(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 October 2009 (29.10.2009)

PCT

(10) International Publication Number
WO 2009/132220 A2

(51) International Patent Classification:
C12N 9/88 (2006.01) *C12N 5/10* (2006.01)
C12N 15/52 (2006.01)

(21) International Application Number:
PCT/US2009/041581

(22) International Filing Date:
23 April 2009 (23.04.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/125,336 23 April 2008 (23.04.2008) US

(71) Applicants *(for all designated States except US)*: **DANISCO US INC.** [US/US]; 925 Page Mill Road, Palo Alto, CA 94304-1013 (US). **THE GOODYEAR TIRE & RUBBER COMPANY** [US/US]; 1144 East Market Street, Akron, OH 44316-0001 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CERVIN, Marguerite, A.** [CA/US]; 404 Palomar Drive, Redwood City, CA 94062 (US). **WHITED, Gregory, M.** [US/US]; 304 South Road, Belmont, CA 94002 (US). **MIASNIKOV, Andrei** [FI/US]; 1769 Latham Street, #a, Mountain View, CA 94041 (US). **PERES, Caroline, M.** [BE/US]; 2328 Santa Catalina Street, Palo Alto, CA 94303 (US). **WEYLER, Walter** [US/US]; 252 Theresa Street, San Francisco, CA 94112 (US). **WELLS, Derek, H.** [US/US]; 775b Loma Verde Avenue, Palo Alto, CA 94303 (US). **BOTT, Richard, R.** [US/US]; 3032 Hillside Drive, Burlingame, CA 94010 (US).

(74) Agents: **SHIEH-NEWTON, Terri** et al.; Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

— *with sequence listing part of description (Rule 5.2(a))*

(54) **Title**: ISOPRENE SYNTHASE VARIANTS FOR IMPROVED MICROBIAL PRODUCTION OF ISOPRENE

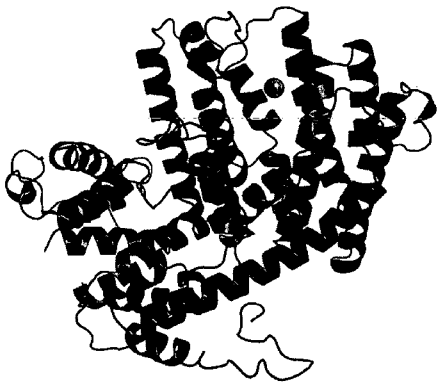


Figure 92

(57) **Abstract**: The present invention provides methods and compositions comprising at least one isoprene synthase enzyme with improved catalytic activity and/or solubility. In particular, the present invention provides variant plant isoprene synthases for increased isoprene production in microbial host cells. Biosynthetically produced isoprene of the present invention finds use in the manufacture of rubber and elastomers.

WO 2009/132220 A2

ISOPRENE SYNTHASE VARIANTS FOR IMPROVED MICROBIAL PRODUCTION OF ISOPRENE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. provisional application serial no. 61/125,336 filed April 23, 2008, which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention provides methods and compositions comprising at least one isoprene synthase enzyme with improved catalytic activity and/or solubility. In particular, the present invention provides variant plant isoprene synthases for increased isoprene production in microbial host cells. Biosynthetically produced isoprene of the present invention finds use in the manufacture of rubber and elastomers.

BACKGROUND OF THE INVENTION

[0003] Isoprenoids are isoprene polymers that find use in pharmaceuticals, neutraceuticals, flavors, fragrances, and rubber products. Natural isoprenoid supplies, however, are limited due to ecological concerns. For this reason, and to provide isoprenoid compositions having fewer impurities and greater uniformity, isoprenoids such as rubber are often produced synthetically.

[0004] Isoprene (2-methyl-1,3-butadiene) is a volatile hydrocarbon that is insoluble in water and soluble in alcohol. Commercially viable quantities of isoprene can be obtained by direct isolation from petroleum C5 cracking fractions or by dehydration of C5 isoalkanes or isoalkenes (Weissermel and Arpe, Industrial Organic Chemistry, 4th ed., Wiley-VCH, pp. 117-122, 2003). The C5 skeleton can also be synthesized from smaller subunits. It would be desirable, however, to have a commercially viable method of producing isoprene that was independent of nonrenewable resources.

[0005] Biosynthetic production of isoprene occurs by two distinct metabolic pathways (Julsing et al., Appl Microbiol Biotechnol, 75:1377-1384, 2007). In eukaryotes and archae, isoprene is formed via the mevalonate (MVA) pathway, while some eubacteria and higher plants produce isoprene via the methylerythritol phosphate (MEP) pathway. Isoprene emissions from plants are light and temperature-dependent with increases linked to leaf development. An isoprene-producing enzyme, isoprene synthase, has been identified in Aspen trees (Silver and Fall, Plant Physiol, 97:1588-1591, 1991; and Silver and Fall, J Biol

Chem, 270:13010-13016, 1995) and is believed to be responsible for the *in vivo* production of isoprene from whole leaves. Bacterial production of isoprene has also been described (Kuzma et al., Curr Microbiol, 30:97-103, 1995; and Wilkins, Chemosphere, 32:1427-1434, 1996), and varies in amount with the phase of bacterial growth and the nutrient content of the culture medium (U.S. Patent No. 5,849,970 to Fall et al.; and Wagner et al., J Bacteriol, 181:4700-4703, 1999, both herein incorporated by reference in their entirety). The levels of isoprene obtainable through bacterial systems of the prior art, however, are insufficient for commercial uses.

[0006] Thus what the art needs is an efficient, large scale, bacterial isoprene production process to provide feedstock for the manufacture of isoprenoids.

[0007] All patents, patent applications, articles and publications mentioned herein are hereby expressly incorporated herein by reference.

SUMMARY OF THE INVENTION

[0008] The present invention provides methods and compositions comprising at least one isoprene synthase enzyme with improved catalytic activity and/or solubility. In particular, the present invention provides variant plant isoprene synthases for increased isoprene production in microbial host cells. Biosynthetically produced isoprene of the present invention finds use in the manufacture of rubber and elastomers.

[0009] Specifically, the present invention provides isolated isoprene synthase variants, wherein the variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a kudzu isoprene synthase comprising the amino acid sequence set forth in SEQ ID NO: 2. In some embodiments, the isoprene synthase variant is a kudzu (*Pueraria sp.*) isoprene synthase variant or a poplar (*Populus sp.*) isoprene synthase variant. In some embodiments, the one or more residues are selected from but not limited to the group consisting of L26, E30, F31, Q33, L35, E36, N37, L39, K40, V41, K43, L44, R61, V62, D63, Q65, K87, E94, N95, L99, D100, N105, K137, E138, G143, E144, N182, L184, K185, G187, N189, T190, P225, H226, K247, T257, E258, M259, D266, N334, D353, S357, I358I, E361, N389, I392, I393, K398, E401, C421, Q423, Q424, E425, D426, H430, L432, R433, S434, D437, R443, L462, E463, H476, N478, D479, Q485, D508, P513, A515, Q532, Y533, L537, G538, R539, Y542, A543, and P557. In some embodiments, the one or more residues are selected from but not limited to the group consisting of P24, N25, Y309, D310, L377, F381, E384, Y399, N402, A403, S406, S407, G409, A411, L413, F449, A456, T457, S458, A459, A460, E461, L462, E463,

R464, G465, E466, T467, T468, N469, M523, S527, and Y531. In some embodiments, the one or more residues are selected from but not limited to the group consisting of A20, N21, Y22, Q23, R271, W278, F299, V302, and S408. The present invention also provides an isolated isoprene synthase variant having an A20G substitution in a kudzu isoprene synthase having the amino acid sequence set forth in SEQ ID NO: 2. In a subset of these embodiments, the variant comprises at least two substitutions (two, three, four, five, six, seven, eight, nine or ten), wherein one of the substitutions is an A20G substitution in a kudzu isoprene synthase having the amino acid sequence set forth in SEQ ID NO: 2. The present invention also provides an isolated isoprene synthase variant having an S408D substitution in a kudzu isoprene synthase having the amino acid sequence set forth in SEQ ID NO: 2. In a subset of these embodiments, the variant comprises at least two substitutions (two, three, four, five, six, seven, eight, nine or ten), wherein one of the substitutions is an S408D substitution in a kudzu isoprene synthase having the amino acid sequence set forth in SEQ ID NO: 2. In some preferred embodiments, the isoprene synthase variant has at least one improved property as compared to wild-type isoprene synthase. In some particularly preferred embodiments, the at least one improved property is selected from but not limited to the group consisting of specific activity (production of isoprene from dimethylallyl diphosphate), and solubility.

[0010] In addition, the present invention further provides a polynucleotide sequence encoding the isoprene synthase variant. Also provided is an expression vector comprising a polynucleotide sequence encoding the isoprene synthase variant in operable combination with a promoter. In further embodiments, the present invention provides a host cell comprising the expression vector. Also provided is a lysate of the host cell, wherein the lysate further comprises lysozyme. In some embodiments, the lysate has a neutral pH (6.5 to 7.5), while in other embodiments the lysate has a basic pH (above 7.5 and below 9.5). The present invention also provides methods of producing isoprene, comprising: (a) providing host cells comprising the expression vector; and (b) culturing the host cells under conditions suitable for producing isoprene. In some embodiments, the methods further comprise (c) recovering the isoprene. In still further embodiments, the methods further comprise (d) polymerizing the isoprene. The present invention further provides methods of detecting isoprene synthase activity, comprising: (a) culturing host cells comprising the expression vector under conditions suitable for producing the isoprene synthase variant; (b) lysing the host cells with a lysis buffer comprising lysozyme to produce a cell lysate; and (c) detecting isoprene synthase activity in the cell lysate by measuring isoprene production from dimethylallyl diphosphate (DMAPP). In some embodiments, the host is selected from but not limited to the

group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells. In some preferred embodiments, the host is selected from but not limited to the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).* In some embodiments, the host cells are cultured in a medium that includes a carbon source selected from but not limited to the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil.

[0011] Moreover, the present invention provides methods of detecting isoprene in a plurality of samples (high-throughput screening), comprising: (a) providing: i) a plurality of samples each comprising isoprene synthase; ii) a glass plate comprising a plurality of wells; and iii) a seal for the glass plate; (b) placing the plurality of samples in the plurality of wells of the glass plate; (c) sealing the glass plate with the seal to produce a sealed glass plate having a headspace associated with the sample in each of the plurality of wells; (d) incubating the glass plate under conditions in which the isoprene synthase is active; and (e) detecting isoprene in the headspace. In some embodiments, the isoprene is detected by gas chromatography-mass spectrometry (GC-MS). In some embodiments, the plurality of samples comprise host cells comprising an expression vector comprising a polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter. In some embodiments, the plurality of samples comprise a lysate of the host cells, lysozyme, and dimethylallyl diphosphate (DMAPP). In some preferred embodiments, the glass plate is a deep-well glass block. In some preferred embodiments, the plurality of wells comprises at least 24 wells (preferably at least 48 wells, more preferably at least 96 wells, still more preferably at least 192 wells, and most preferably at least 384 wells). In particularly preferred embodiments, the plurality of wells each comprise a volume of 2 ml or less (preferably 2 ml to 0.2 ml).

[0012] Additionally the present invention provides a host cell comprising a heterologous polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a kudzu isoprene synthase comprising the amino acid sequence set forth in SEQ ID NO: 2. In some embodiments, the one or more residues are selected from but not limited to the group consisting of L26, E30, F31, Q33, L35, E36, N37, L39, K40, V41, K43, L44, R61, V62, D63, Q65, K87, E94, N95, L99, D100, N105, K137, E138, G143, E144, N182, L184, K185, G187, N189, T190, P225, H226, K247, T257, E258, M259, D266, N334, D353, S357,

I358I, E361, N389, I392, I393, K398, E401, C421, Q423, Q424, E425, D426, H430, L432, R433, S434, D437, R443, L462, E463, H476, N478, D479, Q485, D508, P513, A515, Q532, Y533, L537, G538, R539, Y542, A543, and P557. In some embodiments, the one or more residues are selected from but not limited to the group consisting of P24, N25, Y309, D310, L377, F381, E384, Y399, N402, A403, S406, S407, G409, A411, L413, F449, A456, T457, S458, A459, A460, E461, L462, E463, R464, G465, E466, T467, T468, N469, M523, S527, and Y531. In some embodiments, the one or more residues are selected from but not limited to the group consisting of A20, N21, Y22, Q23, R271, W278, F299, V302, and S408. The present invention also provides an isolated isoprene synthase variant having an A20G substitution and/or an S408D substitution in a kudzu isoprene synthase having the amino acid sequence set forth in SEQ ID NO: 2. In some preferred embodiments, the isoprene synthase variant has at least one improved property as compared to wild-type isoprene synthase. In some particularly preferred embodiments, the at least one improved property is selected from but not limited to the group consisting of specific activity (production of isoprene from dimethylallyl diphosphate), and solubility. In some preferred embodiments, the polynucleotide sequence is contained within a plasmid. In other preferred embodiments, the polynucleotide sequence is integrated into a chromosome of the host cell. In some embodiments, the host is selected from but not limited to the group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells. In some preferred embodiments, the host is selected from but not limited to the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).* In some embodiments, the host cells are cultured in a medium that includes a carbon source selected from but not limited to the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil. In some embodiments, the host cell further comprises a heterologous or native nucleic acid encoding an IDI polypeptide and/or a heterologous or native nucleic acid encoding a DXS polypeptide, sometimes in combination with the native DXP pathway (for example, expression of *dxs* and *idi* in *E. coli* in addition to the native DXP pathway). Alternatively the entire DXP pathway (Figure 15) maybe expressed on a plasmid or integrated on the chromosome as an operon, with a single promoter controlling expression, or promoters of varying strengths (example GI 1.20, GI 1.5, or GI 1.6) controlling one or more of the individual genes. In some embodiments, the host cell further comprises one or more nucleic acids encoding an IDI polypeptide and a DXS polypeptide, while in some preferred embodiments, one vector encodes the isoprene synthase variant, the IDI

polypeptide, and the DXS polypeptide. In some embodiments, the host cell further comprises a heterologous nucleic acid encoding an MVA pathway polypeptide (e.g., an MVA pathway polypeptide from *Saccharomyces cerevisia* or *Enterococcus faecalis*). In some embodiments, the host cell further comprises one or more nucleic acids encoding an MVA pathway polypeptide and a DXS polypeptide, while in some preferred embodiments, one vector encodes the isoprene synthase variant, the MVA pathway polypeptide, and the DXS polypeptide. In some preferred embodiments, the host cell further comprises one or more nucleic acids encoding a DXS polypeptide, an IDI polypeptide, or one or more of the rest of the DXP pathway polypeptides, and a MVA pathway polypeptide. In some embodiments, the vector further comprises a selectable marker (e.g., antibiotic resistance nucleic acid). Also provided are methods of producing isoprene, comprising: (a) culturing the host cells under suitable culture conditions for production of isoprene; and (b) producing the isoprene. In some embodiments, the methods further comprise (c) recovering the isoprene. In some preferred embodiments, the methods further comprise (d) polymerizing isoprene. The present invention also provides methods of producing isoprene synthase, comprising: (a) providing: (i) a host cell; and (ii) a nucleic acid encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a kudzu isoprene synthase comprising the amino acid sequence set forth in SEQ ID NO: 2;

(b) contacting the host cell with the nucleic acid to produce a transformed host cell; and (c) culturing the transformed host cells under suitable culture conditions for production of isoprene synthase.

[0013] In another aspect, the invention provides for isolated poplar isoprene synthase variants. In one embodiment, the variant comprises a truncation in the N-terminal portion of isoprene synthase. In another embodiment, the isoprene synthase variant has an increased specific activity compared to a full length isoprene synthase. In another embodiment, the isoprene synthase is *P. alba* isoprene synthase of SEQ ID NO:120. In another embodiment, wherein the variant is selected from the group consisting of: an MEA variant (SEQ ID NO:122), an MSV variant (SEQ ID NO:124), an MVS variant (SEQ ID NO:126), an MTE variant (SEQ ID NO:128), an MNV variant (SEQ ID NO:130). In another embodiment, the variant is an MEA variant (SEQ ID NO:122). In another embodiment, the variant is selected from the group consisting of: a TRC (-3) variant (SEQ ID NO:136), a TRC (-4) variant (SEQ ID NO:138), a TRC (-5) variant (SEQ ID NO:140), a TRC (-6) variant (SEQ ID NO:142) and

a TRC (-7) variant (SEQ ID NO:144). In another embodiment, the variant is a MET variant of *P. tremuloides* isoprene synthase (SEQ ID NO:146). In another embodiment, the variant is a MET variant of *P. trichocharpa* isoprene synthase (SEQ ID NO:148).

[0014] In another aspect, the invention provides for isolated poplar isoprene synthase variants, wherein the variant comprises a substitution of one or more amino acid residues of a wild type isoprene synthase; and wherein the isoprene synthase variant has increased isoprene synthase activity compared to a wild type isoprene synthase. In one embodiment, the increased isoprene synthase activity is indicated by a host cell comprising the isoprene variant growing at a faster rate in the presence of dimethylallyl pyrophosphate (DMAPP) compared to a host cell comprising a parent isoprene synthase. In another embodiment, the isoprene synthase is the *P. alba* isoprene synthase of SEQ ID NO:120. In another embodiment, the variant comprises one of more amino acid substitutions selected from the group consisting of V10M, F12S, T15A, E18G, V58I, V58F, L70Q, L70V, L70T, T71P, V79L, E89D, G94A, S119F, F120L, G127R, E175V, T212I, S257A, R262G, A266G, F280L, N297K, F305L, L319M, E323K, A328T, D342E, A359T, K366N, E368D, L374M, S396T, V418S, K438N, H440R, T442I, T442A, I449V, A469S, K500R, K505Q, G507S, S509N, F511Y, and N532K. In another embodiment, at least one amino acid substitution is a L70R substitution. In another embodiment, the variant comprises one of more amino acid substitutions selected from the group consisting of G127R/F511Y, L70Q/G94A/R262G/F305L, F12S/ T15A/E18G/N297K, S396T/T442I, V10M/E323K, F120L/A266G, K438N/K500R, V79L/S509N, E175V/S257A/E368D/A469S, T71P/L374M, F280L/H440R, E89D/H440R, V58F/A328T/N532K, S119F/D342E/I449V, and K366N/G507S.

[0015] In another aspect, the invention provides for a crystalline form of a polypeptide comprising the amino acid residues of SEQ ID NO:120 (Figure 19).

[0016] In another aspect, the invention provides for methods of producing isoprene, comprising: (a) providing a host cell comprising an expression vector comprising a polynucleotide sequence encoding an isoprene synthase variant; and (b) culturing the host cell under conditions suitable for producing isoprene. In one embodiment, the method further comprises (c) recovering the isoprene. In another embodiment, the method further comprises (d) polymerizing the isoprene.

[0017] In another aspect, the invention provides for methods of detecting isoprene synthase activity, comprising: (a) culturing a host cell comprising the expression vector under conditions suitable for producing an isoprene synthase variant; (b) lysing the host cells with a

lysis buffer comprising lysozyme to produce a cell lysate; and (c) detecting isoprene synthase activity in the cell lysate by measuring isoprene production from dimethylallyl diphosphate (DMAPP). In one embodiment, the host cell is selected from the group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells. In another embodiment,

the host cell is selected from the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).* In another embodiment, the host cell is cultured in a medium that includes a carbon source selected from the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil.

[0018] In another aspect, the invention provides for host cells comprising a heterologous polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a poplar isoprene synthase. In one embodiment, the isoprene synthase is the *P. alba* isoprene synthase of SEQ ID NO:120. In another embodiment, the variant is selected from the group consisting of: an MEA variant (SEQ ID NO:122), an MSV variant (SEQ ID NO:124), an MVS variant (SEQ ID NO:126), an MTE variant (SEQ ID NO:128), an MNV variant (SEQ ID NO:130). In another embodiment, the variant is selected from the group consisting of: a TRC (-3) variant (SEQ ID NO:136), a TRC (-4) variant (SEQ ID NO:138), a TRC (-5) variant (SEQ ID NO:140), a TRC (-6) variant (SEQ ID NO:142) and a TRC (-7) variant (SEQ ID NO:144). In another embodiment, the variant is a MET variant of *P. tremuloides* isoprene synthase (SEQ ID NO:146). In another embodiment, the variant is a MET variant of *P. trichocharpa* isoprene synthase (SEQ ID NO:148). In another embodiment, the variant comprises one of more amino acid substitutions selected from the group consisting of V10M, F12S, T15A, E18G, V58I, V58F, L70Q, L70V, L70T, T71P, V79L, E89D, G94A, S119F, F120L, G127R, E175V, T212I, S257A, R262G, A266G, F280L, N297K, F305L, L319M, E323K, A328T, D342E, A359T, K366N, E368D, L374M, S396T, V418S, K438N, H440R, T442I, T442A, I449V, A469S, K500R, K505Q, G507S, S509N, F511Y, and N532K. In another embodiment, at least one amino acid substitution is a L70R substitution. In another embodiment, the variant comprises one of more amino acid substitutions selected from the group consisting of G127R/F511Y, L70Q/G94A/R262G/F305L, F12S/ T15A/E18G/N297K, S396T/T442I, V10M/E323K, F120L/A266G, K438N/K500R, V79L/S509N, E175V/S257A/E368D/A469S, T71P/L374M,

F280L/H440R, E89D/H440R, V58F/A328T/N532K, S119F/D342E/I449V, and K366N/G507S. In another embodiment, the polynucleotide sequence is contained within a plasmid. In another embodiment, the polynucleotide sequence is integrated into a chromosome of the host cell.

In another embodiment, the host is selected from the group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells. In another embodiment, the host is selected from the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).* In another embodiment, the host cell is cultured in a medium comprising a carbon source selected from the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil. In another embodiment, the host cell further comprises a heterologous or native nucleic acid encoding an IDI polypeptide and/or a heterologous or native nucleic acid encoding a DXS polypeptide, optionally in combination with the native DXP pathway. In another embodiment, the host cell further comprises one or more nucleic acids encoding an IDI polypeptide and a DXS polypeptide. In another embodiment, the host cell comprises one vector encoding the isoprene synthase variant, the IDI polypeptide, and the DXS polypeptide. In another embodiment, the host cell further comprises a heterologous nucleic acid encoding an MVA pathway polypeptide selected from the group consisting of an MVA pathway polypeptide from *Saccharomyces cerevisia* and *Enterococcus faecalis.* In another embodiment, the host cell further comprises one or more nucleic acids encoding an MVA pathway polypeptide and a DXS polypeptide and wherein one vector encodes the isoprene synthase variant, the MVA pathway polypeptide, and the DXS polypeptide. In another embodiment, the host cell further comprises one or more nucleic acids encoding a DXS polypeptide, an IDI polypeptide, or one or more of the rest of the DXP pathway polypeptides, and a MVA pathway polypeptide.

[0019] In another aspect, the invention provides for methods of producing isoprene, comprising: (a) culturing the host cells comprising a heterologous polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a poplar isoprene synthase under suitable culture conditions for production of isoprene; and (b) producing the isoprene. In one embodiment, the method further comprises (c) recovering the isoprene. In another embodiment, the method further comprises (d) polymerizing isoprene.

[0020] In another aspect, the invention provides for methods of producing isoprene synthase, comprising: (a) providing: (i) a host cell; and (ii) a nucleic acid encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a *P. alba* isoprene synthase of SEQ ID NO:120; (b) contacting the host cell with the nucleic acid to produce a transformed host cell; and (c) culturing the transformed host cells under suitable culture conditions for production of isoprene synthase.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] Figure 1 provides the coding sequence (SEQ ID NO:1) of kudzu (*Pueraria montana*) isoprene synthase, codon-optimized for expression in *Escherichia coli*.

[0022] Figure 2 provides the amino acid sequence (SEQ ID NO:2) of kudzu isoprene synthase.

[0023] Figure 3 provides the coding sequence (SEQ ID NO:6) of poplar (*Populus alba x tremula*) isoprene synthase, codon-optimized for expression in *Escherichia coli*.

[0024] Figure 4 provides the amino acid sequence (SEQ ID NO:7) of poplar (*Populus alba x tremula*) isoprene synthase.

[0025] Figure 5 provides a kudzu isoprene synthase homology model with the cysteine residues highlighted as space filling molecules.

[0026] Figure 6 provides a poplar isoprene synthase homology model with the cysteine residues highlighted as space filling molecules (dark grey). In addition, the cysteine residues from the kudzu model of Figure 5 are superimposed on the poplar model as space filling molecules (light grey).

[0027] Figure 7 provides a graph showing the growth curves of the kudzu IspS cysteine mutants of Example 5.

[0028] Figure 8 shows an SDS-PAGE analysis of kudzu IspS cysteine mutants from lysed cells. Pellet and supernatant fractions were prepared by centrifugation.

[0029] Figure 9 provides a map of plasmid MCM93 (pCR2.1-Kudzu).

[0030] Figure 10 provides the nucleotide sequence of plasmid MCM93 (SEQ ID NO:22).

[0031] Figure 11 provides a map of pET24D-Kudzu.

[0032] Figure 12 provides the nucleotide sequence of pET24D-Kudzu (SEQ ID NO:23).

[0033] Figure 13 shows an SDS-PAGE analysis of kudzu isoprene synthase-containing inclusion bodies. Lane M contains molecular weight markers, while the other lanes contain

increasing amounts of the purified inclusion body preparation. The kudzu isoprene synthase was estimated to have a purity of >90%.

[0034] Figure 14 provides graphs showing isoprene synthase activity of kudzu site evaluation library (SEL) members for positions Y22, A20 and S408. Most members show highly decreased activity, while conservative substitutions show a lesser decrease in activity. Panel A shows assay results for the Y22 library members in comparison with independent wild type samples (circled WT). Panel B shows assay results for the A20 library members in comparison to wild type samples (circled WT). Panel C shows assay results for the S408 library members, indicating that member S408D has 1.5 to 2-fold higher activity than the average of the wild type controls.

[0035] Figure 15 shows the MVA and DXP metabolic pathways for isoprene (based on F. Bouvier et al., Progress in Lipid Res. 44: 357-429, 2005). The following description includes alternative names for each polypeptide in the pathways and a reference that discloses an assay for measuring the activity of the indicated polypeptide (each of these references are each hereby incorporated by reference in their entireties, particularly with respect to assays for polypeptide activity for polypeptides in the MVA and DXP pathways). **Mevalonate Pathway: AACT**; Acetyl-CoA acetyltransferase, MvaE, EC 2.3.1.9. Assay: J. Bacteriol., 184: 2116–2122, 2002; **HMGS**; Hydroxymethylglutaryl-CoA synthase, MvaS, EC 2.3.3.10. Assay: J. Bacteriol., 184: 4065–4070, 2002; **HMGR**; 3-Hydroxy-3-methylglutaryl-CoA reductase, MvaE, EC 1.1.1.34. Assay: J. Bacteriol., 184: 2116–2122, 2002; **MVK**; Mevalonate kinase, ERG12, EC 2.7.1.36. Assay: Curr Genet 19:9-14, 1991. **PMK**; Phosphomevalonate kinase, ERG8, EC 2.7.4.2, Assay: Mol Cell Biol., 11:620–631, 1991; **DPMDC**; Diphosphomevalonate decarboxylase, MVD1, EC 4.1.1.33. Assay: Biochemistry, 33:13355-13362, 1994; **IDI**; Isopentenyl-diphosphate delta-isomerase, IDI1, EC 5.3.3.2. Assay: J. Biol. Chem. 264:19169-19175, 1989. **DXP Pathway: DXS**; 1-Deoxyxylulose-5-phosphate synthase, dxs, EC 2.2.1.7. Assay: PNAS, 94:12857-62, 1997; **DXR**; 1-Deoxy-D-xylulose 5-phosphate reductoisomerase, dxr, EC 2.2.1.7. Assay: Eur. J. Biochem. 269:4446–4457, 2002; **MCT**; 4-Diphosphocytidyl-2C-methyl-D-erythritol synthase, IspD, EC 2.7.7.60. Assay: PNAS, 97: 6451–6456, 2000; **CMK**; 4-Diphosphocytidyl-2-C-methyl-D-erythritol kinase, IspE, EC 2.7.1.148. Assay: PNAS, 97:1062-1067, 2000; **MCS**; 2C-Methyl-D-erythritol 2,4-cyclodiphosphate synthase, IspF, EC 4.6.1.12. Assay: PNAS, 96:11758-11763, 1999; **HDS**; 1-Hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate synthase, ispG, EC 1.17.4.3. Assay: J. Org. Chem., 70:9168 -9174, 2005; **HDR**; 1-Hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate reductase, IspH, EC 1.17.1.2. Assay: JACS, 126:12847-12855, 2004.

[0036] Figure 16 provides a map of pDu27.

[0037] Figure 17 provides the amino acid sequence (SEQ ID NO:118) of 6Xhis N-terminally tagged *P. alba* IspS in pDu27.

[0038] Figure 18 provides the nucleotide sequence (SEQ ID NO:119) of plasmid pDu27.

[0039] Figure 19 provides the amino acid sequence (SEQ ID NO:120) of full length *P. alba* IspS in pET24a. Underlined residues indicate the locations of N-terminal truncations in IspS in plasmids pDu39 through pDu43.

[0040] Figure 20 provides the nucleotide sequence (SEQ ID NO:121) of plasmid P. alba pET24a.

[0041] Figure 21 shows purified IspS displays a lower molecular weight "doublet" by SDS-PAGE analysis.

[0042] Figure 22 shows tryptic peptides identified by mass spectrometry.

[0043] Figure 23 provides maps of pDu40, pDu41, pDu42 and pDu43 harboring N-terminal truncations of *P. alba* IspS.

[0044] Figure 24 provides a map of Pdu39 which is pET24a-*P. alba* MEA untagged (in strain MD09-173).

[0045] Figure 25 provides the amino acid sequence (SEQ ID NO:122) of truncated "MEA" variant of *P. alba* IspS in pDu39.

[0046] Figure 26 provides the nucleotide sequence (SEQ ID NO:123) of plasmid pDu39.

[0047] Figure 27 provides the amino acid sequence (SEQ ID NO:124) of truncated "MSV" variant *P. alba* IspS in pDu41.

[0048] Figure 28 provides the nucleotide sequence (SEQ ID NO:125) of plasmid pDu41 (pET24a-P.alba(MSV) Untagged).

[0049] Figure 29 provides the amino acid sequence (SEQ ID NO:126) of truncated "MVS" variant *P. alba* IspS in pDu43.

[0050] Figure 30 provides the nucleotide sequence (SEQ ID NO:127) of plasmid pDu43 (pET24a-P.alba(MVS) Untagged).

[0051] Figure 31 provides the amino acid sequence (SEQ ID NO:128) of truncated "MTE" variant of *P. alba* IspS in pDu42.

[0052] Figure 32 provides the nucleotide sequence (SEQ ID NO:129) of plasmid pDu42 (pET24a-P.alba(MTE) Untagged).

[0053] Figure 33 provides the amino acid sequence (SEQ ID NO:130) of truncated "MNV" P. alba IspS in pDu40.

[0054] Figure 34 provides the nucleotide sequence (SEQ ID NO:131) of plasmid pDu40 (pET24a-P.alba(MNV) Untagged).

[0055] Figure 35 provides maps of MD09-161 and MD09-163, C-terminally TEV, 6XHis-tagged IspS variants.

[0056] Figure 36 provides the amino acid sequence (SEQ ID NO:132) of P. alba MEA(+)TEV in MD09-163.

[0057] Figure 37 provides the nucleotide sequence (SEQ ID NO:133) of plasmid MD09-163 (pET24a-P.alba MEA(+)TEV. CDS is underlined, TEV protease site is bold.

[0058] Figure 38 provides the amino acid sequence (SEQ ID NO:134) of P. alba FL(+)TEV in MD09-161.

[0059] Figure 39 provides the nucleotide sequence (SEQ ID NO:135) of plasmid MD09-161 (pET24a-P.alba FL(+)TEV. CDS is underlined, TEV protease site is bold.

[0060] Figure 40 shows a graph representing specific activities of MD09-167, Full length (FL), MD09-165, and Truncated isoprene synthase (MD09-173). Reactions were run at 30 °C for 15 minutes in a solution containing 100 mM Tris, 100 mM NaCl, 50 mM $MgCl_2$, 5 mM DMAPP, and 2.5-4.5 μg isoprene synthase in the supernatant of whole cell lysate.

[0061] Figure 41 shows graphs demonstrating Rate/[E] vs. [DMAPP]. X's represent MD09-173, circles represent MD09-167, diamonds represent MD09-165 and squares represent full length IspS.

[0062] Figure 42 shows a graph showing Isoprene synthase activity vs. [DMAPP]. X's represent data generated with MD09-173 truncated isoprene synthase. Circles represent data generated with MD09-167 isoprene synthase. Diamonds represent data generated with MD09-165 isoprene synthase. Squares represent data generated with full length isoprene synthase. Each data set was run in triplicate from independently grown cultures.

[0063] Figure 43 shows graphs demonstrating the effects of varying k_{cat} and K_M and K_i on reaction rate. In panel A, line 1 represents the rate equation of truncated isoprene synthase activity divided by the rate equation of full length isoprene synthase plotted at varying DMAPP concentrations. Line 2 represents the rate equation of full length isoprene synthase in which the k_{cat} has been substituted by the k_{cat} of the truncated isoprene synthase divided by the rate equation of the full length isoprene synthase. Line 3 represents the rate equation of full length isoprene synthase in which the K_M has been substituted by the K_M of the truncated isoprene synthase divided by the rate equation of the full length isoprene synthase. Line 4 represents the rate equation of full length isoprene synthase in which the K_i has been substituted by the K_i of the truncated isoprene synthase divided by the rate equation of the

full length isoprene synthase. Panel B shows a graph demonstrating data fit to the ratio of the rate equation of truncated isoprene synthase to full length isoprene synthase vs.[DMAPP].

[0064] Figure 44 shows a graph demonstrating growth inhibition of MCM531 by Mevalonic Acid (MVA). Cells were grown in TM3 medium in a microtiter plate with different concentrations of MVA. OD_{600} of quadruplicate wells was measured at the indicated times.

[0065] Figure 45 shows graphs demonstrating DMAPP assays of L70 SSL plate. Dark bars represent either the full length (P. alba pET24a) or pDU39 (truncated) controls. The variants in wells C3 (27), D3 (39), or E3 (51) were chosen for further analysis.

[0066] Figure 46 shows a graph demonstrating the average specific activity of all variants selected for DMAPP assay with protein determination. Error bars show one standard deviation. All 3 L70R variants display higher activity than the control (WT).

[0067] Figure 47 shows a graph demonstrating the average specific activity of all 3 L70R variants compared to the "MEA" truncated *P. alba* IspS enzyme. Error bars show one standard deviation.

[0068] Figure 48 provides maps of plasmids pDu47-3, pDu47-4, and pDu47-5.

[0069] Figure 49 provides maps of plasmids pDu47-6, pDu47-7, and pDu48.

[0070] Figure 50 provides maps of plasmids pDu49, pDu50 and pDu50-4.

[0071] Figure 51 provides the amino acid sequence (SEQ ID NO:136) of *P. alba* TRC (-3) in pDu47-3.

[0072] Figure 52 provides the nucleotide sequence (SEQ ID NO:137) of plasmid pDu47-3.

[0073] Figure 53 provides the amino acid sequence (SEQ ID NO:138) of *P. alba* TRC (-4) in pDu47-4.

[0074] Figure 54 provides the nucleotide sequence (SEQ ID NO:139) of plasmid pDu47-4.

[0075] Figure 55 provides the amino acid sequence (SEQ ID NO:140) of *P. alba* TRC (-5) in pDu47-5.

[0076] Figure 56 provides the nucleotide sequence (SEQ ID NO:141) of plasmid pDu47-5.

[0077] Figure 57 provides the amino acid sequence (SEQ ID NO:142) of *P. alba* TRC (-6) in pDu47-6.

[0078] Figure 58 provides the nucleotide sequence (SEQ ID NO:143) of plasmid pDu47-6.

[0079] Figure 59 provides the amino acid sequence (SEQ ID NO:144) of *P. alba* TRC (-7) in pDu47-7.

[0080] Figure 60 provides the nucleotide sequence (SEQ ID NO:145) of plasmid pDu47-7.

[0081] Figure 61 provides the amino acid sequence (SEQ ID NO:146) of *P. tremuloides* TRC (MET) in pDu48.

[0082] Figure 62 provides the nucleotide sequence (SEQ ID NO:147) of plasmid pDu48.

[0083] Figure 63 provides the amino acid sequence (SEQ ID NO:148) of *P. trichocarpa* (TRC) in pDu49.

[0084] Figure 64 provides the nucleotide sequence (SEQ ID NO:149) of plasmid pDu49.

[0085] Figure 65 provides the amino acid sequence (SEQ ID NO:150) of Kudzu TRC (MEA) in pDu50.

[0086] Figure 66 provides the nucleotide sequence (SEQ ID NO:151) of plasmid pDu50.

[0087] Figure 67 provides the amino acid sequence (SEQ ID NO:152) of KudzuTRC (-4) in pDu50-4.

[0088] Figure 68 provides the nucleotide sequence (SEQ ID NO:153) of plasmid pDu50-4.

[0089] Figure 69 shows graphs demonstrating raw and OD-normalized data from DMAPP assay of truncated variants of IspS.

[0090] Figure 70 shows a graph reprensenting the specific activity of IspS truncations. *P. alba*, *P. tremuloides* and *P. trichocharpa* truncations were compared for specific activity relative to the *P. alba* "full length" variant.

[0091] Figure 71 provides a map of plasmid p9795.

[0092] Figure 72 porvides the nucleotide sequence of plasmid p9795 (SEQ ID NO:154).

[0093] Figure 73 provides a map of plasmid pTrcKudzu.

[0094] Figure 74 provides the nucleotide sequence (SEQ ID NO:155) of plasmid pTrcKudzu.

[0095] Figure 75 provides a map of plasmid pMAL-C4X.

[0096] Figure 76 provides the nucleotide sequence (SEQ ID NO:156) of plasmid pMAL-C4X.

[0097] Figure 77 provides a map of plasmid pMAL-C4X-Kudzu.

[0098] Figure 78 provides the nucleotide sequence (SEQ ID NO:157) of plasmid pMAL-C4X-Kudzu.

[0099] Figure 79 provides maps of plasmids pET24 P. tremuloides pET24a and P. trichocharpa pET24a.

[0100] Figure 80 provides the amino acid sequence (SEQ ID NO:158) of *P. tremuloides* IspS in P. trichocharpa pET24a.

[0101] Figure 81 provides the nucleotide sequence (SEQ ID NO:159) of plasmid P. tremuloides pET24a.

[0102] Figure 82 provides the amino acid sequence (SEQ ID NO:160) of *P. trichocharpa* IspS in P. trichocharpa pET24a.

[0103] Figure 83 provides the nucleotide sequence (SEQ ID NO:161) of plasmid P. trichocharpa pET24a.

[0104] Figure 84 provides maps of plasmids pDu30, pDu31, and pDu32.

[0105] Figure 85 provides the amino acid sequence (SEQ ID NO:162) of IspS variant P.albaTRC-pET200 in pDu30.

[0106] Figure 86 provides the nucleotide sequence (SEQ ID NO:163) of pDu30.

[0107] Figure 87 provides the amino acid sequence (SEQ ID NO:164) of IspS variant P.tremTRC-pET200 in pDu31.

[0108] Figure 88 provides the nucleotide sequence (SEQ ID NO:165) of pDu31.

[00100] Figure 89 provides the amino acid sequence (SEQ ID NO:166) of IspS variant P.trichTRC-pET200 in pDu32.

[0109] Figure 90 provides the nucleotide sequence (SEQ ID NO:167) of pDu32.

[0110] Figure 91 provides the three-dimensional structure of *P. tremuloides* IspS shown as a dimer. Chain A is in dark gray, chain B is in medium gray and the single magnesium ion foung in each active site is light gray.

[0111] Figure 92 provides a monomer view of the structure of *P. tremuloides* IspS. The magnesium is shown as a light gray sphere and the N- and C-terminals are indicated.

[0112] Figure 93 shows the structural alignments between (A) BdpS and LS, (B) BdpS and poplar IspS, (C) LS and poplar IspS, and (D) TEAS and poplar IspS. In each case the first structure is in light gray and the second is in dark gray. Divalent cations are shown as spheres.

[0113] Figure 94 shows the three dimensional structure of loops in BdpS and LS. Panel A shows the N-terminal loop of Ls in light gray and the N-terminal loop of BdpS in dark gray. Panel B shows that Loop I and Loop II are structurally homologous.

[0114] Figure 95 shows the N-teminal loop of BdpS (dark gray) and poplar IspS (light gray) are structurally divergent. Panel A shows the N-terminal loop and panel B shows Loop I and Loop II.

[0115] Figure 96 shows the N-teminal loop of LS (light gray) and poplar IspS (dark gray) are structurally divergent. Panel A shows the N-terminal loop and panel B shows Loop I and Loop II.

[0116] Figure 97 shows the N-teminal loop of TEAS (light gray) and poplar IspS (dark gray) are structurally divergent. Panel A shows the N-terminal loop and panel B shows Loop I and Loop II. Loop I is disordered in TEAS.

GENERAL DESCRIPTION OF THE INVENTION

[0117] The present invention provides methods and compositions comprising at least one isoprene synthase enzyme with improved catalytic activity and/or solubility. In particular, the present invention provides variant plant isoprene synthases for increased isoprene production in microbial host cells. Biosynthetically produced isoprene of the present invention finds use in the manufacture of rubber and elastomers.

[0118] Unless otherwise indicated, the practice of the present invention involves conventional techniques commonly used in molecular biology, microbiology, and recombinant DNA, which are within the skill of the art. Such techniques are known to those of skill in the art and are described in numerous texts and reference works (See e.g., Sambrook et al., "Molecular Cloning: A Laboratory Manual," Second Edition, Cold Spring Harbor, 1989; and Ausubel et al., "Current Protocols in Molecular Biology," 1987).

[0119] Unless defined otherwise herein, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. For example, Singleton and Sainsbury, Dictionary of Microbiology and Molecular Biology, 2d Ed., John Wiley and Sons, NY (1994); and Hale and Marham, The Harper Collins Dictionary of Biology, Harper Perennial, NY (1991) provide those of skill in the art with a general dictionaries of many of the terms used in the invention. Although any methods and materials similar or equivalent to those described herein find use in the practice of the present invention, the preferred methods and materials are described herein. Accordingly, the terms defined immediately below are more fully described by reference to the Specification as a whole.

[0120] Furthermore, the headings provided herein are not limitations of the various aspects or embodiments of the invention, which can be had by reference to the specification as a whole. Accordingly, the terms defined immediately below are more fully defined by reference to the specification as a whole. Nonetheless, in order to facilitate understanding of the invention, a number of terms are defined below.

Definitions

[0121] Unless defined otherwise herein, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although any methods and materials similar or equivalent to those described herein find use in the practice of the present invention, the preferred methods and materials are described herein. Accordingly, the terms defined immediately below are more fully described by reference to the Specification as a whole.

[0122] As used herein, the singular terms "a," "an," and "the" include the plural reference unless the context clearly indicates otherwise. Unless otherwise indicated, nucleic acids are written left to right in 5' to 3' orientation; amino acid sequences are written left to right in amino to carboxy orientation, respectively. It is to be understood that this invention is not limited to the particular methodology, protocols, and reagents described, as these may vary, depending upon the context they are used by those of skill in the art.

[0123] It is intended that every maximum numerical limitation given throughout this specification includes every lower numerical limitation, as if such lower numerical limitations were expressly written herein. Every minimum numerical limitation given throughout this specification will include every higher numerical limitation, as if such higher numerical limitations were expressly written herein. Every numerical range given throughout this specification will include every narrower numerical range that falls within such broader numerical range, as if such narrower numerical ranges were all expressly written herein.

[0124] All documents cited are, in relevant part, incorporated herein by reference. However, the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention.

[0125] As used herein, the term 2-methyl-1,3-butadiene (CAS# 78-79-5) ("isoprene") refers to the direct and final volatile C5 hydrocarbon product from the elimination of pyrophosphate from 3,3-dimethylallyl pyrophosphate (DMAPP), and does not involve the linking or polymerization of [an] IPP molecule(s) to [a] DMAPP molecule(s). As used herein, the terms "isoprene synthase," and "IspS," refer to the enzymes that catalyze the elimination or pyrophosphate from diemethylallyl diphosphate (DMAPP) to form isoprene. In some preferred embodiments, the IspS is an enzyme obtained from plants such as kudzu, poplar or red oak. In some embodiments, the term "IspS" refers to a naturally occurring mature enzyme or portion thereof.

[0126] Related (and derivative) proteins comprise "variant proteins." In some preferred embodiments, variant proteins differ from a parent protein (e.g., kudzu IspS set forth as SEQ ID NO:2 or poplar IspS) and one another by a small number of amino acid residues. The number of differing amino acid residues may be one or more, preferably 1, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, or more amino acid residues. In some preferred embodiments, the number of different amino acids between variants is between 1 and 10. In some particularly preferred embodiments, related proteins and particularly variant proteins comprise at least 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, or 99% amino acid sequence identity. Additionally, a related protein or a variant protein as used herein

refers to a protein that differs from another related protein or a parent protein in the number of prominent regions. For example, in some embodiments, variant proteins have 1, 2, 3, 4, 5, or 10 corresponding prominent regions that differ from the parent protein.

[0127] Several methods are known in the art that are suitable for generating variants of the enzymes of the present invention, including but not limited to site-saturation mutagenesis, scanning mutagenesis, insertional mutagenesis, random mutagenesis, site-directed mutagenesis, and directed-evolution, as well as various other recombinatorial approaches.

[0128] Characterization of wild-type and mutant proteins is accomplished via any means or "test" suitable and is preferably based on the assessment of properties of interest. For example one or more of the following properties are assessed in some embodiments of the present invention: pH stability; temperature stability; oxidative stability; proteolytic stability; solubility; Km and/or specific activity of the conversion of DMAPP to isoprene *in vitro;* Km and/or specific activity of the conversion of DMAPP to isoprene *in vivo* in the context of a host organism (e.g., *E. coli*); and expression of enzyme(s) of the DXP pathway and/or the MVA pathway. Indeed, it is contemplated that enzymes having various degrees of stability, solubility, activity, and/or expression level in one or more of test conditions will find use in the present invention.

[0129] As used herein the term "gene" refers to a polynucleotide (*e.g.,* a DNA segment) that encodes a polypeptide and includes regions preceding and following the coding regions as well as intervening sequences (introns) between individual coding segments (exons).

[0130] As used herein, "homologous genes" refers to a pair of genes from different, but usually related species, which correspond to each other and which are identical or very similar to each other. The term encompasses genes that are separated by speciation (*i.e.*, the development of new species) (*e.g.,* orthologous genes), as well as genes that have been separated by genetic duplication (*e.g.,* paralogous genes).

[0131] As used herein, "ortholog" and "orthologous genes" refer to genes in different species that have evolved from a common ancestral gene (*i.e.,* a homologous gene) by speciation. Typically, orthologs retain the same function during the course of evolution. Identification of orthologs finds use in the reliable prediction of gene function in newly sequenced genomes.

[0132] As used herein, "paralog" and "paralogous genes" refer to genes that are related by duplication within a genome. While orthologs retain the same function through the course of evolution, paralogs evolve new functions, even though some functions are often related to the original one.

[0133] As used herein, "homology" refers to sequence similarity or identity, with identity being preferred. This homology is determined using standard techniques known in the art (*See e.g.*, Smith and Waterman, Adv Appl Math, 2:482, 1981; Needleman and Wunsch, J Mol Biol, 48:443, 1970; Pearson and Lipman, Proc Natl Acad Sci USA, 85:2444, 1988; programs such as GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, Madison, WI; and Devereux *et al.*, Nucl Acid Res, 12:387-395, 1984).

[0134] As used herein, an "analogous sequence" is one wherein the function of the gene is essentially the same as the gene based on the kudzu isoprene synthase (IspS) or poplar IspS (IspS). Additionally, analogous genes include at least 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99% or 100% sequence identity with the sequence of the kudzu isoprene synthase. In additional embodiments more than one of the above properties applies to the sequence. Analogous sequences are determined by known methods of sequence alignment. A commonly used alignment method is BLAST, although as indicated above and below, there are other methods that also find use in aligning sequences.

[0135] One example of a useful algorithm is PILEUP. PILEUP creates a multiple sequence alignment from a group of related sequences using progressive, pair-wise alignments. It can also plot a tree showing the clustering relationships used to create the alignment. PILEUP uses a simplification of the progressive alignment method of Feng and Doolittle (Feng and Doolittle, J Mol Evol, 35:351-360, 1987). The method is similar to that described by Higgins and Sharp (Higgins and Sharp, CABIOS 5:151-153, 1989). Useful PILEUP parameters including a default gap weight of 3.00, a default gap length weight of 0.10, and weighted end gaps.

[0136] Another example of a useful algorithm is the BLAST algorithm, described by Altschul *et al.*, (Altschul *et al.*, J Mol Biol, 215:403-410, 1990; and Karlin *et al.*, Proc Natl Acad Sci USA, 90:5873-5787, 1993). A particularly useful BLAST program is the WU-BLAST-2 program (*See*, Altschul *et al.*, Meth Enzymol, 266:460-480, 1996). WU-BLAST-2 uses several search parameters, most of which are set to the default values. The adjustable parameters are set with the following values: overlap span =1, overlap fraction = 0.125, word threshold (T) = 11. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched. However, the values may be adjusted to increase sensitivity. A % amino acid sequence identity value is determined by the number of matching identical residues divided

by the total number of residues of the "longer" sequence in the aligned region. The "longer" sequence is the one having the most actual residues in the aligned region (gaps introduced by WU-Blast-2 to maximize the alignment score are ignored).

[0137] Thus, "percent (%) nucleic acid sequence identity" is defined as the percentage of nucleotide residues in a candidate sequence that are identical to the nucleotide residues of the starting sequence (*i.e.*, the sequence of interest). A preferred method utilizes the BLASTN module of WU-BLAST-2 set to the default parameters, with overlap span and overlap fraction set to 1 and 0.125, respectively.

[0138] As used herein, the term "hybridization" refers to the process by which a strand of nucleic acid joins with a complementary strand through base pairing, as known in the art.

[0139] A nucleic acid sequence is considered to be "selectively hybridizable" to a reference nucleic acid sequence if the two sequences specifically hybridize to one another under moderate to high stringency hybridization and wash conditions. Hybridization conditions are based on the melting temperature (Tm) of the nucleic acid binding complex or probe. For example, "maximum stringency" typically occurs at about Tm-5°C (5° below the Tm of the probe); "high stringency" at about 5-10°C below the Tm; "intermediate stringency" at about 10-20°C below the Tm of the probe; and "low stringency" at about 20-25°C below the Tm. Functionally, maximum stringency conditions may be used to identify sequences having strict identity or near-strict identity with the hybridization probe; while intermediate or low stringency hybridization can be used to identify or detect polynucleotide sequence homologs.

[0140] Moderate and high stringency hybridization conditions are well known in the art. An example of high stringency conditions includes hybridization at about 42°C in 50% formamide, 5X SSC, 5X Denhardt's solution, 0.5% SDS and 100 μg/ml denatured carrier DNA followed by washing two times in 2X SSC and 0.5% SDS at room temperature and two additional times in 0.1X SSC and 0.5% SDS at 42°C. An example of moderate stringent conditions include an overnight incubation at 37°C in a solution comprising 20% formamide, 5 x SSC (150mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1x SSC at about 37 - 50°C. Those of skill in the art know how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

[0141] As used herein, "recombinant" includes reference to a cell or vector, that has been modified by the introduction of a heterologous nucleic acid sequence or that the cell is

derived from a cell so modified. Thus, for example, recombinant cells express genes that are not found in identical form within the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all as a result of deliberate human intervention. "Recombination," "recombining," and generating a "recombined" nucleic acid are generally the assembly of two or more nucleic acid fragments wherein the assembly gives rise to a chimeric gene.

[0142] In a preferred embodiment, mutant DNA sequences are generated with site saturation mutagenesis in at least one codon. In another preferred embodiment, site saturation mutagenesis is performed for two or more codons. In a further embodiment, mutant DNA sequences have more than 50%, more than 55%, more than 60%, more than 65%, more than 70%, more than 75%, more than 80%, more than 85%, more than 90%, more than 95%, or more than 98% homology with the wild-type sequence. In alternative embodiments, mutant DNA is generated *in vivo* using any known mutagenic procedure such as, for example, radiation, nitrosoguanidine and the like. The desired DNA sequence is then isolated and used in the methods provided herein.

[0143] As used herein, the term "target sequence" refers to a DNA sequence in the host cell that encodes the sequence where it is desired for the incoming sequence to be inserted into the host cell genome. In some embodiments, the target sequence encodes a functional wild-type gene or operon, while in other embodiments the target sequence encodes a functional mutant gene or operon, or a non-functional gene or operon.

[0144] As used herein, a "flanking sequence" refers to any sequence that is either upstream or downstream of the sequence being discussed (*e.g.,* for genes A-B-C, gene B is flanked by the A and C gene sequences). In a preferred embodiment, the incoming sequence is flanked by a homology box on each side. In another embodiment, the incoming sequence and the homology boxes comprise a unit that is flanked by stuffer sequence on each side. In some embodiments, a flanking sequence is present on only a single side (either 3' or 5'), but in preferred embodiments, it is on each side of the sequence being flanked. In some embodiments, a flanking sequence is present on only a single side (either 3' or 5'), while in preferred embodiments, it is present on each side of the sequence being flanked.

[0145] As used herein, the term "stuffer sequence" refers to any extra DNA that flanks homology boxes (typically vector sequences). However, the term encompasses any non-homologous DNA sequence. Not to be limited by any theory, a stuffer sequence provides a noncritical target for a cell to initiate DNA uptake.

[0146] As used herein, the terms "amplification" and "gene amplification" refer to a process by which specific DNA sequences are disproportionately replicated such that the amplified gene becomes present in a higher copy number than was initially present in the genome. In some embodiments, selection of cells by growth in the presence of a drug (*e.g.*, an inhibitor of an inhibitable enzyme) results in the amplification of either the endogenous gene encoding the gene product required for growth in the presence of the drug or by amplification of exogenous (*i.e.*, input) sequences encoding this gene product, or both.

[0147] "Amplification" is a special case of nucleic acid replication involving template specificity. It is to be contrasted with non-specific template replication (*i.e.*, replication that is template-dependent but not dependent on a specific template). Template specificity is here distinguished from fidelity of replication (*i.e.*, synthesis of the proper polynucleotide sequence) and nucleotide (ribo- or deoxyribo-) specificity. Template specificity is frequently described in terms of "target" specificity. Target sequences are "targets" in the sense that they are sought to be sorted out from other nucleic acid. Amplification techniques have been designed primarily for this sorting out.

[0148] As used herein, the term "co-amplification" refers to the introduction into a single cell of an amplifiable marker in conjunction with other gene sequences (*i.e.*, comprising one or more non-selectable genes such as those contained within an expression vector) and the application of appropriate selective pressure such that the cell amplifies both the amplifiable marker and the other, non-selectable gene sequences. The amplifiable marker may be physically linked to the other gene sequences or alternatively two separate pieces of DNA, one containing the amplifiable marker and the other containing the non-selectable marker, may be introduced into the same cell.

[0149] As used herein, the terms "amplifiable marker," "amplifiable gene," and "amplification vector" refer to a gene or a vector encoding a gene, which permits the amplification of that gene under appropriate growth conditions.

[0150] "Template specificity" is achieved in most amplification techniques by the choice of enzyme. Amplification enzymes are enzymes that, under conditions they are used, will process only specific sequences of nucleic acid in a heterogeneous mixture of nucleic acid. For example, in the case of Qß replicase, MDV-1 RNA is the specific template for the replicase (*See e.g.*, Kacian *et al.*, Proc Natl Acad Sci USA 69:3038, 1972) and other nucleic acids are not replicated by this amplification enzyme. Similarly, in the case of T7 RNA polymerase, this amplification enzyme has a stringent specificity for its own promoters (*See*, Chamberlin *et al.*, Nature 228:227, 1970). In the case of T4 DNA ligase, the enzyme will not

ligate the two oligonucleotides or polynucleotides, where there is a mismatch between the oligonucleotide or polynucleotide substrate and the template at the ligation junction (*See*, Wu and Wallace, Genomics 4:560, 1989). Finally, *Taq* and *Pfu* polymerases, by virtue of their ability to function at high temperature, are found to display high specificity for the sequences bounded and thus defined by the primers; the high temperature results in thermodynamic conditions that favor primer hybridization with the target sequences and not hybridization with non-target sequences.

[0151] As used herein, the term "amplifiable nucleic acid" refers to nucleic acids, which may be amplified by any amplification method. It is contemplated that "amplifiable nucleic acid" will usually comprise "sample template."

[0152] As used herein, the term "sample template" refers to nucleic acid originating from a sample, which is analyzed for the presence of "target" (defined below). In contrast, "background template" is used in reference to nucleic acid other than sample template, which may or may not be present in a sample. Background template is most often inadvertent. It may be the result of carryover, or it may be due to the presence of nucleic acid contaminants sought to be purified away from the sample. For example, nucleic acids from organisms other than those to be detected may be present as background in a test sample.

[0153] As used herein, the term "primer" refers to an oligonucleotide, whether occurring naturally as in a purified restriction digest or produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced, (*i.e.*, in the presence of nucleotides and an inducing agent such as DNA polymerase and at a suitable temperature and pH). The primer is preferably single stranded for maximum efficiency in amplification, but may alternatively be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. Preferably, the primer is an oligodeoxyribonucleotide. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent. The exact lengths of the primers will depend on many factors, including temperature, source of primer and the use of the method.

[0154] As used herein, the term "probe" refers to an oligonucleotide (*i.e.*, a sequence of nucleotides), whether occurring naturally as in a purified restriction digest or produced synthetically, recombinantly or by PCR amplification, which is capable of hybridizing to another oligonucleotide of interest. A probe may be single-stranded or double-stranded. Probes are useful in the detection, identification and isolation of particular gene sequences. It

is contemplated that any probe used in the present invention will be labeled with any "reporter molecule," so that is detectable in any detection system, including, but not limited to enzyme (*e.g.,* ELISA, as well as enzyme-based histochemical assays), fluorescent, radioactive, and luminescent systems. It is not intended that the present invention be limited to any particular detection system or label.

[0155] As used herein, the term "target," when used in reference to the polymerase chain reaction, refers to the region of nucleic acid bounded by the primers used for polymerase chain reaction. Thus, the "target" is sought to be sorted out from other nucleic acid sequences. A "segment" is defined as a region of nucleic acid within the target sequence.

[0156] As used herein, in one embodiment, the term "polymerase chain reaction" ("PCR") refers to the methods of U.S. Patent Nos. 4,683,195 4,683,202, and 4,965,188, hereby incorporated by reference, which include methods for increasing the concentration of a segment of a target sequence in a mixture of genomic DNA without cloning or purification. This process for amplifying the target sequence consists of introducing a large excess of two oligonucleotide primers to the DNA mixture containing the desired target sequence, followed by a precise sequence of thermal cycling in the presence of a DNA polymerase. The two primers are complementary to their respective strands of the double stranded target sequence. To effect amplification, the mixture is denatured and the primers then annealed to their complementary sequences within the target molecule. Following annealing, the primers are extended with a polymerase so as to form a new pair of complementary strands. The steps of denaturation, primer annealing and polymerase extension can be repeated many times (*i.e.*, denaturation, annealing and extension constitute one "cycle"; there can be numerous "cycles") to obtain a high concentration of an amplified segment of the desired target sequence. The length of the amplified segment of the desired target sequence is determined by the relative positions of the primers with respect to each other, and therefore, this length is a controllable parameter. By virtue of the repeating aspect of the process, the method is referred to as the "polymerase chain reaction" (hereinafter "PCR"). Because the desired amplified segments of the target sequence become the predominant sequences (in terms of concentration) in the mixture, they are said to be "PCR amplified".

[0157] As used herein, the term "amplification reagents" refers to those reagents (deoxyribonucleotide triphosphates, buffer, etc.), needed for amplification except for primers, nucleic acid template and the amplification enzyme. Typically, amplification reagents along with other reaction components are placed and contained in a reaction vessel (test tube, microwell, etc.).

[0158] With PCR, it is possible to amplify a single copy of a specific target sequence in genomic DNA to a level detectable by several different methodologies (*e.g.,* hybridization with a labeled probe; incorporation of biotinylated primers followed by avidin-enzyme conjugate detection; incorporation of ^{32}P-labeled deoxynucleotide triphosphates, such as dCTP or dATP, into the amplified segment). In addition to genomic DNA, any oligonucleotide or polynucleotide sequence can be amplified with the appropriate set of primer molecules. In particular, the amplified segments created by the PCR process itself are, themselves, efficient templates for subsequent PCR amplifications.

[0159] As used herein, the terms "PCR product," "PCR fragment," and "amplification product" refer to the resultant mixture of compounds after two or more cycles of the PCR steps of denaturation, annealing and extension are complete. These terms encompass the case where there has been amplification of one or more segments of one or more target sequences.

[0160] As used herein, the term "RT-PCR" refers to the replication and amplification of RNA sequences. In this method, reverse transcription is coupled to PCR, most often using a one enzyme procedure in which a thermostable polymerase is employed, as described in U.S. Patent No. 5,322,770, herein incorporated by reference. In RT-PCR, the RNA template is converted to cDNA due to the reverse transcriptase activity of the polymerase, and then amplified using the polymerizing activity of the polymerase (*i.e.,* as in other PCR methods).

[0161] As used herein, the terms "restriction endonucleases" and "restriction enzymes" refer to bacterial enzymes, each of which cut double-stranded DNA at or near a specific nucleotide sequence.

[0162] A "restriction site" refers to a nucleotide sequence recognized and cleaved by a given restriction endonuclease and is frequently the site for insertion of DNA fragments. In certain embodiments of the invention restriction sites are engineered into the selective marker and into 5' and 3' ends of the DNA construct.

[0163] As used herein, the term "chromosomal integration" refers to the process whereby an incoming sequence is introduced into the chromosome of a host cell. The homologous regions of the transforming DNA align with homologous regions of the chromosome. Subsequently, the sequence between the homology boxes is replaced by the incoming sequence in a double crossover (*i.e.*, homologous recombination). In some embodiments of the present invention, homologous sections of an inactivating chromosomal segment of a DNA construct align with the flanking homologous regions of the indigenous chromosomal region of the *Escherichia* chromosome. Subsequently, the indigenous chromosomal region is deleted by the DNA construct in a double crossover (*i.e.*, homologous recombination).

[0164] "Homologous recombination" means the exchange of DNA fragments between two DNA molecules or paired chromosomes at the site of identical or nearly identical nucleotide sequences. In a preferred embodiment, chromosomal integration is homologous recombination. "Homologous sequences" as used herein means a nucleic acid or polypeptide sequence having 100%, 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, 90%, 88%, 85%, 80%, 75%, or 70% sequence identity to another nucleic acid or polypeptide sequence when optimally aligned for comparison. In some embodiments, homologous sequences have between 85% and 100% sequence identity, while in other embodiments there is between 90% and 100% sequence identity, and in more preferred embodiments, there is 95% and 100% sequence identity.

[0165] As used herein "amino acid" refers to peptide or protein sequences or portions thereof. The terms "protein," "peptide," and "polypeptide" are used interchangeably.

[0166] As used herein, the term "heterologous protein" refers to a protein or polypeptide that does not naturally occur in the host cell. Examples of heterologous proteins include enzymes such as isoprene synthases. In some embodiments, the genes encoding the proteins are naturally occurring genes, while in other embodiments mutated and/or synthetic genes are used.

[0167] As used herein, "homologous protein" refers to a protein or polypeptide native or naturally occurring in a cell. In preferred embodiments, the cell is a Gram-negative cell, while in particularly preferred embodiments the cell is an *Escherichia* host cell.

[0168] An enzyme is "overexpressed" in a host cell if the enzyme is expressed in the cell at a higher level that the level at which it is expressed in a corresponding wild-type cell.

[0169] The terms "protein" and "polypeptide" are used interchangeability herein. The 3-letter code for amino acids as defined in conformity with the IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN) is used through out this disclosure. It is also understood that a polypeptide may be coded for by more than one nucleotide sequence due to the degeneracy of the genetic code.

[0170] The term "mature" form of a protein or peptide refers to the final functional form of the protein or peptide. To exemplify, a mature form of kudzu isoprene synthase includes the amino acid sequence of SEQ ID NO:2.

[0171] The term "precursor" form of a protein or peptide refers to a mature form of the protein having a prosequence operably linked to the amino or carbonyl terminus of the protein. The precursor may also have a "signal" sequence operably linked, to the amino terminus of the prosequence. The precursor may also have additional polynucleotides that are

involved in post-translational activity (*e.g.*, polynucleotides cleaved therefrom to leave the mature form of a protein or peptide).

[0172] "Naturally occurring enzyme" refers to an enzyme having the unmodified amino acid sequence identical to that found in nature. Naturally occurring enzymes include native enzymes, those enzymes naturally expressed or found in the particular microorganism.

[0173] The term "identical" in the context of two nucleic acids or polypeptide sequences refers to the residues in the two sequences that are the same when aligned for maximum correspondence, as measured using one of the following sequence comparison or analysis algorithms.

[0174] The term "optimal alignment" refers to the alignment giving the highest percent identity score.

[0175] "Percent sequence identity," "percent amino acid sequence identity," "percent gene sequence identity," and/or "percent nucleic acid/polynucloetide sequence identity," with respect to two amino acid, polynucleotide and/or gene sequences (as appropriate), refer to the percentage of residues that are identical in the two sequences when the sequences are optimally aligned. Thus, 80% amino acid sequence identity means that 80% of the amino acids in two optimally aligned polypeptide sequences are identical.

[0176] The phrase "substantially identical" in the context of two nucleic acids or polypeptides thus refers to a polynucleotide or polypeptide that comprising at least 70% sequence identity, preferably at least 75%, preferably at least 80%, preferably at least 85%, preferably at least 90%, preferably at least 95%, preferably at least 97% , preferably at least 98% and preferably at least 99% sequence identity as compared to a reference sequence using the programs or algorithms (*e.g.*, BLAST, ALIGN, CLUSTAL) using standard parameters. One indication that two polypeptides are substantially identical is that the first polypeptide is immunologically cross-reactive with the second polypeptide. Typically, polypeptides that differ by conservative amino acid substitutions are immunologically cross-reactive. Thus, a polypeptide is substantially identical to a second polypeptide, for example, where the two peptides differ only by a conservative substitution. Another indication that two nucleic acid sequences are substantially identical is that the two molecules hybridize to each other under stringent conditions (*e.g.*, within a range of medium to high stringency).

[0177] The term "isolated" or "purified" refers to a material that is removed from its original environment (*e.g.*, the natural environment if it is naturally occurring). For example, the material is said to be "purified" when it is present in a particular composition in a higher or lower concentration than exists in a naturally occurring or wild type organism (e.g., kudzu)

or in combination with components not normally present upon expression from a naturally occurring or wild type organism. For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such polynucleotides could be part of a vector, and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of its natural environment. In preferred embodiments, a nucleic acid or protein is said to be purified, for example, if it gives rise to essentially one band in an electrophoretic gel or blot.

[0178] The term "isolated", when used in reference to a DNA sequence, refers to a DNA sequence that has been removed from its natural genetic milieu and is thus free of other extraneous or unwanted coding sequences, and is in a form suitable for use within genetically engineered protein production systems. Similarly, the term "isolated", when used in reference to a recombinant DNA sequence, refers to a DNA sequence that has been removed from the genetic milieu of the host organism and is thus free of other extraneous or unwanted coding sequences (e.g., kudzu IspS expression vector propagated in *E. coli*). Such isolated molecules are those that are separated from their natural environment and include cDNA and genomic clones. Isolated DNA molecules of the present invention are free of other genes with which they are ordinarily associated, but may include naturally occurring 5' and 3' untranslated regions such as promoters and terminators. The identification of associated regions will be evident to one of ordinary skill in the art (*See e.g.*, Dynan and Tijan, Nature 316:774-78, 1985). The term "an isolated DNA sequence" is alternatively referred to as "a cloned DNA sequence".

[0179] The term "isolated," when used in reference to a protein, refers to a protein that is found in a condition other than its native environment. In a preferred form, the isolated protein is substantially free of other proteins, particularly other homologous proteins. Similarly, the term "isolated", when used in reference to a recombinantly produced protein, refers to a protein that has been removed from the proteinaceous milieu of the host organism and is thus free of other extraneous or unwanted proteins (e.g., recombinant kudzu IspS produced in *E. coli*). An isolated protein is more than 10% pure, preferably more than 20% pure, and even more preferably more than 30% pure, as determined by SDS-PAGE. Further aspects of the invention encompass the protein in a highly purified form (*i.e.,* more than 40% pure, more than 60% pure, more than 80% pure, more than 90% pure, more than 95% pure, more than 97% pure, and even more than 99% pure), as determined by SDS-PAGE.

[0180] The following cassette mutagenesis method may be used to facilitate the construction of the enzyme variants of the present invention, although other methods may be used. First, as described herein, a naturally-occurring gene encoding the enzyme is obtained and sequenced in whole or in part. Then, the sequence is scanned for a point at which it is desired to make a mutation (deletion, insertion or substitution) of one or more amino acids in the encoded enzyme. The sequences flanking this point are evaluated for the presence of restriction sites for replacing a short segment of the gene with an oligonucleotide pool which when expressed will encode various mutants. Such restriction sites are preferably unique sites within the protein gene so as to facilitate the replacement of the gene segment. However, any convenient restriction site that is not overly redundant in the enzyme gene may be used, provided the gene fragments generated by restriction digestion can be reassembled in proper sequence. If restriction sites are not present at locations within a convenient distance from the selected point (from 10 to 15 nucleotides), such sites are generated by substituting nucleotides in the gene in such a fashion that neither the reading frame nor the amino acids encoded are changed in the final construction. Mutation of the gene in order to change its sequence to conform to the desired sequence is accomplished by M13 primer extension in accord with generally known methods. The task of locating suitable flanking regions and evaluating the needed changes to arrive at two convenient restriction site sequences is made routine by the redundancy of the genetic code, a restriction enzyme map of the gene and the large number of different restriction enzymes. Note that if a convenient flanking restriction site is available, the above method need be used only in connection with the flanking region that does not contain a site.

[0181] Once the naturally-occurring DNA and/or synthetic DNA is cloned, the restriction sites flanking the positions to be mutated are digested with the cognate restriction enzymes and a plurality of end termini-complementary oligonucleotide cassettes are ligated into the gene. The mutagenesis is simplified by this method because all of the oligonucleotides can be synthesized so as to have the same restriction sites, and no synthetic linkers are necessary to create the restriction sites.

[0182] As used herein, "corresponding to," refers to a residue at the enumerated position in a protein or peptide, or a residue that is analogous, homologous, or equivalent to an enumerated residue in a protein or peptide. As used herein, "corresponding region," generally refers to an analogous position along related proteins or a parent protein.

[0183] As used herein, the term, "combinatorial mutagenesis" refers to methods in which libraries of variants of a starting sequence are generated. In these libraries, the variants

contain one or several mutations chosen from a predefined set of mutations. In addition, the methods provide means to introduce random mutations, which were not members of the predefined set of mutations. In some embodiments, the methods include those set forth in U.S. Application No. 09/699,250, hereby incorporated by reference. In alternative embodiments, combinatorial mutagenesis methods encompass commercially available kits (*e.g.,* QUIKCHANGE Multisite mutagenesis kit, Stratagene, San Diego, CA).

[0184] As used herein, the term "library of mutants" refers to a population of cells which are identical in most of their genome but include different homologues of one or more genes. Such libraries can be used, for example, to identify genes or operons with improved traits.

[0185] As used herein, the terms "starting gene" and "parent gene" refer to a gene of interest that encodes a protein of interest that is to be improved and/or changed using the present invention.

[0186] As used herein, the terms "multiple sequence alignment" and "MSA" refer to the sequences of multiple homologs of a starting gene that are aligned using an algorithm (*e.g.*, Clustal W).

[0187] As used herein, the terms "consensus sequence" and "canonical sequence" refer to an archetypical amino acid sequence against which all variants of a particular protein or sequence of interest are compared. The terms also refer to a sequence that sets forth the nucleotides that are most often present in a DNA sequence of interest. For each position of a gene, the consensus sequence gives the amino acid that is most abundant in that position in the MSA.

[0188] As used herein, the term "consensus mutation" refers to a difference in the sequence of a starting gene and a consensus sequence. Consensus mutations are identified by comparing the sequences of the starting gene and the consensus sequence obtained from a MSA. In some embodiments, consensus mutations are introduced into the starting gene such that it becomes more similar to the consensus sequence. Consensus mutations also include amino acid changes that change an amino acid in a starting gene to an amino acid that is more frequently found in an MSA at that position relative to the frequency of that amino acid in the starting gene. Thus, the term consensus mutation comprises all single amino acid changes that replace an amino acid of the starting gene with an amino acid that is more abundant than the amino acid in the MSA.

[0189] The terms "modified sequence" and "modified genes" are used interchangeably herein to refer to a sequence that includes a deletion, insertion or interruption of naturally occurring nucleic acid sequence. In some preferred embodiments, the expression product of

the modified sequence is a truncated protein (*e.g.*, if the modification is a deletion or interruption of the sequence). In some particularly preferred embodiments, the truncated protein retains biological activity. In alternative embodiments, the expression product of the modified sequence is an elongated protein (*e.g.,* modifications comprising an insertion into the nucleic acid sequence). In some embodiments, an insertion leads to a truncated protein (*e.g.,* when the insertion results in the formation of a stop codon). Thus, an insertion may result in either a truncated protein or an elongated protein as an expression product.

[0190] As used herein, the terms "mutant sequence" and "mutant gene" are used interchangeably and refer to a sequence that has an alteration in at least one codon occurring in a host cell's wild-type sequence. The expression product of the mutant sequence is a protein with an altered amino acid sequence relative to the wild-type. The expression product may have an altered functional capacity (*e.g.,* enhanced enzymatic activity).

[0191] The terms "mutagenic primer" or "mutagenic oligonucleotide" (used interchangeably herein) are intended to refer to oligonucleotide compositions which correspond to a portion of the template sequence and which are capable of hybridizing thereto. With respect to mutagenic primers, the primer will not precisely match the template nucleic acid, the mismatch or mismatches in the primer being used to introduce the desired mutation into the nucleic acid library. As used herein, "non-mutagenic primer" or "non-mutagenic oligonucleotide" refers to oligonucleotide compositions that match precisely to the template nucleic acid. In one embodiment of the invention, only mutagenic primers are used. In another preferred embodiment of the invention, the primers are designed so that for at least one region at which a mutagenic primer has been included, there is also non-mutagenic primer included in the oligonucleotide mixture. By adding a mixture of mutagenic primers and non-mutagenic primers corresponding to at least one of the mutagenic primers, it is possible to produce a resulting nucleic acid library in which a variety of combinatorial mutational patterns are presented. For example, if it is desired that some of the members of the mutant nucleic acid library retain their parent sequence at certain positions while other members are mutant at such sites, the non-mutagenic primers provide the ability to obtain a specific level of non-mutant members within the nucleic acid library for a given residue. The methods of the invention employ mutagenic and non-mutagenic oligonucleotides which are generally between 10-50 bases in length, more preferably about 15-45 bases in length. However, it may be necessary to use primers that are either shorter than 10 bases or longer than 50 bases to obtain the mutagenesis result desired. With respect to corresponding mutagenic and non-mutagenic primers, it is not necessary that the corresponding

oligonucleotides be of identical length, but only that there is overlap in the region corresponding to the mutation to be added.

[0192] Primers may be added in a pre-defined ratio according to the present invention. For example, if it is desired that the resulting library have a significant level of a certain specific mutation and a lesser amount of a different mutation at the same or different site, by adjusting the amount of primer added, it is possible to produce the desired biased library. Alternatively, by adding lesser or greater amounts of non-mutagenic primers, it is possible to adjust the frequency with which the corresponding mutation(s) are produced in the mutant nucleic acid library.

[0193] The terms "wild-type sequence" or "wild-type gene" are used interchangeably herein, to refer to a sequence that is native or naturally occurring in a host cell. In some embodiments, the wild-type sequence refers to a sequence of interest that is the starting point of a protein-engineering project. The wild-type sequence may encode either a homologous or heterologous protein. A homologous protein is one the host cell would produce without intervention. A heterologous protein is one that the host cell would not produce but for the intervention.

[0194] As used herein the term "lysate" refers to a solution containing the contents of lysed cells. In some embodiments, the lysate is a bacterial cell lysate (e.g., *E. coli* cells lysed using READYLYSE™ lysozyme solution from Epicentre; or *E. coli* cells lysed using a French Pressure cell).

[0195] As used herein the term "lysozyme" refers to a glycosidase that hydrolyzes the bond between N-acetyl muramic acid and N-acetul glucosamine, thus cleaving an important polymer in the cell wall of many bacteria. Suitable lysozymes for use with the present invention include but are not limited to hen egg white lysozyme (Sigma), T4 lysozyme, recombinant non-mammalian, non-avian lysozyme (READYLYSE™), or a fungal lysozyme.

[0196] As used herein, the term "headspace" refers to the vapor/air mixture trapped above a solid or liquid sample in a sealed vessel.

[0197] As used herein, the terms "high throughput screening" and "HTS" refer to measuring isoprene in at least 96 samples in 4 hours or less. In preferred embodiments, the sample volume is less than 2 mL.

[0198] Unless otherwise noted, all component or composition levels are in reference to the active level of that component or composition, and are exclusive of impurities, for example, residual solvents or by-products, which may be present in commercially available sources.

[0199] Enzyme components weights are based on total active protein. All percentages and ratios are calculated by weight unless otherwise indicated. All percentages and ratios are calculated based on the total composition unless otherwise.

DETAILED DESCRIPTION OF THE INVENTION

[0200] Isoprene monomer is employed in the manufacture of polyisoprene and various copolymers (with isobutylene, butadiene, styrene, or other monomers). To build a strain (prokaryotic or eukaryotic) capable of producing commercially viable levels of isoprene requires optimization of the entire pathway, either MVA to isoprene or DXP to isoprene. A key enzyme in the pathway is isoprene synthase (IspS), which converts the precursor DMAPP to isoprene. The only isoprene synthases (IspS) identified to date are those from plants such as poplar, English oak and kudzu vine. Although some bacteria, such as *Bacillus subtilis*, also produce isoprene, a prokaryotic IspS has yet to be identified and the native IspS activity in *Bacillus* is not sufficient for a commercial process. The plant IspS enzymes identified to date have been partially characterized in part by expression in *E. coli* and some of the kinetic parameters of these enzymes have been determined *in vitro* with purified protein. However, the kinetic parameters (Km, rate etc) of the native IspS enzymes are insufficient for commercial production of isoprene in a biological host.

[0201] To solve this problem as described herein, a plant IspS is expressed in a bacterial host. In addition the IspS is engineered for a change in a property of interest. Characterization of wild-type and mutant IspS is accomplished via any means or "test" suitable and is preferably based on the assessment of properties of interest. Properties of interest include but are not limited to: pH optima, temperature stability (e.g., T_m value), intracellular and extracellular solubility, K_m value, k_{cat} value, or specific activity, as well as sensitivity to potential inhibitors including substrate or product inhibition. Oxidative and proteolytic stability are also of interest. Furthermore, activation or inhibition due to metal ion effects and ionic strength is of interest. These properties and parameters can be assessed by the conversion of DMAPP to isoprene *in vitro* with purified or partially purified isoprene synthase or *in vivo* in the context of a host organism such as *E. coli* expressing the DXP pathway, the MVA pathway, or both. It is contemplated that enzymes having various degrees of stability, solubility, activity, and/or expression level in one or more of test conditions will find use in the present invention for the production of isoprene in a diversity of hosts. High throughput methods such as those described in Example 10 are required to investigate these properties in an economical manner.

[0202] The invention features compositions and methods for the production of increased amounts of isoprene. In particular, these compositions and methods increase the rate of isoprene production and increase the total amount of isoprene that is produced. The biosynthetic processes for isoprene production described herein are a desirable alternative to using natural rubber. As discussed further below, the amount of isoprene produced by cells can be greatly increased by introducing a heterologous nucleic acid encoding an isoprene synthase (IspS) polypeptide into the cells. Isoprene synthase polypeptides convert dimethylallyl diphosphate (DMAPP) into isoprene. As shown in the examples, a heterologous *Pueraria montana* (kudzu) isoprene synthase polypeptide and variants thereof was expressed in Gram-negative bacterial cells (e.g., *Escherichia coli*). Also shown in the examples and contemplated within the scope of the invention are poplar isoprene synthase polypeptide and variants thereof was expressed in Gram-negative bacterial cells (e.g., *Escherichia coli*).

[0203] Heterologous expression of a plant IspS in bacterial host cells resulted in the production of more isoprene than the corresponding cells lacking the plant IspS.

[0204] It has been shown that mutating amino-acid residues on the surface of protease enzymes can improve their activity, expression, and stability (WO2008/153925, WO2008/153934, WO2008/153935). Surprisingly, we have found that mutating amino-acid residues on the surface of a completely different enzyme, isoprene synthase, can enhance its expression, solubility, and activity. L70R is an example of such a beneficial surface mutation.

[0205] Elucidation of the three-dimensional structure of an enzyme is essential for accurately identifying amino-acid residues on its surface. Homology modeling using structures with sequences approximately 40% identical to isoprene synthase (e.g., bornyl synthase and limonene synthase, the enzymes of known structure with closest identity to isoprene synthase) can reveal gross aspects of the modeled enzyme structure, but is insufficient to precisely identify surface-exposed residues and quantify their degree of surface exposure. Surface exposure of an amino-acid residue is quantified by the percentage of solvent-accessible surface area of its side chain.

[0206] The following classes of mutations in isoprene synthase may improve solubility of the enzyme by targeting amino-acid residues that are >50% solvent-exposed, preferably >65% solvent-exposed, and most preferably >85% solvent-exposed:

Hydrophobic → positively charged, and vice versa

Hydrophobic → negatively charged, and vice versa

Hydrophobic → neutral polar, and vice versa

Neutral polar → positively charged, and vice versa

Neutral polar → negatively charged, and vice versa

Positively charged → negatively charged, and vice versa

[0207] Additionally isoprene production by cells containing a heterologous isoprene synthase nucleic acid can be enhanced by increasing the amount of a 1-deoxy-D-xylulose-5-phosphate synthase (DXS) polypeptide, and/or an isopentenyl diphosphate isomerase (IDI) polypeptide, expressed by the cells. For example, a DXS nucleic acid and/or an IDI nucleic acid can be introduced into the cells. The DXS nucleic acid may be a heterologous nucleic acid or a duplicate copy of an endogenous nucleic acid. Similarly, the IDI nucleic acid may be a heterologous nucleic acid or a duplicate copy of an endogenous nucleic acid. In some embodiments, the amount of DXS and/or IDI polypeptide is increased by replacing the endogenous DXS and/or IDI promoters or regulatory regions with other promoters and/or regulatory regions that result in greater transcription of the DXS and/or IDI nucleic acids. In some embodiments, the cells contain both a heterologous nucleic acid encoding an isoprene synthase polypeptide (*e.g.*, a plant isoprene synthase nucleic acid) and a duplicate copy of an endogenous nucleic acid encoding an isoprene synthase polypeptide.

[0208] The encoded DXS and IDI polypeptides are part of the DXP pathway for the biosynthesis of isoprene (Figure 15). DXS polypeptides convert pyruvate and D-glyceraldehyde-3-phosphate into 1-deoxy-D-xylulose-5-phosphate. While not intending to be bound by any particular theory, it is believed that increasing the amount of DXS polypeptide increases the flow of carbon through the DXP pathway, leading to greater isoprene production. IDI polypeptides catalyze the interconversion of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP). While not intending to be bound by any particular theory, it is believed that increasing the amount of IDI polypeptide in cells increases the amount of IPP that is converted into DMAPP, which in turn is converted into isoprene.

[0209] In some embodiments the production of isoprene by cells containing a heterologous isoprene synthase nucleic acid can be augmented by increasing expression of a MVA polypeptide in the cells (Figure 15). Exemplary MVA pathways polypeptides include any of the following polypeptides: acetyl-CoA acetyltransferase (AA-CoA thiolase) polypeptides, 3-hydroxy-3-methylglutaryl-CoA synthase (HMG-CoA synthase) polypeptides, 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase) polypeptides, mevalonate kinase (MVK) polypeptides, phosphomevalonate kinase (PMK) polypeptides, diphosphomevalonte decarboxylase (MVD) polypeptides, IDI polypeptides, and polypeptides (*e.g.*, fusion polypeptides) having an activity of two or more MVA pathway polypeptides. For example,

one or more MVA pathway nucleic acids can be introduced into the cells. In some embodiments, the cells contain the upper MVA pathway, which includes AA-CoA thiolase, HMG-CoA synthase, and HMG-CoA reductase nucleic acids. In some embodiments, the cells contain the lower MVA pathway, which includes MVK, PMK, MVD, and IDI nucleic acids. In some embodiments, the cells contain the entire MVA pathway, which includes AA-CoA thiolase, HMG-CoA synthase, HMG-CoA reductase, MVK, PMK, MVD, and IDI nucleic acids. The MVA pathway nucleic acids may be heterologous nucleic acids or duplicate copies of endogenous nucleic acids. In some embodiments, the amount of one or more MVA pathway polypeptides is increased by replacing the endogenous promoters or regulatory regions for the MVA pathway nucleic acids with other promoters and/or regulatory regions that result in greater transcription of the MVA pathway nucleic acids. In some embodiments, the cells contain both a heterologous nucleic acid encoding an isoprene synthase polypeptide (*e.g.*, a plant isoprene synthase nucleic acid) and a duplicate copy of an endogenous nucleic acid encoding an isoprene synthase polypeptide.

[0210] In some embodiments, at least a portion of the cells maintain the heterologous isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acid for at least about 5, 10, 20, 50, 75, 100, 200, 300, or more cell divisions in a continuous culture (such as a continuous culture without dilution). In some embodiments of any of the aspects of the invention, the nucleic acid comprising the heterologous or duplicate copy of an endogenous isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acid also comprises a selective marker, such as a kanamycin, ampicillin, carbenicillin, gentamicin, hygromycin, phleomycin, bleomycin, neomycin, or chloramphenicol antibiotic resistance nucleic acid.

I. Exemplary Polypeptides and Nucleic Acids

[0211] Various isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids can be used in the compositions and methods of the invention.

[0212] As used herein, "polypeptides" includes polypeptides, proteins, peptides, fragments of polypeptides, and fusion polypeptides that include part or all of a first polypeptide (*e.g.*, an isoprene synthase, DXS, IDI, or MVA pathway polypeptide) and part or all of a second polypeptide (*e.g.*, a peptide that facilitates purification or detection of the fusion polypeptide, such as a His-tag). In some embodiments, the fusion polypeptide has an activity of two or more MVA pathway polypeptides (such as AA-CoA thiolase and HMG-CoA reductase polypeptides). In some embodiments, the polypeptide is a naturally-occurring polypeptide

(such as the polypeptide encoded by an *Enterococcus faecalis mvaE* nucleic acid) that has an activity of two or more MVA pathway polypeptides.

[0213] In various embodiments, a polypeptide has at least or about 50, 100, 150, 175, 200, 250, 300, 350, 400, or more amino acids. In some embodiments, the polypeptide fragment contains at least or about 25, 50, 75, 100, 150, 200, 300, or more contiguous amino acids from a full-length polypeptide and has at least or about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% of an activity of a corresponding full-length polypeptide. In particular embodiments the polypeptide includes a segment of or the entire amino acid sequence of any naturally-occurring isoprene synthase, DXS, IDI, or MVA pathway polypeptide. In some embodiments, the polypeptide has one or more mutations compared to the sequence of a wild-type (*i.e.*, a sequence occurring in nature) isoprene synthase, DXS, IDI, or MVA pathway polypeptide.

[0214] In some embodiments, the polypeptide is an isolated polypeptide. As used herein, an "isolated polypeptide" is not part of a library of polypeptides, such as a library of 2, 5, 10, 20, 50 or more different polypeptides and is separated from at least one component with which it occurs in nature. An isolated polypeptide can be obtained, for example, by expression of a recombinant nucleic acid encoding the polypeptide.

[0215] In some embodiments, the polypeptide is a heterologous polypeptide. By "heterologous polypeptide" is meant a polypeptide whose amino acid sequence is not identical to that of another polypeptide naturally expressed in the same host cell.

[0216] As used herein, a "nucleic acid" refers to two or more deoxyribonucleotides and/or ribonucleotides in either single or double-stranded form. In some embodiments, the nucleic acid is a recombinant nucleic acid. By "recombinant nucleic acid" means a nucleic acid of interest that is free of one or more nucleic acids (*e.g.*, genes), which in the genome occurring in nature of the organism from which the nucleic acid of interest is derived, flank the nucleic acid of interest. The term therefore includes, for example, a recombinant DNA which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (*e.g.*, a cDNA, a genomic DNA fragment, or a cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences.

[0217] In various embodiments, the nucleic acid is a recombinant nucleic acid. For instance, in some embodiments, an isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is operably linked to another nucleic acid encoding all or a portion of another polypeptide such that the recombinant nucleic acid encodes a fusion polypeptide that includes

an isoprene synthase, DXS, IDI, or MVA pathway polypeptide and all or part of another polypeptide (*e.g.*, a peptide that facilitates purification or detection of the fusion polypeptide, such as a His-tag). In some embodiments, part or all of a recombinant nucleic acid is chemically synthesized. In some embodiments, the nucleic acid is a heterologous nucleic acid. By "heterologous nucleic acid" is meant a nucleic acid whose nucleic acid sequence is not identical to that of another nucleic acid naturally found in the same host cell.

[0218] In particular embodiments the nucleic acid includes a segment of or the entire nucleic acid sequence of any naturally-occurring isoprene synthase, DXS, IDI, or MVA pathway nucleic acid. In some embodiments, the nucleic acid includes at least or about 50, 100, 150, 200, 300, 400, 500, 600, 700, 800, or more contiguous nucleotides from a naturally-occurring isoprene synthase nucleic acid DXS, IDI, or MVA pathway nucleic acid. In some embodiments, the nucleic acid has one or more mutations compared to the sequence of a wild-type (*i.e.*, a sequence occurring in nature) isoprene synthase, DXS, IDI, or MVA pathway nucleic acid. In some embodiments, the nucleic acid has one or more mutations (*e.g.*, a silent mutation) that increase the transcription or translation of isoprene synthase, DXS, IDI, or MVA pathway nucleic acid. In some embodiments, the nucleic acid is a degenerate variant of any nucleic acid encoding an isoprene synthase, DXS, IDI, or MVA pathway polypeptide.

[0219] "Codon degeneracy" refers to divergence in the genetic code permitting variation of the nucleotide sequence without affecting the amino acid sequence of an encoded polypeptide. The skilled artisan is well aware of the "codon-bias" exhibited by a specific host cell in usage of nucleotide codons to specify a given amino acid. Therefore, when synthesizing a nucleic acid for improved expression in a host cell, it is desirable in some embodiments to design the nucleic acid such that its frequency of codon usage approaches the frequency of preferred codon usage of the host cell.

[0220] The accession numbers of exemplary isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids are listed in Appendix 1 of U.S. Application No. 61/013,574, herein incorporated by reference in its entirety, particularly with respect to the amino acid and nucleic acid sequences of isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids). The Kegg database also contains the amino acid and nucleic acid sequences of numerous exemplary isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids (*See, e.g.,* the world-wide web at "genome.jp/kegg/pathway/map/map00100.html" and the sequences therein, which are each hereby incorporated by reference in their entireties, particularly with respect to the amino

acid and nucleic acid sequences of isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids). In some embodiments, one or more of the isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and/or nucleic acids have a sequence identical to a sequence publicly available on December 12, 2007, such as any of the sequences that correspond to any of the accession numbers in Appendix 1 of U.S. Application No. 61/013,574, or any of the sequences present in the Kegg database as of the date of this filing. Additional exemplary isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and nucleic acids are described further below.

Exemplary Isoprene Synthase Polypeptides and Nucleic Acids

[0221] As noted above, isoprene synthase polypeptides convert dimethylallyl diphosphate (DMAPP) into isoprene. Exemplary isoprene synthase polypeptides include polypeptides, fragments of polypeptides, peptides, and fusions polypeptides that have at least one activity of an isoprene synthase polypeptide. Standard methods can be used to determine whether a polypeptide has isoprene synthase polypeptide activity by measuring the ability of the polypeptide to convert DMAPP into isoprene *in vitro*, in a cell extract, or *in vivo*. Isoprene synthase polypeptide activity in the cell extract can be measured, for example, as described in Silver *et al.*, J. Biol. Chem. 270:13010-13016, 1995 and references therein, which are each hereby incorporated by reference in their entireties, particularly with respect to assays for isoprene synthase polypeptide activity. DMAPP (Sigma) is evaporated to dryness under a stream of nitrogen and rehydrated to a concentration of 100 mM in 100 mM potassium phosphate buffer pH 8.2 and stored at -20 °C. To perform the assay, a solution of 5 μl of 1M $MgCl_2$, 1 mM (250 μg/ml) DMAPP, 65 μl of Plant Extract Buffer (PEB) (50 mM Tris-HCl, pH 8.0, 20 mM $MgCl_2$, 5% glycerol, and 2 mM DTT) is added to 25 μl of cell extract in a 20 ml Headspace vial with a metal screw cap and teflon coated silicon septum (Agilent Technologies) and cultured at 37 °C for 15 minutes with shaking. The reaction is quenched by adding 200 μl of 250 mM EDTA or by heat inactivation, and isoprene is quantified by GC/MS.

[0222] Exemplary isoprene synthase nucleic acids include nucleic acids that encode a polypeptide, fragment of a polypeptide, peptide, or fusion polypeptide that has at least one activity of an isoprene synthase polypeptide. Exemplary isoprene synthase polypeptides and nucleic acids include naturally-occurring polypeptides and nucleic acids from any of the

source organisms described herein as well as mutant polypeptides and nucleic acids derived from any of the source organisms described herein.

[0223] In some embodiments, the isoprene synthase polypeptide or nucleic acid is from the family Fabaceae, the family Salicaceae, or the family Fagaceae. In some embodiments, the isoprene synthase polypeptide or nucleic acid is a naturally-occurring polypeptide or nucleic acid from *Pueraria montana* (kudzu) (Sharkey *et al.*, Plant Physiology 137: 700-712, 2005), poplar (such as *Populus alba x tremula* CAC35696) Miller *et al.*, Planta 213: 483-487, 2001) aspen (such as *Populus tremuloides*) Silver *et al.*, JBC 270(22): 13010-1316, 1995), or English Oak (*Quercus robur*) (Zimmer *et al.*, WO 98/02550), which are each hereby incorporated by reference in their entireties, particularly with respect to isoprene synthase nucleic acids and the expression of isoprene synthase polypeptides. Suitable isoprene synthases include, but are not limited to, those identified by GenBank Accession Nos. AY341431, AY316691, AY279379, AJ457070, and AY182241, which are each hereby incorporated by reference in their entireties, particularly with respect to sequences of isoprene synthase nucleic acids and polypeptides. In some embodiments, the isoprene synthase polypeptide or nucleic acid is not a naturally-occurring polypeptide or nucleic acid from *Quercus robur* (*i.e.*, the isoprene synthase polypeptide or nucleic acid is an isoprene synthase polypeptide or nucleic acid other than a naturally-occurring polypeptide or nucleic acid from *Quercus robur*). In some embodiments, the isoprene synthase nucleic acid or polypeptide is not a naturally-occurring polypeptide or nucleic acid from poplar (such as *Populus alba x tremula* CAC35696).

Exemplary DXS Polypeptides and Nucleic Acids

[0224] As noted above, 1-deoxy-D-xylulose-5-phosphate synthase (DXS) polypeptides convert pyruvate and D-glyceraldehyde-3-phosphate into 1-deoxy-D-xylulose-5-phosphate. Exemplary DXS polypeptides include polypeptides, fragments of polypeptides, peptides, and fusions polypeptides that have at least one activity of a DXS polypeptide. Standard methods (such as those described herein) can be used to determine whether a polypeptide has DXS polypeptide activity by measuring the ability of the polypeptide to convert pyruvate and D-glyceraldehyde-3-phosphate into 1-deoxy-D-xylulose-5-phosphate *in vitro*, in a cell extract, or *in vivo*. Exemplary DXS nucleic acids include nucleic acids that encode a polypeptide, fragment of a polypeptide, peptide, or fusion polypeptide that has at least one activity of a DXS polypeptide. Exemplary DXS polypeptides and nucleic acids include naturally-occurring polypeptides and nucleic acids from any of the source organisms described herein

as well as mutant polypeptides and nucleic acids derived from any of the source organisms described herein.

Exemplary IDI Polypeptides and Nucleic Acids

[0225] Isopentenyl diphosphate isomerase polypeptides (isopentenyl-diphosphate delta-isomerase or IDI) catalzyes the interconversion of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP) (*e.g.*, converting IPP into DMAPP and/or converting DMAPP into IPP). Exemplary IDI polypeptides include polypeptides, fragments of polypeptides, peptides, and fusions polypeptides that have at least one activity of an IDI polypeptide. Standard methods (such as those described herein) can be used to determine whether a polypeptide has IDI polypeptide activity by measuring the ability of the polypeptide to interconvert IPP and DMAPP *in vitro*, in a cell extract, or *in vivo*. Exemplary IDI nucleic acids include nucleic acids that encode a polypeptide, fragment of a polypeptide, peptide, or fusion polypeptide that has at least one activity of an IDI polypeptide. Exemplary IDI polypeptides and nucleic acids include naturally-occurring polypeptides and nucleic acids from any of the source organisms described herein as well as mutant polypeptides and nucleic acids derived from any of the source organisms described herein.

Exemplary MVA Pathway Polypeptides and Nucleic Acids

[0226] Exemplary MVA pathway polypeptides include acetyl-CoA acetyltransferase (AA-CoA thiolase) polypeptides, 3-hydroxy-3-methylglutaryl-CoA synthase (HMG-CoA synthase) polypeptides, 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase) polypeptides, mevalonate kinase (MVK) polypeptides, phosphomevalonate kinase (PMK) polypeptides, diphosphomevalonte decarboxylase (MVD) polypeptides, IDI polypeptides, and polypeptides (*e.g.*, fusion polypeptides) having an activity of two or more MVA pathway polypeptides. In particular, MVA pathway polypeptides include polypeptides, fragments of polypeptides, peptides, and fusions polypeptides that have at least one activity of an MVA pathway polypeptide. Exemplary MVA pathway nucleic acids include nucleic acids that encode a polypeptide, fragment of a polypeptide, peptide, or fusion polypeptide that has at least one activity of an MVA pathway polypeptide. Exemplary MVA pathway polypeptides and nucleic acids include naturally-occurring polypeptides and nucleic acids from any of the source organisms described herein as well as mutant polypeptides and nucleic acids derived from any of the source organisms described herein.

[0227] In particular, acetyl-CoA acetyltransferase polypeptides (AA-CoA thiolase or AACT) convert two molecules of acetyl-CoA into acetoacetyl-CoA. Standard methods (such as those described herein) can be used to determine whether a polypeptide has AA-CoA thiolase polypeptide activity by measuring the ability of the polypeptide to convert two molecules of acetyl-CoA into acetoacetyl-CoA *in vitro*, in a cell extract, or *in vivo*.

[0228] 3-hydroxy-3-methylglutaryl-CoA synthase (HMG-CoA synthase or HMGS) polypeptides convert acetoacetyl-CoA into 3-hydroxy-3-methylglutaryl-CoA. Standard methods (such as those described herein) can be used to determine whether a polypeptide has HMG-CoA synthase polypeptide activity by measuring the ability of the polypeptide to convert acetoacetyl-CoA into 3-hydroxy-3-methylglutaryl-CoA *in vitro*, in a cell extract, or *in vivo*.

[0229] 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase or HMGR) polypeptides convert 3-hydroxy-3-methylglutaryl-CoA into mevalonate. Standard methods (such as those described herein) can be used to determine whether a polypeptide has HMG-CoA reductase polypeptide activity by measuring the ability of the polypeptide to convert 3-hydroxy-3-methylglutaryl-CoA into mevalonate *in vitro*, in a cell extract, or *in vivo*.

[0230] Mevalonate kinase (MVK) polypeptides phosphorylates mevalonate to form mevalonate-5-phosphate. Standard methods (such as those described herein) can be used to determine whether a polypeptide has MVK polypeptide activity by measuring the ability of the polypeptide to convert mevalonate into mevalonate-5-phosphate *in vitro*, in a cell extract, or *in vivo*.

[0231] Phosphomevalonate kinase (PMK) polypeptides phosphorylates mevalonate-5-phosphate to form mevalonate-5-diphosphate. Standard methods (such as those described herein) can be used to determine whether a polypeptide has PMK polypeptide activity by measuring the ability of the polypeptide to convert mevalonate-5-phosphate into mevalonate-5-diphosphate *in vitro*, in a cell extract, or *in vivo*.

[0232] Diphosphomevalonte decarboxylase (MVD or DPMDC) polypeptides convert mevalonate-5-diphosphate into isopentenyl diphosphate polypeptides (IPP). Standard methods (such as those described herein) can be used to determine whether a polypeptide has MVD polypeptide activity by measuring the ability of the polypeptide to convert mevalonate-5-diphosphate into IPP *in vitro*, in a cell extract, or *in vivo*.

Exemplary Methods for Isolating Nucleic Acids

[0233] Isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids can be isolated using standard methods. Methods of obtaining desired nucleic acids from a source organism of interest (such as a bacterial genome) are common and well known in the art of molecular biology (*see*, for example, WO 2004/033646 and references cited therein, which are each hereby incorporated by reference in their entireties, particularly with respect to the isolation of nucleic acids of interest). For example, if the sequence of the nucleic acid is known (such as any of the known nucleic acids described herein), suitable genomic libraries may be created by restriction endonuclease digestion and may be screened with probes complementary to the desired nucleic acid sequence. Once the sequence is isolated, the DNA may be amplified using standard primer directed amplification methods such as polymerase chain reaction (PCR) (U.S. Patent No. 4,683,202, which is incorporated by reference in its entirety, particularly with respect to PCR methods) to obtain amounts of DNA suitable for transformation using appropriate vectors. Alternatively, isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids (such as any isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids with a known nucleic acid sequence) can be chemically synthesized using standard methods.

[0234] Additional isoprene synthase, DXS, IDI, or MVA pathway polypeptides and nucleic acids that may be suitable for use in the compositions and methods described herein can be identified using standard methods. For example, cosmid libraries of the chromosomal DNA of organisms known to produce isoprene naturally can be constructed in organisms such as *E. coli*, and then screened for isoprene production. Additional methods for obtaining isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids include screening a metagenomic library by assay (such as the headspace assay described herein) or by PCR using primers directed against nucleotides encoding for a length of conserved amino acids (for example, at least 3 conserved amino acids). Conserved amino acids can be identified by aligning amino acid sequences of known isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides. Conserved amino acids for isoprene synthase polypeptides can be identified based on aligned sequences of known isoprene synthase polypeptides. An organism found to produce isoprene naturally can be subjected to standard protein purification methods (which are well known in the art) and the resulting purified polypeptide can be sequenced using standard methods. Other methods are found in the literature (See, e.g., Julsing et al., Applied. Microbiol. Biotechnol. 75: 1377-84, 2007; and Withers et al., Appl Environ Microbiol. 73:6277-83, 2007, which are each hereby incorporated by reference in their entireties, particularly with respect to identification of nucleic acids involved in the synthesis of isoprene).

[0235] Additionally, standard sequence alignment and/or structure prediction programs can be used to identify additional DXS, IDI, or MVA pathway polypeptides and nucleic acids based on the similarity of their primary and/or predicted polypeptide secondary structure with that of known DXS, IDI, or MVA pathway polypeptides and nucleic acids. Standard databases such as the swissprot-trembl database (world-wide web at "expasy.org", Swiss Institute of Bioinformatics Swiss-Prot group CMU - 1 rue Michel Servet CH-1211 Geneva 4, Switzerland) can also be used to identify isoprene synthase, DXS, IDI, or MVA pathway polypeptides and nucleic acids. The secondary and/or tertiary structure of an isoprene synthase, DXS, IDI, or MVA pathway polypeptide can be predicted using the default settings of standard structure prediction programs, such as PredictProtein (Rost et al., The PredictProtein Server. Nucleic Acids Research 32(Web Server issue):W321-W326, 2004). Alternatively, the actual secondary and/or tertiary structure of an isoprene synthase, DXS, IDI, or MVA pathway polypeptide can be determined using standard methods. Additional isoprene synthase, DXS, IDI, or MVA pathway nucleic acids can also be identified by hybridization to probes generated from known isoprene synthase, DXS, IDI, or MVA pathway nucleic acids.

Exemplary Promoters and Vectors

[0236] Any of the isoprene synthase, DXS, IDI, or MVA pathway nucleic acid described herein can be included in one or more vectors. Accordingly, the invention also features vectors with one more nucleic acids encoding any of the isoprene synthase, DXS, IDI, or MVA pathway polypeptides that are described herein. As used herein, a "vector" means a construct that is capable of delivering, and desirably expressing one or more nucleic acids of interest in a host cell. Examples of vectors include, but are not limited to, plasmids, viral vectors, DNA or RNA expression vectors, cosmids, and phage vectors. In some embodiments, the vector contains a nucleic acid under the control of an expression control sequence.

[0237] As used herein, an "expression control sequence" means a nucleic acid sequence that directs transcription of a nucleic acid of interest. An expression control sequence can be a promoter, such as a constitutive or an inducible promoter, or an enhancer. An "inducible promoter" is a promoter that is active under environmental or developmental regulation. The expression control sequence is operably linked to the nucleic acid segment to be transcribed.

[0238] In some embodiments, the vector contains a selective marker. The term "selective marker" refers to a nucleic acid capable of expression in a host cell that allows for ease of

selection of those host cells containing an introduced nucleic acid or vector. Examples of selectable markers include, but are not limited to, antibiotic resistance nucleic acids (*e.g.*, kanamycin, ampicillin, carbenicillin, gentamicin, hygromycin, phleomycin, bleomycin, neomycin, or chloramphenicol) and/or nucleic acids that confer a metabolic advantage, such as a nutritional advantage on the host cell. In some embodiments, an isoprene synthase, DXS, IDI, or MVA pathway nucleic acid integrates into a chromosome of the cells without a selective marker.

[0239] Suitable vectors are those that are compatible with the host cell employed. Suitable vectors can be derived, for example, from a bacterium, a virus (such as bacteriophage T7 or a M-13 derived phage), a cosmid, a yeast, or a plant. Protocols for obtaining and using such vectors are known in the art (*See, e.g.,* Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, 1989, which is hereby incorporated by reference in its entirety, particularly with respect to the use of vectors).

[0240] Promoters are well known in the art. Any promoter that functions in the host cell can be used for expression of an isoprene synthase, DXS, IDI, or MVA pathway nucleic acid in the host cell. Initiation control regions or promoters, which are useful to drive expression of isoprene synthase, DXS, IDI, or MVA pathway nucleic acids in various host cells are numerous and familiar to those skilled in the art (*see*, for example, WO 2004/033646 and references cited therein, which are each hereby incorporated by reference in their entireties, particularly with respect to vectors for the expression of nucleic acids of interest). Virtually any promoter capable of driving these nucleic acids is suitable for the present invention including, but not limited to lac, trp, λP_L, λP_R, T7, tac, and trc (useful for expression in *E. coli*).

[0241] In some embodiments, a glucose isomerase promoter is used (*see*, for example, U.S. Patent No. 7,132,527 and references cited therein, which are each hereby incorporated by reference in their entireties, particularly with respect promoters and plasmid systems for expressing polypeptides of interest). Reported glucose isomerase promoter mutants can be used to vary the level of expression of the polypeptide encoded by a nucleic acid operably linked to the glucose isomerase promoter (U.S. Patent No. 7,132,527). In various embodiments, the glucose isomerase promoter is contained in a low, medium, or high copy plasmid (U.S. Patent No. 7,132,527).

[0242] In various embodiments, an isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acid is contained in a low copy plasmid (*e.g.*, a plasmid that is maintained at about 1

to about 4 copies per cell), medium copy plasmid (*e.g.*, a plasmid that is maintained at about 10 to about 15 copies per cell), or high copy plasmid (*e.g.*, a plasmid that is maintained at about 50 or more copies per cell). In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is operably linked to a T7 promoter. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid operably linked to a T7 promoter is contained in a medium or high copy plasmid. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is operably linked to a Trc promoter. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid operably linked to a Trc promoter is contained in a medium or high copy plasmid. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is operably linked to a Lac promoter. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid operably linked to a Lac promoter is contained in a low copy plasmid. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is operably linked to an endogenous promoter, such as an endogenous *Escherichia, Panteoa, Bacillus, Yarrowia, Streptomyces,* or *Trichoderma* promoter or an endogenous alkaline serine protease, isoprene synthase, DXS, IDI, or MVA pathway promoter. In some embodiments, the heterologous or extra endogenous isoprene synthase, DXS, IDI, or MVA pathway nucleic acid operably linked to an endogenous promoter is contained in a high copy plasmid. In some embodiments, the vector is a replicating plasmid that does not integrate into a chromosome in the cells. In some embodiments part or all of the vector integrates into a chromosome in the cells.

[0243] In some embodiments, the expression vector also includes a termination sequence. Termination control regions may also be derived from various genes native to the host cell. In some embodiments, the termination sequence and the promoter sequence are derived from the same source. In another embodiment, the termination sequence is endogenous to the host cell.

[0244] In some embodiments, the promoter, coding, region, and terminator all originate from the isoprene synthase, DXS, IDI, or MVA pathway nucleic acid to be expressed. In some embodiments, the coding region for an isoprene synthase, DXS, IDI, or MVA pathway nucleic acid is inserted into a general-purpose expression vector such that it is under the transcriptional control of the expression construct promoter and terminator sequences. In

some embodiments, genes or part thereof are inserted downstream of the strong *cbh*1 promoter.

[0245] An isoprene synthase, DXS, IDI, or MVA pathway nucleic acid can be incorporated into a vector, such as an expression vector, using standard techniques (Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, 1982, which is hereby incorporated by reference in its entirety, particularly with respect to the screening of appropriate DNA sequences and the construction of vectors). Methods used to ligate the DNA construct comprising a nucleic acid of interest (such as an isoprene synthase, DXS, IDI, or MVA pathway nucleic acid), a promoter, a terminator, and other sequences and to insert them into a suitable vector are well known in the art. For example, restriction enzymes can be used to cleave the isoprene synthase, DXS, IDI, or MVA pathway nucleic acid and the vector. Then, the compatible ends of the cleaved isoprene synthase, DXS, IDI, or MVA pathway nucleic acid and the cleaved vector can be ligated. Linking is generally accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide linkers are used in accordance with conventional practice (*see*, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, 1989, and Bennett and Lasure, More Gene Manipulations in Fungi, Academic Press, San Diego, pp 70–76, 1991, which are each hereby incorporated by reference in their entireties, particularly with respect to oligonucleotide linkers). Additionally, vectors can be constructed using known recombination techniques (*e.g.*, Invitrogen Life Technologies, Gateway Technology).

[0246] In some embodiments, it may be desirable to over-express isoprene synthase, DXS, IDI, or MVA pathway nucleic acids at levels far higher than currently found in naturally-occurring cells. This result may be accomplished by the selective cloning of the nucleic acids encoding those polypeptides into multicopy plasmids or placing those nucleic acids under a strong inducible or constitutive promoter. Methods for over-expressing desired polypeptides are common and well known in the art of molecular biology and examples may be found in Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, 1989, which is hereby incorporated by reference in its entirety, particularly with respect to cloning techniques.

[0247] The following resources include descriptions of additional general methodology useful in accordance with the invention: Kreigler, Gene Transfer and Expression; A Laboratory Manual, 1990; and Ausubel *et al.*, Eds. Current Protocols in Molecular Biology,

1994, which are each hereby incorporated by reference in their entireties, particularly with respect to molecular biology and cloning techniques.

Exemplary Source Organisms

[0248] Isoprene synthase, DXS, IDI, or MVA pathway nucleic acids (and their encoded polypeptides) can be obtained from any organism that naturally contains isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids. As noted above, isoprene is formed naturally by a variety of organisms, such as bacteria, yeast, plants, and animals. Organisms contain the MVA pathway, DXP pathway, or both the MVA and DXP pathways for producing isoprene (Figure 15). Thus, DXS nucleic acids can be obtained, *e.g.*, from any organism that contains the DXP pathway or contains both the MVA and DXP pathways. IDI and isoprene synthase nucleic acids can be obtained, *e.g.*, from any organism that contains the MVA pathway, DXP pathway, or both the MVA and DXP pathways. MVA pathway nucleic acids can be obtained, *e.g.*, from any organism that contains the MVA pathway or contains both the MVA and DXP pathways.

[0249] In some embodiments, the nucleic acid sequence of the isoprene synthase, DXS, IDI, or MVA pathway nucleic is identical to the sequence of a nucleic acid that is produced by any of the following organisms in nature. In some embodiments, the amino acid sequence of the isoprene synthase, DXS, IDI, or MVA pathway polypeptide is identical to the sequence of a polypeptide that is produced by any of the following organisms in nature. In some embodiments, the isoprene synthase, DXS, IDI, or MVA pathway nucleic acid or polypeptide is a mutant nucleic acid or polypeptide derived from any of the organisms described herein. As used herein, "derived from" refers to the source of the nucleic acid or polypeptide into which one or more mutations is introduced. For example, a polypeptide that is "derived from a plant polypeptide" refers to polypeptide of interest that results from introducing one or more mutations into the sequence of a wild-type (*i.e.*, a sequence occurring in nature) plant polypeptide.

[0250] In some embodiments, the source organism is a bacterium, such as strains of *Escherichia* (e.g., *E. coli*), or strains of *Bacillus* (e.g., *B. subtilis*).

[0251] As used herein, "the genus *Escherichia*" includes all species within the genus "*Escherichia*," as known to those of skill in the art, including but not limited to *E. coli, E. adecarboxylata, E. albertii, E. blattae, E. fergusonii, E. hermannii, E. senegalensis, and E. vulneris.* The genus "*Escherichia*" is defined as Gram-negative, non-spore forming,

facultatively anaerobic, rod-shaped bacteria are classified as members of the Family *Enterobacteriaceae*, Order *Enterobacteriales*, Class *Gamma Proteobacteria*.

[0252] As used herein, "the genus *Bacillus*" includes all species within the genus "*Bacillus*," as known to those of skill in the art, including but not limited to *B. subtilis*, *B. licheniformis*, *B. lentus*, *B. brevis*, *B. stearothermophilus*, *B. alkalophilus*, *B. amyloliquefaciens*, *B. clausii*, *B. halodurans*, *B. megaterium*, *B. coagulans*, *B. circulans*, *B. lautus*, and *B. thuringiensis*. It is recognized that the genus *Bacillus* continues to undergo taxonomical reorganization. Thus, it is intended that the genus include species that have been reclassified, including but not limited to such organisms as *B. stearothermophilus*, which is now named "*Geobacillus stearothermophilus*." The production of resistant endospores in the presence of oxygen is considered the defining feature of the genus *Bacillus*, although this characteristic also applies to the recently named *Alicyclobacillus*, *Amphibacillus*, *Aneurinibacillus*, *Anoxybacillus*, *Brevibacillus*, *Filobacillus*, *Gracilibacillus*, *Halobacillus*, *Paenibacillus*, *Salibacillus*, *Thermobacillus*, *Ureibacillus*, and *Virgibacillus*.

Exemplary Host Cells

[0253] A variety of host cells can be used to express isoprene synthase, DXS, IDI, and/or MVA pathway polypeptides and to produce isoprene in the methods of the claimed invention. Exemplary host cells include cells from any of the organisms listed in the prior section under the heading "*Exemplary Source Organisms*." The host cell may be a cell that naturally produces isoprene or a cell that does not naturally produce isoprene. In some embodiments, the host cell naturally produces isoprene using the DXP pathway, and an isoprene synthase, DXS, and/or IDI nucleic acid is added to enhance production of isoprene using this pathway. In some embodiments, the host cell naturally produces isoprene using the MVA pathway, and an isoprene synthase and/or one or more MVA pathway nucleic acids are added to enhance production of isoprene using this pathway. In some embodiments, the host cell naturally produces isoprene using the DXP pathway and one or more MVA pathway nucleic acids are added to produce isoprene using part or all of the MVA pathway as well as the DXP pathway. In some embodiments, the host cell naturally produces isoprene using both the DXP and MVA pathways and one or more isoprene synthase, DXS, IDI, or MVA pathway nucleic acids are added to enhance production of isoprene by one or both of these pathways.

Exemplary Transformation Methods

[0254] Isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acids or vectors containing them can be inserted into a host cell (*e.g.*, a bacterial cell) using standard techniques for expression of the encoded isoprene synthase, DXS, IDI, and/or MVA pathway polypeptide. Introduction of a DNA construct or vector into a host cell can be performed using techniques such as transformation, electroporation, nuclear microinjection, transduction, transfection (*e.g.*, lipofection mediated or DEAE-Dextrin mediated transfection or transfection using a recombinant phage virus), incubation with calcium phosphate DNA precipitate, high velocity bombardment with DNA-coated microprojectiles, and protoplast fusion. General transformation techniques are known in the art (*see*, *e.g.*, Current Protocols in Molecular Biology (F. M. Ausubel *et al.* (eds) Chapter 9, 1987; Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, 1989; and Campbell *et al.*, *Curr Genet,* 16:53-56, 1989, which are each hereby incorporated by reference in their entireties, particularly with respect to transformation methods). The introduced nucleic acids may be integrated into chromosomal DNA or maintained as extrachromosomal replicating sequences.

Exemplary Cell Culture Media

[0255] The invention also includes a cell or a population of cells in culture that produce isoprene. By "cells in culture" is meant two or more cells in a solution (*e.g.*, a cell medium) that allows the cells to undergo one or more cell divisions. "Cells in culture" do not include plant cells that are part of a living, multicellular plant containing cells that have differentiated into plant tissues. In various embodiments, the cell culture includes at least or about 10, 20, 50, 100, 200, 500, 1,000, 5,000, 10,000 or more cells.

[0256] Any carbon source can be used to cultivate the host cells. The term "carbon source" refers to one or more carbon-containing compounds capable of being metabolized by a host cell or organism. For example, the cell medium used to cultivate the host cells may include any carbon source suitable for maintaining the viability or growing the host cells.

[0257] In some embodiments, the carbon source is a carbohydrate (such as monosaccharide, disaccharide, oligosaccharide, or polysaccharides), invert sugar (*e.g.*, enzymatically treated sucrose syrup), glycerol, glycerine (*e.g.*, a glycerine byproduct of a biodiesel or soap-making process), dihydroxyacetone, one-carbon source, fatty acid (*e.g.*, a saturated fatty acid, unsaturated fatty acid, or polyunsaturated fatty acid), lipid, phospholipid, glycerolipid, monoglyceride, diglyceride, triglyceride, polypeptide (*e.g.,* a microbial or plant protein or peptide), renewable carbon source (*e.g.*, a biomass carbon source such as a hydrolyzed biomass carbon source; beet sugar or cane sugar molasses), yeast extract,

component from a yeast extract, polymer, acid, alcohol, aldehyde, ketone, amino acid, succinate, lactate, acetate, ethanol, or any combination of two or more of the foregoing. In some embodiments, the carbon source is a product of photosynthesis, including, but not limited to, glucose.

[0258] Exemplary monosaccharides include glucose and fructose; exemplary oligosaccharides include lactose and sucrose, and exemplary polysaccharides include starch and cellulose. Exemplary carbohydrates include C6 sugars (*e.g.*, fructose, mannose, galactose, or glucose) and C5 sugars (*e.g.*, xylose or arabinose). In some embodiments, the cell medium includes a carbohydrate as well as a carbon source other than a carbohydrate (*e.g.*, glycerol, glycerine, dihydroxyacetone, one-carbon source, fatty acid, lipid, phospholipid, glycerolipid, monoglyceride, diglyceride, triglyceride, renewable carbon source, or a component from a yeast extract). In some embodiments, the cell medium includes a carbohydrate as well as a polypeptide (*e.g.*, a microbial or plant protein or peptide). In some embodiments, the microbial polypeptide is a polypeptide from yeast or bacteria. In some embodiments, the plant polypeptide is a polypeptide from soy, corn, canola, jatropha, palm, peanut, sunflower, coconut, mustard, rapeseed, cottonseed, palm kernel, olive, safflower, sesame, or linseed.

[0259] In some embodiments, the concentration of the carbohydrate is at least or about 5 grams per liter of broth (g/L, wherein the volume of broth includes both the volume of the cell medium and the volume of the cells), such as at least or about 10, 15, 20, 30, 40, 50, 60, 80, 100, 150, 200, 300, 400, or more g/L. In some embodiments, the concentration of the carbohydrate is between about 50 and about 400 g/L, such as between about 100 and about 360 g/L, between about 120 and about 360 g/L, or between about 200 and about 300 g/L. In some embodiments, this concentration of carbohydrate includes the total amount of carbohydrate that is added before and/or during the culturing of the host cells.

[0260] Exemplary lipids are any substance containing one or more fatty acids that are C4 and above fatty acids that are saturated, unsaturated, or branched.

[0261] Exemplary fatty acids include compounds of the formula R-COOH, where "R" is a hydrocarbon. Exemplary unsaturated fatty acids include compounds where "R" includes at least one carbon-carbon double bond. Exemplary unsaturated fatty acids include, but are not limited to, oleic acid, vaccenic acid, linoleic acid, palmitelaidic acid, and arachidonic acid. Exemplary polyunsaturated fatty acids include compounds where "R" includes a plurality of carbon-carbon double bonds. Exemplary saturated fatty acids include compounds where "R" is a saturated aliphatic group. In some embodiments, the carbon source includes one or

more C_{12}-C_{22} fatty acids, such as a C_{12} saturated fatty acid, a C_{14} saturated fatty acid, a C_{16} saturated fatty acid, a C_{18} saturated fatty acid, a C_{20} saturated fatty acid, or a C_{22} saturated fatty acid. In an exemplary embodiment, the fatty acid is palmitic acid. In some embodiments, the carbon source is a salt of a fatty acid (*e.g.*, an unsaturated fatty acid), a derivative of a fatty acid (*e.g.*, an unsaturated fatty acid), or a salt of a derivative of fatty acid (*e.g.*, an unsaturated fatty acid). Suitable salts include, but are not limited to, lithium salts, potassium salts, sodium salts, and the like. Di- and triglycerols are fatty acid esters of glycerol.

[0262] In some embodiments, the concentration of the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride is at least or about 1 gram per liter of broth (g/L, wherein the volume of broth includes both the volume of the cell medium and the volume of the cells), such as at least or about 5, 10, 15, 20, 30, 40, 50, 60, 80, 100, 150, 200, 300, 400, or more g/L. In some embodiments, the concentration of the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride is between about 10 and about 400 g/L, such as between about 25 and about 300 g/L, between about 60 and about 180 g/L, or between about 75 and about 150 g/L. In some embodiments, the concentration includes the total amount of the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride that is added before and/or during the culturing of the host cells. In some embodiments, the carbon source includes both (i) a lipid, fatty acid, monoglyceride, diglyceride, or triglyceride and (ii) a carbohydrate, such as glucose. In some embodiments, the ratio of the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride to the carbohydrate is about 1:1 on a carbon basis (*i.e.*, one carbon in the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride per carbohydrate carbon). In particular embodiments, the amount of the lipid, fatty acid, monoglyceride, diglyceride, or triglyceride is between about 60 and 180 g/L, and the amount of the carbohydrate is between about 120 and 360 g/L.

[0263] Exemplary microbial polypeptide carbon sources include one or more polypeptides from yeast or bacteria. Exemplary plant polypeptide carbon sources include one or more polypeptides from soy, corn, canola, jatropha, palm, peanut, sunflower, coconut, mustard, rapeseed, cottonseed, palm kernel, olive, safflower, sesame, or linseed.

[0264] Exemplary renewable carbon sources include cheese whey permeate, cornsteep liquor, sugar beet molasses, barley malt, and components from any of the foregoing. Exemplary renewable carbon sources also include glucose, hexose, pentose and xylose present in biomass, such as corn, switchgrass, sugar cane, cell waste of fermentation processes, and protein by-product from the milling of soy, corn, or wheat. In some embodiments, the biomass carbon source is a lignocellulosic, hemicellulosic, or cellulosic

material such as, but are not limited to, a grass, wheat, wheat straw, bagasse, sugar cane bagasse, soft wood pulp, corn, corn cob or husk, corn kernel, fiber from corn kernels, corn stover, switch grass, rice hull product, or a by-product from wet or dry milling of grains (*e.g.*, corn, sorghum, rye, triticate, barley, wheat, and/or distillers grains). Exemplary cellulosic materials include wood, paper and pulp waste, herbaceous plants, and fruit pulp. In some embodiments, the carbon source includes any plant part, such as stems, grains, roots, or tubers. In some embodiments, all or part of any of the following plants are used as a carbon source: corn, wheat, rye, sorghum, triticate, rice, millet, barley, cassava, legumes, such as beans and peas, potatoes, sweet potatoes, bananas, sugarcane, and/or tapioca. In some embodiments, the carbon source is a biomass hydrolysate, such as a biomass hydrolysate that includes both xylose and glucose or that includes both sucrose and glucose.

[0265] In some embodiments, the renewable carbon source (such as biomass) is pretreated before it is added to the cell culture medium. In some embodiments, the pretreatment includes enzymatic pretreatment, chemical pretreatment, or a combination of both enzymatic and chemical pretreatment (*see*, for example, Farzaneh *et al.*, *Bioresource Technology* 96 (18): 2014-2018, 2005; U.S. Patent No. 6,176,176; U.S. Patent No. 6,106,888; which are each hereby incorporated by reference in their entireties, particularly with respect to the pretreatment of renewable carbon sources). In some embodiments, the renewable carbon source is partially or completely hydrolyzed before it is added to the cell culture medium.

[0266] In some embodiments, the renewable carbon source (such as corn stover) undergoes ammonia fiber expansion (AFEX) pretreatment before it is added to the cell culture medium (*see*, for example, Farzaneh *et al.*, *Bioresource Technology* 96 (18): 2014-2018, 2005). During AFEX pretreatment, a renewable carbon source is treated with liquid anhydrous ammonia at moderate temperatures (such as about 60 to about 100 °C) and high pressure (such as about 250 to about 300 psi) for about 5 minutes. Then, the pressure is rapidly released. In this process, the combined chemical and physical effects of lignin solubilization, hemicellulose hydrolysis, cellulose decrystallization, and increased surface area enables near complete enzymatic conversion of cellulose and hemicellulose to fermentable sugars. AFEX pretreatment has the advantage that nearly all of the ammonia can be recovered and reused, while the remaining serves as nitrogen source for microbes in downstream processes. Also, a wash stream is not required for AFEX pretreatment. Thus, dry matter recovery following the AFEX treatment is essentially 100%. AFEX is basically a dry-to-dry process. The treated renewable carbon source is stable for long periods and can be fed at very high solid loadings in enzymatic hydrolysis or fermentation processes. Cellulose and hemicellulose are well preserved in the AFEX process,

with little or no degradation. There is no need for neutralization prior to the enzymatic hydrolysis of a renewable carbon source that has undergone AFEX pretreatment. Enzymatic hydrolysis of AFEX-treated carbon sources produces clean sugar streams for subsequent fermentation use.

[0267] In some embodiments, the concentration of the carbon source (*e.g.*, a renewable carbon source) is equivalent to at least or about 0.1, 0.5, 1, 1.5 2, 3, 4, 5, 10, 15, 20, 30, 40, or 50% glucose (w/v). The equivalent amount of glucose can be determined by using standard HPLC methods with glucose as a reference to measure the amount of glucose generated from the carbon source. In some embodiments, the concentration of the carbon source (*e.g.*, a renewable carbon source) is equivalent to between about 0.1 and about 20% glucose, such as between about 0.1 and about 10% glucose, between about 0.5 and about 10% glucose, between about 1 and about 10% glucose, between about 1 and about 5% glucose, or between about 1 and about 2% glucose.

[0268] In some embodiments, the carbon source includes yeast extract or one or more components of yeast extract. In some embodiments, the concentration of yeast extract is at least 1 gram of yeast extract per liter of broth (g/L, wherein the volume of broth includes both the volume of the cell medium and the volume of the cells), such at least or about 5, 10, 15, 20, 30, 40, 50, 60, 80, 100, 150, 200, 300, or more g/L. In some embodiments, the concentration of yeast extract is between about 1 and about 300 g/L, such as between about 1 and about 200 g/L, between about 5 and about 200 g/L, between about 5 and about 100 g/L, or between about 5 and about 60 g/L. In some embodiments, the concentration includes the total amount of yeast extract that is added before and/or during the culturing of the host cells. In some embodiments, the carbon source includes both yeast extract (or one or more components thereof) and another carbon source, such as glucose. In some embodiments, the ratio of yeast extract to the other carbon source is about 1:5, about 1:10, or about 1:20 (w/w).

[0269] Additionally the carbon source may also be one-carbon substrates such as carbon dioxide, or methanol. Glycerol production from single carbon sources (*e.g.*, methanol, formaldehyde, or formate) has been reported in methylotrophic yeasts (Yamada *et al.*, *Agric. Biol. Chem.,* 53(2) 541-543, 1989, which is hereby incorporated by reference in its entirety, particularly with respect to carbon sources) and in bacteria (Hunter *et. al.*, *Biochemistry,* 24, 4148-4155, 1985, which is hereby incorporated by reference in its entirety, particularly with respect to carbon sources). These organisms can assimilate single carbon compounds, ranging in oxidation state from methane to formate, and produce glycerol. The pathway of carbon assimilation can be through ribulose monophosphate, through serine, or through xylulose-

momophosphate (Gottschalk, Bacterial Metabolism, Second Edition, Springer-Verlag: New York, 1986, which is hereby incorporated by reference in its entirety, particularly with respect to carbon sources). The ribulose monophosphate pathway involves the condensation of formate with ribulose-5-phosphate to form a six carbon sugar that becomes fructose and eventually the three carbon product glyceraldehyde-3-phosphate. Likewise, the serine pathway assimilates the one-carbon compound into the glycolytic pathway via methylenetetrahydrofolate.

[0270] In addition to one and two carbon substrates, methylotrophic organisms are also known to utilize a number of other carbon containing compounds such as methylamine, glucosamine and a variety of amino acids for metabolic activity. For example, methylotrophic yeast are known to utilize the carbon from methylamine to form trehalose or glycerol (Bellion *et al.*, *Microb. Growth Cl Compd.,* [Int. Symp.], 7th ed., 415-32. Editors: Murrell *et al.*, Publisher: Intercept, Andover, UK, 1993, which is hereby incorporated by reference in its entirety, particularly with respect to carbon sources). Similarly, various species of *Candida* metabolize alanine or oleic acid (Sulter *et al.*, *Arch. Microbiol.* 153(5), 485-9, 1990, which is hereby incorporated by reference in its entirety, particularly with respect to carbon sources).

[0271] In some embodiments, cells are cultured in a standard medium containing physiological salts and nutrients (*see*, *e.g.*, Pourquie, J. *et al.*, Biochemistry and Genetics of Cellulose Degradation, *eds.* Aubert *et al.*, Academic Press, pp. 71-86, 1988; and Ilmen *et al.*, *Appl. Environ. Microbiol.* 63:1298-1306, 1997, hereby incorporated by reference, particularly with respect to cell media). Exemplary growth media are common commercially prepared media such as Luria Bertani (LB) broth, Sabouraud Dextrose (SD) broth, or Yeast medium (YM) broth. Other defined or synthetic growth media may also be used, and the appropriate medium for growth of particular host cells are known by someone skilled in the art of microbiology or fermentation science.

[0272] In addition to an appropriate carbon source, the cell medium desirably contains suitable minerals, salts, cofactors, buffers, and other components known to those skilled in the art suitable for the growth of the cultures or the enhancement of isoprene production (*see*, for example, WO 2004/033646 and references cited therein and WO 96/35796 and references cited therein, which are each hereby incorporated by reference in their entireties, particularly with respect cell medias and cell culture conditions). In some embodiments where an isoprene synthase, DXS, IDI, and/or MVA pathway nucleic acid is under the control of an inducible promoter, the inducing agent (*e.g.*, a sugar, metal salt or antimicrobial), is desirably added to the medium at a concentration effective to induce expression of an isoprene

synthase, DXS, IDI, and/or MVA pathway polypeptide. In some embodiments, cell medium has an antibiotic (such as kanamycin) that corresponds to the antibiotic resistance nucleic acid (such as a kanamycin resistance nucleic acid) on a vector that has one or more DXS, IDI, or MVA pathway nucleic acids.

Exemplary Production of Isoprene

[0273] In some embodiments, the cells are cultured in a culture medium under conditions permitting the production of isoprene by the cells. In some embodiments, the cells in culture produce isoprene at greater than or about 1, 10, 25, 50, 100, 150, 200, 250, 300, 400, 500, 600, 700, 800, 900, 1,000, 1,250, 1,500, 1,750, 2,000, 2,500, 3,000, 4,000, 5,000, or more nmole of isoprene/gram of cells for the wet weight of the cells/hour (nmole/g_{wcm}/hr). In some embodiments, the amount of isoprene is between about 2 to about 5,000 nmole/g_{wcm}/hr, such as between about 2 to about 100 nmole/g_{wcm}/hr, about 100 to about 500 nmole/g_{wcm}/hr, about 150 to about 500 nmole/g_{wcm} /hr, about 500 to about 1,000 nmole/g_{wcm}/hr, about 1,000 to about 2,000 nmole/g_{wcm}/hr, or about 2,000 to about 5,000 nmole/g_{wcm}/hr. The amount of isoprene in units of nmole/g_{wcm}/hr can be measured as disclosed in U.S. Patent No. 5,849,970, which is hereby incorporated by reference in its entirety, particularly with respect to the measurement of isoprene production. For example, two mL of headspace (*e.g.*, headspace from a culture such as 2 mL of culture cultured in sealed vials at 32 °C with shaking at 200 rpm for approximately 3 hours) are analyzed for isoprene using a standard gas chromatography system, such as a system operated isothermally (85 °C) with an n-octane/porasil C column (Alltech Associates, Inc., Deerfield, IL) and coupled to a RGD2 mercuric oxide reduction gas detector (Trace Analytical, Menlo Park, CA) (*see*, for example, Greenberg et al, *Atmos. Environ.* 27A: 2689-2692, 1993; Silver *et al.*, *Plant Physiol.* 97:1588-1591, 1991, which are each hereby incorporated by reference in their entireties, particularly with respect to the measurement of isoprene production). The gas chromatography area units are converted to nmol isoprene via a standard isoprene concentration calibration curve. In some embodiments, the value for the grams of cells for the wet weight of the cells is calculated by obtaining the A_{600} value for a sample of the cell culture, and then converting the A_{600} value to grams of cells based on a calibration curve of wet weights for cell cultures with a known A_{600} value. In some embodiments, the grams of the cells is estimated by assuming that one liter of broth (including cell medium and cells) with an A_{600} value of 1 has a wet cell weight of 1 gram. The value is also divided by the number of hours the culture has been incubating for, such as three hours.

[0274] In some embodiments, the cells in culture produce isoprene at greater than or about 1, 10, 25, 50, 100, 150, 200, 250, 300, 400, 500, 600, 700, 800, 900, 1,000, 1,250, 1,500, 1,750, 2,000, 2,500, 3,000, 4,000, 5,000, 10,000, 100,000, or more ng of isoprene/gram of cells for the wet weight of the cells/hr ($ng/g_{wcm}/h$). In some embodiments, the amount of isoprene is between about 2 to about 5,000 $ng/g_{wcm}/h$, such as between about 2 to about 100 $ng/g_{wcm}/h$, about 100 to about 500 $ng/g_{wcm}/h$, about 500 to about 1,000 $ng/g_{wcm}/h$, about 1,000 to about 2,000 $ng/g_{wcm}/h$, or about 2,000 to about 5,000 $ng/g_{wcm}/h$. The amount of isoprene in $ng/g_{wcm}/h$ can be calculated by multiplying the value for isoprene production in the units of $nmole/g_{wcm}/hr$ discussed above by 68.1 (as described in Equation 5 below).

[0275] In some embodiments, the cells in culture produce a cumulative titer (total amount) of isoprene at greater than or about 1, 10, 25, 50, 100, 150, 200, 250, 300, 400, 500, 600, 700, 800, 900, 1,000, 1,250, 1,500, 1,750, 2,000, 2,500, 3,000, 4,000, 5,000, 10,000, 50,000, 100,000, or more mg of isoprene/L of broth (mg/L_{broth}, wherein the volume of broth includes the volume of the cells and the cell medium). In some embodiments, the amount of isoprene is between about 2 to about 5,000 mg/L_{broth}, such as between about 2 to about 100 mg/L_{broth}, about 100 to about 500 mg/L_{broth}, about 500 to about 1,000 mg/L_{broth}, about 1,000 to about 2,000 mg/L_{broth}, or about 2,000 to about 5,000 mg/L_{broth}. The specific productivity of isoprene in mg of isoprene/L of headspace from shake flask or similar cultures can be measured by taking a 1 ml sample from the cell culture at an OD_{600} value of approximately 1.0, putting it in a 20 mL vial, incubating for 30 minutes, and then measuring the amount of isoprene in the headspace. If the OD_{600} value is not 1.0, then the measurement can be normalized to an OD_{600} value of 1.0 by dividing by the OD_{600} value. The value of mg isoprene/L headspace can be converted to $mg/L_{broth}/hr/OD_{600}$ of culture broth by multiplying by a factor of 38. The value in units of $mg/L_{broth}/hr/OD_{600}$ can be multiplied by the number of hours and the OD_{600} value to obtain the cumulative titer in units of mg of isoprene/L of broth.

[0276] The instantaneous isoprene production rate in $mg/L_{broth}/hr$ in a fermentor can be measured by taking a sample of the fermentor off-gas, analyzing it for the amount of isoprene (in units such as mg of isoprene per L_{gas}), and multiplying this value by the rate at which off-gas is passed though each liter of broth (*e.g.*, at 1 vvm (volume of air/volume of broth/minute) this is 60 L_{gas} per hour). Thus, an off-gas level of 1 mg/L_{gas} corresponds to an instantaneous production rate of 60 $mg/L_{broth}/hr$ at air flow of 1 vvm. If desired, the value in the units $mg/L_{broth}/hr$ can be divided by the OD_{600} value to obtain the specific rate in units of $mg/L_{broth}/hr/OD$. The average value of mg isoprene/L_{gas} can be converted to the total product productivity (grams of isoprene per liter of fermentation broth, mg/L_{broth}) by multiplying this

average off-gas isoprene concentration by the total amount of off-gas sparged per liter of fermentation broth during the fermentation. Thus, an average off-gas isoprene concentration of 0.5 mg/L_{broth}/hr over 10 hours at 1 vvm corresponds to a total product concentration of 300 mg isoprene/L_{broth}.

[0277] In some embodiments, the cells in culture convert greater than or about 0.0015, 0.002, 0.005, 0.01, 0.02, 0.05, 0.1, 0.12, 0.14, 0.16, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.2, 1.4, or 1.6% of the carbon in the cell culture medium into isoprene. In some embodiments, the percent conversion of carbon into isoprene is between about 0.002 to about 1.6%, such as about 0.002 to about 0.005%, about 0.005 to about 0.01%, about 0.01 to about 0.05%, about 0.05 to about 0.15%, 0.15 to about 0.2%, about 0.2 to about 0.3%, about 0.3 to about 0.5%, about 0.5 to about 0.8%, about 0.8 to about 1.0%, or about 1.0 to about 1.6%. The percent conversion of carbon into isoprene (also referred to as "% carbon yield") can be measured by dividing the moles carbon in the isoprene produced by the moles carbon in the carbon source (such as the moles of carbon in batched and fed glucose and yeast extract). This number is multiplied by 100% to give a percentage value (as indicated in Equation 1).

Equation 1

[0278] % Carbon Yield = (moles carbon in isoprene produced)/(moles carbon in carbon source) * 100

[0279] For this calculation, yeast extract can be assumed to contain 50% w/w carbon.

Equation 2

[0280] % Carbon Yield = (39.1 g isoprene * 1/68.1mol/g * 5 C/mol)/[(181221 g glucose * 1/180 mol/g * 6 C/mol) + (17780 g yeast extract * 0.5 * 1/12 mol/g)] * 100 = 0.042%

[0281] One skilled in the art can readily convert the rates of isoprene production or amount of isoprene produced into any other units. Exemplary equations are listed below for interconverting between units.

Units for Rate of Isoprene production (total and specific)

Equation 3

[0282] 1 g isoprene/L_{broth}/hr = 14.7 mmol isoprene/L_{broth}/hr (total volumetric rate)

Equation 4

[0283] 1 nmol isoprene /g_{wcm}/hr = 1 nmol isoprene /L_{broth}/hr/OD_{600} (This conversion assumes that one liter of broth with an OD_{600} value of 1 has a wet cell weight of 1 gram.)

Equation 5

[0284] 1 nmol isoprene/g_{wcm}/hr = 68.1 ng isoprene/g_{wcm}/hr (given the molecular weight of isoprene)

Equation 6

[0285] 1 nmol isoprene/L_{gas} O_2/hr = 90 nmol isoprene/L_{broth}/hr (at an O_2 flow rate of 90 L/hr per L of culture broth)

Equation 7

[0286] 1 μg isoprene/L_{gas} isoprene in off-gas = 60 μg isoprene/L_{broth}/hr at a flow rate of 60 L_{gas} per L_{broth} (1 vvm)

Units for Titer (total and specific)

Equation 8

[0287] 1 nmol isoprene/mg cell protein = 150 nmol isoprene/L_{broth}/OD_{600} (This conversion assumes that one liter of broth with an OD_{600} value of 1 has a total cell protein of approximately 150 mg) (specific productivity)

Equation 9

[0288] 1 g isoprene/L_{broth} = 14.7 mmol isoprene/L_{broth} (total titer)

[0289] If desired, Equation 10 can be used to convert any of the units that include the wet weight of the cells into the corresponding units that include the dry weight of the cells.

Equation 10

[0290] Dry weight of cells = (wet weight of cells)/3.3

[0291] In some embodiments encompassed by the invention, a cell comprising a heterologous nucleic acid encoding an isoprene synthase polypeptide produces an amount of isoprene that is at least or about 2-fold, 3-fold, 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 150-fold, 200-fold, 400-fold, or greater than the amount of isoprene produced from a

corresponding cell grown under essentially the same conditions without the heterologous nucleic acid encoding the isoprene synthase polypeptide.

[0292] In some embodiments encompassed by the invention, a cell comprising a heterologous nucleic acid encoding an isoprene synthase polypeptide and one or more heterologous nucleic acids encoding a DXS, IDI, and/or MVA pathway polypeptide produces an amount of isoprene that is at least or about 2-fold, 3-fold, 5-fold, 10-fold, 25-fold, 50-fold, 100-fold, 150-fold, 200-fold, 400-fold, or greater than the amount of isoprene produced from a corresponding cell grown under essentially the same conditions without the heterologous nucleic acids.

Exemplary Isoprene Purification Methods

[0293] In some embodiments, any of the methods described herein further include recovering the isoprene. For example, the isoprene produced using the compositions and methods of the invention can be recovered using standard techniques. such as gas stripping, fractionation, adsorption/desorption, pervaporation, thermal or vacuum desorption of isoprene from a solid phase, or extraction of isoprene immobilized or absorbed to a solid phase with a solvent (see, for example, U.S. Patent Nos. 4,703,007 and 4,570,029, which are each hereby incorporated by reference in their entireties, particularly with respect to isoprene recovery and purification methods). In some embodiments, the recovery of isoprene involves the isolation of isoprene in a liquid form (such as a neat solution of isoprene or a solution of isoprene in a solvent). Gas stripping involves the removal of isoprene vapor from the fermentation off-gas stream in a continuous manner. Such removal can be achieved in several different ways including, but not limited to, adsorption to a solid phase, partition into a liquid phase, or direct condensation. In some embodiments, membrane enrichment of a dilute isoprene vapor stream above the dew point of the vapor resulting in the condensation of liquid isoprene.

[0294] The recovery of isoprene may involve one step or multiple steps. In some embodiments, the removal of isoprene vapor from the fermentation off-gas and the conversion of isoprene to a liquid phase are performed simultaneously. For example, isoprene can be directly condensed from the off-gas stream to form a liquid. In some embodiments, the removal of isoprene vapor from the fermentation off-gas and the conversion of isoprene to a liquid phase are performed sequentially. For example, isoprene may be adsorbed to a solid phase and then extracted from the solid phase with a solvent.

[0295] In some embodiments, any of the methods described herein further include purifying the isoprene. For example, the isoprene produced using the compositions and methods of the invention can be purified using standard techniques. Purification refers to a process through which isoprene is separated from one or more components that are present when the isoprene is produced. In some embodiments, the isoprene is obtained as a substantially pure liquid. Examples of purification methods include (i) distillation from a solution in a liquid extractant and (ii) chromatography. As used herein, "purified isoprene" means isoprene that has been separated from one or more components that are present when the isoprene is produced. In some embodiments, the isoprene is at least about 20%, by weight, free from other components that are present when the isoprene is produced. In various embodiments, the isoprene is at least or about 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, or 99%, by weight, pure. Purity can be assayed by any appropriate method, *e.g.*, by column chromatography, HPLC analysis, or GC-MS analysis.

[0296]

[0297] Crystal Structure of Isoprene Synthase

[0298] The invention also contemplates crystalline forms of plant isoprene synthase (e.g., poplar and kudzu) and its variants as described *supra* and in the Examples. In one embodiment, the invention comprises any polypeptide which has the crystal structure of poplar isoprene synthase as disclosed in Table 16-7.

EXPERIMENTAL

[0299] The following examples are provided in order to demonstrate and further illustrate certain preferred embodiments and aspects of the present invention and are not to be construed as limiting the scope thereof.

[0300] In the experimental disclosure which follows, the following abbreviations apply: °C (degrees Centigrade); rpm (revolutions per minute); H_2O (water); diH_2O (deionized water); aa and AA (amino acid); bp (base pair); kb (kilobase pair); kD (kilodaltons); gm (grams); µg and ug (micrograms); mg (milligrams); ng (nanograms); µl and ul (microliters); ml (milliliters); mm (millimeters); qs (quantity sufficient); nm (nanometers); µm and um (micrometer); M (molar); mM (millimolar); µM and uM (micromolar); pM (picomolar); U (units); MW (molecular weight); sec (seconds); min (minute/minutes); hr (hour/hours); OD_{600} (optical density at 600 nm); BSA (bovine serum albumin); DMAPP (dimethylallyl diphosphate); DTT (dithiothreitol); EtOH (ethanol); IPTG (isopropyl-beta-D-

thiogalactopyranoside); isoprene (2-methyl-1,3-butadiene); IspS (isoprene synthase); PAGE (polyacrylamide gel electrophoresis); PBS (phosphate buffered saline [150 mM NaCl, 10 mM sodium phosphate buffer, pH 7.2]); and SDS (sodium dodecyl sulfate).

[0301] The following abbreviations apply to companies whose products or services may have been referred to in the experimental examples: Agilent (Agilent Technologies, Santa Clara, CA); Becton Coulter (Becton Coulter, Inc., Fullerton, CA); Bio-Rad (Bio-Rad Laboratories, Hercules, CA); Cayman Chemical (Cayman Chemical Co., Ann Arbor, MI); CTC Analytics (CTC Analytics A.G., Zwingen, Switzerland); EMS (Electron Microscopy Supply, Hatfield, PA); Epicentre (Epicentre Biotechnologies, Madison, WI); Integrated DNA Technologies (Integrated DNA Technologies, Coralville, IA); Invitrogen (Invitrogen Corp., Carlsbad, CA); Molecular Dynamics (Molecular Dynamics, Sunnyvale, CA); Novagen (Novagen, Inc., Madison, WI); Perkin Elmer (Perkin Elmer, Waltham, MA); Roche (Roche Applied Science, Indianopolis, IN); Sigma (Sigma-Aldrich, St. Louis, MO); Stratagene (Stratagene Cloning Systems, La Jolla, CA); Qiagen (Qiagen, Inc., Valencia, CA); Takara (Takara Bio USA, Madison, WI); Thomson Instrument (Thomson Instrument Co., Oceanside, CA); V&P Scientific (V&P Scientific, Inc., San Diego, CA); and Zinsser (Zinsser North America, Northridge, CA).

EXAMPLE 1

Cloning of Kudzu Isoprene Synthase for Expression in Recombinant Bacteria

[0302] In this example, methods used to produce kudzu isoprene synthase (IspS) in *E. coli* are described. The protein sequence for the kudzu (*Pueraria montana*) isoprene synthase gene (IspS) was obtained from GenBank (AAQ84170). A kudzu isoprene synthase gene, optimized for *E. coli* codon usage, was purchased from DNA2.0 (Menlo Park, CA), and is set forth as SEQ ID NO:1 (Figure 1). The isoprene synthase gene was removed from the supplied plasmid by restriction endonuclease digestion with *Bsp*LU11I /*Pst*I, gel-purified, and ligated into pTrcHis2B (Invitrogen) that had been digested with *Nco*I/*Pst*I. The construct was designed such that the stop codon in the isoprene synthase gene was 5' to the *Pst*I site. As a result, when the construct was expressed the His-Tag is not attached to the isoprene synthase protein. The resulting plasmid, pTrcKudzu, was verified by sequencing.

[0303] The isoprene synthase gene was also cloned into pET16b (Novagen). In this case, the isoprene synthase gene was inserted into pET16b such that the recombinant isoprene synthase protein contained the N-terminal His tag. The isoprene synthase gene was amplified

from pTrcKudzu by PCR using the primer set pET-His-Kudzu-2F: 5'-CGTGAGATCA TATGTGTGCG ACCTCTTCTC AATTTAC (SEQ ID NO:3) and pET-His-Kudzu-R: 5'-CGGTCGACGG ATCCCTGCAG TTAGACATAC ATCAGCTG (SEQ ID NO:4). These primers added an *Nde*I site at the 5'-end and a *Bam*H1 site at the 3' end of the gene respectively. The plasmid pTrcKudzu, described above, was used as template DNA, HERCULASE DNA polymerase (Stratagene) was used according to manufacturer's directions, and primers were added at a concentration of 10 pM. The PCR was carried out in a total volume of 25 µl. The PCR product was digested with *Nde*I/*Bam*H1 and cloned into pET16b digested with the same enzymes. The ligation mix was transformed into *E. coli* Top10 (Invitrogen) and the correct clone selected by sequencing. The resulting plasmid designated pETNHisKudzu is then transformed into BL21(λDE3)pLysS (Novagen) cells for expression from the T7 promoter.

[0304] The kudzu isoprene synthase gene was also cloned into the low copy number plasmid pCL1920 (Lerner and Inouye, Nucl Acids Res, 18:4631, 1990). Primers were used to amplify the kudzu isoprene synthase gene from pTrcKudzu described above. The forward primer added a *Hin*dIII site and an *E. coli* consensus RBS to the 5' end. The *Pst*I cloning site was already present in pTrcKudzu just 3' of the stop codon so the reverse primer was constructed such that the final PCR product includes the *Pst*I site. The sequences of the primers were: HindIII-rbs-Kudzu F: 5'-CATATGAAAG CTTGTATCGA TTAAATAAGG AGGAATAAAC C (SEQ ID NO:5) and BamH1-Kudzu R: 5'-CGGTCGACGG ATCCCTGCAG TTAGACATAC ATCAGCTG (SEQ ID NO:4). The PCR product was amplified using HERCULASE DNA polymerase (Stratagene) with primers at a concentration of 10 pM and with 1 ng of template DNA (pTrcKudzu). The amplification protocol included 30 cycles of (95° C for 1 minute, 60° C for 1 minute, 72° C for 2 minutes). The product was digested with *Hin*dIII and *Pst*I and ligated into pCL1920, which had also been digested with *Hin*dIII and *Pst*I. The ligation mix was transformed into *E. coli* Top10. Several transformants were verified by sequence analysis. The resulting plasmid was designated pCL-lac-Kudzu.

[0305] In order to remove the beta-lactamase gene, pTrcKudzu was digested with *Bsp*HI, treated with shrimp alkaline phosphatase (SAP), incubated at 65ºC for 10 min to heat kill the SAP, then end-filled by incubating with 2 units of Klenow fragment (New England BioLabs)and dNTPS. The 5 kb fragment was purified from an agarose gel and ligated to the Kan(R) gene. The Kan(R) gene was prepared by PCR amplification from pCR-Blunt-II-TOPO (Invitrogen) using primers MCM22 and MCM23 and Taq DNA polymerase according

to the Manufacturer's instructions. The PCR fragment was digested with *Hin*dIII and *Pvu*I, and end-filled using Klenow Fragment and dNTPs. The ligation mixture was transformed into *E. coli* Top 10 chemically competent cells and a transformant carrying a plasmid conferring kanamycin resistance, pTrcKudzu(kan), was selected on Luria Agar containing kanamycin (50μg/ml). The sequences of the primers were: MCM22 5'- gatcaagctt AACCGGAATTGCCAGCTG (SEQ ID NO:15); and MCM23 5'- gatccgatcgTCAGAAGAACTCGTCAAGAAGGC (SEQ ID NO:16).

EXAMPLE 2

Cloning of Poplar Isoprene Synthase for Expression in Recombinant Bacteria

[0306] In this example, methods used to produce poplar isoprene synthase (IspS) in *E. coli* are described. The protein sequence for the poplar (*Populus alba x Populus tremula*) isoprene synthase (Schnitzler et al., Planta 222:777-786, 2005) was obtained from GenBank (CAC35696). A gene, codon optimized for *E. coli*, was purchased from DNA2.0 and is set forth as SEQ ID NO:6 (Figure 3). The isoprene synthase gene was removed from the supplied plasmid (p9796-poplar) by restriction endonuclease digestion with *Bsp*LU11I /*Pst*I, gel-purified, and ligated into pTrcHis2B that had been digested with *Nco*I/*Pst*I. The construct is cloned such that the stop codon in the insert is before the *Pst*I site, which results in a construct in which the His-Tag is not attached to the isoprene synthase protein. The resulting plasmid, pTrcPoplar, was verified by sequencing using commercially available primers that hybridize within the vector sequence (Forward and Reverse), as well as the primer Poplar InSeq 5'-GAGAAAATCG GTAAGGAACT GG (SEQ ID NO:8).

EXAMPLE 3

Isoprene Production in Recombinant Bacteria

[0307] In this example, methods used to produce and measure isoprene in recombinant *E. coli* are described.

I. Determination of isoprene production

[0308] For the shake flask cultures, one ml of a culture was transferred from shake flasks to 20 ml CTC headspace vials (Agilent vial Catalog No. 5188 2753, and cap Catalog No. 5188 2759). The cap was screwed on tightly and the vials incubated at the equivalent temperature

with shaking at 250 rpm. After 30 minutes, the vials were removed from the incubator and analyzed as described below. In cases where isoprene production in fermentors was determined, samples were taken from the off-gas of the fermentor and analyzed directly.

[0309] The analysis was performed using an Agilent 6890 GC/MS system interfaced with a CTC Analytics CombiPAL autosampler operating in headspace mode. An Agilent HP-5MS GC/MS column (30 m x 0.25 mm; 0.25 μm film thickness) was used for separation of analytes. The sampler was set up to inject 500 μL of headspace gas. The GC/MS method utilized helium as the carrier gas at a flow of 1 ml/min. The injection port was held at 250° C with a split ratio of 50:1. The oven temperature was held at 37° C for the 2 min duration of the analysis. The Agilent 5793N mass selective detector was run in single ion monitoring (SIM) mode on m/z 67. The detector was switched off from 1.4 to 1.7 minutes to allow the elution of permanent gases. Under these conditions, isoprene (2-methyl-1,3-butadiene) was observed to elute at 1.78 minutes. A calibration table was used to quantify the absolute amount of isoprene and was found to be linear from 1 μg/L to 200 μg/L. The limit of detection was estimated to be 50 to 100 ng/L using this method.

II. Production of isoprene in shake flasks

[0310] The vectors described above were introduced into *E. coli* strain BL21(λDE3)pLysS (Novagen) to produce strains BL21/ptrcKudzu, BL21/pCL-lac-Kudzu and BL21/pETHisKudzu. The strains were spread for isolation onto LA (Luria agar) containing the appropriate antibiotic (50 μg/ml carbenicillin for BL21/ptrcKudzu and BL21/pETHisKudzu or 50 μg/ml spectinomycin for BL21/pCL-lac-Kudzu) and incubated overnight at 37° C. Single colonies were inoculated into 250 ml baffled shake flasks containing 20 ml Luria Bertani broth (LB) and the appropriate antibiotic. Cultures were grown overnight at 20° C with shaking at 200 rpm. The OD_{600} of the overnight cultures was measured and the cultures were diluted into a 250 ml baffled shake flask containing 30 ml MAGICMEDIA expression medium (Invitrogen) containing the appropriate antibiotic to an OD_{600} ~ 0.05. The culture was incubated at 30° C with shaking at 200 rpm. When the OD_{600} ~ 0.5 - 0.8, 400 μM IPTG was added and the cells were incubated for a further 6 hours at 30° C with shaking at 200 rpm. At 0, 2, 4 and 6 hours after induction with IPTG, 1 ml aliquots of the cultures were collected, the OD_{600} was determined and the amount of isoprene produced was measured as described above.

III. Production of Isoprene from BL21/ptrcKudzu in 14 liter fermentation

[0311] Large-scale production of isoprene from *E. coli* containing the recombinant kudzu isoprene synthase gene was determined from a fed-batch culture. The recipe for the fermentation media (TM2) per liter of fermentation medium was as follows: K_2HPO_4 13.6 g, KH_2PO_4 13.6 g, $MgSO_4$ * $7H_2O$ 2 g, citric acid monohydrate 2 g, ferric ammonium citrate 0.3 g, $(NH_4)_2SO_4$ 3.2 g, yeast extract 5 g, 1000X Modified Trace Metal Solution 1 ml. All of the components were added together and dissolved in diH_2O. The pH was adjusted to 6.8 with potassium hydroxide (KOH) and qs to volume. The final product was filter sterilized with 0.22 μM filter, but not autoclaved. The recipe for 1000X Modified Trace Metal Solution was as follows: Citric Acids * H_2O 40 g, $MnSO_4$ * H_2O 30 g, NaCl 10 g, $FeSO_4$ * $7H_2O$ 1 g, $CoCl_2$ * $6H_2O$ 1 g, ZnSO * $7H_2O$ 1 g, $CuSO_4$ * $5H_2O$ 100 mg, H_3BO_3 100 mg, $NaMoO_4$ * $2H_2O$ 100 mg. Each component was dissolved one at a time in diH_2O, the pH was adjusted to 3.0 with HCl/NaOH, then qs to volume and filter sterilized with a 0.22 μ filter.

[0312] This experiment was carried out in 14 L bioreactor to monitor isoprene formation from glucose at the desired fermentation, pH 6.7 and temperature 34° C. An inoculum of *E. coli* strain BL21/ptrcKudzu taken from a frozen vial was prepared in soytone-yeast extract-glucose medium in two 600 ml flasks.. After the inoculum grew to OD_{550} = 0.6, two 600 ml flasks were centrifuged and the contents resuspended in 70 ml supernatant to transfer the cell pellet (70 ml of OD 3.1 material) to the bioreactor. At various times after inoculation, samples were removed and the amount of isoprene produced was determined as described above.

EXAMPLE 4

Selection of Sites for Improvement of Plant Isoprene Synthases

[0313] The isoprene synthases of plants were expected to be homologous to the terpene synthases. The three-dimensional structures of two homologous terpene synthases have been determined from bornyl diphosphate synthase (pdb entry 1N1B) and 5-epi-aristolochene synthase (pdb entry 5EAU). These enzymes share only 32% homology but their tertiary structure is conserved. In addition, the structures of intermediate complexes with both enzymes have shown that not only tertiary folding, but also detailed interactions in the active sites of these enzymes are highly conserved.

[0314] The kudzu and poplar isoprene synthases have higher sequence identity than was seen between the bornyl diphosphate synthase and the 5-epi-aristolochene synthase as shown in Table 4-1 below.

Table 4-1. Percent Identity of Various Enzymes

	BDP-synthase	5EA-synthase	Kudzu IspS
Poplar IspS	40.1	32.9	54.4
Kudzu IspS	40.7	33.8	
5ES synthase	31.9		

[0315] A homology model of the poplar isoprene synthase has been made based on the bornyl diphosphate synthase (BDP-synthase) pdb entry 1N24 (~40% sequence identity). The homology model appears to be plausible based on the close similarity of 10 trial models created using the program MOE written and supported by The Chemical Computing Group, Inc. The plausibility is based on the conservation of common amino acid residues at sites found to be involved in catalysis in the BDP-synthase structure.

[0316] A comparison of the active site from the structure of BDP-synthase and the homology model of poplar IspS indicates that the active site involved in metal ion binding and phosphate recognition is conserved. In particular, Lys 272, Asp 309, Asp 313, Glu 387, Arg 450 and Asn 453 of poplar IspS were observed to overlap equivalent residues in BDP-synthase. In this example, amino acid residue positions for poplar IspS are derived from SEQ ID NO:7. The positioning of an intermediate of the BDP-synthase was also compared with the poplar IspS homology model. Based on this, it was possible to identify the analogous binding region and the approach direction that isopentenyl diphosphate would require in order to bind and react with the poplar IspS enzyme.

[0317] A homology model of the kudzu isoprene synthase has been made based on bornyl diphosphate synthase pdb entry 1N24 having (~40% sequence identity). A comparison of the active site from the structure of BDP-synthase with the homology model of kudzu IspS indicates that numerous active site residues involved in metal ion binding and phosphate recognition are conserved. In particular, Arg 269, Asp 306, Asp 310, Glu 384, Arg 450 and Asn 453 of kudzu IspS were observed to overlap equivalent residues in BDP-synthase.

[0318] A comparison of the active site residues identified in the homology models of poplar and kudzu IspS revealed that residues from one homology model are also quite homologous with similar residues, appearing with only minor shifts in the relative position numbers for some of the residues, in the other homology model. Based on the homology models, sites in poplar and kudzu IspS were identified as candidates for mutagenesis to produce variant IspS enzymes with improved performance. Briefly, sites were selected in the

IspS that might alter the interaction of the metal binding, the diphosphate recognition, the IPP chain binding and/or the approach to the active site.

I. Diphosphate/ Metal Binding Sites

[0319] The side chains of amino acid residues in the poplar IspS that are found in proximity to the metal and diphosphate (DPP) binding side chains were identified. These residues include Phe 384, Tyr 402, Ala 406, Ser 409, Ala 460 and Asn 469. The inventors note that Lys 272 is incorrect based on homology to other known poplar IspS sequences, which have an Arg at this position.

II. Substrate Access Loop

[0320] The substrate access loop of poplar IspS is in a region that deviates from the BDP-synthase structure. In the BDP-synthase structure the residues form a segment that creates a cover. Without being bound by theory, the inventors expect that this segment in the actual three-dimensional structure of poplar IspS will form a similar structure. As such the residues in this loop, including residues 455-466, will be in a position to alter the activity of the poplar IspS enzyme. In the poplar IspS enzyme residues 454-466 have the following sequence: LASASAEIARGET (SEQ ID NO:9).

III. Isoprenyl Binding Site

[0321] The complex of BDP-synthase and the product of the reaction, bornyl diphosphate (pdb entry 1N24), was used to identify residues in the poplar model that may modulate substrate specificity and/or reaction rate (altered on and off rates of substrate and product). These residues include Arg 274, Trp 281 Phe 302, Val 305, Ser 411, Gln 415, Phe 449, Ser 537 and Glu 540.

Table 4-2. Candidate Mutagenesis Sites

	Poplar Amino Acid	Kudzu Amino Acid / codon
DPP/metal sites	Phe 384	Phe 381 / 1141-1143
	Tyr 402	Tyr 399 / 1195-1197
	Ala 406	Ala 403 / 1207-1209
	Ser 409	Ser 406 / 1216-1218
	Asn 469	Asn 469 / 1405-1407

Extra DPP sites	Tyr 312	Tyr 309 / 925-927
	Asp 313	Asp 310 / 928-930
	Leu 380	Leu 377 / 1129-1131
	Glu 387	Glu 384 / 1150-1152
	Asn 404	Asn 402 / 1204-1206
	Ser 410	Ser 407 / 1219-1221
N_terminal access segment	22	20 / 58-60
	23	21 / 61-63
	24	22 / 64-66
	25	23 / 67-69
	26	24 / 70-72
	27	25 / 73-75
Substrate access loop	Leu 454	Ala 456 / 4102-4104
	Ala 455	Thr 457 / 4105-4107
	Ser 456	Ser 458 / 4108-4110
	Ala 457	Ala 459 / 4111-4113
	Ser 458	Ala 460 / 4114-4116
	Ala 459	Glu 461 / 4117-4119
	Glu 460	Leu 462 / 4120-4122
	Ile 461	Glu 463 / 4123-4125
	Ala 462	
	Arg 463	Arg 464 / 4126-4128
	Gly 464	Gly 465 / 4129-4131
	Glu 465	Glu 466 / 4132-4134
	Thr 466	Thr 467 / 4135-4137
		Thr 468 / 4138-4140
Isoprenyl binding site	Arg 274	Arg 271 / 811-813
	Trp 281	Trp 278 / 832-834
	Phe 302	Phe 299 / 895-897
	Val 305	Val 302 / 904-906
	Ser 411	Ser 408 / 1222-1224
	Gln 415	
	Phe 449	Phe 449 / 1345-1347
	Ser 537	Ser 458 / 1372-1374
	Glu 540	Tyr 531 / 1591-1593
Extra Isoprenyl sites	Gly 412	Gly 409 / 1225-1227

	Leu 414	Ala 411 / 1231-1233
	Leu 416	Leu 413 / 1237-1239
	Leu 521	Met 523 / 1567-1569
	Ser 525	Ser 527 / 1579-1581

EXAMPLE 5

Mutation of Non-Conserved Cysteines in Kudzu Isoprene Synthase

[0322] The kudzu and poplar isoprene synthase (IspS) homology models, based on the bornyl diphosphate synthase crystal structure, were compared with respect to the positions of the cysteine residues. Cysteines have the potential to form disulfide bonds and stabilize structures. The non-conserved cysteines, contemplated to affect solubility and/or activity, were altered by site-directed mutagenesis. The kudzu IspS amino acid sequence used for the modeling is shown in Figure 2 (SEQ ID NO:2). There are eight cysteines in kudzu IspS at positions 57, 291, 343, 378, 421, 446, 451 and 529 (relative to the mature form of the protein) as shown in the homology model of Figure 5. In contrast, there are five cysteines in poplar IspS amino acid sequence has five cysteines, as shown in the homology model of Figure 6 upon which the kudzu cysteines are superimposed. Several of the cysteines are apparently conserved between the poplar and kudzu IspS sequences indicating that these positions are important in stabilizing the structure, activity and/or other protein function. The remaining cysteines (nonconserved residues 57, 291, 421 and 446) in kudzu were mutated to serine as described herein.

I. Mutagenesis

[0323] The QUIKCHANGE® Multi-Site Directed Mutagenesis Kit (Stratagene) was used as per the manufacturer's directions. The following primers were utilized for mutagenesis:

C57S-F 5'- CTGGAGGAAGAAGTTCGC **TCC**
ATGATCAACCGTGTAGAC (SEQ ID NO:10);

C291S-F 5'- CGCCAGACCCGCAGTTTGGTGAA **TCT**
CGCAAAGCTGTTACTAAAATG (SEQ ID NO:11);

C421S-F 5'-CGCCGTCTTACTTTTCCGTA **TCC**
CAGCAGCAGGAAGACATC (SEQ ID NO:12);

C446S-F 5'-CATGGTCTGGTGCGTTCTAGC **TCC**
GTTATCTTCCGCCTGTGC (SEQ ID NO:13); and

C421S-R 5'-GATGTCTTCCTGCTGCTG **GGA**

TACGGAAAAGTAAGACGGCG (SEQ ID NO:14).

[0324] The plasmid pTrcKudzu(kan) described in Example 1 was used as template DNA. The primers C57S-F, C291S-F, C421S-F, and C446-F were combined in a single reaction (100 pmol). Template DNA was added (~200 nanograms) and 0.5 μl of Quiksolution was added to the recommended volumes of enzyme and buffer. The PCR reaction was carried out in an Eppendorf PCR machine using an annealing temperature of 55°C and an extension time of 12 minutes for 30 cycles. Other parameters of the cycle were as indicated in the instructions. The PCR mix was treated with *Dpn*I for 4 hours at 37°C (2 x 1 μl for 2 h each) and then 5 μl of the reaction were transformed into *E. coli* Top10 (Invitrogen) chemically competent cells and plated on Luria agar containing kanamycin (50 μg/ml). After overnight incubation at 37°C, several colonies were picked and inoculated into 5 ml of Luria Broth containing kanamycin (50 μg/ml). The plasmids were isolated using the QIAprep Spin Miniprep kit (Qiagen), and the IspS genes were sequenced in their entirety. Various single and combinations of mutations were made as indicated in the Table 5-1 below.

Table 5-1. BL21(λDE3) Cells Transformed with Mutated pTrcKudzu Plasmids*

Strain*	C57S	C291S	C421S	C446S
C1	+	+		
C2		+		+
C4	+	+		+
C6	+			+
C11				+
C20			+	
C6-4	+		+	+

[0325] All the variant plasmids were transformed into chemically competent BL21(λDE3) cells (Novagen). In a second reaction pTrcKudzu(kan) and plasmid DNA isolated from C6 were used as templates in a QUIKCHANGE® site directed mutagenesis kit (Stratagene) single site reaction with C421S-F and C421S-R primers. After confirmation by sequencing, two additional strains were obtained.

II. Cell Growth and Isoprene Production

[0326] Cells were grown in 5 ml tubes containing Luria Broth supplemented with 50 mg/L kanamycin at 30°C overnight with agitation. These cultures were diluted into TM3 broth supplemented with 10 g/L glucose and 50 mg/L kanamycin. The culture volume was 25 ml in a 250 ml baffled Bellco Delong flask in which cells were grown at 30°C with agitation (225 rpm). Samples were taken aseptically, as indicated, for optical density measurements at A_{600}. The results are shown in Figure 7. The cultures were induced at 3.33 hrs with 200 μM IPTG and allowed to continue growth until harvest at 7.8 hr. The cultures were centrifuged at 10,000 X g for 10 min, the supernatants decanted and the cell pellets frozen at -80°C overnight.

[0327] Frozen cell pellets were thawed and resuspended in 2 ml PEB (50 mM Tris-HCl, pH 8.0, 20 mM MgCl, 2 mM dithiothreitol, and 50% [v/v] glycerol). Cells were lysed by French pressure cell disruption, one pass, at 20,000 psi. The lysate was centrifuged for 15 min at 10,000 X g. The supernatants were decanted and the pellets resuspended in 2 ml PEB. The pellets and supernatants were analyzed by SDS-PAGE, 4-12% NuPage gels (Invitrogen), run in MES buffer under reducing conditions. The molecular weight standard was SeeBlue2 (Invitrogen). The results are shown in Figure 8. The IspS protein concentrations were estimated using the BCA assay (Pierce) using BSA as standard (Table 5-2).

III. Assays for Isoprene Synthase Activity and Solubility

[0328] Briefly the activity of the supernatants was measured by reaction with DMAPP, and the isoprene evolved was quantified by GC/MS.

[0329] Headspace Assay. A sample of 200 μl of the desired culture is inoculated into 2 ml CTC headspace vials (Agilent vial Catalog No. 5188 2753, and cap Catalog No. 5188 2759). The cap was screwed on tightly and the vials were incubated at 37°C with shaking at 250 rpm. After 30 minutes the vials were removed from the incubator and cooled briefly with ambient tap water. The vials were placed into the CombiPal Headspace auto sampler for analysis by GC-MS. The analysis was performed using an Agilent 6890 GC/MS system interfaced with a CTC Analytics CombiPAL autosampler operating in headspace mode. An Agilent HP-5MS GC/MS column (30 m x 0.25 mm; 0.25 μm film thickness) was used for separation of analytes. The sampler was set up to inject 500 μL of headspace gas. The GC/MS method utilized helium as the carrier gas at a flow of 1 ml/min. The injection port was held at 250°C with a split ratio of 50:1. The oven temperature was held at 37°C for the 2 min duration of the analysis. The Agilent 5793N mass selective detector was run in single ion

monitoring (SIM) mode on m/z 67. The detector was switched off from 1.4 to 1.7 minutes to allow the elution of permanent gases. Under these conditions isoprene (2-methyl-1,3-butadiene) was observed to elute at 1.78 minutes. A calibration table was used to quantify the absolute amount of isoprene and was found to be linear from 1 μg/L to 200 μg/L. The limit of detection was estimated to be 50-100 ng/L using this method.

[0330] DMAPP Assay. An aliquot of 95 μl of the supernatant fraction from the centrifuged French Pressure cell lysate was added to the headspace vials. A 5 μL aliquot of 8 mM DMAPP in 100 mM potassium phosphate buffer, pH 8.2 was added, the vials sealed and allowed to incubate at room temperature for 30 min. The amount of isoprene produced was measured by GC/MS as described above and reported in Table 5-2.

Table 5-2. Isoprene Synthase Activity from Crude Extracts of Cysteine Mutants

Supernatant	Activity (mU/ml)	Protein (mg/ml)	Specific Activity (mU/mgP)
Wt	59.0	2.48	23.79
C1	5.3	2.64	2.01
C2	0.2	3.52	0.06
C4	0.5	3.22	0.16
C6	9.0	3.32	2.71
C11	0.1	4.26	0.03

[0331] The values shown in Table 5-2 are averages of reactions with two different concentrations of extract. All proteins containing any of the cysteine mutations resulted in severe diminution of enzyme activity and an apparent decrease of soluble protein as judged by a relative increase in the proportion of protein in the insoluble (pellet) fraction.

EXAMPLE 6

Mutation of Residues in Poplar Isoprene Synthase

[0332] Alignment of the amino acid sequences of kudzu and poplar isoprene synthases with other synthases was done using Vector Nti (Invitrogen). The aligned sequences included: beta-ocimene synthase *Lotus corniculatus* (AAT86042); putative terpene synthetase *Medficago trunculata* (AAV36465); hypothetical protein *Vitis vinifera* (can65805); hypothetical protein *Vitis vinifera* (CAN62729); pinene synthase *Quercus ilex* (CAK55186); IspS *Pueraria montana* (kudzu) Sharkey (AAQ84170); monoterpene synthase *Eucaliptus globulus* (BAF02832); IspS *Populus nigra* Fortunati (CAL69918); IspS *Populus tremuloides*

Sharkey (AAQ16588); IspS *Populus alba* (BAD98243); and IspS *Populus alba x tremula* Zimmer (CAC35696). The sequence from the database of *Populus alba x tremula* (CAC35696) exhibited different amino acids at positions 272 and 497 that were otherwise highly conserved. Additionally based on analysis of the homology model of poplar IspS, position 453 was identified as a third candidate for mutagenesis.

I. Mutagenesis

[0333] The QUIKCHANGE® Multi-Site Directed Mutagenesis kit (Stratagene) was used as per the manufacturer's directions to introduce the following mutations singly and in combination into the *Populus alba x tremula* IspS sequence (SEQ ID NO:7): K272R; C497W; and N453D. The following primers were utilized for mutagenesis:
Poplar K272R 5'-ccaaactgcacttcg ctcgtgaccgcctgattgag (SEQ ID NO:17);
Poplar N453D 5'-atctttcgcctgtgcgacgacctggcaagc (SEQ ID NO:18); and
Poplar C497W 5'-tgaatctgatcgacgaaacctggaagaaaatgaacaaagaaaaac (SEQ ID NO:19).
The following primer, Poplar InSeq, 5'-gagaaaatcggtaaggaactgg (SEQ ID NO:8) was used for sequencing.

[0334] Mutagenesis was done according to the manufacturer's directions, with all three mutagenesis primers being added to a single reaction mix (100 ng each) with pTrcPoplar as the template DNA (100 ng). Addition of 0.5 μl of Quik Solution aided the mutagenesis reaction. The suggested PCR cycle was run with an annealing temperature of 55°C and an extension time of 12 min. Other parameters were as indicated in the instructions. The PCR mix was digested with *Dpn*I for 4 hrs at 37°C (1 μl each x 2 h) and then 5 μl of the reaction was transformed into *E. coli* Top10 chemically competent cells (Invitrogen). Several colonies were selected and grown up in 5 ml of Luria Broth (LB) containing carbenicillin (50 μg/ml). Plasmids were isolated using the Qiagen QIAprep spin mini-prep kit and sent for sequencing using forward and reverse primers that hybridized to the vector, as well as the Poplar InSeq primer.

[0335] The resulting variants of pTrcPoplar were obtained: pTrcPoplar K272R, pTrcPoplar K272R/N453D; pTrcPoplar K272R/N453D/C497W; and pTrcPoplar 272R/497W. These plasmids were transformed into BL21(λDE3)pLysS chemically competent cells (Novagen) for analysis. The variants were analyzed for headspace activity (production of isoprene from whole cells), solubility, and specific activity.

II. Cell Growth and Isoprene Production

[0336] The variants, the parent Poplar strain, and the strain containing pTrcKudzu were grown overnight at 37°C in 5 ml of Luria Bertani medium containing either carbenicillin (50 μg/ml-Poplar strains) or kanamycin (50 μg/ml-Kudzu strain). These cultures were diluted into TM3 broth to an OD_{600} of 0.05, supplemented with 10g/L glucose and either 50 μg/ml carbenicillin (Poplar mutants and wild type) or 50 mg/L kanamycin (BL21/pTrcKudzu). The recipe for TM3 broth is as follows: K_2HPO_4 (13.6 g/l) KH_2PO_4 (13.6 g/l), $MgSO_4$ * $7H_2O$ (2 g/l) Citric Acid Monohydrate (2 g/L) Ferric Ammonium Citrate (0.3 g/L) $(NH_4)_2SO_4$ (3.2 g/L) yeast extract (0.2 g/L) 1 ml of 1000x Trace Elements solution, pH adjusted to 6.8 with ammonium hydroxide qs to volume with sterile diH_2O and filter sterilized with a 0.22 micron filter. The recipe for 1000X Trace Elements solution is as follows: Citric Acids * H_2O (40 g/L), $MnSO_4$ * H_2O (30 g/L), NaCl (10 g/L), $FeSO_4$ * 7 H_2O (1 g/L), $CoCl_2$ * 6 H_2O (1 g/L), ZnSO * 7 H_2O (1 g/L), $CuSO_4$ * 5 H_2O (100 mg/L), H_3BO_3 (100 mg/L), $NaMoO_4$ * 2 H_2O (100 mg/L). Each component was dissolved one at a time in diH_2O, pH adjusted to 3.0 with HCl/NaOH, qs to volume and filter sterilized with a 0.22 micron filter.

[0337] The diluted culture volume was 25 ml in a 250 ml baffled Bellco Delong flask for growth at 30°C with agitation (225 rpm). Samples were taken aseptically, as indicated, for optical density measurements at A_{600}. Two sets of cultures were set up, one for induction with 0.2 mM IPTG and one that remained un-induced. After 3 hours of growth at 30°C with shaking at 200 rpm (OD_{600}~0.5), one set of the cultures was induced with 0.2 mM IPTG and incubated for a further 3 h at 30°C with shaking at 200 rpm, the un-induced set was further incubated for the same amount of time. The OD_{600} was determined for all cultures prior to the induction time (3 h post inoculation) and at the time of the measurement of isoprene by the Headspace assay (3 h post-induction, total of 6 h of growth). The cell cultures were centrifuged at 7000 x g for 15 minutes in a Sorvall superspeed centrifuge to pellet the cells. The supernatant was removed and the cell pellet frozen for use in an in vitro assay for isoprene synthase activity. Results of the growth and headspace assays are shown in the following tables.

Table 6-1. Growth of *E. coli* Strains Expressing Poplar IspS Variants (OD_{600} values)

Strain	Pre-induction (after 3h growth)	Post-induction (3h with IPTG)	Non-induced (after 6h growth)
pTrcPoplar	0.49	3.3	4.7

K272R			
pTrcPoplar K272R/N453D	0.48	3.7	4.8
pTrcPoplar K272R/N453D/C497W	0.41	3.1	5.1
pTrcPoplar K272R/497W H2	0.45	0.8	0.97
pTrcPoplar WT	0.49	3.5	4.7
pTrcKudzu WT	0.44	3.3	4.2

Table 6-2. Production of Isoprene by *E. coli* Strains Expressing Poplar IspS Variants (μg/L)

Strain	Pre-induction (after 3h growth)	Post-induction (3h with IPTG)	Non-induced (after 6h growth)
pTrcPoplar K272R	n/a	0	0
pTrcPoplar K272R/N453D	n/a	0	0
pTrcPoplar K272R/N453D/C497W	n/a	0	0
pTrcPoplar K272R/497W H2	n/a	0	0
pTrcPoplar WT	n/a	0	0
pTrcKudzu WT	n/a	1.3	0.29

[0338] Surprisingly, the strain expressing the kudzu IspS demonstrated any measurable isoprene production. This is unexpected given that kinetic properties of the poplar enzymes were reported in the literature to be superior to those of kudzu enzymes. In particular, the prior art describes the specific activity (U/mg) and K_m (μM) of recombinant kudzu IspS to be 0.075 and 7,700 respectively, native aspen IspS to be 0.5 and 8,000 respectively, and recombinant poplar IspS to be 0.16 and 9,000 respectively (Silver and Fall, J Biol Chem, 270:13010-1316, 1995; Miller et al., Planta, 213:483-487, 2001; and Sharkey et al., Plant Physiology, 137:700-712, 2005). The published K_m values for the three enzymes are all quite high and within range of each other, but the specific activity for kudzu isoprene synthase is significantly worse than that of the other two isoprene synthases.

III. Assays for Isoprene Synthase Activity and Solubility

[0339] By using the DMAPP assay, the activity of isoprene synthase can be measured directly as DMAPP is the direct substrate for the enzyme. The cell pellets of the poplar parent and mutant strains, as well as the wild type kudzu were thawed and resuspended in 2 ml PEB (50 mM Tris-HCl, pH 8.0, 20 mM MgCl, 2 mM dithiothreitol, and 50% [v/v] glycerol). Cells were lysed by French pressure cell disruption, one pass, at 20,000 psi. The lysate (1 ml) was then centrifuged in a microfuge for 20 min at 20,000 rpm at 4°C. The supernatant was removed and the pellet resuspended in 1 ml of PEB. The supernatant and pellet samples were analyzed by SDS-PAGE, and DMAPP assay, while the total protein content was determined by BCA.

Table 6-3. DMAPP Assay of Isoprene Production from the Supernatant of the Centrifuged Cell Lysate

Strain	OD600 (prior to lysis)	Total Protein (mg/ml)	Isoprene/ Total Protein
Induced			
pTrcPoplar K272R	3.3	1.70	0.03
pTrcPoplar K272R/N453D	3.6	1.3	0.08
pTrcPoplar K272R/N453D/C497W	3.1	1.10	0.08
pTrcPoplar K272R/497W H2	0.803	0.80	0.11
pTrcPoplar WT	3.5	1.30	0.06
pTrcKudzu WT	3.3	1.50	11.15
Uninduced			
pTrcPoplar K272R	4.7	1.7	0.26
pTrcPoplar K272R/N453D	4.8	1.8	0.07
pTrcPoplar K272R/N453D/C497W	5.2	1.9	0.02
pTrcPoplar K272R/497W H2	0.969	1.0	0.17
pTrcPoplar WT	4.6	1.7	0.05
pTrcKudzu WT	4.2	1.9	1.62

[0340] Production was normalized to total cell lysate supernatant protein.

Table 6-4. DMAPP Assay of Isoprene Production from the Pellet of the Centrifuged Cell Lysate

Strain	OD600 (prior to lysis)	Total Protein (mg/ml)	Isoprene/ Total Protein
Induced			
pTrcPoplar K272R	3.3	1.02	0.118
pTrcPoplar K272R/N453D	3.6	1.36	0.000
pTrcPoplar K272R/N453D/C497W	3.1	1.49	0.040
pTrcPoplar K272R/C497W H2	0.80	1.38	0.043
pTrcPoplar WT	3.5	1.57	0.050
pTrcKudzu WT	3.3	1.47	0.040
Uninduced			
pTrcPoplar K272R	4.7	1.40	0.170
pTrcPoplar K272R/N453D	4.8	1.53	0.120
pTrcPoplar K272R/N453D/C497W	5.2	1.42	0.131
pTrcPoplar K272R/C497W H2	0.97	1.55	0.080
pTrcPoplar WT	4.6	1.38	0.120
pTrcKudzu WT	4.2	1.55	0.120

[0341] Production was normalized to total cell lysate pellet protein.

[0342] The poplar variant K272R/C497W showed a 1.8x increase in activity as compared to the wild type in the supernatant fraction of the induced cultures. Likewise, the poplar variants K272R and K272R/C497W showed a 5.2x and 3.4x increase in activity as compared to the wild type in the supernatant fraction of the uninduced cultures. Moreover the poplar variant K272R showed a 2x increase in activity as compared to wild type in the pellet of the induced cultures. However, the most striking result was that the kudzu IspS is more active than the poplar IspS employed herein (185x). In the above tables, H2 is the name of the clone designated pTrcPoplar K272R/C497W H2.

EXAMPLE 7

Subcloning of Kudzu Isoprene Synthase

[0343] In this Example, methods used in the construction of kudzu isoprene synthase (IspS) SELs are described. To create an expression vector for construction of site evaluation libraries (SEL), the kudzu isoprene synthase gene was subcloned into the pET24d vector (Novagen) from the pCR2.1 vector (Invitrogen). The kudzu IspS gene was amplified from pTrcKudzu template DNA using primers MCM50 5'-GATCATGCAT TCGCCCTTAG GAGGTAAAAA AACATGTGTG CGACCTCTTC TCAATTTACT (SEQ ID NO:20); and MCM53 5'-CGGTCGACGG ATCCCTGCAG TTAGACATAC ATCAGCTG (SEQ ID NO:21). PCR reactions were carried out using Taq DNA Polymerase (Invitrogen), and the resulting PCR product was cloned into pCR2.1-TOPO TA cloning vector (Invitrogen), and transformed into *E. coli* Top10 chemically competent cells (Invitrogen). Transformants were plated on L agar containing carbenicillin (50 μg/ml) and incubated overnight at 37°C. Five ml Luria Broth cultures containing carbenicillin 50 μg/ml were inoculated with single transformants and grown overnight at 37°C. Five colonies were screened for the correct insert by sequencing of plasmid DNA isolated from 1 ml of liquid culture (Luria Broth) and purified using the QIAprep Spin Mini-prep Kit (Qiagen). The resulting plasmid, designated MCM93, contains the kudzu IspS coding sequence in a pCR2.1 backbone (Figure 9). The sequence of MCM93 (SEQ ID NO:22) is shown in Figure 10.

[0344] The kudzu coding sequence was removed by restriction endonuclease digestion with *Pci*I and *Bam*H1 (Roche) and gel purified using the QIAquick Gel Extraction kit (Qiagen). The pET24d vector DNA was digested with *Nco*I and *Bam*HI (Roche), treated with shrimp alkaline phosphatase (Roche), and purified using the QIAprep Spin Mini-prep Kit (Qiagen). The kudzu IspS fragment was ligated to the *Nco*I/*Bam*H1 digested pET24d using the Rapid DNA Ligation Kit (Roche) at a 5:1 fragment to vector ratio in a total volume of 20 μl. A portion of the ligation mixture (5 μl) was transformed into *E. coli* Top 10 chemically competent cells and plated on L agar containing kanamycin (50 μg/ml). The correct transformant was confirmed by sequencing and transformed into chemically competent BL21(λDE3)pLysS cells (Novagen). A single colony was selected after overnight growth at 37°C on L agar containing kanamycin (50 μg/ml). A map of the resulting plasmid designated as pET24D-Kudzu is shown in Figure 11. The sequence of pET24D-Kudzu (SEQ ID NO:23) is shown in Figure 12. IspS Activity was confirmed using the headspace assay as described in Example 5).

EXAMPLE 8

Construction of Isoprene Synthase Site Evaluation Libraries (SELs)

[0345] In order to improve the kinetic parameters of a plant IspS SELs are prepared at sites selected from homology models of both the kudzu and the poplar IspS enzymes. While it is predicted from the homology models that engineering at the indicated sites would improve both enzymes, in this embodiment, kudzu SELs are described. Kudzu IspS surface sites of interest include but are not limited to: 26 L, 30 E, 31 F, 33 Q, 35 L, 36 E, 37 N, 39 L, 40 K, 41 V, 43 K, 44 L, 61 R, 62 V, 63 D, 65 Q, 87 K, 94 E, 95 N, 99 L, 100 D, 105 N, 137 K, 138 E, 143 G, 144 E, 182 N, 184 L, 185 K, 187 G, 189 N, 190 T, 225 P, 226 H, 247 K, 257 T, 258 E, 259 M, 266 D, 334 N, 353 D, 357 S, 358 I, 361 E, 389 N, 392 I, 393 I, 398 K, 401 E, 421 C, 423 Q, 424 Q, 425 E, 426 D, 430 H, 432 L, 433 R, 434 S, 437 D, 443 R, 462 L, 463 E, 476 H, 478 N, 479 D, 485 Q, 508 D, 513 P, 515 A, 532 Q, 533 Y, 537 L, 538 G, 539 R, 542 Y, 543 A, and 557 P. Kudzu IspS active site positions of interest include but are not limited to: 24 P, 25 N, 309 Y, 310 D, 377 L, 381 F, 384 E, 399 Y, 402 N, 403 A, 406 S, 407 S, 409 G, 411 A, 413 L, 449 F, 456 A, 457 T, 458 S, 458 S, 459 A, 460 A, 461 E, 462 L, 463 E, 464 R, 465 G, 466 E, 467 T, 468 T, 469 N, 523 M, 527 S, and 531 Y. Additional kudzu IspS active site positions of interest include but are not limited to: 20 A, 21 N, 22 Y, 23 Q, 271 R, 278 W, 299 F, 302 V, and 408 S. Each library SEL contains clones, maximally including 20 different variants. For example, kudzu isoprene synthase SEL 531 contains variants in which the DNA triplet coding for tyrosine at position 531 of the mature kudzu enzyme is replaced by another DNA triplet encoding: alanine, aspartic acid, cysteine, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, arginine, serine, threonine, valine, or tryptophan. Briefly, DNA triplets of specific positions in the DNA coding strand of the mature IspS are replaced. The mutated IspS nucleic acids are subsequently ligated to a suitable expression vector and used to transform suitable host cells.

[0346] Site evaluation libraries are created either by ordering synthetic constructs (e.g., DNA2.0) or by ordering primers with the "nns" sequence in place of the codon to be mutated. The primers are then be used to mutate the gene to produce an SEL at the indicated site using commercially available mutagenesis kits (e.g., Stratagene) as has been described (e.g., WO0507682A2). The mutated codons are identified by sequence analysis. The site libraries are arrayed in 96 well master plates, and frozen for later use. Cultures are grown from the master plates and prepared for screening.

[0347] The desired end products are IspS enzymes that function optimally in a host metabolically engineered to maximize carbon flow through IspS. To this end several stages of

screening are used to ensure that correct parameters are being addressed. Exemplary screens include but are not limited to: expression, DMAPP feeding for production of HG, microreactor, protein determination, and headspace assays. Expression screen: One example of a method to analyze the level of protein expression is as follows. Soluble and insoluble fractions of cell lysates (obtained from lysed cell cultures) are prepared by centrifugation. The resulting supernatants and pellets are analyzed by SDS-PAGE. The percent soluble protein is determined by densitometry analysis of the protein present in the supernatant versus the pellet.

[0348] In an exemplary embodiment, kudzu site evaluation libraries are constructed in the pET24D expression vector. The pET24D-Kudzu vector, containing the kudzu isoprene synthase gene, serves as the template DNA.

Materials:

pET24D-Kudzu vector (~50 ng/μl)

Kudzu IS site-directed mutagenic primers (Integrated DNA Technologies)

QUIKCHANGE® Multi Site-Directed Mutagenesis Kit (Stratagene)

MJ Research PTC-200 Peltier Thermal Cylcer (Bio-Rad Laboratories)

One Shot TOP10 competent cells (Invitrogen)

QIAprep Spin Miniprep Kit (Qiagen)

BL21(λDE3) pLysS competent cells (Invitrogen)

Luria Broth (LB) agar plates

Methods:

[0349] The method of mutagenesis was based on the codon-specific mutation approach, in which the creation of all possible mutations in a specific DNA triplet was performed using a single forward primer with a length of 25 to 45 nucleotides, enclosing a specific designed triple DNA sequence NNS (N = A, C, T or G and S = C or G) corresponding with the sequence of the codon to be mutated. This method results in the random incorporation of nucleotides at a specific pET24D-kudzu codon of interest. Table 8-1 lists the oligonucleotide primers used for mutagenesis, with the number in the primer name corresponding with the codon position in the mature kudzu isoprene synthase enzyme sequence. All oligonucleotide primers were synthesized (Integrated DNA Technologies) on a 100 nmole scale and PAGE purified.

Table 8-1. Kudzu IspS Codon-Specific Mutation Primers

Name	SEQ ID	Primer Sequence
IS_A20	NO:24	CATAATTCCCGTCGTTCCNNSAACTATCAGCCAAACCTG
IS_N21	NO:25	CATAATTCCCGTCGTTCCGCANNSTATCAGCCAAACCTGTG
IS_Y22	NO:26	CCCGTCGTTCCGCAAACNNSCAGCCAAACCTGTGGAATTTC
IS_Q23	NO:27	GTCGTTCCGCAAACTATNNSCCAAACCTGTGGAATTTC
IS_R271	NO:28	CTGGATTTTGTACGCGACNNSCTGATGGAAGTTTATTTC
IS_W278	NO:29	CTGATGGAAGTTTATTTCNNSGCACTGGGTATGGCGCC
IS_F299	NO:30	CAAAGCTGTTACTAAAATGNNSGGTCTGGTGACGATCATC
IS_V302	NO:31	CTAAAATGTTTGGTCTGNNSACGATCATCGATGACGTG
IS_S408	NO:32	GAAAACGCCAGCGTTTCCTCCNNSGGTGTAGCGCTGCTGGC

[0350] A PCR reaction was set up in a 0.5ml thin-walled PCR tube following the manufacturer's protocol for the QUIKCHANGE® Multi Site-Directed Mutagenesis Kit (Stratagene): 1μl pET24 Kudzu vector (50ng/μl); 1μl Kudzu IS site-directed forward mutagenic primer (10μM); 2.5μl 10X QUIKCHANGE® Multi Reaction buffer; 1μl dNTP Mix, 1μl QUIKCHANGE® Multi enzyme blend (2.5U/μl); and 18.5μl distilled autoclaved water to provide a 25μl total reaction mix. The pET24 Kudzu SELs were amplified using the following conditions: 95°C, for 1 min (1^{st} cycle only), followed by 95°C for 1 min, 55°C for 1 min, 65°C for 12 min, and repeat cycling 29 times. Then the reaction mixture was subjected to *Dpn*I digestion (supplied with QUIKCHANGE® Multi Site-Directed Mutagenesis Kit) by addition of 1.5μl *Dpn*I restriction enzyme to each tube, and incubated at 37°C for 2 hours to digest the parental pET24D-kudzu vector. The *DpnI*-treated PCR reaction was then transformed into One Shot TOP10 competent cells (Invitrogen), plated onto LB agar plates containing 50μg/ml kanamycin, and incubated overnight at 37°C. The next day, 96 random colonies were picked and sequenced to identify a minimum of 15 of the possible 19 amino acid variants. Upon identification of the site-directed variants, each variant clone was then inoculated in a 5ml tube of LB + 50μg/ml kanamycin and grown overnight at 37°C with shaking (250 rpm). The following day plasmid DNA was purified using the QIAprep Spin Miniprep Kit (Qiagen). The variants were then transformed into One Shot BL21(λDE3) pLysS competent cells (Invitrogen) for protein expression screening, plated on LB agar plates containing 50μg/ml kanamycin and 30μg/ml chloramphenicol and incubated overnight at 37°C.

[0351] An alternative method for producing pET24D-Kudzu SELs in *E. coli* BL21(λDE3) pLysS cells was also successfully employed. The TOP10 competent cell transformants obtained from the *DpnI*-treated PCR reaction described above were harvested by applying 3ml of LB media to the top of the agar and resuspending the cells by scraping with a sterile plate spreader. The 3ml of pooled, resuspended cells were then used to inoculate a 25ml shake flask containing LB + 50μg/ml kanamycin. The pooled culture was then grown overnight at 37°C with shaking (250rpm). The following day plasmid DNA was purified from the pooled cultures using the QIAprep Spin Miniprep Kit (Qiagen). The pooled plasmid DNA was then transformed into One Shot BL21(λDE3) pLysS competent cells for protein expression screening as described above.

[0352] To make a master plate, the correct constructs are arrayed in quadruplicate in 96 well plates. One colony of the correct sequence is used to inoculate 4 wells and the plates are grown for several hours to overnight at 37°C in LB containing 50 μg/ml kanamycin with shaking (200 rpm). Sterile glycerol is added to the cultures to a final concentration of 15% (for a final total volume of 150-200 μl/well). The plates are then sealed using BREATHE-EASIER (EMS Catalog No. 70536-20) membranes and stored at -80°C.

EXAMPLE 9

Production and Purification of Isoprene Synthase Inclusion Bodies

[0353] Inclusion bodies containing kudzu isoprene synthase were formed when the enzyme is overexpressed in the presence of the chaperone GroELS in the strain BL21(λDE3). Briefly pETNHisKudzu (U.S. Application No. 61/013,574, herein incorporated by reference) was subcloned into pGro7 (Takara Catalog No. 3340) according to the manufacturer's instructions. A 500 mL of culture was grown essentially as described (Whittington et al., Proc Natl Acad Sci USA, 99:15375-15380, 2002). Despite the presence of chaperone and low temperature of cultivation the culture yielded predominantly inclusion bodies and only low levels of soluble active protein. The inclusion bodies were harvested using the IFOLD Protein Refolding System (Novagen Catalog No. 71552-3) according to the manufacturer's instructions. This procedure led to a high yield (>50 mg) of recombinant kudzu isoprene synthase. The purity of the inclusion body is shown in Figure 13. This preparation was used for the production of rabbit polyclonal anti-isoprene synthase antisera (Invitrogen).

EXAMPLE 10

High Throughput Biochemical Screen of Isoprene Synthase Variants

[0354] This example describes high throughput methods for the determination of isoprene synthase activity. Libraries of BL21(λDE3)pLysS *E.coli* host cells capable of expressing isoprene synthase variants are arrayed in 96-well plates and stored frozen at -80°C as 15% glycerol stocks as described above in Example 8. To analyze a plate of up to 96 variants, a replica stamp of the glycerol stock master plate is made with a 96-pin MULTI-BLOT floating pin tool (V&P Scientific Catalog No. VP 408AF) onto Luria broth agar containing appropriate antibiotic(s) (e.g., 30 μg/mL chloramphenicol, 50 μg/mL kanamycin). The replica plate is incubated over night at 30°C to allow growth of bacterial patches. Using the same floating pin replicator a 96-square deep well plate containing 250 μL of TM3 medium supplemented with 0.08% Biospringer yeast extract and 1% glucose plus antibiotics (30 μg/mL chloramphenicol, 50 μg/mL kanamycin) is inoculated from the agar plate and incubated overnight at 30°C. The recipe for TM3 broth is as follows: K_2HPO_4 (13.6 g/l) KH_2PO_4 (13.6 g/l), $MgSO_4$ * $7H_2O$ (2 g/l) Citric Acid Monohydrate (2 g/L) Ferric Ammonium Citrate (0.3 g/L) $(NH_4)_2SO_4$ (3.2 g/L) yeast extract (0.2 g/L) 1 ml of 1000x Trace Elements solution, pH adjusted to 6.8 with ammonium hydroxide qs to volume with sterile diH_2O and filter sterilized with a 0.22 micron filter. The recipe for 1000X Trace Elements solution is as follows: Citric Acids * H_2O (40 g/L), $MnSO_4$ * H_2O (30 g/L), NaCl (10 g/L), $FeSO_4$ * 7 H_2O (1 g/L), $CoCl_2$ * 6 H_2O (1 g/L), ZnSO * 7 H_2O (1 g/L), $CuSO_4$ * 5 H_2O (100 mg/L), H_3BO_3 (100 mg/L), $NaMoO_4$ * 2 H_2O (100 mg/L). Each component was dissolved one at a time in diH_2O, pH adjusted to 3.0 with HCl/NaOH, qs to volume and filter sterilized with a 0.22 micron filter. The overnight cultures are diluted with the same medium to an OD_{600} of 0.05 and grown in another 96-square deep well plate (Thomson Instrument, Catalog No. 951652C), with each well containing 600 μL of the dilution. The dilutions are grown at 30°C with shaking to an OD_{600} of 0.8 and are then induced with IPTG added to a concentration of 400 μM. The plate is grown for 5 hours and OD_{600} is determined for quality control and normalization.

[0355] A volume of 400 μL of culture is transferred into a new 96-well plate (Perkin Elmer, Catalog No. 6008290) and cells are harvested by centrifugation in a Beckman Coulter Allegra 6R centrifuge at 2500 x g. The pellet is resuspended in 200 μL of hypotonic buffer (5mM $MgCL_2$, 5mM Tris HCl, 5mM DTT pH 8.0) and the plate is frozen at – 80°C for a minimum time of 60 min. Cell lysate is prepared by thawing the plate and adding 32 μL of isoprene synthase DMAPP assay buffer (57mM Tris HCl, 19 mM $MgCl_2$, 74 μg/mL DNase I

(Sigma Catalog No. DN-25), $2.63x10^5$ U/mL of READYLYSE lysozyme solution (Epicentre Catalog No. R1802M), and 5 mg/mL of molecular biology grade BSA. The plate is incubated with shaking at 25°C for 30 min and then placed on ice. For isoprene production, an 80 μL aliquot of lysate is transferred to a 96-deep well glass plate (Zinsser Catalog No. 3600600) and 20 μL of a 10 mM DMAPP solution in 100mM $KHPO_4$, pH 8.2 (Cayman Chemical Catalog No. 63180) is added. The plate is sealed with an aluminum plate seal (Beckman Coultor Catalog No. 538619) and incubated with shaking at 30°C of 60 minutes. The enzymatic reactions are terminated by heating the glass block (70°C for 5 min). The headspace of each well is quantitatively analyzed as described in Example 5.

[0356] To determine protein concentration 5μL or more of lysate is run on precast gels (Invitrogen Catalog No. NP0301BOX) for western blot analysis after transfer to a nitrocellulose membrane (Invitrogen Catalog No. LC2000). The primary antibody employed is an anti-isoprene synthase antibody of Example 9. Primary antibody binding is followed by development with a secondary antibody labeled with Alexa Fluor 488 (Invitrogen Catalog No. A-11008) to permit quantitative signal determination. The western blot procedure was carried out as described by Invitrogen. The fluorescence signal was recorded with a Molecular Dynamics STORM instrument using the blue filter setting and quantitatively analyzed with the Molecular Dynamics IMAGEQUANT image analysis software package. Specific activity of the library members was calculated from the ratio of the amount of isoprene produced divided by either the A_{600} of the induction cultures or the isoprene synthase protein concentration determined by western blot. Isoprene synthase protein standard was calibrated by standard gel densitometry with BSA stained with Coomassie brilliant blue R250 serving as primary standard. Increased, decreased, or no change in specific activity of the entire library was tabulated for further analysis. Figure 14 provides graphs showing isoprene synthase activity of kudzu site evaluation library (SEL) members for positions Y22, A20, and S408. Most members show highly decreased activity relative to wild type, while conservative substitutions show a lesser decrease in activity. . Activity of variant A20G approximates that of the wild type kudzu enzyme, indicating that it is a candidate partner for a combinatorial mutant. Interestingly, variant S408D of library S408 showed an increase in activity compared to wild type thus providing another candidate partner for a combinatorial mutant.

Example 11

Isoprene Synthase Truncations

[0357] This example describes the identification of the amino acid sequence of the protein in the lower band of the doublet seen in purified poplar IspS preparations (see Figure 21). A series of N-terminally truncated IspS molecules based on putative cleavage sites identified by mass spectrometry was also generated. A shorter N-terminal truncation of IspS (the "MEA" truncation in pDu39, see below) was also generated, to examine the effect of further truncation on IspS activity (Williams DC, McGarvey DJ, Katahira EJ, Croteau R (1998) Biochemistry 37:12213–12220).

I. Construction of an N-terminally 6XHis-tagged IspS (in pDu27) for protein purification:

[0358] The full length *P. alba* IspS from the template P. alba pET24a (Figures 19 and 20) was prepared by PCR. The following PCR reaction was prepared: 1µl (Template)-P. alba pET24a, 5 µl 10X PfuUltraII Fusion buffer, 1 µl dNTP's (10 mM), 1µl primer (50 µM) primer F-(MCM219), 1 µl primer (50 µM) primer R-(MCM182), 41 µl diH_2O and 1 µl of PfuUltra II Fusion DNA Polymerase (Stratagene). PCR cycling parameters were as follows: 95 °C 1 min., 95 °C 1 min, 55 °C 20 sec., 72 °C 27 sec. for 29 cycles followed by 72 °C 3 min and 4 °C until cool, using an Eppendorf Mastercycler. The PCR product was gel extracted and purified, using 0.8% E-gel (Invitrogen) and Qiagen QIAquick Gel Extraction and QIAprep Spin Miniprep kits, according to the manufacturer's recommended protocol. A 3 µl aliquot of purified product was ligated to the pET200D/TOPO vector (Invitrogen), according to the manufacturer's protocol. The reaction was incubated for 5 minutes at room temperature, and the 6 µl topoisomerase mixture was then transformed into *E. coli* Top10 chemically competent cells (Invitrogen) according to the manufacturer's protocol. Transformants were selected for on LB plates containing kanamycin (50 µg/ml) (Kan50), and incubated at 37 °C overnight. Five colonies were picked and screened using PuReTaq Ready-To-Go PCR Beads (Amersham) using the T7 Forward and MCM182 primers. Clones harboring inserts of the correct size were further verified by sequencing using the T7 Forward and T7 Reverse primers (Quintara Biosciences). One construct, pDu27 (Figures 16-18), was chosen for further study. A 1 µl aliquot of the plasmid preparation was transformed into BL21(λDE3)*pLysS* (Invitrogen) according to the manufacturer's protocol. Transformants were selected for on LB plates containing Kan50+ and chloramphenicol (35 µg/ml) (Cm35) and incubated at 37 °C overnight. The resulting strain was used for expression and purification of N-terminally 6XHis-tagged P. alba IspS.

[0359]

II. Purification of 6XHis-tagged IspS

Expression of 6XHis-tagged IspS

[0360] N-terminally 6XHis-tagged IspS was expressed and purified from strain MD08-99. The growth procedure is suitable for histidine tagged enzymes expressed in BL21(λDE3)*pLysS* cells. A 10 ml of overnight culture was prepared for each 1L of planned growth. The appropriate antibiotics (50 mg/ml kanamycin, 50 mg/ml chloramphenicol, and/or 50 mg/ml Carbenecillin) was added to 10 ml of LB medium in a 25 ml flask and was inoculated with 1 colony from a fresh plate of cells or directly from glycerol frozen cell stock. Cultures were grown at 30 °C overnight with shaking at ~220 rpm. Day cultures were prepared in 1 liter of LB medium with appropriate antibiotics for each culture. Each 1L day culture was inoculated with 10 ml of overnight culture and grown at 30-37 °C with shaking at ~220 rpm until the OD_{600} reached ~0.4-0.6. Day cultures were then induced with 400 μM IPTG and allowed to continue growing at 30°C with shaking at 220 rpm for ~5-6 hours. Cells were then harvested by centrifugation at 10,000 x g for 10 min, 4 °C. Following Harvest, cells were used directly or stored at -80°C until ready to process.

Purification of 6XHis-tagged IspS

[0361] For purification of histidine tagged enzymes from BL21(λDE3)pLysS cells, cells were gently resuspended in fresh Lysis buffer (Lysis buffer: Ni wash buffer + 0.5 mM PMSF, 0.01% Tween-20, 1 mg/ml lysozyme, 0.2 mg/ml DNaseI; Ni wash buffer: 50 mM NaH_2PO_4, 300 mM NaCl, 20 mM Imidazole, pH 8.0). Approximately 40-50 ml of lysis buffer was used per 1L of cell pellet. Cells were then incubated on ice for approximately 30 min. The cell suspension was then lysed fully by passing 2-3 times through a french pressure cell (large french press cell at 1200 psi/High setting) until lysate started to look clear. A sample of the lysate was saved for activity assay and gel analysis (~100 μl). The lysate was then clarified by centrifuging the lysate at 30,000xg for 30 min, 4°C in a Sorvall Discovery 90SE ultracentrifuge. The supernatant was removed and retained. A sample of the "clarified lysate" was saved for activity assay and gel analysis (~100 μl).

[0362] The clarified lysate was run over HisTrap HP columns (GE Healthcare) using a gradient from 0-100% Ni buffer B. Samples were then analyzed by SDS-PAGE gel (4-12% gel NUPAGE, Invitrogen) according to manufacturer's directions. Desired fractions were concentrated on spin filters (Vivaspin-20, Sartoris,) and then desalted over a HiPrep 26/10

Desalting column (GE heathcare) packed with Sephadex G25 resin. The G-25 buffer consisted of 50 mM HEPES, 50 mM NaCl, and 1 mM DTT, pH 7.4. The desired sample was then purified over a HiTrap Q HP column (GE) using a gradient elution from 0% Q seph buffer A to 100% Q seph buffer B (Q seph buffer A: 50 mM Tris, 0.05 M NaCl, 1 mM DTT, pH 7.6 and Q seph buffer B: 50 mM Tris, 1.0 M NaCl, 1 mM DTT, pH 7.6). Fractions containing the desired protein were analyzed and concentrated. Sample buffer was then exchanged into 50 mM HEPES, 50 mM NaCL, pH 7.4 with 1 mM DTT by passing the sample over a Hi Prep 26/10 Desalting column (GE heathcare) packed with Sephadex G25 resin. A final polishing step of Gel filtration was used when necessary. The sample was passed through a Hi Load 26/60 Superdex 200 prep grade (GE) in gel fitration buffer: (50 mM HEPES, 150 mM NaCl, 1mM DTT, pH 7.4). Fractions were then analyzed and concentrated. The samples were then stored at -80 °C. For preparation for analysis of the band, the sample is run on an SDS-PAGE gel (4-12% NUPAGE gel, Invitrogen), stained and the desired band excised and processed as described below.

III. Mass Spectrometry of Isoprene Synthase

Sample preparation

[0363] An In-Gel Digestion and LCQ-Deca Mass Spectrometry Procedure was utilized (Modified Rosenfeld in-gel Digest Protocol) (Rosenfeld *et al*, Anal. Biochem. (1992) 203, 173-179; Hellman *et al*, Anal Biochem, (1995) 224, 451-455). The purified sample of Isoprene synthase was run on a 4-12% SDS-PAGE (NUPAGE, Invitrogen) and stained with Coomassie Brilliant Blue R-250 (Thermo Scientific) or SimplyBlue Safe Stain (Invitrogen). Band(s) of interest were excised from the gel and destained. Each gel slice was diced into small pieces ~1 mm x 1mm and placed into 0.65 mL "slick" (siliconized) tubes from PGC Scientific. Approximately 100µL of 25mM NH_4HCO_3/50% ACN/H_2O was added to each tube and vortexed for 10 min. Supernatants were extracted and discarded. These steps were repeated twice. Then gel pieces were then run in a Savant SpeedVac to dryness (~ 20 to 30 min).

[0364] Samples were then reducted and alkylated. For reduction, 25 µL (or enough to cover) of 10 mM DTT in 25 mM NH_4HCO_3 (prepared fresh) were added to dried gels. Tubes were then vortexed and spun briefly. Reactions were incubated at 50 °C for 1 hour. For alkylation, supernatants were removed and 25 µL or more of 55 mM iodoacetamide (IAA) in 25 mM NH_4HCO_3 were added to the gel. Reaction tubes were vortexed and spun briefly

again. Reactions were allowed in dark for 1 hour at room temperature. Supernatants were removed and gels were washed with ~ 100 µL of 25mM NH_4HCO_3/50% ACN/H_2O, by vortexing for 10 min and briefly spinning. Supernatant were removed and the wash step was repeated once. Gel pieces were then dried in a SpeedVac (~ 15 -30 min).

[0365] Digestion buffer was prepared by adding 400 µL of 0.1% n-octyl B-D-glucopyranosidase water to 100 uL of 8M Urea. 400 uL of this digestion buffer was added to 20 ug of freshly prepared Trypsin. 0.05 µg/µL of sequencing-grade Trypsin was prepared from one vial of 20 µg sequencing grade trypsin (Promega) that was dissolved into 400 uL of 1.6 M Urea solution. Trypsin enzyme solution was added enough to cover gel pieces. Tubes were covered with parafilm and incubated at 37 °C overnight (16-20 hrs). It was ensured that there is a little extra buffer above the gel.

[0366] Peptides were extracted from gels by briefly vortexing and spinning the digest. The digest solution was transferred with gel loading tips into a 0.65 mL siliconized tube. 50 µL (enough to cover) of 50% ACN/0.1% FA/H_2O were added to the gel pieces and samples were vortexed for 10 min, spun, and then sonicated for five min. Extracted peptides were pooled together in one tube. Extraction steps were repeated two to three more times until the gel pieces became white in appearance and shrank in size. Extracted digests were vortexed, spun and dried in a Speed Vac to a volume of 55 µL. In cases where the volume was less than 55 µL, enough 0.1% FA was added to make up a final volume of 55 µL.

Mass Spectrometry

[0367] The sample was injected onto a Thermofinnigan (San Jose, CA) LCQ-Deca electrospray ionization (ESI) ion-trap mass spectrometer. A Vydac C18 column (5µ, 300A, 0.2 x 150 mm, Michrom Bioresources, Auburn, CA) was used with a flow rate of 200 µL/min. The injection volume was 50 uL, and was filtered through an on-line trapping cartridge (Peptide CapTrap, Michrom Bioresources, Auburn, CA) before loading onto the column. Separation of the in-gel digest was performed with the following gradient (Solvent A: 0.1% trifluoroacetic acid in H2O (J.T. Baker, Phillipsburg, NJ), Solvent B: 0.08% trifluoroacetic acid in acetonitrile (J.T. Baker, Phillipsburg, NJ)):

Table 11-1. Gradient Table

	min	A%	B%

0	0.00	100	0
1	10.00	86	14
2	16.00	81	19
3	20.00	78	22
4	21.00	77	23
5	22.00	75	25
6	24.00	73	27
7	32.00	69	31
8	34.00	66	34
9	37.00	64	36
10	47.00	60	40
11	50.00	30	70
12	55.00	100	0
13	60.00	100	0
14	65.00	100	0
15		100	0

Mass Spectrometry Results

[0368] An aliquot of 6.4 µg of protein was loaded into 5 lanes on a 4-12% bis-tris NUPAGE gel (Invitrogen), MOPS buffer, 50 min run. As described above, the gel was stained for 2 minutes, and then de-stained for 15 minutes. The gel was washed in H_2O, then all bands were excised, cut into small pieces, and destained. Gel pieces were reduced and alkyated with DTT/IAA for 1 hour each at 52 °C and RT, respectively. Trypsin was added for an overnight digestion. Extracted peptides were run on the LCQ-Deca. Figures 21 and 22 show the results for the mass spectrometry analysis. The lower doublet band (in Figure 21) is identified as IspS. Figure 22 shows that N-terminal truncations were observed after amino acids 39, 40, 42, and 44 (according to the peptide sequence of the N-terminally His-tagged IspS protein in pDu27). The C-terminus of IspS is intact.

IV. Construction of N-terminally truncated IspS variants:

[0369] All truncated constructs without affinity tags were generated using the QuickChange Site-directed Mutagenesis kit (Stratagene) using the template P. alba pET24a

for PCR amplification. Approximately 50 ng of template DNA was used for amplification (with an Eppendorf Mastercycler Gradient PCR Machine) of the mutagenized PCR product with the Forward (For) and Reverse (Rev) primer pairs that correspond to each relevant truncation (QC MSV For and QC MSV Rev, for example, see Table 11-2). The following PCR reaction mixtures were used: 1 µl P. alba pET24a, 5 µl 10X PfuUltra HF buffer, 1 µl dNTP's, 1 ul (50 µM) primer-For (*e.g.* QC MSV For), 1 µl (50 µM) primer-Rev (*e.g.* QC MSV Rev), 2 µl DMSO, 39 µl diH_2O, 1 µl PfuUltra HF Polymerase (Stratagene). The following PCR cycling parameters were used: 95 °C 1 min, 95 °C 30 sec., 55 °C 1 min., 68 °C 7.3 min. for one cycle followed by 95 °C 30 sec., 55 °C 1 min., 68 °C 7.3 min for a total of 18 cycles and then followed by 4 °C. The PCR products were treated with 1-2 µl of *Dpn*I (Roche) for 1-3 hour at 37 °C. A 5 µl aliquot of the *Dpn*I treated products was visualized on a 0.8% E-gel (Invitrogen). A 1 µl aliquot of each product was transformed into chemically competent *E. coli* Top10 cells (Invitrogen) according to the manufacturer's protocol. Transformants were selected for on LB medium containing kanamycin at a concentration of 50 µg/ml (Kan50), and incubated overnight at 37 °C. Five colonies of each transformation were selected and grown to stationary phase in 3 ml liquid LB Kan50. Plasmids were purified using a Qiagen miniprep kit according to the manufacturer's recommended protocol. Purified plasmids were sequenced (by Quintara Biosciences) with T7 Forward and Reverse primers, and confirmed for their respective truncation. The resulting plasmids (pDU39 through pDU43, see Table 11-4, Figures 23-34) were transformed into chemically competent *E. coli* BL21(λDE3) *pLysS* (Invitrogen) according to the manufacturer's recommended protocol. Table X describes the strains used for expression of truncated IspS enzymes.

[0370] Constructs with affinity (6XHis) and proteolysis (TEV, Tobacco Etch Virus) tags were generated using P. alba pET24a as a template for PCR reactions. PCR reaction mixtures were prepared as follows: 1ul (P. alba pET24a), 5ul 10X PfuUltraII Fusion buffer, 1ul dNTP's (10 mM), 1ul primer (50 µM) Alba FL-NdeI-For or Alba TRC (MEA)-NdeI-F, 1ul primer (50uM) Alba FLTRC (+) TEV-R, 41 ul diH_2O and 1ul of PfuUltra II Fusion DNA Polymerase from Stratagene. PCR cycling parameters were as follows: 95 °C 1 min., 95 °C 30 sec., 55 °C 20 sec., 72 °C 25 sec. for one cycle and then repeating 95°C 30 sec., 55 °C 20 sec., 72 °C 25 sec. for an additional 28 cycles, followed by 72°C 3min and then 4 °C. After amplification and verification of the correct molecular weight of the product by visualization on 0.8% E-gel (Invitrogen), PCR products were digested with restriction enzymes *Nde*I and *Xho*I (Roche) for 2 hours at 37 °C, and then gel purified using the Qiaquick Gel Purification system (Qiagen) according to the manufacturer's recommended protocol. 3 µl of purified

product was ligated to pET-24a (Invitrogen) that was digested with *Nde*I and *Xho*I (Roche), gel purified and dephosphorylated (using SAP, shrimp alkaline phosphatase) (Promega) according to the manufacturer's recommended protocols. T4 ligase (NEB) was used for the ligation reaction, which was incubated overnight at 16 °C. The ligation reaction was dialyzed into water for 30 min., and 2 µl of the reaction were used to electroporate MCM331 (see below) competent cells. Cells were allowed to recover at 30 °C for 2 hours, and then selected on Kan50 with 5 mM (R)-(-)-Mevalonolactone (MVA) (Sigma) spread onto the plate. Positive transformants were inoculated into 3 ml of liquid LB Kan50, and plasmids were isolated using the QIAPrep Spin miniprep kit (Qiagen). Inserts were verified by restriction digestion using *Nde*I and *Xho*I (Roche) and positive clones were sequenced (Quintara Biosciences) with T7 promoter and T7 terminator sequencing primers. 1 µl of each plasmid (see Table 11-4 for plasmid description and Figures 35-39) was transformed into chemically competent *E. coli* BL21(λDE3) pLysS (Invitrogen) according to the manufacturer's recommended protocol. Transformants were selected on LB Kan50 + Cm35 (Chloramphenicol 35 ug/ml) plates and incubated at 37 °C. See Table 11-5 for a description of all expression strains.

[0371] Strain MCM331 was prepared as follows. A synthetic operon containing mevalonate kinase, mevalonate phosphate kinase, mevalonate pyrophosphate decarboxylase, and the IPP isomerase was integrated into the chromosome of *E. coli*. If desired, expression may be altered by integrating different promoters 5' of the operon.

i) Target vector construction

[0372] The attTn7 site was selected for integration. Regions of homology upstream (attTn7 up) (primers MCM78 and MCM79) and downstream (attTn7 down) (primers MCM88 and MCM89) were amplified by PCR from MG1655 cells. A 50 µL reaction with 1 µL 10 µM primers, 3 µL ddH_2O, 45 µL Invitrogen Platinum PCR Supermix High Fidelity, and a scraped colony of MG1655 was denatured for 2:00 at 94 °C, cycled 25 times (2:00 at 94 °C, 0:30 at 50 °C, and 1:00 at 68 °C), extended for 7:00 at 72 °C, and cooled to 4 °C. This resulting DNA was cloned into pCR2.1 (Invitrogen) according to the manufacturer's instructions, resulting in plasmids MCM278 (attTn7 up) and MCM252 (attTn7 down). The 832 bp *Apa*I-*Pvu*I fragment digested and gel purified from MCM252 was cloned into *Apa*I-*Pvu*I digested and gel purified plasmid pR6K, creating plasmid MCM276. The 825bp *Pst*I-*Not*I fragment digested and gel purified from MCM278 was cloned into *Pst*I-*Not*I digested and gel purified MCM276, creating plasmid MCM281.

ii) Cloning of lower pathway and promoter

[0373] MVK-PMK-MVD-IDI genes were amplified from pTrcKKDyIkIS with primers MCM104 and MCM105 using Roche Expand Long PCR System according to the manufacturer's instructions. This product was digested with *Not*I and *Apa*I and cloned into MCM281 which had been digested with *Not*I and *Apa*I and gel purified. Primers MCM120 and MCM127 were used to amplify CMR cassette from the GeneBridges FRT-gb2-Cm-FRT template DNA using Stratagene Pfu Ultra II. A PCR program of denaturing at 95 °C for 4:00, 5 cycles of 95 °C for 0:20, 55 °C for 0:20, 72 °C for 2:00, 25 cycles of 95 °C for 0:20, 58 °C for 0:20, 72 °C for 2:00, 72 °C for 10:00, and then cooling to 4 °C was used with four 50 uL PCR reactions containing 1uL ~10ng/μL template, 1 μL each primer, 1.25 μL 10mM dNTPs, 5 μL 10x buffer, 1 μL enzyme, and 39.75 μL ddH_20. Reactions were pooled, purified on a Qiagen PCR cleanup column, and used to electroporate water-washed Pir1 cells containing plasmid MCM296. Electroporation was carried out in 2 mM cuvettes at 2.5V and 200 ohms. Electroporation reactions were recovered in LB for 3 hr at 30 °C. Transformant MCM330 was selected on LA with CMP5, Kan50.

iii) Integration into *E. coli* chromosome

[0374] Miniprepped DNA (Qiaquick Spin kit) from MCM330 was digested with SnaBI and used to electroporate BL21(DE3) (Novagen) or MG1655 containing GeneBridges plasmid pRedET Carb. Cells were grown at 30 °C to ~OD1 then induced with 0.4% L-arabinose at 37 °C for 1.5 hours. These cells were washed three times in 4 C ddH_2O before electroporation with 2 μL of DNA. Integrants were selected on L agar with containing chloramphenicol (5 μg/ml) and subsequently confirmed to not grow on L agar + Kanamycin (50 μg/ml). BL21 integrant MCM331 and MG1655 integrant MCM333 were frozen.

Table 11-2. Primers

MCM219	caccatgcgttgtagcgtgtcca (SEQ ID NO:33)
MCM182	gggcccgtttaaactttaactagactctgcagttagcgttcaaacggcagaa (SEQ ID NO:34)
QC MSV For	gaaggagatatacatatgagcgtgtccaccgaaaatg (SEQ ID NO:35)
QC MSV Rev	cattttcggtggacacgctcatatgtatatctccttc (SEQ ID NO:36)
QC MVS For	gaaggagatatacatatggtgtccaccgaaaatgtgtc (SEQ ID NO:37)
QC MVS Rev	gacacattttcggtggacaccatatgtatatctccttc (SEQ ID NO:38)
QC MTE For	gaaggagatatacatatgaccgaaaatgtgtctttcac (SEQ ID NO:39)
QC MTE Rev	gtgaaagacacattttcggtcatatgtatatctccttc (SEQ ID NO:40)
QC MNV For	gaaggagatatacatatgaatgtgtctttcaccgaaac (SEQ ID NO:41)
QC MNV Rev	gtttcggtgaaagacacattcatatgtatatctccttc (SEQ ID NO:42)
QC MEA For	gaaggagatatacatatggaagctcgtcgttctgcg (SEQ ID NO:43)
QC MEA Rev	cgcagaacgacgagcttccatatgtatatctccttc (SEQ ID NO:44)
Alba FL-NdeI-For	gaaggagatatacatatgcgttgtagcgtg (SEQ ID NO:45)

Alba FLTRC (+) TEV-R	cccgcgcttactcgaggccctgaaaatacaggttttcgcg ttcaaacggcagaatcggtt (SEQ ID NO:46)
Alba TRC (MEA)-NdeI-F	gaaactgaaacccatatggaagctcgtcgttctgc (SEQ ID NO:47)

Table 11-3. Primers for construction of strain MCM331

MCM78	attTn7 up rev for integration construct	gcatgctcgagcggccgcTTTTAATCAAACATCCTGCCAACTC (SEQ ID NO:48)
MCM79	attTn7 down rev for integration construct	gatcgaagggcgatcgTGTCACAGTCTGGCGAAACCG (SEQ ID NO:49)
MCM88	attTn7 up forw for integration construct	ctgaattctgcagatatcTGTTTTTCCACTCTTCGTTCACTTT (SEQ ID NO:50)
MCM89	attTn7 down forw for integration construct	tctagagggcccAAGAAAAATGCCCCGCTTACG (SEQ ID NO:51)
MCM104	GI1.2 promoter – MVK	Gatcgcggccgcgcccttgacgatgccacatcctgagcaa Ataattcaaccactaattgtgagcggataacacaaggagg Aaacagctatgtcattaccgttcttaacttc (SEQ ID NO:52)
MCM105	aspA terminator – yIDI	Gatcgggccccaagaaaaaaggcacgtcatctgacgtgcc Ttttttatttgtagacgcgttgttatagcattcta (SEQ ID NO:53)
MCM120	Forward of attTn7: attTn7 homology, GB marker homology	aaagtagccgaagatgacggtttgtcacatggagtt ggcaggatgtttgattaaaagcAATTAACCCTCACTA AAGGGCGG (SEQ ID NO:54)
MCM127	Rev complement of 1.2 GI: GB marker homology(extra long), promoter, RBS, ATG	AGAGTGTTCACCAAAAATAATAACCTTTCCCGGTGCAgaa Gttaagaacggtaatgacatagctgtttcctccttgtgtt Atccgctcacaattagtggttgaattatttgctcaggatg tggcatcgtcaagggcTAATACGACTCACTATAGGGCTCG (SEQ ID NO:55)

Table 11-4. Plasmids for expression of IspS variants

MD09-161	pET24a-P.alba FL C-Term (+) TEV, His tag/MCM331
MD09-163	pET24a-P.alba TRC (MEA) C-Term (+) TEV, His tag/MCM331
pDu27	Alba-FL-pET200/D-TOPO
pDu39	Mtg pET24a-P.alba-MEA /Top10 (Untagged)
pDu40	Mtg pET24a-P.alba-MNV/Top10 (Untagged)
pDu41	Mtg pET24a-P.alba-MSV/Top10 (Untagged)
pDu42	Mtg pET24a-P.alba-MTE/Top10 (Untagged)
pDu43	Mtg pET24a-P.alba-MVS/Top10 (Untagged)

Table 11-5. Strains for expression of IspS variants

MD08-99	Alba-FL-pET200/D-TOPO (pDu27) in BL21 (λDE3) pLysS
MD09-165	BL21(λDE3)pLysS, pET24a-P.alba FL C-Term (+) TEV, His tag
MD09-167	BL21(λDE3) pLysS, pET24a-P.alba TRC (MEA) C-Term (+) TEV, His tag
MD09-173	BL21(λDE3)pLysS, pET24a-P.alba (MEA) Untagged (pDu39)
MD09-174	BL21(λDE3)pLysS, pET24a-P.alba (MNV) Untagged (pDu40)
MD09-175	BL21(λDE3)pLysS, pET24a-P.alba (MSV) Untagged (pDu41)

MD09-176	BL21(λDE3)pLysS, pET24a-P.alba (MTE) Untagged (pDu42)
MD09-177	BL21(λDE3)pLysS, pET24a-P.alba (MVS) Untagged (pDu43)

V. Biochemical Analysis of IspS Truncations

[0375] The relative activity of the various N-terminally truncated IspS enzymes was determined by DMAPP assay. The strains described above were analyzed via DMAPP assay in a 96-well plate. All strains were assayed in quadruplicate. The "Full Length" variant refers to the IspS enzyme expressed in BL21(λDE3) pLysS (Invitrogen) from the P. alba pET24a plasmid.

Table 11-6. DMAPP Assay of N-terminal Truncations

Activity Data				Avg	OD
Variant	**Average**	**Std Dev**	**%CV**	**OD_{600}**	**Normalized**
MD09-173	1125.6	93.7	8.3	5.2	217.6
MD09-174	118.6	8.0	6.7	5.2	22.8
MD09-175	1064.6	71.7	6.7	4.9	219.0
MD09-176	1179.1	64.7	5.5	4.9	238.7
MD09-177	831.7	89.6	10.8	4.9	168.2
Full Length	805.8	65.1	8.1	5.0	161.3

[0376] Results: Table X shows that when normalized for OD_{600}, strains MD09-173 (with plasmid pDu39), MD09-175 (pDu41), MD09-176 (pDu42), and MD09-177 (pDu43) all displayed higher DMAPP activity than the "Full Length" wild type IspS enzyme (in strain BL21(λDE3) *pLysS* with P. alba pET24a).

VI. Detailed Kinetic Analysis of the "MEA" Truncation in IspS

[0377] The relative specific activity was determined and the kinetics of "N-terminally truncated" *P. alba* isoprene synthases were examined compared to "Full length" *P. alba* isoprene synthases. Four strains expressing four different constructs were used in this analysis: BL21(λDE3) *pLysS* with P. alba pET24a; MD09-173; MD09-165; and MD09-167 (Strains described above in detail). These strains express "full length" *P. alba* IspS, "truncated" P. alba IspS (the MEA truncation), "full length" C-terminally TEV and His-tagged *P. alba* IspS, and "truncated" C-terminally TEV and His-tagged *P. alba* IspS, respectively. In the experiments described below, "truncated" refers specifically to the MEA variant of *P. alba* IspS.

[0378] All strains were inoculated into LB containing 30 mg/L chloramphenicol(Cm) and 50 mg/L kanamycin and grown overnight in 2 mL culture tubes at 37 °C. The overnight cultures were diluted 1:100 in 25 mL of LB broth containing 30 mg/L chloramphenicol(Cm) and 50 mg/L kanamycin the following morning and grown at 37 °C until OD~0.5. Each strain was grown in triplicate. The cultures were then induced with 400 uM IPTG and incubated at 30 °C for 4 hours. 20 mL of each culture were centrifuged at 3000 x g for 20 min. and the supernatant was discarded. The pellets were frozen at -80 °C overnight. Pellets were resuspended in 2 mL of a buffer containing 100 mM Tris, 100 mM NaCl, 0.25 mg/mL lysozyme and 0.25 mg/mL DNAase, pH 8. Cell suspensions were french pressed at 20,000 psi twice and the lysate was then centrifuged at 14000 x g for 20 minutes to yield cell free extract that was used for kinetic studies and protein concentration determination.

[0379] To measure specific activity, 5 μL of cell free extract from each strain was incubated with 5 mM DMAPP, 50 mM $MgCl_2$ in a buffer containing 100 mM Tris and 100 mM NaCl (pH 8) to a final volume of 100 μL for 15 min. at 30 °C in gas tight 2 mL vials. Reactions were terminated with the addition of 100 μL of 500 uM EDTA, pH 8. Samples were analyzed by GC-MS to determine the concentration of isoprene in the headspace of the vials.

[0380] To determine k_{cat} and K_M, 5 uL of cell free extract from each strain was incubated with DMAPP at concentrations ranging from 0.625 to 40 mM DMAPP in a buffer containing 100 mM Tris, 50 mM $MgCl_2$ and 100 mM NaCl (pH 8) to a final volume of 100 μL for 15 min. at 30 °C in gas tight 2 mL vials. Reactions were terminated with the addition of 100 μL of 500 mM EDTA, pH 8. Samples were analyzed by GC-MS to determine the concentration of isoprene in the headspace of the vials. Data were analyzed using Kaleidagraph and fit to following equation for uncompetitive substrate inhibition: $rate/E = k_{cat}*S/(K_M+S*(1+S/K_i))$. All data were run in triplicate with the exception of MD09-167 with 2.5 mM DMAPP which was run in duplicate.

[0381] Cell free extract was run on a Caliper microfluidic electrophoresis instrument (Caliper Life Sciences, Hopkinton, MA, USA) in order to quantify the amount of isoprene synthase in each sample. The microfluidic chip and protein samples were prepared according to the manufacturer's instructions (LabChip® HT Protein Express, P/N 760301). Culture lysates were prepared in 96-well mictrotiter plates by adding 50 mM Tris pH 8.0 containing 0.1% Tween 20, 0.1 mg/ml lysozyme, 1.0 ug/ml DNAse at room temperature for 30 minutes, followed by centrifugation. Supernatants were then transferred to another 96 well plate and stored at -20 ºC until use, when they were thawed at room temperature for 30 minutes. After

shaking briefly, the 2 µl of each culture sample was transferred to a 96-well PCR plate (Bio-Rad, Hercules, CA,USA) containing 7 µl samples buffer (Caliper) followed by heating the plate to 90 °C for 5 minutes on a thermostatically controlled plate heater. The plate was allowed to cool before adding 35 µl water to each sample. The plate was then placed in the instrument along with a protein standard supplied and calibrated by the manufacturer. The instrument functions by mixing the sample with a fluorescent dye that attaches non-covalently to the proteins, followed by electrophoresis through a gel matrix. As the proteins move past a focal point in the chip, the fluorescence signal is recorded and the protein concentration is determined by quantitating the signal relative to the signal generated by a calibrated set of protein standards.

Table 11-7. k_{cat} and K_M and specific activity values for isoprene synthases

Isoprene Synthase	k_{cat} ± S.D. (s^{-1})	K_M ± S.D.(mM)	K_i ± S.D.(mM)	S.A. (nmol/mg/min)
Full Length	0.72±0.09	2.4±0.3	15.7±0.2	420±60
Truncated	1.5±0.2	1.8±0.2	9.8±0.9	800±100
MD09-165	0.8±0.1	2.4±0.5	19±4	440±80
MD09-167	1.1±0.3	2±1	8.7±0.9	610±60

[0382] Parameters were determined by fitting the following uncompetitive substrate inhibition equation to data obtained for rate/[E] vs. [DMAPP]:

$$\frac{rate}{[E]} = \frac{k_{cat} * [S]}{K_M + [S] * \left((1 + \frac{[S]}{K_i} \right)}$$

[0383] The specific activities (S.A.) were calculated for reactions containing 5 mM DMAPP, 50 mM $MgCl_2$, 100 mM Tris, 100 mM NaCl, and 2.5-4.5 µg isoprene synthase from the supernatant of whole cell lysate. Reactions were performed at 30 ºC for 15 minutes in triplicate using independently grown cultures.

Results/Discussion:

[0384] The specific activity of each protein was determined (Figure 40 and Table 11-7). The specific activity of truncated isoprene synthase was approximately 2-fold greater than the specific activity of full length isoprene synthase. The C-terminally His-tagged full length isoprene synthase yielded approximately the same specific activity as the full length isoprene

synthase. The C-terminally His-tagged truncated isoprene synthase gave a specific activity that was less than the non-tagged truncated isoprene synthase, but greater than the specific activity of both full length isoprene synthases.

[0385] The rate of conversion of DMAPP to isoprene was analyzed over a range of DMAPP concentrations in order to determine the k_{cat} and K_M parameters of the enzymes (Figures 41 and 42 and Table 11-7). The enzymes all exhibited rate profiles consistent with uncompetitive substrate inhibition by DMAPP. The K_i for the full length constructs was greater than the K_i for truncated constructs as determined by altering K_i and observing the best fit (R-value) to the data (data not shown). All data has been fit to a K_i of 10 mM in the figures in this document. The K_Ms of truncated isoprene synthase decreased relative to the full length isoprene synthases. Therefore, as the substrate concentration decreases the ratio between the isoprene synthase activity of the truncated isoprene synthase to the full length isoprene synthase will increase (Figure 43). The k_{cats} of truncated isoprene synthases increased relative to the full length isoprene synthases. This results in greater isoprene synthase activity for the truncated isoprene synthases than the full length isoprene synthases at all substrate concentrations (Figure 43). The ratio of the isoprene synthase activity of the truncated isoprene synthase to the full length isoprene synthase at varying DMAPP levels was determined (Figure 43).

[0386] Conclusions: "Truncated" isoprene synthases exhibit increased k_{cat} values and decreased K_M values with respect to the catalysis of the conversion of DMAPP to isoprene compared to "full length" isoprene synthases. The specific activity of "truncated" isoprene synthases is increased relative to the specific activity of "full length" isoprene synthases. The most active isoprene synthase was non-tagged truncated isoprene synthase "MEA" variant (in strain MD09-173). The truncated isoprene synthase may increase the isoprene synthase activity in organisms used for production of isoprene compared to the full length isoprene synthase.

Example 12

Isoprene Synthase Enrichment – Relief of DMAPP Toxicity

[0387] This example identifies residue changes within IspS that confer better activity to the enzyme through kinetic improvement, increased expression, increased solubility, or any other means by which DMAPP is more effectively converted to isoprene by Isoprene Synthase. This procedure allows for the relief of cytotoxic intracellular levels of DMAPP by expression of improved IspS variants. In a population of cells expressing a heterogeneous mixture of

IspS variants, the best enzymes should allow for better growth of their host strain, and should be enriched in the mixed population.

I. Strain Construction

[0388] Construction of Strains MCM518-521 and 528-531 in which Lambda promoters drive integrated mKKDyI was as follows. Primers MCM120 and MCM224 (Table 12-1) were used to amplify the resistance cassette from the GeneBridges FRT-gb2-Cm-FRT template using Stratagene Herculase II Fusion kit according to the manufacturer's protocol. Four 50 μL reactions were cycled as follows: 95°C, 2 min; (95 °C, 20 sec, 55 °C, 20 sec, 72 °C, 1 min) for 30 cycles; 72 °C, 3 min; and 4°C until cool. The four reactions were pooled and purified on a Qiagen PCR column according to the manufacturer's protocol and eluted with 60 μL EB at 55 °C.

[0389] Plasmid pRedET-carb (GeneBridges) was electroporated into MCM446. Transformants were recovered by shaking for one hour in SOC (Invitrogen) at 30 °C and then selected on LB containing carbenicillin (50 μg/ml) (carb50) plates at 30 °C overnight. A carbenicillin resistant colony was frozen as MCM508 (Table 12-2).

[0390] Strain MCM508 was grown from a fresh streak in 5mL LB/carb50 at 30 °C to an OD_{600} of ~0.5. 40mM L-arabinose was added and culture was incubated at 37 °C for 1.5 hrs. Cells were harvested and electroporated with 3 μL of purified amplicons as previously, and then recovered in 500 μL SOC at 37 °C for 1.5-3hrs. Transformants were selected on LB/kan10 plates at 37 °C.

[0391] Recombination of the amplicon at the target locus was confirmed by PCR with primers GB-DW and MCM208. The resulting amplicons were sequenced to identify four clones with the sequences below. Carbenicillin-sensitive clones were frozen as strains MCM518-521.

[0392] MCM518-521 were restreaked on LB kan10 plates and grown overnight at 37 °C.

[0393] Strains MCM518-521 were cultured in LB/kan10 at 37 °C and then electrotransformed with plasmid pCP20 (Datsenko KA, Wanner BL. One-step inactivation of chromosomal genes in *Escherichia coli* K-12 using PCR products. Proc Natl Acad Sci U S A. 2000 Jun 6;97(12):6640-5). Cells were recovered in 500 μL SOC, shaking at 30 °C for 1hour. Transformants were selected on LB/carb50 plates at 30 °C overnight. The following morning a colony from each transformation was grown at 30 °C in liquid LB/carb50 until visibly turbid. The culture was then shifted to 37 °C for at least 3 hrs. Cells were streaked from this culture onto LB plates and grown overnight at 37 °C.

[0394] The following day colonies were patched to LB, LB/carb50 and LB/kan10. Clones that grew on neither carb50 nor kan10 and were cultured in liquid LB from the patch on LB and frozen as MCM528-531.

DNA Sequences

[0395] These assemblies include the new promoters inserted on the chromosome in strains MCM518-521, as well as the very beginning of the mMVK ORF. Upstream of these assemblies is sequence from the GeneBridges FRT-gb2-Cm-FRT cassette. Downstream is the remainder of the mMVK ORF and then the rest of the lower MVA pathway integron from strain MCM508.

MCM518

aaagaccgaccaagcgacgtctgagagctccctggcgaattcggtaccaataaaagagcttt
attttcatgatctgtgtgttggttttgtgtgcggcgcggaagttcctattctctagaaagt
ataggaacttcctcgagccctatagtgagtcgtattaaattcatataaaaaacatacagata
accatctgcggtgataaattatctctggcggtgttgacataaataccactggcggtgatact
gagcacatcagcaggacgcactgaccaccatgaaggtgcaaaggaggtaaaaaaacatggta
tcctgttctgcgccgggtaagatttacctgttcggtgaacacgccgtagtttatggcgaaac
tgcaattgcgtgtgcggtggaactgcgtacccgtgttcgcgcggaactcaatgactctatca
ctattcagagc (SEQ ID NO:56)

MCM519

aaagaccgaccaagcgacgtctgagagctccctggcgaattcggtaccaataaaagagcttt
attttcatgatctgtgtgttggttttgtgtgcggcgcggaagttcctattctctagaaagt
ataggaacttcctcgagccctatagtgagtcgtattaaattcatataaaaaacatacagata
accatctgcggtgataaattatctctggcggtgttgacctaaataccactggcggtgatact
gagcacatcagcaggacgcactgaccaccatgaaggtgcaaaggaggtaaaaaaacatggta
tcctgttctgcgccgggtaagatttacctgttcggtgaacacgccgtagtttatggcgaaac
tgcaattgcgtgtgcggtggaactgcgtacccgtgttcgcgcggaactcaatgactctatca
ctattcagagc (SEQ ID NO:57)

MCM520

aaagaccgaccaagcgacgtctgagagctccctggcgaattcggtaccaataaaagagcttt
attttcatgatctgtgtgttggttttgtgtgcggcgcggaagttcctattctctagaaagt

ataggaacttcctcgagccctatagtgagtcgtattaaattcatataaaaaacatacagata
accatctgcggtgataaattatctctggcggtgttgacctaaataccactggcggtgatact
gagcacatcagcaggacgcactgaccaccatgaaggtgcaaaggtaaaaaaacatggtatcc
tgttctgcgccgggtaagatttacctgttcggtgaacacgccgtagtttatggcgaaactgc
aattgcgtgtgcggtggaactgcgtacccgtgttcgcgcggaactcaatgactctatcacta
ttcagagc (SEQ ID NO:58)

MCM521 (in strains MCM531 and MD09-171)

aaagaccgaccaagcgacgtctgagagctccctggcgaattcggtaccaataaaagagcttt
attttcatgatctgtgtgttggttttgtgtgcggcgcggaagttcctattctctagaaagt
ataggaacttcctcgagccctatagtgagtcgtattaaattcatataaaaaacatacagata
accatctgcggtgataaattatctctggcggtgttgacgtaaataccactggcggtgatact
gagcacatcagcaggacgcactgaccaccatgaaggtgcaaaggaggtaaaaaaacatggta
tcctgttctgcgccgggtaagatttacctgttcggtgaacacgccgtagtttatggcgaaac
tgcaattgcgtgtgcggtggaactgcgtacccgtgttcgcgcggaactcaatgactctatca
ctattcagagc (SEQ ID NO:59)

[0396] The neo-PL.2-mKKDyI (from MCM521) was transduced into BL21(λDE3) to generate strain MD09-171. A P1 lysate of MCM521 was made and transduced into BL21(λDE3) according to standard molecular biology techniques (Miller, A Short Course in Bacterial Genetics). Transductants were selected on Kan20 LB medium plates. Positive colonies were further verified by PCR to confirm the presence of PL.2-mKKDyI in the BL21(λDE3) strain. 1 µl of pCP20 plasmid was then transformed into this strain and selected for on LB + Carb50 and incubated at 30 °C. Positive transformants were subsequently streaked on an LB plate and incubated at 37 °C for loss of the pCP20 plasmid. To confirm the loss of the neomycin (kanamycin) resistance marker, colonies that grew at 37 °C were patched onto LB Kan20, LB Carb50, and plain LB plates. The strains with integrated PL.2 mKKDyI without the kanamycin resistance marker that have lost pCP20 should be sensitive to kanamycin and carbenicillin. 4 KanS CarbS were used to check by PCR for the presence of mKKDyI in BL21(λDE3) with the parental BL21(λDE3) strain as a control. Once PCR confirmed the presence of mKKDyI, the resulting strain was transformed with 1 µl of the pLysS plasmid (Invitrogen). The resulting strain, MD09-171, was used for the enrichment experiments described below.

Table 12-1. Primers used for strain construction

MCM120	aaagtagccgaagatgacggtttgtcacatggagttggcaggatgtttgat taaaagcaattaaccctcactaaagggcgg (SEQ ID NO:60)
MCM208	gctctgaatagtgatagagtca (SEQ ID NO:61)
MCM224	taaatcttacccggcgcagaacaggataccatgttttttacctcctttgc accttcatggtggtcagtgcgtcctgctgatgtgctcagtatcac cgccagtggtatttangtcaacaccgccagagataatttatcaccgcagat ggttatctgtatgtttttttatatgaatttaatacgactcactatag ggctcg (SEQ ID NO:62)
GB-DW	aaagaccgaccaagcgacgtctga (SEQ ID NO:63)
MCM161	caccatggtatcctgttctgcg (SEQ ID NO:64)
MCM162	ttaatctactttcagaccttgc (SEQ ID NO:65)
MCM143	aggaggtggtctcaaatgactgccgacaacaatagta (SEQ ID NO:66)
MCM144	aggaggtggtctcagcgctctgcagttatagcattctatgaatttgcctg (SEQ ID NO:67)

Table 12-2. Strains

Strain	Description	Parent
MCM508	BL21 gi1.6-mKKDyI + predet.-carb	MCM446
MCM518	BL21 neo-PL.6-mKKDyI, clone10	MCM508
MCM519	BL21 neo-PL.0-mKKDyI, clone11	MCM508
MCM520	BL21 neo-PL.0-mKKDyI (bad RBS in front of mMVK), clone13	MCM508
MCM521	BL21 neo-PL.2-mKKDyI, clone15	MCM508
MCM528	BL21 PL.6-mKKDyI, loopedout	MCM518
MCM529	BL21 PL.0-mKKDyI, loopedout	MCM519
MCM530	BL21 PL.0-mKKDyI (bad RBS in front of mMVK), loopedout	MCM520
MCM531	BL21 PL.2-mKKDyI, loopedout	MCM521
MD09-171	BL21 (λDE3) PL.2-mKKDyI, loopedout + pLysS	MCM521

II. Growth Inhibition of MCM531 by Mevalonic Acid

[0397] An overnight culture of MCM531 (see strain description) was back-diluted to an OD_{600} of 0.05 (this corresponds to an OD_{600} of approx 0.005 in a 96-well plate reader) (SpectraMax M2, Molecular Devices). The diluted culture was then aliquotted into separate wells in a 96-well deep-well plate into standard TM3 medium (13.6 g K_2PO_4, 13.6 g KH_2PO_4, 2.0 g $MgSO_4*7H_2O$) supplemented with 1% glucose and 0.8 g/L Biospringer yeast extract (1% Yeast extract final))with 0, 1, 5, 10, 15 or 20 mM MVA added. Figure 44 shows the growth curve of MCM531 in the various concentrations of MVA. Each MVA concentration was assayed in quadruplicate, error bars were negligible. Figure 44 shows that

MCM531 was severely inhibited for growth at concentrations of 5 mM MVA and higher.

III. Mutagenesis of IspS and Selection/Enrichment Assay

[0398] To generate a randomly mutagenized IspS open reading frame, the GeneMorph II EZ Clone domain mutagenesis kit (Stratagene) was used according to the manufacturer's recommended protocol. Specific primers to amplify the template (Pdu39 (pET24a-P. alba (MEA))) are described below (Table 12-3, pET24 Megaprime Forward and Reverse). To achieve the desired mutation frequency, the protocol outlined in the GeneMorph II kit was followed. To generate 2 to 3 residue changes per molecule, approximately 150 ng of starting template DNA was used for the initial PCR reaction. More or less template was used to generate IspS enzymes with either fewer or more residue changes, respectively. The resulting mutant "megaprimers" were then used to amplify the rest of the plasmid according to the manufacturer's recommended protocol.

[0399] The final PCR product from the GeneMorph II kit was treated with *Dpn*I according to the manufacturer's recommended protocol. Prior to transformation into *E. coli*, it was necessary to desalt the PCR reaction by microdialysis. Typically, approximately 20 µl of the PCR reaction was subjected to microdialysis and used for electroporation into strain MD09-171 (Table 12-2) by standard molecular biology procedures. After electroporation, cells were recovered for 2 hours at 30 °C, and then plated onto LB medium Kan50 Cm35. The entire transformation volume was plated to recover all mutations generated by the mutagenesis procedure.

[0400] For enrichment, all transformants were scraped and pooled together. An aliquot from each pool was frozen for storage in the -80. Prior to the enrichment, strains (control or experimental pools) were inoculated directly into LB with Kan50 and grown for a few hours, to minimize the loss of pool heterogeneity. After this recovery period, cells were diluted into liquid TM3 medium (described above) with Kan50, 5 mM MVA, and 200 µM IPTG. (The exact dilution was determined empirically for each pool/source of medium/control reaction). Cultures were then placed in the shaking incubator at 34°C until an OD_{600} of no more than 5. At this point, plasmids were purified from 1 ml of the "enriched" culture via miniprep protocol (Qiagen). This plasmid preparation was then transformed into electrocompetent MD09-171 cells as described above. The transformed cells were recovered for 2 hours in LB medium without antibiotics, and then subjected to a subsequent round of enrichment by dilution into TM3 with Kan50, 5 mM MVA and 200 µM IPTG as described above. This culture was placed into the shaking incubator at 34°C until it reached an OD_{600} of no more

than 5, as described above. Plasmids were then purified, retransformed and subjected to further rounds of "enrichment." The enrichment process continued for 5 or 6 rounds of selection, plasmid purification, and retransformation. The process continued until the culture was homogeneous, *i.e.* contained only one variant of IspS by sequencing analysis.

[0401] After the last round of enrichment, the plasmid pool was transformed into chemically competent *E. coli* Top10 cells (Invitrogen) per the manufacturer's recommended protocol, recovered, plated onto LB medium with Kan50, and sent for complete sequencing (Quintara Biosciences) for comparison to the wild type sequence of P. alba IspS. Primers used for sequencing are described below.

Table 12-3. Primers used for IspS mutagenesis and sequencing

pET24 Megaprime Forward	gtttaactttaagaaggagatatacat
pET24 Megaprime Reverse	gagctcgaattcggatcctta
alba sequencing reverse	ctcgtacaggctcaggatag
alba sequencing reverse2	ttacgtcccaacgctcaact
EWL1000	gcactgtctttccgtctgctgc
QB1493	cttcggcaacgcatggaaat

IV. Individual Residue Changes Identified by Enrichment/DMAPP Toxicity Relief:

[0402] Plasmids isolated from selection/enrichment were fully sequenced. The following residue changes were confirmed by sequencing (Quintara Biosciences). The residue numbering corresponds to the P. alba "Full Length" sequence (in P. alba pET24a; SEQ ID NO:120), where the starting methionine is amino acid number 1. Identified residue changes included: V10M, F12S, T15A, E18G, V58I, V58F, L70Q, L70V, L70T, T71P, V79L, E89D, G94A, S119F, F120L, G127R, E175V, T212I, S257A, R262G, A266G, F280L, N297K, F305L, L319M, E323K, A328T, D342E, A359T, K366N, E368D, L374M, S396T, V418S, K438N, H440R, T442I, T442A, I449V, A469S, K500R, K505Q, G507S, S509N, F511Y, and N532K.

[0403] Combinations of Residue Changes (in a single IspS enzyme) Identified by Enrichment/DMAPP Toxicity Relief: G127R/F511Y, L70Q/G94A/R262G/F305L, F12S/ T15A/E18G/N297K, S396T/T442I, V10M/E323K, F120L/A266G, K438N/K500R, V79L/S509N, E175V/S257A/E368D/A469S, T71P/L374M, F280L/H440R, E89D/H440R, V58F/A328T/N532K, S119F/D342E/I449V, and K366N/G507S.

Example 13

Construction of Site Saturation Libraries (SSLs) and Biochemical Analysis of the L70R Variant

[0404] This example includes an examination of possible amino acid substitutions at sites identified by the selection/enrichment procedure described above and other sites of potential interest (active site, conserved between Poplar species) for their effect on solubility, expression, and activity of IspS.

I. Strain Construction

[0405] Residues identified by the selection/enrichment procedure (L70, G94, R262, F305) described above were chosen for analysis. In addition, residues that are putatively involved in substrate binding (F303, V3065, F385, S412, Q416, F450), and residues that are different between the various Poplar species (*e.g.* V418, T442) were chosen for further analysis (numbering corresponds to the "full length" amino acid sequence of *P. alba* IspS). To generate a randomized pool of amino acid substitutions (the Site Saturation Library, SSL), pDu39 (see description above) was subjected to QuickChange (Stratagene) mutagenesis with the QC primers indicated below (Table 13-1), according to the manufacturer's recommended protocol. The PCR Reaction was prepared as follows:
1 µl pDu39, 5 µl 10X PfuUltra HF buffer, 1 µl dNTP's, 1 µl (50 µM) primer-For (e.g. QC L69 F), 1 µl (50uM) primer-Rev (e.g. QC L69 R), 2 µl DMSO, 39 µl diH2O, and1 µl PfuUltra HF Polymerase (Stratagene). The PCR cycling parameters for QuickChange were as follows: 95°C 1 min, 95°C 30 sec., 55°C 1 min., 68°C 7.3 min. for one cycle followed by 95°C 30 sec., 55°C 1 min., 68°C 7.3 min for 17 more cycles. The temperature was then reduced to 4°C. Incorporation of the bases NNK at the codon for the residues described above allows for the insertion of codons that represent all 20 possible amino acids at the given site. 1 µl of the resulting pools of mutagenized PCR products was *Dpn*I treated (described above), and transformed into chemically competent *E. coli* Top10 cells (Invitrogen) according to the manufacturer's recommended protocol. Entire transformation reactions were recovered in 1 ml LB medium without antibiotics at 37 °C for 1 hour and plated onto LB Kan50. The next day, all transformants were scraped off of the LB plates, mixed thoroughly, and plasmids were purified via miniprep (Qiagen). Pools of plasmids were then transformed into chemically competent BL21(λDE3)pLysS cells (Invitrogen) according to the manufacturer's protocol. The transformation reactions were recovered in 1 ml LB medium at 37 °C for 1 hour and then plated onto LB Kan50 Cm35 at dilutions sufficient to generate separation of positive colonies. After overnight incubation at 37 °C,

individual colonies were inoculated into individual wells in a 96-well deep-well microtiter plate (VWR) containing 500 ul of liquid LB Kan50 Cm35 each. In eight wells (typically column 12, A through H) strain MD09-173 (see above) or BL21(λDE3)pLysS with P. alba pET24a (Full Length) was inoculated as a control for the DMAPP assay. The microtiter plates were then sealed with a semi-permeable membrane (Breathe-Easier, Diversified Biotech), and incubated overnight at 30 ℃ in a shaking incubator (Vertiga). The next day, 100 µl samples from each well within a 96-well plate were mixed with 50 µl of 50% glycerol in a new 200 ul 96-well plate, and frozen at -80 °C until further analysis. This plate was then used for the DMAPP assay described below.

Table 13-1. Primers used for mutagenesis

QC L70 F	gaaaaagcagaatttnnkaccctgctggaactg (SEQ ID NO:68)
QC L70 R	cagttccagcagggtmnnaaattctgcttttc (SEQ ID NO:69)
QC G94 F	gagtctgatatccgtnnkgcgctggatcgcttc (SEQ ID NO:70)
QC G94 R	gaagcgatccagcgcmnnacggatatcagactc (SEQ ID NO:71)
QC R262 F	tcccgttggtggcgtnnkgtgggtctggcgacc (SEQ ID NO:72)
QC R262 R	ggtcgccagacccacmnnacgccaccaacggga (SEQ ID NO:73)
QC F303 F	tccgtcgcaaaaatgnnktctttcgtaaccatt (SEQ ID NO:74)
QC F303 R	aatggttacgaaagamnncatttttgcgacgga (SEQ ID NO:75)
QC F305 F	gcaaaaatgttttctnnkgtaaccattatcgac (SEQ ID NO:76)
QC F305 R	gtcgataatggttacmnnagaaaacatttttgc (SEQ ID NO:77)
QC V306 F	aaaatgttttctttcnnkaccattatcgacgat (SEQ ID NO:78)
QC V306 R	atcgtcgataatggtmnngaaagaaaacatttt (SEQ ID NO:79)
QC F385 F	gacctgtgcaacgctnnkctgcaagaagccaag (SEQ ID NO:80)
QC F385 R	cttggcttcttgcagmnnagcgttgcacaggtc (SEQ ID NO:81)
QC S412 F	gcatggaaatcctctnnkggcccgctgcaactg (SEQ ID NO:82)
QC S412 R	cagttgcagcgggccmnnagaggatttccatgc (SEQ ID NO:83)
QC Q416 F	tcttctggcccgctgnnkctggtgttcgcttac (SEQ ID NO:84)
QC Q416 R	gtaagcgaacaccagmnncagcgggccagaaga (SEQ ID NO:85)
QC V418 F	ggcccgctgcaactgnnkttcgcttacttcgct (SEQ ID NO:86)
QC V418 R	agcgaagtaagcgaamnncagttgcagcgggcc (SEQ ID NO:87)
QC T442 F	caaaaataccatgacnnkatctctcgtccttcc (SEQ ID NO:88)
QC T442 R	ggaaggacgagagatmnngtcatggtatttttg (SEQ ID NO:89)
QC F450 F	cgtccttcccatatcnnkcgtctgtgcaatgac (SEQ ID NO:90)
QC F450 R	gtcattgcacagacgmnngatatgggaaggacg (SEQ ID NO:91)

II. Generation of a "Winner" Plate for Secondary Assay and Identification of L70R as a Variant with Increased Specific Activity

[0406] Variants that displayed increased specific isoprene production when compared to wild type were chosen for further analysis. Figure 45 shows a typical data set of an SSL plate for an individual residue, in this case L70. From this particular plate, the samples in wells C3 (27), D3 (39), and E3 (51) were chosen for further analysis. Other variants at different residues (listed above) that showed increased isoprene productivity, when subjected to DMAPP analysis, were isolated from their original SSL plates stored at -80 °C (described above), and re-arrayed onto a new "winner" plate for secondary screening. Two wells containing MD09-173 were included as controls. All variants were sequenced (Quintara Biosciences) and subjected to the DMAPP assay as described above. See Table 13-2 for sequencing results. For the DMAPP assay, a single growth of each variant was assayed, and therefore a single lysate generated, but in quadruplicate to generate statistically significant data. Samples were assayed at the OD_{600} indicated in Table 13-2. Protein analysis was performed on all lysates using the Western Breeze Western blot kit (Invitrogen) followed by fluorescence detection on a Storm860 (see below)

III. DMAPP Assay – Growth, Lysis and Isoprene Measurement

[0407] A patch plate was prepared from a glycerol stock plate using a VP-Scientific Replication Tool patch LB Agar CM35/Kan50 large patch plate from overnight glycerol stock Plate. Cultures were incubated at 30°C overnight (20 to 24 hr). Plates were stored at 4°C for up to a week.

[0408] An overnight growth plate was prepared from 500 mL of LB CM35/Kan50 media. 300 µL/well of LB CM35/Kan50 media were dispensed into deep 96 well plate. Using the V&S Replication Tool, the patch inoculum was transferred to a deep 96 well plate. Media was inoculated by dipping the tool then shaking the pin within the well. The overnight growth plate was sealed with a Breathe-Easier Sealing Membrane. The plate was incubated at 30 °C overnight in a Vertiga Shaking Incubator at 800 rpm for 16 to 18 hours.

[0409] A deep 96 well day growth plate was prepared by dispensing 588 µL/well of LB CM35/Kan50 media. The overnight growth plate was removed from the incubator and cultures were diluted 50-fold. 12 µL of overnight oulture was transferred to a day growth plate containing 588 µL/well of supplemented LB media. The overnight growth plate was sealed with a new Breathe-Easier Sealing Membrane and was incubated at 34 °C and 800 rpm for 2.25 hr in the Vertiga Shaking Incubator.

[0410] To induce the expression of IspS, thawed 12 mM IPTG was poured into 50 mL or 100 mL sterile reservoir and dispensed 20 µL/well into each 600 µL/well culture. Overnight

growth plate was resealed with Breathe-Easier Sealing Membrane and incubated at 34°C and 800 rpm for 4 hours in the Vertiga Shaking Incubator.

[0411] To harvest cell, 200 µL of induced culture was transferred to 450 µL Nunc storage plate. The plate was centrifuged at 3300 rpm for 20 min at 4 °C in a low speed benchtop centrifuge. 180 µL supernatant was removed with a pipettor and discarded. The plate was sealed with an aluminum foil membrane, covered with a plastic plate lid and stored frozen at -80 °C.

[0412] The OD_{600} of the plates were read. 150 µL 1x PBS was dispensed into a 96 well Costar Read Plate (#9017). 50 µL of culture sample was then transferred to the read plate. The OD_{600} reading was then taked with a Spectramax Plate Reader.

[0413] Lysis: The harvest plate was defrosted in a room temperature water bath for 4 min and then incubated in Thermomixer at 25°C at 1200 rpm for 1 min. Lysis buffer was dispensed at 80 µL/well to 20 µL/well of harvest cells. 1.25X Lysis Working Stock buffer was prepared from 6.25 ml 1M Tris pH 8, 625 µl 10% Tween 20, 312.5 µl 0.2 M PMSF, 462.5 µl 10 mg/ml DNAse I (Sigma), 1.25 ml 1 M $MgCl_2$, 132.5 µl 25000 U/µl Lysozyme (Epicentre Technologies) and 40.968 ml dIH_20. Plates were incubated on a Thermomixer at 25°C and 1200 rpm for 30 min. 1x Lysis Buffer stock was prepared by diluting 19 ml of 1.25x Lysis Working stock with 4.75 ml dIH_2O.

[0414] DMAPP Working Stock was prepared as follows.

Dimethylallyl Pyrophosphate (triammonium salt) 25 mg (Cayman Chemicals, Cat No. 63180)

final	total vol	diluent	stock vol	stock	dilution	Reagent	Units	Plate(s)
30	840	840	solid	25000	1	DMAPP	mg/mL	1
3	2500	2250	250	30	10	DMAPP	mg/mL	1

[0415] The Diluent was 0.1 M Potassium Phosphate. 200 uL/well was dispensed for transfer to sample wells and was stored on ice.

[0416] DMAPP Reaction: 1x Lysis Buffer was dispensed at 65 µL/well. 15 µL/well of lysate was transferred to the respective sample wells in a 96 Deep well Zinsser Glass Block. DMAPP reagent was dispensed at 20 µL/well. The glass block was sealed with an aluminum foil membrane and incubated at 25 °C at 450 rpm for 45 min. The reaction was stopped by transferring the Glass Block to a 70 °C water bath and incubating for 6 min. GC Analysis was performed as previously described.

IV. Western blot of Isoprene Synthase with Fluorescence labeled Secondary Antibody.

[0417] Samples were prepared and run on NativePAGE™ Novex® Bis-Tris Gels (Invitrogen) according to the manufacturer's protocol. After completion of the run the gels were immediately transferred to Nitrocellulose membranes using the XCell II™ Blot Module (Invitrogen) according to the manufacturer's recommended protocol. After transfer, the membrane was placed in 15 ml of the appropriate Blocking Solution (Ultra filtered Water 31.5 ml, Blocker/Diluent (Part A) 9 ml, Blocker/Diluent (Part B) 4.5 ml) in the covered, plastic dish provided in the kit and incubated for 30 minutes on a rotary shaker set at 1 revolution/sec. The Blocking Solution was decanted and the membrane rinsed 2 times with 20 ml of water for 5 minutes. The membrane was incubated with 15 ml of Primary Antibody (Ab) Solution (24 µl of primary Ab in 15 ml Blocking solution) for 1 hour, followed by washing 3 times 5 minutes with 20 ml of 1x Antibody Wash Solution. The membrane was then incubated in 15 ml of SecondaryAntibody Solution (15ul secondary Ab (Alexa Fluor 488 goat anti-rabbit IgG (H+L, Invitrogen)) in 15 of blocking solution) for 30 minutes. The membrane was washed 3 times at 5 minutes with 20 ml of Antibody Wash, and rinsed two times 2 minutes with 20 ml of water. The membrane was dried between paper towels and stored at room temperature for further detection. The fluorescent bands were detected and quantified using the Storm 860 Molecular Imager (GMI, Inc).

V. Results:

[0418] Table 13-2 shows all of the relevant data for each variant assayed: sequencing results, residue change, average isoprene production, protein concentration, and average specific activity (of all 4 replicates). Figure 46 shows the graphical representation of the data shown in Table 13-2. Specific activity was calculated by multiplying the isoprene produced (µg/l) by 0.0414 and then dividing by protein concentration (mg/ml). This conversion factor (0.0414) accounts for the total headspace volume in a sealed 2 ml GC vial (1.9 ml), the lysate volume (15 ul), the duration of the DMAPP assay (45 min), and the molecular weight of isoprene. Thus, specific activity values are given in nmol isoprene/mg Isps/min.

[0419] The data in Table 13-2 and the graph in Figure 46 show that of all variants analyzed, all three L70R variants displayed higher specific activity than wild type. To analyze the L70R variants further, the specific activity values for all 3 isolates (4 replicates of each) were averaged and compared to the controls (2 isolates, 4 replicates each). Therefore, there were 12 measurements for the L70R variant, and 8 for wild type. These data are shown

below in Table 13-3. When corrected for protein, the L70R variants displayed a 25% increase in activity over MD09-173 (the MEA truncation). Figure 47 shows the average specific activity for all L70R variants compared to MEA. Error bars show one standard deviation. The two data sets for L70R and the MEA control were subjected to a Student's T-Test for statistical analysis, which yielded a P-value of 6.0011×10^{-5}.

Table 13-2. Sequencing Results, Isoprene Production, Protein concentration, and Specific Activity for all residues in the Winner Plate

Residue	WT codon	Mutant codon	Amino acid change	OD600	Avg. Isoprene produced (4 replicates)	Std. Dev. (isoprene)	Protein concentration (mg/ml)	Avg. Specific Activity (4 replicates)	Std. Dev. (Specific Activity)
L70	CTG	TGG	W	2.6488	663.00	18.64	0.139	198.020	5.566
L70	CTG	CGG	R	3.4944	1235.72	48.82	0.127	401.451	15.860
L70	CTG	CGT	R	3.32416	944.77	19.15	0.121	322.523	6.539
L70	CTG	CGT	R	3.37232	947.11	17.74	0.106	371.375	6.957
L70	CTG	TGG	W	2.83584	774.49	32.60	0.129	248.925	10.477
G94	GGT	GAG	E	3.304	1070.41	20.52	0.144	307.731	5.898
G94	GGT	GGG	G	3.40816	982.64	27.37	0.133	306.891	8.549
R262	CGT	CGT	R	3.01616	861.08	29.13	0.116	307.227	10.395
R262	CGT	CGG	R	3.31744	965.44	19.25	0.136	294.311	5.868
F305	TTC	TTT	F	2.90864	788.46	15.15	0.119	274.297	5.270
F305	TTC	CTG	L	2.7776	626.70	22.91	0.141	183.823	6.719
WT1				3.71392	991.65	35.78	0.144	285.216	10.292
F305	TTC	TTC	F	2.604	694.03	35.93	0.118	244.488	12.658
V306	GTA	GTA	V	3.33648	912.56	38.76	nd	nd	nd
V306	GTA	GTA	V	3.17632	892.97	56.10	0.137	269.415	16.927
F385	TTC	TTC	F	2.89184	721.24	29.36	0.134	223.380	9.094
Q416	CAA	CAG	Q	3.00272	953.07	57.38	0.149	264.718	15.938

V418	GTG	ATG	M	2.14144	767.25	27.94	0.164	194.099	7.067
V418	GTG	ACG	T	3.24688	973.57	75.08	0.192	209.801	16.179
V418	GTG	ACG	T	3.13264	936.98	68.50	0.171	226.197	16.536
T442	ACC	GTA	V	3.07552	951.64	38.06	0.154	255.496	10.217
F450	TTC	TTC	F	2.93328	911.44	50.88	0.126	299.018	16.691
V418	GTG	ACG	T	3.08896	1057.71	46.28	0.183	238.887	10.454
WT2				3.37568	960.25	58.16	0.131	304.346	18.434

[0420] Note that sequence of all plasmids is identical to Pdu39 (see above) with the exception of the indicated codon. The L70R variants are highlighted in gray.

Table 13-3. Average Specific Activity of all L70R variants relative to the MEA control.

VariantAverage	Specific Activity	Standard Deviation
L70R	365.116	35.31977
WT (the MEA control)	294.7809	17.19228

See Figure 47 for bar graph.

Example 14

Truncations of *P. alba*, *P. tremuloides*, *P. trichocharpa*, and Kudzu Isoprene Synthases

[0421] This example describes the generation of a series of truncations in the IspS enzymes of *P. alba*, *P. tremuloides*, *P. trichocharpa*, and Kudzu and to determine their effect on activity.

I. Strain Construction

[0422] All isoprene synthase genes were codon optimized for *E. coli*, synthesized, and cloned into pET24a by DNA2.0 (Menlo Park, CA). All truncated constructs were generated using the QuickChange Site-Directed Mutagensis kit (Stratagene) using the previously described templates P. alba pET24a (for plasmids pDu47-3 through -7, Figures 48, 49, 51-60), P. tremuloides pET24a (plasmid pDu48, Figures 49C, 61 and 62), P. trichocharpa pET24a (pDu49, Figures 50A, 63, 64), or pET24d-Kudzu (pDu50 and 50-4, Figures 50B, 50C, 65-68) for PCR amplification. Approximately 50 ng of template DNA was used for

amplification (with an Eppendorf Mastercycler Gradient PCR Machine) of the PCR product with the Forward (For) and Reverse (Rev) primer pairs that correspond to each relevant truncation (QC Trunc -3 F and QC Trunc -3 R, for example, see Table 14-1). PCR reactions mixtures were as follows: 1 µl P. alba pET24a (or other template), 5 µl 10X PfuUltra HF buffer, 1 µl dNTP's (10 mM), 1 µl (50uM) primer-For, 1 µl (50 µM) primer-Rev, 1.5 µl DMSO, 39.5 µl diH_2O and 1 µl PfuUltra HF Polymerase. PCR cycle parameters were as follows: (95 °C 1 min., 95 °C 1 min., 55 °C 1 min., 68 °C 7.30 min.) for 18 cycles then 4°C until cool using an Eppendorf Mastercycler Gradient Machine. The PCR products were treated with 1-2 µl of *Dpn*I (Roche) for 1-3 hour at 37 °C. 5 µl of the *Dpn*I treated products were visualized on a 0.8% E-gel (Invitrogen). 1 µl of each product was transformed into chemically competent *E. coli* Top10 cells (Invitrogen) (according to the manufacturer's protocol). Transformants were selected for on LB medium containing kanamycin at a concentration of 50 µg/ml (Kan50), and incubated overnight at 37 °C. Five colonies of each transformation were selected and grown to stationary phase in 3 ml liquid LB Kan50. Plasmids were purified using a QIAPrep Spin miniprep kit (Qiagen) according to the manufacturer's recommended protocol. Purified plasmids were sequenced (by Quintara Biosciences) with T7 Forward and Reverse primers, compared to the parental sequence, and confirmed for their respective truncation. The resulting plasmids (pDu47-3 through pDu50-4, see Table 14-2) were transformed into chemically competent *E. coli* BL21(DE3) pLysS (Invitrogen) according to the manufacturer's recommended protocol. Table 14-3 describes the strains used for expression of truncated IspS enzymes.

[0423] After overnight incubation at 37 °C, individual colonies were inoculated into individual wells in a 96-well deep-well microtiter plate (VWR) containing 500 µl of liquid LB Kan50 CM35 each. Microtiter plates were then sealed with a semi-permeable membrane (Breathe-Easier, Diversified Biotech), and incubated overnight at 30 °C in a shaking incubator (Vertiga). The next day, 100 µl samples from each well within a 96-well plate were mixed with 50 µl of 50% glycerol in a new 200 µl 96-well plate, and frozen at -80 °C until further analysis. This plate was then used for the DMAPP assay as described in Example 13. Table 14-4 shows the average specific productivity of all samples, and Figure 69 shows the graphical representation of the same data.

[0424] DMAPP activity and protein quantitation was determined as described in Example 13.

[0425] Specific activity was calculated by multiplying the isoprene produced (µg/l) by 0.00776 and then dividing by protein concentration (mg/ml). This conversion factor

(0.00776) accounts for the total headspace volume in a sealed 2 ml GC vial (1.9 ml), the lysate volume (80 µl), the duration of the DMAPP assay (45 min), and the molecular weight of isoprene. Thus, specific activity values are given in nmol isoprene/mg IspS/min.

Table 14-1. Primers

QC Trunc -3 F	gaaggagatatacatatgaccgaagctcgtcgt (SEQ ID NO:92)
QC Trunc -3 R	acgacgagcttcggtcatatgtatatctccttc (SEQ ID NO:93)
QC Trunc -4 F	gaaggagatatacatatggaaaccgaagctcgt (SEQ ID NO:94)
QC Trunc -4 R	acgagcttcggtttccatatgtatatctccttc (SEQ ID NO:95)
QC Trunc -5 F	gaaggagatatacatatgactgaaaccgaagct (SEQ ID NO:96)
QC Trunc -5 R	agcttcggtttcagtcatatgtatatctccttc (SEQ ID NO:97)
QC Trunc -6 F	gaaggagatatacatatggaaactgaaaccgaa (SEQ ID NO:98)
QC Trunc -6 R	ttcggtttcagtttccatatgtatatctccttc (SEQ ID NO:99)
QC Trunc -7 F	gaaggagatatacatatgaccgaaactgaaacc (SEQ ID NO:100)
QC Trunc -7 F	ggtttcagtttcggtcatatgtatatctccttc (SEQ ID NO:101)
QC Kudzu MEA F	agaaggagatataccatggaagctcgtcgttccgcaaac (SEQ ID NO:102)
QC Kudzu MEA R	gtttgcggaacgacgagcttccatggtatatctccttct (SEQ ID NO:103)
QC Kudzu -4 F	agaaggagatataccatggagcataattcccgt (SEQ ID NO:104)
QC Kudzu -4 R	acgggaattatgctccatggtatatctccttct (SEQ ID NO:105)
QC Trem/Trich -2 F	gaaggagatatacatatggaaacgcgtcgttct (SEQ ID NO:106)
QC Trem/Trich -2 R	agaacgacgcgtttccatatgtatatctccttc (SEQ ID NO:107)

Table 14-2. Plasmids

pDu47-3	Mtg pET24a-P.alba TRC (-3)
pDu47-4	Mtg pET24a-P.alba TRC (-4)
pDu47-5	Mtg pET24a-P.alba TRC (-5)
pDu47-6	Mtg pET24a-P.alba TRC (-6)
pDu47-7	Mtg pET24a-P.alba TRC (-7)
pDu48	Mtg pET24a-P.tremu TRC (MET)
pDu49	Mtg pET24a-P.tricho TRC (MET)
pDu50	Mtg pET24d-Kudzu TRC (MEA)
pDu50-4	Mtg pET24d-Kudzu TRC (-4)

Table 14-3. Strains

MD09-197-3	BL21(DE3)pLysS, pDu47-3
MD09-197-4	BL21(DE3)pLysS, pDu47-4
MD09-197-5	BL21(DE3)pLysS, pDu47-5
MD09-197-6	BL21(DE3)pLysS, pDu47-6
MD09-197-7	BL21(DE3)pLysS, pDu47-7
MD09-198	BL21(DE3)pLysS, pDu48
MD09-199	BL21(DE3)pLysS, pDu49
MD09-200	BL21(DE3)pLysS, pDu50
MD09-200-4	BL21(DE3)pLysS, pDu50-4

Table 14-4. Specific Productivity of Variants listed above

Isoprene Produced (µg/l)					OD_{600}		OD
Sample	Sample	Average	Std Dev	%CV	Raw	xDF xCF	Norm
IspS N terminal Truncation Variants	MD09-197-3	3381	154	5	0.3060	3.4	986.6
	MD09-197-4	3000	206	7	0.3160	3.5	847.7
	MD09-197-5	2932	266	9	0.3200	3.6	818.2
	MD09-197-6	2450	217	9	0.3040	3.4	719.4
	MD09-197-7	2285	397	17	0.3020	3.4	675.5
	MD09-198	1916	106	6	0.3330	3.7	513.6
	MD09-199	2031	108	5	0.2140	2.4	847.6
	MD09-200	141	8	6	0.3700	4.1	34.0
	MD09-200-4	1829	197	11	0.2760	3.1	591.5
	MD09-173	2414	201	8	0.3400	3.8	633.9
	MD09-176	2826	354	13	0.3260	3.7	773.9
	BL21 DE3 pLysS + P alba pET24a	2175	117	5	0.2990	3.3	649.6

[0426]

[0427] A second experiment was conducted with the strains outlined in Table 14-5. Control was BL21 DE3 pLysS with P. alba pET24a (full length P. alba IspS).

[0428]

[0429] Table 14-5. Strains

MD09-197-3	BL21(DE3)pLysS, pDu47-3
MD09-197-4	BL21(DE3)pLysS, pDu47-4
MD09-197-5	BL21(DE3)pLysS, pDu47-5
MD09-197-6	BL21(DE3)pLysS, pDu47-6
MD09-197-7	BL21(DE3)pLysS, pDu47-7
MD09-198	BL21(DE3)pLysS, pDu48
MD09-199	BL21(DE3)pLysS, pDu49
MD09-173	BL21(DE3)pLysS, pET24a-P.alba (MEA) Untagged (pDu39)
MD09-174	BL21(DE3)pLysS, pET24a-P.alba (MNV) Untagged (pDu40)
MD09-175	BL21(DE3)pLysS, pET24a-P.alba (MSV) Untagged (pDu41)
MD09-176	BL21(DE3)pLysS, pET24a-P.alba (MTE) Untagged (pDu42)
MD09-177	BL21(DE3)pLysS, pET24a-P.alba (MVS) Untagged (pDu43)
MD09-197-3	BL21(DE3)pLysS, pDu47-3
MD09-197-4	BL21(DE3)pLysS, pDu47-4

[0430]

[0431] Results

[0432] All truncations of *P. alba* IspS and two from *P. tremuloides* and *P. trichocharpa* were assayed in parallel to compare their relevant specific activities via DMAPP assay and quantitative Western blot. At least two samples per variant were assayed for isoprene

production and amount of IspS in mg/ml. Variant MD09-174 produced little isoprene and expressed little protein, yet displayed high specific activity. High specific activities were also displayed by MD09-173, MD09-176, and MD09-197-3 (see Table 14-6 and Figure 70). The highest levels of protein (µg) in 3 µg total protein were displayed by MD09-176 and MD09-197-3, indicating that these variants are more effectively expressed in the *E. coli* BL21 DE3 host strain.

[0433]

[0434] Table 14-6. Specific Activity of truncations.

Strain	Average Specific Activity	Standard Deviation	Average ug IspS/ 3 µg total protein
P. alba FL	240.16239	31.0423851	0.198
MD09-175	331.8755329	8.958408319	0.188
MD09-177	340.1959506	39.72104203	0.150
MD09-176	363.516921	3.376026129	0.202
MD09-174	452.7792122	27.71567075	0.018
MD09-197-7	279.2042431	23.82331163	0.158
MD09-197-6	309.8357305	7.903564316	0.164
MD09-197-5	293.22592	20.97161876	0.165
MD09-197-4	321.3926574	56.13760028	0.186
MD09-197-3	333.0604155	45.92710529	0.207
MD09-173	368.4597405	37.80631246	0.159
MD09-198	297.6476631	56.81405985	0.154
MD09-199	256.7342861	8.239697653	0.216

[0435]

Example 15

Constructs for Three-Dimensional Structure Determination

I. Construction of pMAL-C4X Kudzu

[0436] A synthetic gene, coding for isoprene synthase (IspS) of the Kudzu vine (*Pueraria lobata*) and codon-optimized for E. coli, was purchased from DNA2.0 (Menlo Park, CA) and provided as plasmid p9795 (Figure 71 and 72). The insert was removed by digestion with *Bsp*LU11I/*Pst*I, gel-purified, and religated into *Nco*I/*Pst*I-digested pTrcHis2B (Invitrogen, Carlsbad, California). The resulting plasmid was named pTrcKudzu (Figure 73: map of pTrcKudzu). The stop codon in the insert is before the *Pst*I site, which results in a construct in which the His-Tag is not attached to the IspS protein.

[0437] A PCR reaction was performed to amplify the *E. coli* codon-optimized Kudzu gene using plasmid pTrcKudzu as the DNA template, primers EL-959 and EL-960, 10mM dNTP

(Roche, Indianapolis, IN), and Pfu Ultra II Fusion DNA polymerase (Stratagene, La Jolla, CA) according to manufacturer's protocol. PCR conditions were as follows: 95 °C for 2 min (first cycle only), 95 °C for 25 sec, 60 °C for 25 sec, 72 °C for 30 sec, repeat for 28 cycles, with final extension at 72 °C for 1 min. The PCR product was then purified using the QIAquick PCR Purification Kit (Qiagen Inc, Valencia, CA).

[0438] The Kudzu PCR product (1 µg) was digested using *Eco*RI and *Hind*III restriction endonucleases (Roche) according to manufacturer's protocol. The digest was incubated 37 °C for 30 minutes to minimize digestion of the internal *Eco*RI site that is present in the Kudzu gene. The digested PCR fragment was then purified using the QIAquick PCR Purification Kit. The vector pMAL-C4X (0.5 µg) (New England Biolabs, Ipswich, MA; Figures 75 and 76) was digested using *Eco*RI and *Hind*III restriction endonucleases (Roche) according to manufacturer's protocol. The digested vector was then gel purified using the QIAquick Gel Extraction Kit (Qiagen Inc). A DNA ligation reaction was performed using T4 DNA ligase (New England Biolabs) with a 5:1 ratio of digested Kudzu PCR product to digested pMAL-C4X vector according to manufacturer's protocol. An aliquot of the ligation reaction was then transformed into TOP10 chemically competent cells (Invitrogen Corp). Transformants were selected on LA + 50 µg/µl carbenicillin plates.

[0439] Screening of transformants containing the Kudzu gene was performed by picking colonies and performing PCR with primers EL-957 and EL-966 using PuReTaq Ready-To-Go PCR beads (GE Healthcare, Piscataway, NJ) according to manufacturer's protocol. PCR conditions were as follows: 95 °C for 2 min (first cycle only), 95 °C for 30 sec, 50 °C for 30 sec, 72 °C for 40 sec, repeat for 28 cycles, with final extension at 72 °C for 1 min. PCR products were analyzed on a 2% E-gel (Invitrogen Corp) looking for a 600 bp fragment. Colonies containing the correct sized PCR product insert were submitted for DNA sequencing using primers EL-950, EL-951, EL-953, and EL-957. DNA sequencing confirmed the construction of plasmid pMAL-C4X Kudzu (Figures 77 - 79).

Table 15-1 Primer sequences

Primer name	Primer sequence
EL-950	CGGTGAACTGAAAGGTGACGTCC (SEQ ID NO:108)
EL-951	GGACGTTAACGCTATTAACACCCTG (SEQ ID NO:109)
EL-953	CACATCGTCGATCAGCTCCAGC (SEQ ID NO:110)
EL-957	GGTCGTCAGACTGTCGATGAAGCC (SEQ ID NO:111)
EL-959	GCTTATGAATTCTGTGCGACCTCTTCTCAATTTACTCAG (SEQ ID NO:112)
EL-960	GCTTATAAGCTTAGACATACATCAGCTGGTTAATCGGG (SEQ ID NO:113)

EL-966	CTCCTCCAGCAGGTTCTCACC (SEQ ID NO:114)

[0440] Plasmid pMAL-C4X Kudzu was transformed into OneShot BL21(λDE3) chemically competent cells (Invitrogen Corp). Expression strain transformants were selected on LA + 50 mg/ml carbenicillin plates.

II. IspS Variants for Crystal Structure Trials

[0441] This example describes methods to generate affinity tagged isoprene synthase (IspS) enzymes for expression, purification and crystallization.

Strain Construction

[0442] For constructs in the pET200D-TOPO vector (Invitrogen), PCR products of the IspS enzymes from *P. alba*, *P. tremuloides*, and *P. trichocharpa* were gel extracted and purified (Qiagen), using 0.8% E-gel (Invitrogen), according to the manufacturer's recommended protocol. PCR reactions for pET200 constructs are as follows: Reaction mixture was 1µl (Templates)-pET24a-P.alba, 5 µl 10X PfuUltraII Fusion buffer, 1 µl dNTP's (10 mM), 1 µl primer (50uM) primer F-(MCM219 or 218), 1 µl primer (50uM) primer R-(MCM182), 41 µl diH2O and 1 µl of PfuUltra II Fusion DNA Polymerase from Stratagene; Cycle Parameter were 95°C 1 min., 95°C 1 min, 55°C 20 sec., 72°C 27 sec. for 29 cycles followed by 72°C for 3 min and then 4° C until cool, using an Eppendorf Mastercycler. Similar reactions were performed for *P. tremuloides*, *P. trichocarpa*, and Kudzu. 3 µl of purified product was then ligated to the pET200D/TOPO vector (Invitrogen), according to the manufacturer's protocol. The reaction was incubated for 5 minutes at room temperature, and the 6 µl topoisomerase mixture was then transformed into E. coli Top10 chemically competent cells (Invitrogen) according to the manufacturer's protocol. Transformants were selected for on LB Kan50, and incubated at 37 °C overnight. Five colonies per construct were chosen and screened using PuReTaq Ready-To-Go PCR Beads (Amersham) using the T7 Forward and MCM182 primers (Table 15-2). Clones harboring inserts of the correct size were further verified by plasmid miniprep using the QIAPrep Spin Miniprep kit (Qiagen) followed by sequencing using the T7 Forward and T7 Reverse primers (Quintara Biosciences). One fully sequenced construct for each IspS variant (see below for details and sequence/Figures 79-90), was chosen for further study. 1 µl of each plasmid was transformed into BL21(λDE3) pLysS (Invitrogen) according to the manufacturer's protocol. Transformants were selected for on LB medium with Kan50 + Cm35 and incubated at 37°C overnight. The resulting strains were used for expression and purification of various IspS enzymes for crystallography studies.

[0443] Construction of N-terminally 6His-tagged IspS plasmids, strains and purification is described in Example 11.

Table 15-2. Primers

MCM219	caccatgcgttgtagcgtgtcca (SEQ ID NO: 114)
MCM182	gggcccgtttaaactttaactagactctgcagttagcgttcaaacggcagaa (SEQ ID NO:115)
MCM218	caccatgcgtcgttctgcgaactac (SEQ ID NO:116)

Table 15-3. Plasmids

P. alba pET24a	pET24a with "full length" IspS from P. alba
P. trichocharpa pET24a	pET24a with "full length" IspS from P. trichocharpa
P. tremuloides pET24a	pET24a with "full length" IspS from P. tremuloides
MBP-Kudzu	
pDu27	P. albaFL-pET200/Top 10
pDu30	P. albaTRC-pET200/Top10
pDu31	P. tremTRC-pET200/Top 10
pDu32	P. trichTRC-pET200/Top10
MD09-161	pET24a-P.alba FL C-Term (+) TEV, His tag/MCM331
MD09-163	pET24a-P.alba TRC (MEA) C-Term (+) TEV, His tag/MCM331

Table 15-4. Strains

MBP-Kudzu	
MD08-99	BL21 DE3 pLys + pDu27
MD08-100	BL21 DE3 pLys + pDu30
MD08-102	BL21 DE3 pLys + pDu31
MD08-104	BL21 DE3 pLys + pDu32
MD09-165	BL21(DE3)pLysS, pET24a-P.alba FL C-Term (+) TEV, His tag
MD09-167	BL21(DE3) pLysS, pET24a-P.alba TRC (MEA) C-Term (+) TEV, His tag

III. Digestion of TEV (Tobacco Etch Virus) or EK (Enterokinase)-tagged enzymes

TEV Cleavage (IspS from strains MD09-165 and MD09-167)

[0444] Strains MD09-165 and MD09-167 are described in Example 11. For digestion, enzymes were purified through a Ni charged sepharose (GE Healthcare) and desalted into 50 mM HEPES, 50 mM NaCl pH 7.4 buffer containing 1 mM DTT. Digestion was performed with TurboTEV Protease from Eton Bioscience Inc. One unit of TurboTEV per 10 μg of purified protein was used. The digest was performed at 4°C overnight. Samples were passed through another Ni column equilibrated in the Ni buffer to remove uncleaved enzyme, tag, TurboTEV protease (that is also tagged) and impurities. The Ni column pass though and washes were analyzed using SDS-PAGE gel (NUPAGE, Invitrogen) and DMAPP activity

assays. Samples containing pure enzyme were pooled and desalted into 50 mM NaCl pH 7.4 buffer containing 1 mM DTT and stored at -80°C.

EK Cleavage (IspS from strains MD08-102 and MD08-104)

[0445] For digestion enzymes were purified through a Ni charged sepharose (GE Healthcare) and desalted into 50 mM HEPES, 50 mM NaCl pH 7.4 buffer containing 1 mM DTT.

[0446] Digestion was performed with EKMax (E180-02) (Invitrogen) using 1 unit of EKMax per 20 μg of purified protein at 4 °C overnight. Samples were passed over EK Away resin (Invitrogen) to remove excess enterokinase. Samples were batched onto Ni charged sepharose resin (equilibrated in the Ni wash buffer) and incubated for 30 min at 4 °C, with occasional inverting. This removed uncleaved enzyme, tag, and impurities. The Ni column pass through and washes were analyzed using SDS-PAGE gel (4-12% NUPAGE, Invitrogen) and DMAPP activity assays. Samples containing pure enzyme were pooled and desalted into 50 mM HEPES, 50 mM NaCl pH 7.4 buffer containing 1 mM DTT and stored at -80°C.

IV. Purification of MBP-IspS

[0447] Construction of pMAL-C4X Kudzu for the expression of MBP-Kudzu isoprene synthase is described above. MBP-Kudzu isoprene synthase production from *E. coli* grown in batch culture at the 15-L scale.

Medium Recipe (per liter fermentation medium)

[0448] K_2HPO_4 7.5 g, $MgSO_4 * 7H_2O$ 2 g, citric acid monohydrate 2 g, ferric ammonium citrate 0.3 g, yeast extract 0.5 g, 1000X Modified Trace Metal Solution 1 ml. All of the components were added together and dissolved in diH_2O. This solution was autoclaved. The pH was adjusted to 7.0 with ammonium hydroxide (30%) and q.s. to volume. Glucose 10 g, thiamine * HCl 0.1 g, and antibiotics were added after sterilization and pH adjustment.

1000X Modified Trace Metal Solution

[0449] Citric Acids * H_2O 40 g, $MnSO_4 * H_2O$ 30 g, NaCl 10 g, $FeSO_4 * 7H_2O$ 1 g, $CoCl_2 * 6H_2O$ 1 g, ZnSO * $7H_2O$ 1 g, $CuSO_4 * 5H_2O$ 100 mg, H_3BO_3 100 mg, $NaMoO_4 * 2H_2O$ 100 mg. Each component is dissolved one at a time in diH_2O, pH to 3.0 with HCl/NaOH, then q.s. to volume and filter sterilized with 0.22 micron filter.

[0450] Fermentation was performed in a 15-L bioreactor with BL21 (DE3) *E. coli* cells containing the pMAL-C4X plasmid expressing a maltose binding protein (MBP)-Kudzu

isoprene synthase fusion molecule. This experiment was carried out to produce isoprene synthase at the desired fermentation pH 7.0 and temperature 30 °C. A frozen vial of the *E. coli* strain was thawed and inoculated into tryptone-yeast extract medium. After the inoculum grew to OD 1.0, measured at 550 nm (OD_{550}), 120 mL was used to inoculate a 15-L bioreactor bringing the initial volume to 9-L.

[0451] Expression of the desired molecule was achieved by adding isopropyl-beta-D-1-thiogalactopyranoside (IPTG). The IPTG concentration was brought to 1 mM when the OD_{550} reached a value of 10. Cells containing the desired product were harvested 3 hrs after IPTG addition.

MBP-IspS Purification

[0452] The broth was centrifuged for 15 min at 10000 x g. The pellet was collected and frozen at -80 ºC until further purification. Cells were resuspended in MBP-Bind Buffer (5% glycerol, 20 mM Tris pH 7.4, 200 mM NaCl, 2 mM DTT, 1mg/ml lysozyme) and passed through the french press three times at 20000 psi. The lysate was then ultracentrifuged at 100000 x g for 1 hour to yield a relatively clear solution. The supernatant was pipetted from the top of the tube without disturbing the gelatinous material on the bottom of the centrifuge tube. Gel filtration was performed on the supernatant using a Superdex-200 26/60 column (GE healthcare). The column was developed using MBP-Bind buffer at a flow rate of 3 mL/min at 23 ºC. Fractions were tested for DMAPP activity as described below. Active fractions were pooled and loaded onto 25 mL amylose resin (New England Biolabs). The column was washed with 10 column volumes MBP-Bind buffer and the protein was then eluted with 2 column volumes of MBP-Bind buffer containing 10 mM maltose to yield >90% pure MBP-IspS.

V. DMAPP Assay

[0453] The following reaction mixture was used for the DMAPP assay: 25 µL lysate mixture, 5 µL $MgCl_2$ (1 M), 5 µL DMAPP (100mM), and 65 µL 100 mM Tris pH 8, 100 mM NaCl for a total volume of 100 µL. The reaction is performed at 30 ºC for 15 minutes in a gas tight 1.8 mL GC tube. Reactions are terminated by the addition of 100 µL 500 mM EDTA (pH 8). The amount of isoprene produced was measured by GC/MS as described above.

Example 16

Three-dimensional structure of IspS

[0454] Seven constructs of plant isoprene synthase (IspS) were prepared to generate crystals suitable for x-ray diffraction. These were: a construct containing N-terminal histidine-tagged maltose binding protein and kudzu IspS (MBP-kudzu), full-length *P. alba* IspS with N-terminal histidine-tag (MD08-99), *P. alba* IspS with the first nineteen N-terminal residues removed (MD08-100), this construct also had the N-terminal his-tag removed after purification. Full-length, untagged *P. alba* IspS (strain RM11608-2). A truncated *P. alba* IspS construct featuring two additional residues before the twin-arginine motif was generated (MD09-167). *P. tricharpa* IspS was generated, which contains both an N-terminal his-tag and N-terminal truncation (MD08-104), and another construct composed of IspS from *P. tremuloides* was generated with an N-terminal his-tag and N-terminal truncation (MD08-102). Construction of strains expressing various isoprene synthases are described above.

[0455] Each construct was purified and a concentrated protein solution was then prepared for surveying possible crystallization conditions. Each construct was purified independently and surveyed as described below. All in-house crystallization screens were set up using the hanging drop vapor diffusion method. At a minimum, each construct was surveyed using the following commercial screens: the Crystal Screen from Hampton Research (Aliso Viejo, CA) and the JCSG+ Suite from Qiagen (Valencia, CA).

[0456] Purified MBP-kudzu using was set up using the following commercial screens: the Crystal Screen from Hampton Research and the JCSG+ Suite from. Additionally, purified MBP-kudzu was sent to the Hauptman-Woodward Institute (Buffalo, NY) for high-throughput screening, where no fewer than 1536 conditions were surveyed. The purified MBP-kudzu fusion precipitated out of solution in the majority of conditions, and no protein crystals were observed.

[0457] The next construct used for crystallization screening was MD08-99 (full-length *P. alba* IspS with N-terminal histidine-tag). MD08-99 was purified and the histidine-tag was removed. The same three initial crystallization screens were performed as for MBP-kudzu. The Hampton Research Crystal Screen and Qiagen JCSG+ Suite were each performed at multiple protein concentrations. Small needle-like crystals were observed in some Hampton Research Crystal Screen conditions. Further attempts to improve the crystals involved co-crystallization with the IspS inhibitor sodium ibandronate (Sigma-Aldrich, St Louis, MO). Taken together, an additional 288 crystallization conditions were attempted with variations of pH, concentration, and crystallization reagents. The nine best crystals were then prepared for data collection and tested in-house on a Rigaku RU200 rotating anode generator and R-AXIS IV++, and they either did not diffract x-rays or were salt crystals.

[0458] The first nineteen N-terminal residues of *P. alba* IspS were removed to produce construct MD08-100. This construct had the N-terminal histidine-tag removed after purification. In house crystallization screens were performed using the Hampton Research Crystal Screen and Qiagen JCSG+ Suite, each with multiple protein concentrations. Initial crystal hits included hexagonal plates that diffracted to 16Å resolution, and small rods that diffracted to 5Å resolution using the in-house x-ray generator. In an attempt to improve the crystals, MD08-100 was co-crystallized with either sodium ibandronate or sodium pyrophosphate (Sigma-Aldrich, St Louis, MO), both of which are inhibitors of the IspS activity. Neither inhibitor resulted in improved crystals or improved diffraction. An additional 168 crystallization conditions were attempted with variations of pH, concentration, and crystallization reagents. The twenty-one most promising MD08-100 crystals were screened for diffraction, with the best resolution obtained being 5Å.

[0459] Full-length, untagged *P. alba* IspS (strain RM11608-2) from a fermentation run was purified. An initial screen was set up using the Hampton Research Crystal Screen, and crystals were observed in four different conditions. All four crystals were tested for diffraction in-house, with three being salt crystals and one not diffracting.

[0460] A truncated *P. alba* IspS construct featuring two additional residues before the twin-arginine motif was generated (MD09-167). This construct contains a C-terminal histidine-tag, and crystallization experiments were set up with the tag either cleaved or not cleaved, at varying protein concentrations, and with or without sodium pyrophosphate. Initial crystallization screens were done as per MBP-kudzu. Crystals from this construct were observed in numerous conditions; optimization included 528 variations of pH, precipitating agents, concentrations, and inhibitors. From the optimization experiments, fifteen different MD09-167 crystals were screened in-house for diffraction. In an effort to improve the resolution, various crystal freezing conditions were tested, with the effect of improving the diffraction limits from 10Å to 6.5Å.

[0461] A new construct containing *P. tricharpa* IspS was generated, which contains both an N-terminal histidine-tag and an N-terminal truncation (MD08-104). Purified MD08-104 with cleaved histidine-tag was surveyed using the Hampton Research Crystal Screen and the Qiagen JCSG+ suite. This construct generated heavier precipitate than the *P. alba* IspS constructs. Very small needles were observed, with none of the crystals being suitable for diffraction.

[0462] Another construct composed of IspS from *P. tremuloides* was generated with an N-terminal histidine-tag and an N-terminal truncation (MD08-102). Purified MD08-102 with

and without cleaved histidine-tag was set up using the Hampton Research Crystal Screen and the Qiagen JCSG+ Suite at varying protein concentrations. Rod and plate-like crystals were observed in some conditions and an additional 120 experiments were performed to improve the crystals by varying pH, concentration, and crystallization reagents. From the optimization experiments, ten crystals were tested in-house, with the initial best diffraction reaching 5Å. Upon further modification of the freezing conditions of the crystals, a crystal was found that diffracted to 3.3Å from the non-cleaved histidine-tagged protein. This crystal was grown by mixing 2 μL of protein (10 mg/ml, with 30mM $MgCl_2$) with 2 μL of precipitant solution [10% (wt/vol) polyethylene glycol 8000, 0.1 M HEPES, pH 7.5, 8% ethylene glycol] and equilibrated against 500 μL of precipitant. A cluster of rod-shaped crystals appeared after three weeks. The crystals belong to the tetragonal space group P43212, and have unit cell dimensions a = 154.2, b = 154.2, c = 142.7.

[0463] In-house x-ray diffraction data were collected under a nitrogen stream at 100 K using a Rigaku RU200 generator and R-AXIS IV++ detector. Before flash-freezing the crystal in liquid nitrogen, it was cryoprotected by swiping it through a solution containing 10% (wt/vol) polyethylene glycol 8000, 0.1 M HEPES, pH 7.5, and 25% ethylene glycol. Data were integrated using Mosflm (Leslie, A. (1998) J. of Appl. Crystallography 30, 1036-1040) and scaled using SCALA (Collaborative Computational Project, N. (1994) Acta Crystallographica Section D 50, 760-763). The data were then phased by molecular replacement using MrBUMP (Keegan, R. M., and Winn, M. D. (2007) Acta Crystallographica Section D 63, 447-457; Vagin, A., and Teplyakov, A. (1997) J. of Appl. Crystallography 30, 1022-1025), with a monomer of limonene synthase (Protein Data Bank ID 2ONH)(Berman, H., *et al.* (2007) Nucl. Acids Res. 35, D301-303) as the starting model. The crystal contains one dimer in the asymmetric unit with a solvent content of 66%.

[0464] A 3.05Å data set from the same crystal was then collected using beamline 11-1 of the Stanford Synchrotron Radiation Laboratory. These data were also processed using Mosflm and SCALA. Data collection and refinement statistics are given in Table 16-1.

[0465] Refinement with Refmac5 (Collaborative Computational Project, N. (1994) Acta Crystallographica Section D 50, 760-763) was used with iterative manual rebuilding steps using the visualization program Coot (Emsley, P., and Cowtan, K. (2004) Acta Crystallographica Section D 60, 2126-2132). During refinement, the geometry of the protein was checked using Molprobity (Davis, I. W., *et al.* (2007) Nucl. Acids Res., gkm216).

[0466] The fold of poplar IspS is similar to bornyl diphosphate synthase (Whittington, D. A., *et al.* (2002) Proc. Natl Acad. Sci. USA 99, 15375-15380), limonene synthase (Hyatt, D.

C., et al. (2007) Proc. Natl Acad. Sci. USA 104, 5360-5365), and tobacco 5-epi-aristolochene synthase (Starks, C. M., *et al.* (1997) Science 277, 1815-1820) . The structure consists of two helical domains, a C-terminal domain containing the active site and N-terminal domain (Figures 90 and 91). Coordinates are provided in Table 16-7.

Table 16-1. Data Collection and Refinement Statistics

Data Collection	
Space Group	$P4_32_12$
Cell dimensions	
a, b, c (Å)	154.2, 154.2, 142.7
a, ß, γ, (°)	90.0, 90.0, 90.0
Resolution (Å)	37.8 – 3.05
R_{merge}	16.4 (72.9)[a]
<I/sI>	10.3 (2.6)
Completeness (%)	99.8 (100)
Redundancy	7.3 (7.4)
Refinement	
Resolution (Å)	37.8 – 3.05
No. measured reflections	248741
No. Unique reflections	34201
R_{work}	21.1
R_{free}	27.1
rmsd bonds, (Å)	0.011
rmsd angles, (°)	1.28
No. of Atoms	
Protein, ions[b]	8331
Water	18

Flexible Loops

[0467] The unique and unexpected discovery coming from the determination of the three dimensional structure of isoprene synthase is that several crucial loops forming the active site are flexible. The discovery can be immediately seen when the known structure of other terpene synthases are compared with the structure of isoprene synthase (Figure 94). Overall, the structures are highly conserved in the conformation of secondary structure and connectivity loops. (In this example of the *Poplar tremuloides* IspS from construct P.tremTRC-pET200, the numbering convention is such that the first number of the complete sequence containing the tag is -35, with the first residue of IspS being 1.) However, three segments, forming a considerable portion of the substrate binding pocket, notably the truncated N-terminus, along with two loops comprised of residues 438-453 (Loop I) and

residues 512-527 (Loop II) are seen to diverge (Figures 95 to 97). This has been attributed to the absence of substrate complexed with the enzyme in our structure determination.

[0468] In comparing the enzyme with BdpS, for example, we find that the loops corresponding to residues 498-513 and 573-587 are composed of the same number of residues and have a homologous, but not identical amino sequence in these regions. We expect that the related terpene synthases will be found to display similar flexibility in the segments as these structure become more thoroughly studied. The residues in terpene synthases corresponding to these variable loop regions are enumerated in Table 16-2.

Table 16-2. Residues corresponding to variable loops in terpene synthases

	Poplar IspS	LS	BdpS	TEAS
N-term I	Met 1	Met 57	Ile 54	Val 14
	Arg 2	Arg 58	Arg 55	Arg 15
	Arg 3	Arg 59	Arg 56	Pro 16
	Ser 4	Ser 60	Ser 57	Val 17
	Ala 5	Gly 61	Gly 58	Ala 18
	Asn 6	Asn 62	Asn 59	Asp 19
	Tyr 7	Tyr 63	Tyr 60	Phe 20
	Glu 8	Asn 64	Gln 61	Ser 21
	Pro 9	Pro 65	Pro 62	Pro 22
	Asn 10	Ser 66	Ala 63	Ser 23
	Ser 11	Arg 67	Leu 64	Leu 24
	Trp 12	Trp 68	Trp 65	Trp 25
	Asp 13	Asp 69	Asp 66	Gly 26
	Tyr 14	Val 70	Ser 67	Asp 27
	Asp 15	Asn 71	Asn 68	Gln 28
	Tyr 16	Phe 72	Tyr 69	Phe 29
N-term II	Leu 17	Ile 73	Ile 70	Leu 30
	Leu 18	Gln 74	Gln 71	Ser 31
	Ser 19	Ser 75	Ser 72	Phe 32
	Ser 20	Leu 76	Leu 73	Ser 34
	Asp 21	Leu 77	Asn 74	Ile 35
	Thr 22	Ser 78	Thr 75	Asp 36
	Asp 23	Asp 79	Pro 76	Asn 37
	Glu 24	Tyr 80	Tyr 77	Gln 38
	Ser 25	Lys 81	Thr 78	Val 39
	Ile 26	Glu 82	Glu 79	Ala 40
	Glu 27	Asp 83	Glu 80	Glu 41
	Val 28	Lys 84	Arg 81	Lys 42

Loop I	Leu 438	Leu 498	Leu 498	Thr 446
	Ala 439	Gly 499	Gly 499	Ala 447
	Ser 440	Thr 500	Thr 500	The 448
	Ala 441	Ser 501	Ser 502	Tyr 449
	Ser 442	Val 502	Tyr 503	Glu 450
	Ala 443	Glu 503	Phe 504	Val 451
	Glu 444	Glu 504	Glu 505	Glu 452
	Ile 445	Val 505	Leu 506	Lys 453
	Ala 446	Ser 506	Ala 507	Ser 454
	Arg 447	Arg 507	Arg 508	Arg 455
	Gly 448	Gly 508	Gly 509	Gly 456
	Glu 449	Asp 509	Asp 510	Gln 457
	Thr 450	Val 510	Val 511	Ile 458
	Ala 451	Pro 511	Pro 512	Ala 459
	Asn 452	Lys 512	Lys 513	Thr 460
	Ser 453	Ser 513	Thr 514	Gly 461
Loop II	Tyr 512	Tyr 576	Tyr 573	Tyr 520
				Ile 521
	His 513	His 577	Leu 574	His 522
	Asn 514	Asn 578	His 575	Asn 523
	Gly 515	Gly 579	Gly 576	Leu 524
	Asp 516	Asp 580	Asp 577	Asp 525
	Ala 517	Gly 581	Gly 578	Gly 526
	His 518	His 582	Phe 579	Tyr 527
	Thr 519	Gly 583	Gly 580	The 528
	Ser 520	Thr 584	Val 581	His 529
	Pro 521	Gln 585	Gln 582	Pro 530
	Asp 522	His 585	His 583	Glu 531
	Glu 523	Pro 586	Ser 584	Lys 532
	Leu 524	Ile 587	Lys 585	Val 533
	Thr 525	Ile 588	Thr 586	Lue 534
	Arg 526	His 589	Tyr 587	Lys 535

[0469] This important finding can be exploited for the engineering of improved isoprene synthase in a straightforward manner. It would be desirable to exploit the flexibility to enhance enzyme performance by making substitutions in the amino aids forming these segments to facilitate the transitions the enzyme must undergo in the steps of binding substrate and allowing rearrangement of substrate in different kinetic steps that are postulated

to occur during enzymatic de-phosphorylation and for electron transfer to convert DMAPP to isoprene.

[0470] The structure provides the new insight that these loops can be present in at least two conformations: the "open" form in the absence of substrate, as we have see in the uncomplexed structure of the isoprene synthase, and a "closed," or active form when the substrate is bound. It would therefore also be beneficial to modify residues coming in contact with the loops in the active form as described in Table 16-3.

Table 16-3. Residues coming within 5 angstroms of flexible elements

	P trem IspS	1N1B	2ONG	5EAS[e]
N-term neigbors	L17, L18, S19, S20, S239, R243, F253, A254, R255, D256, R257, I259, E260, D293, Y295, D296, V297, Y298, G299, T300, E303, Y325, L374, Y375, elements of loop I, elements of loop II, V529, L530, T534	70I, 71Q, 72S, 73L, 298S, 302S, 312F, 313V, 314R, 315D, 316R, 318V, 319E, 352D, 354Y, 355D, 356V, 357Y, 358G, 359T, 362E, 384Y, 433Y, 434H, elements of loop I, elements of loop II , 589I, 590A , 594F	I73, Q74, S75, L76, F299, R303, F313, A314, R315, A316, R317, V319, E320, D353, Y355, D356, V357, Y358, G359, T360, E363, Y385, F434, Y435, elements of loop I, elements of loop II, M590, T591, F595	L30, S31, F32, S33, S248, K252, Y262, A263, R264, D265, R266, V268, E269, D302, F304, D305, A306, Y307, G308, T309, E312, Y334, F383, I384, elements of loop I, elements of loop II, I538, I538, V543
Loop I neighbors	Elements of N-term, D293, Y295, V297, E370, A371, W373, L374, S378, T379, P380, F382, Y385, F386, R433, L434 C435, N436, D437, V454, S455, C456, Y457, M458, T469, V472, I476, Y512, elements of loop II	Elements of N-term, 352D, 354Y, 356V, 429E, 430A, 432W, 433Y, 437Y, 438T, 439P, 441L, 444Y, 445L, 493R, 494L, 495P, 496D, 497D, 514I, 515Q, 516C, 517Y, 518M, 529V, 532V, 536I, 572Y, elements of loop II	Elements of N-term, D353, Y355, V357, E430, A431, W433, F434, H438, K439, P440, L442, Y445, L446, R493, L494, A495, D496, D497, L514, Q515, C516, Y517, M518, R529, V532, I536, Y573, elements of loop II	Elements of N-term, D304, F304, A306, E379, S380, W382, F383, Y387, T388, P389, V391, Y394, L395, R441, V442, I443, D444, D445, I462, E463, C464, C465, M466, M477, F480, A484, Y520, elements of loop II
Loop II neighbors	Elements of N-terminus, E187, L188, R255, R257, F270, E271, Q273, Y274, F285, V288, A439, S440, S442, S508, H509, C510, T511, Y512, R528, V529, L530, S531, V532	Elements of N-terminus, 246D, 247L, 314R, 316R, 329E, 330S, 332F, 333W, 344I, 348I, 499G, 500T, 503Y, 568A, 569Q, 570F, 571I, 572Y, 588H, 589I, 590A, 591G, 592L	Elements of N-terminus, D247, I248, R315, R317, E330, P331, Q333, H334, N345, I347, G499, T500, V502, A569, Q570, L571, M572, Y573, Q589, M590, T591, R592, T593	Elements of N-terminus, E195, Q196, R264, R266, F279, E280, Q282, Y283, I294, I297, A447, T448, E450, V516, E517, V518, T519, Y520, H537, I538, I539, N540, L541

Selection of Sites for Improvement of Plant Isoprene Synthase

[0471] The isoprene synthases of plants were expected to be homologous to the terpene synthases. The three-dimensional structures of three homologous terpene synthases have been determined: *Salvia officinalis* bornyl diphosphate synthase (BdpS; pdb entry 1N1B), *Mentha spicata* limonene synthase (LS; pdb entry 2ONG), and tobacco 5-epi-aristolochene synthase (TEAS; pdb entry 5EAS). These enzymes share only 33% homology but their tertiary structure is conserved. Sequence identity is shown in Table 16-4, and structural homology between the structures is shown in Table 16-5. In addition, the structures of intermediate complexes with all three related enzymes have shown that not only tertiary

folding, but also detailed interactions in the active sites of these enzymes are highly conserved.

Table 16-4. Percent Identity of Terpene Cyclases.

	P trem IspS	1N1B	2ONG	5EAS[e]
P alba IspS[a]	98.6	40.7	41.3	33.2
P trem IspS[b]		41.0	41.4	33.2
1N1B[c]			51.4	33.8
2ONG[d]				33.3

[a] Polar alba isoprene synthase
[b] Polar tremuloides isoprene synthase
[c] bornyl diphosphate synthase
[d] limonene synthase
[e] 5-epi-aristolochene synthase

Table 16-5. Structural Alignment of Terpene Synthases

	1N1B[b]	2ONG[c]	5EAS[d]
P trem IspS[a]	1.40 (465)[e]	1.29 (468)	1.62 (458)
1N1B		1.27 (520)	1.97 (476)
2ONG			1.83 (477)

[a] *Polar tremuloides* isoprene synthase
[b] bornyl diphosphate synthase
[c] limonene synthase
[d] 5-epi-aristolochene synthase
[e] Root mean square deviation in Å for Ca atoms, with the number of aligned residues in parenthesis

[0472] In this example of the *Poplar tremuloides* IspS from construct P.tremTRC-pET200, the numbering convention is such that the first number of the complete sequence containing the tag is -35, with the first residue of IspS being 1.

[0473] A comparison of the active site from the structure of BdpS and the structure of poplar IspS indicates that the active site involved in metal ion binding and phosphate recognition is conserved. In particular, Arg 255, Asp 292, Asp 296, Glu 370, Arg 433 and

Asn 436 of poplar IspS were observed to overlap equivalent residues in BdpS. The positioning of an intermediate of the BdpS was also compared with the poplar IspS structure. Based on this it was possible to identify the analogous binding region and the approach direction that dimethylallyl pyrophosphate would require in order to bind and react with the poplar IspS enzyme.

[0474] Based on the structure of poplar IspS, sites in the poplar IspS were identified as candidates for mutagenesis to produce variant IspS enzymes with improved performance. Briefly, sites were selected in the IspS that might alter the interaction of the metal binding, diphosphate recognition, DMAPP chain binding and/or the approach to the active site.

I. Diphosphate/ Metal Binding Sites

[0475] The side chains of amino acid residues in the poplar IspS that are found in proximity to the metal and diphosphate binding side chains were identified. These residues include Asp 293, Tyr 385, Ser 392, and Asp 437. Engineering of these sites may result in increased enzyme activity.

II. Substrate Access Loops

[0476] The substrate access loops of poplar IspS are in regions that deviate from the BdpS structure. In the BdpS structure the residues create a cover over the active site. It is likely that upon substrate binding the structure of poplar IspS will form a similar structure. As such the residues in these loops, including residues 440-453 and 512-524, may be in a position to alter the activity of the poplar IspS. In the poplar IspS enzyme, residues 440-453 have the sequence SASAEIARGETANS and residues 512-526 have the sequence YHNGDAHTSPDEL.

III. Isoprenyl Binding Site

[0477] The complex of BdpS and the product of the reaction, bornyl diphosphate (PDB entry 1N24), was used to identify residues in the poplar IspS structure that with protein engineering may be used modulate substrate specificity and/or reaction rate (altered on and off rates of substrate and product). These residues include Ser 261, Trp 264, Phe 285, Thr 289, Ser 393, Ser 394, Phe 432, and Try 512.

Table 16-6. Candidate mutagenesis sites.

	Poplar IspS
DPP/Metal Binding Sites	Asp 293
	Tyr 385
	Ser 392
	Asp 437
Substrate Access Loop I	Ser 440
	Ala 441
	Ser 442
	Ala 443
	Glu 444
	Ile 445
	Ala 446
	Arg 447
	Gly 448
	Glu 449
	Thr 450
	Ala 451
	Asn 452
	Ser 453
Substate Access Loop II	Tyr 512
	His 513
	Asn 514
	Gly 515
	Asp 516
	Ala 517
	His 518
	Thr 519
	Ser 520
	Pro 521
	Asp 522
	Glu 523
	Leu 524
Isoprenyl Binding Site	Ser 261
	Trp 264
	Phe 285
	Thr 289
	Ser 393
	Ser 394
	Phe 432

	Tyr 512

Table 16-7. Coordinates of *P. tremuloides* IspS

```
HEADER    ----                              XX-XXX-XX   xxxx
COMPND    ---
REMARK   3
REMARK   3 REFINEMENT.
REMARK   3   PROGRAM     : REFMAC 5.5.0088
REMARK   3   AUTHORS     : MURSHUDOV,VAGIN,DODSON
REMARK   3
REMARK   3    REFINEMENT TARGET : MAXIMUM LIKELIHOOD
REMARK   3
REMARK   3  DATA USED IN REFINEMENT.
REMARK   3   RESOLUTION RANGE HIGH (ANGSTROMS) :   3.05
REMARK   3   RESOLUTION RANGE LOW  (ANGSTROMS) : 110.17
REMARK   3   DATA CUTOFF           (SIGMA(F)) : NONE
REMARK   3   COMPLETENESS FOR RANGE       (%) :  99.67
REMARK   3   NUMBER OF REFLECTIONS            :  32446
REMARK   3
REMARK   3  FIT TO DATA USED IN REFINEMENT.
REMARK   3   CROSS-VALIDATION METHOD         : THROUGHOUT
REMARK   3   FREE R VALUE TEST SET SELECTION  : RANDOM
REMARK   3   R VALUE     (WORKING + TEST SET) :  .21396
REMARK   3   R VALUE           (WORKING SET) :  .21092
REMARK   3   FREE R VALUE                     :  .27112
REMARK   3   FREE R VALUE TEST SET SIZE   (%) :  5.1
REMARK   3   FREE R VALUE TEST SET COUNT      :  1727
REMARK   3
REMARK   3  FIT IN THE HIGHEST RESOLUTION BIN.
REMARK   3   TOTAL NUMBER OF BINS USED        :    20
REMARK   3   BIN RESOLUTION RANGE HIGH        :  3.050
REMARK   3   BIN RESOLUTION RANGE LOW         :  3.129
REMARK   3   REFLECTION IN BIN     (WORKING SET) :    2359
REMARK   3   BIN COMPLETENESS (WORKING+TEST) (%) :  100.00
REMARK   3   BIN R VALUE           (WORKING SET) :    .288
REMARK   3   BIN FREE R VALUE SET COUNT       :    127
REMARK   3   BIN FREE R VALUE                 :    .352
REMARK   3
REMARK   3  NUMBER OF NON-HYDROGEN ATOMS USED IN REFINEMENT.
REMARK   3   ALL ATOMS             :   8349
REMARK   3
REMARK   3  B VALUES.
REMARK   3   FROM WILSON PLOT          (A**2) : NULL
REMARK   3   MEAN B VALUE      (OVERALL, A**2) :  24.592
REMARK   3   OVERALL ANISOTROPIC B VALUE.
REMARK   3    B11 (A**2) :     .41
REMARK   3    B22 (A**2) :     .41
REMARK   3    B33 (A**2) :    -.81
REMARK   3    B12 (A**2) :     .00
REMARK   3    B13 (A**2) :     .00
REMARK   3    B23 (A**2) :     .00
REMARK   3
REMARK   3  ESTIMATED OVERALL COORDINATE ERROR.
REMARK   3   ESU BASED ON R VALUE                            (A): NULL
REMARK   3   ESU BASED ON FREE R VALUE                       (A):   .427
REMARK   3   ESU BASED ON MAXIMUM LIKELIHOOD                 (A):   .327
REMARK   3   ESU FOR B VALUES BASED ON MAXIMUM LIKELIHOOD (A**2):  39.836
```

```
REMARK   3
REMARK   3 CORRELATION COEFFICIENTS.
REMARK   3  CORRELATION COEFFICIENT FO-FC      :   .916
REMARK   3  CORRELATION COEFFICIENT FO-FC FREE :   .868
REMARK   3
REMARK   3 RMS DEVIATIONS FROM IDEAL VALUES       COUNT    RMS    WEIGHT
REMARK   3  BOND LENGTHS REFINED ATOMS       (A):  8495 ;  .011 ;  .022
REMARK   3  BOND LENGTHS OTHERS              (A):  5804 ;  .001 ;  .020
REMARK   3  BOND ANGLES REFINED ATOMS   (DEGREES): 11476 ; 1.279 ; 1.953
REMARK   3  BOND ANGLES OTHERS          (DEGREES): 14093 ;  .882 ; 3.000
REMARK   3  TORSION ANGLES, PERIOD 1    (DEGREES):  1020 ; 7.002 ; 5.000
REMARK   3  TORSION ANGLES, PERIOD 2    (DEGREES):   435 ;35.412 ;24.299
REMARK   3  TORSION ANGLES, PERIOD 3    (DEGREES):  1525 ;18.250 ;15.000
REMARK   3  TORSION ANGLES, PERIOD 4    (DEGREES):    58 ;16.811 ;15.000
REMARK   3  CHIRAL-CENTER RESTRAINTS       (A**3):  1266 ;  .070 ;  .200
REMARK   3  GENERAL PLANES REFINED ATOMS      (A):  9416 ;  .005 ;  .020
REMARK   3  GENERAL PLANES OTHERS             (A):  1780 ;  .001 ;  .020
REMARK   3
REMARK   3 ISOTROPIC THERMAL FACTOR RESTRAINTS.    COUNT   RMS    WEIGHT
REMARK   3  MAIN-CHAIN BOND REFINED ATOMS  (A**2):  5104 ;  .514 ; 1.500
REMARK   3  MAIN-CHAIN BOND OTHER ATOMS    (A**2):  2068 ;  .059 ; 1.500
REMARK   3  MAIN-CHAIN ANGLE REFINED ATOMS (A**2):  8204 ; 1.000 ; 2.000
REMARK   3  SIDE-CHAIN BOND REFINED ATOMS  (A**2):  3391 ; 1.218 ; 3.000
REMARK   3  SIDE-CHAIN ANGLE REFINED ATOMS (A**2):  3272 ; 2.157 ; 4.500
REMARK   3
REMARK   3 NCS RESTRAINTS STATISTICS
REMARK   3  NUMBER OF DIFFERENT NCS GROUPS :  1
REMARK   3
REMARK   3 NCS GROUP NUMBER             :  1
REMARK   3   CHAIN NAMES                : A B
REMARK   3   NUMBER OF COMPONENTS NCS GROUP :   1
REMARK   3    COMPONENT C  SSSEQI  TO  C   SSSEQI   CODE
REMARK   3        1    A      17      A      541     6
REMARK   3        1    B      17      B      541     6
REMARK   3              GROUP CHAIN       COUNT   RMS     WEIGHT
REMARK   3 LOOSE POSITIONAL   1   1    (A):   7038 ;  .37 ;  5.00
REMARK   3 LOOSE THERMAL      1   1  (A**2):   7038 ;  1.09 ; 10.00
REMARK   3
REMARK   3 TWIN DETAILS
REMARK   3  NUMBER OF TWIN DOMAINS  : NULL
REMARK   3
REMARK   3
REMARK   3 TLS DETAILS
REMARK   3  NUMBER OF TLS GROUPS  :   8
REMARK   3  ATOM RECORD CONTAINS RESIDUAL B FACTORS ONLY
REMARK   3
REMARK   3  TLS GROUP :    1
REMARK   3   NUMBER OF COMPONENTS GROUP :   1
REMARK   3   COMPONENTS       C SSSEQI   TO  C SSSEQI
REMARK   3   RESIDUE RANGE :   A      17       A      219
REMARK   3   ORIGIN FOR THE GROUP (A): -64.7667  37.6643   -.0896
REMARK   3   T TENSOR
REMARK   3     T11:   .0648 T22:   .0357
REMARK   3     T33:   .0787 T12:   .0200
REMARK   3     T13:   .0129 T23:   -.0089
REMARK   3   L TENSOR
REMARK   3     L11:  3.7204 L22:  1.5111
REMARK   3     L33:  2.6701 L12:   .5715
REMARK   3     L13:   .6692 L23:   -.9699
REMARK   3   S TENSOR
```

```
REMARK   3    S11:   .0562 S12:   .0478 S13:  -.1976
REMARK   3    S21:  -.1702 S22:  -.0055 S23:   .1376
REMARK   3    S31:   .0900 S32:  -.2188 S33:  -.0507
REMARK   3
REMARK   3  TLS GROUP :    2
REMARK   3   NUMBER OF COMPONENTS GROUP :    1
REMARK   3   COMPONENTS       C SSSEQI   TO  C SSSEQI
REMARK   3   RESIDUE RANGE :   A     220       A     287
REMARK   3   ORIGIN FOR THE GROUP (A): -59.5787   8.4529   -.7693
REMARK   3   T TENSOR
REMARK   3    T11:   .1615 T22:   .0645
REMARK   3    T33:   .1539 T12:  -.0314
REMARK   3    T13:  -.0461 T23:   .0198
REMARK   3   L TENSOR
REMARK   3    L11:  2.4192 L22:  4.6709
REMARK   3    L33:   .7709 L12: -3.2943
REMARK   3    L13:  -.1814 L23:  -.0705
REMARK   3   S TENSOR
REMARK   3    S11:   .0055 S12:  -.0699 S13:  -.2073
REMARK   3    S21:  -.1805 S22:   .0996 S23:   .3781
REMARK   3    S31:   .2596 S32:   .0887 S33:  -.1051
REMARK   3
REMARK   3  TLS GROUP :    3
REMARK   3   NUMBER OF COMPONENTS GROUP :    1
REMARK   3   COMPONENTS       C SSSEQI   TO  C SSSEQI
REMARK   3   RESIDUE RANGE :   A     288       A     374
REMARK   3   ORIGIN FOR THE GROUP (A): -40.1866   1.6932    .5805
REMARK   3   T TENSOR
REMARK   3    T11:   .1149 T22:   .1003
REMARK   3    T33:   .1629 T12:   .0153
REMARK   3    T13:   .0224 T23:   .0164
REMARK   3   L TENSOR
REMARK   3    L11:   .2271 L22:   .7399
REMARK   3    L33:  4.8529 L12:   .3413
REMARK   3    L13:   .4755 L23:  -.1746
REMARK   3   S TENSOR
REMARK   3    S11:  -.0449 S12:  -.0288 S13:  -.1131
REMARK   3    S21:  -.1346 S22:  -.0665 S23:  -.2749
REMARK   3    S31:  -.0040 S32:   .1558 S33:   .1114
REMARK   3
REMARK   3  TLS GROUP :    4
REMARK   3   NUMBER OF COMPONENTS GROUP :    1
REMARK   3   COMPONENTS       C SSSEQI   TO  C SSSEQI
REMARK   3   RESIDUE RANGE :   A     375       A     541
REMARK   3   ORIGIN FOR THE GROUP (A): -47.2220  21.5399   6.9217
REMARK   3   T TENSOR
REMARK   3    T11:   .1551 T22:   .1194
REMARK   3    T33:   .1485 T12:  -.0666
REMARK   3    T13:   .0275 T23:   .0272
REMARK   3   L TENSOR
REMARK   3    L11:  2.2352 L22:  2.1698
REMARK   3    L33:  2.3370 L12:  -.4501
REMARK   3    L13:  2.2662 L23:  -.1852
REMARK   3   S TENSOR
REMARK   3    S11:   .0233 S12:  -.3041 S13:  -.0323
REMARK   3    S21:   .3375 S22:   .0236 S23:   .0121
REMARK   3    S31:   .0592 S32:  -.2979 S33:  -.0469
REMARK   3
REMARK   3  TLS GROUP :    5
REMARK   3   NUMBER OF COMPONENTS GROUP :    1
```

REMARK 3 COMPONENTS C SSSEQI TO C SSSEQI
REMARK 3 RESIDUE RANGE : B 17 B 219
REMARK 3 ORIGIN FOR THE GROUP (A): -73.9834 -39.9016 -18.5783
REMARK 3 T TENSOR
REMARK 3 T11: .0658 T22: .1153
REMARK 3 T33: .1251 T12: -.0621
REMARK 3 T13: -.0164 T23: -.0098
REMARK 3 L TENSOR
REMARK 3 L11: 4.6230 L22: 1.7260
REMARK 3 L33: 3.8816 L12: -.4202
REMARK 3 L13: -1.8646 L23: -.9046
REMARK 3 S TENSOR
REMARK 3 S11: -.0685 S12: .0375 S13: -.0003
REMARK 3 S21: .1931 S22: .0510 S23: -.0097
REMARK 3 S31: .0317 S32: -.2047 S33: .0175
REMARK 3
REMARK 3 TLS GROUP : 6
REMARK 3 NUMBER OF COMPONENTS GROUP : 1
REMARK 3 COMPONENTS C SSSEQI TO C SSSEQI
REMARK 3 RESIDUE RANGE : B 220 B 287
REMARK 3 ORIGIN FOR THE GROUP (A): -62.1586 -12.7634 -18.1912
REMARK 3 T TENSOR
REMARK 3 T11: .1825 T22: .0804
REMARK 3 T33: .1512 T12: .0549
REMARK 3 T13: .0773 T23: .0208
REMARK 3 L TENSOR
REMARK 3 L11: 5.4421 L22: 4.0606
REMARK 3 L33: 1.5369 L12: 4.6706
REMARK 3 L13: -2.0058 L23: -1.5537
REMARK 3 S TENSOR
REMARK 3 S11: .1622 S12: .0431 S13: .3257
REMARK 3 S21: .1755 S22: .0292 S23: .2977
REMARK 3 S31: -.1910 S32: -.0506 S33: -.1914
REMARK 3
REMARK 3 TLS GROUP : 7
REMARK 3 NUMBER OF COMPONENTS GROUP : 1
REMARK 3 COMPONENTS C SSSEQI TO C SSSEQI
REMARK 3 RESIDUE RANGE : B 288 B 374
REMARK 3 ORIGIN FOR THE GROUP (A): -41.6930 -10.8250 -19.6636
REMARK 3 T TENSOR
REMARK 3 T11: .1424 T22: .0604
REMARK 3 T33: .1153 T12: .0184
REMARK 3 T13: .0146 T23: .0276
REMARK 3 L TENSOR
REMARK 3 L11: .6426 L22: .8163
REMARK 3 L33: 2.3437 L12: -.1831
REMARK 3 L13: -.5246 L23: .4917
REMARK 3 S TENSOR
REMARK 3 S11: .0592 S12: -.0206 S13: .0071
REMARK 3 S21: .0906 S22: -.0229 S23: -.1585
REMARK 3 S31: -.0355 S32: .0262 S33: -.0363
REMARK 3
REMARK 3 TLS GROUP : 8
REMARK 3 NUMBER OF COMPONENTS GROUP : 1
REMARK 3 COMPONENTS C SSSEQI TO C SSSEQI
REMARK 3 RESIDUE RANGE : B 375 B 541
REMARK 3 ORIGIN FOR THE GROUP (A): -53.4886 -28.3212 -26.0670
REMARK 3 T TENSOR
REMARK 3 T11: .1107 T22: .1220
REMARK 3 T33: .1514 T12: .0692

```
REMARK   3     T13:  -.0073 T23:   .0518
REMARK   3   L TENSOR
REMARK   3     L11:  2.6766 L22:  1.8433
REMARK   3     L33:  2.6389 L12:   .1130
REMARK   3     L13: -2.4696 L23:   .6986
REMARK   3   S TENSOR
REMARK   3     S11:   .1115 S12:   .3882 S13:   .0569
REMARK   3     S21:  -.0725 S22:  -.0724 S23:   .1450
REMARK   3     S31:  -.1453 S32:  -.4044 S33:  -.0392
REMARK   3
REMARK   3
REMARK   3  BULK SOLVENT MODELLING.
REMARK   3   METHOD USED :  MASK
REMARK   3   PARAMETERS FOR MASK CALCULATION
REMARK   3   VDW PROBE RADIUS   :  1.40
REMARK   3   ION PROBE RADIUS   :   .80
REMARK   3   SHRINKAGE RADIUS   :   .80
REMARK   3
REMARK   3  OTHER REFINEMENT REMARKS:
REMARK   3  HYDROGENS HAVE BEEN ADDED IN THE RIDING POSITIONS
REMARK   3  U VALUES      : RESIDUAL ONLY
REMARK   3
CISPEP   1 ALA A  446    ARG A  447                .00
CISPEP   2 GLY A  515    ASP A  516                .00
CISPEP   3 THR B   22    ASP B   23               .00
CISPEP   4 ALA B  446    ARG B  447                .00
CISPEP   5 GLY B  515    ASP B  516                .00
CRYST1  155.800  155.800  143.690  90.00  90.00  90.00 P 43 21 2
SCALE1      .006418  .000000  .000000        .00000
SCALE2      .000000  .006418  .000000        .00000
SCALE3      .000000  .000000  .006959        .00000
ATOM     1  N   LEU A  17    -63.930  24.416 -19.202  1.00 30.90         N
ATOM     2  CA  LEU A  17    -64.132  23.019 -19.731  1.00 31.43         C
ATOM     4  CB  LEU A  17    -63.308  22.800 -21.021  1.00 31.35         C
ATOM     7  CG  LEU A  17    -64.002  23.016 -22.386  1.00 31.95         C
ATOM     9  CD1 LEU A  17    -62.989  23.068 -23.550  1.00 31.88         C
ATOM    13  CD2 LEU A  17    -65.052  21.915 -22.676  1.00 31.95         C
ATOM    17  C   LEU A  17    -63.783  21.952 -18.660  1.00 31.39         C
ATOM    18  O   LEU A  17    -63.142  22.291 -17.651  1.00 31.61         O
ATOM    22  N   LEU A  18    -64.216  20.693 -18.877  1.00 31.11         N
ATOM    23  CA  LEU A  18    -63.986  19.529 -17.957  1.00 30.78         C
ATOM    25  CB  LEU A  18    -62.503  19.072 -17.935  1.00 30.97         C
ATOM    28  CG  LEU A  18    -61.303  19.949 -17.496  1.00 31.10         C
ATOM    30  CD1 LEU A  18    -61.406  20.430 -16.064  1.00 30.71         C
ATOM    34  CD2 LEU A  18    -59.977  19.173 -17.703  1.00 31.87         C
ATOM    38  C   LEU A  18    -64.531  19.665 -16.522  1.00 30.38         C
ATOM    39  O   LEU A  18    -64.837  18.667 -15.883  1.00 29.86         O
ATOM    41  N   SER A  19    -64.587  20.900 -16.023  1.00 30.45         N
ATOM    42  CA  SER A  19    -65.335  21.276 -14.815  1.00 30.37         C
ATOM    44  CB  SER A  19    -64.604  22.417 -14.026  1.00 30.02         C
ATOM    47  OG  SER A  19    -64.881  23.741 -14.489  1.00 28.00         O
ATOM    49  C   SER A  19    -66.784  21.654 -15.218  1.00 31.03         C
ATOM    50  O   SER A  19    -67.666  21.711 -14.367  1.00 30.95         O
ATOM    52  N   SER A  20    -67.023  21.880 -16.519  1.00 31.85         N
ATOM    53  CA  SER A  20    -68.355  22.247 -17.051  1.00 32.37         C
ATOM    55  CB  SER A  20    -68.291  22.507 -18.579  1.00 32.39         C
ATOM    58  OG  SER A  20    -67.387  23.542 -18.931  1.00 31.77         O
ATOM    60  C   SER A  20    -69.357  21.124 -16.744  1.00 33.04         C
ATOM    61  O   SER A  20    -69.076  20.254 -15.922  1.00 33.08         O
ATOM    63  N   ASP A  21    -70.522  21.136 -17.393  1.00 33.88         N
```

```
ATOM   64 CA  ASP A 21    -71.512  20.069 -17.206  1.00 34.48       C
ATOM   66 CB  ASP A 21    -72.907  20.655 -17.127  1.00 34.59       C
ATOM   69 CG  ASP A 21    -73.022  21.661 -16.006  1.00 35.54       C
ATOM   70 OD1 ASP A 21    -72.041  21.836 -15.251  1.00 35.31       O
ATOM   71 OD2 ASP A 21    -74.082  22.289 -15.870  1.00 38.72       O
ATOM   72 C   ASP A 21    -71.409  18.975 -18.260  1.00 34.94       C
ATOM   73 O   ASP A 21    -72.134  18.947 -19.269  1.00 34.58       O
ATOM   75 N   THR A 22    -70.457  18.086 -17.989  1.00 35.66       N
ATOM   76 CA  THR A 22    -70.340  16.799 -18.657  1.00 36.27       C
ATOM   78 CB  THR A 22    -68.895  16.576 -19.168  1.00 36.30       C
ATOM   80 OG1 THR A 22    -67.968  17.278 -18.322  1.00 36.04       O
ATOM   82 CG2 THR A 22    -68.755  17.088 -20.604  1.00 36.11       C
ATOM   86 C   THR A 22    -70.792  15.714 -17.648  1.00 36.83       C
ATOM   87 O   THR A 22    -69.968  15.022 -17.035  1.00 37.05       O
ATOM   89 N   ASP A 23    -72.121  15.599 -17.494  1.00 37.27       N
ATOM   90 CA  ASP A 23    -72.790  14.802 -16.441  1.00 37.25       C
ATOM   92 CB  ASP A 23    -72.962  15.659 -15.167  1.00 37.17       C
ATOM   95 CG  ASP A 23    -71.625  16.081 -14.549  1.00 37.74       C
ATOM   96 OD1 ASP A 23    -70.714  15.241 -14.436  1.00 38.88       O
ATOM   97 OD2 ASP A 23    -71.472  17.256 -14.164  1.00 38.91       O
ATOM   98 C   ASP A 23    -74.172  14.351 -16.956  1.00 37.18       C
ATOM   99 O   ASP A 23    -75.137  15.112 -16.846  1.00 37.10       O
ATOM  101 N   GLU A 24    -74.280  13.134 -17.501  1.00 37.23       N
ATOM  102 CA  GLU A 24    -75.406  12.815 -18.410  1.00 37.58       C
ATOM  104 CB  GLU A 24    -74.941  13.007 -19.865  1.00 37.77       C
ATOM  107 CG  GLU A 24    -74.424  14.417 -20.239  1.00 37.98       C
ATOM  110 CD  GLU A 24    -74.121  14.556 -21.746  1.00 38.35       C
ATOM  111 OE1 GLU A 24    -74.284  13.564 -22.503  1.00 38.12       O
ATOM  112 OE2 GLU A 24    -73.721  15.661 -22.174  1.00 38.18       O
ATOM  113 C   GLU A 24    -76.139  11.440 -18.323  1.00 37.79       C
ATOM  114 O   GLU A 24    -77.323  11.397 -17.960  1.00 37.90       O
ATOM  116 N   SER A 25    -75.462  10.345 -18.696  1.00 37.92       N
ATOM  117 CA  SER A 25    -76.140   9.070 -19.048  1.00 38.09       C
ATOM  119 CB  SER A 25    -75.167   8.076 -19.723  1.00 38.11       C
ATOM  122 OG  SER A 25    -74.503   7.239 -18.787  1.00 38.02       O
ATOM  124 C   SER A 25    -76.917   8.374 -17.907  1.00 38.42       C
ATOM  125 O   SER A 25    -76.635   8.581 -16.724  1.00 38.15       O
ATOM  127 N   ILE A 26    -77.861   7.511 -18.312  1.00 39.00       N
ATOM  128 CA  ILE A 26    -78.993   7.042 -17.476  1.00 39.30       C
ATOM  130 CB  ILE A 26    -78.594   5.965 -16.429  1.00 39.34       C
ATOM  132 CG1 ILE A 26    -77.892   4.791 -17.120  1.00 39.37       C
ATOM  135 CD1 ILE A 26    -77.766   3.531 -16.253  1.00 39.46       C
ATOM  139 CG2 ILE A 26    -79.836   5.423 -15.714  1.00 39.29       C
ATOM  143 C   ILE A 26    -79.716   8.260 -16.852  1.00 39.66       C
ATOM  144 O   ILE A 26    -79.274   8.831 -15.838  1.00 39.49       O
ATOM  146 N   GLU A 27    -80.837   8.623 -17.486  1.00 39.99       N
ATOM  147 CA  GLU A 27    -81.450   9.965 -17.383  1.00 40.11       C
ATOM  149 CB  GLU A 27    -82.395  10.183 -18.587  1.00 40.19       C
ATOM  152 CG  GLU A 27    -81.632  10.311 -19.904  1.00 40.60       C
ATOM  155 CD  GLU A 27    -82.528  10.434 -21.116  1.00 41.06       C
ATOM  156 OE1 GLU A 27    -83.328   9.502 -21.367  1.00 41.10       O
ATOM  157 OE2 GLU A 27    -82.409  11.458 -21.830  1.00 41.36       O
ATOM  158 C   GLU A 27    -82.144  10.264 -16.042  1.00 40.02       C
ATOM  159 O   GLU A 27    -81.977   9.518 -15.071  1.00 40.01       O
ATOM  161 N   VAL A 28    -82.899  11.370 -16.005  1.00 39.84       N
ATOM  162 CA  VAL A 28    -83.463  11.960 -14.779  1.00 39.65       C
ATOM  164 CB  VAL A 28    -83.884  10.905 -13.694  1.00 39.78       C
ATOM  166 CG1 VAL A 28    -84.472  11.596 -12.456  1.00 39.87       C
ATOM  170 CG2 VAL A 28    -84.887   9.880 -14.274  1.00 39.49       C
ATOM  174 C   VAL A 28    -82.469  12.980 -14.206  1.00 39.46       C
```

ATOM 175 O VAL A 28 -82.798 13.717 -13.270 1.00 39.38 O
ATOM 177 N HIS A 29 -81.264 13.025 -14.786 1.00 39.30 N
ATOM 178 CA HIS A 29 -80.236 14.006 -14.412 1.00 39.23 C
ATOM 180 CB HIS A 29 -78.866 13.344 -14.186 1.00 39.45 C
ATOM 183 CG HIS A 29 -78.910 12.139 -13.296 1.00 41.29 C
ATOM 184 ND1 HIS A 29 -78.407 12.140 -12.007 1.00 42.51 N
ATOM 186 CE1 HIS A 29 -78.585 10.942 -11.472 1.00 43.37 C
ATOM 188 NE2 HIS A 29 -79.181 10.164 -12.365 1.00 43.18 N
ATOM 190 CD2 HIS A 29 -79.393 10.888 -13.515 1.00 42.55 C
ATOM 192 C HIS A 29 -80.090 15.110 -15.464 1.00 38.60 C
ATOM 193 O HIS A 29 -79.049 15.774 -15.499 1.00 38.61 O
ATOM 195 N LYS A 30 -81.110 15.320 -16.311 1.00 37.87 N
ATOM 196 CA LYS A 30 -81.265 16.610 -17.001 1.00 37.22 C
ATOM 198 CB LYS A 30 -82.283 16.542 -18.140 1.00 37.09 C
ATOM 201 CG LYS A 30 -81.764 15.794 -19.360 1.00 37.00 C
ATOM 204 CD LYS A 30 -82.831 15.653 -20.457 1.00 36.89 C
ATOM 207 CE LYS A 30 -82.413 14.637 -21.531 1.00 36.48 C
ATOM 210 NZ LYS A 30 -83.422 14.458 -22.611 1.00 35.46 N
ATOM 214 C LYS A 30 -81.648 17.649 -15.938 1.00 36.88 C
ATOM 215 O LYS A 30 -82.516 18.499 -16.136 1.00 36.71 O
ATOM 217 N ASP A 31 -80.982 17.506 -14.788 1.00 36.58 N
ATOM 218 CA ASP A 31 -80.895 18.476 -13.720 1.00 36.18 C
ATOM 220 CB ASP A 31 -80.518 17.751 -12.396 1.00 36.20 C
ATOM 223 CG ASP A 31 -79.863 18.669 -11.342 1.00 36.65 C
ATOM 224 OD1 ASP A 31 -80.055 19.901 -11.390 1.00 38.17 O
ATOM 225 OD2 ASP A 31 -79.147 18.150 -10.449 1.00 35.46 O
ATOM 226 C ASP A 31 -79.811 19.426 -14.226 1.00 35.74 C
ATOM 227 O ASP A 31 -78.628 19.279 -13.918 1.00 35.44 O
ATOM 229 N LYS A 32 -80.220 20.343 -15.096 1.00 35.30 N
ATOM 230 CA LYS A 32 -79.360 21.449 -15.507 1.00 34.69 C
ATOM 232 CB LYS A 32 -78.698 21.188 -16.849 1.00 34.63 C
ATOM 235 CG LYS A 32 -77.699 20.042 -16.765 1.00 34.51 C
ATOM 238 CD LYS A 32 -76.953 19.853 -18.078 1.00 34.48 C
ATOM 241 CE LYS A 32 -76.859 18.387 -18.503 1.00 33.77 C
ATOM 244 NZ LYS A 32 -77.002 18.244 -19.985 1.00 32.92 N
ATOM 248 C LYS A 32 -80.162 22.745 -15.459 1.00 34.01 C
ATOM 249 O LYS A 32 -80.468 23.380 -16.473 1.00 33.41 O
ATOM 251 N ALA A 33 -80.540 23.051 -14.219 1.00 33.21 N
ATOM 252 CA ALA A 33 -80.785 24.381 -13.766 1.00 32.60 C
ATOM 254 CB ALA A 33 -81.619 24.347 -12.484 1.00 32.28 C
ATOM 258 C ALA A 33 -79.411 25.031 -13.524 1.00 32.31 C
ATOM 259 O ALA A 33 -79.335 26.081 -12.901 1.00 32.80 O
ATOM 261 N LYS A 34 -78.323 24.389 -13.968 1.00 31.70 N
ATOM 262 CA LYS A 34 -77.035 25.071 -14.186 1.00 31.12 C
ATOM 264 CB LYS A 34 -75.863 24.089 -14.128 1.00 31.23 C
ATOM 267 CG LYS A 34 -75.118 24.077 -12.791 1.00 31.76 C
ATOM 270 CD LYS A 34 -73.584 24.412 -12.921 1.00 31.49 C
ATOM 273 CE LYS A 34 -72.685 23.269 -12.506 1.00 30.50 C
ATOM 276 NZ LYS A 34 -72.951 22.090 -13.348 1.00 29.53 N
ATOM 280 C LYS A 34 -77.024 25.884 -15.518 1.00 30.50 C
ATOM 281 O LYS A 34 -76.977 25.353 -16.625 1.00 29.82 O
ATOM 283 N LYS A 35 -76.927 27.191 -15.337 1.00 29.97 N
ATOM 284 CA LYS A 35 -77.632 28.233 -16.098 1.00 29.41 C
ATOM 286 CB LYS A 35 -78.852 27.704 -16.867 1.00 29.53 C
ATOM 289 CG LYS A 35 -80.166 27.594 -16.077 1.00 30.18 C
ATOM 292 CD LYS A 35 -81.030 28.858 -16.203 1.00 31.25 C
ATOM 295 CE LYS A 35 -82.375 28.721 -15.486 1.00 31.85 C
ATOM 298 NZ LYS A 35 -83.298 29.865 -15.783 1.00 31.73 N
ATOM 302 C LYS A 35 -78.053 29.277 -15.026 1.00 28.53 C
ATOM 303 O LYS A 35 -78.246 30.460 -15.307 1.00 28.53 O

ATOM 305 N LEU A 36 -78.225 28.791 -13.796 1.00 27.29 N
ATOM 306 CA LEU A 36 -77.998 29.576 -12.594 1.00 26.21 C
ATOM 308 CB LEU A 36 -78.088 28.679 -11.364 1.00 25.76 C
ATOM 311 CG LEU A 36 -79.468 28.350 -10.832 1.00 24.08 C
ATOM 313 CD1 LEU A 36 -79.376 27.233 -9.836 1.00 22.16 C
ATOM 317 CD2 LEU A 36 -80.051 29.586 -10.213 1.00 23.45 C
ATOM 321 C LEU A 36 -76.587 30.137 -12.665 1.00 25.93 C
ATOM 322 O LEU A 36 -76.290 31.221 -12.137 1.00 26.11 O
ATOM 324 N GLU A 37 -75.714 29.332 -13.260 1.00 25.24 N
ATOM 325 CA GLU A 37 -74.381 29.739 -13.650 1.00 24.85 C
ATOM 327 CB GLU A 37 -73.678 28.566 -14.313 1.00 24.74 C
ATOM 330 CG GLU A 37 -72.182 28.667 -14.285 1.00 23.93 C
ATOM 333 CD GLU A 37 -71.519 27.490 -14.937 1.00 22.32 C
ATOM 334 OE1 GLU A 37 -72.203 26.738 -15.657 1.00 20.57 O
ATOM 335 OE2 GLU A 37 -70.303 27.322 -14.728 1.00 22.27 O
ATOM 336 C GLU A 37 -74.391 30.927 -14.600 1.00 24.69 C
ATOM 337 O GLU A 37 -73.666 31.891 -14.389 1.00 24.49 O
ATOM 339 N ALA A 38 -75.203 30.850 -15.650 1.00 24.68 N
ATOM 340 CA ALA A 38 -75.352 31.960 -16.599 1.00 24.87 C
ATOM 342 CB ALA A 38 -76.453 31.656 -17.609 1.00 24.53 C
ATOM 346 C ALA A 38 -75.643 33.278 -15.880 1.00 25.08 C
ATOM 347 O ALA A 38 -75.009 34.295 -16.135 1.00 25.21 O
ATOM 349 N GLU A 39 -76.591 33.228 -14.956 1.00 25.35 N
ATOM 350 CA GLU A 39 -77.050 34.400 -14.219 1.00 25.51 C
ATOM 352 CB GLU A 39 -78.283 34.014 -13.396 1.00 25.95 C
ATOM 355 CG GLU A 39 -79.302 35.119 -13.136 1.00 27.03 C
ATOM 358 CD GLU A 39 -80.715 34.557 -12.906 1.00 28.70 C
ATOM 359 OE1 GLU A 39 -81.006 33.416 -13.346 1.00 27.40 O
ATOM 360 OE2 GLU A 39 -81.540 35.266 -12.289 1.00 31.12 O
ATOM 361 C GLU A 39 -75.970 34.966 -13.306 1.00 25.11 C
ATOM 362 O GLU A 39 -75.870 36.167 -13.164 1.00 25.28 O
ATOM 364 N VAL A 40 -75.182 34.107 -12.672 1.00 24.86 N
ATOM 365 CA VAL A 40 -74.079 34.568 -11.824 1.00 24.69 C
ATOM 367 CB VAL A 40 -73.511 33.420 -10.952 1.00 24.56 C
ATOM 369 CG1 VAL A 40 -72.239 33.857 -10.240 1.00 23.69 C
ATOM 373 CG2 VAL A 40 -74.553 32.955 -9.955 1.00 24.68 C
ATOM 377 C VAL A 40 -72.971 35.148 -12.698 1.00 24.76 C
ATOM 378 O VAL A 40 -72.337 36.139 -12.362 1.00 24.16 O
ATOM 380 N ARG A 41 -72.744 34.506 -13.831 1.00 25.25 N
ATOM 381 CA ARG A 41 -71.727 34.948 -14.769 1.00 25.66 C
ATOM 383 CB ARG A 41 -71.576 33.927 -15.896 1.00 25.88 C
ATOM 386 CG ARG A 41 -70.726 34.385 -17.062 1.00 27.04 C
ATOM 389 CD ARG A 41 -71.519 35.178 -18.095 1.00 27.90 C
ATOM 392 NE ARG A 41 -70.653 35.635 -19.180 1.00 29.20 N
ATOM 394 CZ ARG A 41 -70.946 36.615 -20.034 1.00 29.94 C
ATOM 395 NH1 ARG A 41 -70.077 36.945 -20.980 1.00 29.86 N
ATOM 398 NH2 ARG A 41 -72.096 37.273 -19.957 1.00 30.54 N
ATOM 401 C ARG A 41 -72.104 36.301 -15.335 1.00 25.60 C
ATOM 402 O ARG A 41 -71.237 37.113 -15.612 1.00 25.77 O
ATOM 404 N ARG A 42 -73.400 36.521 -15.537 1.00 25.50 N
ATOM 405 CA ARG A 42 -73.900 37.810 -15.979 1.00 25.39 C
ATOM 407 CB ARG A 42 -75.389 37.723 -16.313 1.00 25.09 C
ATOM 410 CG ARG A 42 -76.077 39.062 -16.445 1.00 23.84 C
ATOM 413 CD ARG A 42 -77.459 38.906 -16.980 1.00 22.37 C
ATOM 416 NE ARG A 42 -78.448 38.554 -15.965 1.00 21.69 N
ATOM 418 CZ ARG A 42 -79.705 38.206 -16.248 1.00 22.99 C
ATOM 419 NH1 ARG A 42 -80.122 38.146 -17.517 1.00 24.16 N
ATOM 422 NH2 ARG A 42 -80.557 37.900 -15.275 1.00 22.94 N
ATOM 425 C ARG A 42 -73.666 38.889 -14.925 1.00 26.00 C
ATOM 426 O ARG A 42 -73.173 39.959 -15.244 1.00 26.17 O

ATOM 428 N GLU A 43 -74.014 38.621 -13.673 1.00 26.66 N
ATOM 429 CA GLU A 43 -73.930 39.662 -12.650 1.00 27.47 C
ATOM 431 CB GLU A 43 -74.749 39.304 -11.401 1.00 27.97 C
ATOM 434 CG GLU A 43 -76.274 39.266 -11.661 1.00 31.05 C
ATOM 437 CD GLU A 43 -76.869 40.636 -12.063 1.00 34.68 C
ATOM 438 OE1 GLU A 43 -76.804 41.571 -11.222 1.00 37.63 O
ATOM 439 OE2 GLU A 43 -77.398 40.773 -13.205 1.00 34.52 O
ATOM 440 C GLU A 43 -72.494 40.035 -12.275 1.00 27.15 C
ATOM 441 O GLU A 43 -72.292 41.118 -11.716 1.00 27.49 O
ATOM 443 N ILE A 44 -71.517 39.166 -12.588 1.00 26.57 N
ATOM 444 CA ILE A 44 -70.090 39.456 -12.334 1.00 25.80 C
ATOM 446 CB ILE A 44 -69.206 38.187 -12.187 1.00 25.52 C
ATOM 448 CG1 ILE A 44 -69.624 37.320 -11.010 1.00 24.69 C
ATOM 451 CD1 ILE A 44 -68.828 36.061 -10.899 1.00 23.08 C
ATOM 455 CG2 ILE A 44 -67.790 38.581 -11.916 1.00 25.73 C
ATOM 459 C ILE A 44 -69.522 40.286 -13.472 1.00 25.40 C
ATOM 460 O ILE A 44 -68.745 41.211 -13.236 1.00 25.26 O
ATOM 462 N ASN A 45 -69.912 39.945 -14.700 1.00 25.14 N
ATOM 463 CA ASN A 45 -69.480 40.669 -15.906 1.00 25.02 C
ATOM 465 CB ASN A 45 -69.696 39.813 -17.151 1.00 24.69 C
ATOM 468 CG ASN A 45 -68.662 38.735 -17.302 1.00 24.01 C
ATOM 469 OD1 ASN A 45 -67.470 39.013 -17.395 1.00 23.81 O
ATOM 470 ND2 ASN A 45 -69.111 37.490 -17.344 1.00 23.28 N
ATOM 473 C ASN A 45 -70.177 42.014 -16.114 1.00 25.52 C
ATOM 474 O ASN A 45 -69.704 42.836 -16.890 1.00 25.40 O
ATOM 476 N ASN A 46 -71.308 42.210 -15.437 1.00 26.33 N
ATOM 477 CA ASN A 46 -72.085 43.453 -15.468 1.00 26.72 C
ATOM 479 CB ASN A 46 -73.102 43.404 -14.322 1.00 26.31 C
ATOM 482 CG ASN A 46 -73.935 44.641 -14.209 1.00 24.24 C
ATOM 483 OD1 ASN A 46 -73.948 45.472 -15.091 1.00 22.38 O
ATOM 484 ND2 ASN A 46 -74.645 44.766 -13.106 1.00 21.64 N
ATOM 487 C ASN A 46 -71.185 44.680 -15.349 1.00 28.11 C
ATOM 488 O ASN A 46 -70.603 44.933 -14.304 1.00 28.16 O
ATOM 490 N GLU A 47 -71.084 45.441 -16.433 1.00 29.93 N
ATOM 491 CA GLU A 47 -70.128 46.558 -16.544 1.00 31.30 C
ATOM 493 CB GLU A 47 -69.933 46.969 -18.013 1.00 31.28 C
ATOM 496 CG GLU A 47 -69.737 45.795 -19.020 1.00 32.37 C
ATOM 499 CD GLU A 47 -71.060 45.127 -19.545 1.00 32.69 C
ATOM 500 OE1 GLU A 47 -72.055 45.833 -19.816 1.00 32.16 O
ATOM 501 OE2 GLU A 47 -71.087 43.880 -19.699 1.00 32.41 O
ATOM 502 C GLU A 47 -70.582 47.774 -15.729 1.00 32.47 C
ATOM 503 O GLU A 47 -69.760 48.525 -15.230 1.00 32.86 O
ATOM 505 N LYS A 48 -71.898 47.945 -15.585 1.00 33.93 N
ATOM 506 CA LYS A 48 -72.491 49.075 -14.861 1.00 34.85 C
ATOM 508 CB LYS A 48 -73.660 49.672 -15.684 1.00 35.08 C
ATOM 511 CG LYS A 48 -73.221 50.119 -17.126 1.00 36.58 C
ATOM 514 CD LYS A 48 -74.035 51.277 -17.751 1.00 37.93 C
ATOM 517 CE LYS A 48 -75.353 50.799 -18.415 1.00 39.02 C
ATOM 520 NZ LYS A 48 -75.159 49.990 -19.669 1.00 39.11 N
ATOM 524 C LYS A 48 -72.926 48.632 -13.465 1.00 35.26 C
ATOM 525 O LYS A 48 -74.011 48.954 -13.015 1.00 35.04 O
ATOM 527 N ALA A 49 -72.051 47.890 -12.790 1.00 36.29 N
ATOM 528 CA ALA A 49 -72.321 47.348 -11.456 1.00 37.18 C
ATOM 530 CB ALA A 49 -71.828 45.923 -11.353 1.00 37.20 C
ATOM 534 C ALA A 49 -71.618 48.191 -10.418 1.00 37.88 C
ATOM 535 O ALA A 49 -70.480 48.610 -10.638 1.00 38.17 O
ATOM 537 N GLU A 50 -72.278 48.404 -9.280 1.00 38.53 N
ATOM 538 CA GLU A 50 -71.730 49.242 -8.213 1.00 39.08 C
ATOM 540 CB GLU A 50 -72.790 49.545 -7.146 1.00 39.43 C
ATOM 543 CG GLU A 50 -72.708 50.953 -6.600 1.00 40.86 C

ATOM 546 CD GLU A 50 -73.089 52.010 -7.639 1.00 42.77 C
ATOM 547 OE1 GLU A 50 -74.225 52.530 -7.570 1.00 45.07 O
ATOM 548 OE2 GLU A 50 -72.265 52.320 -8.530 1.00 43.35 O
ATOM 549 C GLU A 50 -70.560 48.521 -7.600 1.00 38.89 C
ATOM 550 O GLU A 50 -70.699 47.378 -7.201 1.00 39.05 O
ATOM 552 N PHE A 51 -69.411 49.181 -7.536 1.00 38.99 N
ATOM 553 CA PHE A 51 -68.161 48.502 -7.196 1.00 39.52 C
ATOM 555 CB PHE A 51 -67.000 49.494 -7.098 1.00 40.05 C
ATOM 558 CG PHE A 51 -66.460 49.948 -8.431 1.00 42.80 C
ATOM 559 CD1 PHE A 51 -66.135 49.014 -9.435 1.00 45.21 C
ATOM 561 CE1 PHE A 51 -65.612 49.425 -10.675 1.00 46.12 C
ATOM 563 CZ PHE A 51 -65.403 50.790 -10.917 1.00 47.21 C
ATOM 565 CE2 PHE A 51 -65.726 51.741 -9.913 1.00 46.72 C
ATOM 567 CD2 PHE A 51 -66.247 51.310 -8.679 1.00 45.05 C
ATOM 569 C PHE A 51 -68.223 47.687 -5.905 1.00 39.05 C
ATOM 570 O PHE A 51 -67.897 46.506 -5.900 1.00 39.28 O
ATOM 572 N LEU A 52 -68.648 48.307 -4.813 1.00 38.42 N
ATOM 573 CA LEU A 52 -68.709 47.610 -3.528 1.00 37.94 C
ATOM 575 CB LEU A 52 -69.084 48.594 -2.413 1.00 38.53 C
ATOM 578 CG LEU A 52 -68.057 49.726 -2.181 1.00 40.46 C
ATOM 580 CD1 LEU A 52 -68.691 51.101 -1.787 1.00 41.88 C
ATOM 584 CD2 LEU A 52 -67.020 49.274 -1.141 1.00 41.83 C
ATOM 588 C LEU A 52 -69.667 46.406 -3.532 1.00 36.72 C
ATOM 589 O LEU A 52 -69.517 45.494 -2.724 1.00 36.84 O
ATOM 591 N THR A 53 -70.649 46.398 -4.431 1.00 35.37 N
ATOM 592 CA THR A 53 -71.545 45.247 -4.569 1.00 34.11 C
ATOM 594 CB THR A 53 -72.867 45.594 -5.277 1.00 33.87 C
ATOM 596 OG1 THR A 53 -73.339 46.863 -4.828 1.00 33.49 O
ATOM 598 CG2 THR A 53 -73.917 44.535 -4.983 1.00 33.70 C
ATOM 602 C THR A 53 -70.853 44.148 -5.359 1.00 33.04 C
ATOM 603 O THR A 53 -70.893 42.977 -4.973 1.00 32.90 O
ATOM 605 N LEU A 54 -70.228 44.528 -6.467 1.00 31.76 N
ATOM 606 CA LEU A 54 -69.469 43.578 -7.286 1.00 31.13 C
ATOM 608 CB LEU A 54 -68.721 44.308 -8.392 1.00 30.92 C
ATOM 611 CG LEU A 54 -68.028 43.437 -9.424 1.00 30.27 C
ATOM 613 CD1 LEU A 54 -69.034 42.769 -10.310 1.00 29.56 C
ATOM 617 CD2 LEU A 54 -67.108 44.306 -10.242 1.00 31.15 C
ATOM 621 C LEU A 54 -68.466 42.808 -6.443 1.00 30.60 C
ATOM 622 O LEU A 54 -68.378 41.587 -6.543 1.00 30.30 O
ATOM 624 N LEU A 55 -67.725 43.551 -5.618 1.00 30.09 N
ATOM 625 CA LEU A 55 -66.730 43.000 -4.695 1.00 29.47 C
ATOM 627 CB LEU A 55 -66.006 44.126 -3.944 1.00 29.44 C
ATOM 630 CG LEU A 55 -65.069 45.017 -4.781 1.00 29.74 C
ATOM 632 CD1 LEU A 55 -64.609 46.255 -4.003 1.00 29.43 C
ATOM 636 CD2 LEU A 55 -63.859 44.234 -5.286 1.00 29.64 C
ATOM 640 C LEU A 55 -67.340 42.024 -3.696 1.00 28.87 C
ATOM 641 O LEU A 55 -66.746 40.991 -3.383 1.00 28.98 O
ATOM 643 N GLU A 56 -68.525 42.330 -3.198 1.00 28.01 N
ATOM 644 CA GLU A 56 -69.160 41.419 -2.256 1.00 27.64 C
ATOM 646 CB GLU A 56 -70.172 42.173 -1.395 1.00 28.19 C
ATOM 649 CG GLU A 56 -69.497 43.167 -.459 1.00 29.75 C
ATOM 652 CD GLU A 56 -70.457 43.858 .478 1.00 33.04 C
ATOM 653 OE1 GLU A 56 -71.667 43.538 .481 1.00 34.46 O
ATOM 654 OE2 GLU A 56 -69.988 44.737 1.226 1.00 36.78 O
ATOM 655 C GLU A 56 -69.776 40.200 -2.945 1.00 26.37 C
ATOM 656 O GLU A 56 -69.914 39.146 -2.333 1.00 26.02 O
ATOM 658 N LEU A 57 -70.134 40.347 -4.218 1.00 25.30 N
ATOM 659 CA LEU A 57 -70.569 39.212 -5.036 1.00 24.17 C
ATOM 661 CB LEU A 57 -71.125 39.680 -6.382 1.00 23.71 C
ATOM 664 CG LEU A 57 -71.417 38.568 -7.390 1.00 22.27 C

ATOM 666 CD1 LEU A 57 -72.515 37.675 -6.858 1.00 19.31 C
ATOM 670 CD2 LEU A 57 -71.752 39.167 -8.768 1.00 20.30 C
ATOM 674 C LEU A 57 -69.404 38.267 -5.284 1.00 23.69 C
ATOM 675 O LEU A 57 -69.547 37.051 -5.136 1.00 23.83 O
ATOM 677 N ILE A 58 -68.261 38.822 -5.682 1.00 22.82 N
ATOM 678 CA ILE A 58 -67.070 38.019 -5.925 1.00 22.39 C
ATOM 680 CB ILE A 58 -65.884 38.899 -6.355 1.00 22.21 C
ATOM 682 CG1 ILE A 58 -66.088 39.386 -7.792 1.00 21.83 C
ATOM 685 CD1 ILE A 58 -65.002 40.314 -8.320 1.00 20.43 C
ATOM 689 CG2 ILE A 58 -64.565 38.131 -6.245 1.00 22.64 C
ATOM 693 C ILE A 58 -66.719 37.227 -4.662 1.00 22.35 C
ATOM 694 O ILE A 58 -66.520 36.002 -4.706 1.00 21.95 O
ATOM 696 N ASP A 59 -66.676 37.951 -3.543 1.00 22.32 N
ATOM 697 CA ASP A 59 -66.396 37.396 -2.215 1.00 22.26 C
ATOM 699 CB ASP A 59 -66.570 38.500 -1.171 1.00 22.67 C
ATOM 702 CG ASP A 59 -66.126 38.092 .213 1.00 23.91 C
ATOM 703 OD1 ASP A 59 -65.271 37.182 .338 1.00 23.77 O
ATOM 704 OD2 ASP A 59 -66.641 38.718 1.178 1.00 27.12 O
ATOM 705 C ASP A 59 -67.304 36.216 -1.901 1.00 21.79 C
ATOM 706 O ASP A 59 -66.828 35.102 -1.668 1.00 21.71 O
ATOM 708 N ASN A 60 -68.610 36.466 -1.926 1.00 21.51 N
ATOM 709 CA ASN A 60 -69.619 35.418 -1.759 1.00 21.28 C
ATOM 711 CB ASN A 60 -71.012 36.006 -1.958 1.00 21.25 C
ATOM 714 CG ASN A 60 -71.476 36.827 -.776 1.00 21.82 C
ATOM 715 OD1 ASN A 60 -71.067 36.598 .364 1.00 20.81 O
ATOM 716 ND2 ASN A 60 -72.361 37.783 -1.043 1.00 23.63 N
ATOM 719 C ASN A 60 -69.445 34.240 -2.725 1.00 21.22 C
ATOM 720 O ASN A 60 -69.444 33.053 -2.303 1.00 20.95 O
ATOM 722 N VAL A 61 -69.308 34.566 -4.018 1.00 20.83 N
ATOM 723 CA VAL A 61 -69.147 33.536 -5.043 1.00 20.57 C
ATOM 725 CB VAL A 61 -68.915 34.122 -6.466 1.00 20.53 C
ATOM 727 CG1 VAL A 61 -68.382 33.042 -7.430 1.00 19.44 C
ATOM 731 CG2 VAL A 61 -70.190 34.758 -7.006 1.00 19.75 C
ATOM 735 C VAL A 61 -67.981 32.646 -4.644 1.00 20.62 C
ATOM 736 O VAL A 61 -68.080 31.431 -4.699 1.00 20.56 O
ATOM 738 N GLN A 62 -66.888 33.255 -4.209 1.00 20.76 N
ATOM 739 CA GLN A 62 -65.703 32.481 -3.898 1.00 21.18 C
ATOM 741 CB GLN A 62 -64.461 33.379 -3.824 1.00 21.39 C
ATOM 744 CG GLN A 62 -64.007 33.920 -5.165 1.00 21.64 C
ATOM 747 CD GLN A 62 -62.608 34.512 -5.135 1.00 22.04 C
ATOM 748 OE1 GLN A 62 -61.890 34.483 -6.145 1.00 23.18 O
ATOM 749 NE2 GLN A 62 -62.217 35.062 -3.989 1.00 20.39 N
ATOM 752 C GLN A 62 -65.891 31.681 -2.607 1.00 21.09 C
ATOM 753 O GLN A 62 -65.544 30.485 -2.554 1.00 21.30 O
ATOM 755 N ARG A 63 -66.448 32.325 -1.583 1.00 20.63 N
ATOM 756 CA ARG A 63 -66.590 31.677 -.273 1.00 20.54 C
ATOM 758 CB ARG A 63 -67.025 32.686 .786 1.00 20.57 C
ATOM 761 CG ARG A 63 -66.031 33.823 .930 1.00 22.55 C
ATOM 764 CD ARG A 63 -66.214 34.632 2.179 1.00 24.93 C
ATOM 767 NE ARG A 63 -66.123 33.781 3.355 1.00 27.75 N
ATOM 769 CZ ARG A 63 -66.496 34.151 4.573 1.00 30.24 C
ATOM 770 NH1 ARG A 63 -66.971 35.385 4.782 1.00 31.79 N
ATOM 773 NH2 ARG A 63 -66.399 33.285 5.581 1.00 30.07 N
ATOM 776 C ARG A 63 -67.557 30.499 -.338 1.00 19.81 C
ATOM 777 O ARG A 63 -67.283 29.431 .209 1.00 19.67 O
ATOM 779 N LEU A 64 -68.661 30.684 -1.057 1.00 19.04 N
ATOM 780 CA LEU A 64 -69.636 29.617 -1.246 1.00 18.44 C
ATOM 782 CB LEU A 64 -70.865 30.167 -1.954 1.00 18.59 C
ATOM 785 CG LEU A 64 -71.662 31.170 -1.140 1.00 18.32 C
ATOM 787 CD1 LEU A 64 -72.669 31.852 -2.034 1.00 18.10 C

ATOM 791 CD2 LEU A 64 -72.334 30.444 .004 1.00 18.29 C
ATOM 795 C LEU A 64 -69.089 28.436 -2.037 1.00 17.80 C
ATOM 796 O LEU A 64 -69.802 27.453 -2.252 1.00 17.79 O
ATOM 798 N GLY A 65 -67.850 28.573 -2.515 1.00 17.07 N
ATOM 799 CA GLY A 65 -67.084 27.480 -3.081 1.00 16.27 C
ATOM 802 C GLY A 65 -67.137 27.406 -4.588 1.00 15.77 C
ATOM 803 O GLY A 65 -66.893 26.347 -5.154 1.00 15.78 O
ATOM 805 N LEU A 66 -67.439 28.521 -5.246 1.00 15.24 N
ATOM 806 CA LEU A 66 -67.621 28.537 -6.701 1.00 14.93 C
ATOM 808 CB LEU A 66 -68.977 29.146 -7.021 1.00 14.84 C
ATOM 811 CG LEU A 66 -70.204 28.334 -6.619 1.00 13.97 C
ATOM 813 CD1 LEU A 66 -71.391 29.260 -6.650 1.00 13.74 C
ATOM 817 CD2 LEU A 66 -70.415 27.125 -7.534 1.00 11.22 C
ATOM 821 C LEU A 66 -66.533 29.314 -7.454 1.00 15.09 C
ATOM 822 O LEU A 66 -66.621 29.497 -8.678 1.00 14.81 O
ATOM 824 N GLY A 67 -65.510 29.758 -6.720 1.00 15.21 N
ATOM 825 CA GLY A 67 -64.404 30.526 -7.280 1.00 14.98 C
ATOM 828 C GLY A 67 -63.873 29.952 -8.569 1.00 14.60 C
ATOM 829 O GLY A 67 -63.891 30.619 -9.579 1.00 14.63 O
ATOM 831 N TYR A 68 -63.419 28.706 -8.523 1.00 14.57 N
ATOM 832 CA TYR A 68 -62.831 28.029 -9.688 1.00 14.72 C
ATOM 834 CB TYR A 68 -62.608 26.539 -9.372 1.00 14.73 C
ATOM 837 CG TYR A 68 -63.858 25.689 -9.330 1.00 12.47 C
ATOM 838 CD1 TYR A 68 -64.163 24.826 -10.366 1.00 10.68 C
ATOM 840 CE1 TYR A 68 -65.310 24.043 -10.340 1.00 10.55 C
ATOM 842 CZ TYR A 68 -66.163 24.119 -9.258 1.00 10.41 C
ATOM 843 OH TYR A 68 -67.311 23.349 -9.212 1.00 6.97 O
ATOM 845 CE2 TYR A 68 -65.864 24.979 -8.210 1.00 11.44 C
ATOM 847 CD2 TYR A 68 -64.722 25.750 -8.252 1.00 11.29 C
ATOM 849 C TYR A 68 -63.648 28.141 -10.980 1.00 15.31 C
ATOM 850 O TYR A 68 -63.106 28.230 -12.083 1.00 15.01 O
ATOM 852 N ARG A 69 -64.959 28.136 -10.816 1.00 16.03 N
ATOM 853 CA ARG A 69 -65.884 28.083 -11.922 1.00 16.67 C
ATOM 855 CB ARG A 69 -67.224 27.649 -11.348 1.00 16.58 C
ATOM 858 CG ARG A 69 -68.332 27.445 -12.335 1.00 16.07 C
ATOM 861 CD ARG A 69 -69.378 26.578 -11.701 1.00 14.26 C
ATOM 864 NE ARG A 69 -68.915 25.205 -11.677 1.00 12.82 N
ATOM 866 CZ ARG A 69 -69.063 24.346 -12.676 1.00 12.42 C
ATOM 867 NH1 ARG A 69 -69.676 24.694 -13.792 1.00 12.27 N
ATOM 870 NH2 ARG A 69 -68.601 23.119 -12.553 1.00 13.23 N
ATOM 873 C ARG A 69 -66.010 29.409 -12.692 1.00 17.62 C
ATOM 874 O ARG A 69 -66.281 29.401 -13.892 1.00 17.10 O
ATOM 876 N PHE A 70 -65.811 30.529 -11.985 1.00 19.11 N
ATOM 877 CA PHE A 70 -65.936 31.891 -12.530 1.00 19.96 C
ATOM 879 CB PHE A 70 -67.024 32.666 -11.763 1.00 19.89 C
ATOM 882 CG PHE A 70 -68.365 32.010 -11.784 1.00 18.68 C
ATOM 883 CD1 PHE A 70 -69.158 32.082 -12.903 1.00 18.05 C
ATOM 885 CE1 PHE A 70 -70.376 31.452 -12.938 1.00 18.03 C
ATOM 887 CZ PHE A 70 -70.825 30.754 -11.851 1.00 17.26 C
ATOM 889 CE2 PHE A 70 -70.051 30.672 -10.736 1.00 17.60 C
ATOM 891 CD2 PHE A 70 -68.822 31.300 -10.700 1.00 17.86 C
ATOM 893 C PHE A 70 -64.627 32.661 -12.400 1.00 21.34 C
ATOM 894 O PHE A 70 -64.629 33.862 -12.171 1.00 21.25 O
ATOM 896 N GLU A 71 -63.501 31.977 -12.541 1.00 23.19 N
ATOM 897 CA GLU A 71 -62.211 32.591 -12.214 1.00 24.60 C
ATOM 899 CB GLU A 71 -61.127 31.524 -12.073 1.00 25.03 C
ATOM 902 CG GLU A 71 -59.717 32.059 -11.861 1.00 27.10 C
ATOM 905 CD GLU A 71 -58.712 30.949 -11.549 1.00 30.10 C
ATOM 906 OE1 GLU A 71 -59.084 30.007 -10.796 1.00 32.05 O
ATOM 907 OE2 GLU A 71 -57.558 31.027 -12.051 1.00 30.50 O

ATOM 908 C GLU A 71 -61.809 33.644 -13.241 1.00 25.23 C
ATOM 909 O GLU A 71 -61.362 34.717 -12.862 1.00 25.54 O
ATOM 911 N SER A 72 -61.979 33.345 -14.530 1.00 25.91 N
ATOM 912 CA SER A 72 -61.641 34.294 -15.588 1.00 26.37 C
ATOM 914 CB SER A 72 -61.656 33.606 -16.941 1.00 26.32 C
ATOM 917 OG SER A 72 -62.985 33.278 -17.291 1.00 27.28 O
ATOM 919 C SER A 72 -62.609 35.476 -15.608 1.00 26.84 C
ATOM 920 O SER A 72 -62.197 36.601 -15.852 1.00 27.02 O
ATOM 922 N ASP A 73 -63.893 35.214 -15.361 1.00 27.45 N
ATOM 923 CA ASP A 73 -64.895 36.277 -15.246 1.00 27.87 C
ATOM 925 CB ASP A 73 -66.289 35.705 -14.968 1.00 27.99 C
ATOM 928 CG ASP A 73 -66.842 34.913 -16.140 1.00 29.49 C
ATOM 929 OD1 ASP A 73 -67.215 35.530 -17.155 1.00 30.90 O
ATOM 930 OD2 ASP A 73 -66.916 33.667 -16.054 1.00 31.85 O
ATOM 931 C ASP A 73 -64.518 37.221 -14.121 1.00 27.86 C
ATOM 932 O ASP A 73 -64.598 38.435 -14.286 1.00 28.05 O
ATOM 934 N ILE A 74 -64.118 36.652 -12.985 1.00 27.88 N
ATOM 935 CA ILE A 74 -63.698 37.422 -11.821 1.00 27.98 C
ATOM 937 CB ILE A 74 -63.348 36.521 -10.637 1.00 27.71 C
ATOM 939 CG1 ILE A 74 -64.607 36.007 -9.960 1.00 27.60 C
ATOM 942 CD1 ILE A 74 -64.355 34.846 -9.023 1.00 27.67 C
ATOM 946 CG2 ILE A 74 -62.551 37.272 -9.621 1.00 26.82 C
ATOM 950 C ILE A 74 -62.472 38.252 -12.133 1.00 28.80 C
ATOM 951 O ILE A 74 -62.475 39.453 -11.917 1.00 29.00 O
ATOM 953 N ARG A 75 -61.415 37.616 -12.628 1.00 29.80 N
ATOM 954 CA ARG A 75 -60.197 38.341 -12.968 1.00 30.79 C
ATOM 956 CB ARG A 75 -59.286 37.507 -13.841 1.00 31.33 C
ATOM 959 CG ARG A 75 -58.506 36.441 -13.115 1.00 34.25 C
ATOM 962 CD ARG A 75 -57.286 36.009 -13.929 1.00 37.53 C
ATOM 965 NE ARG A 75 -56.238 37.019 -13.799 1.00 40.89 N
ATOM 967 CZ ARG A 75 -54.934 36.807 -13.967 1.00 44.24 C
ATOM 968 NH1 ARG A 75 -54.459 35.602 -14.294 1.00 45.02 N
ATOM 971 NH2 ARG A 75 -54.089 37.821 -13.796 1.00 45.88 N
ATOM 974 C ARG A 75 -60.548 39.596 -13.727 1.00 30.95 C
ATOM 975 O ARG A 75 -60.163 40.685 -13.336 1.00 31.27 O
ATOM 977 N ARG A 76 -61.293 39.435 -14.815 1.00 31.31 N
ATOM 978 CA ARG A 76 -61.712 40.567 -15.638 1.00 31.62 C
ATOM 980 CB ARG A 76 -62.593 40.106 -16.794 1.00 31.97 C
ATOM 983 CG ARG A 76 -61.833 39.392 -17.895 1.00 32.91 C
ATOM 986 CD ARG A 76 -62.615 39.453 -19.205 1.00 34.43 C
ATOM 989 NE ARG A 76 -63.925 38.803 -19.128 1.00 35.66 N
ATOM 991 CZ ARG A 76 -64.115 37.480 -19.106 1.00 37.15 C
ATOM 992 NH1 ARG A 76 -63.085 36.632 -19.129 1.00 37.93 N
ATOM 995 NH2 ARG A 76 -65.347 36.992 -19.048 1.00 37.64 N
ATOM 998 C ARG A 76 -62.453 41.629 -14.849 1.00 31.41 C
ATOM 999 O ARG A 76 -62.144 42.798 -14.966 1.00 31.35 O
ATOM 1001 N ALA A 77 -63.437 41.230 -14.058 1.00 31.53 N
ATOM 1002 CA ALA A 77 -64.136 42.177 -13.211 1.00 31.73 C
ATOM 1004 CB ALA A 77 -65.074 41.468 -12.275 1.00 31.69 C
ATOM 1008 C ALA A 77 -63.107 42.950 -12.423 1.00 32.23 C
ATOM 1009 O ALA A 77 -63.116 44.176 -12.411 1.00 32.42 O
ATOM 1011 N LEU A 78 -62.198 42.223 -11.786 1.00 32.95 N
ATOM 1012 CA LEU A 78 -61.168 42.838 -10.963 1.00 33.51 C
ATOM 1014 CB LEU A 78 -60.319 41.775 -10.265 1.00 33.10 C
ATOM 1017 CG LEU A 78 -60.959 41.077 -9.081 1.00 32.30 C
ATOM 1019 CD1 LEU A 78 -59.960 40.104 -8.472 1.00 30.80 C
ATOM 1023 CD2 LEU A 78 -61.438 42.117 -8.056 1.00 31.89 C
ATOM 1027 C LEU A 78 -60.249 43.752 -11.753 1.00 34.70 C
ATOM 1028 O LEU A 78 -59.790 44.753 -11.214 1.00 35.18 O
ATOM 1030 N ASP A 79 -59.955 43.404 -13.007 1.00 35.91 N

```
ATOM  1031  CA  ASP A  79     -59.054  44.205 -13.828  1.00 36.89           C
ATOM  1033  CB  ASP A  79     -58.637  43.452 -15.083  1.00 37.06           C
ATOM  1036  CG  ASP A  79     -57.518  44.150 -15.821  1.00 38.41           C
ATOM  1037  OD1 ASP A  79     -57.800  45.080 -16.615  1.00 39.85           O
ATOM  1038  OD2 ASP A  79     -56.347  43.775 -15.592  1.00 40.78           O
ATOM  1039  C   ASP A  79     -59.721  45.505 -14.220  1.00 37.75           C
ATOM  1040  O   ASP A  79     -59.105  46.568 -14.177  1.00 37.82           O
ATOM  1042  N   ARG A  80     -60.984  45.401 -14.615  1.00 38.99           N
ATOM  1043  CA  ARG A  80     -61.814  46.558 -14.923  1.00 39.88           C
ATOM  1045  CB  ARG A  80     -63.191  46.106 -15.427  1.00 40.41           C
ATOM  1048  CG  ARG A  80     -64.025  47.183 -16.122  1.00 42.77           C
ATOM  1051  CD  ARG A  80     -65.347  46.624 -16.718  1.00 45.79           C
ATOM  1054  NE  ARG A  80     -66.107  45.799 -15.765  1.00 48.55           N
ATOM  1056  CZ  ARG A  80     -66.136  44.457 -15.742  1.00 50.37           C
ATOM  1057  NH1 ARG A  80     -65.450  43.724 -16.636  1.00 49.78           N
ATOM  1060  NH2 ARG A  80     -66.868  43.835 -14.805  1.00 50.77           N
ATOM  1063  C   ARG A  80     -61.946  47.409 -13.668  1.00 39.80           C
ATOM  1064  O   ARG A  80     -61.840  48.630 -13.742  1.00 40.37           O
ATOM  1066  N   PHE A  81     -62.136  46.771 -12.516  1.00 39.62           N
ATOM  1067  CA  PHE A  81     -62.216  47.505 -11.245  1.00 39.61           C
ATOM  1069  CB  PHE A  81     -62.392  46.561 -10.053  1.00 39.74           C
ATOM  1072  CG  PHE A  81     -62.282  47.247  -8.712  1.00 38.81           C
ATOM  1073  CD1 PHE A  81     -63.238  48.153  -8.315  1.00 39.03           C
ATOM  1075  CE1 PHE A  81     -63.153  48.787  -7.100  1.00 39.69           C
ATOM  1077  CZ  PHE A  81     -62.095  48.515  -6.261  1.00 39.54           C
ATOM  1079  CE2 PHE A  81     -61.134  47.608  -6.647  1.00 38.66           C
ATOM  1081  CD2 PHE A  81     -61.228  46.986  -7.865  1.00 38.27           C
ATOM  1083  C   PHE A  81     -61.006  48.378 -10.970  1.00 39.58           C
ATOM  1084  O   PHE A  81     -61.165  49.535 -10.581  1.00 39.76           O
ATOM  1086  N   VAL A  82     -59.810  47.817 -11.142  1.00 39.50           N
ATOM  1087  CA  VAL A  82     -58.575  48.562 -10.892  1.00 39.47           C
ATOM  1089  CB  VAL A  82     -57.314  47.659 -10.977  1.00 39.37           C
ATOM  1091  CG1 VAL A  82     -56.108  48.426 -11.521  1.00 39.06           C
ATOM  1095  CG2 VAL A  82     -57.009  47.079  -9.614  1.00 39.23           C
ATOM  1099  C   VAL A  82     -58.457  49.755 -11.833  1.00 39.54           C
ATOM  1100  O   VAL A  82     -58.222  50.884 -11.378  1.00 39.45           O
ATOM  1102  N   SER A  83     -58.678  49.513 -13.126  1.00 39.65           N
ATOM  1103  CA  SER A  83     -58.469  50.535 -14.157  1.00 39.82           C
ATOM  1105  CB  SER A  83     -58.196  49.880 -15.526  1.00 39.84           C
ATOM  1108  OG  SER A  83     -59.138  48.870 -15.829  1.00 40.00           O
ATOM  1110  C   SER A  83     -59.617  51.561 -14.219  1.00 39.62           C
ATOM  1111  O   SER A  83     -60.149  51.853 -15.286  1.00 39.59           O
ATOM  1113  N   SER A  84     -59.957  52.108 -13.052  1.00 39.44           N
ATOM  1114  CA  SER A  84     -60.926  53.197 -12.910  1.00 39.13           C
ATOM  1116  CB  SER A  84     -62.238  52.834 -13.618  1.00 39.03           C
ATOM  1119  OG  SER A  84     -62.620  51.505 -13.325  1.00 37.97           O
ATOM  1121  C   SER A  84     -61.243  53.580 -11.446  1.00 39.17           C
ATOM  1122  O   SER A  84     -62.189  54.341 -11.230  1.00 39.58           O
ATOM  1124  N   GLY A  85     -60.482  53.077 -10.457  1.00 38.74           N
ATOM  1125  CA  GLY A  85     -60.795  53.282  -9.024  1.00 38.26           C
ATOM  1128  C   GLY A  85     -61.724  52.238  -8.413  1.00 37.79           C
ATOM  1129  O   GLY A  85     -61.529  51.799  -7.273  1.00 36.84           O
ATOM  1131  N   SER A  94     -63.557  54.187   1.994  1.00 28.27           N
ATOM  1132  CA  SER A  94     -64.069  52.892   2.476  1.00 28.03           C
ATOM  1134  CB  SER A  94     -64.856  52.225   1.359  1.00 27.84           C
ATOM  1137  OG  SER A  94     -65.234  50.921   1.743  1.00 28.20           O
ATOM  1139  C   SER A  94     -62.992  51.910   2.934  1.00 27.83           C
ATOM  1140  O   SER A  94     -62.339  51.325   2.090  1.00 28.15           O
ATOM  1142  N   LEU A  95     -62.815  51.705   4.245  1.00 27.70           N
ATOM  1143  CA  LEU A  95     -61.813  50.728   4.751  1.00 27.59           C
```

ATOM 1145 CB LEU A 95 -61.692 50.747 6.282 1.00 27.49 C
ATOM 1148 CG LEU A 95 -60.871 49.596 6.909 1.00 27.47 C
ATOM 1150 CD1 LEU A 95 -59.400 49.900 6.902 1.00 27.70 C
ATOM 1154 CD2 LEU A 95 -61.292 49.274 8.329 1.00 27.50 C
ATOM 1158 C LEU A 95 -62.173 49.314 4.318 1.00 27.71 C
ATOM 1159 O LEU A 95 -61.303 48.537 3.914 1.00 27.73 O
ATOM 1161 N HIS A 96 -63.461 48.989 4.437 1.00 27.74 N
ATOM 1162 CA HIS A 96 -64.003 47.715 3.977 1.00 27.54 C
ATOM 1164 CB HIS A 96 -65.497 47.680 4.230 1.00 27.57 C
ATOM 1167 CG HIS A 96 -66.161 46.482 3.654 1.00 28.65 C
ATOM 1168 ND1 HIS A 96 -65.790 45.201 3.988 1.00 30.59 N
ATOM 1170 CE1 HIS A 96 -66.540 44.341 3.325 1.00 31.88 C
ATOM 1172 NE2 HIS A 96 -67.384 45.021 2.570 1.00 32.06 N
ATOM 1174 CD2 HIS A 96 -67.166 46.364 2.758 1.00 30.47 C
ATOM 1176 C HIS A 96 -63.705 47.450 2.492 1.00 27.09 C
ATOM 1177 O HIS A 96 -63.128 46.425 2.150 1.00 27.18 O
ATOM 1179 N GLY A 97 -64.079 48.386 1.625 1.00 26.55 N
ATOM 1180 CA GLY A 97 -63.760 48.300 .205 1.00 26.26 C
ATOM 1183 C GLY A 97 -62.277 48.112 -.088 1.00 26.23 C
ATOM 1184 O GLY A 97 -61.918 47.334 -.974 1.00 26.39 O
ATOM 1186 N THR A 98 -61.415 48.815 .653 1.00 25.83 N
ATOM 1187 CA THR A 98 -59.967 48.755 .435 1.00 25.36 C
ATOM 1189 CB THR A 98 -59.204 49.847 1.215 1.00 25.07 C
ATOM 1191 OG1 THR A 98 -59.796 51.123 .980 1.00 23.62 O
ATOM 1193 CG2 THR A 98 -57.755 49.905 .780 1.00 24.88 C
ATOM 1197 C THR A 98 -59.416 47.389 .845 1.00 25.69 C
ATOM 1198 O THR A 98 -58.622 46.802 .111 1.00 25.66 O
ATOM 1200 N ALA A 99 -59.847 46.890 2.008 1.00 25.95 N
ATOM 1201 CA ALA A 99 -59.468 45.540 2.495 1.00 25.93 C
ATOM 1203 CB ALA A 99 -59.945 45.330 3.929 1.00 25.82 C
ATOM 1207 C ALA A 99 -59.984 44.404 1.595 1.00 25.64 C
ATOM 1208 O ALA A 99 -59.204 43.599 1.102 1.00 25.38 O
ATOM 1210 N LEU A 100 -61.290 44.348 1.371 1.00 25.46 N
ATOM 1211 CA LEU A 100 -61.856 43.335 .474 1.00 25.55 C
ATOM 1213 CB LEU A 100 -63.361 43.540 .326 1.00 25.37 C
ATOM 1216 CG LEU A 100 -64.118 42.464 -.443 1.00 25.41 C
ATOM 1218 CD1 LEU A 100 -64.038 41.115 .281 1.00 26.01 C
ATOM 1222 CD2 LEU A 100 -65.555 42.893 -.639 1.00 25.19 C
ATOM 1226 C LEU A 100 -61.196 43.353 -.919 1.00 25.70 C
ATOM 1227 O LEU A 100 -60.819 42.301 -1.469 1.00 25.36 O
ATOM 1229 N SER A 101 -61.064 44.550 -1.489 1.00 25.77 N
ATOM 1230 CA SER A 101 -60.434 44.688 -2.805 1.00 25.67 C
ATOM 1232 CB SER A 101 -60.629 46.098 -3.375 1.00 25.83 C
ATOM 1235 OG SER A 101 -59.840 47.064 -2.688 1.00 26.98 O
ATOM 1237 C SER A 101 -58.947 44.336 -2.756 1.00 25.01 C
ATOM 1238 O SER A 101 -58.427 43.705 -3.672 1.00 24.94 O
ATOM 1240 N PHE A 102 -58.270 44.737 -1.687 1.00 24.30 N
ATOM 1241 CA PHE A 102 -56.852 44.436 -1.560 1.00 23.99 C
ATOM 1243 CB PHE A 102 -56.295 44.963 -.229 1.00 23.84 C
ATOM 1246 CG PHE A 102 -54.860 44.606 .027 1.00 23.24 C
ATOM 1247 CD1 PHE A 102 -53.849 45.504 -.259 1.00 23.56 C
ATOM 1249 CE1 PHE A 102 -52.507 45.182 -.007 1.00 24.50 C
ATOM 1251 CZ PHE A 102 -52.175 43.941 .540 1.00 24.27 C
ATOM 1253 CE2 PHE A 102 -53.180 43.042 .834 1.00 23.95 C
ATOM 1255 CD2 PHE A 102 -54.520 43.376 .576 1.00 23.45 C
ATOM 1257 C PHE A 102 -56.673 42.928 -1.679 1.00 23.65 C
ATOM 1258 O PHE A 102 -55.890 42.442 -2.501 1.00 23.55 O
ATOM 1260 N ARG A 103 -57.443 42.202 -.880 1.00 23.20 N
ATOM 1261 CA ARG A 103 -57.298 40.765 -.764 1.00 22.84 C
ATOM 1263 CB ARG A 103 -58.250 40.231 .291 1.00 23.01 C

ATOM 1266 CG ARG A 103 -58.054 38.774 .597 1.00 23.93 C
ATOM 1269 CD ARG A 103 -58.703 38.376 1.937 1.00 23.84 C
ATOM 1272 NE ARG A 103 -60.150 38.538 1.919 1.00 22.36 N
ATOM 1274 CZ ARG A 103 -60.982 37.763 1.240 1.00 20.62 C
ATOM 1275 NH1 ARG A 103 -60.512 36.773 .490 1.00 20.19 N
ATOM 1278 NH2 ARG A 103 -62.288 38.003 1.293 1.00 20.32 N
ATOM 1281 C ARG A 103 -57.602 40.117 -2.082 1.00 22.34 C
ATOM 1282 O ARG A 103 -56.826 39.303 -2.576 1.00 22.37 O
ATOM 1284 N LEU A 104 -58.729 40.496 -2.667 1.00 21.98 N
ATOM 1285 CA LEU A 104 -59.129 39.926 -3.951 1.00 21.60 C
ATOM 1287 CB LEU A 104 -60.503 40.442 -4.378 1.00 21.23 C
ATOM 1290 CG LEU A 104 -61.590 39.832 -3.522 1.00 20.30 C
ATOM 1292 CD1 LEU A 104 -62.949 40.401 -3.856 1.00 19.53 C
ATOM 1296 CD2 LEU A 104 -61.554 38.344 -3.725 1.00 19.71 C
ATOM 1300 C LEU A 104 -58.101 40.198 -5.040 1.00 21.48 C
ATOM 1301 O LEU A 104 -57.743 39.294 -5.780 1.00 21.62 O
ATOM 1303 N LEU A 105 -57.623 41.432 -5.139 1.00 21.14 N
ATOM 1304 CA LEU A 105 -56.655 41.747 -6.173 1.00 21.05 C
ATOM 1306 CB LEU A 105 -56.352 43.248 -6.205 1.00 20.94 C
ATOM 1309 CG LEU A 105 -57.465 44.165 -6.732 1.00 20.06 C
ATOM 1311 CD1 LEU A 105 -57.060 45.617 -6.580 1.00 17.92 C
ATOM 1315 CD2 LEU A 105 -57.804 43.857 -8.174 1.00 19.18 C
ATOM 1319 C LEU A 105 -55.372 40.908 -5.997 1.00 21.32 C
ATOM 1320 O LEU A 105 -54.840 40.357 -6.976 1.00 21.37 O
ATOM 1322 N ARG A 106 -54.893 40.777 -4.763 1.00 21.25 N
ATOM 1323 CA ARG A 106 -53.678 40.003 -4.528 1.00 21.33 C
ATOM 1325 CB ARG A 106 -53.151 40.211 -3.117 1.00 21.53 C
ATOM 1328 CG ARG A 106 -51.772 39.588 -2.917 1.00 22.60 C
ATOM 1331 CD ARG A 106 -51.098 40.091 -1.666 1.00 23.60 C
ATOM 1334 NE ARG A 106 -50.374 41.330 -1.897 1.00 24.60 N
ATOM 1336 CZ ARG A 106 -49.606 41.916 -.989 1.00 26.54 C
ATOM 1337 NH1 ARG A 106 -49.469 41.380 .225 1.00 26.98 N
ATOM 1340 NH2 ARG A 106 -48.967 43.041 -1.295 1.00 27.19 N
ATOM 1343 C ARG A 106 -53.888 38.517 -4.767 1.00 21.19 C
ATOM 1344 O ARG A 106 -52.998 37.821 -5.278 1.00 21.18 O
ATOM 1346 N GLN A 107 -55.061 38.028 -4.378 1.00 21.09 N
ATOM 1347 CA GLN A 107 -55.425 36.635 -4.618 1.00 20.76 C
ATOM 1349 CB GLN A 107 -56.861 36.378 -4.168 1.00 20.51 C
ATOM 1352 CG GLN A 107 -57.329 34.941 -4.327 1.00 19.68 C
ATOM 1355 CD GLN A 107 -58.790 34.772 -4.010 1.00 18.26 C
ATOM 1356 OE1 GLN A 107 -59.395 35.591 -3.334 1.00 17.44 O
ATOM 1357 NE2 GLN A 107 -59.366 33.698 -4.497 1.00 18.48 N
ATOM 1360 C GLN A 107 -55.304 36.306 -6.094 1.00 20.93 C
ATOM 1361 O GLN A 107 -54.917 35.212 -6.447 1.00 21.45 O
ATOM 1363 N HIS A 108 -55.642 37.260 -6.951 1.00 21.09 N
ATOM 1364 CA HIS A 108 -55.686 37.030 -8.379 1.00 21.28 C
ATOM 1366 CB HIS A 108 -57.024 37.541 -8.913 1.00 21.02 C
ATOM 1369 CG HIS A 108 -58.182 36.706 -8.478 1.00 19.70 C
ATOM 1370 ND1 HIS A 108 -58.637 35.632 -9.210 1.00 19.91 N
ATOM 1372 CE1 HIS A 108 -59.641 35.060 -8.571 1.00 19.27 C
ATOM 1374 NE2 HIS A 108 -59.851 35.720 -7.449 1.00 18.10 N
ATOM 1376 CD2 HIS A 108 -58.950 36.753 -7.367 1.00 18.98 C
ATOM 1378 C HIS A 108 -54.456 37.621 -9.108 1.00 22.21 C
ATOM 1379 O HIS A 108 -54.505 37.980 -10.304 1.00 21.80 O
ATOM 1381 N GLY A 109 -53.345 37.686 -8.375 1.00 23.19 N
ATOM 1382 CA GLY A 109 -52.055 38.007 -8.956 1.00 24.17 C
ATOM 1385 C GLY A 109 -51.813 39.470 -9.275 1.00 25.25 C
ATOM 1386 O GLY A 109 -50.767 39.802 -9.845 1.00 25.26 O
ATOM 1388 N PHE A 110 -52.755 40.349 -8.917 1.00 26.42 N
ATOM 1389 CA PHE A 110 -52.575 41.783 -9.154 1.00 27.33 C

ATOM 1391 CB PHE A 110 -53.895 42.546 -9.067 1.00 27.36 C
ATOM 1394 CG PHE A 110 -54.838 42.250 -10.193 1.00 27.83 C
ATOM 1395 CD1 PHE A 110 -54.633 42.801 -11.439 1.00 28.69 C
ATOM 1397 CE1 PHE A 110 -55.490 42.529 -12.488 1.00 28.91 C
ATOM 1399 CZ PHE A 110 -56.568 41.702 -12.295 1.00 28.85 C
ATOM 1401 CE2 PHE A 110 -56.787 41.146 -11.060 1.00 28.67 C
ATOM 1403 CD2 PHE A 110 -55.923 41.418 -10.013 1.00 28.39 C
ATOM 1405 C PHE A 110 -51.582 42.369 -8.163 1.00 28.25 C
ATOM 1406 O PHE A 110 -51.449 41.890 -7.024 1.00 28.71 O
ATOM 1408 N GLU A 111 -50.886 43.411 -8.607 1.00 29.05 N
ATOM 1409 CA GLU A 111 -49.951 44.142 -7.760 1.00 29.66 C
ATOM 1411 CB GLU A 111 -48.902 44.803 -8.648 1.00 30.37 C
ATOM 1414 CG GLU A 111 -47.750 45.509 -7.947 1.00 33.30 C
ATOM 1417 CD GLU A 111 -46.916 46.342 -8.946 1.00 38.00 C
ATOM 1418 OE1 GLU A 111 -46.312 45.750 -9.885 1.00 39.60 O
ATOM 1419 OE2 GLU A 111 -46.886 47.594 -8.802 1.00 40.87 O
ATOM 1420 C GLU A 111 -50.724 45.184 -6.935 1.00 28.98 C
ATOM 1421 O GLU A 111 -51.293 46.123 -7.495 1.00 28.45 O
ATOM 1423 N VAL A 112 -50.787 44.961 -5.618 1.00 28.47 N
ATOM 1424 CA VAL A 112 -51.284 45.950 -4.655 1.00 28.09 C
ATOM 1426 CB VAL A 112 -52.564 45.501 -3.908 1.00 27.76 C
ATOM 1428 CG1 VAL A 112 -53.745 45.466 -4.836 1.00 27.38 C
ATOM 1432 CG2 VAL A 112 -52.360 44.167 -3.252 1.00 27.80 C
ATOM 1436 C VAL A 112 -50.193 46.199 -3.631 1.00 28.15 C
ATOM 1437 O VAL A 112 -49.339 45.354 -3.436 1.00 27.90 O
ATOM 1439 N SER A 113 -50.241 47.354 -2.974 1.00 28.54 N
ATOM 1440 CA SER A 113 -49.194 47.782 -2.047 1.00 28.93 C
ATOM 1442 CB SER A 113 -48.563 49.064 -2.564 1.00 29.12 C
ATOM 1445 OG SER A 113 -47.692 49.644 -1.619 1.00 29.57 O
ATOM 1447 C SER A 113 -49.780 48.041 -.685 1.00 29.13 C
ATOM 1448 O SER A 113 -50.937 48.426 -.581 1.00 28.90 O
ATOM 1450 N GLN A 114 -48.985 47.857 .367 1.00 29.84 N
ATOM 1451 CA GLN A 114 -49.524 48.019 1.736 1.00 30.40 C
ATOM 1453 CB GLN A 114 -48.568 47.507 2.830 1.00 30.34 C
ATOM 1456 CG GLN A 114 -47.199 48.159 2.844 1.00 30.61 C
ATOM 1459 CD GLN A 114 -46.456 47.928 4.147 1.00 30.77 C
ATOM 1460 OE1 GLN A 114 -46.876 47.129 4.982 1.00 31.92 O
ATOM 1461 NE2 GLN A 114 -45.341 48.624 4.324 1.00 30.02 N
ATOM 1464 C GLN A 114 -49.939 49.440 2.068 1.00 30.62 C
ATOM 1465 O GLN A 114 -50.573 49.644 3.094 1.00 30.73 O
ATOM 1467 N GLU A 115 -49.592 50.407 1.216 1.00 30.94 N
ATOM 1468 CA GLU A 115 -49.963 51.794 1.458 1.00 31.45 C
ATOM 1470 CB GLU A 115 -48.881 52.777 .975 1.00 31.86 C
ATOM 1473 CG GLU A 115 -48.489 52.723 -.509 1.00 33.48 C
ATOM 1476 CD GLU A 115 -47.006 53.100 -.759 1.00 36.13 C
ATOM 1477 OE1 GLU A 115 -46.106 52.668 .022 1.00 38.72 O
ATOM 1478 OE2 GLU A 115 -46.741 53.811 -1.754 1.00 35.70 O
ATOM 1479 C GLU A 115 -51.338 52.125 .895 1.00 31.45 C
ATOM 1480 O GLU A 115 -51.716 53.283 .808 1.00 31.80 O
ATOM 1482 N ALA A 116 -52.108 51.105 .549 1.00 31.58 N
ATOM 1483 CA ALA A 116 -53.524 51.286 .284 1.00 31.67 C
ATOM 1485 CB ALA A 116 -54.071 50.092 -.461 1.00 31.62 C
ATOM 1489 C ALA A 116 -54.273 51.473 1.596 1.00 31.88 C
ATOM 1490 O ALA A 116 -55.428 51.874 1.604 1.00 31.82 O
ATOM 1492 N PHE A 117 -53.608 51.161 2.702 1.00 32.39 N
ATOM 1493 CA PHE A 117 -54.193 51.271 4.030 1.00 32.87 C
ATOM 1495 CB PHE A 117 -53.884 50.003 4.856 1.00 32.79 C
ATOM 1498 CG PHE A 117 -54.539 48.758 4.323 1.00 31.03 C
ATOM 1499 CD1 PHE A 117 -53.782 47.749 3.760 1.00 28.79 C
ATOM 1501 CE1 PHE A 117 -54.379 46.620 3.265 1.00 28.36 C

```
ATOM  1503  CZ  PHE A 117     -55.754  46.489   3.316  1.00 29.50       C
ATOM  1505  CE2 PHE A 117     -56.527  47.493   3.872  1.00 29.91       C
ATOM  1507  CD2 PHE A 117     -55.917  48.613   4.375  1.00 30.09       C
ATOM  1509  C   PHE A 117     -53.683  52.493   4.773  1.00 33.71       C
ATOM  1510  O   PHE A 117     -54.012  52.678   5.937  1.00 33.61       O
ATOM  1512  N   SER A 118     -52.886  53.325   4.107  1.00 35.09       N
ATOM  1513  CA  SER A 118     -52.186  54.429   4.779  1.00 36.12       C
ATOM  1515  CB  SER A 118     -51.073  54.990   3.895  1.00 36.09       C
ATOM  1518  OG  SER A 118     -51.607  55.747   2.820  1.00 35.96       O
ATOM  1520  C   SER A 118     -53.134  55.552   5.184  1.00 37.17       C
ATOM  1521  O   SER A 118     -52.873  56.255   6.166  1.00 37.22       O
ATOM  1523  N   GLY A 119     -54.231  55.705   4.436  1.00 38.40       N
ATOM  1524  CA  GLY A 119     -55.227  56.735   4.708  1.00 39.47       C
ATOM  1527  C   GLY A 119     -56.255  56.398   5.778  1.00 40.62       C
ATOM  1528  O   GLY A 119     -57.259  57.086   5.877  1.00 40.74       O
ATOM  1530  N   PHE A 120     -56.024  55.344   6.563  1.00 42.13       N
ATOM  1531  CA  PHE A 120     -56.906  54.971   7.684  1.00 43.27       C
ATOM  1533  CB  PHE A 120     -57.510  53.586   7.455  1.00 43.21       C
ATOM  1536  CG  PHE A 120     -58.176  53.439   6.134  1.00 42.36       C
ATOM  1537  CD1 PHE A 120     -59.418  54.006   5.911  1.00 41.23       C
ATOM  1539  CE1 PHE A 120     -60.035  53.880   4.691  1.00 40.87       C
ATOM  1541  CZ  PHE A 120     -59.414  53.182   3.675  1.00 41.03       C
ATOM  1543  CE2 PHE A 120     -58.167  52.618   3.883  1.00 40.92       C
ATOM  1545  CD2 PHE A 120     -57.556  52.746   5.106  1.00 41.30       C
ATOM  1547  C   PHE A 120     -56.179  54.952   9.019  1.00 44.71       C
ATOM  1548  O   PHE A 120     -56.732  54.489  10.025  1.00 44.80       O
ATOM  1550  N   LYS A 121     -54.939  55.430   9.021  1.00 46.38       N
ATOM  1551  CA  LYS A 121     -54.153  55.519  10.235  1.00 47.81       C
ATOM  1553  CB  LYS A 121     -52.722  55.050   9.957  1.00 47.86       C
ATOM  1556  CG  LYS A 121     -52.648  53.537   9.648  1.00 48.24       C
ATOM  1559  CD  LYS A 121     -51.417  53.119   8.823  1.00 49.41       C
ATOM  1562  CE  LYS A 121     -50.095  53.142   9.621  1.00 49.88       C
ATOM  1565  NZ  LYS A 121     -49.944  52.005  10.584  1.00 49.89       N
ATOM  1569  C   LYS A 121     -54.257  56.964  10.735  1.00 49.00       C
ATOM  1570  O   LYS A 121     -54.712  57.839  10.000  1.00 49.11       O
ATOM  1572  N   ASP A 122     -53.899  57.206  11.995  1.00 50.51       N
ATOM  1573  CA  ASP A 122     -54.078  58.537  12.596  1.00 51.46       C
ATOM  1575  CB  ASP A 122     -54.604  58.443  14.050  1.00 51.29       C
ATOM  1578  CG  ASP A 122     -53.570  57.919  15.036  1.00 50.73       C
ATOM  1579  OD1 ASP A 122     -52.353  58.025  14.777  1.00 49.90       O
ATOM  1580  OD2 ASP A 122     -53.988  57.398  16.088  1.00 49.66       O
ATOM  1581  C   ASP A 122     -52.792  59.358  12.502  1.00 52.60       C
ATOM  1582  O   ASP A 122     -51.830  58.953  11.835  1.00 52.65       O
ATOM  1584  N   GLN A 123     -52.802  60.512  13.172  1.00 53.88       N
ATOM  1585  CA  GLN A 123     -51.680  61.456  13.195  1.00 54.66       C
ATOM  1587  CB  GLN A 123     -51.993  62.594  14.178  1.00 55.01       C
ATOM  1590  CG  GLN A 123     -53.249  63.442  13.831  1.00 56.15       C
ATOM  1593  CD  GLN A 123     -52.943  64.736  13.064  1.00 57.64       C
ATOM  1594  OE1 GLN A 123     -51.779  65.102  12.859  1.00 59.10       O
ATOM  1595  NE2 GLN A 123     -54.001  65.438  12.652  1.00 57.63       N
ATOM  1598  C   GLN A 123     -50.365  60.772  13.591  1.00 54.87       C
ATOM  1599  O   GLN A 123     -49.309  61.078  13.034  1.00 54.67       O
ATOM  1601  N   ASN A 124     -50.458  59.834  14.538  1.00 55.21       N
ATOM  1602  CA  ASN A 124     -49.300  59.137  15.109  1.00 55.39       C
ATOM  1604  CB  ASN A 124     -49.421  59.122  16.637  1.00 55.52       C
ATOM  1607  CG  ASN A 124     -49.833  60.478  17.202  1.00 55.98       C
ATOM  1608  OD1 ASN A 124     -49.093  61.460  17.091  1.00 56.93       O
ATOM  1609  ND2 ASN A 124     -51.026  60.540  17.797  1.00 55.99       N
ATOM  1612  C   ASN A 124     -49.116  57.705  14.589  1.00 55.27       C
ATOM  1613  O   ASN A 124     -48.530  56.864  15.271  1.00 55.18       O
```

ATOM 1615 N GLY A 125 -49.626 57.430 13.391 1.00 55.18 N
ATOM 1616 CA GLY A 125 -49.311 56.190 12.672 1.00 55.08 C
ATOM 1619 C GLY A 125 -49.994 54.897 13.119 1.00 54.90 C
ATOM 1620 O GLY A 125 -49.543 53.806 12.750 1.00 55.24 O
ATOM 1622 N ASN A 126 -51.072 55.008 13.900 1.00 54.23 N
ATOM 1623 CA ASN A 126 -51.871 53.853 14.329 1.00 53.39 C
ATOM 1625 CB ASN A 126 -51.927 53.782 15.852 1.00 53.27 C
ATOM 1628 CG ASN A 126 -50.596 53.425 16.466 1.00 52.81 C
ATOM 1629 OD1 ASN A 126 -49.636 53.113 15.764 1.00 52.29 O
ATOM 1630 ND2 ASN A 126 -50.532 53.460 17.789 1.00 52.53 N
ATOM 1633 C ASN A 126 -53.274 53.978 13.771 1.00 52.82 C
ATOM 1634 O ASN A 126 -53.724 55.081 13.494 1.00 52.69 O
ATOM 1636 N PHE A 127 -53.968 52.857 13.607 1.00 52.17 N
ATOM 1637 CA PHE A 127 -55.287 52.875 12.962 1.00 51.56 C
ATOM 1639 CB PHE A 127 -55.805 51.451 12.721 1.00 51.35 C
ATOM 1642 CG PHE A 127 -55.119 50.730 11.587 1.00 50.06 C
ATOM 1643 CD1 PHE A 127 -54.068 49.856 11.831 1.00 48.90 C
ATOM 1645 CE1 PHE A 127 -53.437 49.187 10.789 1.00 47.59 C
ATOM 1647 CZ PHE A 127 -53.857 49.383 9.495 1.00 47.40 C
ATOM 1649 CE2 PHE A 127 -54.906 50.244 9.234 1.00 47.96 C
ATOM 1651 CD2 PHE A 127 -55.533 50.915 10.276 1.00 48.85 C
ATOM 1653 C PHE A 127 -56.303 53.690 13.776 1.00 51.35 C
ATOM 1654 O PHE A 127 -56.347 53.594 15.002 1.00 51.09 O
ATOM 1656 N LEU A 128 -57.100 54.500 13.083 1.00 51.15 N
ATOM 1657 CA LEU A 128 -58.143 55.280 13.727 1.00 51.09 C
ATOM 1659 CB LEU A 128 -59.039 55.979 12.694 1.00 51.17 C
ATOM 1662 CG LEU A 128 -58.463 57.046 11.746 1.00 51.31 C
ATOM 1664 CD1 LEU A 128 -59.571 57.628 10.855 1.00 50.76 C
ATOM 1668 CD2 LEU A 128 -57.762 58.157 12.508 1.00 50.98 C
ATOM 1672 C LEU A 128 -58.996 54.353 14.581 1.00 51.06 C
ATOM 1673 O LEU A 128 -59.573 53.393 14.078 1.00 50.94 O
ATOM 1675 N GLU A 129 -59.053 54.637 15.879 1.00 51.12 N
ATOM 1676 CA GLU A 129 -59.916 53.913 16.808 1.00 50.99 C
ATOM 1678 CB GLU A 129 -60.019 54.665 18.132 1.00 51.14 C
ATOM 1681 CG GLU A 129 -58.850 54.431 19.049 1.00 52.04 C
ATOM 1684 CD GLU A 129 -58.903 53.069 19.697 1.00 53.22 C
ATOM 1685 OE1 GLU A 129 -58.040 52.219 19.376 1.00 54.19 O
ATOM 1686 OE2 GLU A 129 -59.823 52.848 20.516 1.00 53.51 O
ATOM 1687 C GLU A 129 -61.314 53.712 16.260 1.00 50.66 C
ATOM 1688 O GLU A 129 -61.791 52.587 16.200 1.00 50.83 O
ATOM 1690 N ASN A 130 -61.960 54.799 15.839 1.00 50.28 N
ATOM 1691 CA ASN A 130 -63.389 54.765 15.486 1.00 50.03 C
ATOM 1693 CB ASN A 130 -63.910 56.182 15.193 1.00 50.09 C
ATOM 1696 CG ASN A 130 -63.286 56.805 13.960 1.00 50.37 C
ATOM 1697 OD1 ASN A 130 -62.504 56.177 13.249 1.00 51.44 O
ATOM 1698 ND2 ASN A 130 -63.634 58.056 13.701 1.00 50.27 N
ATOM 1701 C ASN A 130 -63.804 53.782 14.369 1.00 49.56 C
ATOM 1702 O ASN A 130 -64.993 53.581 14.131 1.00 49.44 O
ATOM 1704 N LEU A 131 -62.828 53.175 13.699 1.00 49.21 N
ATOM 1705 CA LEU A 131 -63.087 52.103 12.729 1.00 48.78 C
ATOM 1707 CB LEU A 131 -61.846 51.832 11.875 1.00 48.64 C
ATOM 1710 CG LEU A 131 -61.445 52.939 10.898 1.00 48.26 C
ATOM 1712 CD1 LEU A 131 -60.029 52.709 10.375 1.00 47.76 C
ATOM 1716 CD2 LEU A 131 -62.441 53.039 9.754 1.00 47.32 C
ATOM 1720 C LEU A 131 -63.516 50.798 13.394 1.00 48.58 C
ATOM 1721 O LEU A 131 -64.093 49.939 12.731 1.00 48.64 O
ATOM 1723 N LYS A 132 -63.225 50.645 14.689 1.00 48.23 N
ATOM 1724 CA LYS A 132 -63.650 49.474 15.465 1.00 47.80 C
ATOM 1726 CB LYS A 132 -63.156 49.587 16.913 1.00 47.71 C
ATOM 1729 CG LYS A 132 -63.930 50.615 17.728 1.00 47.80 C

ATOM 1732 CD LYS A 132 -63.430 50.779 19.153 1.00 47.75 C
ATOM 1735 CE LYS A 132 -64.438 51.577 19.982 1.00 47.22 C
ATOM 1738 NZ LYS A 132 -63.769 52.364 21.033 1.00 46.65 N
ATOM 1742 C LYS A 132 -65.182 49.308 15.446 1.00 47.56 C
ATOM 1743 O LYS A 132 -65.696 48.204 15.616 1.00 47.76 O
ATOM 1745 N GLU A 133 -65.901 50.413 15.249 1.00 47.18 N
ATOM 1746 CA GLU A 133 -67.371 50.412 15.191 1.00 46.79 C
ATOM 1748 CB GLU A 133 -67.898 51.850 15.337 1.00 46.95 C
ATOM 1751 CG GLU A 133 -67.840 52.376 16.776 1.00 47.56 C
ATOM 1754 CD GLU A 133 -67.613 53.886 16.863 1.00 48.41 C
ATOM 1755 OE1 GLU A 133 -68.247 54.648 16.093 1.00 47.67 O
ATOM 1756 OE2 GLU A 133 -66.798 54.304 17.721 1.00 48.92 O
ATOM 1757 C GLU A 133 -67.949 49.770 13.918 1.00 46.10 C
ATOM 1758 O GLU A 133 -69.140 49.446 13.874 1.00 46.11 O
ATOM 1760 N ASP A 134 -67.103 49.601 12.896 1.00 45.11 N
ATOM 1761 CA ASP A 134 -67.477 48.995 11.608 1.00 44.06 C
ATOM 1763 CB ASP A 134 -66.934 49.868 10.474 1.00 43.97 C
ATOM 1766 CG ASP A 134 -67.380 49.411 9.104 1.00 44.08 C
ATOM 1767 OD1 ASP A 134 -68.072 48.373 8.972 1.00 43.42 O
ATOM 1768 OD2 ASP A 134 -67.020 50.116 8.141 1.00 44.84 O
ATOM 1769 C ASP A 134 -66.910 47.570 11.526 1.00 43.12 C
ATOM 1770 O ASP A 134 -65.788 47.357 11.080 1.00 43.19 O
ATOM 1772 N ILE A 135 -67.708 46.594 11.944 1.00 41.85 N
ATOM 1773 CA ILE A 135 -67.216 45.247 12.216 1.00 40.75 C
ATOM 1775 CB ILE A 135 -68.183 44.507 13.170 1.00 40.80 C
ATOM 1777 CG1 ILE A 135 -68.227 45.226 14.524 1.00 41.21 C
ATOM 1780 CD1 ILE A 135 -69.353 46.283 14.633 1.00 42.86 C
ATOM 1784 CG2 ILE A 135 -67.776 43.063 13.373 1.00 40.88 C
ATOM 1788 C ILE A 135 -66.980 44.457 10.933 1.00 39.67 C
ATOM 1789 O ILE A 135 -66.166 43.537 10.901 1.00 39.37 O
ATOM 1791 N LYS A 136 -67.690 44.828 9.877 1.00 38.62 N
ATOM 1792 CA LYS A 136 -67.465 44.256 8.554 1.00 37.88 C
ATOM 1794 CB LYS A 136 -68.525 44.749 7.561 1.00 38.33 C
ATOM 1797 CG LYS A 136 -69.955 44.342 7.879 1.00 40.17 C
ATOM 1800 CD LYS A 136 -70.486 43.262 6.911 1.00 42.97 C
ATOM 1803 CE LYS A 136 -71.624 42.389 7.536 1.00 44.00 C
ATOM 1806 NZ LYS A 136 -72.950 43.086 7.726 1.00 43.82 N
ATOM 1810 C LYS A 136 -66.097 44.687 8.047 1.00 36.38 C
ATOM 1811 O LYS A 136 -65.399 43.914 7.388 1.00 36.24 O
ATOM 1813 N ALA A 137 -65.728 45.931 8.341 1.00 34.51 N
ATOM 1814 CA ALA A 137 -64.463 46.474 7.876 1.00 33.41 C
ATOM 1816 CB ALA A 137 -64.432 47.981 8.058 1.00 33.43 C
ATOM 1820 C ALA A 137 -63.291 45.827 8.600 1.00 32.30 C
ATOM 1821 O ALA A 137 -62.288 45.481 7.995 1.00 31.89 O
ATOM 1823 N ILE A 138 -63.437 45.662 9.905 1.00 31.41 N
ATOM 1824 CA ILE A 138 -62.395 45.074 10.737 1.00 30.60 C
ATOM 1826 CB ILE A 138 -62.770 45.131 12.238 1.00 30.20 C
ATOM 1828 CG1 ILE A 138 -62.914 46.576 12.689 1.00 29.92 C
ATOM 1831 CD1 ILE A 138 -61.681 47.414 12.417 1.00 30.50 C
ATOM 1835 CG2 ILE A 138 -61.706 44.470 13.085 1.00 29.73 C
ATOM 1839 C ILE A 138 -62.140 43.631 10.320 1.00 30.34 C
ATOM 1840 O ILE A 138 -60.972 43.203 10.212 1.00 30.65 O
ATOM 1842 N LEU A 139 -63.227 42.884 10.098 1.00 29.69 N
ATOM 1843 CA LEU A 139 -63.134 41.523 9.562 1.00 29.23 C
ATOM 1845 CB LEU A 139 -64.517 40.917 9.332 1.00 28.92 C
ATOM 1848 CG LEU A 139 -65.066 40.185 10.545 1.00 29.06 C
ATOM 1850 CD1 LEU A 139 -66.541 39.875 10.352 1.00 28.20 C
ATOM 1854 CD2 LEU A 139 -64.250 38.922 10.813 1.00 28.59 C
ATOM 1858 C LEU A 139 -62.382 41.546 8.247 1.00 29.00 C
ATOM 1859 O LEU A 139 -61.444 40.773 8.035 1.00 29.50 O

ATOM 1861 N SER A 140 -62.790 42.458 7.372 1.00 28.14 N
ATOM 1862 CA SER A 140 -62.222 42.526 6.054 1.00 27.40 C
ATOM 1864 CB SER A 140 -62.912 43.619 5.260 1.00 27.35 C
ATOM 1867 OG SER A 140 -63.310 43.103 4.015 1.00 28.43 O
ATOM 1869 C SER A 140 -60.720 42.777 6.123 1.00 26.77 C
ATOM 1870 O SER A 140 -59.975 42.269 5.298 1.00 27.29 O
ATOM 1872 N LEU A 141 -60.285 43.563 7.105 1.00 25.89 N
ATOM 1873 CA LEU A 141 -58.872 43.897 7.283 1.00 25.20 C
ATOM 1875 CB LEU A 141 -58.717 45.164 8.155 1.00 25.00 C
ATOM 1878 CG LEU A 141 -57.298 45.670 8.489 1.00 24.35 C
ATOM 1880 CD1 LEU A 141 -56.497 45.974 7.232 1.00 22.75 C
ATOM 1884 CD2 LEU A 141 -57.329 46.893 9.385 1.00 22.81 C
ATOM 1888 C LEU A 141 -58.140 42.721 7.920 1.00 24.92 C
ATOM 1889 O LEU A 141 -57.034 42.380 7.521 1.00 24.77 O
ATOM 1891 N TYR A 142 -58.751 42.101 8.921 1.00 24.51 N
ATOM 1892 CA TYR A 142 -58.163 40.913 9.514 1.00 24.36 C
ATOM 1894 CB TYR A 142 -59.120 40.325 10.538 1.00 24.18 C
ATOM 1897 CG TYR A 142 -58.774 38.941 11.046 1.00 23.72 C
ATOM 1898 CD1 TYR A 142 -57.878 38.763 12.091 1.00 22.97 C
ATOM 1900 CE1 TYR A 142 -57.593 37.500 12.582 1.00 24.25 C
ATOM 1902 CZ TYR A 142 -58.229 36.386 12.030 1.00 25.75 C
ATOM 1903 OH TYR A 142 -57.967 35.100 12.500 1.00 26.97 O
ATOM 1905 CE2 TYR A 142 -59.120 36.551 10.988 1.00 25.02 C
ATOM 1907 CD2 TYR A 142 -59.390 37.820 10.511 1.00 24.01 C
ATOM 1909 C TYR A 142 -57.877 39.896 8.423 1.00 24.39 C
ATOM 1910 O TYR A 142 -56.822 39.276 8.380 1.00 24.19 O
ATOM 1912 N GLU A 143 -58.841 39.760 7.527 1.00 24.59 N
ATOM 1913 CA GLU A 143 -58.820 38.728 6.521 1.00 24.70 C
ATOM 1915 CB GLU A 143 -60.194 38.636 5.853 1.00 24.69 C
ATOM 1918 CG GLU A 143 -60.651 37.219 5.547 1.00 27.21 C
ATOM 1921 CD GLU A 143 -61.127 36.426 6.774 1.00 30.20 C
ATOM 1922 OE1 GLU A 143 -60.261 35.776 7.393 1.00 33.40 O
ATOM 1923 OE2 GLU A 143 -62.351 36.421 7.097 1.00 30.50 O
ATOM 1924 C GLU A 143 -57.701 39.010 5.518 1.00 24.08 C
ATOM 1925 O GLU A 143 -56.984 38.090 5.126 1.00 24.53 O
ATOM 1927 N ALA A 144 -57.537 40.281 5.147 1.00 23.30 N
ATOM 1928 CA ALA A 144 -56.515 40.715 4.173 1.00 22.79 C
ATOM 1930 CB ALA A 144 -56.787 42.154 3.740 1.00 22.49 C
ATOM 1934 C ALA A 144 -55.073 40.598 4.701 1.00 22.42 C
ATOM 1935 O ALA A 144 -54.128 40.380 3.935 1.00 22.36 O
ATOM 1937 N SER A 145 -54.909 40.713 6.012 1.00 21.80 N
ATOM 1938 CA SER A 145 -53.593 40.822 6.600 1.00 21.36 C
ATOM 1940 CB SER A 145 -53.726 41.170 8.066 1.00 21.21 C
ATOM 1943 OG SER A 145 -54.337 40.100 8.753 1.00 21.59 O
ATOM 1945 C SER A 145 -52.797 39.537 6.476 1.00 21.30 C
ATOM 1946 O SER A 145 -51.571 39.533 6.701 1.00 21.50 O
ATOM 1948 N PHE A 146 -53.488 38.439 6.154 1.00 21.00 N
ATOM 1949 CA PHE A 146 -52.827 37.127 6.030 1.00 20.41 C
ATOM 1951 CB PHE A 146 -53.796 35.979 6.338 1.00 20.20 C
ATOM 1954 CG PHE A 146 -54.130 35.873 7.798 1.00 19.91 C
ATOM 1955 CD1 PHE A 146 -53.382 35.087 8.637 1.00 20.48 C
ATOM 1957 CE1 PHE A 146 -53.679 35.012 9.992 1.00 20.59 C
ATOM 1959 CZ PHE A 146 -54.731 35.740 10.508 1.00 19.15 C
ATOM 1961 CE2 PHE A 146 -55.464 36.536 9.691 1.00 19.10 C
ATOM 1963 CD2 PHE A 146 -55.155 36.615 8.343 1.00 20.16 C
ATOM 1965 C PHE A 146 -52.174 36.964 4.680 1.00 19.76 C
ATOM 1966 O PHE A 146 -51.305 36.116 4.523 1.00 19.46 O
ATOM 1968 N LEU A 147 -52.550 37.819 3.729 1.00 19.34 N
ATOM 1969 CA LEU A 147 -51.933 37.804 2.402 1.00 19.13 C
ATOM 1971 CB LEU A 147 -52.905 38.367 1.347 1.00 18.67 C

ATOM 1974 CG LEU A 147 -53.964 37.334 .919 1.00 18.11 C
ATOM 1976 CD1 LEU A 147 -55.090 37.248 1.961 1.00 15.10 C
ATOM 1980 CD2 LEU A 147 -54.494 37.609 -.499 1.00 16.50 C
ATOM 1984 C LEU A 147 -50.582 38.525 2.369 1.00 19.10 C
ATOM 1985 O LEU A 147 -49.992 38.715 1.311 1.00 19.44 O
ATOM 1987 N ALA A 148 -50.075 38.882 3.542 1.00 19.13 N
ATOM 1988 CA ALA A 148 -48.967 39.806 3.664 1.00 18.84 C
ATOM 1990 CB ALA A 148 -48.762 40.167 5.117 1.00 18.78 C
ATOM 1994 C ALA A 148 -47.723 39.184 3.113 1.00 18.85 C
ATOM 1995 O ALA A 148 -47.548 37.975 3.206 1.00 18.80 O
ATOM 1997 N LEU A 149 -46.869 40.013 2.523 1.00 19.08 N
ATOM 1998 CA LEU A 149 -45.507 39.601 2.215 1.00 19.32 C
ATOM 2000 CB LEU A 149 -45.056 40.145 .863 1.00 19.14 C
ATOM 2003 CG LEU A 149 -45.819 39.650 -.364 1.00 19.16 C
ATOM 2005 CD1 LEU A 149 -45.036 39.929 -1.645 1.00 18.43 C
ATOM 2009 CD2 LEU A 149 -46.089 38.175 -.259 1.00 20.09 C
ATOM 2013 C LEU A 149 -44.527 40.029 3.304 1.00 19.60 C
ATOM 2014 O LEU A 149 -44.797 40.916 4.113 1.00 19.20 O
ATOM 2016 N GLU A 150 -43.384 39.361 3.309 1.00 20.42 N
ATOM 2017 CA GLU A 150 -42.286 39.674 4.215 1.00 21.03 C
ATOM 2019 CB GLU A 150 -41.098 38.741 3.948 1.00 21.03 C
ATOM 2022 CG GLU A 150 -40.491 38.176 5.205 1.00 22.23 C
ATOM 2025 CD GLU A 150 -39.433 37.117 4.941 1.00 24.34 C
ATOM 2026 OE1 GLU A 150 -39.189 36.786 3.753 1.00 24.53 O
ATOM 2027 OE2 GLU A 150 -38.843 36.625 5.940 1.00 25.82 O
ATOM 2028 C GLU A 150 -41.887 41.130 4.011 1.00 21.29 C
ATOM 2029 O GLU A 150 -41.619 41.544 2.885 1.00 21.13 O
ATOM 2031 N GLY A 151 -41.893 41.903 5.094 1.00 21.89 N
ATOM 2032 CA GLY A 151 -41.636 43.341 5.030 1.00 22.25 C
ATOM 2035 C GLY A 151 -42.871 44.221 5.152 1.00 22.67 C
ATOM 2036 O GLY A 151 -42.757 45.397 5.462 1.00 22.84 O
ATOM 2038 N GLU A 152 -44.055 43.669 4.918 1.00 23.19 N
ATOM 2039 CA GLU A 152 -45.263 44.474 4.937 1.00 23.76 C
ATOM 2041 CB GLU A 152 -46.350 43.813 4.100 1.00 23.79 C
ATOM 2044 CG GLU A 152 -46.037 43.890 2.615 1.00 23.98 C
ATOM 2047 CD GLU A 152 -47.147 43.368 1.749 1.00 23.72 C
ATOM 2048 OE1 GLU A 152 -47.226 43.771 .574 1.00 22.11 O
ATOM 2049 OE2 GLU A 152 -47.939 42.542 2.241 1.00 25.41 O
ATOM 2050 C GLU A 152 -45.722 44.719 6.365 1.00 24.47 C
ATOM 2051 O GLU A 152 -46.586 44.006 6.906 1.00 24.70 O
ATOM 2053 N ASN A 153 -45.134 45.744 6.969 1.00 25.00 N
ATOM 2054 CA ASN A 153 -45.287 45.978 8.404 1.00 25.59 C
ATOM 2056 CB ASN A 153 -44.221 46.957 8.902 1.00 25.55 C
ATOM 2059 CG ASN A 153 -44.386 48.331 8.308 1.00 25.57 C
ATOM 2060 OD1 ASN A 153 -44.114 48.557 7.128 1.00 24.52 O
ATOM 2061 ND2 ASN A 153 -44.867 49.256 9.117 1.00 27.05 N
ATOM 2064 C ASN A 153 -46.679 46.486 8.772 1.00 25.92 C
ATOM 2065 O ASN A 153 -47.172 46.238 9.872 1.00 26.02 O
ATOM 2067 N ILE A 154 -47.310 47.197 7.847 1.00 26.35 N
ATOM 2068 CA ILE A 154 -48.638 47.751 8.082 1.00 26.57 C
ATOM 2070 CB ILE A 154 -49.013 48.779 7.007 1.00 26.45 C
ATOM 2072 CG1 ILE A 154 -48.159 50.023 7.164 1.00 26.36 C
ATOM 2075 CD1 ILE A 154 -48.060 50.790 5.883 1.00 27.92 C
ATOM 2079 CG2 ILE A 154 -50.467 49.152 7.089 1.00 26.25 C
ATOM 2083 C ILE A 154 -49.674 46.643 8.111 1.00 26.96 C
ATOM 2084 O ILE A 154 -50.650 46.741 8.851 1.00 27.12 O
ATOM 2086 N LEU A 155 -49.467 45.588 7.320 1.00 27.35 N
ATOM 2087 CA LEU A 155 -50.422 44.475 7.304 1.00 27.76 C
ATOM 2089 CB LEU A 155 -50.238 43.594 6.067 1.00 27.73 C
ATOM 2092 CG LEU A 155 -51.090 43.990 4.875 1.00 27.31 C

ATOM 2094 CD1 LEU A 155 -50.980 45.456 4.683 1.00 28.13 C
ATOM 2098 CD2 LEU A 155 -50.633 43.262 3.623 1.00 27.79 C
ATOM 2102 C LEU A 155 -50.340 43.642 8.582 1.00 28.22 C
ATOM 2103 O LEU A 155 -51.361 43.237 9.112 1.00 27.95 O
ATOM 2105 N ASP A 156 -49.128 43.395 9.068 1.00 28.95 N
ATOM 2106 CA ASP A 156 -48.944 42.723 10.348 1.00 29.71 C
ATOM 2108 CB ASP A 156 -47.450 42.461 10.639 1.00 30.23 C
ATOM 2111 CG ASP A 156 -46.938 41.125 10.027 1.00 32.82 C
ATOM 2112 OD1 ASP A 156 -47.765 40.240 9.658 1.00 36.27 O
ATOM 2113 OD2 ASP A 156 -45.700 40.961 9.923 1.00 34.48 O
ATOM 2114 C ASP A 156 -49.570 43.539 11.469 1.00 29.66 C
ATOM 2115 O ASP A 156 -50.109 42.969 12.425 1.00 29.81 O
ATOM 2117 N GLU A 157 -49.514 44.866 11.345 1.00 29.69 N
ATOM 2118 CA GLU A 157 -50.129 45.768 12.329 1.00 29.57 C
ATOM 2120 CB GLU A 157 -49.581 47.186 12.178 1.00 29.71 C
ATOM 2123 CG GLU A 157 -48.164 47.326 12.712 1.00 30.53 C
ATOM 2126 CD GLU A 157 -47.455 48.544 12.169 1.00 31.96 C
ATOM 2127 OE1 GLU A 157 -48.167 49.491 11.741 1.00 33.56 O
ATOM 2128 OE2 GLU A 157 -46.195 48.546 12.166 1.00 31.54 O
ATOM 2129 C GLU A 157 -51.649 45.771 12.230 1.00 29.16 C
ATOM 2130 O GLU A 157 -52.330 45.819 13.241 1.00 29.00 O
ATOM 2132 N ALA A 158 -52.172 45.716 11.010 1.00 28.86 N
ATOM 2133 CA ALA A 158 -53.606 45.570 10.792 1.00 28.79 C
ATOM 2135 CB ALA A 158 -53.893 45.456 9.301 1.00 28.44 C
ATOM 2139 C ALA A 158 -54.171 44.352 11.536 1.00 28.93 C
ATOM 2140 O ALA A 158 -55.265 44.402 12.098 1.00 28.77 O
ATOM 2142 N LYS A 159 -53.416 43.260 11.528 1.00 29.19 N
ATOM 2143 CA LYS A 159 -53.849 42.022 12.143 1.00 29.57 C
ATOM 2145 CB LYS A 159 -52.929 40.880 11.710 1.00 29.62 C
ATOM 2148 CG LYS A 159 -53.297 39.513 12.258 1.00 30.27 C
ATOM 2151 CD LYS A 159 -52.765 38.365 11.387 1.00 31.78 C
ATOM 2154 CE LYS A 159 -51.259 38.132 11.525 1.00 33.15 C
ATOM 2157 NZ LYS A 159 -50.911 36.696 11.248 1.00 33.88 N
ATOM 2161 C LYS A 159 -53.866 42.160 13.670 1.00 29.99 C
ATOM 2162 O LYS A 159 -54.767 41.642 14.332 1.00 30.29 O
ATOM 2164 N VAL A 160 -52.886 42.862 14.236 1.00 30.07 N
ATOM 2165 CA VAL A 160 -52.840 43.047 15.696 1.00 30.03 C
ATOM 2167 CB VAL A 160 -51.520 43.691 16.162 1.00 29.88 C
ATOM 2169 CG1 VAL A 160 -51.515 43.863 17.671 1.00 28.94 C
ATOM 2173 CG2 VAL A 160 -50.341 42.848 15.707 1.00 30.23 C
ATOM 2177 C VAL A 160 -53.996 43.925 16.149 1.00 30.05 C
ATOM 2178 O VAL A 160 -54.544 43.752 17.234 1.00 30.31 O
ATOM 2180 N PHE A 161 -54.355 44.862 15.290 1.00 30.08 N
ATOM 2181 CA PHE A 161 -55.407 45.808 15.558 1.00 30.09 C
ATOM 2183 CB PHE A 161 -55.255 46.993 14.598 1.00 29.92 C
ATOM 2186 CG PHE A 161 -56.370 47.974 14.654 1.00 28.52 C
ATOM 2187 CD1 PHE A 161 -56.347 49.005 15.554 1.00 27.92 C
ATOM 2189 CE1 PHE A 161 -57.361 49.903 15.600 1.00 28.06 C
ATOM 2191 CZ PHE A 161 -58.411 49.783 14.733 1.00 28.76 C
ATOM 2193 CE2 PHE A 161 -58.441 48.757 13.826 1.00 28.31 C
ATOM 2195 CD2 PHE A 161 -57.429 47.869 13.789 1.00 28.16 C
ATOM 2197 C PHE A 161 -56.746 45.123 15.388 1.00 30.55 C
ATOM 2198 O PHE A 161 -57.598 45.203 16.258 1.00 30.53 O
ATOM 2200 N ALA A 162 -56.930 44.438 14.271 1.00 31.34 N
ATOM 2201 CA ALA A 162 -58.193 43.770 14.023 1.00 32.26 C
ATOM 2203 CB ALA A 162 -58.217 43.139 12.643 1.00 32.31 C
ATOM 2207 C ALA A 162 -58.500 42.734 15.118 1.00 33.09 C
ATOM 2208 O ALA A 162 -59.557 42.814 15.735 1.00 33.83 O
ATOM 2210 N ILE A 163 -57.587 41.799 15.393 1.00 33.59 N
ATOM 2211 CA ILE A 163 -57.826 40.799 16.438 1.00 34.02 C

ATOM 2213 CB ILE A 163 -56.597 39.907 16.745 1.00 33.98 C
ATOM 2215 CG1 ILE A 163 -56.235 39.008 15.566 1.00 34.37 C
ATOM 2218 CD1 ILE A 163 -54.878 38.317 15.722 1.00 34.38 C
ATOM 2222 CG2 ILE A 163 -56.883 38.995 17.919 1.00 33.38 C
ATOM 2226 C ILE A 163 -58.225 41.472 17.744 1.00 34.75 C
ATOM 2227 O ILE A 163 -59.189 41.064 18.373 1.00 35.03 O
ATOM 2229 N SER A 164 -57.501 42.504 18.156 1.00 35.76 N
ATOM 2230 CA SER A 164 -57.763 43.117 19.463 1.00 36.59 C
ATOM 2232 CB SER A 164 -56.828 44.293 19.735 1.00 36.59 C
ATOM 2235 OG SER A 164 -57.350 45.485 19.164 1.00 36.46 O
ATOM 2237 C SER A 164 -59.196 43.611 19.556 1.00 37.42 C
ATOM 2238 O SER A 164 -59.860 43.420 20.571 1.00 37.38 O
ATOM 2240 N HIS A 165 -59.661 44.251 18.486 1.00 38.51 N
ATOM 2241 CA HIS A 165 -60.990 44.851 18.467 1.00 39.40 C
ATOM 2243 CB HIS A 165 -61.008 46.097 17.574 1.00 39.76 C
ATOM 2246 CG HIS A 165 -60.467 47.323 18.251 1.00 42.06 C
ATOM 2247 ND1 HIS A 165 -59.205 47.821 18.000 1.00 44.21 N
ATOM 2249 CE1 HIS A 165 -58.998 48.893 18.748 1.00 45.04 C
ATOM 2251 NE2 HIS A 165 -60.080 49.106 19.478 1.00 44.99 N
ATOM 2253 CD2 HIS A 165 -61.011 48.135 19.192 1.00 43.76 C
ATOM 2255 C HIS A 165 -62.078 43.872 18.060 1.00 39.38 C
ATOM 2256 O HIS A 165 -63.248 44.244 18.067 1.00 39.43 O
ATOM 2258 N LEU A 166 -61.683 42.632 17.745 1.00 39.54 N
ATOM 2259 CA LEU A 166 -62.589 41.550 17.326 1.00 39.55 C
ATOM 2261 CB LEU A 166 -62.001 40.766 16.154 1.00 39.28 C
ATOM 2264 CG LEU A 166 -62.156 41.339 14.752 1.00 38.23 C
ATOM 2266 CD1 LEU A 166 -61.361 40.501 13.805 1.00 37.53 C
ATOM 2270 CD2 LEU A 166 -63.594 41.367 14.332 1.00 37.21 C
ATOM 2274 C LEU A 166 -62.842 40.555 18.438 1.00 40.08 C
ATOM 2275 O LEU A 166 -63.991 40.220 18.733 1.00 40.42 O
ATOM 2277 N LYS A 167 -61.766 40.074 19.052 1.00 40.58 N
ATOM 2278 CA LYS A 167 -61.875 39.090 20.133 1.00 41.09 C
ATOM 2280 CB LYS A 167 -60.491 38.632 20.595 1.00 41.13 C
ATOM 2283 CG LYS A 167 -59.897 39.399 21.768 1.00 42.16 C
ATOM 2286 CD LYS A 167 -58.421 39.035 22.013 1.00 44.45 C
ATOM 2289 CE LYS A 167 -58.070 37.561 21.654 1.00 45.56 C
ATOM 2292 NZ LYS A 167 -56.610 37.237 21.798 1.00 46.20 N
ATOM 2296 C LYS A 167 -62.678 39.584 21.337 1.00 41.23 C
ATOM 2297 O LYS A 167 -62.994 38.793 22.215 1.00 41.47 O
ATOM 2299 N GLU A 168 -62.995 40.884 21.352 1.00 41.49 N
ATOM 2300 CA GLU A 168 -63.704 41.583 22.437 1.00 41.42 C
ATOM 2302 CB GLU A 168 -65.201 41.730 22.100 1.00 41.27 C
ATOM 2305 CG GLU A 168 -65.995 40.424 22.016 1.00 41.01 C
ATOM 2308 CD GLU A 168 -66.928 40.328 20.787 1.00 40.84 C
ATOM 2309 OE1 GLU A 168 -66.701 41.040 19.770 1.00 39.82 O
ATOM 2310 OE2 GLU A 168 -67.884 39.509 20.845 1.00 39.04 O
ATOM 2311 C GLU A 168 -63.484 41.004 23.843 1.00 41.66 C
ATOM 2312 O GLU A 168 -62.435 41.231 24.469 1.00 41.46 O
ATOM 2314 N GLU A 172 -71.668 38.961 21.192 1.00 55.65 N
ATOM 2315 CA GLU A 172 -73.052 39.153 20.721 1.00 56.00 C
ATOM 2317 CB GLU A 172 -73.876 37.880 20.937 1.00 56.27 C
ATOM 2320 CG GLU A 172 -73.198 36.620 20.390 1.00 57.12 C
ATOM 2323 CD GLU A 172 -74.056 35.363 20.516 1.00 58.18 C
ATOM 2324 OE1 GLU A 172 -75.300 35.480 20.622 1.00 58.84 O
ATOM 2325 OE2 GLU A 172 -73.480 34.249 20.498 1.00 58.98 O
ATOM 2326 C GLU A 172 -73.766 40.386 21.334 1.00 55.70 C
ATOM 2327 O GLU A 172 -74.956 40.347 21.688 1.00 54.95 O
ATOM 2329 N LYS A 173 -72.987 41.458 21.486 1.00 55.58 N
ATOM 2330 CA LYS A 173 -73.496 42.831 21.466 1.00 55.43 C
ATOM 2332 CB LYS A 173 -72.649 43.741 22.357 1.00 55.51 C

ATOM 2335 CG LYS A 173 -72.527 43.223 23.793 1.00 56.07 C
ATOM 2338 CD LYS A 173 -72.803 44.291 24.868 1.00 55.87 C
ATOM 2341 CE LYS A 173 -73.111 43.642 26.221 1.00 55.20 C
ATOM 2344 NZ LYS A 173 -72.893 44.576 27.348 1.00 54.63 N
ATOM 2348 C LYS A 173 -73.449 43.297 20.009 1.00 55.01 C
ATOM 2349 O LYS A 173 -74.091 44.274 19.625 1.00 54.97 O
ATOM 2351 N ILE A 174 -72.647 42.581 19.223 1.00 54.57 N
ATOM 2352 CA ILE A 174 -72.713 42.550 17.767 1.00 54.22 C
ATOM 2354 CB ILE A 174 -71.429 41.845 17.227 1.00 54.21 C
ATOM 2356 CG1 ILE A 174 -70.196 42.724 17.474 1.00 54.73 C
ATOM 2359 CD1 ILE A 174 -68.858 41.949 17.553 1.00 55.78 C
ATOM 2363 CG2 ILE A 174 -71.532 41.504 15.759 1.00 54.06 C
ATOM 2367 C ILE A 174 -73.957 41.744 17.384 1.00 53.88 C
ATOM 2368 O ILE A 174 -74.587 41.134 18.250 1.00 53.83 O
ATOM 2370 N GLY A 175 -74.332 41.747 16.107 1.00 53.59 N
ATOM 2371 CA GLY A 175 -75.351 40.817 15.613 1.00 53.51 C
ATOM 2374 C GLY A 175 -75.130 39.395 16.126 1.00 53.43 C
ATOM 2375 O GLY A 175 -74.119 39.105 16.760 1.00 53.80 O
ATOM 2377 N LYS A 176 -76.070 38.495 15.861 1.00 53.10 N
ATOM 2378 CA LYS A 176 -75.926 37.098 16.286 1.00 52.68 C
ATOM 2380 CB LYS A 176 -77.291 36.522 16.677 1.00 52.99 C
ATOM 2383 CG LYS A 176 -78.003 37.387 17.746 1.00 54.12 C
ATOM 2386 CD LYS A 176 -79.201 36.697 18.436 1.00 54.57 C
ATOM 2389 CE LYS A 176 -79.503 37.369 19.792 1.00 54.79 C
ATOM 2392 NZ LYS A 176 -80.458 36.598 20.653 1.00 55.20 N
ATOM 2396 C LYS A 176 -75.246 36.267 15.196 1.00 51.83 C
ATOM 2397 O LYS A 176 -74.393 35.433 15.486 1.00 51.69 O
ATOM 2399 N GLU A 177 -75.609 36.520 13.940 1.00 50.90 N
ATOM 2400 CA GLU A 177 -74.975 35.854 12.800 1.00 50.19 C
ATOM 2402 CB GLU A 177 -75.792 36.062 11.507 1.00 50.41 C
ATOM 2405 CG GLU A 177 -75.506 37.368 10.735 1.00 51.03 C
ATOM 2408 CD GLU A 177 -76.403 37.572 9.507 1.00 52.17 C
ATOM 2409 OE1 GLU A 177 -75.955 38.276 8.569 1.00 52.63 O
ATOM 2410 OE2 GLU A 177 -77.546 37.048 9.479 1.00 52.03 O
ATOM 2411 C GLU A 177 -73.549 36.369 12.607 1.00 49.10 C
ATOM 2412 O GLU A 177 -72.626 35.597 12.321 1.00 49.53 O
ATOM 2414 N LEU A 178 -73.388 37.681 12.770 1.00 47.39 N
ATOM 2415 CA LEU A 178 -72.110 38.371 12.575 1.00 45.63 C
ATOM 2417 CB LEU A 178 -72.352 39.877 12.615 1.00 45.59 C
ATOM 2420 CG LEU A 178 -71.280 40.809 12.085 1.00 45.45 C
ATOM 2422 CD1 LEU A 178 -70.969 40.515 10.620 1.00 45.45 C
ATOM 2426 CD2 LEU A 178 -71.765 42.233 12.279 1.00 44.63 C
ATOM 2430 C LEU A 178 -71.095 37.979 13.634 1.00 44.06 C
ATOM 2431 O LEU A 178 -69.902 38.012 13.387 1.00 43.70 O
ATOM 2433 N ALA A 179 -71.586 37.611 14.810 1.00 42.54 N
ATOM 2434 CA ALA A 179 -70.753 37.041 15.847 1.00 41.66 C
ATOM 2436 CB ALA A 179 -71.545 36.884 17.122 1.00 41.69 C
ATOM 2440 C ALA A 179 -70.193 35.695 15.416 1.00 40.75 C
ATOM 2441 O ALA A 179 -69.078 35.351 15.769 1.00 40.61 O
ATOM 2443 N GLU A 180 -70.974 34.931 14.664 1.00 39.88 N
ATOM 2444 CA GLU A 180 -70.518 33.639 14.143 1.00 39.40 C
ATOM 2446 CB GLU A 180 -71.710 32.781 13.718 1.00 39.74 C
ATOM 2449 CG GLU A 180 -72.650 32.415 14.865 1.00 40.88 C
ATOM 2452 CD GLU A 180 -73.913 31.710 14.398 1.00 42.02 C
ATOM 2453 OE1 GLU A 180 -74.380 32.022 13.271 1.00 43.05 O
ATOM 2454 OE2 GLU A 180 -74.437 30.857 15.166 1.00 41.93 O
ATOM 2455 C GLU A 180 -69.565 33.805 12.960 1.00 38.29 C
ATOM 2456 O GLU A 180 -68.739 32.940 12.699 1.00 38.23 O
ATOM 2458 N GLN A 181 -69.704 34.911 12.240 1.00 36.92 N
ATOM 2459 CA GLN A 181 -68.748 35.299 11.223 1.00 35.74 C

ATOM 2461 CB GLN A 181 -69.272 36.516 10.463 1.00 35.94 C
ATOM 2464 CG GLN A 181 -68.931 36.537 8.975 1.00 36.93 C
ATOM 2467 CD GLN A 181 -69.693 35.492 8.176 1.00 37.72 C
ATOM 2468 OE1 GLN A 181 -70.769 35.067 8.567 1.00 38.78 O
ATOM 2469 NE2 GLN A 181 -69.139 35.083 7.050 1.00 38.11 N
ATOM 2472 C GLN A 181 -67.406 35.632 11.881 1.00 34.64 C
ATOM 2473 O GLN A 181 -66.348 35.411 11.294 1.00 34.73 O
ATOM 2475 N VAL A 182 -67.448 36.158 13.102 1.00 33.29 N
ATOM 2476 CA VAL A 182 -66.224 36.488 13.842 1.00 32.28 C
ATOM 2478 CB VAL A 182 -66.433 37.653 14.855 1.00 32.10 C
ATOM 2480 CG1 VAL A 182 -66.328 38.991 14.166 1.00 31.51 C
ATOM 2484 CG2 VAL A 182 -65.420 37.594 15.957 1.00 31.69 C
ATOM 2488 C VAL A 182 -65.613 35.298 14.575 1.00 31.49 C
ATOM 2489 O VAL A 182 -64.396 35.230 14.668 1.00 31.43 O
ATOM 2491 N SER A 183 -66.422 34.378 15.106 1.00 30.56 N
ATOM 2492 CA SER A 183 -65.860 33.174 15.744 1.00 30.16 C
ATOM 2494 CB SER A 183 -66.926 32.253 16.327 1.00 30.29 C
ATOM 2497 OG SER A 183 -67.796 32.934 17.214 1.00 32.35 O
ATOM 2499 C SER A 183 -65.111 32.403 14.692 1.00 29.30 C
ATOM 2500 O SER A 183 -63.974 31.981 14.903 1.00 29.32 O
ATOM 2502 N HIS A 184 -65.768 32.252 13.546 1.00 28.24 N
ATOM 2503 CA HIS A 184 -65.215 31.578 12.379 1.00 27.36 C
ATOM 2505 CB HIS A 184 -66.245 31.653 11.254 1.00 27.41 C
ATOM 2508 CG HIS A 184 -65.930 30.807 10.064 1.00 26.90 C
ATOM 2509 ND1 HIS A 184 -65.484 29.511 10.166 1.00 27.76 N
ATOM 2511 CE1 HIS A 184 -65.321 29.009 8.955 1.00 27.47 C
ATOM 2513 NE2 HIS A 184 -65.661 29.929 8.075 1.00 26.52 N
ATOM 2515 CD2 HIS A 184 -66.059 31.058 8.742 1.00 26.61 C
ATOM 2517 C HIS A 184 -63.898 32.200 11.940 1.00 26.69 C
ATOM 2518 O HIS A 184 -62.881 31.525 11.862 1.00 26.44 O
ATOM 2520 N ALA A 185 -63.909 33.498 11.675 1.00 26.11 N
ATOM 2521 CA ALA A 185 -62.711 34.176 11.205 1.00 25.63 C
ATOM 2523 CB ALA A 185 -62.970 35.627 11.109 1.00 25.74 C
ATOM 2527 C ALA A 185 -61.552 33.917 12.153 1.00 25.33 C
ATOM 2528 O ALA A 185 -60.451 33.572 11.725 1.00 25.79 O
ATOM 2530 N LEU A 186 -61.814 34.066 13.450 1.00 24.77 N
ATOM 2531 CA LEU A 186 -60.776 33.940 14.470 1.00 24.05 C
ATOM 2533 CB LEU A 186 -61.256 34.498 15.814 1.00 23.63 C
ATOM 2536 CG LEU A 186 -61.516 36.012 15.903 1.00 22.51 C
ATOM 2538 CD1 LEU A 186 -62.057 36.399 17.266 1.00 20.79 C
ATOM 2542 CD2 LEU A 186 -60.273 36.793 15.613 1.00 21.13 C
ATOM 2546 C LEU A 186 -60.316 32.497 14.613 1.00 24.02 C
ATOM 2547 O LEU A 186 -59.169 32.250 14.943 1.00 24.27 O
ATOM 2549 N GLU A 187 -61.201 31.543 14.347 1.00 23.88 N
ATOM 2550 CA GLU A 187 -60.836 30.117 14.348 1.00 23.53 C
ATOM 2552 CB GLU A 187 -62.029 29.270 13.919 1.00 23.66 C
ATOM 2555 CG GLU A 187 -61.945 27.828 14.316 1.00 25.26 C
ATOM 2558 CD GLU A 187 -63.049 26.971 13.693 1.00 28.04 C
ATOM 2559 OE1 GLU A 187 -63.672 27.393 12.681 1.00 28.67 O
ATOM 2560 OE2 GLU A 187 -63.288 25.858 14.225 1.00 29.72 O
ATOM 2561 C GLU A 187 -59.686 29.838 13.395 1.00 22.92 C
ATOM 2562 O GLU A 187 -58.765 29.091 13.729 1.00 22.53 O
ATOM 2564 N LEU A 188 -59.763 30.446 12.209 1.00 22.46 N
ATOM 2565 CA LEU A 188 -58.799 30.246 11.121 1.00 22.07 C
ATOM 2567 CB LEU A 188 -58.802 28.794 10.635 1.00 22.11 C
ATOM 2570 CG LEU A 188 -57.876 28.362 9.493 1.00 22.17 C
ATOM 2572 CD1 LEU A 188 -56.456 28.051 9.961 1.00 21.62 C
ATOM 2576 CD2 LEU A 188 -58.464 27.134 8.822 1.00 22.40 C
ATOM 2580 C LEU A 188 -59.237 31.137 9.985 1.00 21.69 C
ATOM 2581 O LEU A 188 -60.380 31.075 9.563 1.00 21.53 O

ATOM 2583 N PRO A 189 -58.333 31.973 9.474 1.00 21.46 N
ATOM 2584 CA PRO A 189 -58.745 32.935 8.472 1.00 21.18 C
ATOM 2586 CB PRO A 189 -57.592 33.936 8.486 1.00 21.03 C
ATOM 2589 CG PRO A 189 -56.423 33.118 8.757 1.00 21.21 C
ATOM 2592 CD PRO A 189 -56.873 31.992 9.668 1.00 21.61 C
ATOM 2595 C PRO A 189 -58.946 32.314 7.076 1.00 20.96 C
ATOM 2596 O PRO A 189 -58.418 31.247 6.793 1.00 21.02 O
ATOM 2597 N LEU A 190 -59.714 32.994 6.226 1.00 20.89 N
ATOM 2598 CA LEU A 190 -60.018 32.533 4.867 1.00 20.74 C
ATOM 2600 CB LEU A 190 -60.597 33.690 4.053 1.00 20.76 C
ATOM 2603 CG LEU A 190 -62.090 33.924 4.259 1.00 21.35 C
ATOM 2605 CD1 LEU A 190 -62.537 35.196 3.578 1.00 20.54 C
ATOM 2609 CD2 LEU A 190 -62.889 32.712 3.720 1.00 23.39 C
ATOM 2613 C LEU A 190 -58.814 31.971 4.112 1.00 20.35 C
ATOM 2614 O LEU A 190 -58.859 30.871 3.546 1.00 20.08 O
ATOM 2616 N HIS A 191 -57.734 32.746 4.132 1.00 19.81 N
ATOM 2617 CA HIS A 191 -56.537 32.448 3.364 1.00 18.89 C
ATOM 2619 CB HIS A 191 -55.548 33.592 3.536 1.00 18.92 C
ATOM 2622 CG HIS A 191 -54.372 33.520 2.623 1.00 18.51 C
ATOM 2623 ND1 HIS A 191 -54.482 33.647 1.258 1.00 18.08 N
ATOM 2625 CE1 HIS A 191 -53.281 33.544 .718 1.00 18.96 C
ATOM 2627 NE2 HIS A 191 -52.397 33.371 1.684 1.00 17.01 N
ATOM 2629 CD2 HIS A 191 -53.054 33.355 2.884 1.00 17.94 C
ATOM 2631 C HIS A 191 -55.889 31.142 3.759 1.00 18.32 C
ATOM 2632 O HIS A 191 -55.217 30.531 2.942 1.00 17.98 O
ATOM 2634 N ARG A 192 -56.093 30.719 5.006 1.00 18.06 N
ATOM 2635 CA ARG A 192 -55.502 29.480 5.523 1.00 17.99 C
ATOM 2637 CB ARG A 192 -54.940 29.722 6.909 1.00 17.77 C
ATOM 2640 CG ARG A 192 -53.822 30.683 6.881 1.00 18.47 C
ATOM 2643 CD ARG A 192 -53.082 30.748 8.196 1.00 19.80 C
ATOM 2646 NE ARG A 192 -52.174 31.900 8.224 1.00 20.33 N
ATOM 2648 CZ ARG A 192 -51.176 32.048 9.077 1.00 20.10 C
ATOM 2649 NH1 ARG A 192 -50.928 31.113 9.972 1.00 21.72 N
ATOM 2652 NH2 ARG A 192 -50.407 33.119 9.019 1.00 20.79 N
ATOM 2655 C ARG A 192 -56.477 28.311 5.590 1.00 18.00 C
ATOM 2656 O ARG A 192 -56.067 27.170 5.871 1.00 18.21 O
ATOM 2658 N ARG A 193 -57.758 28.588 5.335 1.00 17.59 N
ATOM 2659 CA ARG A 193 -58.779 27.563 5.382 1.00 17.16 C
ATOM 2661 CB ARG A 193 -60.141 28.164 5.741 1.00 17.45 C
ATOM 2664 CG ARG A 193 -61.109 27.132 6.322 1.00 18.70 C
ATOM 2667 CD ARG A 193 -62.479 27.682 6.686 1.00 20.20 C
ATOM 2670 NE ARG A 193 -62.423 28.682 7.751 1.00 22.59 N
ATOM 2672 CZ ARG A 193 -62.386 28.435 9.067 1.00 24.12 C
ATOM 2673 NH1 ARG A 193 -62.395 27.198 9.575 1.00 22.66 N
ATOM 2676 NH2 ARG A 193 -62.348 29.469 9.898 1.00 26.36 N
ATOM 2679 C ARG A 193 -58.871 26.842 4.058 1.00 16.63 C
ATOM 2680 O ARG A 193 -58.861 27.461 3.005 1.00 15.93 O
ATOM 2682 N THR A 194 -58.955 25.518 4.149 1.00 16.72 N
ATOM 2683 CA THR A 194 -59.332 24.638 3.051 1.00 16.88 C
ATOM 2685 CB THR A 194 -59.520 23.250 3.592 1.00 16.43 C
ATOM 2687 OG1 THR A 194 -58.252 22.605 3.583 1.00 17.74 O
ATOM 2689 CG2 THR A 194 -60.454 22.441 2.754 1.00 18.43 C
ATOM 2693 C THR A 194 -60.607 25.112 2.384 1.00 17.28 C
ATOM 2694 O THR A 194 -61.441 25.734 3.022 1.00 17.44 O
ATOM 2696 N GLN A 195 -60.765 24.855 1.091 1.00 18.05 N
ATOM 2697 CA GLN A 195 -61.925 25.402 .397 1.00 18.76 C
ATOM 2699 CB GLN A 195 -61.768 25.381 -1.114 1.00 18.87 C
ATOM 2702 CG GLN A 195 -63.145 25.523 -1.761 1.00 20.75 C
ATOM 2705 CD GLN A 195 -63.095 25.922 -3.179 1.00 23.41 C
ATOM 2706 OE1 GLN A 195 -62.031 26.088 -3.733 1.00 27.07 O

```
ATOM  2707 NE2 GLN A 195    -64.248  26.090  -3.791  1.00 25.02       N
ATOM  2710 C   GLN A 195    -63.243  24.704    .765  1.00 18.93       C
ATOM  2711 O   GLN A 195    -64.169  25.333   1.291  1.00 19.42       O
ATOM  2713 N   ARG A 196    -63.345  23.418    .443  1.00 18.90       N
ATOM  2714 CA  ARG A 196    -64.577  22.685    .663  1.00 18.68       C
ATOM  2716 CB  ARG A 196    -64.356  21.186    .454  1.00 18.53       C
ATOM  2719 CG  ARG A 196    -64.851  20.644   -.888  1.00 18.31       C
ATOM  2722 CD  ARG A 196    -64.705  21.622  -2.037  1.00 17.93       C
ATOM  2725 NE  ARG A 196    -65.930  21.720  -2.834  1.00 18.52       N
ATOM  2727 CZ  ARG A 196    -66.480  22.857  -3.256  1.00 18.63       C
ATOM  2728 NH1 ARG A 196    -65.938  24.014  -2.937  1.00 19.84       N
ATOM  2731 NH2 ARG A 196    -67.582  22.844  -3.999  1.00 18.53       N
ATOM  2734 C   ARG A 196    -65.070  22.982   2.061  1.00 19.02       C
ATOM  2735 O   ARG A 196    -66.276  23.085   2.284  1.00 19.30       O
ATOM  2737 N   LEU A 197    -64.127  23.152   2.990  1.00 19.09       N
ATOM  2738 CA  LEU A 197    -64.444  23.432   4.379  1.00 19.19       C
ATOM  2740 CB  LEU A 197    -63.203  23.346   5.262  1.00 19.14       C
ATOM  2743 CG  LEU A 197    -63.135  22.097   6.130  1.00 19.99       C
ATOM  2745 CD1 LEU A 197    -64.476  21.899   6.811  1.00 21.56       C
ATOM  2749 CD2 LEU A 197    -62.016  22.198   7.161  1.00 20.06       C
ATOM  2753 C   LEU A 197    -65.071  24.781   4.553  1.00 19.52       C
ATOM  2754 O   LEU A 197    -66.052  24.902   5.252  1.00 19.85       O
ATOM  2756 N   GLU A 198    -64.488  25.803   3.941  1.00 20.11       N
ATOM  2757 CA  GLU A 198    -65.051  27.147   3.986  1.00 20.47       C
ATOM  2759 CB  GLU A 198    -64.079  28.156   3.385  1.00 20.84       C
ATOM  2762 CG  GLU A 198    -64.659  29.539   3.069  1.00 22.30       C
ATOM  2765 CD  GLU A 198    -65.206  30.260   4.283  1.00 24.40       C
ATOM  2766 OE1 GLU A 198    -64.852  29.894   5.418  1.00 25.34       O
ATOM  2767 OE2 GLU A 198    -65.991  31.217   4.106  1.00 26.83       O
ATOM  2768 C   GLU A 198    -66.360  27.186   3.226  1.00 20.57       C
ATOM  2769 O   GLU A 198    -67.212  28.009   3.529  1.00 20.65       O
ATOM  2771 N   ALA A 199    -66.519  26.298   2.240  1.00 20.76       N
ATOM  2772 CA  ALA A 199    -67.751  26.229   1.452  1.00 20.52       C
ATOM  2774 CB  ALA A 199    -67.521  25.492    .166  1.00 20.44       C
ATOM  2778 C   ALA A 199    -68.907  25.611   2.232  1.00 20.55       C
ATOM  2779 O   ALA A 199    -69.988  26.158   2.202  1.00 20.17       O
ATOM  2781 N   VAL A 200    -68.701  24.493   2.933  1.00 21.10       N
ATOM  2782 CA  VAL A 200    -69.791  23.935   3.774  1.00 21.51       C
ATOM  2784 CB  VAL A 200    -69.509  22.576   4.485  1.00 21.18       C
ATOM  2786 CG1 VAL A 200    -69.618  21.460   3.525  1.00 21.27       C
ATOM  2790 CG2 VAL A 200    -68.161  22.569   5.200  1.00 21.23       C
ATOM  2794 C   VAL A 200    -70.170  24.905   4.860  1.00 21.99       C
ATOM  2795 O   VAL A 200    -71.338  25.022   5.186  1.00 22.99       O
ATOM  2797 N   TRP A 201    -69.204  25.590   5.440  1.00 22.10       N
ATOM  2798 CA  TRP A 201    -69.551  26.565   6.433  1.00 22.58       C
ATOM  2800 CB  TRP A 201    -68.315  27.144   7.121  1.00 22.92       C
ATOM  2803 CG  TRP A 201    -68.667  27.957   8.310  1.00 23.65       C
ATOM  2804 CD1 TRP A 201    -68.758  27.520   9.588  1.00 25.08       C
ATOM  2806 NE1 TRP A 201    -69.127  28.549  10.417  1.00 26.35       N
ATOM  2808 CE2 TRP A 201    -69.290  29.683   9.669  1.00 25.48       C
ATOM  2809 CD2 TRP A 201    -69.010  29.344   8.332  1.00 24.77       C
ATOM  2810 CE3 TRP A 201    -69.095  30.336   7.355  1.00 24.92       C
ATOM  2812 CZ3 TRP A 201    -69.450  31.616   7.739  1.00 24.96       C
ATOM  2814 CH2 TRP A 201    -69.720  31.918   9.078  1.00 25.08       C
ATOM  2816 CZ2 TRP A 201    -69.648  30.968  10.056  1.00 24.68       C
ATOM  2818 C   TRP A 201    -70.351  27.662   5.758  1.00 22.71       C
ATOM  2819 O   TRP A 201    -71.482  27.921   6.140  1.00 22.76       O
ATOM  2821 N   SER A 202    -69.776  28.272   4.727  1.00 23.04       N
ATOM  2822 CA  SER A 202    -70.335  29.500   4.165  1.00 23.29       C
ATOM  2824 CB  SER A 202    -69.304  30.205   3.290  1.00 23.20       C
```

ATOM 2827 OG SER A 202 -68.306 30.807 4.111 1.00 23.07 O
ATOM 2829 C SER A 202 -71.666 29.341 3.432 1.00 23.66 C
ATOM 2830 O SER A 202 -72.392 30.310 3.265 1.00 23.38 O
ATOM 2832 N ILE A 203 -71.996 28.124 3.016 1.00 24.49 N
ATOM 2833 CA ILE A 203 -73.321 27.859 2.460 1.00 25.07 C
ATOM 2835 CB ILE A 203 -73.391 26.530 1.653 1.00 24.74 C
ATOM 2837 CG1 ILE A 203 -72.494 26.587 .423 1.00 24.36 C
ATOM 2840 CD1 ILE A 203 -72.344 25.255 -.281 1.00 23.81 C
ATOM 2844 CG2 ILE A 203 -74.795 26.292 1.156 1.00 24.45 C
ATOM 2848 C ILE A 203 -74.338 27.858 3.607 1.00 25.91 C
ATOM 2849 O ILE A 203 -75.350 28.554 3.546 1.00 26.26 O
ATOM 2851 N GLU A 204 -74.051 27.104 4.662 1.00 26.69 N
ATOM 2852 CA GLU A 204 -74.929 27.053 5.824 1.00 27.40 C
ATOM 2854 CB GLU A 204 -74.286 26.217 6.931 1.00 27.65 C
ATOM 2857 CG GLU A 204 -75.132 26.032 8.183 1.00 29.02 C
ATOM 2860 CD GLU A 204 -76.530 25.491 7.903 1.00 30.44 C
ATOM 2861 OE1 GLU A 204 -76.746 24.858 6.844 1.00 31.22 O
ATOM 2862 OE2 GLU A 204 -77.417 25.703 8.753 1.00 31.96 O
ATOM 2863 C GLU A 204 -75.258 28.451 6.342 1.00 27.61 C
ATOM 2864 O GLU A 204 -76.409 28.778 6.526 1.00 27.78 O
ATOM 2866 N ALA A 205 -74.240 29.274 6.547 1.00 28.15 N
ATOM 2867 CA ALA A 205 -74.416 30.637 7.050 1.00 28.41 C
ATOM 2869 CB ALA A 205 -73.062 31.285 7.274 1.00 28.41 C
ATOM 2873 C ALA A 205 -75.234 31.520 6.136 1.00 28.84 C
ATOM 2874 O ALA A 205 -76.050 32.302 6.610 1.00 28.54 O
ATOM 2876 N TYR A 206 -74.978 31.408 4.832 1.00 29.84 N
ATOM 2877 CA TYR A 206 -75.581 32.281 3.805 1.00 30.41 C
ATOM 2879 CB TYR A 206 -74.801 32.170 2.493 1.00 30.20 C
ATOM 2882 CG TYR A 206 -75.180 33.173 1.425 1.00 29.62 C
ATOM 2883 CD1 TYR A 206 -74.721 34.482 1.484 1.00 30.32 C
ATOM 2885 CE1 TYR A 206 -75.047 35.412 .489 1.00 29.70 C
ATOM 2887 CZ TYR A 206 -75.830 35.028 -.578 1.00 28.41 C
ATOM 2888 OH TYR A 206 -76.155 35.956 -1.548 1.00 26.74 O
ATOM 2890 CE2 TYR A 206 -76.291 33.724 -.659 1.00 28.16 C
ATOM 2892 CD2 TYR A 206 -75.958 32.806 .335 1.00 28.39 C
ATOM 2894 C TYR A 206 -77.038 31.918 3.561 1.00 31.15 C
ATOM 2895 O TYR A 206 -77.858 32.781 3.268 1.00 31.30 O
ATOM 2897 N ARG A 207 -77.341 30.631 3.676 1.00 32.05 N
ATOM 2898 CA ARG A 207 -78.691 30.128 3.555 1.00 32.81 C
ATOM 2900 CB ARG A 207 -78.684 28.623 3.813 1.00 32.86 C
ATOM 2903 CG ARG A 207 -80.028 27.941 3.673 1.00 34.01 C
ATOM 2906 CD ARG A 207 -80.066 26.632 4.450 1.00 35.11 C
ATOM 2909 NE ARG A 207 -79.096 25.669 3.939 1.00 35.35 N
ATOM 2911 CZ ARG A 207 -79.353 24.737 3.022 1.00 36.00 C
ATOM 2912 NH1 ARG A 207 -80.562 24.611 2.478 1.00 35.55 N
ATOM 2915 NH2 ARG A 207 -78.381 23.918 2.640 1.00 37.05 N
ATOM 2918 C ARG A 207 -79.609 30.826 4.550 1.00 33.57 C
ATOM 2919 O ARG A 207 -80.783 31.003 4.263 1.00 33.82 O
ATOM 2921 N LYS A 208 -79.064 31.223 5.707 1.00 34.58 N
ATOM 2922 CA LYS A 208 -79.835 31.830 6.812 1.00 35.21 C
ATOM 2924 CB LYS A 208 -79.137 31.599 8.159 1.00 35.05 C
ATOM 2927 CG LYS A 208 -78.847 30.147 8.496 1.00 34.78 C
ATOM 2930 CD LYS A 208 -78.583 29.974 9.980 1.00 34.44 C
ATOM 2933 CE LYS A 208 -77.992 28.619 10.309 1.00 34.16 C
ATOM 2936 NZ LYS A 208 -76.540 28.693 10.572 1.00 33.81 N
ATOM 2940 C LYS A 208 -80.075 33.333 6.663 1.00 36.06 C
ATOM 2941 O LYS A 208 -81.032 33.857 7.226 1.00 36.19 O
ATOM 2943 N LYS A 209 -79.197 34.032 5.946 1.00 36.93 N
ATOM 2944 CA LYS A 209 -79.412 35.445 5.652 1.00 37.77 C
ATOM 2946 CB LYS A 209 -78.284 35.998 4.779 1.00 38.18 C

ATOM 2949 CG LYS A 209 -76.928 36.134 5.458 1.00 39.90 C
ATOM 2952 CD LYS A 209 -75.982 37.023 4.621 1.00 42.39 C
ATOM 2955 CE LYS A 209 -74.531 37.016 5.169 1.00 44.21 C
ATOM 2958 NZ LYS A 209 -74.350 37.688 6.509 1.00 44.75 N
ATOM 2962 C LYS A 209 -80.738 35.600 4.911 1.00 37.89 C
ATOM 2963 O LYS A 209 -81.049 34.785 4.036 1.00 38.20 O
ATOM 2965 N GLU A 210 -81.518 36.632 5.243 1.00 37.87 N
ATOM 2966 CA GLU A 210 -82.847 36.797 4.630 1.00 37.72 C
ATOM 2968 CB GLU A 210 -83.821 37.578 5.549 1.00 38.19 C
ATOM 2971 CG GLU A 210 -83.850 39.130 5.404 1.00 39.68 C
ATOM 2974 CD GLU A 210 -85.270 39.736 5.534 1.00 41.27 C
ATOM 2975 OE1 GLU A 210 -86.172 39.100 6.136 1.00 41.67 O
ATOM 2976 OE2 GLU A 210 -85.482 40.859 5.019 1.00 42.17 O
ATOM 2977 C GLU A 210 -82.760 37.394 3.219 1.00 36.68 C
ATOM 2978 O GLU A 210 -83.605 37.103 2.371 1.00 36.39 O
ATOM 2980 N ASP A 211 -81.725 38.198 2.969 1.00 35.65 N
ATOM 2981 CA ASP A 211 -81.481 38.777 1.632 1.00 34.94 C
ATOM 2983 CB ASP A 211 -81.064 40.257 1.740 1.00 35.22 C
ATOM 2986 CG ASP A 211 -79.811 40.477 2.599 1.00 35.84 C
ATOM 2987 OD1 ASP A 211 -79.379 39.557 3.341 1.00 35.60 O
ATOM 2988 OD2 ASP A 211 -79.276 41.606 2.536 1.00 36.73 O
ATOM 2989 C ASP A 211 -80.451 37.989 .811 1.00 33.73 C
ATOM 2990 O ASP A 211 -79.753 38.556 -.021 1.00 33.40 O
ATOM 2992 N ALA A 212 -80.366 36.682 1.057 1.00 32.53 N
ATOM 2993 CA ALA A 212 -79.506 35.783 .293 1.00 31.40 C
ATOM 2995 CB ALA A 212 -79.569 34.382 .889 1.00 30.79 C
ATOM 2999 C ALA A 212 -79.940 35.762 -1.176 1.00 30.60 C
ATOM 3000 O ALA A 212 -81.124 35.594 -1.467 1.00 30.37 O
ATOM 3002 N ASN A 213 -79.000 35.967 -2.097 1.00 29.71 N
ATOM 3003 CA ASN A 213 -79.304 35.809 -3.520 1.00 29.27 C
ATOM 3005 CB ASN A 213 -78.144 36.315 -4.402 1.00 29.30 C
ATOM 3008 CG ASN A 213 -78.442 36.217 -5.911 1.00 29.07 C
ATOM 3009 OD1 ASN A 213 -78.437 37.215 -6.624 1.00 29.38 O
ATOM 3010 ND2 ASN A 213 -78.691 35.015 -6.389 1.00 28.37 N
ATOM 3013 C ASN A 213 -79.634 34.328 -3.785 1.00 28.81 C
ATOM 3014 O ASN A 213 -78.784 33.455 -3.658 1.00 29.04 O
ATOM 3016 N GLN A 214 -80.880 34.053 -4.145 1.00 28.04 N
ATOM 3017 CA GLN A 214 -81.376 32.692 -4.191 1.00 27.32 C
ATOM 3019 CB GLN A 214 -82.906 32.700 -4.178 1.00 27.47 C
ATOM 3022 CG GLN A 214 -83.505 33.269 -2.889 1.00 27.68 C
ATOM 3025 CD GLN A 214 -83.294 32.359 -1.688 1.00 27.54 C
ATOM 3026 OE1 GLN A 214 -83.940 31.320 -1.571 1.00 28.19 O
ATOM 3027 NE2 GLN A 214 -82.392 32.748 -.790 1.00 26.90 N
ATOM 3030 C GLN A 214 -80.858 31.902 -5.385 1.00 26.71 C
ATOM 3031 O GLN A 214 -80.863 30.668 -5.355 1.00 26.91 O
ATOM 3033 N VAL A 215 -80.439 32.600 -6.442 1.00 25.81 N
ATOM 3034 CA VAL A 215 -79.789 31.947 -7.588 1.00 24.88 C
ATOM 3036 CB VAL A 215 -79.651 32.894 -8.808 1.00 24.81 C
ATOM 3038 CG1 VAL A 215 -78.459 32.483 -9.680 1.00 24.94 C
ATOM 3042 CG2 VAL A 215 -80.935 32.907 -9.620 1.00 23.74 C
ATOM 3046 C VAL A 215 -78.415 31.427 -7.176 1.00 24.18 C
ATOM 3047 O VAL A 215 -78.073 30.282 -7.430 1.00 23.74 O
ATOM 3049 N LEU A 216 -77.650 32.283 -6.510 1.00 23.78 N
ATOM 3050 CA LEU A 216 -76.299 31.961 -6.036 1.00 23.33 C
ATOM 3052 CB LEU A 216 -75.680 33.195 -5.373 1.00 23.10 C
ATOM 3055 CG LEU A 216 -74.194 33.192 -5.059 1.00 22.91 C
ATOM 3057 CD1 LEU A 216 -73.383 32.962 -6.312 1.00 22.88 C
ATOM 3061 CD2 LEU A 216 -73.826 34.518 -4.424 1.00 22.03 C
ATOM 3065 C LEU A 216 -76.333 30.797 -5.050 1.00 22.92 C
ATOM 3066 O LEU A 216 -75.598 29.826 -5.201 1.00 23.38 O

ATOM 3068 N LEU A 217 -77.214 30.890 -4.060 1.00 22.09 N
ATOM 3069 CA LEU A 217 -77.367 29.851 -3.054 1.00 21.14 C
ATOM 3071 CB LEU A 217 -78.488 30.225 -2.090 1.00 21.11 C
ATOM 3074 CG LEU A 217 -78.782 29.236 -.961 1.00 21.08 C
ATOM 3076 CD1 LEU A 217 -77.703 29.267 .101 1.00 19.87 C
ATOM 3080 CD2 LEU A 217 -80.146 29.535 -.360 1.00 21.46 C
ATOM 3084 C LEU A 217 -77.682 28.517 -3.685 1.00 20.38 C
ATOM 3085 O LEU A 217 -77.133 27.508 -3.286 1.00 20.04 O
ATOM 3087 N GLU A 218 -78.579 28.512 -4.661 1.00 19.97 N
ATOM 3088 CA GLU A 218 -79.027 27.260 -5.273 1.00 19.72 C
ATOM 3090 CB GLU A 218 -80.220 27.499 -6.212 1.00 19.87 C
ATOM 3093 CG GLU A 218 -81.005 26.228 -6.627 1.00 21.03 C
ATOM 3096 CD GLU A 218 -82.303 26.535 -7.424 1.00 22.59 C
ATOM 3097 OE1 GLU A 218 -82.643 27.730 -7.619 1.00 23.61 O
ATOM 3098 OE2 GLU A 218 -82.983 25.578 -7.863 1.00 22.31 O
ATOM 3099 C GLU A 218 -77.854 26.613 -6.009 1.00 19.03 C
ATOM 3100 O GLU A 218 -77.522 25.452 -5.764 1.00 18.97 O
ATOM 3102 N LEU A 219 -77.203 27.381 -6.878 1.00 18.06 N
ATOM 3103 CA LEU A 219 -76.012 26.907 -7.573 1.00 17.15 C
ATOM 3105 CB LEU A 219 -75.439 28.029 -8.418 1.00 16.75 C
ATOM 3108 CG LEU A 219 -74.196 27.717 -9.231 1.00 16.01 C
ATOM 3110 CD1 LEU A 219 -74.511 26.832 -10.404 1.00 12.99 C
ATOM 3114 CD2 LEU A 219 -73.577 29.028 -9.675 1.00 16.20 C
ATOM 3118 C LEU A 219 -74.973 26.409 -6.570 1.00 16.75 C
ATOM 3119 O LEU A 219 -74.377 25.355 -6.757 1.00 16.47 O
ATOM 3121 N ALA A 220 -74.786 27.169 -5.496 1.00 16.40 N
ATOM 3122 CA ALA A 220 -73.858 26.808 -4.422 1.00 16.15 C
ATOM 3124 CB ALA A 220 -73.906 27.830 -3.302 1.00 16.13 C
ATOM 3128 C ALA A 220 -74.137 25.436 -3.862 1.00 16.03 C
ATOM 3129 O ALA A 220 -73.253 24.603 -3.799 1.00 16.30 O
ATOM 3131 N ILE A 221 -75.371 25.201 -3.447 1.00 16.24 N
ATOM 3132 CA ILE A 221 -75.731 23.916 -2.857 1.00 16.33 C
ATOM 3134 CB ILE A 221 -77.203 23.895 -2.352 1.00 15.94 C
ATOM 3136 CG1 ILE A 221 -77.410 24.879 -1.203 1.00 15.36 C
ATOM 3139 CD1 ILE A 221 -78.842 25.234 -.962 1.00 14.49 C
ATOM 3143 CG2 ILE A 221 -77.571 22.537 -1.836 1.00 15.18 C
ATOM 3147 C ILE A 221 -75.509 22.841 -3.911 1.00 17.06 C
ATOM 3148 O ILE A 221 -74.899 21.819 -3.653 1.00 16.51 O
ATOM 3150 N LEU A 222 -75.981 23.138 -5.117 1.00 18.53 N
ATOM 3151 CA LEU A 222 -76.006 22.207 -6.243 1.00 19.25 C
ATOM 3153 CB LEU A 222 -76.657 22.891 -7.445 1.00 19.18 C
ATOM 3156 CG LEU A 222 -77.037 21.972 -8.597 1.00 19.65 C
ATOM 3158 CD1 LEU A 222 -78.318 22.489 -9.268 1.00 19.24 C
ATOM 3162 CD2 LEU A 222 -75.869 21.788 -9.597 1.00 18.75 C
ATOM 3166 C LEU A 222 -74.618 21.751 -6.630 1.00 20.07 C
ATOM 3167 O LEU A 222 -74.381 20.558 -6.778 1.00 20.55 O
ATOM 3169 N ASP A 223 -73.710 22.711 -6.797 1.00 20.92 N
ATOM 3170 CA ASP A 223 -72.330 22.427 -7.189 1.00 21.43 C
ATOM 3172 CB ASP A 223 -71.621 23.723 -7.585 1.00 21.63 C
ATOM 3175 CG ASP A 223 -70.202 23.495 -8.070 1.00 22.51 C
ATOM 3176 OD1 ASP A 223 -69.296 23.282 -7.225 1.00 24.67 O
ATOM 3177 OD2 ASP A 223 -69.990 23.544 -9.296 1.00 22.73 O
ATOM 3178 C ASP A 223 -71.573 21.722 -6.060 1.00 21.79 C
ATOM 3179 O ASP A 223 -70.843 20.764 -6.313 1.00 21.73 O
ATOM 3181 N TYR A 224 -71.755 22.182 -4.820 1.00 22.14 N
ATOM 3182 CA TYR A 224 -71.120 21.529 -3.686 1.00 22.22 C
ATOM 3184 CB TYR A 224 -71.462 22.190 -2.355 1.00 22.38 C
ATOM 3187 CG TYR A 224 -70.673 21.542 -1.249 1.00 22.65 C
ATOM 3188 CD1 TYR A 224 -69.356 21.864 -1.053 1.00 22.59 C
ATOM 3190 CE1 TYR A 224 -68.622 21.258 -.098 1.00 23.38 C

ATOM 3192 CZ TYR A 224 -69.177 20.288 .670 1.00 23.22 C
ATOM 3193 OH TYR A 224 -68.402 19.684 1.620 1.00 23.93 O
ATOM 3195 CE2 TYR A 224 -70.483 19.931 .500 1.00 23.36 C
ATOM 3197 CD2 TYR A 224 -71.221 20.547 -.464 1.00 23.41 C
ATOM 3199 C TYR A 224 -71.485 20.065 -3.605 1.00 22.52 C
ATOM 3200 O TYR A 224 -70.641 19.233 -3.311 1.00 22.93 O
ATOM 3202 N ASN A 225 -72.742 19.749 -3.856 1.00 22.94 N
ATOM 3203 CA ASN A 225 -73.187 18.374 -3.801 1.00 23.44 C
ATOM 3205 CB ASN A 225 -74.706 18.310 -3.729 1.00 23.34 C
ATOM 3208 CG ASN A 225 -75.210 18.579 -2.352 1.00 22.62 C
ATOM 3209 OD1 ASN A 225 -74.749 17.977 -1.407 1.00 23.33 O
ATOM 3210 ND2 ASN A 225 -76.146 19.494 -2.223 1.00 22.52 N
ATOM 3213 C ASN A 225 -72.694 17.523 -4.959 1.00 24.26 C
ATOM 3214 O ASN A 225 -72.408 16.328 -4.767 1.00 24.88 O
ATOM 3216 N MET A 226 -72.607 18.119 -6.150 1.00 24.67 N
ATOM 3217 CA MET A 226 -72.167 17.395 -7.349 1.00 24.95 C
ATOM 3219 CB MET A 226 -72.421 18.237 -8.594 1.00 25.37 C
ATOM 3222 CG MET A 226 -71.785 17.713 -9.873 1.00 27.23 C
ATOM 3225 SD MET A 226 -70.837 19.010 -10.708 1.00 31.73 S
ATOM 3226 CE MET A 226 -72.185 20.000 -11.367 1.00 31.30 C
ATOM 3230 C MET A 226 -70.688 17.045 -7.247 1.00 24.70 C
ATOM 3231 O MET A 226 -70.291 15.929 -7.568 1.00 24.91 O
ATOM 3233 N ILE A 227 -69.873 17.995 -6.799 1.00 24.43 N
ATOM 3234 CA ILE A 227 -68.456 17.726 -6.598 1.00 24.18 C
ATOM 3236 CB ILE A 227 -67.656 18.971 -6.154 1.00 24.15 C
ATOM 3238 CG1 ILE A 227 -67.628 20.021 -7.253 1.00 23.64 C
ATOM 3241 CD1 ILE A 227 -66.853 21.246 -6.880 1.00 23.11 C
ATOM 3245 CG2 ILE A 227 -66.229 18.603 -5.827 1.00 24.36 C
ATOM 3249 C ILE A 227 -68.329 16.645 -5.546 1.00 23.98 C
ATOM 3250 O ILE A 227 -67.609 15.689 -5.747 1.00 24.35 O
ATOM 3252 N GLN A 228 -69.048 16.779 -4.439 1.00 23.79 N
ATOM 3253 CA GLN A 228 -69.020 15.754 -3.382 1.00 23.66 C
ATOM 3255 CB GLN A 228 -70.077 16.010 -2.305 1.00 23.64 C
ATOM 3258 CG GLN A 228 -69.972 15.049 -1.145 1.00 22.91 C
ATOM 3261 CD GLN A 228 -70.891 15.417 -.033 1.00 23.26 C
ATOM 3262 OE1 GLN A 228 -72.082 15.098 -.069 1.00 25.64 O
ATOM 3263 NE2 GLN A 228 -70.357 16.083 .978 1.00 21.77 N
ATOM 3266 C GLN A 228 -69.243 14.349 -3.893 1.00 23.54 C
ATOM 3267 O GLN A 228 -68.664 13.412 -3.357 1.00 23.59 O
ATOM 3269 N SER A 229 -70.105 14.194 -4.893 1.00 23.27 N
ATOM 3270 CA SER A 229 -70.394 12.868 -5.406 1.00 23.35 C
ATOM 3272 CB SER A 229 -71.753 12.812 -6.095 1.00 23.31 C
ATOM 3275 OG SER A 229 -71.836 13.823 -7.060 1.00 24.31 O
ATOM 3277 C SER A 229 -69.287 12.394 -6.331 1.00 23.19 C
ATOM 3278 O SER A 229 -69.130 11.194 -6.512 1.00 23.44 O
ATOM 3280 N VAL A 230 -68.512 13.306 -6.914 1.00 23.14 N
ATOM 3281 CA VAL A 230 -67.269 12.874 -7.552 1.00 23.00 C
ATOM 3283 CB VAL A 230 -66.469 13.998 -8.253 1.00 22.75 C
ATOM 3285 CG1 VAL A 230 -65.091 13.470 -8.667 1.00 21.87 C
ATOM 3289 CG2 VAL A 230 -67.222 14.539 -9.459 1.00 21.74 C
ATOM 3293 C VAL A 230 -66.417 12.268 -6.452 1.00 23.35 C
ATOM 3294 O VAL A 230 -65.917 11.173 -6.589 1.00 23.68 O
ATOM 3296 N TYR A 231 -66.284 12.968 -5.340 1.00 23.96 N
ATOM 3297 CA TYR A 231 -65.414 12.509 -4.274 1.00 24.60 C
ATOM 3299 CB TYR A 231 -65.486 13.426 -3.051 1.00 24.69 C
ATOM 3302 CG TYR A 231 -64.963 14.837 -3.211 1.00 24.11 C
ATOM 3303 CD1 TYR A 231 -64.071 15.190 -4.214 1.00 24.31 C
ATOM 3305 CE1 TYR A 231 -63.592 16.491 -4.322 1.00 24.63 C
ATOM 3307 CZ TYR A 231 -63.994 17.441 -3.406 1.00 25.13 C
ATOM 3308 OH TYR A 231 -63.554 18.754 -3.456 1.00 24.64 O

ATOM 3310 CE2 TYR A 231 -64.863 17.086 -2.402 1.00 25.76 C
ATOM 3312 CD2 TYR A 231 -65.329 15.800 -2.308 1.00 24.28 C
ATOM 3314 C TYR A 231 -65.785 11.111 -3.833 1.00 25.26 C
ATOM 3315 O TYR A 231 -64.917 10.315 -3.488 1.00 25.44 O
ATOM 3317 N GLN A 232 -67.079 10.819 -3.833 1.00 26.04 N
ATOM 3318 CA GLN A 232 -67.566 9.532 -3.362 1.00 26.57 C
ATOM 3320 CB GLN A 232 -69.060 9.621 -3.057 1.00 26.44 C
ATOM 3323 CG GLN A 232 -69.339 10.397 -1.778 1.00 26.25 C
ATOM 3326 CD GLN A 232 -70.786 10.819 -1.630 1.00 26.53 C
ATOM 3327 OE1 GLN A 232 -71.667 10.305 -2.318 1.00 27.77 O
ATOM 3328 NE2 GLN A 232 -71.040 11.759 -.723 1.00 25.51 N
ATOM 3331 C GLN A 232 -67.238 8.414 -4.351 1.00 27.44 C
ATOM 3332 O GLN A 232 -66.852 7.319 -3.935 1.00 27.33 O
ATOM 3334 N ARG A 233 -67.373 8.691 -5.649 1.00 28.66 N
ATOM 3335 CA ARG A 233 -66.905 7.768 -6.685 1.00 29.86 C
ATOM 3337 CB ARG A 233 -67.212 8.292 -8.090 1.00 30.08 C
ATOM 3340 CG ARG A 233 -66.378 7.634 -9.179 1.00 32.80 C
ATOM 3343 CD ARG A 233 -66.913 7.923 -10.572 1.00 36.74 C
ATOM 3346 NE ARG A 233 -66.962 9.363 -10.860 1.00 40.33 N
ATOM 3348 CZ ARG A 233 -68.069 10.119 -10.891 1.00 43.12 C
ATOM 3349 NH1 ARG A 233 -69.276 9.600 -10.655 1.00 44.55 N
ATOM 3352 NH2 ARG A 233 -67.971 11.418 -11.169 1.00 43.38 N
ATOM 3355 C ARG A 233 -65.401 7.518 -6.514 1.00 30.34 C
ATOM 3356 O ARG A 233 -64.962 6.374 -6.412 1.00 30.55 O
ATOM 3358 N ASP A 234 -64.621 8.591 -6.461 1.00 31.00 N
ATOM 3359 CA ASP A 234 -63.187 8.487 -6.205 1.00 31.48 C
ATOM 3361 CB ASP A 234 -62.594 9.870 -5.942 1.00 31.56 C
ATOM 3364 CG ASP A 234 -62.573 10.741 -7.167 1.00 32.78 C
ATOM 3365 OD1 ASP A 234 -62.911 10.249 -8.276 1.00 34.25 O
ATOM 3366 OD2 ASP A 234 -62.215 11.930 -7.011 1.00 34.81 O
ATOM 3367 C ASP A 234 -62.885 7.596 -5.010 1.00 31.70 C
ATOM 3368 O ASP A 234 -61.985 6.780 -5.053 1.00 31.56 O
ATOM 3370 N LEU A 235 -63.647 7.766 -3.943 1.00 32.43 N
ATOM 3371 CA LEU A 235 -63.366 7.102 -2.685 1.00 33.04 C
ATOM 3373 CB LEU A 235 -64.072 7.833 -1.553 1.00 32.57 C
ATOM 3376 CG LEU A 235 -63.884 7.252 -.167 1.00 30.85 C
ATOM 3378 CD1 LEU A 235 -62.428 7.261 .174 1.00 28.78 C
ATOM 3382 CD2 LEU A 235 -64.703 8.050 .823 1.00 29.93 C
ATOM 3386 C LEU A 235 -63.789 5.637 -2.686 1.00 34.69 C
ATOM 3387 O LEU A 235 -63.123 4.812 -2.065 1.00 35.29 O
ATOM 3389 N ARG A 236 -64.893 5.299 -3.354 1.00 36.09 N
ATOM 3390 CA ARG A 236 -65.290 3.893 -3.458 1.00 37.26 C
ATOM 3392 CB ARG A 236 -66.672 3.736 -4.103 1.00 37.64 C
ATOM 3395 CG ARG A 236 -67.839 4.000 -3.157 1.00 39.15 C
ATOM 3398 CD ARG A 236 -69.162 3.528 -3.741 1.00 40.25 C
ATOM 3401 NE ARG A 236 -69.385 4.046 -5.095 1.00 41.64 N
ATOM 3403 CZ ARG A 236 -69.837 5.269 -5.392 1.00 42.54 C
ATOM 3404 NH1 ARG A 236 -70.115 6.147 -4.430 1.00 42.18 N
ATOM 3407 NH2 ARG A 236 -70.012 5.621 -6.668 1.00 43.04 N
ATOM 3410 C ARG A 236 -64.266 3.108 -4.262 1.00 37.81 C
ATOM 3411 O ARG A 236 -64.104 1.912 -4.060 1.00 38.07 O
ATOM 3413 N GLU A 237 -63.584 3.801 -5.168 1.00 38.69 N
ATOM 3414 CA GLU A 237 -62.639 3.189 -6.102 1.00 39.45 C
ATOM 3416 CB GLU A 237 -62.452 4.108 -7.338 1.00 40.25 C
ATOM 3419 CG GLU A 237 -62.268 3.387 -8.710 1.00 43.02 C
ATOM 3422 CD GLU A 237 -60.835 3.458 -9.287 1.00 46.64 C
ATOM 3423 OE1 GLU A 237 -60.093 4.440 -8.997 1.00 48.03 O
ATOM 3424 OE2 GLU A 237 -60.466 2.519 -10.047 1.00 48.35 O
ATOM 3425 C GLU A 237 -61.310 2.905 -5.408 1.00 38.70 C
ATOM 3426 O GLU A 237 -60.832 1.782 -5.440 1.00 38.33 O

ATOM 3428 N THR A 238 -60.726 3.908 -4.764 1.00 38.40 N
ATOM 3429 CA THR A 238 -59.504 3.669 -4.009 1.00 38.74 C
ATOM 3431 CB THR A 238 -58.710 4.965 -3.593 1.00 38.78 C
ATOM 3433 OG1 THR A 238 -59.294 5.583 -2.444 1.00 38.38 O
ATOM 3435 CG2 THR A 238 -58.612 5.963 -4.743 1.00 38.94 C
ATOM 3439 C THR A 238 -59.802 2.834 -2.773 1.00 39.05 C
ATOM 3440 O THR A 238 -58.886 2.294 -2.153 1.00 39.17 O
ATOM 3442 N SER A 239 -61.076 2.717 -2.408 1.00 39.34 N
ATOM 3443 CA SER A 239 -61.443 1.841 -1.304 1.00 39.47 C
ATOM 3445 CB SER A 239 -62.844 2.149 -.792 1.00 39.34 C
ATOM 3448 OG SER A 239 -63.087 1.428 .396 1.00 39.94 O
ATOM 3450 C SER A 239 -61.313 .367 -1.699 1.00 39.53 C
ATOM 3451 O SER A 239 -60.834 -.439 -.900 1.00 39.53 O
ATOM 3453 N ARG A 240 -61.728 .021 -2.921 1.00 39.69 N
ATOM 3454 CA ARG A 240 -61.559 -1.341 -3.439 1.00 39.79 C
ATOM 3456 CB ARG A 240 -62.105 -1.492 -4.867 1.00 40.34 C
ATOM 3459 CG ARG A 240 -63.624 -1.715 -4.947 1.00 43.03 C
ATOM 3462 CD ARG A 240 -64.104 -2.125 -6.364 1.00 46.66 C
ATOM 3465 NE ARG A 240 -63.780 -1.136 -7.416 1.00 50.46 N
ATOM 3467 CZ ARG A 240 -64.535 -.082 -7.775 1.00 53.13 C
ATOM 3468 NH1 ARG A 240 -64.112 .732 -8.749 1.00 53.13 N
ATOM 3471 NH2 ARG A 240 -65.707 .178 -7.178 1.00 54.02 N
ATOM 3474 C ARG A 240 -60.089 -1.704 -3.414 1.00 38.94 C
ATOM 3475 O ARG A 240 -59.732 -2.795 -2.978 1.00 39.09 O
ATOM 3477 N TRP A 241 -59.246 -.775 -3.862 1.00 37.92 N
ATOM 3478 CA TRP A 241 -57.787 -.947 -3.842 1.00 36.93 C
ATOM 3480 CB TRP A 241 -57.099 .318 -4.388 1.00 36.57 C
ATOM 3483 CG TRP A 241 -55.624 .333 -4.209 1.00 34.71 C
ATOM 3484 CD1 TRP A 241 -54.702 -.312 -4.969 1.00 33.50 C
ATOM 3486 NE1 TRP A 241 -53.441 -.068 -4.482 1.00 32.62 N
ATOM 3488 CE2 TRP A 241 -53.538 .747 -3.392 1.00 31.16 C
ATOM 3489 CD2 TRP A 241 -54.896 1.022 -3.191 1.00 32.61 C
ATOM 3490 CE3 TRP A 241 -55.268 1.837 -2.117 1.00 32.63 C
ATOM 3492 CZ3 TRP A 241 -54.293 2.345 -1.307 1.00 31.31 C
ATOM 3494 CH2 TRP A 241 -52.956 2.053 -1.537 1.00 31.81 C
ATOM 3496 CZ2 TRP A 241 -52.560 1.252 -2.577 1.00 31.18 C
ATOM 3498 C TRP A 241 -57.263 -1.274 -2.444 1.00 36.67 C
ATOM 3499 O TRP A 241 -56.540 -2.247 -2.252 1.00 36.32 O
ATOM 3501 N TRP A 242 -57.647 -.460 -1.471 1.00 36.59 N
ATOM 3502 CA TRP A 242 -57.150 -.593 -.100 1.00 36.80 C
ATOM 3504 CB TRP A 242 -57.694 .582 .734 1.00 36.47 C
ATOM 3507 CG TRP A 242 -57.113 .754 2.107 1.00 35.59 C
ATOM 3508 CD1 TRP A 242 -57.806 .831 3.270 1.00 35.14 C
ATOM 3510 NE1 TRP A 242 -56.950 .999 4.328 1.00 34.47 N
ATOM 3512 CE2 TRP A 242 -55.667 1.032 3.859 1.00 34.64 C
ATOM 3513 CD2 TRP A 242 -55.728 .884 2.461 1.00 35.26 C
ATOM 3514 CE3 TRP A 242 -54.531 .882 1.732 1.00 35.22 C
ATOM 3516 CZ3 TRP A 242 -53.342 1.024 2.409 1.00 34.30 C
ATOM 3518 CH2 TRP A 242 -53.318 1.169 3.799 1.00 34.70 C
ATOM 3520 CZ2 TRP A 242 -54.467 1.173 4.542 1.00 34.63 C
ATOM 3522 C TRP A 242 -57.482 -1.975 .524 1.00 37.34 C
ATOM 3523 O TRP A 242 -56.628 -2.623 1.126 1.00 36.53 O
ATOM 3525 N ARG A 243 -58.720 -2.421 .348 1.00 38.54 N
ATOM 3526 CA ARG A 243 -59.149 -3.734 .822 1.00 39.71 C
ATOM 3528 CB ARG A 243 -60.669 -3.896 .687 1.00 40.10 C
ATOM 3531 CG ARG A 243 -61.495 -3.134 1.747 1.00 42.18 C
ATOM 3534 CD ARG A 243 -62.826 -2.623 1.169 1.00 45.18 C
ATOM 3537 NE ARG A 243 -63.506 -3.656 .369 1.00 48.22 N
ATOM 3539 CZ ARG A 243 -64.374 -3.431 -.629 1.00 49.95 C
ATOM 3540 NH1 ARG A 243 -64.717 -2.182 -.991 1.00 50.13 N

ATOM 3543 NH2 ARG A 243 -64.911 -4.477 -1.273 1.00 49.77 N
ATOM 3546 C ARG A 243 -58.438 -4.852 .068 1.00 40.08 C
ATOM 3547 O ARG A 243 -58.084 -5.870 .665 1.00 40.45 O
ATOM 3549 N ARG A 244 -58.236 -4.663 -1.236 1.00 40.42 N
ATOM 3550 CA ARG A 244 -57.499 -5.621 -2.063 1.00 40.65 C
ATOM 3552 CB ARG A 244 -57.370 -5.100 -3.503 1.00 41.29 C
ATOM 3555 CG ARG A 244 -56.939 -6.126 -4.560 1.00 43.27 C
ATOM 3558 CD ARG A 244 -58.090 -7.062 -4.952 1.00 46.01 C
ATOM 3561 NE ARG A 244 -57.595 -8.337 -5.485 1.00 48.77 N
ATOM 3563 CZ ARG A 244 -57.075 -9.332 -4.752 1.00 51.17 C
ATOM 3564 NH1 ARG A 244 -56.968 -9.234 -3.422 1.00 51.63 N
ATOM 3567 NH2 ARG A 244 -56.656 -10.448 -5.353 1.00 52.11 N
ATOM 3570 C ARG A 244 -56.120 -5.861 -1.465 1.00 40.12 C
ATOM 3571 O ARG A 244 -55.728 -7.000 -1.235 1.00 39.96 O
ATOM 3573 N VAL A 245 -55.399 -4.778 -1.201 1.00 39.78 N
ATOM 3574 CA VAL A 245 -54.099 -4.858 -.543 1.00 39.68 C
ATOM 3576 CB VAL A 245 -53.430 -3.458 -.437 1.00 39.70 C
ATOM 3578 CG1 VAL A 245 -53.133 -2.914 -1.824 1.00 39.54 C
ATOM 3582 CG2 VAL A 245 -52.145 -3.507 .395 1.00 39.41 C
ATOM 3586 C VAL A 245 -54.262 -5.472 .841 1.00 39.73 C
ATOM 3587 O VAL A 245 -53.455 -6.291 1.253 1.00 39.53 O
ATOM 3589 N GLY A 246 -55.312 -5.051 1.544 1.00 40.11 N
ATOM 3590 CA GLY A 246 -55.705 -5.617 2.839 1.00 40.35 C
ATOM 3593 C GLY A 246 -54.621 -5.648 3.894 1.00 40.58 C
ATOM 3594 O GLY A 246 -54.396 -6.676 4.510 1.00 40.68 O
ATOM 3596 N LEU A 247 -53.963 -4.522 4.129 1.00 41.15 N
ATOM 3597 CA LEU A 247 -52.778 -4.519 4.982 1.00 41.71 C
ATOM 3599 CB LEU A 247 -51.808 -3.422 4.537 1.00 41.60 C
ATOM 3602 CG LEU A 247 -50.334 -3.815 4.441 1.00 40.83 C
ATOM 3604 CD1 LEU A 247 -50.158 -5.014 3.539 1.00 40.54 C
ATOM 3608 CD2 LEU A 247 -49.534 -2.644 3.918 1.00 39.92 C
ATOM 3612 C LEU A 247 -53.136 -4.385 6.471 1.00 42.60 C
ATOM 3613 O LEU A 247 -52.588 -5.111 7.313 1.00 42.06 O
ATOM 3615 N ALA A 248 -54.064 -3.475 6.788 1.00 43.75 N
ATOM 3616 CA ALA A 248 -54.603 -3.352 8.162 1.00 44.52 C
ATOM 3618 CB ALA A 248 -55.712 -2.296 8.210 1.00 44.31 C
ATOM 3622 C ALA A 248 -55.129 -4.706 8.695 1.00 45.10 C
ATOM 3623 O ALA A 248 -54.969 -5.041 9.875 1.00 44.96 O
ATOM 3625 N THR A 249 -55.742 -5.477 7.802 1.00 45.91 N
ATOM 3626 CA THR A 249 -56.328 -6.768 8.154 1.00 46.50 C
ATOM 3628 CB THR A 249 -57.303 -7.277 7.041 1.00 46.48 C
ATOM 3630 OG1 THR A 249 -56.583 -8.039 6.063 1.00 46.20 O
ATOM 3632 CG2 THR A 249 -58.033 -6.102 6.350 1.00 46.70 C
ATOM 3636 C THR A 249 -55.257 -7.840 8.447 1.00 47.06 C
ATOM 3637 O THR A 249 -55.531 -8.813 9.159 1.00 47.22 O
ATOM 3639 N LYS A 250 -54.049 -7.661 7.905 1.00 47.52 N
ATOM 3640 CA LYS A 250 -52.952 -8.620 8.096 1.00 47.91 C
ATOM 3642 CB LYS A 250 -52.319 -8.976 6.744 1.00 48.09 C
ATOM 3645 CG LYS A 250 -52.911 -10.229 6.088 1.00 48.91 C
ATOM 3648 CD LYS A 250 -52.210 -11.510 6.585 1.00 49.88 C
ATOM 3651 CE LYS A 250 -53.066 -12.760 6.349 1.00 50.12 C
ATOM 3654 NZ LYS A 250 -52.385 -14.011 6.791 1.00 49.99 N
ATOM 3658 C LYS A 250 -51.880 -8.129 9.078 1.00 48.13 C
ATOM 3659 O LYS A 250 -51.252 -8.939 9.759 1.00 47.89 O
ATOM 3661 N LEU A 251 -51.667 -6.812 9.134 1.00 48.63 N
ATOM 3662 CA LEU A 251 -50.758 -6.187 10.114 1.00 48.83 C
ATOM 3664 CB LEU A 251 -49.981 -5.020 9.485 1.00 48.74 C
ATOM 3667 CG LEU A 251 -48.569 -5.296 8.960 1.00 48.51 C
ATOM 3669 CD1 LEU A 251 -48.472 -6.594 8.174 1.00 47.96 C
ATOM 3673 CD2 LEU A 251 -48.102 -4.115 8.116 1.00 48.76 C

ATOM 3677 C LEU A 251 -51.559 -5.703 11.324 1.00 49.17 C
ATOM 3678 O LEU A 251 -52.176 -4.632 11.304 1.00 49.28 O
ATOM 3680 N HIS A 252 -51.521 -6.486 12.393 1.00 49.53 N
ATOM 3681 CA HIS A 252 -52.470 -6.322 13.494 1.00 50.02 C
ATOM 3683 CB HIS A 252 -52.598 -7.647 14.266 1.00 50.42 C
ATOM 3686 CG HIS A 252 -52.860 -8.834 13.380 1.00 52.23 C
ATOM 3687 ND1 HIS A 252 -54.032 -8.989 12.667 1.00 53.75 N
ATOM 3689 CE1 HIS A 252 -53.978 -10.113 11.973 1.00 54.43 C
ATOM 3691 NE2 HIS A 252 -52.810 -10.689 12.201 1.00 54.52 N
ATOM 3693 CD2 HIS A 252 -52.090 -9.910 13.077 1.00 53.70 C
ATOM 3695 C HIS A 252 -52.161 -5.147 14.441 1.00 49.64 C
ATOM 3696 O HIS A 252 -52.951 -4.849 15.336 1.00 49.61 O
ATOM 3698 N PHE A 253 -51.027 -4.483 14.229 1.00 49.37 N
ATOM 3699 CA PHE A 253 -50.652 -3.273 14.973 1.00 49.15 C
ATOM 3701 CB PHE A 253 -49.144 -3.273 15.260 1.00 49.07 C
ATOM 3704 CG PHE A 253 -48.307 -3.112 14.025 1.00 48.30 C
ATOM 3705 CD1 PHE A 253 -48.028 -1.851 13.518 1.00 48.10 C
ATOM 3707 CE1 PHE A 253 -47.290 -1.702 12.349 1.00 48.21 C
ATOM 3709 CZ PHE A 253 -46.825 -2.825 11.675 1.00 47.88 C
ATOM 3711 CE2 PHE A 253 -47.101 -4.090 12.175 1.00 47.66 C
ATOM 3713 CD2 PHE A 253 -47.842 -4.226 13.338 1.00 47.74 C
ATOM 3715 C PHE A 253 -50.974 -2.006 14.176 1.00 49.31 C
ATOM 3716 O PHE A 253 -50.846 -.893 14.702 1.00 49.01 O
ATOM 3718 N ALA A 254 -51.365 -2.185 12.910 1.00 49.48 N
ATOM 3719 CA ALA A 254 -51.412 -1.095 11.931 1.00 49.63 C
ATOM 3721 CB ALA A 254 -51.344 -1.663 10.524 1.00 49.64 C
ATOM 3725 C ALA A 254 -52.650 -.224 12.061 1.00 49.77 C
ATOM 3726 O ALA A 254 -53.761 -.735 12.219 1.00 49.86 O
ATOM 3728 N ARG A 255 -52.452 1.090 11.975 1.00 49.93 N
ATOM 3729 CA ARG A 255 -53.562 2.042 11.908 1.00 50.27 C
ATOM 3731 CB ARG A 255 -53.094 3.468 12.237 1.00 50.43 C
ATOM 3734 CG ARG A 255 -52.678 3.736 13.696 1.00 50.82 C
ATOM 3737 CD ARG A 255 -52.242 5.211 13.887 1.00 51.32 C
ATOM 3740 NE ARG A 255 -51.003 5.522 13.155 1.00 51.81 N
ATOM 3742 CZ ARG A 255 -50.571 6.746 12.829 1.00 51.67 C
ATOM 3743 NH1 ARG A 255 -51.264 7.839 13.146 1.00 51.63 N
ATOM 3746 NH2 ARG A 255 -49.427 6.877 12.162 1.00 51.52 N
ATOM 3749 C ARG A 255 -54.160 2.040 10.497 1.00 50.32 C
ATOM 3750 O ARG A 255 -53.416 2.081 9.504 1.00 50.35 O
ATOM 3752 N ASP A 256 -55.492 2.005 10.412 1.00 50.17 N
ATOM 3753 CA ASP A 256 -56.190 2.090 9.128 1.00 50.18 C
ATOM 3755 CB ASP A 256 -57.259 1.009 9.037 1.00 50.37 C
ATOM 3758 CG ASP A 256 -58.095 1.130 7.780 1.00 50.96 C
ATOM 3759 OD1 ASP A 256 -59.252 1.601 7.881 1.00 52.00 O
ATOM 3760 OD2 ASP A 256 -57.581 .787 6.693 1.00 50.94 O
ATOM 3761 C ASP A 256 -56.838 3.470 8.945 1.00 49.85 C
ATOM 3762 O ASP A 256 -57.812 3.804 9.624 1.00 50.13 O
ATOM 3764 N ARG A 257 -56.315 4.263 8.013 1.00 49.11 N
ATOM 3765 CA ARG A 257 -56.712 5.665 7.913 1.00 48.59 C
ATOM 3767 CB ARG A 257 -55.622 6.553 8.529 1.00 48.79 C
ATOM 3770 CG ARG A 257 -55.318 6.275 10.006 1.00 49.85 C
ATOM 3773 CD ARG A 257 -56.538 6.480 10.908 1.00 51.01 C
ATOM 3776 NE ARG A 257 -56.198 7.274 12.089 1.00 51.80 N
ATOM 3778 CZ ARG A 257 -55.779 6.791 13.260 1.00 52.00 C
ATOM 3779 NH1 ARG A 257 -55.643 5.486 13.468 1.00 51.64 N
ATOM 3782 NH2 ARG A 257 -55.501 7.638 14.245 1.00 52.62 N
ATOM 3785 C ARG A 257 -56.988 6.112 6.477 1.00 47.58 C
ATOM 3786 O ARG A 257 -56.476 7.144 6.031 1.00 47.40 O
ATOM 3788 N LEU A 258 -57.814 5.352 5.761 1.00 46.18 N
ATOM 3789 CA LEU A 258 -58.094 5.672 4.358 1.00 44.78 C

ATOM 3791 CB LEU A 258 -58.777 4.508 3.629 1.00 44.57 C
ATOM 3794 CG LEU A 258 -58.917 4.731 2.121 1.00 43.79 C
ATOM 3796 CD1 LEU A 258 -57.557 4.661 1.478 1.00 43.89 C
ATOM 3800 CD2 LEU A 258 -59.850 3.733 1.492 1.00 42.88 C
ATOM 3804 C LEU A 258 -58.970 6.907 4.259 1.00 43.52 C
ATOM 3805 O LEU A 258 -58.643 7.849 3.545 1.00 43.42 O
ATOM 3807 N ILE A 259 -60.080 6.895 4.983 1.00 41.98 N
ATOM 3808 CA ILE A 259 -61.072 7.948 4.843 1.00 40.89 C
ATOM 3810 CB ILE A 259 -62.349 7.703 5.693 1.00 41.02 C
ATOM 3812 CG1 ILE A 259 -62.846 6.248 5.570 1.00 41.82 C
ATOM 3815 CD1 ILE A 259 -64.029 5.872 6.508 1.00 42.29 C
ATOM 3819 CG2 ILE A 259 -63.446 8.662 5.262 1.00 40.47 C
ATOM 3823 C ILE A 259 -60.424 9.253 5.273 1.00 39.74 C
ATOM 3824 O ILE A 259 -60.607 10.291 4.635 1.00 39.25 O
ATOM 3826 N GLU A 260 -59.650 9.191 6.355 1.00 38.46 N
ATOM 3827 CA GLU A 260 -58.951 10.366 6.846 1.00 37.44 C
ATOM 3829 CB GLU A 260 -58.183 10.072 8.140 1.00 37.74 C
ATOM 3832 CG GLU A 260 -59.041 9.934 9.393 1.00 38.71 C
ATOM 3835 CD GLU A 260 -59.469 8.501 9.693 1.00 41.00 C
ATOM 3836 OE1 GLU A 260 -59.273 7.594 8.842 1.00 42.70 O
ATOM 3837 OE2 GLU A 260 -60.012 8.281 10.800 1.00 42.43 O
ATOM 3838 C GLU A 260 -57.995 10.841 5.764 1.00 35.94 C
ATOM 3839 O GLU A 260 -57.981 12.020 5.418 1.00 36.10 O
ATOM 3841 N SER A 261 -57.222 9.908 5.212 1.00 34.02 N
ATOM 3842 CA SER A 261 -56.263 10.229 4.152 1.00 32.47 C
ATOM 3844 CB SER A 261 -55.407 9.015 3.774 1.00 32.51 C
ATOM 3847 OG SER A 261 -54.253 8.940 4.584 1.00 33.14 O
ATOM 3849 C SER A 261 -56.894 10.764 2.889 1.00 30.82 C
ATOM 3850 O SER A 261 -56.199 11.306 2.062 1.00 30.79 O
ATOM 3852 N PHE A 262 -58.194 10.589 2.713 1.00 29.25 N
ATOM 3853 CA PHE A 262 -58.861 11.091 1.514 1.00 27.98 C
ATOM 3855 CB PHE A 262 -60.011 10.185 1.119 1.00 27.57 C
ATOM 3858 CG PHE A 262 -60.473 10.423 -.251 1.00 26.11 C
ATOM 3859 CD1 PHE A 262 -59.763 9.914 -1.318 1.00 25.14 C
ATOM 3861 CE1 PHE A 262 -60.169 10.147 -2.605 1.00 24.32 C
ATOM 3863 CZ PHE A 262 -61.284 10.917 -2.840 1.00 24.36 C
ATOM 3865 CE2 PHE A 262 -61.987 11.445 -1.785 1.00 25.23 C
ATOM 3867 CD2 PHE A 262 -61.575 11.201 -.492 1.00 25.61 C
ATOM 3869 C PHE A 262 -59.394 12.507 1.707 1.00 27.29 C
ATOM 3870 O PHE A 262 -59.275 13.359 .821 1.00 27.39 O
ATOM 3872 N TYR A 263 -60.025 12.723 2.856 1.00 26.19 N
ATOM 3873 CA TYR A 263 -60.415 14.052 3.310 1.00 25.22 C
ATOM 3875 CB TYR A 263 -60.975 13.942 4.735 1.00 25.21 C
ATOM 3878 CG TYR A 263 -61.037 15.199 5.578 1.00 25.37 C
ATOM 3879 CD1 TYR A 263 -62.020 16.152 5.385 1.00 24.95 C
ATOM 3881 CE1 TYR A 263 -62.084 17.282 6.197 1.00 26.54 C
ATOM 3883 CZ TYR A 263 -61.158 17.455 7.229 1.00 27.44 C
ATOM 3884 OH TYR A 263 -61.186 18.567 8.059 1.00 28.97 O
ATOM 3886 CE2 TYR A 263 -60.185 16.512 7.438 1.00 27.10 C
ATOM 3888 CD2 TYR A 263 -60.136 15.390 6.626 1.00 26.91 C
ATOM 3890 C TYR A 263 -59.190 14.946 3.238 1.00 24.29 C
ATOM 3891 O TYR A 263 -59.267 16.077 2.757 1.00 24.13 O
ATOM 3893 N TRP A 264 -58.055 14.415 3.682 1.00 23.01 N
ATOM 3894 CA TRP A 264 -56.789 15.121 3.567 1.00 22.32 C
ATOM 3896 CB TRP A 264 -55.642 14.261 4.119 1.00 22.26 C
ATOM 3899 CG TRP A 264 -54.326 14.874 3.860 1.00 22.16 C
ATOM 3900 CD1 TRP A 264 -53.614 14.821 2.699 1.00 22.68 C
ATOM 3902 NE1 TRP A 264 -52.456 15.538 2.818 1.00 23.08 N
ATOM 3904 CE2 TRP A 264 -52.407 16.083 4.072 1.00 23.07 C
ATOM 3905 CD2 TRP A 264 -53.579 15.686 4.753 1.00 22.18 C

ATOM 3906 CE3 TRP A 264 -53.782 16.119 6.066 1.00 22.57 C
ATOM 3908 CZ3 TRP A 264 -52.824 16.925 6.657 1.00 23.43 C
ATOM 3910 CH2 TRP A 264 -51.656 17.297 5.955 1.00 24.14 C
ATOM 3912 CZ2 TRP A 264 -51.433 16.886 4.663 1.00 23.64 C
ATOM 3914 C TRP A 264 -56.485 15.523 2.112 1.00 21.50 C
ATOM 3915 O TRP A 264 -56.179 16.682 1.820 1.00 21.29 O
ATOM 3917 N ALA A 265 -56.561 14.547 1.213 1.00 20.41 N
ATOM 3918 CA ALA A 265 -56.242 14.760 -.187 1.00 19.63 C
ATOM 3920 CB ALA A 265 -56.298 13.437 -.953 1.00 19.39 C
ATOM 3924 C ALA A 265 -57.176 15.792 -.798 1.00 19.07 C
ATOM 3925 O ALA A 265 -56.760 16.573 -1.633 1.00 18.99 O
ATOM 3927 N VAL A 266 -58.431 15.814 -.359 1.00 18.78 N
ATOM 3928 CA VAL A 266 -59.396 16.828 -.818 1.00 18.56 C
ATOM 3930 CB VAL A 266 -60.839 16.541 -.278 1.00 18.41 C
ATOM 3932 CG1 VAL A 266 -61.405 15.298 -.935 1.00 18.88 C
ATOM 3936 CG2 VAL A 266 -61.780 17.709 -.505 1.00 17.21 C
ATOM 3940 C VAL A 266 -58.947 18.257 -.450 1.00 18.43 C
ATOM 3941 O VAL A 266 -59.250 19.200 -1.171 1.00 18.83 O
ATOM 3943 N GLY A 267 -58.230 18.411 .663 1.00 17.96 N
ATOM 3944 CA GLY A 267 -57.714 19.712 1.067 1.00 17.45 C
ATOM 3947 C GLY A 267 -56.687 20.180 .070 1.00 17.20 C
ATOM 3948 O GLY A 267 -56.574 21.365 -.215 1.00 17.41 O
ATOM 3950 N VAL A 268 -55.959 19.219 -.480 1.00 16.88 N
ATOM 3951 CA VAL A 268 -54.822 19.487 -1.319 1.00 16.62 C
ATOM 3953 CB VAL A 268 -53.833 18.300 -1.290 1.00 16.19 C
ATOM 3955 CG1 VAL A 268 -52.691 18.536 -2.240 1.00 15.50 C
ATOM 3959 CG2 VAL A 268 -53.310 18.121 .103 1.00 15.30 C
ATOM 3963 C VAL A 268 -55.262 19.788 -2.736 1.00 17.15 C
ATOM 3964 O VAL A 268 -54.748 20.710 -3.350 1.00 17.12 O
ATOM 3966 N ALA A 269 -56.217 19.014 -3.243 1.00 17.99 N
ATOM 3967 CA ALA A 269 -56.688 19.158 -4.622 1.00 18.79 C
ATOM 3969 CB ALA A 269 -55.958 18.183 -5.551 1.00 18.26 C
ATOM 3973 C ALA A 269 -58.196 18.938 -4.672 1.00 19.70 C
ATOM 3974 O ALA A 269 -58.665 17.834 -4.958 1.00 19.50 O
ATOM 3976 N PHE A 270 -58.945 20.011 -4.417 1.00 21.09 N
ATOM 3977 CA PHE A 270 -60.393 19.910 -4.211 1.00 22.32 C
ATOM 3979 CB PHE A 270 -60.925 21.108 -3.404 1.00 22.49 C
ATOM 3982 CG PHE A 270 -61.193 22.321 -4.246 1.00 23.31 C
ATOM 3983 CD1 PHE A 270 -62.423 22.483 -4.883 1.00 24.16 C
ATOM 3985 CE1 PHE A 270 -62.662 23.569 -5.683 1.00 23.84 C
ATOM 3987 CZ PHE A 270 -61.675 24.497 -5.871 1.00 23.93 C
ATOM 3989 CE2 PHE A 270 -60.448 24.349 -5.242 1.00 23.33 C
ATOM 3991 CD2 PHE A 270 -60.213 23.268 -4.443 1.00 23.11 C
ATOM 3993 C PHE A 270 -61.173 19.820 -5.515 1.00 23.21 C
ATOM 3994 O PHE A 270 -62.142 19.069 -5.599 1.00 23.48 O
ATOM 3996 N GLU A 271 -60.771 20.599 -6.522 1.00 24.16 N
ATOM 3997 CA GLU A 271 -61.595 20.744 -7.741 1.00 25.01 C
ATOM 3999 CB GLU A 271 -61.065 21.863 -8.655 1.00 25.19 C
ATOM 4002 CG GLU A 271 -59.563 21.909 -8.794 1.00 27.45 C
ATOM 4005 CD GLU A 271 -58.857 22.910 -7.857 1.00 30.03 C
ATOM 4006 OE1 GLU A 271 -58.905 24.145 -8.147 1.00 29.41 O
ATOM 4007 OE2 GLU A 271 -58.227 22.431 -6.865 1.00 30.71 O
ATOM 4008 C GLU A 271 -61.799 19.391 -8.484 1.00 24.95 C
ATOM 4009 O GLU A 271 -60.972 18.480 -8.352 1.00 25.70 O
ATOM 4011 N PRO A 272 -62.918 19.242 -9.224 1.00 24.59 N
ATOM 4012 CA PRO A 272 -63.399 17.915 -9.656 1.00 24.38 C
ATOM 4014 CB PRO A 272 -64.675 18.243 -10.430 1.00 24.25 C
ATOM 4017 CG PRO A 272 -65.105 19.536 -9.869 1.00 24.53 C
ATOM 4020 CD PRO A 272 -63.855 20.295 -9.639 1.00 24.42 C
ATOM 4023 C PRO A 272 -62.475 17.111 -10.549 1.00 24.29 C

ATOM 4024 O PRO A 272 -62.406 15.886 -10.410 1.00 24.45 O
ATOM 4025 N GLN A 273 -61.777 17.781 -11.462 1.00 24.13 N
ATOM 4026 CA GLN A 273 -60.998 17.064 -12.461 1.00 24.13 C
ATOM 4028 CB GLN A 273 -60.523 17.983 -13.567 1.00 23.84 C
ATOM 4031 CG GLN A 273 -59.556 19.041 -13.117 1.00 24.37 C
ATOM 4034 CD GLN A 273 -60.222 20.360 -12.775 1.00 25.22 C
ATOM 4035 OE1 GLN A 273 -61.392 20.412 -12.367 1.00 25.71 O
ATOM 4036 NE2 GLN A 273 -59.468 21.441 -12.932 1.00 24.95 N
ATOM 4039 C GLN A 273 -59.808 16.327 -11.877 1.00 24.33 C
ATOM 4040 O GLN A 273 -59.224 15.486 -12.555 1.00 24.91 O
ATOM 4042 N TYR A 274 -59.462 16.607 -10.626 1.00 24.27 N
ATOM 4043 CA TYR A 274 -58.211 16.119 -10.067 1.00 24.38 C
ATOM 4045 CB TYR A 274 -57.639 17.180 -9.138 1.00 24.36 C
ATOM 4048 CG TYR A 274 -57.066 18.398 -9.819 1.00 24.35 C
ATOM 4049 CD1 TYR A 274 -56.249 18.291 -10.935 1.00 24.13 C
ATOM 4051 CE1 TYR A 274 -55.716 19.409 -11.542 1.00 23.75 C
ATOM 4053 CZ TYR A 274 -55.968 20.646 -11.019 1.00 24.14 C
ATOM 4054 OH TYR A 274 -55.431 21.762 -11.597 1.00 24.45 O
ATOM 4056 CE2 TYR A 274 -56.755 20.780 -9.903 1.00 24.92 C
ATOM 4058 CD2 TYR A 274 -57.297 19.658 -9.308 1.00 24.74 C
ATOM 4060 C TYR A 274 -58.319 14.796 -9.310 1.00 24.63 C
ATOM 4061 O TYR A 274 -57.681 14.613 -8.276 1.00 24.47 O
ATOM 4063 N SER A 275 -59.097 13.852 -9.821 1.00 25.00 N
ATOM 4064 CA SER A 275 -59.254 12.575 -9.116 1.00 25.11 C
ATOM 4066 CB SER A 275 -60.244 11.664 -9.842 1.00 25.14 C
ATOM 4069 OG SER A 275 -61.537 12.252 -9.852 1.00 25.96 O
ATOM 4071 C SER A 275 -57.907 11.885 -8.963 1.00 24.94 C
ATOM 4072 O SER A 275 -57.544 11.439 -7.877 1.00 24.57 O
ATOM 4074 N ASP A 276 -57.149 11.822 -10.052 1.00 25.01 N
ATOM 4075 CA ASP A 276 -55.840 11.187 -9.990 1.00 24.92 C
ATOM 4077 CB ASP A 276 -55.102 11.257 -11.324 1.00 25.02 C
ATOM 4080 CG ASP A 276 -55.827 10.495 -12.407 1.00 26.27 C
ATOM 4081 OD1 ASP A 276 -56.372 9.411 -12.080 1.00 26.65 O
ATOM 4082 OD2 ASP A 276 -55.880 10.991 -13.563 1.00 28.21 O
ATOM 4083 C ASP A 276 -55.026 11.798 -8.881 1.00 24.30 C
ATOM 4084 O ASP A 276 -54.454 11.064 -8.099 1.00 24.64 O
ATOM 4086 N CYS A 277 -55.005 13.124 -8.772 1.00 23.61 N
ATOM 4087 CA CYS A 277 -54.210 13.746 -7.715 1.00 22.91 C
ATOM 4089 CB CYS A 277 -54.262 15.268 -7.748 1.00 22.83 C
ATOM 4092 SG CYS A 277 -53.048 15.994 -6.615 1.00 22.43 S
ATOM 4094 C CYS A 277 -54.653 13.251 -6.357 1.00 22.39 C
ATOM 4095 O CYS A 277 -53.822 12.833 -5.559 1.00 22.23 O
ATOM 4097 N ARG A 278 -55.962 13.262 -6.115 1.00 22.01 N
ATOM 4098 CA ARG A 278 -56.519 12.813 -4.829 1.00 21.40 C
ATOM 4100 CB ARG A 278 -58.021 13.053 -4.753 1.00 21.07 C
ATOM 4103 CG ARG A 278 -58.382 14.509 -4.754 1.00 20.39 C
ATOM 4106 CD ARG A 278 -59.852 14.698 -4.527 1.00 20.05 C
ATOM 4109 NE ARG A 278 -60.683 14.331 -5.675 1.00 18.86 N
ATOM 4111 CZ ARG A 278 -60.993 15.144 -6.679 1.00 18.58 C
ATOM 4112 NH1 ARG A 278 -60.530 16.391 -6.730 1.00 18.45 N
ATOM 4115 NH2 ARG A 278 -61.775 14.702 -7.647 1.00 19.04 N
ATOM 4118 C ARG A 278 -56.224 11.358 -4.530 1.00 21.12 C
ATOM 4119 O ARG A 278 -55.804 11.050 -3.434 1.00 21.59 O
ATOM 4121 N ASN A 279 -56.412 10.467 -5.493 1.00 20.94 N
ATOM 4122 CA ASN A 279 -56.168 9.044 -5.243 1.00 21.08 C
ATOM 4124 CB ASN A 279 -56.672 8.182 -6.401 1.00 21.54 C
ATOM 4127 CG ASN A 279 -58.199 8.346 -6.642 1.00 23.94 C
ATOM 4128 OD1 ASN A 279 -58.920 8.941 -5.823 1.00 26.47 O
ATOM 4129 ND2 ASN A 279 -58.685 7.825 -7.769 1.00 25.52 N
ATOM 4132 C ASN A 279 -54.699 8.798 -4.972 1.00 20.30 C

ATOM 4133 O ASN A 279 -54.337 8.200 -3.977 1.00 19.95 O
ATOM 4135 N SER A 280 -53.851 9.297 -5.856 1.00 20.02 N
ATOM 4136 CA SER A 280 -52.409 9.335 -5.612 1.00 19.32 C
ATOM 4138 CB SER A 280 -51.725 10.304 -6.580 1.00 19.35 C
ATOM 4141 OG SER A 280 -50.624 9.705 -7.212 1.00 19.77 O
ATOM 4143 C SER A 280 -52.122 9.745 -4.166 1.00 18.55 C
ATOM 4144 O SER A 280 -51.514 8.976 -3.436 1.00 18.98 O
ATOM 4146 N VAL A 281 -52.580 10.923 -3.743 1.00 17.45 N
ATOM 4147 CA VAL A 281 -52.235 11.444 -2.416 1.00 17.01 C
ATOM 4149 CB VAL A 281 -52.650 12.934 -2.235 1.00 17.20 C
ATOM 4151 CG1 VAL A 281 -52.492 13.376 -.787 1.00 16.76 C
ATOM 4155 CG2 VAL A 281 -51.826 13.847 -3.128 1.00 17.13 C
ATOM 4159 C VAL A 281 -52.861 10.607 -1.301 1.00 16.82 C
ATOM 4160 O VAL A 281 -52.217 10.314 -.289 1.00 16.81 O
ATOM 4162 N ALA A 282 -54.118 10.225 -1.481 1.00 16.55 N
ATOM 4163 CA ALA A 282 -54.774 9.304 -.559 1.00 16.31 C
ATOM 4165 CB ALA A 282 -56.174 8.951 -1.060 1.00 16.08 C
ATOM 4169 C ALA A 282 -53.946 8.036 -.355 1.00 16.31 C
ATOM 4170 O ALA A 282 -53.671 7.653 .762 1.00 16.16 O
ATOM 4172 N LYS A 283 -53.539 7.395 -1.443 1.00 16.92 N
ATOM 4173 CA LYS A 283 -52.773 6.139 -1.368 1.00 17.39 C
ATOM 4175 CB LYS A 283 -52.454 5.596 -2.773 1.00 17.31 C
ATOM 4178 CG LYS A 283 -53.680 5.066 -3.519 1.00 17.85 C
ATOM 4181 CD LYS A 283 -53.389 4.527 -4.941 1.00 18.98 C
ATOM 4184 CE LYS A 283 -54.709 4.275 -5.718 1.00 19.79 C
ATOM 4187 NZ LYS A 283 -54.695 3.091 -6.625 1.00 20.11 N
ATOM 4191 C LYS A 283 -51.483 6.338 -.591 1.00 17.82 C
ATOM 4192 O LYS A 283 -51.170 5.577 .331 1.00 17.37 O
ATOM 4194 N MET A 284 -50.744 7.381 -.964 1.00 18.49 N
ATOM 4195 CA MET A 284 -49.434 7.622 -.373 1.00 18.82 C
ATOM 4197 CB MET A 284 -48.688 8.795 -1.047 1.00 18.84 C
ATOM 4200 CG MET A 284 -48.118 8.506 -2.444 1.00 18.47 C
ATOM 4203 SD MET A 284 -47.540 6.819 -2.718 1.00 19.50 S
ATOM 4204 CE MET A 284 -49.088 5.982 -3.094 1.00 19.36 C
ATOM 4208 C MET A 284 -49.575 7.848 1.115 1.00 18.95 C
ATOM 4209 O MET A 284 -48.901 7.166 1.892 1.00 19.29 O
ATOM 4211 N PHE A 285 -50.465 8.762 1.507 1.00 18.94 N
ATOM 4212 CA PHE A 285 -50.671 9.082 2.930 1.00 19.26 C
ATOM 4214 CB PHE A 285 -51.714 10.185 3.073 1.00 19.72 C
ATOM 4217 CG PHE A 285 -51.575 11.016 4.328 1.00 21.97 C
ATOM 4218 CD1 PHE A 285 -50.335 11.202 4.954 1.00 24.49 C
ATOM 4220 CE1 PHE A 285 -50.209 11.996 6.086 1.00 25.11 C
ATOM 4222 CZ PHE A 285 -51.321 12.634 6.597 1.00 26.40 C
ATOM 4224 CE2 PHE A 285 -52.566 12.470 5.977 1.00 26.44 C
ATOM 4226 CD2 PHE A 285 -52.678 11.670 4.846 1.00 24.55 C
ATOM 4228 C PHE A 285 -51.097 7.879 3.770 1.00 18.74 C
ATOM 4229 O PHE A 285 -50.700 7.729 4.924 1.00 18.31 O
ATOM 4231 N SER A 286 -51.903 7.019 3.169 1.00 18.49 N
ATOM 4232 CA SER A 286 -52.281 5.772 3.791 1.00 18.38 C
ATOM 4234 CB SER A 286 -53.302 5.065 2.926 1.00 18.45 C
ATOM 4237 OG SER A 286 -54.389 5.949 2.687 1.00 19.82 O
ATOM 4239 C SER A 286 -51.070 4.888 4.048 1.00 18.08 C
ATOM 4240 O SER A 286 -50.931 4.376 5.146 1.00 18.18 O
ATOM 4242 N PHE A 287 -50.195 4.714 3.054 1.00 17.72 N
ATOM 4243 CA PHE A 287 -48.911 4.024 3.279 1.00 17.23 C
ATOM 4245 CB PHE A 287 -48.133 3.801 1.977 1.00 17.09 C
ATOM 4248 CG PHE A 287 -48.513 2.555 1.258 1.00 17.26 C
ATOM 4249 CD1 PHE A 287 -48.220 1.315 1.802 1.00 18.31 C
ATOM 4251 CE1 PHE A 287 -48.583 .129 1.131 1.00 18.47 C
ATOM 4253 CZ PHE A 287 -49.237 .198 -.091 1.00 17.88 C

ATOM 4255 CE2 PHE A 287 -49.530 1.441 -.642 1.00 17.57 C
ATOM 4257 CD2 PHE A 287 -49.168 2.608 .031 1.00 17.79 C
ATOM 4259 C PHE A 287 -48.022 4.787 4.277 1.00 16.92 C
ATOM 4260 O PHE A 287 -47.369 4.173 5.143 1.00 17.18 O
ATOM 4262 N VAL A 288 -47.989 6.113 4.174 1.00 16.00 N
ATOM 4263 CA VAL A 288 -47.148 6.883 5.080 1.00 15.45 C
ATOM 4265 CB VAL A 288 -47.289 8.399 4.863 1.00 15.21 C
ATOM 4267 CG1 VAL A 288 -46.433 9.162 5.852 1.00 14.24 C
ATOM 4271 CG2 VAL A 288 -46.898 8.757 3.450 1.00 14.46 C
ATOM 4275 C VAL A 288 -47.479 6.499 6.527 1.00 15.46 C
ATOM 4276 O VAL A 288 -46.590 6.160 7.299 1.00 14.79 O
ATOM 4278 N THR A 289 -48.759 6.494 6.880 1.00 15.62 N
ATOM 4279 CA THR A 289 -49.110 6.272 8.274 1.00 16.09 C
ATOM 4281 CB THR A 289 -50.602 6.557 8.588 1.00 15.72 C
ATOM 4283 OG1 THR A 289 -51.422 5.827 7.708 1.00 16.52 O
ATOM 4285 CG2 THR A 289 -50.927 8.007 8.371 1.00 16.56 C
ATOM 4289 C THR A 289 -48.677 4.879 8.727 1.00 16.34 C
ATOM 4290 O THR A 289 -48.234 4.707 9.881 1.00 16.68 O
ATOM 4292 N ILE A 290 -48.737 3.904 7.820 1.00 16.29 N
ATOM 4293 CA ILE A 290 -48.347 2.538 8.166 1.00 16.56 C
ATOM 4295 CB ILE A 290 -48.734 1.516 7.096 1.00 16.48 C
ATOM 4297 CG1 ILE A 290 -50.247 1.440 6.944 1.00 16.91 C
ATOM 4300 CD1 ILE A 290 -50.677 .564 5.811 1.00 16.52 C
ATOM 4304 CG2 ILE A 290 -48.262 .145 7.488 1.00 16.52 C
ATOM 4308 C ILE A 290 -46.842 2.456 8.402 1.00 16.94 C
ATOM 4309 O ILE A 290 -46.404 1.968 9.443 1.00 17.06 O
ATOM 4311 N ILE A 291 -46.048 2.942 7.451 1.00 17.22 N
ATOM 4312 CA ILE A 291 -44.595 2.969 7.640 1.00 17.20 C
ATOM 4314 CB ILE A 291 -43.842 3.534 6.405 1.00 17.32 C
ATOM 4316 CG1 ILE A 291 -44.172 2.744 5.125 1.00 17.61 C
ATOM 4319 CD1 ILE A 291 -44.004 1.265 5.250 1.00 18.21 C
ATOM 4323 CG2 ILE A 291 -42.336 3.550 6.637 1.00 16.64 C
ATOM 4327 C ILE A 291 -44.262 3.794 8.886 1.00 17.36 C
ATOM 4328 O ILE A 291 -43.420 3.413 9.670 1.00 17.06 O
ATOM 4330 N ASP A 292 -44.950 4.906 9.093 1.00 18.12 N
ATOM 4331 CA ASP A 292 -44.627 5.755 10.227 1.00 18.83 C
ATOM 4333 CB ASP A 292 -45.511 7.017 10.285 1.00 19.22 C
ATOM 4336 CG ASP A 292 -45.185 7.920 11.485 1.00 19.93 C
ATOM 4337 OD1 ASP A 292 -44.062 8.460 11.544 1.00 21.80 O
ATOM 4338 OD2 ASP A 292 -46.048 8.080 12.375 1.00 20.46 O
ATOM 4339 C ASP A 292 -44.745 4.947 11.509 1.00 18.96 C
ATOM 4340 O ASP A 292 -43.902 5.094 12.394 1.00 19.05 O
ATOM 4342 N ASP A 293 -45.774 4.097 11.610 1.00 19.05 N
ATOM 4343 CA ASP A 293 -45.951 3.273 12.817 1.00 18.99 C
ATOM 4345 CB ASP A 293 -47.237 2.443 12.790 1.00 18.95 C
ATOM 4348 CG ASP A 293 -48.496 3.272 12.921 1.00 19.27 C
ATOM 4349 OD1 ASP A 293 -48.483 4.361 13.523 1.00 21.51 O
ATOM 4350 OD2 ASP A 293 -49.536 2.812 12.421 1.00 19.61 O
ATOM 4351 C ASP A 293 -44.783 2.322 12.935 1.00 19.07 C
ATOM 4352 O ASP A 293 -44.244 2.135 14.024 1.00 19.35 O
ATOM 4354 N ILE A 294 -44.390 1.730 11.805 1.00 19.10 N
ATOM 4355 CA ILE A 294 -43.320 .727 11.786 1.00 19.04 C
ATOM 4357 CB ILE A 294 -43.137 .109 10.386 1.00 18.49 C
ATOM 4359 CG1 ILE A 294 -44.343 -.754 10.038 1.00 17.60 C
ATOM 4362 CD1 ILE A 294 -44.204 -1.504 8.752 1.00 16.77 C
ATOM 4366 CG2 ILE A 294 -41.895 -.745 10.348 1.00 18.77 C
ATOM 4370 C ILE A 294 -41.974 1.273 12.298 1.00 19.55 C
ATOM 4371 O ILE A 294 -41.234 .550 12.974 1.00 19.75 O
ATOM 4373 N TYR A 295 -41.649 2.525 11.983 1.00 19.75 N
ATOM 4374 CA TYR A 295 -40.411 3.103 12.476 1.00 19.91 C

ATOM 4376 CB TYR A 295 -39.856 4.178 11.542 1.00 19.66 C
ATOM 4379 CG TYR A 295 -39.206 3.695 10.245 1.00 18.19 C
ATOM 4380 CD1 TYR A 295 -37.821 3.727 10.075 1.00 16.19 C
ATOM 4382 CE1 TYR A 295 -37.222 3.331 8.882 1.00 14.68 C
ATOM 4384 CZ TYR A 295 -38.004 2.906 7.828 1.00 15.04 C
ATOM 4385 OH TYR A 295 -37.428 2.485 6.631 1.00 12.25 O
ATOM 4387 CE2 TYR A 295 -39.383 2.871 7.975 1.00 16.48 C
ATOM 4389 CD2 TYR A 295 -39.975 3.271 9.172 1.00 17.01 C
ATOM 4391 C TYR A 295 -40.647 3.677 13.858 1.00 20.73 C
ATOM 4392 O TYR A 295 -39.749 3.635 14.717 1.00 21.64 O
ATOM 4394 N ASP A 296 -41.843 4.200 14.103 1.00 21.38 N
ATOM 4395 CA ASP A 296 -42.100 4.865 15.391 1.00 22.20 C
ATOM 4397 CB ASP A 296 -43.421 5.644 15.391 1.00 22.69 C
ATOM 4400 CG ASP A 296 -43.567 6.548 16.607 1.00 23.85 C
ATOM 4401 OD1 ASP A 296 -42.568 7.179 17.014 1.00 25.49 O
ATOM 4402 OD2 ASP A 296 -44.689 6.648 17.145 1.00 26.12 O
ATOM 4403 C ASP A 296 -42.106 3.890 16.549 1.00 22.10 C
ATOM 4404 O ASP A 296 -41.376 4.082 17.506 1.00 22.14 O
ATOM 4406 N VAL A 297 -42.900 2.828 16.435 1.00 22.25 N
ATOM 4407 CA VAL A 297 -43.163 1.937 17.570 1.00 22.22 C
ATOM 4409 CB VAL A 297 -44.635 2.116 18.057 1.00 22.07 C
ATOM 4411 CG1 VAL A 297 -44.958 3.587 18.215 1.00 21.63 C
ATOM 4415 CG2 VAL A 297 -45.618 1.459 17.099 1.00 20.76 C
ATOM 4419 C VAL A 297 -42.861 .422 17.373 1.00 22.49 C
ATOM 4420 O VAL A 297 -42.517 -.255 18.343 1.00 22.40 O
ATOM 4422 N TYR A 298 -42.990 -.117 16.157 1.00 22.69 N
ATOM 4423 CA TYR A 298 -43.065 -1.579 15.993 1.00 22.90 C
ATOM 4425 CB TYR A 298 -44.089 -1.974 14.934 1.00 22.77 C
ATOM 4428 CG TYR A 298 -44.341 -3.469 14.932 1.00 23.74 C
ATOM 4429 CD1 TYR A 298 -45.249 -4.043 15.819 1.00 25.72 C
ATOM 4431 CE1 TYR A 298 -45.484 -5.435 15.833 1.00 26.12 C
ATOM 4433 CZ TYR A 298 -44.798 -6.247 14.954 1.00 25.59 C
ATOM 4434 OH TYR A 298 -45.027 -7.593 14.970 1.00 25.33 O
ATOM 4436 CE2 TYR A 298 -43.890 -5.702 14.062 1.00 24.79 C
ATOM 4438 CD2 TYR A 298 -43.661 -4.317 14.061 1.00 24.20 C
ATOM 4440 C TYR A 298 -41.750 -2.258 15.649 1.00 23.02 C
ATOM 4441 O TYR A 298 -41.387 -3.257 16.256 1.00 22.80 O
ATOM 4443 N GLY A 299 -41.069 -1.747 14.634 1.00 23.47 N
ATOM 4444 CA GLY A 299 -39.839 -2.361 14.149 1.00 23.36 C
ATOM 4447 C GLY A 299 -38.631 -1.978 14.984 1.00 23.27 C
ATOM 4448 O GLY A 299 -38.532 -.858 15.501 1.00 23.35 O
ATOM 4450 N THR A 300 -37.702 -2.918 15.098 1.00 23.11 N
ATOM 4451 CA THR A 300 -36.459 -2.682 15.797 1.00 22.90 C
ATOM 4453 CB THR A 300 -35.869 -3.957 16.386 1.00 22.83 C
ATOM 4455 OG1 THR A 300 -35.328 -4.756 15.328 1.00 22.61 O
ATOM 4457 CG2 THR A 300 -36.928 -4.732 17.162 1.00 22.18 C
ATOM 4461 C THR A 300 -35.482 -2.120 14.796 1.00 23.00 C
ATOM 4462 O THR A 300 -35.606 -2.364 13.602 1.00 23.13 O
ATOM 4464 N LEU A 301 -34.496 -1.394 15.309 1.00 23.07 N
ATOM 4465 CA LEU A 301 -33.596 -.572 14.498 1.00 22.84 C
ATOM 4467 CB LEU A 301 -32.515 .007 15.403 1.00 22.80 C
ATOM 4470 CG LEU A 301 -31.965 1.412 15.182 1.00 22.39 C
ATOM 4472 CD1 LEU A 301 -32.983 2.365 14.587 1.00 22.44 C
ATOM 4476 CD2 LEU A 301 -31.482 1.919 16.536 1.00 22.19 C
ATOM 4480 C LEU A 301 -32.964 -1.358 13.361 1.00 22.95 C
ATOM 4481 O LEU A 301 -32.910 -.888 12.232 1.00 22.50 O
ATOM 4483 N ASP A 302 -32.511 -2.569 13.673 1.00 23.35 N
ATOM 4484 CA ASP A 302 -31.929 -3.469 12.670 1.00 23.65 C
ATOM 4486 CB ASP A 302 -31.332 -4.747 13.328 1.00 24.12 C
ATOM 4489 CG ASP A 302 -29.984 -4.498 14.057 1.00 25.23 C

ATOM 4490 OD1 ASP A 302 -29.003 -4.051 13.409 1.00 26.43 O
ATOM 4491 OD2 ASP A 302 -29.896 -4.780 15.277 1.00 26.92 O
ATOM 4492 C ASP A 302 -32.945 -3.859 11.581 1.00 23.11 C
ATOM 4493 O ASP A 302 -32.544 -4.086 10.445 1.00 23.05 O
ATOM 4495 N GLU A 303 -34.235 -3.965 11.927 1.00 22.63 N
ATOM 4496 CA GLU A 303 -35.295 -4.248 10.931 1.00 22.40 C
ATOM 4498 CB GLU A 303 -36.625 -4.675 11.589 1.00 22.20 C
ATOM 4501 CG GLU A 303 -36.537 -5.956 12.426 1.00 22.66 C
ATOM 4504 CD GLU A 303 -37.832 -6.341 13.159 1.00 22.69 C
ATOM 4505 OE1 GLU A 303 -38.614 -5.449 13.568 1.00 22.23 O
ATOM 4506 OE2 GLU A 303 -38.051 -7.558 13.338 1.00 21.64 O
ATOM 4507 C GLU A 303 -35.533 -3.017 10.067 1.00 22.35 C
ATOM 4508 O GLU A 303 -35.658 -3.105 8.841 1.00 22.27 O
ATOM 4510 N LEU A 304 -35.597 -1.866 10.724 1.00 22.34 N
ATOM 4511 CA LEU A 304 -35.776 -.607 10.040 1.00 22.26 C
ATOM 4513 CB LEU A 304 -35.861 .537 11.052 1.00 22.49 C
ATOM 4516 CG LEU A 304 -37.089 .517 11.973 1.00 23.05 C
ATOM 4518 CD1 LEU A 304 -37.109 1.708 12.932 1.00 23.46 C
ATOM 4522 CD2 LEU A 304 -38.353 .511 11.142 1.00 23.96 C
ATOM 4526 C LEU A 304 -34.634 -.383 9.063 1.00 22.09 C
ATOM 4527 O LEU A 304 -34.873 .094 7.969 1.00 22.32 O
ATOM 4529 N GLU A 305 -33.408 -.740 9.450 1.00 21.91 N
ATOM 4530 CA GLU A 305 -32.259 -.685 8.541 1.00 21.93 C
ATOM 4532 CB GLU A 305 -30.988 -1.194 9.219 1.00 22.35 C
ATOM 4535 CG GLU A 305 -30.363 -.258 10.249 1.00 24.12 C
ATOM 4538 CD GLU A 305 -29.751 1.002 9.649 1.00 26.11 C
ATOM 4539 OE1 GLU A 305 -29.275 1.846 10.454 1.00 25.68 O
ATOM 4540 OE2 GLU A 305 -29.756 1.146 8.391 1.00 27.67 O
ATOM 4541 C GLU A 305 -32.475 -1.524 7.295 1.00 21.54 C
ATOM 4542 O GLU A 305 -32.010 -1.162 6.220 1.00 21.75 O
ATOM 4544 N LEU A 306 -33.155 -2.660 7.448 1.00 21.21 N
ATOM 4545 CA LEU A 306 -33.459 -3.557 6.316 1.00 20.66 C
ATOM 4547 CB LEU A 306 -33.880 -4.956 6.795 1.00 20.26 C
ATOM 4550 CG LEU A 306 -32.725 -5.854 7.220 1.00 19.57 C
ATOM 4552 CD1 LEU A 306 -33.261 -7.150 7.777 1.00 20.18 C
ATOM 4556 CD2 LEU A 306 -31.791 -6.120 6.061 1.00 18.29 C
ATOM 4560 C LEU A 306 -34.535 -2.967 5.416 1.00 20.23 C
ATOM 4561 O LEU A 306 -34.412 -2.966 4.197 1.00 19.97 O
ATOM 4563 N PHE A 307 -35.588 -2.457 6.023 1.00 19.99 N
ATOM 4564 CA PHE A 307 -36.635 -1.861 5.237 1.00 20.00 C
ATOM 4566 CB PHE A 307 -37.771 -1.388 6.118 1.00 20.08 C
ATOM 4569 CG PHE A 307 -39.011 -1.115 5.370 1.00 19.05 C
ATOM 4570 CD1 PHE A 307 -39.895 -2.118 5.119 1.00 18.77 C
ATOM 4572 CE1 PHE A 307 -41.037 -1.873 4.421 1.00 20.07 C
ATOM 4574 CZ PHE A 307 -41.296 -.621 3.959 1.00 19.63 C
ATOM 4576 CE2 PHE A 307 -40.411 .391 4.199 1.00 19.27 C
ATOM 4578 CD2 PHE A 307 -39.278 .142 4.900 1.00 19.17 C
ATOM 4580 C PHE A 307 -36.087 -.695 4.447 1.00 20.25 C
ATOM 4581 O PHE A 307 -36.356 -.589 3.242 1.00 20.08 O
ATOM 4583 N THR A 308 -35.325 .167 5.137 1.00 20.51 N
ATOM 4584 CA THR A 308 -34.737 1.379 4.538 1.00 20.60 C
ATOM 4586 CB THR A 308 -33.860 2.177 5.541 1.00 20.41 C
ATOM 4588 OG1 THR A 308 -34.672 2.661 6.611 1.00 20.05 O
ATOM 4590 CG2 THR A 308 -33.198 3.376 4.864 1.00 20.38 C
ATOM 4594 C THR A 308 -33.895 1.009 3.331 1.00 20.82 C
ATOM 4595 O THR A 308 -34.057 1.571 2.243 1.00 20.45 O
ATOM 4597 N ASP A 309 -33.020 .031 3.522 1.00 21.32 N
ATOM 4598 CA ASP A 309 -32.138 -.399 2.449 1.00 21.88 C
ATOM 4600 CB ASP A 309 -31.042 -1.324 2.971 1.00 22.44 C
ATOM 4603 CG ASP A 309 -30.164 -1.847 1.857 1.00 25.69 C

ATOM 4604 OD1 ASP A 309 -29.599 -1.010 1.089 1.00 28.02 O
ATOM 4605 OD2 ASP A 309 -30.076 -3.100 1.730 1.00 30.59 O
ATOM 4606 C ASP A 309 -32.928 -1.085 1.357 1.00 21.17 C
ATOM 4607 O ASP A 309 -32.601 -.948 .188 1.00 20.95 O
ATOM 4609 N ALA A 310 -33.965 -1.818 1.757 1.00 20.99 N
ATOM 4610 CA ALA A 310 -34.885 -2.474 .828 1.00 20.91 C
ATOM 4612 CB ALA A 310 -35.931 -3.244 1.591 1.00 20.77 C
ATOM 4616 C ALA A 310 -35.567 -1.501 -.123 1.00 21.08 C
ATOM 4617 O ALA A 310 -35.745 -1.816 -1.305 1.00 20.76 O
ATOM 4619 N VAL A 311 -35.958 -.334 .402 1.00 21.51 N
ATOM 4620 CA VAL A 311 -36.594 .719 -.396 1.00 21.50 C
ATOM 4622 CB VAL A 311 -37.424 1.715 .477 1.00 21.73 C
ATOM 4624 CG1 VAL A 311 -38.724 1.076 .941 1.00 21.01 C
ATOM 4628 CG2 VAL A 311 -37.765 2.993 -.292 1.00 21.88 C
ATOM 4632 C VAL A 311 -35.553 1.445 -1.230 1.00 21.67 C
ATOM 4633 O VAL A 311 -35.811 1.728 -2.389 1.00 21.71 O
ATOM 4635 N GLU A 312 -34.381 1.724 -.663 1.00 22.25 N
ATOM 4636 CA GLU A 312 -33.248 2.284 -1.443 1.00 23.00 C
ATOM 4638 CB GLU A 312 -31.951 2.331 -.608 1.00 23.36 C
ATOM 4641 CG GLU A 312 -31.897 3.383 .511 1.00 24.72 C
ATOM 4644 CD GLU A 312 -30.526 3.469 1.189 1.00 27.09 C
ATOM 4645 OE1 GLU A 312 -30.083 4.608 1.458 1.00 30.07 O
ATOM 4646 OE2 GLU A 312 -29.885 2.418 1.454 1.00 27.86 O
ATOM 4647 C GLU A 312 -32.954 1.498 -2.731 1.00 23.13 C
ATOM 4648 O GLU A 312 -32.851 2.064 -3.803 1.00 22.88 O
ATOM 4650 N ARG A 313 -32.819 .188 -2.615 1.00 23.74 N
ATOM 4651 CA ARG A 313 -32.400 -.628 -3.743 1.00 24.46 C
ATOM 4653 CB ARG A 313 -31.758 -1.916 -3.232 1.00 25.01 C
ATOM 4656 CG ARG A 313 -30.421 -1.667 -2.481 1.00 27.74 C
ATOM 4659 CD ARG A 313 -29.715 -2.963 -2.072 1.00 31.41 C
ATOM 4662 NE ARG A 313 -30.675 -3.921 -1.499 1.00 34.94 N
ATOM 4664 CZ ARG A 313 -31.203 -4.974 -2.138 1.00 37.87 C
ATOM 4665 NH1 ARG A 313 -30.861 -5.282 -3.402 1.00 38.35 N
ATOM 4668 NH2 ARG A 313 -32.079 -5.746 -1.495 1.00 38.82 N
ATOM 4671 C ARG A 313 -33.523 -.914 -4.739 1.00 24.27 C
ATOM 4672 O ARG A 313 -33.257 -1.178 -5.898 1.00 24.17 O
ATOM 4674 N TRP A 314 -34.770 -.873 -4.282 1.00 24.59 N
ATOM 4675 CA TRP A 314 -35.939 -1.042 -5.142 1.00 24.66 C
ATOM 4677 CB TRP A 314 -36.175 .234 -5.961 1.00 24.39 C
ATOM 4680 CG TRP A 314 -37.575 .382 -6.386 1.00 22.61 C
ATOM 4681 CD1 TRP A 314 -38.073 .204 -7.635 1.00 21.66 C
ATOM 4683 NE1 TRP A 314 -39.429 .403 -7.634 1.00 21.42 N
ATOM 4685 CE2 TRP A 314 -39.829 .707 -6.360 1.00 20.99 C
ATOM 4686 CD2 TRP A 314 -38.683 .701 -5.550 1.00 21.41 C
ATOM 4687 CE3 TRP A 314 -38.817 .991 -4.191 1.00 21.48 C
ATOM 4689 CZ3 TRP A 314 -40.080 1.277 -3.693 1.00 21.38 C
ATOM 4691 CH2 TRP A 314 -41.204 1.269 -4.523 1.00 20.84 C
ATOM 4693 CZ2 TRP A 314 -41.099 .985 -5.857 1.00 20.87 C
ATOM 4695 C TRP A 314 -35.831 -2.286 -6.038 1.00 25.65 C
ATOM 4696 O TRP A 314 -36.069 -2.238 -7.259 1.00 25.69 O
ATOM 4698 N ASP A 315 -35.480 -3.400 -5.404 1.00 26.79 N
ATOM 4699 CA ASP A 315 -35.253 -4.667 -6.087 1.00 28.01 C
ATOM 4701 CB ASP A 315 -33.801 -5.097 -5.890 1.00 28.07 C
ATOM 4704 CG ASP A 315 -33.553 -6.536 -6.296 1.00 29.92 C
ATOM 4705 OD1 ASP A 315 -34.262 -7.026 -7.197 1.00 32.58 O
ATOM 4706 OD2 ASP A 315 -32.648 -7.194 -5.722 1.00 32.73 O
ATOM 4707 C ASP A 315 -36.202 -5.710 -5.518 1.00 28.91 C
ATOM 4708 O ASP A 315 -36.019 -6.163 -4.399 1.00 29.17 O
ATOM 4710 N VAL A 316 -37.218 -6.091 -6.283 1.00 30.25 N
ATOM 4711 CA VAL A 316 -38.233 -7.012 -5.778 1.00 31.47 C

ATOM 4713 CB VAL A 316 -39.396 -7.156 -6.755 1.00 31.56 C
ATOM 4715 CG1 VAL A 316 -40.668 -7.590 -6.027 1.00 30.99 C
ATOM 4719 CG2 VAL A 316 -39.033 -8.141 -7.862 1.00 31.84 C
ATOM 4723 C VAL A 316 -37.663 -8.405 -5.540 1.00 32.86 C
ATOM 4724 O VAL A 316 -38.170 -9.153 -4.708 1.00 32.99 O
ATOM 4726 N ASN A 317 -36.607 -8.750 -6.278 1.00 34.55 N
ATOM 4727 CA ASN A 317 -35.940 -10.060 -6.160 1.00 35.53 C
ATOM 4729 CB ASN A 317 -35.013 -10.298 -7.367 1.00 35.68 C
ATOM 4732 CG ASN A 317 -35.752 -10.264 -8.713 1.00 35.92 C
ATOM 4733 OD1 ASN A 317 -36.634 -11.092 -8.971 1.00 36.95 O
ATOM 4734 ND2 ASN A 317 -35.368 -9.323 -9.585 1.00 34.17 N
ATOM 4737 C ASN A 317 -35.126 -10.225 -4.871 1.00 36.40 C
ATOM 4738 O ASN A 317 -34.385 -11.195 -4.747 1.00 36.47 O
ATOM 4740 N ALA A 318 -35.239 -9.265 -3.944 1.00 37.52 N
ATOM 4741 CA ALA A 318 -34.614 -9.335 -2.613 1.00 38.45 C
ATOM 4743 CB ALA A 318 -33.371 -8.465 -2.557 1.00 38.43 C
ATOM 4747 C ALA A 318 -35.631 -8.902 -1.554 1.00 39.28 C
ATOM 4748 O ALA A 318 -35.361 -8.094 -.662 1.00 39.55 O
ATOM 4750 N ILE A 319 -36.823 -9.456 -1.698 1.00 40.17 N
ATOM 4751 CA ILE A 319 -37.905 -9.310 -.740 1.00 40.49 C
ATOM 4753 CB ILE A 319 -39.275 -9.588 -1.469 1.00 40.64 C
ATOM 4755 CG1 ILE A 319 -40.473 -9.078 -.683 1.00 40.88 C
ATOM 4758 CD1 ILE A 319 -41.799 -9.535 -1.280 1.00 40.86 C
ATOM 4762 CG2 ILE A 319 -39.460 -11.082 -1.801 1.00 40.50 C
ATOM 4766 C ILE A 319 -37.656 -10.319 .393 1.00 40.69 C
ATOM 4767 O ILE A 319 -38.136 -10.138 1.504 1.00 40.88 O
ATOM 4769 N ASN A 320 -36.886 -11.374 .104 1.00 40.79 N
ATOM 4770 CA ASN A 320 -36.689 -12.483 1.049 1.00 40.64 C
ATOM 4772 CB ASN A 320 -36.240 -13.761 .314 1.00 40.73 C
ATOM 4775 CG ASN A 320 -37.370 -14.422 -.468 1.00 40.98 C
ATOM 4776 OD1 ASN A 320 -38.556 -14.309 -.119 1.00 40.77 O
ATOM 4777 ND2 ASN A 320 -37.001 -15.131 -1.529 1.00 41.31 N
ATOM 4780 C ASN A 320 -35.711 -12.175 2.169 1.00 40.16 C
ATOM 4781 O ASN A 320 -35.546 -12.978 3.077 1.00 40.15 O
ATOM 4783 N ASP A 321 -35.067 -11.017 2.101 1.00 39.66 N
ATOM 4784 CA ASP A 321 -34.111 -10.615 3.126 1.00 39.51 C
ATOM 4786 CB ASP A 321 -33.114 -9.571 2.575 1.00 40.17 C
ATOM 4789 CG ASP A 321 -32.595 -9.904 1.152 1.00 42.12 C
ATOM 4790 OD1 ASP A 321 -32.425 -11.115 .820 1.00 44.15 O
ATOM 4791 OD2 ASP A 321 -32.354 -8.934 .375 1.00 43.28 O
ATOM 4792 C ASP A 321 -34.851 -10.030 4.337 1.00 38.27 C
ATOM 4793 O ASP A 321 -34.304 -9.987 5.443 1.00 38.15 O
ATOM 4795 N LEU A 322 -36.089 -9.583 4.108 1.00 36.72 N
ATOM 4796 CA LEU A 322 -36.887 -8.875 5.104 1.00 35.38 C
ATOM 4798 CB LEU A 322 -37.894 -7.942 4.422 1.00 35.15 C
ATOM 4801 CG LEU A 322 -37.370 -6.840 3.503 1.00 34.83 C
ATOM 4803 CD1 LEU A 322 -38.479 -6.286 2.626 1.00 34.45 C
ATOM 4807 CD2 LEU A 322 -36.742 -5.740 4.316 1.00 34.89 C
ATOM 4811 C LEU A 322 -37.683 -9.834 5.963 1.00 34.57 C
ATOM 4812 O LEU A 322 -37.975 -10.933 5.527 1.00 34.27 O
ATOM 4814 N PRO A 323 -38.039 -9.402 7.189 1.00 33.93 N
ATOM 4815 CA PRO A 323 -39.070 -9.917 8.067 1.00 33.49 C
ATOM 4817 CB PRO A 323 -39.151 -8.840 9.141 1.00 33.31 C
ATOM 4820 CG PRO A 323 -37.791 -8.419 9.311 1.00 33.67 C
ATOM 4823 CD PRO A 323 -37.154 -8.496 7.941 1.00 34.20 C
ATOM 4826 C PRO A 323 -40.429 -10.036 7.425 1.00 33.33 C
ATOM 4827 O PRO A 323 -40.776 -9.232 6.579 1.00 33.35 O
ATOM 4828 N ASP A 324 -41.209 -11.005 7.891 1.00 33.37 N
ATOM 4829 CA ASP A 324 -42.511 -11.329 7.313 1.00 33.36 C
ATOM 4831 CB ASP A 324 -43.137 -12.542 8.037 1.00 33.59 C

ATOM 4834 CG ASP A 324 -42.496 -13.881 7.619 1.00 34.18 C
ATOM 4835 OD1 ASP A 324 -41.885 -13.915 6.518 1.00 36.44 O
ATOM 4836 OD2 ASP A 324 -42.607 -14.887 8.371 1.00 32.19 O
ATOM 4837 C ASP A 324 -43.484 -10.149 7.289 1.00 32.90 C
ATOM 4838 O ASP A 324 -44.108 -9.885 6.255 1.00 33.36 O
ATOM 4840 N TYR A 325 -43.606 -9.423 8.392 1.00 32.10 N
ATOM 4841 CA TYR A 325 -44.515 -8.279 8.400 1.00 31.65 C
ATOM 4843 CB TYR A 325 -44.718 -7.726 9.815 1.00 31.68 C
ATOM 4846 CG TYR A 325 -43.618 -6.846 10.352 1.00 31.35 C
ATOM 4847 CD1 TYR A 325 -42.507 -7.389 10.992 1.00 31.31 C
ATOM 4849 CE1 TYR A 325 -41.497 -6.574 11.504 1.00 31.46 C
ATOM 4851 CZ TYR A 325 -41.613 -5.192 11.392 1.00 32.41 C
ATOM 4852 OH TYR A 325 -40.637 -4.336 11.893 1.00 32.78 O
ATOM 4854 CE2 TYR A 325 -42.723 -4.644 10.769 1.00 32.17 C
ATOM 4856 CD2 TYR A 325 -43.713 -5.470 10.261 1.00 31.47 C
ATOM 4858 C TYR A 325 -44.094 -7.179 7.424 1.00 31.17 C
ATOM 4859 O TYR A 325 -44.947 -6.458 6.920 1.00 31.09 O
ATOM 4861 N MET A 326 -42.796 -7.068 7.145 1.00 30.73 N
ATOM 4862 CA MET A 326 -42.277 -6.036 6.225 1.00 30.49 C
ATOM 4864 CB MET A 326 -40.832 -5.702 6.565 1.00 30.16 C
ATOM 4867 CG MET A 326 -40.725 -4.918 7.830 1.00 29.57 C
ATOM 4870 SD MET A 326 -39.057 -4.376 8.166 1.00 28.39 S
ATOM 4871 CE MET A 326 -39.407 -2.787 8.933 1.00 26.18 C
ATOM 4875 C MET A 326 -42.371 -6.418 4.748 1.00 30.59 C
ATOM 4876 O MET A 326 -42.786 -5.603 3.920 1.00 30.48 O
ATOM 4878 N LYS A 327 -41.936 -7.643 4.438 1.00 30.68 N
ATOM 4879 CA LYS A 327 -42.170 -8.299 3.143 1.00 30.56 C
ATOM 4881 CB LYS A 327 -42.267 -9.830 3.326 1.00 30.84 C
ATOM 4884 CG LYS A 327 -41.052 -10.607 2.844 1.00 32.35 C
ATOM 4887 CD LYS A 327 -40.990 -12.019 3.412 1.00 34.43 C
ATOM 4890 CE LYS A 327 -40.221 -12.941 2.462 1.00 35.77 C
ATOM 4893 NZ LYS A 327 -39.691 -14.162 3.150 1.00 37.20 N
ATOM 4897 C LYS A 327 -43.453 -7.811 2.515 1.00 29.89 C
ATOM 4898 O LYS A 327 -43.447 -7.220 1.436 1.00 29.85 O
ATOM 4900 N LEU A 328 -44.544 -8.046 3.230 1.00 29.10 N
ATOM 4901 CA LEU A 328 -45.871 -7.781 2.730 1.00 28.77 C
ATOM 4903 CB LEU A 328 -46.899 -8.336 3.709 1.00 28.81 C
ATOM 4906 CG LEU A 328 -48.349 -8.364 3.257 1.00 28.82 C
ATOM 4908 CD1 LEU A 328 -48.519 -9.260 2.046 1.00 29.09 C
ATOM 4912 CD2 LEU A 328 -49.202 -8.845 4.411 1.00 29.16 C
ATOM 4916 C LEU A 328 -46.057 -6.291 2.564 1.00 28.61 C
ATOM 4917 O LEU A 328 -46.582 -5.828 1.554 1.00 29.00 O
ATOM 4919 N CYS A 329 -45.612 -5.532 3.557 1.00 28.24 N
ATOM 4920 CA CYS A 329 -45.737 -4.086 3.504 1.00 27.95 C
ATOM 4922 CB CYS A 329 -45.311 -3.459 4.834 1.00 28.21 C
ATOM 4925 SG CYS A 329 -45.280 -1.630 4.817 1.00 32.39 S
ATOM 4927 C CYS A 329 -44.921 -3.541 2.327 1.00 26.34 C
ATOM 4928 O CYS A 329 -45.459 -2.853 1.475 1.00 26.23 O
ATOM 4930 N PHE A 330 -43.642 -3.882 2.269 1.00 24.82 N
ATOM 4931 CA PHE A 330 -42.790 -3.514 1.130 1.00 23.82 C
ATOM 4933 CB PHE A 330 -41.397 -4.137 1.283 1.00 23.64 C
ATOM 4936 CG PHE A 330 -40.492 -3.873 .117 1.00 22.63 C
ATOM 4937 CD1 PHE A 330 -39.845 -2.658 -.008 1.00 21.68 C
ATOM 4939 CE1 PHE A 330 -39.020 -2.393 -1.082 1.00 21.07 C
ATOM 4941 CZ PHE A 330 -38.829 -3.343 -2.046 1.00 22.00 C
ATOM 4943 CE2 PHE A 330 -39.474 -4.568 -1.944 1.00 22.60 C
ATOM 4945 CD2 PHE A 330 -40.309 -4.824 -.865 1.00 22.36 C
ATOM 4947 C PHE A 330 -43.348 -3.863 -.281 1.00 22.99 C
ATOM 4948 O PHE A 330 -43.350 -3.012 -1.182 1.00 22.98 O
ATOM 4950 N LEU A 331 -43.789 -5.101 -.492 1.00 21.65 N

ATOM 4951 CA LEU A 331 -44.306 -5.484 -1.816 1.00 20.74 C
ATOM 4953 CB LEU A 331 -44.573 -6.990 -1.912 1.00 20.57 C
ATOM 4956 CG LEU A 331 -44.959 -7.575 -3.277 1.00 19.82 C
ATOM 4958 CD1 LEU A 331 -43.936 -7.246 -4.329 1.00 19.00 C
ATOM 4962 CD2 LEU A 331 -45.128 -9.092 -3.165 1.00 19.11 C
ATOM 4966 C LEU A 331 -45.568 -4.710 -2.159 1.00 19.98 C
ATOM 4967 O LEU A 331 -45.753 -4.324 -3.300 1.00 20.15 O
ATOM 4969 N ALA A 332 -46.431 -4.495 -1.172 1.00 19.09 N
ATOM 4970 CA ALA A 332 -47.619 -3.675 -1.353 1.00 18.46 C
ATOM 4972 CB ALA A 332 -48.406 -3.587 -.045 1.00 18.20 C
ATOM 4976 C ALA A 332 -47.248 -2.279 -1.856 1.00 17.91 C
ATOM 4977 O ALA A 332 -47.890 -1.745 -2.744 1.00 17.98 O
ATOM 4979 N LEU A 333 -46.197 -1.706 -1.295 1.00 17.62 N
ATOM 4980 CA LEU A 333 -45.753 -.353 -1.637 1.00 17.60 C
ATOM 4982 CB LEU A 333 -44.725 .132 -.598 1.00 17.59 C
ATOM 4985 CG LEU A 333 -44.122 1.533 -.761 1.00 17.16 C
ATOM 4987 CD1 LEU A 333 -45.166 2.629 -.554 1.00 16.99 C
ATOM 4991 CD2 LEU A 333 -42.979 1.704 .200 1.00 15.89 C
ATOM 4995 C LEU A 333 -45.100 -.320 -3.005 1.00 17.70 C
ATOM 4996 O LEU A 333 -45.321 .603 -3.795 1.00 17.86 O
ATOM 4998 N TYR A 334 -44.248 -1.319 -3.234 1.00 17.63 N
ATOM 4999 CA TYR A 334 -43.542 -1.531 -4.489 1.00 17.44 C
ATOM 5001 CB TYR A 334 -42.893 -2.908 -4.444 1.00 17.50 C
ATOM 5004 CG TYR A 334 -41.897 -3.169 -5.523 1.00 18.03 C
ATOM 5005 CD1 TYR A 334 -40.698 -2.473 -5.569 1.00 18.83 C
ATOM 5007 CE1 TYR A 334 -39.764 -2.725 -6.542 1.00 18.13 C
ATOM 5009 CZ TYR A 334 -40.016 -3.678 -7.478 1.00 18.78 C
ATOM 5010 OH TYR A 334 -39.096 -3.929 -8.439 1.00 21.71 O
ATOM 5012 CE2 TYR A 334 -41.180 -4.391 -7.462 1.00 19.74 C
ATOM 5014 CD2 TYR A 334 -42.118 -4.139 -6.472 1.00 19.59 C
ATOM 5016 C TYR A 334 -44.500 -1.497 -5.649 1.00 17.43 C
ATOM 5017 O TYR A 334 -44.264 -.803 -6.636 1.00 17.64 O
ATOM 5019 N ASN A 335 -45.589 -2.253 -5.504 1.00 17.30 N
ATOM 5020 CA ASN A 335 -46.574 -2.448 -6.553 1.00 17.23 C
ATOM 5022 CB ASN A 335 -47.544 -3.551 -6.166 1.00 17.32 C
ATOM 5025 CG ASN A 335 -46.952 -4.920 -6.332 1.00 18.16 C
ATOM 5026 OD1 ASN A 335 -45.913 -5.090 -6.989 1.00 18.99 O
ATOM 5027 ND2 ASN A 335 -47.616 -5.921 -5.749 1.00 18.49 N
ATOM 5030 C ASN A 335 -47.365 -1.218 -6.812 1.00 17.12 C
ATOM 5031 O ASN A 335 -47.613 -.852 -7.965 1.00 17.36 O
ATOM 5033 N THR A 336 -47.789 -.602 -5.722 1.00 17.20 N
ATOM 5034 CA THR A 336 -48.601 .593 -5.779 1.00 17.36 C
ATOM 5036 CB THR A 336 -48.888 1.104 -4.381 1.00 17.20 C
ATOM 5038 OG1 THR A 336 -49.611 .103 -3.657 1.00 16.26 O
ATOM 5040 CG2 THR A 336 -49.688 2.384 -4.452 1.00 17.18 C
ATOM 5044 C THR A 336 -47.893 1.691 -6.550 1.00 17.84 C
ATOM 5045 O THR A 336 -48.511 2.388 -7.360 1.00 18.07 O
ATOM 5047 N ILE A 337 -46.595 1.831 -6.298 1.00 18.14 N
ATOM 5048 CA ILE A 337 -45.817 2.904 -6.895 1.00 18.50 C
ATOM 5050 CB ILE A 337 -44.584 3.209 -6.066 1.00 18.31 C
ATOM 5052 CG1 ILE A 337 -45.014 3.997 -4.837 1.00 18.58 C
ATOM 5055 CD1 ILE A 337 -44.043 3.866 -3.735 1.00 20.66 C
ATOM 5059 CG2 ILE A 337 -43.570 3.988 -6.867 1.00 16.98 C
ATOM 5063 C ILE A 337 -45.447 2.548 -8.314 1.00 19.29 C
ATOM 5064 O ILE A 337 -45.556 3.387 -9.214 1.00 19.17 O
ATOM 5066 N ASN A 338 -45.033 1.299 -8.513 1.00 20.16 N
ATOM 5067 CA ASN A 338 -44.861 .767 -9.864 1.00 20.93 C
ATOM 5069 CB ASN A 338 -44.409 -.695 -9.830 1.00 21.07 C
ATOM 5072 CG ASN A 338 -42.953 -.845 -9.439 1.00 21.61 C
ATOM 5073 OD1 ASN A 338 -42.232 .143 -9.308 1.00 22.40 O

ATOM 5074 ND2 ASN A 338 -42.509 -2.086 -9.260 1.00 21.92 N
ATOM 5077 C ASN A 338 -46.123 .914 -10.719 1.00 21.44 C
ATOM 5078 O ASN A 338 -46.022 1.202 -11.904 1.00 21.25 O
ATOM 5080 N GLU A 339 -47.303 .747 -10.128 1.00 22.21 N
ATOM 5081 CA GLU A 339 -48.532 1.000 -10.880 1.00 23.31 C
ATOM 5083 CB GLU A 339 -49.768 .464 -10.164 1.00 24.13 C
ATOM 5086 CG GLU A 339 -50.146 -.936 -10.660 1.00 28.69 C
ATOM 5089 CD GLU A 339 -50.939 -1.740 -9.638 1.00 35.06 C
ATOM 5090 OE1 GLU A 339 -51.899 -1.136 -9.067 1.00 39.51 O
ATOM 5091 OE2 GLU A 339 -50.596 -2.952 -9.414 1.00 36.64 O
ATOM 5092 C GLU A 339 -48.725 2.463 -11.269 1.00 22.71 C
ATOM 5093 O GLU A 339 -49.215 2.743 -12.372 1.00 22.48 O
ATOM 5095 N ILE A 340 -48.339 3.390 -10.390 1.00 22.19 N
ATOM 5096 CA ILE A 340 -48.406 4.813 -10.734 1.00 21.64 C
ATOM 5098 CB ILE A 340 -48.135 5.739 -9.538 1.00 21.33 C
ATOM 5100 CG1 ILE A 340 -49.229 5.596 -8.482 1.00 21.29 C
ATOM 5103 CD1 ILE A 340 -48.925 6.306 -7.150 1.00 20.00 C
ATOM 5107 CG2 ILE A 340 -48.091 7.177 -9.982 1.00 20.28 C
ATOM 5111 C ILE A 340 -47.414 5.128 -11.861 1.00 21.78 C
ATOM 5112 O ILE A 340 -47.786 5.826 -12.818 1.00 22.13 O
ATOM 5114 N ALA A 341 -46.179 4.609 -11.771 1.00 21.34 N
ATOM 5115 CA ALA A 341 -45.147 4.892 -12.787 1.00 21.03 C
ATOM 5117 CB ALA A 341 -43.837 4.268 -12.406 1.00 20.55 C
ATOM 5121 C ALA A 341 -45.592 4.426 -14.183 1.00 21.32 C
ATOM 5122 O ALA A 341 -45.228 5.036 -15.217 1.00 21.11 O
ATOM 5124 N TYR A 342 -46.393 3.355 -14.196 1.00 21.45 N
ATOM 5125 CA TYR A 342 -47.008 2.861 -15.414 1.00 21.41 C
ATOM 5127 CB TYR A 342 -47.627 1.468 -15.208 1.00 21.31 C
ATOM 5130 CG TYR A 342 -48.336 .957 -16.450 1.00 19.60 C
ATOM 5131 CD1 TYR A 342 -47.613 .463 -17.521 1.00 16.69 C
ATOM 5133 CE1 TYR A 342 -48.231 .032 -18.643 1.00 15.50 C
ATOM 5135 CZ TYR A 342 -49.595 .085 -18.728 1.00 15.88 C
ATOM 5136 OH TYR A 342 -50.196 -.352 -19.877 1.00 16.46 O
ATOM 5138 CE2 TYR A 342 -50.352 .558 -17.681 1.00 16.50 C
ATOM 5140 CD2 TYR A 342 -49.725 .997 -16.556 1.00 18.17 C
ATOM 5142 C TYR A 342 -48.064 3.830 -15.899 1.00 22.08 C
ATOM 5143 O TYR A 342 -48.094 4.169 -17.048 1.00 22.07 O
ATOM 5145 N ASP A 343 -48.942 4.283 -15.032 1.00 23.41 N
ATOM 5146 CA ASP A 343 -49.970 5.211 -15.481 1.00 24.66 C
ATOM 5148 CB ASP A 343 -50.851 5.674 -14.318 1.00 25.10 C
ATOM 5151 CG ASP A 343 -51.720 4.552 -13.732 1.00 26.06 C
ATOM 5152 OD1 ASP A 343 -52.107 3.613 -14.477 1.00 26.39 O
ATOM 5153 OD2 ASP A 343 -52.032 4.642 -12.516 1.00 27.29 O
ATOM 5154 C ASP A 343 -49.316 6.420 -16.142 1.00 25.22 C
ATOM 5155 O ASP A 343 -49.755 6.874 -17.192 1.00 25.47 O
ATOM 5157 N ASN A 344 -48.260 6.936 -15.528 1.00 25.87 N
ATOM 5158 CA ASN A 344 -47.508 8.042 -16.127 1.00 26.41 C
ATOM 5160 CB ASN A 344 -46.498 8.605 -15.134 1.00 26.56 C
ATOM 5163 CG ASN A 344 -47.152 9.407 -14.073 1.00 26.95 C
ATOM 5164 OD1 ASN A 344 -47.495 10.568 -14.296 1.00 29.13 O
ATOM 5165 ND2 ASN A 344 -47.367 8.799 -12.916 1.00 26.36 N
ATOM 5168 C ASN A 344 -46.785 7.674 -17.416 1.00 26.53 C
ATOM 5169 O ASN A 344 -46.658 8.508 -18.304 1.00 26.74 O
ATOM 5171 N LEU A 345 -46.280 6.448 -17.510 1.00 26.56 N
ATOM 5172 CA LEU A 345 -45.634 6.019 -18.739 1.00 26.37 C
ATOM 5174 CB LEU A 345 -44.890 4.693 -18.550 1.00 26.32 C
ATOM 5177 CG LEU A 345 -43.995 4.339 -19.750 1.00 25.96 C
ATOM 5179 CD1 LEU A 345 -42.706 5.133 -19.665 1.00 25.07 C
ATOM 5183 CD2 LEU A 345 -43.724 2.835 -19.874 1.00 24.75 C
ATOM 5187 C LEU A 345 -46.679 5.908 -19.856 1.00 26.38 C

ATOM 5188 O LEU A 345 -46.435 6.335 -20.966 1.00 26.52 O
ATOM 5190 N LYS A 346 -47.839 5.340 -19.563 1.00 26.59 N
ATOM 5191 CA LYS A 346 -48.880 5.176 -20.572 1.00 26.89 C
ATOM 5193 CB LYS A 346 -50.065 4.367 -20.011 1.00 26.80 C
ATOM 5196 CG LYS A 346 -51.073 3.931 -21.062 1.00 26.26 C
ATOM 5199 CD LYS A 346 -52.210 3.080 -20.517 1.00 26.15 C
ATOM 5202 CE LYS A 346 -53.227 3.849 -19.689 1.00 26.40 C
ATOM 5205 NZ LYS A 346 -53.136 3.506 -18.223 1.00 27.67 N
ATOM 5209 C LYS A 346 -49.372 6.537 -21.071 1.00 27.52 C
ATOM 5210 O LYS A 346 -49.562 6.742 -22.272 1.00 27.57 O
ATOM 5212 N ASP A 347 -49.567 7.472 -20.148 1.00 28.10 N
ATOM 5213 CA ASP A 347 -50.309 8.689 -20.465 1.00 28.58 C
ATOM 5215 CB ASP A 347 -51.305 9.017 -19.329 1.00 28.85 C
ATOM 5218 CG ASP A 347 -52.426 7.950 -19.197 1.00 30.01 C
ATOM 5219 OD1 ASP A 347 -52.827 7.349 -20.223 1.00 30.51 O
ATOM 5220 OD2 ASP A 347 -52.910 7.704 -18.069 1.00 32.61 O
ATOM 5221 C ASP A 347 -49.407 9.871 -20.804 1.00 28.22 C
ATOM 5222 O ASP A 347 -49.778 10.710 -21.611 1.00 28.39 O
ATOM 5224 N LYS A 348 -48.228 9.930 -20.206 1.00 28.03 N
ATOM 5225 CA LYS A 348 -47.301 11.021 -20.467 1.00 28.01 C
ATOM 5227 CB LYS A 348 -46.785 11.648 -19.164 1.00 28.39 C
ATOM 5230 CG LYS A 348 -47.834 12.305 -18.257 1.00 30.18 C
ATOM 5233 CD LYS A 348 -47.143 12.898 -17.003 1.00 32.40 C
ATOM 5236 CE LYS A 348 -48.124 13.121 -15.874 1.00 33.59 C
ATOM 5239 NZ LYS A 348 -49.319 13.878 -16.341 1.00 35.48 N
ATOM 5243 C LYS A 348 -46.107 10.551 -21.260 1.00 27.25 C
ATOM 5244 O LYS A 348 -45.241 11.345 -21.566 1.00 27.60 O
ATOM 5246 N GLY A 349 -46.036 9.271 -21.583 1.00 26.47 N
ATOM 5247 CA GLY A 349 -44.863 8.742 -22.261 1.00 26.01 C
ATOM 5250 C GLY A 349 -43.559 9.109 -21.587 1.00 25.67 C
ATOM 5251 O GLY A 349 -42.613 9.472 -22.250 1.00 25.85 O
ATOM 5253 N GLU A 350 -43.498 9.032 -20.269 1.00 25.55 N
ATOM 5254 CA GLU A 350 -42.272 9.374 -19.555 1.00 25.76 C
ATOM 5256 CB GLU A 350 -42.332 10.814 -19.021 1.00 26.34 C
ATOM 5259 CG GLU A 350 -42.179 11.928 -20.106 1.00 29.04 C
ATOM 5262 CD GLU A 350 -40.745 12.101 -20.598 1.00 32.08 C
ATOM 5263 OE1 GLU A 350 -39.853 12.170 -19.716 1.00 35.46 O
ATOM 5264 OE2 GLU A 350 -40.516 12.174 -21.839 1.00 31.64 O
ATOM 5265 C GLU A 350 -42.084 8.414 -18.400 1.00 24.87 C
ATOM 5266 O GLU A 350 -43.067 8.046 -17.760 1.00 25.16 O
ATOM 5268 N ASN A 351 -40.833 8.009 -18.145 1.00 23.71 N
ATOM 5269 CA ASN A 351 -40.494 7.189 -16.980 1.00 22.88 C
ATOM 5271 CB ASN A 351 -39.351 6.229 -17.287 1.00 22.88 C
ATOM 5274 CG ASN A 351 -39.141 5.215 -16.184 1.00 22.98 C
ATOM 5275 OD1 ASN A 351 -39.006 5.584 -15.035 1.00 22.68 O
ATOM 5276 ND2 ASN A 351 -39.139 3.924 -16.529 1.00 24.38 N
ATOM 5279 C ASN A 351 -40.126 8.058 -15.786 1.00 22.40 C
ATOM 5280 O ASN A 351 -39.097 8.741 -15.785 1.00 22.66 O
ATOM 5282 N ILE A 352 -40.965 8.021 -14.760 1.00 21.55 N
ATOM 5283 CA ILE A 352 -40.770 8.860 -13.591 1.00 20.75 C
ATOM 5285 CB ILE A 352 -42.002 9.788 -13.360 1.00 20.95 C
ATOM 5287 CG1 ILE A 352 -43.263 8.970 -13.022 1.00 20.82 C
ATOM 5290 CD1 ILE A 352 -44.237 9.698 -12.122 1.00 20.21 C
ATOM 5294 CG2 ILE A 352 -42.266 10.669 -14.582 1.00 19.85 C
ATOM 5298 C ILE A 352 -40.516 8.016 -12.339 1.00 20.37 C
ATOM 5299 O ILE A 352 -40.574 8.513 -11.224 1.00 20.55 O
ATOM 5301 N LEU A 353 -40.236 6.733 -12.519 1.00 19.98 N
ATOM 5302 CA LEU A 353 -40.061 5.828 -11.387 1.00 19.42 C
ATOM 5304 CB LEU A 353 -39.894 4.392 -11.870 1.00 19.27 C
ATOM 5307 CG LEU A 353 -39.989 3.318 -10.799 1.00 19.01 C

ATOM 5309 CD1 LEU A 353 -41.164 3.574 -9.867 1.00 18.35 C
ATOM 5313 CD2 LEU A 353 -40.085 1.938 -11.468 1.00 18.74 C
ATOM 5317 C LEU A 353 -38.890 6.240 -10.523 1.00 19.11 C
ATOM 5318 O LEU A 353 -39.022 6.319 -9.314 1.00 18.96 O
ATOM 5320 N PRO A 354 -37.746 6.549 -11.142 1.00 19.06 N
ATOM 5321 CA PRO A 354 -36.631 7.069 -10.367 1.00 19.29 C
ATOM 5323 CB PRO A 354 -35.749 7.717 -11.438 1.00 19.25 C
ATOM 5326 CG PRO A 354 -35.997 6.942 -12.638 1.00 19.08 C
ATOM 5329 CD PRO A 354 -37.409 6.472 -12.572 1.00 19.00 C
ATOM 5332 C PRO A 354 -37.024 8.122 -9.328 1.00 19.33 C
ATOM 5333 O PRO A 354 -36.534 8.057 -8.193 1.00 19.73 O
ATOM 5334 N TYR A 355 -37.891 9.063 -9.721 1.00 18.83 N
ATOM 5335 CA TYR A 355 -38.206 10.221 -8.898 1.00 18.79 C
ATOM 5337 CB TYR A 355 -38.836 11.359 -9.707 1.00 19.10 C
ATOM 5340 CG TYR A 355 -38.142 11.708 -11.009 1.00 20.15 C
ATOM 5341 CD1 TYR A 355 -36.940 12.403 -11.027 1.00 20.78 C
ATOM 5343 CE1 TYR A 355 -36.321 12.719 -12.232 1.00 22.19 C
ATOM 5345 CZ TYR A 355 -36.918 12.347 -13.438 1.00 22.19 C
ATOM 5346 OH TYR A 355 -36.341 12.660 -14.657 1.00 23.29 O
ATOM 5348 CE2 TYR A 355 -38.113 11.677 -13.430 1.00 21.62 C
ATOM 5350 CD2 TYR A 355 -38.720 11.371 -12.227 1.00 21.05 C
ATOM 5352 C TYR A 355 -39.155 9.864 -7.777 1.00 18.43 C
ATOM 5353 O TYR A 355 -39.081 10.460 -6.709 1.00 18.61 O
ATOM 5355 N LEU A 356 -40.058 8.917 -8.023 1.00 17.92 N
ATOM 5356 CA LEU A 356 -40.993 8.467 -6.994 1.00 17.38 C
ATOM 5358 CB LEU A 356 -42.136 7.658 -7.597 1.00 17.17 C
ATOM 5361 CG LEU A 356 -42.956 8.366 -8.682 1.00 17.56 C
ATOM 5363 CD1 LEU A 356 -43.933 7.419 -9.371 1.00 17.47 C
ATOM 5367 CD2 LEU A 356 -43.698 9.548 -8.112 1.00 18.08 C
ATOM 5371 C LEU A 356 -40.241 7.623 -5.978 1.00 17.10 C
ATOM 5372 O LEU A 356 -40.332 7.859 -4.783 1.00 17.62 O
ATOM 5374 N THR A 357 -39.464 6.656 -6.442 1.00 16.64 N
ATOM 5375 CA THR A 357 -38.775 5.769 -5.513 1.00 16.18 C
ATOM 5377 CB THR A 357 -38.104 4.554 -6.213 1.00 16.04 C
ATOM 5379 OG1 THR A 357 -37.092 4.996 -7.123 1.00 15.93 O
ATOM 5381 CG2 THR A 357 -39.142 3.732 -6.962 1.00 14.99 C
ATOM 5385 C THR A 357 -37.764 6.544 -4.686 1.00 16.16 C
ATOM 5386 O THR A 357 -37.599 6.278 -3.506 1.00 16.07 O
ATOM 5388 N LYS A 358 -37.107 7.524 -5.291 1.00 16.20 N
ATOM 5389 CA LYS A 358 -36.186 8.365 -4.543 1.00 16.46 C
ATOM 5391 CB LYS A 358 -35.518 9.386 -5.453 1.00 16.80 C
ATOM 5394 CG LYS A 358 -34.612 10.388 -4.741 1.00 18.30 C
ATOM 5397 CD LYS A 358 -33.352 9.738 -4.168 1.00 20.21 C
ATOM 5400 CE LYS A 358 -32.335 10.811 -3.768 1.00 21.96 C
ATOM 5403 NZ LYS A 358 -31.163 10.275 -3.019 1.00 22.95 N
ATOM 5407 C LYS A 358 -36.936 9.083 -3.440 1.00 16.26 C
ATOM 5408 O LYS A 358 -36.448 9.161 -2.320 1.00 16.15 O
ATOM 5410 N ALA A 359 -38.126 9.593 -3.763 1.00 16.11 N
ATOM 5411 CA ALA A 359 -38.937 10.332 -2.798 1.00 16.10 C
ATOM 5413 CB ALA A 359 -40.221 10.768 -3.406 1.00 15.71 C
ATOM 5417 C ALA A 359 -39.215 9.476 -1.588 1.00 16.52 C
ATOM 5418 O ALA A 359 -39.247 9.970 -.442 1.00 16.82 O
ATOM 5420 N TRP A 360 -39.398 8.187 -1.843 1.00 16.79 N
ATOM 5421 CA TRP A 360 -39.704 7.247 -.780 1.00 17.25 C
ATOM 5423 CB TRP A 360 -40.390 6.006 -1.352 1.00 17.41 C
ATOM 5426 CG TRP A 360 -41.852 6.129 -1.318 1.00 17.06 C
ATOM 5427 CD1 TRP A 360 -42.664 6.451 -2.346 1.00 17.94 C
ATOM 5429 NE1 TRP A 360 -43.967 6.489 -1.926 1.00 18.03 N
ATOM 5431 CE2 TRP A 360 -44.002 6.193 -.592 1.00 17.72 C
ATOM 5432 CD2 TRP A 360 -42.684 5.965 -.179 1.00 16.60 C

ATOM 5433 CE3 TRP A 360 -42.441 5.654 1.155 1.00 16.65 C
ATOM 5435 CZ3 TRP A 360 -43.508 5.573 2.022 1.00 16.91 C
ATOM 5437 CH2 TRP A 360 -44.811 5.807 1.586 1.00 17.82 C
ATOM 5439 CZ2 TRP A 360 -45.080 6.114 .282 1.00 18.49 C
ATOM 5441 C TRP A 360 -38.490 6.865 .073 1.00 17.52 C
ATOM 5442 O TRP A 360 -38.603 6.767 1.297 1.00 17.38 O
ATOM 5444 N ALA A 361 -37.344 6.651 -.568 1.00 17.82 N
ATOM 5445 CA ALA A 361 -36.122 6.336 .157 1.00 18.11 C
ATOM 5447 CB ALA A 361 -34.982 6.050 -.805 1.00 17.92 C
ATOM 5451 C ALA A 361 -35.781 7.507 1.063 1.00 18.52 C
ATOM 5452 O ALA A 361 -35.434 7.327 2.229 1.00 18.48 O
ATOM 5454 N ASP A 362 -35.911 8.711 .521 1.00 19.16 N
ATOM 5455 CA ASP A 362 -35.627 9.925 1.276 1.00 19.90 C
ATOM 5457 CB ASP A 362 -35.797 11.167 .387 1.00 20.39 C
ATOM 5460 CG ASP A 362 -34.596 11.424 -.530 1.00 21.84 C
ATOM 5461 OD1 ASP A 362 -33.630 10.625 -.561 1.00 22.88 O
ATOM 5462 OD2 ASP A 362 -34.630 12.453 -1.231 1.00 24.83 O
ATOM 5463 C ASP A 362 -36.532 10.039 2.510 1.00 19.91 C
ATOM 5464 O ASP A 362 -36.074 10.427 3.591 1.00 19.76 O
ATOM 5466 N LEU A 363 -37.813 9.707 2.346 1.00 19.95 N
ATOM 5467 CA LEU A 363 -38.747 9.688 3.478 1.00 19.85 C
ATOM 5469 CB LEU A 363 -40.175 9.415 3.006 1.00 19.70 C
ATOM 5472 CG LEU A 363 -41.219 9.293 4.123 1.00 18.58 C
ATOM 5474 CD1 LEU A 363 -41.189 10.551 4.965 1.00 18.37 C
ATOM 5478 CD2 LEU A 363 -42.597 9.073 3.551 1.00 16.43 C
ATOM 5482 C LEU A 363 -38.368 8.613 4.488 1.00 20.24 C
ATOM 5483 O LEU A 363 -38.314 8.875 5.691 1.00 20.52 O
ATOM 5485 N CYS A 364 -38.129 7.397 3.997 1.00 20.29 N
ATOM 5486 CA CYS A 364 -37.741 6.308 4.874 1.00 20.39 C
ATOM 5488 CB CYS A 364 -37.595 4.985 4.111 1.00 20.37 C
ATOM 5491 SG CYS A 364 -39.208 4.201 3.666 1.00 20.69 S
ATOM 5493 C CYS A 364 -36.467 6.683 5.646 1.00 20.59 C
ATOM 5494 O CYS A 364 -36.386 6.445 6.863 1.00 20.82 O
ATOM 5496 N ASN A 365 -35.495 7.314 4.980 1.00 20.35 N
ATOM 5497 CA ASN A 365 -34.282 7.716 5.697 1.00 20.14 C
ATOM 5499 CB ASN A 365 -33.188 8.203 4.754 1.00 20.18 C
ATOM 5502 CG ASN A 365 -32.359 7.064 4.184 1.00 20.55 C
ATOM 5503 OD1 ASN A 365 -31.706 6.316 4.925 1.00 20.40 O
ATOM 5504 ND2 ASN A 365 -32.365 6.938 2.854 1.00 21.25 N
ATOM 5507 C ASN A 365 -34.590 8.746 6.779 1.00 19.92 C
ATOM 5508 O ASN A 365 -33.997 8.685 7.857 1.00 19.94 O
ATOM 5510 N ALA A 366 -35.531 9.658 6.507 1.00 19.58 N
ATOM 5511 CA ALA A 366 -36.036 10.578 7.537 1.00 19.39 C
ATOM 5513 CB ALA A 366 -37.083 11.507 6.971 1.00 18.79 C
ATOM 5517 C ALA A 366 -36.597 9.784 8.730 1.00 19.75 C
ATOM 5518 O ALA A 366 -36.215 10.049 9.891 1.00 19.53 O
ATOM 5520 N PHE A 367 -37.460 8.797 8.447 1.00 19.69 N
ATOM 5521 CA PHE A 367 -37.985 7.925 9.502 1.00 20.11 C
ATOM 5523 CB PHE A 367 -38.952 6.857 8.967 1.00 20.47 C
ATOM 5526 CG PHE A 367 -40.293 7.370 8.494 1.00 21.35 C
ATOM 5527 CD1 PHE A 367 -40.985 8.347 9.180 1.00 21.54 C
ATOM 5529 CE1 PHE A 367 -42.224 8.775 8.732 1.00 21.47 C
ATOM 5531 CZ PHE A 367 -42.798 8.213 7.612 1.00 21.87 C
ATOM 5533 CE2 PHE A 367 -42.135 7.230 6.924 1.00 22.60 C
ATOM 5535 CD2 PHE A 367 -40.894 6.798 7.373 1.00 22.90 C
ATOM 5537 C PHE A 367 -36.871 7.179 10.252 1.00 20.12 C
ATOM 5538 O PHE A 367 -36.940 7.009 11.476 1.00 19.88 O
ATOM 5540 N LEU A 368 -35.868 6.696 9.516 1.00 20.30 N
ATOM 5541 CA LEU A 368 -34.775 5.931 10.133 1.00 20.19 C
ATOM 5543 CB LEU A 368 -33.783 5.413 9.085 1.00 20.08 C

ATOM 5546 CG LEU A 368 -32.743 4.363 9.514 1.00 19.30 C
ATOM 5548 CD1 LEU A 368 -33.384 3.227 10.260 1.00 18.66 C
ATOM 5552 CD2 LEU A 368 -31.968 3.807 8.319 1.00 18.16 C
ATOM 5556 C LEU A 368 -34.063 6.812 11.128 1.00 20.41 C
ATOM 5557 O LEU A 368 -33.842 6.407 12.257 1.00 20.01 O
ATOM 5559 N GLN A 369 -33.751 8.036 10.711 1.00 20.89 N
ATOM 5560 CA GLN A 369 -33.037 8.970 11.564 1.00 21.49 C
ATOM 5562 CB GLN A 369 -32.782 10.280 10.832 1.00 21.58 C
ATOM 5565 CG GLN A 369 -32.071 11.359 11.677 1.00 21.20 C
ATOM 5568 CD GLN A 369 -30.639 11.006 11.976 1.00 20.04 C
ATOM 5569 OE1 GLN A 369 -30.282 10.650 13.108 1.00 19.10 O
ATOM 5570 NE2 GLN A 369 -29.803 11.095 10.956 1.00 18.75 N
ATOM 5573 C GLN A 369 -33.763 9.265 12.870 1.00 22.21 C
ATOM 5574 O GLN A 369 -33.122 9.343 13.909 1.00 22.41 O
ATOM 5576 N GLU A 370 -35.080 9.455 12.822 1.00 23.05 N
ATOM 5577 CA GLU A 370 -35.856 9.718 14.046 1.00 23.71 C
ATOM 5579 CB GLU A 370 -37.329 10.041 13.726 1.00 24.04 C
ATOM 5582 CG GLU A 370 -37.484 11.293 12.862 1.00 26.84 C
ATOM 5585 CD GLU A 370 -38.897 11.910 12.834 1.00 30.36 C
ATOM 5586 OE1 GLU A 370 -39.886 11.161 12.586 1.00 31.90 O
ATOM 5587 OE2 GLU A 370 -38.992 13.164 13.014 1.00 31.62 O
ATOM 5588 C GLU A 370 -35.755 8.523 14.994 1.00 23.60 C
ATOM 5589 O GLU A 370 -35.534 8.689 16.199 1.00 23.33 O
ATOM 5591 N ALA A 371 -35.904 7.322 14.435 1.00 23.72 N
ATOM 5592 CA ALA A 371 -35.771 6.091 15.201 1.00 23.91 C
ATOM 5594 CB ALA A 371 -35.991 4.868 14.312 1.00 23.76 C
ATOM 5598 C ALA A 371 -34.392 6.051 15.840 1.00 24.20 C
ATOM 5599 O ALA A 371 -34.277 5.804 17.035 1.00 24.54 O
ATOM 5601 N LYS A 372 -33.355 6.333 15.049 1.00 24.38 N
ATOM 5602 CA LYS A 372 -31.979 6.273 15.530 1.00 24.39 C
ATOM 5604 CB LYS A 372 -30.970 6.466 14.393 1.00 24.43 C
ATOM 5607 CG LYS A 372 -30.623 5.164 13.645 1.00 25.20 C
ATOM 5610 CD LYS A 372 -29.188 5.149 13.069 1.00 26.09 C
ATOM 5613 CE LYS A 372 -29.114 5.437 11.557 1.00 27.01 C
ATOM 5616 NZ LYS A 372 -29.002 4.200 10.709 1.00 26.82 N
ATOM 5620 C LYS A 372 -31.717 7.268 16.645 1.00 24.59 C
ATOM 5621 O LYS A 372 -31.096 6.908 17.627 1.00 25.13 O
ATOM 5623 N TRP A 373 -32.181 8.507 16.520 1.00 24.78 N
ATOM 5624 CA TRP A 373 -32.006 9.473 17.610 1.00 24.90 C
ATOM 5626 CB TRP A 373 -32.565 10.863 17.266 1.00 24.75 C
ATOM 5629 CG TRP A 373 -31.701 11.677 16.338 1.00 23.59 C
ATOM 5630 CD1 TRP A 373 -30.344 11.663 16.259 1.00 22.38 C
ATOM 5632 NE1 TRP A 373 -29.915 12.539 15.298 1.00 21.59 N
ATOM 5634 CE2 TRP A 373 -30.999 13.162 14.744 1.00 21.69 C
ATOM 5635 CD2 TRP A 373 -32.147 12.644 15.376 1.00 22.41 C
ATOM 5636 CE3 TRP A 373 -33.409 13.110 14.976 1.00 21.98 C
ATOM 5638 CZ3 TRP A 373 -33.480 14.072 13.979 1.00 22.08 C
ATOM 5640 CH2 TRP A 373 -32.313 14.567 13.366 1.00 22.31 C
ATOM 5642 CZ2 TRP A 373 -31.067 14.124 13.736 1.00 21.87 C
ATOM 5644 C TRP A 373 -32.678 8.970 18.881 1.00 25.53 C
ATOM 5645 O TRP A 373 -32.101 9.072 19.972 1.00 25.99 O
ATOM 5647 N LEU A 374 -33.881 8.420 18.739 1.00 25.84 N
ATOM 5648 CA LEU A 374 -34.667 7.980 19.893 1.00 26.29 C
ATOM 5650 CB LEU A 374 -36.070 7.562 19.443 1.00 26.32 C
ATOM 5653 CG LEU A 374 -37.227 7.646 20.444 1.00 26.39 C
ATOM 5655 CD1 LEU A 374 -38.456 8.286 19.761 1.00 26.95 C
ATOM 5659 CD2 LEU A 374 -37.583 6.281 21.050 1.00 26.24 C
ATOM 5663 C LEU A 374 -33.982 6.824 20.623 1.00 26.77 C
ATOM 5664 O LEU A 374 -33.995 6.758 21.860 1.00 26.95 O
ATOM 5666 N TYR A 375 -33.383 5.919 19.854 1.00 27.23 N

ATOM 5667 CA TYR A 375 -32.706 4.761 20.425 1.00 27.74 C
ATOM 5669 CB TYR A 375 -32.195 3.814 19.328 1.00 27.78 C
ATOM 5672 CG TYR A 375 -31.526 2.556 19.848 1.00 28.74 C
ATOM 5673 CD1 TYR A 375 -32.264 1.394 20.090 1.00 29.61 C
ATOM 5675 CE1 TYR A 375 -31.652 .232 20.573 1.00 29.89 C
ATOM 5677 CZ TYR A 375 -30.287 .226 20.817 1.00 30.15 C
ATOM 5678 OH TYR A 375 -29.676 -.917 21.286 1.00 30.57 O
ATOM 5680 CE2 TYR A 375 -29.530 1.367 20.579 1.00 30.05 C
ATOM 5682 CD2 TYR A 375 -30.152 2.522 20.096 1.00 29.74 C
ATOM 5684 C TYR A 375 -31.553 5.248 21.275 1.00 27.97 C
ATOM 5685 O TYR A 375 -31.404 4.837 22.422 1.00 28.00 O
ATOM 5687 N ASN A 376 -30.763 6.158 20.719 1.00 28.32 N
ATOM 5688 CA ASN A 376 -29.531 6.590 21.368 1.00 28.71 C
ATOM 5690 CB ASN A 376 -28.569 7.161 20.329 1.00 28.60 C
ATOM 5693 CG ASN A 376 -28.215 6.159 19.255 1.00 28.32 C
ATOM 5694 OD1 ASN A 376 -27.961 4.977 19.527 1.00 25.72 O
ATOM 5695 ND2 ASN A 376 -28.195 6.631 18.015 1.00 29.29 N
ATOM 5698 C ASN A 376 -29.728 7.617 22.484 1.00 29.05 C
ATOM 5699 O ASN A 376 -28.752 8.021 23.136 1.00 29.03 O
ATOM 5701 N LYS A 377 -30.977 8.021 22.716 1.00 29.16 N
ATOM 5702 CA LYS A 377 -31.254 9.178 23.549 1.00 29.27 C
ATOM 5704 CB LYS A 377 -31.051 8.879 25.050 1.00 29.52 C
ATOM 5707 CG LYS A 377 -32.202 8.112 25.723 1.00 30.36 C
ATOM 5710 CD LYS A 377 -32.202 6.638 25.340 1.00 31.54 C
ATOM 5713 CE LYS A 377 -33.322 5.862 26.031 1.00 32.30 C
ATOM 5716 NZ LYS A 377 -33.559 4.509 25.411 1.00 32.13 N
ATOM 5720 C LYS A 377 -30.337 10.299 23.080 1.00 28.92 C
ATOM 5721 O LYS A 377 -29.590 10.867 23.875 1.00 28.94 O
ATOM 5723 N SER A 378 -30.377 10.575 21.776 1.00 28.52 N
ATOM 5724 CA SER A 378 -29.652 11.700 21.201 1.00 28.30 C
ATOM 5726 CB SER A 378 -29.623 11.620 19.678 1.00 28.33 C
ATOM 5729 OG SER A 378 -28.919 10.482 19.237 1.00 29.36 O
ATOM 5731 C SER A 378 -30.355 12.977 21.594 1.00 27.97 C
ATOM 5732 O SER A 378 -31.483 12.947 22.108 1.00 27.91 O
ATOM 5734 N THR A 379 -29.684 14.098 21.344 1.00 27.60 N
ATOM 5735 CA THR A 379 -30.257 15.422 21.581 1.00 27.24 C
ATOM 5737 CB THR A 379 -29.929 15.950 23.002 1.00 27.23 C
ATOM 5739 OG1 THR A 379 -28.512 16.102 23.158 1.00 26.85 O
ATOM 5741 CG2 THR A 379 -30.467 15.007 24.067 1.00 27.48 C
ATOM 5745 C THR A 379 -29.738 16.414 20.548 1.00 26.83 C
ATOM 5746 O THR A 379 -28.834 17.190 20.844 1.00 26.69 O
ATOM 5748 N PRO A 380 -30.305 16.390 19.331 1.00 26.56 N
ATOM 5749 CA PRO A 380 -29.884 17.315 18.278 1.00 26.52 C
ATOM 5751 CB PRO A 380 -30.380 16.648 16.992 1.00 26.46 C
ATOM 5754 CG PRO A 380 -31.281 15.533 17.408 1.00 26.41 C
ATOM 5757 CD PRO A 380 -31.395 15.508 18.887 1.00 26.53 C
ATOM 5760 C PRO A 380 -30.469 18.728 18.386 1.00 26.55 C
ATOM 5761 O PRO A 380 -31.472 18.966 19.063 1.00 26.69 O
ATOM 5762 N THR A 381 -29.840 19.661 17.692 1.00 26.51 N
ATOM 5763 CA THR A 381 -30.299 21.034 17.699 1.00 26.51 C
ATOM 5765 CB THR A 381 -29.261 21.955 17.033 1.00 26.99 C
ATOM 5767 OG1 THR A 381 -28.919 21.431 15.732 1.00 27.65 O
ATOM 5769 CG2 THR A 381 -28.003 22.082 17.930 1.00 26.41 C
ATOM 5773 C THR A 381 -31.635 21.167 16.970 1.00 26.06 C
ATOM 5774 O THR A 381 -31.972 20.347 16.112 1.00 26.03 O
ATOM 5776 N PHE A 382 -32.386 22.218 17.294 1.00 25.52 N
ATOM 5777 CA PHE A 382 -33.681 22.436 16.654 1.00 24.83 C
ATOM 5779 CB PHE A 382 -34.284 23.793 17.011 1.00 24.53 C
ATOM 5782 CG PHE A 382 -35.495 24.113 16.211 1.00 23.77 C
ATOM 5783 CD1 PHE A 382 -36.745 23.715 16.637 1.00 24.50 C

ATOM 5785 CE1 PHE A 382 -37.873 23.977 15.878 1.00 24.49 C
ATOM 5787 CZ PHE A 382 -37.744 24.630 14.673 1.00 24.41 C
ATOM 5789 CE2 PHE A 382 -36.490 25.014 14.235 1.00 23.88 C
ATOM 5791 CD2 PHE A 382 -35.381 24.752 14.999 1.00 23.29 C
ATOM 5793 C PHE A 382 -33.542 22.342 15.150 1.00 24.49 C
ATOM 5794 O PHE A 382 -34.361 21.731 14.485 1.00 24.32 O
ATOM 5796 N ASP A 383 -32.498 22.969 14.627 1.00 24.42 N
ATOM 5797 CA ASP A 383 -32.257 23.005 13.190 1.00 24.19 C
ATOM 5799 CB ASP A 383 -31.101 23.966 12.867 1.00 24.21 C
ATOM 5802 CG ASP A 383 -31.473 25.423 13.050 1.00 23.72 C
ATOM 5803 OD1 ASP A 383 -32.634 25.794 12.837 1.00 25.60 O
ATOM 5804 OD2 ASP A 383 -30.594 26.220 13.383 1.00 24.03 O
ATOM 5805 C ASP A 383 -31.982 21.612 12.599 1.00 24.06 C
ATOM 5806 O ASP A 383 -32.393 21.342 11.473 1.00 24.00 O
ATOM 5808 N ASP A 384 -31.298 20.739 13.336 1.00 23.78 N
ATOM 5809 CA ASP A 384 -31.078 19.379 12.848 1.00 24.11 C
ATOM 5811 CB ASP A 384 -29.981 18.651 13.632 1.00 24.54 C
ATOM 5814 CG ASP A 384 -28.573 19.009 13.159 1.00 26.32 C
ATOM 5815 OD1 ASP A 384 -28.441 19.852 12.232 1.00 28.55 O
ATOM 5816 OD2 ASP A 384 -27.599 18.451 13.728 1.00 27.18 O
ATOM 5817 C ASP A 384 -32.351 18.550 12.905 1.00 23.83 C
ATOM 5818 O ASP A 384 -32.670 17.825 11.955 1.00 24.24 O
ATOM 5820 N TYR A 385 -33.070 18.637 14.017 1.00 23.31 N
ATOM 5821 CA TYR A 385 -34.294 17.861 14.179 1.00 22.89 C
ATOM 5823 CB TYR A 385 -34.833 17.979 15.608 1.00 22.86 C
ATOM 5826 CG TYR A 385 -36.144 17.245 15.807 1.00 22.65 C
ATOM 5827 CD1 TYR A 385 -36.163 15.868 16.030 1.00 22.36 C
ATOM 5829 CE1 TYR A 385 -37.351 15.189 16.206 1.00 22.77 C
ATOM 5831 CZ TYR A 385 -38.545 15.887 16.146 1.00 23.54 C
ATOM 5832 OH TYR A 385 -39.733 15.212 16.309 1.00 24.38 O
ATOM 5834 CE2 TYR A 385 -38.554 17.258 15.913 1.00 22.76 C
ATOM 5836 CD2 TYR A 385 -37.360 17.923 15.744 1.00 22.12 C
ATOM 5838 C TYR A 385 -35.375 18.299 13.190 1.00 22.55 C
ATOM 5839 O TYR A 385 -36.050 17.467 12.584 1.00 22.85 O
ATOM 5841 N PHE A 386 -35.537 19.609 13.042 1.00 22.08 N
ATOM 5842 CA PHE A 386 -36.626 20.155 12.248 1.00 21.62 C
ATOM 5844 CB PHE A 386 -36.857 21.628 12.568 1.00 21.73 C
ATOM 5847 CG PHE A 386 -38.033 22.209 11.851 1.00 21.54 C
ATOM 5848 CD1 PHE A 386 -39.311 21.933 12.273 1.00 21.29 C
ATOM 5850 CE1 PHE A 386 -40.380 22.444 11.623 1.00 22.11 C
ATOM 5852 CZ PHE A 386 -40.193 23.240 10.517 1.00 23.28 C
ATOM 5854 CE2 PHE A 386 -38.920 23.502 10.069 1.00 23.10 C
ATOM 5856 CD2 PHE A 386 -37.853 22.989 10.737 1.00 22.15 C
ATOM 5858 C PHE A 386 -36.369 19.987 10.769 1.00 21.09 C
ATOM 5859 O PHE A 386 -37.278 19.700 10.006 1.00 20.91 O
ATOM 5861 N GLY A 387 -35.127 20.177 10.362 1.00 20.68 N
ATOM 5862 CA GLY A 387 -34.747 19.917 8.985 1.00 20.43 C
ATOM 5865 C GLY A 387 -35.151 18.521 8.544 1.00 19.95 C
ATOM 5866 O GLY A 387 -35.553 18.327 7.398 1.00 20.24 O
ATOM 5868 N ASN A 388 -35.032 17.554 9.451 1.00 19.12 N
ATOM 5869 CA ASN A 388 -35.451 16.182 9.202 1.00 18.73 C
ATOM 5871 CB ASN A 388 -34.744 15.272 10.205 1.00 18.90 C
ATOM 5874 CG ASN A 388 -34.863 13.795 9.871 1.00 18.35 C
ATOM 5875 OD1 ASN A 388 -34.163 13.284 8.993 1.00 17.24 O
ATOM 5876 ND2 ASN A 388 -35.714 13.092 10.614 1.00 17.01 N
ATOM 5879 C ASN A 388 -36.968 16.033 9.350 1.00 18.65 C
ATOM 5880 O ASN A 388 -37.624 15.370 8.551 1.00 18.82 O
ATOM 5882 N ALA A 389 -37.527 16.670 10.371 1.00 18.38 N
ATOM 5883 CA ALA A 389 -38.926 16.477 10.728 1.00 18.02 C
ATOM 5885 CB ALA A 389 -39.203 17.107 12.084 1.00 17.83 C

ATOM 5889 C ALA A 389 -39.949 16.966 9.700 1.00 17.90 C
ATOM 5890 O ALA A 389 -41.095 16.544 9.760 1.00 17.74 O
ATOM 5892 N TRP A 390 -39.585 17.860 8.783 1.00 18.11 N
ATOM 5893 CA TRP A 390 -40.543 18.254 7.731 1.00 18.46 C
ATOM 5895 CB TRP A 390 -40.459 19.737 7.329 1.00 18.59 C
ATOM 5898 CG TRP A 390 -39.143 20.224 6.821 1.00 19.26 C
ATOM 5899 CD1 TRP A 390 -38.224 20.947 7.519 1.00 20.64 C
ATOM 5901 NE1 TRP A 390 -37.138 21.224 6.729 1.00 20.62 N
ATOM 5903 CE2 TRP A 390 -37.352 20.694 5.485 1.00 19.57 C
ATOM 5904 CD2 TRP A 390 -38.607 20.066 5.504 1.00 19.15 C
ATOM 5905 CE3 TRP A 390 -39.060 19.448 4.344 1.00 20.13 C
ATOM 5907 CZ3 TRP A 390 -38.254 19.477 3.224 1.00 20.27 C
ATOM 5909 CH2 TRP A 390 -37.017 20.110 3.239 1.00 19.38 C
ATOM 5911 CZ2 TRP A 390 -36.549 20.724 4.356 1.00 19.49 C
ATOM 5913 C TRP A 390 -40.407 17.343 6.527 1.00 18.73 C
ATOM 5914 O TRP A 390 -41.369 17.143 5.788 1.00 18.32 O
ATOM 5916 N LYS A 391 -39.200 16.806 6.336 1.00 19.30 N
ATOM 5917 CA LYS A 391 -38.969 15.692 5.404 1.00 19.70 C
ATOM 5919 CB LYS A 391 -37.459 15.392 5.244 1.00 19.92 C
ATOM 5922 CG LYS A 391 -36.812 15.953 3.935 1.00 22.08 C
ATOM 5925 CD LYS A 391 -35.257 16.217 4.040 1.00 23.92 C
ATOM 5928 CE LYS A 391 -34.918 17.698 4.426 1.00 24.43 C
ATOM 5931 NZ LYS A 391 -33.699 17.901 5.307 1.00 23.23 N
ATOM 5935 C LYS A 391 -39.731 14.441 5.861 1.00 19.46 C
ATOM 5936 O LYS A 391 -40.284 13.709 5.032 1.00 20.07 O
ATOM 5938 N SER A 392 -39.793 14.202 7.170 1.00 18.95 N
ATOM 5939 CA SER A 392 -40.455 12.998 7.666 1.00 18.63 C
ATOM 5941 CB SER A 392 -39.850 12.508 9.000 1.00 18.75 C
ATOM 5944 OG SER A 392 -40.314 13.230 10.126 1.00 18.94 O
ATOM 5946 C SER A 392 -41.964 13.152 7.771 1.00 18.20 C
ATOM 5947 O SER A 392 -42.654 12.182 8.031 1.00 18.12 O
ATOM 5949 N SER A 393 -42.477 14.360 7.567 1.00 18.07 N
ATOM 5950 CA SER A 393 -43.929 14.591 7.556 1.00 18.02 C
ATOM 5952 CB SER A 393 -44.229 16.078 7.504 1.00 18.08 C
ATOM 5955 OG SER A 393 -43.995 16.558 6.192 1.00 18.01 O
ATOM 5957 C SER A 393 -44.594 13.971 6.340 1.00 17.87 C
ATOM 5958 O SER A 393 -45.778 13.661 6.372 1.00 18.03 O
ATOM 5960 N SER A 394 -43.823 13.841 5.264 1.00 17.69 N
ATOM 5961 CA SER A 394 -44.284 13.306 3.989 1.00 17.59 C
ATOM 5963 CB SER A 394 -45.329 12.180 4.149 1.00 17.61 C
ATOM 5966 OG SER A 394 -46.648 12.681 4.294 1.00 17.18 O
ATOM 5968 C SER A 394 -44.828 14.415 3.115 1.00 17.42 C
ATOM 5969 O SER A 394 -45.345 14.146 2.024 1.00 17.31 O
ATOM 5971 N GLY A 395 -44.711 15.654 3.592 1.00 17.23 N
ATOM 5972 CA GLY A 395 -45.088 16.827 2.807 1.00 17.26 C
ATOM 5975 C GLY A 395 -44.478 16.749 1.415 1.00 17.29 C
ATOM 5976 O GLY A 395 -45.203 16.653 .413 1.00 18.06 O
ATOM 5978 N PRO A 396 -43.145 16.754 1.331 1.00 16.72 N
ATOM 5979 CA PRO A 396 -42.582 16.610 .006 1.00 16.40 C
ATOM 5981 CB PRO A 396 -41.080 16.549 .259 1.00 16.62 C
ATOM 5984 CG PRO A 396 -40.903 16.749 1.775 1.00 17.11 C
ATOM 5987 CD PRO A 396 -42.157 17.252 2.296 1.00 16.87 C
ATOM 5990 C PRO A 396 -43.053 15.374 -.748 1.00 15.89 C
ATOM 5991 O PRO A 396 -43.501 15.498 -1.894 1.00 15.90 O
ATOM 5992 N LEU A 397 -42.973 14.197 -.135 1.00 15.27 N
ATOM 5993 CA LEU A 397 -43.287 12.976 -.886 1.00 14.57 C
ATOM 5995 CB LEU A 397 -43.332 11.733 -.008 1.00 14.36 C
ATOM 5998 CG LEU A 397 -43.541 10.431 -.781 1.00 14.02 C
ATOM 6000 CD1 LEU A 397 -42.690 9.348 -.206 1.00 15.04 C
ATOM 6004 CD2 LEU A 397 -44.985 9.976 -.805 1.00 13.75 C

ATOM 6008 C LEU A 397 -44.618 13.182 -1.542 1.00 14.39 C
ATOM 6009 O LEU A 397 -44.736 12.999 -2.745 1.00 14.57 O
ATOM 6011 N GLN A 398 -45.604 13.607 -.751 1.00 14.08 N
ATOM 6012 CA GLN A 398 -46.962 13.828 -1.245 1.00 13.91 C
ATOM 6014 CB GLN A 398 -47.860 14.363 -.136 1.00 13.99 C
ATOM 6017 CG GLN A 398 -48.274 13.321 .909 1.00 14.01 C
ATOM 6020 CD GLN A 398 -49.189 13.902 1.983 1.00 13.41 C
ATOM 6021 OE1 GLN A 398 -49.941 14.847 1.740 1.00 14.65 O
ATOM 6022 NE2 GLN A 398 -49.122 13.344 3.168 1.00 12.17 N
ATOM 6025 C GLN A 398 -47.015 14.800 -2.403 1.00 13.84 C
ATOM 6026 O GLN A 398 -47.677 14.547 -3.396 1.00 13.46 O
ATOM 6028 N LEU A 399 -46.319 15.922 -2.272 1.00 14.11 N
ATOM 6029 CA LEU A 399 -46.359 16.942 -3.315 1.00 14.37 C
ATOM 6031 CB LEU A 399 -45.900 18.282 -2.756 1.00 14.26 C
ATOM 6034 CG LEU A 399 -46.882 18.830 -1.704 1.00 14.44 C
ATOM 6036 CD1 LEU A 399 -46.250 19.960 -.919 1.00 16.43 C
ATOM 6040 CD2 LEU A 399 -48.191 19.304 -2.317 1.00 12.20 C
ATOM 6044 C LEU A 399 -45.582 16.525 -4.578 1.00 14.68 C
ATOM 6045 O LEU A 399 -46.043 16.784 -5.687 1.00 14.70 O
ATOM 6047 N ILE A 400 -44.443 15.844 -4.419 1.00 14.92 N
ATOM 6048 CA ILE A 400 -43.748 15.221 -5.564 1.00 15.08 C
ATOM 6050 CB ILE A 400 -42.549 14.355 -5.129 1.00 15.35 C
ATOM 6052 CG1 ILE A 400 -41.406 15.254 -4.611 1.00 16.83 C
ATOM 6055 CD1 ILE A 400 -40.234 14.490 -3.958 1.00 17.18 C
ATOM 6059 CG2 ILE A 400 -42.060 13.486 -6.292 1.00 14.03 C
ATOM 6063 C ILE A 400 -44.682 14.329 -6.358 1.00 15.08 C
ATOM 6064 O ILE A 400 -44.672 14.362 -7.574 1.00 15.18 O
ATOM 6066 N PHE A 401 -45.474 13.524 -5.650 1.00 15.16 N
ATOM 6067 CA PHE A 401 -46.501 12.674 -6.258 1.00 14.90 C
ATOM 6069 CB PHE A 401 -47.052 11.663 -5.240 1.00 14.51 C
ATOM 6072 CG PHE A 401 -46.294 10.378 -5.201 1.00 12.92 C
ATOM 6073 CD1 PHE A 401 -46.727 9.282 -5.931 1.00 11.98 C
ATOM 6075 CE1 PHE A 401 -46.032 8.093 -5.917 1.00 11.20 C
ATOM 6077 CZ PHE A 401 -44.881 7.985 -5.165 1.00 12.03 C
ATOM 6079 CE2 PHE A 401 -44.431 9.078 -4.428 1.00 11.98 C
ATOM 6081 CD2 PHE A 401 -45.143 10.263 -4.453 1.00 12.09 C
ATOM 6083 C PHE A 401 -47.641 13.509 -6.806 1.00 15.39 C
ATOM 6084 O PHE A 401 -48.183 13.215 -7.858 1.00 15.51 O
ATOM 6086 N ALA A 402 -48.022 14.545 -6.080 1.00 16.15 N
ATOM 6087 CA ALA A 402 -49.110 15.393 -6.525 1.00 16.90 C
ATOM 6089 CB ALA A 402 -49.391 16.473 -5.505 1.00 16.99 C
ATOM 6093 C ALA A 402 -48.722 16.003 -7.856 1.00 17.50 C
ATOM 6094 O ALA A 402 -49.549 16.100 -8.770 1.00 17.48 O
ATOM 6096 N TYR A 403 -47.444 16.367 -7.963 1.00 18.28 N
ATOM 6097 CA TYR A 403 -46.916 17.046 -9.142 1.00 18.94 C
ATOM 6099 CB TYR A 403 -45.412 17.252 -9.043 1.00 19.03 C
ATOM 6102 CG TYR A 403 -44.823 17.801 -10.314 1.00 19.79 C
ATOM 6103 CD1 TYR A 403 -44.973 19.138 -10.652 1.00 20.80 C
ATOM 6105 CE1 TYR A 403 -44.436 19.643 -11.827 1.00 20.73 C
ATOM 6107 CZ TYR A 403 -43.759 18.804 -12.674 1.00 21.16 C
ATOM 6108 OH TYR A 403 -43.231 19.283 -13.836 1.00 22.98 O
ATOM 6110 CE2 TYR A 403 -43.608 17.476 -12.370 1.00 21.23 C
ATOM 6112 CD2 TYR A 403 -44.137 16.980 -11.195 1.00 20.93 C
ATOM 6114 C TYR A 403 -47.198 16.293 -10.413 1.00 19.39 C
ATOM 6115 O TYR A 403 -47.567 16.904 -11.422 1.00 19.57 O
ATOM 6117 N PHE A 404 -47.023 14.976 -10.376 1.00 19.74 N
ATOM 6118 CA PHE A 404 -47.239 14.177 -11.573 1.00 20.35 C
ATOM 6120 CB PHE A 404 -46.533 12.841 -11.466 1.00 19.96 C
ATOM 6123 CG PHE A 404 -45.048 12.971 -11.387 1.00 18.81 C
ATOM 6124 CD1 PHE A 404 -44.292 13.115 -12.528 1.00 17.42 C

ATOM 6126 CE1 PHE A 404 -42.935 13.239 -12.457 1.00 17.24 C
ATOM 6128 CZ PHE A 404 -42.312 13.237 -11.237 1.00 17.40 C
ATOM 6130 CE2 PHE A 404 -43.056 13.106 -10.093 1.00 17.72 C
ATOM 6132 CD2 PHE A 404 -44.413 12.975 -10.170 1.00 17.93 C
ATOM 6134 C PHE A 404 -48.713 13.994 -11.894 1.00 21.59 C
ATOM 6135 O PHE A 404 -49.072 13.717 -13.046 1.00 21.71 O
ATOM 6137 N ALA A 405 -49.572 14.169 -10.896 1.00 22.87 N
ATOM 6138 CA ALA A 405 -50.990 13.939 -11.099 1.00 24.06 C
ATOM 6140 CB ALA A 405 -51.604 13.408 -9.833 1.00 24.15 C
ATOM 6144 C ALA A 405 -51.724 15.192 -11.556 1.00 25.21 C
ATOM 6145 O ALA A 405 -52.876 15.114 -11.939 1.00 25.51 O
ATOM 6147 N VAL A 406 -51.056 16.336 -11.530 1.00 26.52 N
ATOM 6148 CA VAL A 406 -51.713 17.617 -11.759 1.00 27.68 C
ATOM 6150 CB VAL A 406 -51.694 18.406 -10.434 1.00 27.60 C
ATOM 6152 CG1 VAL A 406 -51.654 19.913 -10.663 1.00 28.07 C
ATOM 6156 CG2 VAL A 406 -52.883 18.009 -9.596 1.00 27.41 C
ATOM 6160 C VAL A 406 -51.097 18.429 -12.925 1.00 29.10 C
ATOM 6161 O VAL A 406 -51.810 19.104 -13.678 1.00 28.53 O
ATOM 6163 N VAL A 407 -49.772 18.356 -13.059 1.00 30.90 N
ATOM 6164 CA VAL A 407 -49.052 19.003 -14.151 1.00 32.15 C
ATOM 6166 CB VAL A 407 -47.574 19.228 -13.777 1.00 32.25 C
ATOM 6168 CG1 VAL A 407 -46.770 19.780 -14.964 1.00 32.22 C
ATOM 6172 CG2 VAL A 407 -47.490 20.154 -12.583 1.00 32.25 C
ATOM 6176 C VAL A 407 -49.134 18.160 -15.421 1.00 33.36 C
ATOM 6177 O VAL A 407 -48.688 17.009 -15.454 1.00 33.40 O
ATOM 6179 N GLN A 408 -49.693 18.767 -16.463 1.00 34.93 N
ATOM 6180 CA GLN A 408 -49.930 18.102 -17.749 1.00 36.16 C
ATOM 6182 CB GLN A 408 -50.779 19.016 -18.638 1.00 36.63 C
ATOM 6185 CG GLN A 408 -51.625 18.270 -19.672 1.00 38.95 C
ATOM 6188 CD GLN A 408 -52.991 18.930 -19.887 1.00 41.80 C
ATOM 6189 OE1 GLN A 408 -53.739 19.150 -18.921 1.00 43.40 O
ATOM 6190 NE2 GLN A 408 -53.323 19.244 -21.151 1.00 41.68 N
ATOM 6193 C GLN A 408 -48.630 17.725 -18.470 1.00 36.22 C
ATOM 6194 O GLN A 408 -48.456 16.588 -18.920 1.00 35.86 O
ATOM 6196 N ASN A 409 -47.726 18.694 -18.578 1.00 36.64 N
ATOM 6197 CA ASN A 409 -46.400 18.441 -19.136 1.00 36.85 C
ATOM 6199 CB ASN A 409 -46.134 19.306 -20.373 1.00 36.73 C
ATOM 6202 CG ASN A 409 -46.808 18.752 -21.604 1.00 36.19 C
ATOM 6203 OD1 ASN A 409 -46.178 18.072 -22.420 1.00 35.00 O
ATOM 6204 ND2 ASN A 409 -48.110 18.994 -21.720 1.00 34.99 N
ATOM 6207 C ASN A 409 -45.312 18.613 -18.095 1.00 36.96 C
ATOM 6208 O ASN A 409 -45.032 19.720 -17.618 1.00 36.81 O
ATOM 6210 N ILE A 410 -44.713 17.488 -17.734 1.00 37.10 N
ATOM 6211 CA ILE A 410 -43.625 17.508 -16.792 1.00 37.27 C
ATOM 6213 CB ILE A 410 -43.265 16.092 -16.295 1.00 37.38 C
ATOM 6215 CG1 ILE A 410 -42.745 15.209 -17.426 1.00 37.84 C
ATOM 6218 CD1 ILE A 410 -42.416 13.824 -16.985 1.00 38.96 C
ATOM 6222 CG2 ILE A 410 -44.491 15.437 -15.676 1.00 37.67 C
ATOM 6226 C ILE A 410 -42.467 18.179 -17.492 1.00 37.12 C
ATOM 6227 O ILE A 410 -42.150 17.839 -18.617 1.00 36.87 O
ATOM 6229 N LYS A 411 -41.896 19.187 -16.851 1.00 37.38 N
ATOM 6230 CA LYS A 411 -40.680 19.813 -17.332 1.00 37.73 C
ATOM 6232 CB LYS A 411 -40.756 21.332 -17.171 1.00 38.15 C
ATOM 6235 CG LYS A 411 -41.979 21.962 -17.837 1.00 39.89 C
ATOM 6238 CD LYS A 411 -41.797 23.463 -18.080 1.00 42.48 C
ATOM 6241 CE LYS A 411 -43.029 24.069 -18.795 1.00 44.22 C
ATOM 6244 NZ LYS A 411 -42.977 25.576 -18.904 1.00 45.31 N
ATOM 6248 C LYS A 411 -39.562 19.244 -16.489 1.00 37.38 C
ATOM 6249 O LYS A 411 -39.721 19.112 -15.281 1.00 37.28 O
ATOM 6251 N LYS A 412 -38.445 18.886 -17.122 1.00 37.24 N

ATOM 6252 CA LYS A 412 -37.333 18.243 -16.413 1.00 36.95 C
ATOM 6254 CB LYS A 412 -36.286 17.701 -17.384 1.00 37.14 C
ATOM 6257 CG LYS A 412 -35.233 16.818 -16.720 1.00 37.89 C
ATOM 6260 CD LYS A 412 -34.334 16.125 -17.757 1.00 39.54 C
ATOM 6263 CE LYS A 412 -33.263 17.068 -18.348 1.00 40.08 C
ATOM 6266 NZ LYS A 412 -32.161 17.399 -17.376 1.00 40.16 N
ATOM 6270 C LYS A 412 -36.664 19.177 -15.419 1.00 36.42 C
ATOM 6271 O LYS A 412 -36.246 18.728 -14.357 1.00 36.56 O
ATOM 6273 N GLU A 413 -36.570 20.466 -15.744 1.00 35.77 N
ATOM 6274 CA GLU A 413 -35.948 21.423 -14.820 1.00 35.38 C
ATOM 6276 CB GLU A 413 -35.688 22.792 -15.489 1.00 35.73 C
ATOM 6279 CG GLU A 413 -36.510 24.013 -14.973 1.00 37.10 C
ATOM 6282 CD GLU A 413 -35.621 25.235 -14.633 1.00 38.51 C
ATOM 6283 OE1 GLU A 413 -34.778 25.125 -13.714 1.00 39.24 O
ATOM 6284 OE2 GLU A 413 -35.768 26.306 -15.266 1.00 39.04 O
ATOM 6285 C GLU A 413 -36.760 21.551 -13.522 1.00 34.43 C
ATOM 6286 O GLU A 413 -36.196 21.801 -12.460 1.00 34.34 O
ATOM 6288 N GLU A 414 -38.074 21.360 -13.616 1.00 33.45 N
ATOM 6289 CA GLU A 414 -38.956 21.407 -12.452 1.00 32.80 C
ATOM 6291 CB GLU A 414 -40.435 21.425 -12.864 1.00 32.83 C
ATOM 6294 CG GLU A 414 -40.923 22.736 -13.478 1.00 33.15 C
ATOM 6297 CD GLU A 414 -42.360 22.668 -14.003 1.00 33.82 C
ATOM 6298 OE1 GLU A 414 -42.876 21.560 -14.231 1.00 35.31 O
ATOM 6299 OE2 GLU A 414 -42.985 23.727 -14.204 1.00 33.98 O
ATOM 6300 C GLU A 414 -38.715 20.222 -11.536 1.00 32.18 C
ATOM 6301 O GLU A 414 -38.407 20.409 -10.372 1.00 32.25 O
ATOM 6303 N ILE A 415 -38.863 19.002 -12.044 1.00 31.63 N
ATOM 6304 CA ILE A 415 -38.725 17.819 -11.181 1.00 31.28 C
ATOM 6306 CB ILE A 415 -39.131 16.472 -11.852 1.00 31.14 C
ATOM 6308 CG1 ILE A 415 -38.349 16.204 -13.133 1.00 31.13 C
ATOM 6311 CD1 ILE A 415 -38.786 14.926 -13.836 1.00 30.72 C
ATOM 6315 CG2 ILE A 415 -40.611 16.454 -12.160 1.00 31.12 C
ATOM 6319 C ILE A 415 -37.316 17.705 -10.636 1.00 31.08 C
ATOM 6320 O ILE A 415 -37.105 17.188 -9.539 1.00 31.22 O
ATOM 6322 N GLU A 416 -36.345 18.208 -11.381 1.00 30.67 N
ATOM 6323 CA GLU A 416 -34.998 18.270 -10.850 1.00 30.55 C
ATOM 6325 CB GLU A 416 -34.011 18.654 -11.955 1.00 30.91 C
ATOM 6328 CG GLU A 416 -32.654 17.967 -11.845 1.00 32.55 C
ATOM 6331 CD GLU A 416 -31.802 18.130 -13.109 1.00 34.91 C
ATOM 6332 OE1 GLU A 416 -32.337 18.563 -14.161 1.00 35.53 O
ATOM 6333 OE2 GLU A 416 -30.590 17.816 -13.052 1.00 36.45 O
ATOM 6334 C GLU A 416 -34.962 19.249 -9.650 1.00 29.74 C
ATOM 6335 O GLU A 416 -34.143 19.097 -8.738 1.00 29.73 O
ATOM 6337 N ASN A 417 -35.864 20.234 -9.652 1.00 28.69 N
ATOM 6338 CA ASN A 417 -36.060 21.134 -8.503 1.00 27.92 C
ATOM 6340 CB ASN A 417 -36.632 22.477 -8.963 1.00 27.75 C
ATOM 6343 CG ASN A 417 -35.572 23.532 -9.095 1.00 26.84 C
ATOM 6344 OD1 ASN A 417 -35.160 24.132 -8.105 1.00 24.88 O
ATOM 6345 ND2 ASN A 417 -35.117 23.765 -10.318 1.00 26.28 N
ATOM 6348 C ASN A 417 -36.917 20.580 -7.356 1.00 27.41 C
ATOM 6349 O ASN A 417 -36.650 20.838 -6.187 1.00 27.15 O
ATOM 6351 N LEU A 418 -37.955 19.834 -7.675 1.00 27.09 N
ATOM 6352 CA LEU A 418 -38.694 19.156 -6.628 1.00 27.02 C
ATOM 6354 CB LEU A 418 -39.921 18.423 -7.200 1.00 26.95 C
ATOM 6357 CG LEU A 418 -41.030 19.284 -7.826 1.00 25.97 C
ATOM 6359 CD1 LEU A 418 -42.127 18.429 -8.447 1.00 24.88 C
ATOM 6363 CD2 LEU A 418 -41.623 20.226 -6.803 1.00 24.50 C
ATOM 6367 C LEU A 418 -37.763 18.196 -5.860 1.00 27.26 C
ATOM 6368 O LEU A 418 -37.834 18.123 -4.644 1.00 27.07 O
ATOM 6370 N GLN A 419 -36.873 17.494 -6.561 1.00 27.67 N

ATOM 6371 CA GLN A 419 -35.924 16.575 -5.909 1.00 28.28 C
ATOM 6373 CB GLN A 419 -35.155 15.758 -6.945 1.00 28.36 C
ATOM 6376 CG GLN A 419 -35.747 14.375 -7.146 1.00 29.43 C
ATOM 6379 CD GLN A 419 -35.052 13.573 -8.215 1.00 29.76 C
ATOM 6380 OE1 GLN A 419 -34.355 14.112 -9.066 1.00 29.93 O
ATOM 6381 NE2 GLN A 419 -35.252 12.270 -8.184 1.00 31.33 N
ATOM 6384 C GLN A 419 -34.922 17.219 -4.947 1.00 28.73 C
ATOM 6385 O GLN A 419 -34.540 16.608 -3.952 1.00 28.90 O
ATOM 6387 N LYS A 420 -34.490 18.440 -5.240 1.00 29.27 N
ATOM 6388 CA LYS A 420 -33.608 19.166 -4.335 1.00 29.81 C
ATOM 6390 CB LYS A 420 -32.758 20.163 -5.129 1.00 30.24 C
ATOM 6393 CG LYS A 420 -31.592 19.513 -5.867 1.00 31.75 C
ATOM 6396 CD LYS A 420 -31.259 20.217 -7.183 1.00 34.14 C
ATOM 6399 CE LYS A 420 -30.140 19.463 -7.953 1.00 36.21 C
ATOM 6402 NZ LYS A 420 -30.073 19.759 -9.439 1.00 36.76 N
ATOM 6406 C LYS A 420 -34.375 19.872 -3.204 1.00 29.98 C
ATOM 6407 O LYS A 420 -33.759 20.547 -2.384 1.00 30.44 O
ATOM 6409 N TYR A 421 -35.706 19.694 -3.162 1.00 30.07 N
ATOM 6410 CA TYR A 421 -36.646 20.309 -2.171 1.00 29.73 C
ATOM 6412 CB TYR A 421 -36.298 19.949 -.712 1.00 29.59 C
ATOM 6415 CG TYR A 421 -36.386 18.468 -.470 1.00 30.57 C
ATOM 6416 CD1 TYR A 421 -37.582 17.785 -.643 1.00 30.87 C
ATOM 6418 CE1 TYR A 421 -37.665 16.414 -.448 1.00 31.28 C
ATOM 6420 CZ TYR A 421 -36.549 15.705 -.068 1.00 31.90 C
ATOM 6421 OH TYR A 421 -36.620 14.347 .124 1.00 32.43 O
ATOM 6423 CE2 TYR A 421 -35.355 16.354 .119 1.00 32.68 C
ATOM 6425 CD2 TYR A 421 -35.274 17.736 -.095 1.00 32.42 C
ATOM 6427 C TYR A 421 -36.850 21.816 -2.347 1.00 29.24 C
ATOM 6428 O TYR A 421 -36.709 22.590 -1.401 1.00 29.26 O
ATOM 6430 N HIS A 422 -37.219 22.214 -3.563 1.00 28.65 N
ATOM 6431 CA HIS A 422 -37.540 23.604 -3.859 1.00 28.26 C
ATOM 6433 CB HIS A 422 -38.150 23.715 -5.256 1.00 28.33 C
ATOM 6436 CG HIS A 422 -38.299 25.124 -5.748 1.00 28.44 C
ATOM 6437 ND1 HIS A 422 -37.225 25.904 -6.106 1.00 28.97 N
ATOM 6439 CE1 HIS A 422 -37.660 27.082 -6.520 1.00 29.40 C
ATOM 6441 NE2 HIS A 422 -38.977 27.090 -6.443 1.00 28.14 N
ATOM 6443 CD2 HIS A 422 -39.399 25.879 -5.965 1.00 27.76 C
ATOM 6445 C HIS A 422 -38.511 24.147 -2.816 1.00 27.74 C
ATOM 6446 O HIS A 422 -39.357 23.408 -2.310 1.00 27.53 O
ATOM 6448 N ASP A 423 -38.384 25.437 -2.505 1.00 27.12 N
ATOM 6449 CA ASP A 423 -39.186 26.072 -1.454 1.00 26.63 C
ATOM 6451 CB ASP A 423 -38.877 27.575 -1.349 1.00 27.05 C
ATOM 6454 CG ASP A 423 -37.456 27.875 -.851 1.00 28.35 C
ATOM 6455 OD1 ASP A 423 -36.951 27.121 .018 1.00 30.99 O
ATOM 6456 OD2 ASP A 423 -36.860 28.884 -1.322 1.00 27.89 O
ATOM 6457 C ASP A 423 -40.689 25.883 -1.698 1.00 25.71 C
ATOM 6458 O ASP A 423 -41.487 25.831 -.749 1.00 26.26 O
ATOM 6460 N ILE A 424 -41.075 25.781 -2.966 1.00 24.01 N
ATOM 6461 CA ILE A 424 -42.479 25.596 -3.327 1.00 22.72 C
ATOM 6463 CB ILE A 424 -42.639 25.391 -4.843 1.00 22.40 C
ATOM 6465 CG1 ILE A 424 -44.029 25.668 -5.318 1.00 21.78 C
ATOM 6468 CD1 ILE A 424 -44.086 25.499 -6.793 1.00 22.22 C
ATOM 6472 CG2 ILE A 424 -42.340 23.985 -5.255 1.00 22.87 C
ATOM 6476 C ILE A 424 -43.103 24.442 -2.562 1.00 21.91 C
ATOM 6477 O ILE A 424 -44.238 24.574 -2.115 1.00 21.73 O
ATOM 6479 N ILE A 425 -42.365 23.334 -2.399 1.00 21.23 N
ATOM 6480 CA ILE A 425 -42.853 22.173 -1.634 1.00 20.73 C
ATOM 6482 CB ILE A 425 -42.622 20.820 -2.330 1.00 20.10 C
ATOM 6484 CG1 ILE A 425 -41.158 20.409 -2.290 1.00 18.72 C
ATOM 6487 CD1 ILE A 425 -40.923 19.075 -2.948 1.00 18.27 C

ATOM 6491 CG2 ILE A 425 -43.146 20.840 -3.741 1.00 19.57 C
ATOM 6495 C ILE A 425 -42.252 22.060 -.242 1.00 21.21 C
ATOM 6496 O ILE A 425 -42.810 21.370 .613 1.00 21.30 O
ATOM 6498 N SER A 426 -41.129 22.721 -.002 1.00 21.56 N
ATOM 6499 CA SER A 426 -40.492 22.620 1.299 1.00 22.23 C
ATOM 6501 CB SER A 426 -39.043 23.082 1.234 1.00 22.36 C
ATOM 6504 OG SER A 426 -38.977 24.501 1.342 1.00 24.09 O
ATOM 6506 C SER A 426 -41.242 23.460 2.334 1.00 22.39 C
ATOM 6507 O SER A 426 -41.390 23.051 3.491 1.00 22.95 O
ATOM 6509 N ARG A 427 -41.701 24.643 1.937 1.00 22.08 N
ATOM 6510 CA ARG A 427 -42.332 25.541 2.905 1.00 21.87 C
ATOM 6512 CB ARG A 427 -42.466 26.955 2.345 1.00 21.99 C
ATOM 6515 CG ARG A 427 -41.170 27.696 2.493 1.00 23.36 C
ATOM 6518 CD ARG A 427 -40.954 28.727 1.433 1.00 26.07 C
ATOM 6521 NE ARG A 427 -39.680 29.407 1.667 1.00 28.18 N
ATOM 6523 CZ ARG A 427 -39.127 30.298 .844 1.00 29.21 C
ATOM 6524 NH1 ARG A 427 -39.723 30.633 -.298 1.00 28.60 N
ATOM 6527 NH2 ARG A 427 -37.962 30.854 1.173 1.00 30.48 N
ATOM 6530 C ARG A 427 -43.651 25.003 3.434 1.00 21.21 C
ATOM 6531 O ARG A 427 -43.817 24.891 4.645 1.00 21.11 O
ATOM 6533 N PRO A 428 -44.573 24.622 2.541 1.00 20.52 N
ATOM 6534 CA PRO A 428 -45.789 23.999 3.040 1.00 20.27 C
ATOM 6536 CB PRO A 428 -46.410 23.369 1.791 1.00 20.44 C
ATOM 6539 CG PRO A 428 -45.864 24.119 .666 1.00 20.63 C
ATOM 6542 CD PRO A 428 -44.521 24.644 1.074 1.00 20.54 C
ATOM 6545 C PRO A 428 -45.450 22.917 4.050 1.00 19.75 C
ATOM 6546 O PRO A 428 -46.089 22.834 5.095 1.00 19.77 O
ATOM 6547 N SER A 429 -44.424 22.123 3.747 1.00 18.97 N
ATOM 6548 CA SER A 429 -44.008 21.045 4.636 1.00 18.45 C
ATOM 6550 CB SER A 429 -42.954 20.180 3.972 1.00 18.35 C
ATOM 6553 OG SER A 429 -43.452 19.716 2.733 1.00 19.12 O
ATOM 6555 C SER A 429 -43.519 21.525 5.985 1.00 17.97 C
ATOM 6556 O SER A 429 -43.733 20.846 6.968 1.00 17.88 O
ATOM 6558 N HIS A 430 -42.879 22.689 6.053 1.00 17.73 N
ATOM 6559 CA HIS A 430 -42.593 23.289 7.359 1.00 17.71 C
ATOM 6561 CB HIS A 430 -41.937 24.668 7.241 1.00 17.97 C
ATOM 6564 CG HIS A 430 -40.558 24.663 6.651 1.00 18.87 C
ATOM 6565 ND1 HIS A 430 -39.940 23.524 6.186 1.00 19.85 N
ATOM 6567 CE1 HIS A 430 -38.746 23.836 5.709 1.00 19.43 C
ATOM 6569 NE2 HIS A 430 -38.573 25.137 5.838 1.00 19.06 N
ATOM 6571 CD2 HIS A 430 -39.693 25.681 6.418 1.00 19.32 C
ATOM 6573 C HIS A 430 -43.914 23.444 8.131 1.00 17.31 C
ATOM 6574 O HIS A 430 -44.023 23.013 9.287 1.00 17.06 O
ATOM 6576 N ILE A 431 -44.913 24.050 7.475 1.00 16.74 N
ATOM 6577 CA ILE A 431 -46.218 24.304 8.091 1.00 16.15 C
ATOM 6579 CB ILE A 431 -47.174 25.057 7.174 1.00 16.18 C
ATOM 6581 CG1 ILE A 431 -46.613 26.428 6.801 1.00 17.05 C
ATOM 6584 CD1 ILE A 431 -46.441 27.352 7.994 1.00 18.34 C
ATOM 6588 CG2 ILE A 431 -48.496 25.263 7.860 1.00 15.28 C
ATOM 6592 C ILE A 431 -46.899 23.021 8.476 1.00 15.75 C
ATOM 6593 O ILE A 431 -47.624 22.980 9.445 1.00 15.95 O
ATOM 6595 N PHE A 432 -46.663 21.969 7.714 1.00 15.59 N
ATOM 6596 CA PHE A 432 -47.192 20.652 8.041 1.00 15.52 C
ATOM 6598 CB PHE A 432 -46.837 19.683 6.913 1.00 15.23 C
ATOM 6601 CG PHE A 432 -47.451 18.318 7.031 1.00 15.98 C
ATOM 6602 CD1 PHE A 432 -48.324 17.972 8.052 1.00 16.55 C
ATOM 6604 CE1 PHE A 432 -48.867 16.700 8.102 1.00 16.04 C
ATOM 6606 CZ PHE A 432 -48.559 15.774 7.130 1.00 15.29 C
ATOM 6608 CE2 PHE A 432 -47.718 16.107 6.114 1.00 15.37 C
ATOM 6610 CD2 PHE A 432 -47.172 17.364 6.061 1.00 16.74 C

ATOM 6612 C PHE A 432 -46.640 20.191 9.392 1.00 15.54 C
ATOM 6613 O PHE A 432 -47.383 20.006 10.343 1.00 15.37 O
ATOM 6615 N ARG A 433 -45.328 20.041 9.483 1.00 15.98 N
ATOM 6616 CA ARG A 433 -44.695 19.542 10.709 1.00 16.20 C
ATOM 6618 CB ARG A 433 -43.176 19.476 10.526 1.00 15.85 C
ATOM 6621 CG ARG A 433 -42.411 19.183 11.804 1.00 16.11 C
ATOM 6624 CD ARG A 433 -42.848 17.890 12.489 1.00 15.70 C
ATOM 6627 NE ARG A 433 -42.811 16.747 11.588 1.00 15.64 N
ATOM 6629 CZ ARG A 433 -43.377 15.571 11.838 1.00 16.27 C
ATOM 6630 NH1 ARG A 433 -44.029 15.359 12.965 1.00 16.82 N
ATOM 6633 NH2 ARG A 433 -43.302 14.598 10.948 1.00 16.96 N
ATOM 6636 C ARG A 433 -45.029 20.411 11.935 1.00 16.46 C
ATOM 6637 O ARG A 433 -45.296 19.890 13.031 1.00 16.31 O
ATOM 6639 N LEU A 434 -45.006 21.731 11.724 1.00 16.47 N
ATOM 6640 CA LEU A 434 -45.123 22.701 12.800 1.00 15.98 C
ATOM 6642 CB LEU A 434 -44.771 24.114 12.303 1.00 15.83 C
ATOM 6645 CG LEU A 434 -43.287 24.486 12.218 1.00 14.95 C
ATOM 6647 CD1 LEU A 434 -43.130 25.918 11.826 1.00 15.09 C
ATOM 6651 CD2 LEU A 434 -42.600 24.281 13.536 1.00 14.37 C
ATOM 6655 C LEU A 434 -46.517 22.660 13.387 1.00 16.19 C
ATOM 6656 O LEU A 434 -46.669 22.564 14.604 1.00 15.92 O
ATOM 6658 N CYS A 435 -47.529 22.715 12.520 1.00 16.78 N
ATOM 6659 CA CYS A 435 -48.936 22.591 12.940 1.00 17.48 C
ATOM 6661 CB CYS A 435 -49.870 22.617 11.726 1.00 17.54 C
ATOM 6664 SG CYS A 435 -50.110 24.233 10.985 1.00 18.80 S
ATOM 6666 C CYS A 435 -49.192 21.296 13.708 1.00 17.84 C
ATOM 6667 O CYS A 435 -50.043 21.250 14.597 1.00 17.92 O
ATOM 6669 N ASN A 436 -48.446 20.257 13.333 1.00 18.24 N
ATOM 6670 CA ASN A 436 -48.603 18.913 13.846 1.00 18.50 C
ATOM 6672 CB ASN A 436 -47.936 17.949 12.867 1.00 18.63 C
ATOM 6675 CG ASN A 436 -48.156 16.487 13.213 1.00 18.58 C
ATOM 6676 OD1 ASN A 436 -48.810 16.129 14.185 1.00 18.80 O
ATOM 6677 ND2 ASN A 436 -47.588 15.633 12.398 1.00 19.29 N
ATOM 6680 C ASN A 436 -47.975 18.755 15.210 1.00 18.83 C
ATOM 6681 O ASN A 436 -48.551 18.153 16.115 1.00 19.00 O
ATOM 6683 N ASP A 437 -46.763 19.255 15.351 1.00 19.29 N
ATOM 6684 CA ASP A 437 -46.097 19.179 16.634 1.00 19.62 C
ATOM 6686 CB ASP A 437 -44.615 19.522 16.510 1.00 19.45 C
ATOM 6689 CG ASP A 437 -43.849 18.480 15.734 1.00 19.36 C
ATOM 6690 OD1 ASP A 437 -44.491 17.586 15.158 1.00 19.89 O
ATOM 6691 OD2 ASP A 437 -42.608 18.543 15.699 1.00 19.86 O
ATOM 6692 C ASP A 437 -46.799 20.106 17.597 1.00 20.01 C
ATOM 6693 O ASP A 437 -46.916 19.790 18.779 1.00 20.30 O
ATOM 6695 N LEU A 438 -47.288 21.233 17.092 1.00 20.40 N
ATOM 6696 CA LEU A 438 -47.996 22.174 17.940 1.00 21.03 C
ATOM 6698 CB LEU A 438 -48.510 23.363 17.126 1.00 21.01 C
ATOM 6701 CG LEU A 438 -47.575 24.565 17.078 1.00 20.32 C
ATOM 6703 CD1 LEU A 438 -47.938 25.524 15.952 1.00 19.14 C
ATOM 6707 CD2 LEU A 438 -47.611 25.263 18.415 1.00 19.73 C
ATOM 6711 C LEU A 438 -49.153 21.496 18.679 1.00 21.81 C
ATOM 6712 O LEU A 438 -49.277 21.633 19.902 1.00 21.55 O
ATOM 6714 N ALA A 439 -49.973 20.754 17.932 1.00 22.76 N
ATOM 6715 CA ALA A 439 -51.138 20.055 18.486 1.00 23.58 C
ATOM 6717 CB ALA A 439 -51.905 19.360 17.386 1.00 23.57 C
ATOM 6721 C ALA A 439 -50.746 19.042 19.542 1.00 24.47 C
ATOM 6722 O ALA A 439 -51.386 18.951 20.575 1.00 24.63 O
ATOM 6724 N SER A 440 -49.685 18.291 19.276 1.00 25.78 N
ATOM 6725 CA SER A 440 -49.242 17.227 20.168 1.00 26.84 C
ATOM 6727 CB SER A 440 -48.566 16.130 19.353 1.00 26.92 C
ATOM 6730 OG SER A 440 -47.321 16.582 18.859 1.00 27.46 O

ATOM 6732 C SER A 440 -48.270 17.691 21.244 1.00 27.68 C
ATOM 6733 O SER A 440 -47.934 16.923 22.132 1.00 28.00 O
ATOM 6735 N ALA A 441 -47.822 18.935 21.174 1.00 28.83 N
ATOM 6736 CA ALA A 441 -46.760 19.419 22.056 1.00 29.73 C
ATOM 6738 CB ALA A 441 -46.529 20.910 21.841 1.00 29.84 C
ATOM 6742 C ALA A 441 -46.982 19.132 23.539 1.00 30.57 C
ATOM 6743 O ALA A 441 -46.306 18.274 24.093 1.00 30.50 O
ATOM 6745 N SER A 442 -47.929 19.827 24.172 1.00 31.90 N
ATOM 6746 CA SER A 442 -47.999 19.862 25.654 1.00 32.95 C
ATOM 6748 CB SER A 442 -49.043 20.870 26.169 1.00 32.91 C
ATOM 6751 OG SER A 442 -50.331 20.614 25.650 1.00 33.50 O
ATOM 6753 C SER A 442 -48.219 18.497 26.289 1.00 33.69 C
ATOM 6754 O SER A 442 -47.754 18.246 27.397 1.00 33.59 O
ATOM 6756 N ALA A 443 -48.922 17.623 25.578 1.00 34.93 N
ATOM 6757 CA ALA A 443 -49.050 16.231 25.980 1.00 35.81 C
ATOM 6759 CB ALA A 443 -49.981 15.488 25.030 1.00 35.72 C
ATOM 6763 C ALA A 443 -47.663 15.580 25.996 1.00 36.71 C
ATOM 6764 O ALA A 443 -47.198 15.115 27.047 1.00 36.94 O
ATOM 6766 N GLU A 444 -46.999 15.567 24.838 1.00 37.47 N
ATOM 6767 CA GLU A 444 -45.688 14.930 24.718 1.00 37.93 C
ATOM 6769 CB GLU A 444 -45.164 14.996 23.277 1.00 37.99 C
ATOM 6772 CG GLU A 444 -45.952 14.100 22.326 1.00 39.24 C
ATOM 6775 CD GLU A 444 -45.419 14.080 20.886 1.00 41.03 C
ATOM 6776 OE1 GLU A 444 -44.612 14.958 20.510 1.00 42.16 O
ATOM 6777 OE2 GLU A 444 -45.827 13.178 20.119 1.00 42.36 O
ATOM 6778 C GLU A 444 -44.694 15.534 25.708 1.00 38.09 C
ATOM 6779 O GLU A 444 -43.924 14.803 26.324 1.00 38.17 O
ATOM 6781 N ILE A 445 -44.739 16.851 25.889 1.00 38.41 N
ATOM 6782 CA ILE A 445 -43.829 17.530 26.814 1.00 38.75 C
ATOM 6784 CB ILE A 445 -43.802 19.065 26.587 1.00 38.69 C
ATOM 6786 CG1 ILE A 445 -43.314 19.396 25.170 1.00 38.18 C
ATOM 6789 CD1 ILE A 445 -43.702 20.775 24.712 1.00 37.58 C
ATOM 6793 CG2 ILE A 445 -42.909 19.753 27.617 1.00 38.26 C
ATOM 6797 C ILE A 445 -44.243 17.194 28.246 1.00 39.35 C
ATOM 6798 O ILE A 445 -45.039 17.901 28.870 1.00 39.44 O
ATOM 6800 N ALA A 446 -43.696 16.092 28.750 1.00 40.02 N
ATOM 6801 CA ALA A 446 -44.082 15.540 30.045 1.00 40.51 C
ATOM 6803 CB ALA A 446 -43.815 16.552 31.170 1.00 40.55 C
ATOM 6807 C ALA A 446 -45.559 15.130 30.029 1.00 40.86 C
ATOM 6808 O ALA A 446 -46.407 16.021 30.121 1.00 40.77 O
ATOM 6810 N ARG A 447 -45.925 13.842 29.899 1.00 41.31 N
ATOM 6811 CA ARG A 447 -45.072 12.633 29.691 1.00 41.58 C
ATOM 6813 CB ARG A 447 -45.272 12.092 28.258 1.00 41.84 C
ATOM 6816 CG ARG A 447 -46.667 11.495 27.991 1.00 42.69 C
ATOM 6819 CD ARG A 447 -46.778 10.901 26.582 1.00 43.92 C
ATOM 6822 NE ARG A 447 -47.764 11.589 25.744 1.00 45.34 N
ATOM 6824 CZ ARG A 447 -47.887 11.435 24.420 1.00 46.56 C
ATOM 6825 NH1 ARG A 447 -47.077 10.623 23.742 1.00 46.71 N
ATOM 6828 NH2 ARG A 447 -48.828 12.107 23.757 1.00 46.97 N
ATOM 6831 C ARG A 447 -43.581 12.728 30.054 1.00 41.38 C
ATOM 6832 O ARG A 447 -43.231 12.747 31.238 1.00 41.92 O
ATOM 6834 N GLY A 448 -42.710 12.736 29.051 1.00 40.88 N
ATOM 6835 CA GLY A 448 -41.312 13.128 29.234 1.00 40.44 C
ATOM 6838 C GLY A 448 -40.579 13.316 27.915 1.00 40.08 C
ATOM 6839 O GLY A 448 -39.364 13.488 27.901 1.00 40.05 O
ATOM 6841 N GLU A 449 -41.323 13.332 26.809 1.00 39.56 N
ATOM 6842 CA GLU A 449 -40.750 13.132 25.486 1.00 39.19 C
ATOM 6844 CB GLU A 449 -41.827 12.668 24.502 1.00 39.52 C
ATOM 6847 CG GLU A 449 -42.403 11.290 24.810 1.00 40.61 C
ATOM 6850 CD GLU A 449 -43.348 10.782 23.715 1.00 42.21 C

ATOM 6851 OE1 GLU A 449 -43.068 11.019 22.503 1.00 41.83 O
ATOM 6852 OE2 GLU A 449 -44.368 10.141 24.082 1.00 42.41 O
ATOM 6853 C GLU A 449 -40.037 14.365 24.921 1.00 38.34 C
ATOM 6854 O GLU A 449 -40.511 15.497 25.031 1.00 38.01 O
ATOM 6856 N THR A 450 -38.904 14.106 24.279 1.00 37.37 N
ATOM 6857 CA THR A 450 -38.047 15.138 23.726 1.00 36.37 C
ATOM 6859 CB THR A 450 -36.607 14.985 24.285 1.00 36.39 C
ATOM 6861 OG1 THR A 450 -35.846 16.153 23.982 1.00 36.63 O
ATOM 6863 CG2 THR A 450 -35.888 13.749 23.706 1.00 36.52 C
ATOM 6867 C THR A 450 -38.013 15.100 22.190 1.00 35.36 C
ATOM 6868 O THR A 450 -37.175 15.764 21.583 1.00 35.43 O
ATOM 6870 N ALA A 451 -38.917 14.338 21.563 1.00 33.98 N
ATOM 6871 CA ALA A 451 -38.920 14.182 20.096 1.00 32.81 C
ATOM 6873 CB ALA A 451 -39.030 12.708 19.708 1.00 32.99 C
ATOM 6877 C ALA A 451 -40.043 14.987 19.459 1.00 31.46 C
ATOM 6878 O ALA A 451 -41.050 14.432 18.996 1.00 31.06 O
ATOM 6880 N ASN A 452 -39.848 16.302 19.432 1.00 29.88 N
ATOM 6881 CA ASN A 452 -40.881 17.225 18.973 1.00 28.81 C
ATOM 6883 CB ASN A 452 -41.957 17.329 20.051 1.00 28.57 C
ATOM 6886 CG ASN A 452 -42.969 18.380 19.757 1.00 28.30 C
ATOM 6887 OD1 ASN A 452 -42.622 19.517 19.468 1.00 29.35 O
ATOM 6888 ND2 ASN A 452 -44.236 18.018 19.836 1.00 28.36 N
ATOM 6891 C ASN A 452 -40.285 18.590 18.641 1.00 27.76 C
ATOM 6892 O ASN A 452 -39.365 19.018 19.296 1.00 28.04 O
ATOM 6894 N SER A 453 -40.807 19.269 17.630 1.00 26.77 N
ATOM 6895 CA SER A 453 -40.226 20.533 17.182 1.00 26.38 C
ATOM 6897 CB SER A 453 -40.912 21.015 15.903 1.00 26.40 C
ATOM 6900 OG SER A 453 -40.796 20.044 14.876 1.00 25.79 O
ATOM 6902 C SER A 453 -40.253 21.643 18.233 1.00 26.12 C
ATOM 6903 O SER A 453 -39.280 22.361 18.385 1.00 25.97 O
ATOM 6905 N VAL A 454 -41.368 21.784 18.942 1.00 26.15 N
ATOM 6906 CA VAL A 454 -41.518 22.780 20.022 1.00 26.21 C
ATOM 6908 CB VAL A 454 -42.975 22.818 20.532 1.00 26.04 C
ATOM 6910 CG1 VAL A 454 -43.122 23.787 21.694 1.00 25.24 C
ATOM 6914 CG2 VAL A 454 -43.913 23.190 19.401 1.00 26.32 C
ATOM 6918 C VAL A 454 -40.617 22.451 21.211 1.00 26.63 C
ATOM 6919 O VAL A 454 -40.173 23.328 21.959 1.00 26.53 O
ATOM 6921 N SER A 455 -40.374 21.160 21.380 1.00 27.21 N
ATOM 6922 CA SER A 455 -39.541 20.651 22.437 1.00 27.60 C
ATOM 6924 CB SER A 455 -39.677 19.141 22.490 1.00 27.31 C
ATOM 6927 OG SER A 455 -38.922 18.625 23.545 1.00 28.13 O
ATOM 6929 C SER A 455 -38.096 21.045 22.181 1.00 28.29 C
ATOM 6930 O SER A 455 -37.445 21.628 23.043 1.00 28.63 O
ATOM 6932 N CYS A 456 -37.599 20.748 20.988 1.00 29.04 N
ATOM 6933 CA CYS A 456 -36.219 21.082 20.640 1.00 29.65 C
ATOM 6935 CB CYS A 456 -35.868 20.535 19.256 1.00 29.52 C
ATOM 6938 SG CYS A 456 -35.959 18.734 19.163 1.00 29.71 S
ATOM 6940 C CYS A 456 -35.955 22.589 20.710 1.00 30.26 C
ATOM 6941 O CYS A 456 -34.887 23.007 21.162 1.00 30.49 O
ATOM 6943 N TYR A 457 -36.924 23.399 20.283 1.00 30.88 N
ATOM 6944 CA TYR A 457 -36.767 24.850 20.308 1.00 31.45 C
ATOM 6946 CB TYR A 457 -37.967 25.557 19.648 1.00 31.55 C
ATOM 6949 CG TYR A 457 -37.691 26.991 19.178 1.00 32.09 C
ATOM 6950 CD1 TYR A 457 -37.378 27.269 17.843 1.00 31.69 C
ATOM 6952 CE1 TYR A 457 -37.128 28.569 17.418 1.00 31.73 C
ATOM 6954 CZ TYR A 457 -37.186 29.613 18.328 1.00 32.84 C
ATOM 6955 OH TYR A 457 -36.945 30.917 17.927 1.00 33.81 O
ATOM 6957 CE2 TYR A 457 -37.492 29.364 19.658 1.00 32.72 C
ATOM 6959 CD2 TYR A 457 -37.746 28.064 20.074 1.00 32.44 C
ATOM 6961 C TYR A 457 -36.571 25.295 21.758 1.00 31.99 C

ATOM 6962 O TYR A 457 -35.648 26.053 22.052 1.00 31.98 O
ATOM 6964 N MET A 458 -37.419 24.799 22.661 1.00 32.76 N
ATOM 6965 CA MET A 458 -37.211 24.987 24.105 1.00 33.37 C
ATOM 6967 CB MET A 458 -38.151 24.097 24.921 1.00 33.43 C
ATOM 6970 CG MET A 458 -39.570 24.593 25.059 1.00 33.70 C
ATOM 6973 SD MET A 458 -40.641 23.312 25.737 1.00 34.59 S
ATOM 6974 CE MET A 458 -39.709 22.763 27.179 1.00 34.71 C
ATOM 6978 C MET A 458 -35.784 24.641 24.517 1.00 33.78 C
ATOM 6979 O MET A 458 -35.101 25.437 25.151 1.00 33.73 O
ATOM 6981 N ARG A 459 -35.347 23.445 24.145 1.00 34.46 N
ATOM 6982 CA ARG A 459 -34.051 22.926 24.581 1.00 35.15 C
ATOM 6984 CB ARG A 459 -33.876 21.447 24.171 1.00 35.68 C
ATOM 6987 CG ARG A 459 -32.494 20.864 24.500 1.00 37.23 C
ATOM 6990 CD ARG A 459 -32.491 19.345 24.752 1.00 39.80 C
ATOM 6993 NE ARG A 459 -33.140 18.538 23.711 1.00 42.88 N
ATOM 6995 CZ ARG A 459 -32.704 18.407 22.453 1.00 45.43 C
ATOM 6996 NH1 ARG A 459 -31.615 19.062 22.035 1.00 47.50 N
ATOM 6999 NH2 ARG A 459 -33.366 17.629 21.595 1.00 44.77 N
ATOM 7002 C ARG A 459 -32.878 23.749 24.072 1.00 34.92 C
ATOM 7003 O ARG A 459 -32.007 24.109 24.849 1.00 35.06 O
ATOM 7005 N THR A 460 -32.854 24.047 22.778 1.00 34.96 N
ATOM 7006 CA THR A 460 -31.674 24.678 22.163 1.00 34.91 C
ATOM 7008 CB THR A 460 -31.494 24.263 20.680 1.00 34.88 C
ATOM 7010 OG1 THR A 460 -32.330 25.067 19.841 1.00 34.39 O
ATOM 7012 CG2 THR A 460 -31.825 22.776 20.488 1.00 35.44 C
ATOM 7016 C THR A 460 -31.672 26.210 22.258 1.00 34.78 C
ATOM 7017 O THR A 460 -30.673 26.837 21.911 1.00 34.92 O
ATOM 7019 N LYS A 461 -32.781 26.806 22.701 1.00 34.41 N
ATOM 7020 CA LYS A 461 -32.811 28.231 23.039 1.00 34.25 C
ATOM 7022 CB LYS A 461 -33.921 28.947 22.265 1.00 34.56 C
ATOM 7025 CG LYS A 461 -33.717 28.986 20.750 1.00 35.84 C
ATOM 7028 CD LYS A 461 -32.519 29.859 20.347 1.00 37.64 C
ATOM 7031 CE LYS A 461 -32.232 29.804 18.838 1.00 38.44 C
ATOM 7034 NZ LYS A 461 -33.141 30.671 18.027 1.00 38.31 N
ATOM 7038 C LYS A 461 -32.974 28.476 24.544 1.00 33.73 C
ATOM 7039 O LYS A 461 -32.994 29.626 24.983 1.00 33.23 O
ATOM 7041 N GLY A 462 -33.078 27.395 25.321 1.00 33.48 N
ATOM 7042 CA GLY A 462 -33.173 27.464 26.784 1.00 33.23 C
ATOM 7045 C GLY A 462 -34.332 28.320 27.239 1.00 32.95 C
ATOM 7046 O GLY A 462 -34.144 29.258 28.004 1.00 33.17 O
ATOM 7048 N ILE A 463 -35.528 28.000 26.757 1.00 32.52 N
ATOM 7049 CA ILE A 463 -36.694 28.843 26.971 1.00 32.32 C
ATOM 7051 CB ILE A 463 -37.006 29.724 25.734 1.00 32.47 C
ATOM 7053 CG1 ILE A 463 -37.152 28.866 24.463 1.00 32.41 C
ATOM 7056 CD1 ILE A 463 -37.359 29.675 23.191 1.00 32.02 C
ATOM 7060 CG2 ILE A 463 -35.937 30.810 25.571 1.00 32.44 C
ATOM 7064 C ILE A 463 -37.902 28.006 27.309 1.00 32.15 C
ATOM 7065 O ILE A 463 -37.886 26.799 27.145 1.00 32.01 O
ATOM 7067 N SER A 464 -38.950 28.670 27.780 1.00 32.27 N
ATOM 7068 CA SER A 464 -40.163 28.006 28.239 1.00 32.52 C
ATOM 7070 CB SER A 464 -40.964 28.974 29.110 1.00 32.65 C
ATOM 7073 OG SER A 464 -41.112 30.224 28.457 1.00 32.69 O
ATOM 7075 C SER A 464 -41.036 27.522 27.079 1.00 32.53 C
ATOM 7076 O SER A 464 -40.968 28.069 25.986 1.00 32.62 O
ATOM 7078 N GLU A 465 -41.857 26.500 27.332 1.00 32.47 N
ATOM 7079 CA GLU A 465 -42.836 26.010 26.353 1.00 32.33 C
ATOM 7081 CB GLU A 465 -43.689 24.868 26.935 1.00 32.34 C
ATOM 7084 CG GLU A 465 -44.756 24.312 25.974 1.00 32.37 C
ATOM 7087 CD GLU A 465 -45.675 23.279 26.611 1.00 32.47 C
ATOM 7088 OE1 GLU A 465 -45.297 22.659 27.630 1.00 31.63 O

ATOM 7089 OE2 GLU A 465 -46.785 23.086 26.074 1.00 32.77 O
ATOM 7090 C GLU A 465 -43.758 27.124 25.864 1.00 32.33 C
ATOM 7091 O GLU A 465 -44.078 27.183 24.676 1.00 32.60 O
ATOM 7093 N GLU A 466 -44.196 28.001 26.767 1.00 32.08 N
ATOM 7094 CA GLU A 466 -45.085 29.097 26.380 1.00 31.79 C
ATOM 7096 CB GLU A 466 -45.606 29.832 27.624 1.00 31.91 C
ATOM 7099 CG GLU A 466 -46.503 31.041 27.304 1.00 32.82 C
ATOM 7102 CD GLU A 466 -47.426 31.472 28.452 1.00 33.67 C
ATOM 7103 OE1 GLU A 466 -47.519 30.756 29.478 1.00 35.09 O
ATOM 7104 OE2 GLU A 466 -48.077 32.533 28.312 1.00 33.12 O
ATOM 7105 C GLU A 466 -44.392 30.052 25.386 1.00 31.13 C
ATOM 7106 O GLU A 466 -45.032 30.603 24.492 1.00 30.87 O
ATOM 7108 N LEU A 467 -43.077 30.194 25.531 1.00 30.57 N
ATOM 7109 CA LEU A 467 -42.265 31.102 24.708 1.00 30.18 C
ATOM 7111 CB LEU A 467 -41.055 31.604 25.524 1.00 30.38 C
ATOM 7114 CG LEU A 467 -40.674 33.087 25.463 1.00 30.39 C
ATOM 7116 CD1 LEU A 467 -41.608 33.900 26.362 1.00 30.23 C
ATOM 7120 CD2 LEU A 467 -39.214 33.308 25.872 1.00 30.31 C
ATOM 7124 C LEU A 467 -41.773 30.401 23.439 1.00 29.47 C
ATOM 7125 O LEU A 467 -41.660 31.010 22.382 1.00 29.17 O
ATOM 7127 N ALA A 468 -41.445 29.121 23.562 1.00 28.93 N
ATOM 7128 CA ALA A 468 -41.095 28.310 22.404 1.00 28.45 C
ATOM 7130 CB ALA A 468 -40.613 26.935 22.830 1.00 28.10 C
ATOM 7134 C ALA A 468 -42.306 28.193 21.494 1.00 28.08 C
ATOM 7135 O ALA A 468 -42.179 28.321 20.285 1.00 28.24 O
ATOM 7137 N THR A 469 -43.479 27.964 22.080 1.00 27.58 N
ATOM 7138 CA THR A 469 -44.719 27.870 21.322 1.00 27.26 C
ATOM 7140 CB THR A 469 -45.928 27.710 22.261 1.00 27.28 C
ATOM 7142 OG1 THR A 469 -46.063 26.330 22.627 1.00 27.55 O
ATOM 7144 CG2 THR A 469 -47.222 28.185 21.597 1.00 27.34 C
ATOM 7148 C THR A 469 -44.916 29.099 20.449 1.00 27.10 C
ATOM 7149 O THR A 469 -45.176 28.989 19.250 1.00 27.11 O
ATOM 7151 N GLU A 470 -44.774 30.267 21.061 1.00 26.88 N
ATOM 7152 CA GLU A 470 -44.944 31.542 20.376 1.00 26.84 C
ATOM 7154 CB GLU A 470 -44.832 32.663 21.400 1.00 27.07 C
ATOM 7157 CG GLU A 470 -45.357 34.003 20.958 1.00 28.47 C
ATOM 7160 CD GLU A 470 -45.140 35.087 22.008 1.00 30.51 C
ATOM 7161 OE1 GLU A 470 -45.029 34.775 23.221 1.00 31.53 O
ATOM 7162 OE2 GLU A 470 -45.083 36.269 21.608 1.00 32.59 O
ATOM 7163 C GLU A 470 -43.926 31.750 19.239 1.00 26.48 C
ATOM 7164 O GLU A 470 -44.261 32.296 18.184 1.00 26.29 O
ATOM 7166 N SER A 471 -42.686 31.316 19.452 1.00 26.12 N
ATOM 7167 CA SER A 471 -41.660 31.386 18.408 1.00 25.85 C
ATOM 7169 CB SER A 471 -40.296 30.933 18.941 1.00 25.96 C
ATOM 7172 OG SER A 471 -39.656 31.939 19.711 1.00 26.53 O
ATOM 7174 C SER A 471 -42.036 30.529 17.208 1.00 25.35 C
ATOM 7175 O SER A 471 -41.761 30.899 16.067 1.00 25.43 O
ATOM 7177 N VAL A 472 -42.653 29.381 17.482 1.00 24.95 N
ATOM 7178 CA VAL A 472 -43.097 28.451 16.438 1.00 24.65 C
ATOM 7180 CB VAL A 472 -43.485 27.055 17.024 1.00 24.57 C
ATOM 7182 CG1 VAL A 472 -44.257 26.222 16.016 1.00 23.23 C
ATOM 7186 CG2 VAL A 472 -42.232 26.309 17.494 1.00 23.83 C
ATOM 7190 C VAL A 472 -44.252 29.039 15.631 1.00 24.71 C
ATOM 7191 O VAL A 472 -44.369 28.776 14.440 1.00 24.63 O
ATOM 7193 N MET A 473 -45.073 29.866 16.269 1.00 24.79 N
ATOM 7194 CA MET A 473 -46.143 30.591 15.565 1.00 24.94 C
ATOM 7196 CB MET A 473 -47.059 31.266 16.576 1.00 25.11 C
ATOM 7199 CG MET A 473 -47.683 30.335 17.560 1.00 25.11 C
ATOM 7202 SD MET A 473 -48.967 29.391 16.780 1.00 25.35 S
ATOM 7203 CE MET A 473 -50.064 29.163 18.189 1.00 26.11 C

ATOM 7207 C MET A 473 -45.613 31.672 14.605 1.00 24.86 C
ATOM 7208 O MET A 473 -46.132 31.849 13.513 1.00 24.57 O
ATOM 7210 N ASN A 474 -44.589 32.405 15.032 1.00 24.89 N
ATOM 7211 CA ASN A 474 -43.951 33.383 14.166 1.00 25.00 C
ATOM 7213 CB ASN A 474 -43.009 34.278 14.966 1.00 25.12 C
ATOM 7216 CG ASN A 474 -43.700 34.966 16.127 1.00 25.77 C
ATOM 7217 OD1 ASN A 474 -43.058 35.312 17.114 1.00 26.96 O
ATOM 7218 ND2 ASN A 474 -45.015 35.163 16.021 1.00 26.31 N
ATOM 7221 C ASN A 474 -43.195 32.707 13.024 1.00 24.84 C
ATOM 7222 O ASN A 474 -42.979 33.313 11.973 1.00 25.07 O
ATOM 7224 N LEU A 475 -42.792 31.455 13.227 1.00 24.46 N
ATOM 7225 CA LEU A 475 -42.218 30.671 12.142 1.00 24.06 C
ATOM 7227 CB LEU A 475 -41.596 29.367 12.653 1.00 24.27 C
ATOM 7230 CG LEU A 475 -40.307 29.072 11.886 1.00 25.08 C
ATOM 7232 CD1 LEU A 475 -39.207 30.000 12.419 1.00 25.89 C
ATOM 7236 CD2 LEU A 475 -39.887 27.622 11.985 1.00 25.33 C
ATOM 7240 C LEU A 475 -43.278 30.365 11.085 1.00 23.26 C
ATOM 7241 O LEU A 475 -43.018 30.479 9.884 1.00 22.90 O
ATOM 7243 N ILE A 476 -44.471 29.978 11.534 1.00 22.53 N
ATOM 7244 CA ILE A 476 -45.544 29.632 10.606 1.00 21.93 C
ATOM 7246 CB ILE A 476 -46.773 29.017 11.308 1.00 21.58 C
ATOM 7248 CG1 ILE A 476 -46.499 27.550 11.664 1.00 21.32 C
ATOM 7251 CD1 ILE A 476 -47.552 26.902 12.598 1.00 20.33 C
ATOM 7255 CG2 ILE A 476 -47.994 29.104 10.428 1.00 20.46 C
ATOM 7259 C ILE A 476 -45.926 30.887 9.853 1.00 22.07 C
ATOM 7260 O ILE A 476 -46.007 30.869 8.626 1.00 22.47 O
ATOM 7262 N ASP A 477 -46.122 31.982 10.584 1.00 21.81 N
ATOM 7263 CA ASP A 477 -46.483 33.245 9.970 1.00 21.56 C
ATOM 7265 CB ASP A 477 -46.643 34.337 11.032 1.00 21.89 C
ATOM 7268 CG ASP A 477 -47.962 34.217 11.817 1.00 23.39 C
ATOM 7269 OD1 ASP A 477 -48.854 33.441 11.375 1.00 24.41 O
ATOM 7270 OD2 ASP A 477 -48.103 34.902 12.875 1.00 23.80 O
ATOM 7271 C ASP A 477 -45.425 33.626 8.947 1.00 21.06 C
ATOM 7272 O ASP A 477 -45.759 33.913 7.795 1.00 20.78 O
ATOM 7274 N GLU A 478 -44.156 33.591 9.361 1.00 20.63 N
ATOM 7275 CA GLU A 478 -43.027 33.919 8.467 1.00 20.45 C
ATOM 7277 CB GLU A 478 -41.680 33.793 9.200 1.00 20.66 C
ATOM 7280 CG GLU A 478 -40.422 34.044 8.339 1.00 22.27 C
ATOM 7283 CD GLU A 478 -39.107 33.579 9.018 1.00 24.72 C
ATOM 7284 OE1 GLU A 478 -38.553 34.367 9.817 1.00 26.19 O
ATOM 7285 OE2 GLU A 478 -38.619 32.442 8.745 1.00 25.66 O
ATOM 7286 C GLU A 478 -43.041 33.042 7.217 1.00 19.54 C
ATOM 7287 O GLU A 478 -42.879 33.544 6.102 1.00 19.02 O
ATOM 7289 N THR A 479 -43.250 31.743 7.413 1.00 18.76 N
ATOM 7290 CA THR A 479 -43.358 30.808 6.294 1.00 18.45 C
ATOM 7292 CB THR A 479 -43.503 29.339 6.774 1.00 18.26 C
ATOM 7294 OG1 THR A 479 -42.334 28.955 7.494 1.00 17.30 O
ATOM 7296 CG2 THR A 479 -43.669 28.394 5.592 1.00 17.93 C
ATOM 7300 C THR A 479 -44.504 31.173 5.314 1.00 18.39 C
ATOM 7301 O THR A 479 -44.280 31.200 4.103 1.00 18.58 O
ATOM 7303 N TRP A 480 -45.709 31.457 5.818 1.00 17.85 N
ATOM 7304 CA TRP A 480 -46.801 31.909 4.942 1.00 17.44 C
ATOM 7306 CB TRP A 480 -48.086 32.225 5.728 1.00 17.67 C
ATOM 7309 CG TRP A 480 -48.969 31.042 5.888 1.00 17.09 C
ATOM 7310 CD1 TRP A 480 -48.996 30.195 6.936 1.00 16.76 C
ATOM 7312 NE1 TRP A 480 -49.914 29.216 6.724 1.00 17.08 N
ATOM 7314 CE2 TRP A 480 -50.501 29.410 5.507 1.00 17.86 C
ATOM 7315 CD2 TRP A 480 -49.930 30.559 4.954 1.00 17.15 C
ATOM 7316 CE3 TRP A 480 -50.356 30.980 3.696 1.00 18.31 C
ATOM 7318 CZ3 TRP A 480 -51.337 30.244 3.039 1.00 19.10 C

ATOM 7320 CH2 TRP A 480 -51.897 29.107 3.622 1.00 18.83 C
ATOM 7322 CZ2 TRP A 480 -51.493 28.673 4.855 1.00 18.86 C
ATOM 7324 C TRP A 480 -46.426 33.124 4.097 1.00 17.10 C
ATOM 7325 O TRP A 480 -46.824 33.215 2.943 1.00 17.22 O
ATOM 7327 N LYS A 481 -45.675 34.062 4.659 1.00 16.60 N
ATOM 7328 CA LYS A 481 -45.275 35.215 3.886 1.00 16.23 C
ATOM 7330 CB LYS A 481 -44.566 36.243 4.747 1.00 16.42 C
ATOM 7333 CG LYS A 481 -45.417 36.954 5.769 1.00 16.42 C
ATOM 7336 CD LYS A 481 -44.555 37.979 6.505 1.00 16.40 C
ATOM 7339 CE LYS A 481 -45.199 38.504 7.782 1.00 16.66 C
ATOM 7342 NZ LYS A 481 -44.184 38.717 8.846 1.00 16.72 N
ATOM 7346 C LYS A 481 -44.357 34.782 2.767 1.00 15.94 C
ATOM 7347 O LYS A 481 -44.451 35.291 1.674 1.00 16.09 O
ATOM 7349 N LYS A 482 -43.461 33.849 3.034 1.00 15.98 N
ATOM 7350 CA LYS A 482 -42.559 33.369 1.996 1.00 16.30 C
ATOM 7352 CB LYS A 482 -41.409 32.563 2.594 1.00 16.51 C
ATOM 7355 CG LYS A 482 -40.354 33.445 3.286 1.00 17.46 C
ATOM 7358 CD LYS A 482 -39.486 32.647 4.241 1.00 18.48 C
ATOM 7361 CE LYS A 482 -38.625 33.548 5.096 1.00 18.94 C
ATOM 7364 NZ LYS A 482 -37.865 32.773 6.129 1.00 20.40 N
ATOM 7368 C LYS A 482 -43.296 32.561 .938 1.00 16.40 C
ATOM 7369 O LYS A 482 -42.941 32.614 -.229 1.00 16.85 O
ATOM 7371 N MET A 483 -44.328 31.824 1.332 1.00 16.57 N
ATOM 7372 CA MET A 483 -45.149 31.100 .366 1.00 16.67 C
ATOM 7374 CB MET A 483 -46.128 30.156 1.057 1.00 16.55 C
ATOM 7377 CG MET A 483 -45.496 28.923 1.675 1.00 16.50 C
ATOM 7380 SD MET A 483 -46.715 27.684 2.194 1.00 17.39 S
ATOM 7381 CE MET A 483 -47.937 28.704 3.025 1.00 17.27 C
ATOM 7385 C MET A 483 -45.928 32.069 -.495 1.00 17.06 C
ATOM 7386 O MET A 483 -46.027 31.867 -1.688 1.00 17.17 O
ATOM 7388 N ASN A 484 -46.483 33.110 .118 1.00 17.72 N
ATOM 7389 CA ASN A 484 -47.305 34.093 -.587 1.00 18.35 C
ATOM 7391 CB ASN A 484 -47.861 35.129 .397 1.00 18.26 C
ATOM 7394 CG ASN A 484 -48.994 34.601 1.248 1.00 17.35 C
ATOM 7395 OD1 ASN A 484 -49.597 33.577 .934 1.00 17.54 O
ATOM 7396 ND2 ASN A 484 -49.304 35.317 2.331 1.00 14.10 N
ATOM 7399 C ASN A 484 -46.541 34.839 -1.677 1.00 19.51 C
ATOM 7400 O ASN A 484 -47.123 35.250 -2.685 1.00 19.49 O
ATOM 7402 N LYS A 485 -45.243 35.035 -1.463 1.00 20.86 N
ATOM 7403 CA LYS A 485 -44.394 35.681 -2.456 1.00 22.12 C
ATOM 7405 CB LYS A 485 -43.070 36.092 -1.823 1.00 22.08 C
ATOM 7408 CG LYS A 485 -42.229 37.060 -2.641 1.00 23.09 C
ATOM 7411 CD LYS A 485 -40.783 37.072 -2.109 1.00 25.38 C
ATOM 7414 CE LYS A 485 -40.098 38.460 -2.135 1.00 26.12 C
ATOM 7417 NZ LYS A 485 -38.943 38.555 -3.086 1.00 26.61 N
ATOM 7421 C LYS A 485 -44.164 34.743 -3.656 1.00 23.36 C
ATOM 7422 O LYS A 485 -44.120 35.191 -4.802 1.00 23.00 O
ATOM 7424 N GLU A 486 -44.027 33.442 -3.400 1.00 24.99 N
ATOM 7425 CA GLU A 486 -43.902 32.479 -4.491 1.00 26.35 C
ATOM 7427 CB GLU A 486 -43.627 31.061 -3.978 1.00 26.55 C
ATOM 7430 CG GLU A 486 -42.985 30.130 -5.033 1.00 28.29 C
ATOM 7433 CD GLU A 486 -41.466 30.324 -5.191 1.00 31.11 C
ATOM 7434 OE1 GLU A 486 -40.981 30.466 -6.341 1.00 32.07 O
ATOM 7435 OE2 GLU A 486 -40.744 30.335 -4.159 1.00 33.04 O
ATOM 7436 C GLU A 486 -45.157 32.501 -5.362 1.00 27.13 C
ATOM 7437 O GLU A 486 -45.064 32.618 -6.583 1.00 27.57 O
ATOM 7439 N LYS A 487 -46.325 32.422 -4.739 1.00 28.12 N
ATOM 7440 CA LYS A 487 -47.582 32.378 -5.485 1.00 29.12 C
ATOM 7442 CB LYS A 487 -48.788 32.260 -4.542 1.00 29.21 C
ATOM 7445 CG LYS A 487 -50.167 32.296 -5.235 1.00 28.57 C

ATOM 7448 CD LYS A 487 -50.403 31.040 -6.036 1.00 27.91 C
ATOM 7451 CE LYS A 487 -51.615 31.141 -6.936 1.00 28.38 C
ATOM 7454 NZ LYS A 487 -52.874 31.460 -6.211 1.00 28.03 N
ATOM 7458 C LYS A 487 -47.756 33.603 -6.352 1.00 30.18 C
ATOM 7459 O LYS A 487 -48.308 33.514 -7.446 1.00 30.21 O
ATOM 7461 N LEU A 488 -47.295 34.743 -5.844 1.00 31.64 N
ATOM 7462 CA LEU A 488 -47.422 36.026 -6.532 1.00 32.65 C
ATOM 7464 CB LEU A 488 -47.426 37.144 -5.494 1.00 32.43 C
ATOM 7467 CG LEU A 488 -48.091 38.446 -5.907 1.00 32.50 C
ATOM 7469 CD1 LEU A 488 -49.593 38.288 -5.943 1.00 32.66 C
ATOM 7473 CD2 LEU A 488 -47.707 39.554 -4.943 1.00 33.38 C
ATOM 7477 C LEU A 488 -46.286 36.242 -7.542 1.00 33.99 C
ATOM 7478 O LEU A 488 -46.536 36.539 -8.705 1.00 33.72 O
ATOM 7480 N GLY A 489 -45.046 36.045 -7.091 1.00 35.85 N
ATOM 7481 CA GLY A 489 -43.845 36.361 -7.874 1.00 37.37 C
ATOM 7484 C GLY A 489 -43.278 35.221 -8.709 1.00 38.76 C
ATOM 7485 O GLY A 489 -42.414 34.467 -8.250 1.00 39.06 O
ATOM 7487 N GLY A 490 -43.760 35.119 -9.947 1.00 40.26 N
ATOM 7488 CA GLY A 490 -43.285 34.130 -10.927 1.00 41.03 C
ATOM 7491 C GLY A 490 -42.193 33.194 -10.436 1.00 41.61 C
ATOM 7492 O GLY A 490 -41.010 33.547 -10.423 1.00 41.62 O
ATOM 7494 N SER A 491 -42.590 31.996 -10.023 1.00 42.17 N
ATOM 7495 CA SER A 491 -41.619 30.962 -9.662 1.00 42.54 C
ATOM 7497 CB SER A 491 -42.279 29.909 -8.741 1.00 42.63 C
ATOM 7500 OG SER A 491 -43.451 29.345 -9.294 1.00 42.44 O
ATOM 7502 C SER A 491 -41.032 30.349 -10.952 1.00 42.50 C
ATOM 7503 O SER A 491 -41.117 30.961 -12.030 1.00 42.57 O
ATOM 7505 N LEU A 492 -40.405 29.177 -10.843 1.00 42.18 N
ATOM 7506 CA LEU A 492 -40.185 28.333 -12.021 1.00 41.96 C
ATOM 7508 CB LEU A 492 -39.110 27.270 -11.782 1.00 42.39 C
ATOM 7511 CG LEU A 492 -37.695 27.671 -11.353 1.00 44.21 C
ATOM 7513 CD1 LEU A 492 -36.783 26.438 -11.498 1.00 45.26 C
ATOM 7517 CD2 LEU A 492 -37.120 28.896 -12.129 1.00 45.51 C
ATOM 7521 C LEU A 492 -41.479 27.610 -12.356 1.00 40.88 C
ATOM 7522 O LEU A 492 -41.713 27.244 -13.504 1.00 40.78 O
ATOM 7524 N PHE A 493 -42.308 27.409 -11.339 1.00 39.61 N
ATOM 7525 CA PHE A 493 -43.500 26.595 -11.460 1.00 38.85 C
ATOM 7527 CB PHE A 493 -43.783 25.911 -10.124 1.00 38.62 C
ATOM 7530 CG PHE A 493 -42.725 24.937 -9.713 1.00 37.16 C
ATOM 7531 CD1 PHE A 493 -42.901 23.587 -9.916 1.00 35.26 C
ATOM 7533 CE1 PHE A 493 -41.934 22.698 -9.546 1.00 34.86 C
ATOM 7535 CZ PHE A 493 -40.769 23.143 -8.966 1.00 35.09 C
ATOM 7537 CE2 PHE A 493 -40.574 24.482 -8.759 1.00 35.45 C
ATOM 7539 CD2 PHE A 493 -41.549 25.374 -9.130 1.00 36.36 C
ATOM 7541 C PHE A 493 -44.714 27.412 -11.890 1.00 38.62 C
ATOM 7542 O PHE A 493 -44.756 28.621 -11.702 1.00 38.86 O
ATOM 7544 N ALA A 494 -45.698 26.731 -12.469 1.00 38.32 N
ATOM 7545 CA ALA A 494 -46.977 27.337 -12.843 1.00 38.09 C
ATOM 7547 CB ALA A 494 -47.658 26.486 -13.906 1.00 38.17 C
ATOM 7551 C ALA A 494 -47.891 27.479 -11.623 1.00 37.76 C
ATOM 7552 O ALA A 494 -48.039 26.541 -10.845 1.00 38.15 O
ATOM 7554 N LYS A 495 -48.541 28.629 -11.484 1.00 37.15 N
ATOM 7555 CA LYS A 495 -49.321 28.947 -10.270 1.00 36.53 C
ATOM 7557 CB LYS A 495 -50.116 30.258 -10.477 1.00 36.90 C
ATOM 7560 CG LYS A 495 -49.235 31.524 -10.582 1.00 37.72 C
ATOM 7563 CD LYS A 495 -50.061 32.826 -10.585 1.00 38.87 C
ATOM 7566 CE LYS A 495 -49.140 34.065 -10.665 1.00 39.78 C
ATOM 7569 NZ LYS A 495 -49.786 35.369 -10.282 1.00 39.78 N
ATOM 7573 C LYS A 495 -50.238 27.809 -9.724 1.00 35.25 C
ATOM 7574 O LYS A 495 -50.261 27.563 -8.523 1.00 34.91 O

```
ATOM  7576  N   PRO A 496     -50.978  27.107 -10.599  1.00 33.76           N
ATOM  7577  CA  PRO A 496     -51.846  26.015 -10.162  1.00 32.74           C
ATOM  7579  CB  PRO A 496     -52.222  25.340 -11.474  1.00 32.99           C
ATOM  7582  CG  PRO A 496     -52.337  26.470 -12.385  1.00 33.75           C
ATOM  7585  CD  PRO A 496     -51.196  27.400 -12.022  1.00 33.83           C
ATOM  7588  C   PRO A 496     -51.194  24.998  -9.267  1.00 31.24           C
ATOM  7589  O   PRO A 496     -51.822  24.522  -8.331  1.00 31.54           O
ATOM  7590  N   PHE A 497     -49.954  24.642  -9.566  1.00 29.40           N
ATOM  7591  CA  PHE A 497     -49.229  23.726  -8.708  1.00 27.76           C
ATOM  7593  CB  PHE A 497     -48.162  22.948  -9.474  1.00 27.62           C
ATOM  7596  CG  PHE A 497     -47.351  22.040  -8.597  1.00 26.33           C
ATOM  7597  CD1 PHE A 497     -47.944  20.969  -7.974  1.00 24.96           C
ATOM  7599  CE1 PHE A 497     -47.218  20.151  -7.156  1.00 25.04           C
ATOM  7601  CZ  PHE A 497     -45.875  20.396  -6.940  1.00 24.79           C
ATOM  7603  CE2 PHE A 497     -45.274  21.457  -7.549  1.00 24.73           C
ATOM  7605  CD2 PHE A 497     -46.010  22.282  -8.366  1.00 25.48           C
ATOM  7607  C   PHE A 497     -48.592  24.407  -7.494  1.00 26.59           C
ATOM  7608  O   PHE A 497     -48.361  23.738  -6.500  1.00 26.77           O
ATOM  7610  N   VAL A 498     -48.291  25.704  -7.535  1.00 24.83           N
ATOM  7611  CA  VAL A 498     -47.869  26.338  -6.289  1.00 23.86           C
ATOM  7613  CB  VAL A 498     -47.181  27.722  -6.455  1.00 23.47           C
ATOM  7615  CG1 VAL A 498     -48.163  28.755  -6.759  1.00 24.57           C
ATOM  7619  CG2 VAL A 498     -46.151  27.690  -7.551  1.00 23.54           C
ATOM  7623  C   VAL A 498     -49.094  26.396  -5.355  1.00 22.97           C
ATOM  7624  O   VAL A 498     -48.978  26.130  -4.161  1.00 23.39           O
ATOM  7626  N   GLU A 499     -50.268  26.687  -5.903  1.00 21.68           N
ATOM  7627  CA  GLU A 499     -51.473  26.719  -5.106  1.00 20.84           C
ATOM  7629  CB  GLU A 499     -52.677  27.136  -5.930  1.00 20.99           C
ATOM  7632  CG  GLU A 499     -53.957  27.352  -5.099  1.00 21.25           C
ATOM  7635  CD  GLU A 499     -53.930  28.630  -4.265  1.00 21.77           C
ATOM  7636  OE1 GLU A 499     -52.982  29.448  -4.383  1.00 20.74           O
ATOM  7637  OE2 GLU A 499     -54.876  28.812  -3.476  1.00 22.76           O
ATOM  7638  C   GLU A 499     -51.766  25.371  -4.497  1.00 20.35           C
ATOM  7639  O   GLU A 499     -52.137  25.308  -3.318  1.00 20.78           O
ATOM  7641  N   THR A 500     -51.629  24.286  -5.264  1.00 19.40           N
ATOM  7642  CA  THR A 500     -51.894  22.970  -4.667  1.00 18.94           C
ATOM  7644  CB  THR A 500     -51.993  21.782  -5.683  1.00 18.96           C
ATOM  7646  OG1 THR A 500     -50.708  21.475  -6.202  1.00 19.44           O
ATOM  7648  CG2 THR A 500     -52.991  22.071  -6.835  1.00 18.75           C
ATOM  7652  C   THR A 500     -50.895  22.674  -3.526  1.00 18.20           C
ATOM  7653  O   THR A 500     -51.280  22.100  -2.519  1.00 17.68           O
ATOM  7655  N   ALA A 501     -49.646  23.119  -3.666  1.00 17.49           N
ATOM  7656  CA  ALA A 501     -48.663  23.021  -2.593  1.00 17.18           C
ATOM  7658  CB  ALA A 501     -47.348  23.563  -3.051  1.00 16.98           C
ATOM  7662  C   ALA A 501     -49.120  23.770  -1.338  1.00 17.38           C
ATOM  7663  O   ALA A 501     -49.098  23.219   -.230  1.00 17.45           O
ATOM  7665  N   ILE A 502     -49.517  25.031  -1.508  1.00 17.29           N
ATOM  7666  CA  ILE A 502     -49.971  25.857   -.386  1.00 17.07           C
ATOM  7668  CB  ILE A 502     -50.353  27.304   -.846  1.00 17.09           C
ATOM  7670  CG1 ILE A 502     -49.092  28.069  -1.286  1.00 17.17           C
ATOM  7673  CD1 ILE A 502     -49.345  29.345  -2.116  1.00 16.25           C
ATOM  7677  CG2 ILE A 502     -51.110  28.076   .265  1.00 16.14           C
ATOM  7681  C   ILE A 502     -51.155  25.168   .285  1.00 17.24           C
ATOM  7682  O   ILE A 502     -51.265  25.163  1.516  1.00 17.03           O
ATOM  7684  N   ASN A 503     -52.022  24.559   -.522  1.00 17.32           N
ATOM  7685  CA  ASN A 503     -53.167  23.823   .022  1.00 17.75           C
ATOM  7687  CB  ASN A 503     -53.986  23.221  -1.121  1.00 17.70           C
ATOM  7690  CG  ASN A 503     -54.760  24.261  -1.888  1.00 18.41           C
ATOM  7691  OD1 ASN A 503     -55.058  25.334  -1.382  1.00 18.94           O
ATOM  7692  ND2 ASN A 503     -55.107  23.939  -3.119  1.00 20.42           N
```

ATOM 7695 C ASN A 503 -52.803 22.727 1.075 1.00 17.74 C
ATOM 7696 O ASN A 503 -53.619 22.387 1.949 1.00 17.96 O
ATOM 7698 N LEU A 504 -51.589 22.185 .993 1.00 17.23 N
ATOM 7699 CA LEU A 504 -51.105 21.249 1.994 1.00 17.10 C
ATOM 7701 CB LEU A 504 -49.745 20.686 1.583 1.00 17.28 C
ATOM 7704 CG LEU A 504 -49.213 19.528 2.426 1.00 17.29 C
ATOM 7706 CD1 LEU A 504 -49.570 18.196 1.762 1.00 17.22 C
ATOM 7710 CD2 LEU A 504 -47.708 19.686 2.616 1.00 16.83 C
ATOM 7714 C LEU A 504 -50.971 21.939 3.347 1.00 16.97 C
ATOM 7715 O LEU A 504 -51.237 21.330 4.379 1.00 16.84 O
ATOM 7717 N ALA A 505 -50.535 23.201 3.330 1.00 16.90 N
ATOM 7718 CA ALA A 505 -50.433 24.015 4.540 1.00 16.68 C
ATOM 7720 CB ALA A 505 -49.739 25.309 4.243 1.00 16.54 C
ATOM 7724 C ALA A 505 -51.826 24.281 5.074 1.00 16.77 C
ATOM 7725 O ALA A 505 -52.087 24.123 6.266 1.00 16.80 O
ATOM 7727 N ARG A 506 -52.726 24.664 4.172 1.00 16.82 N
ATOM 7728 CA ARG A 506 -54.128 24.875 4.521 1.00 16.84 C
ATOM 7730 CB ARG A 506 -54.944 25.274 3.286 1.00 16.86 C
ATOM 7733 CG ARG A 506 -54.649 26.661 2.795 1.00 16.27 C
ATOM 7736 CD ARG A 506 -55.586 27.090 1.726 1.00 15.26 C
ATOM 7739 NE ARG A 506 -55.240 28.436 1.273 1.00 15.31 N
ATOM 7741 CZ ARG A 506 -54.744 28.758 .082 1.00 14.28 C
ATOM 7742 NH1 ARG A 506 -54.519 27.856 -.856 1.00 14.12 N
ATOM 7745 NH2 ARG A 506 -54.471 30.018 -.176 1.00 15.94 N
ATOM 7748 C ARG A 506 -54.732 23.631 5.122 1.00 16.96 C
ATOM 7749 O ARG A 506 -55.480 23.707 6.089 1.00 16.71 O
ATOM 7751 N GLN A 507 -54.415 22.481 4.542 1.00 17.37 N
ATOM 7752 CA GLN A 507 -54.962 21.233 5.048 1.00 17.87 C
ATOM 7754 CB GLN A 507 -54.712 20.075 4.087 1.00 17.80 C
ATOM 7757 CG GLN A 507 -55.293 18.740 4.571 1.00 17.24 C
ATOM 7760 CD GLN A 507 -56.777 18.805 4.860 1.00 16.23 C
ATOM 7761 OE1 GLN A 507 -57.506 19.585 4.250 1.00 16.66 O
ATOM 7762 NE2 GLN A 507 -57.233 17.980 5.790 1.00 14.96 N
ATOM 7765 C GLN A 507 -54.401 20.890 6.423 1.00 18.28 C
ATOM 7766 O GLN A 507 -55.148 20.419 7.287 1.00 18.53 O
ATOM 7768 N SER A 508 -53.096 21.113 6.609 1.00 18.50 N
ATOM 7769 CA SER A 508 -52.435 20.924 7.908 1.00 18.54 C
ATOM 7771 CB SER A 508 -50.979 21.385 7.856 1.00 18.40 C
ATOM 7774 OG SER A 508 -50.259 20.694 6.857 1.00 18.51 O
ATOM 7776 C SER A 508 -53.147 21.752 8.942 1.00 18.78 C
ATOM 7777 O SER A 508 -53.535 21.278 10.006 1.00 18.33 O
ATOM 7779 N HIS A 509 -53.324 23.014 8.599 1.00 19.37 N
ATOM 7780 CA HIS A 509 -54.014 23.922 9.466 1.00 19.92 C
ATOM 7782 CB HIS A 509 -54.126 25.295 8.818 1.00 20.07 C
ATOM 7785 CG HIS A 509 -53.000 26.188 9.174 1.00 19.82 C
ATOM 7786 ND1 HIS A 509 -52.079 26.631 8.255 1.00 19.73 N
ATOM 7788 CE1 HIS A 509 -51.187 27.383 8.866 1.00 20.25 C
ATOM 7790 NE2 HIS A 509 -51.485 27.426 10.149 1.00 21.66 N
ATOM 7792 CD2 HIS A 509 -52.615 26.682 10.368 1.00 20.98 C
ATOM 7794 C HIS A 509 -55.389 23.448 9.839 1.00 20.41 C
ATOM 7795 O HIS A 509 -55.821 23.694 10.934 1.00 20.22 O
ATOM 7797 N CYS A 510 -56.093 22.808 8.918 1.00 21.33 N
ATOM 7798 CA CYS A 510 -57.470 22.396 9.189 1.00 22.03 C
ATOM 7800 CB CYS A 510 -58.278 22.383 7.894 1.00 21.90 C
ATOM 7803 SG CYS A 510 -58.522 24.055 7.270 1.00 21.93 S
ATOM 7805 C CYS A 510 -57.527 21.054 9.908 1.00 22.60 C
ATOM 7806 O CYS A 510 -58.423 20.822 10.706 1.00 22.23 O
ATOM 7808 N THR A 511 -56.553 20.194 9.627 1.00 23.67 N
ATOM 7809 CA THR A 511 -56.421 18.920 10.305 1.00 24.81 C
ATOM 7811 CB THR A 511 -55.437 18.000 9.565 1.00 24.70 C

ATOM 7813 OG1 THR A 511 -56.071 17.485 8.394 1.00 24.45 O
ATOM 7815 CG2 THR A 511 -55.003 16.844 10.448 1.00 24.23 C
ATOM 7819 C THR A 511 -55.965 19.086 11.756 1.00 26.22 C
ATOM 7820 O THR A 511 -56.685 18.717 12.679 1.00 26.12 O
ATOM 7822 N TYR A 512 -54.775 19.643 11.959 1.00 28.08 N
ATOM 7823 CA TYR A 512 -54.177 19.657 13.298 1.00 29.63 C
ATOM 7825 CB TYR A 512 -52.663 19.783 13.238 1.00 29.67 C
ATOM 7828 CG TYR A 512 -52.117 18.579 12.560 1.00 29.56 C
ATOM 7829 CD1 TYR A 512 -51.965 17.395 13.246 1.00 29.66 C
ATOM 7831 CE1 TYR A 512 -51.507 16.273 12.614 1.00 30.94 C
ATOM 7833 CZ TYR A 512 -51.217 16.326 11.263 1.00 32.04 C
ATOM 7834 OH TYR A 512 -50.757 15.209 10.608 1.00 33.78 O
ATOM 7836 CE2 TYR A 512 -51.390 17.492 10.557 1.00 31.29 C
ATOM 7838 CD2 TYR A 512 -51.847 18.600 11.205 1.00 30.53 C
ATOM 7840 C TYR A 512 -54.812 20.676 14.206 1.00 31.11 C
ATOM 7841 O TYR A 512 -55.494 20.277 15.139 1.00 31.34 O
ATOM 7843 N HIS A 513 -54.583 21.969 13.966 1.00 32.89 N
ATOM 7844 CA HIS A 513 -55.505 23.023 14.442 1.00 34.48 C
ATOM 7846 CB HIS A 513 -56.372 23.461 13.225 1.00 35.13 C
ATOM 7849 CG HIS A 513 -57.704 24.108 13.529 1.00 37.10 C
ATOM 7850 ND1 HIS A 513 -58.265 25.040 12.678 1.00 38.69 N
ATOM 7852 CE1 HIS A 513 -59.442 25.416 13.151 1.00 39.23 C
ATOM 7854 NE2 HIS A 513 -59.678 24.751 14.268 1.00 38.18 N
ATOM 7856 CD2 HIS A 513 -58.615 23.915 14.519 1.00 38.17 C
ATOM 7858 C HIS A 513 -56.337 22.503 15.610 1.00 35.00 C
ATOM 7859 O HIS A 513 -56.302 23.074 16.712 1.00 35.48 O
ATOM 7861 N ASN A 514 -57.079 21.419 15.351 1.00 35.23 N
ATOM 7862 CA ASN A 514 -57.934 20.768 16.347 1.00 35.46 C
ATOM 7864 CB ASN A 514 -58.342 19.343 15.903 1.00 35.39 C
ATOM 7867 CG ASN A 514 -59.383 19.345 14.786 1.00 34.01 C
ATOM 7868 OD1 ASN A 514 -59.336 20.185 13.896 1.00 33.36 O
ATOM 7869 ND2 ASN A 514 -60.315 18.406 14.833 1.00 31.13 N
ATOM 7872 C ASN A 514 -57.464 20.751 17.818 1.00 36.15 C
ATOM 7873 O ASN A 514 -56.397 20.211 18.153 1.00 36.13 O
ATOM 7875 N GLY A 515 -58.277 21.430 18.640 1.00 36.95 N
ATOM 7876 CA GLY A 515 -58.427 21.235 20.079 1.00 37.43 C
ATOM 7879 C GLY A 515 -59.724 20.470 20.381 1.00 38.18 C
ATOM 7880 O GLY A 515 -59.636 19.418 21.021 1.00 38.57 O
ATOM 7882 N ASP A 516 -60.930 20.921 19.969 1.00 38.73 N
ATOM 7883 CA ASP A 516 -61.249 22.194 19.293 1.00 39.26 C
ATOM 7885 CB ASP A 516 -61.607 21.904 17.845 1.00 39.51 C
ATOM 7888 CG ASP A 516 -60.523 22.291 16.894 1.00 42.32 C
ATOM 7889 OD1 ASP A 516 -59.613 23.084 17.286 1.00 45.56 O
ATOM 7890 OD2 ASP A 516 -60.578 21.797 15.740 1.00 45.52 O
ATOM 7891 C ASP A 516 -62.466 22.913 19.884 1.00 39.38 C
ATOM 7892 O ASP A 516 -63.032 22.454 20.880 1.00 39.74 O
ATOM 7894 N ALA A 517 -62.850 24.038 19.259 1.00 39.40 N
ATOM 7895 CA ALA A 517 -64.140 24.752 19.481 1.00 39.50 C
ATOM 7897 CB ALA A 517 -65.117 24.403 18.333 1.00 39.27 C
ATOM 7901 C ALA A 517 -64.837 24.566 20.863 1.00 39.90 C
ATOM 7902 O ALA A 517 -64.173 24.428 21.899 1.00 39.89 O
ATOM 7904 N HIS A 518 -66.175 24.617 20.876 1.00 40.33 N
ATOM 7905 CA HIS A 518 -66.973 24.112 22.016 1.00 40.73 C
ATOM 7907 CB HIS A 518 -68.091 25.092 22.396 1.00 41.22 C
ATOM 7910 CG HIS A 518 -67.578 26.419 22.866 1.00 43.58 C
ATOM 7911 ND1 HIS A 518 -67.426 26.725 24.207 1.00 45.88 N
ATOM 7913 CE1 HIS A 518 -66.938 27.950 24.320 1.00 46.42 C
ATOM 7915 NE2 HIS A 518 -66.760 28.446 23.102 1.00 46.25 N
ATOM 7917 CD2 HIS A 518 -67.145 27.506 22.174 1.00 45.24 C
ATOM 7919 C HIS A 518 -67.526 22.725 21.655 1.00 40.17 C

ATOM 7920 O HIS A 518 -68.738 22.501 21.571 1.00 40.02 O
ATOM 7922 N THR A 519 -66.581 21.812 21.448 1.00 39.64 N
ATOM 7923 CA THR A 519 -66.808 20.466 20.918 1.00 39.16 C
ATOM 7925 CB THR A 519 -67.414 20.469 19.453 1.00 39.16 C
ATOM 7927 OG1 THR A 519 -66.847 21.529 18.665 1.00 39.04 O
ATOM 7929 CG2 THR A 519 -68.942 20.633 19.480 1.00 38.82 C
ATOM 7933 C THR A 519 -65.428 19.771 20.978 1.00 38.85 C
ATOM 7934 O THR A 519 -64.391 20.433 20.878 1.00 38.66 O
ATOM 7936 N SER A 520 -65.407 18.455 21.170 1.00 38.37 N
ATOM 7937 CA SER A 520 -64.160 17.745 21.500 1.00 38.08 C
ATOM 7939 CB SER A 520 -64.514 16.320 21.931 1.00 38.06 C
ATOM 7942 OG SER A 520 -64.560 15.475 20.805 1.00 38.66 O
ATOM 7944 C SER A 520 -63.136 17.771 20.327 1.00 37.86 C
ATOM 7945 O SER A 520 -63.420 18.369 19.289 1.00 37.50 O
ATOM 7947 N PRO A 521 -61.948 17.122 20.482 1.00 37.98 N
ATOM 7948 CA PRO A 521 -60.944 17.170 19.379 1.00 37.92 C
ATOM 7950 CB PRO A 521 -59.674 16.527 19.987 1.00 37.87 C
ATOM 7953 CG PRO A 521 -60.091 15.919 21.330 1.00 38.28 C
ATOM 7956 CD PRO A 521 -61.577 16.137 21.526 1.00 38.13 C
ATOM 7959 C PRO A 521 -61.432 16.446 18.110 1.00 37.96 C
ATOM 7960 O PRO A 521 -61.769 17.118 17.140 1.00 38.09 O
ATOM 7961 N ASP A 522 -61.483 15.108 18.107 1.00 38.07 N
ATOM 7962 CA ASP A 522 -62.351 14.393 17.161 1.00 38.14 C
ATOM 7964 CB ASP A 522 -62.132 12.877 17.204 1.00 38.31 C
ATOM 7967 CG ASP A 522 -60.769 12.456 16.640 1.00 39.45 C
ATOM 7968 OD1 ASP A 522 -60.160 13.200 15.827 1.00 39.72 O
ATOM 7969 OD2 ASP A 522 -60.302 11.361 17.025 1.00 41.59 O
ATOM 7970 C ASP A 522 -63.760 14.780 17.591 1.00 37.92 C
ATOM 7971 O ASP A 522 -63.908 15.608 18.474 1.00 38.01 O
ATOM 7973 N GLU A 523 -64.799 14.239 16.974 1.00 37.79 N
ATOM 7974 CA GLU A 523 -66.150 14.818 17.121 1.00 37.83 C
ATOM 7976 CB GLU A 523 -66.618 14.919 18.591 1.00 37.85 C
ATOM 7979 CG GLU A 523 -66.346 13.678 19.483 1.00 39.40 C
ATOM 7982 CD GLU A 523 -66.916 13.802 20.931 1.00 41.49 C
ATOM 7983 OE1 GLU A 523 -67.714 14.737 21.207 1.00 42.81 O
ATOM 7984 OE2 GLU A 523 -66.566 12.957 21.800 1.00 42.04 O
ATOM 7985 C GLU A 523 -66.242 16.203 16.430 1.00 37.51 C
ATOM 7986 O GLU A 523 -67.338 16.751 16.283 1.00 37.70 O
ATOM 7988 N LEU A 524 -65.097 16.775 16.043 1.00 37.03 N
ATOM 7989 CA LEU A 524 -65.044 17.863 15.067 1.00 36.58 C
ATOM 7991 CB LEU A 524 -64.174 19.022 15.559 1.00 36.56 C
ATOM 7994 CG LEU A 524 -63.963 20.225 14.624 1.00 36.35 C
ATOM 7996 CD1 LEU A 524 -63.400 21.376 15.418 1.00 35.74 C
ATOM 8000 CD2 LEU A 524 -65.242 20.681 13.910 1.00 36.53 C
ATOM 8004 C LEU A 524 -64.478 17.287 13.782 1.00 36.20 C
ATOM 8005 O LEU A 524 -65.106 17.363 12.733 1.00 36.14 O
ATOM 8007 N THR A 525 -63.298 16.686 13.869 1.00 35.83 N
ATOM 8008 CA THR A 525 -62.756 15.935 12.748 1.00 35.66 C
ATOM 8010 CB THR A 525 -61.585 15.015 13.173 1.00 35.48 C
ATOM 8012 OG1 THR A 525 -60.776 15.678 14.152 1.00 35.55 O
ATOM 8014 CG2 THR A 525 -60.720 14.641 11.978 1.00 34.73 C
ATOM 8018 C THR A 525 -63.875 15.098 12.123 1.00 35.89 C
ATOM 8019 O THR A 525 -64.040 15.095 10.909 1.00 35.98 O
ATOM 8021 N ARG A 526 -64.667 14.420 12.954 1.00 36.06 N
ATOM 8022 CA ARG A 526 -65.739 13.574 12.448 1.00 36.18 C
ATOM 8024 CB ARG A 526 -66.340 12.718 13.555 1.00 36.56 C
ATOM 8027 CG ARG A 526 -67.416 11.754 13.054 1.00 38.35 C
ATOM 8030 CD ARG A 526 -67.781 10.702 14.092 1.00 41.00 C
ATOM 8033 NE ARG A 526 -67.740 11.207 15.470 1.00 43.08 N
ATOM 8035 CZ ARG A 526 -68.637 12.033 16.024 1.00 44.51 C

```
ATOM  8036 NH1 ARG A 526    -69.681  12.500  15.336  1.00 44.46        N
ATOM  8039 NH2 ARG A 526    -68.476  12.406  17.288  1.00 45.02        N
ATOM  8042 C   ARG A 526    -66.834  14.384  11.774  1.00 35.68        C
ATOM  8043 O   ARG A 526    -67.253  14.035  10.675  1.00 35.84        O
ATOM  8045 N   LYS A 527    -67.309  15.447  12.424  1.00 35.06        N
ATOM  8046 CA  LYS A 527    -68.285  16.343  11.780  1.00 34.61        C
ATOM  8048 CB  LYS A 527    -68.680  17.528  12.683  1.00 34.74        C
ATOM  8051 CG  LYS A 527    -69.818  17.225  13.651  1.00 35.40        C
ATOM  8054 CD  LYS A 527    -70.301  18.452  14.441  1.00 35.99        C
ATOM  8057 CE  LYS A 527    -71.280  18.021  15.556  1.00 36.42        C
ATOM  8060 NZ  LYS A 527    -71.652  19.095  16.530  1.00 36.31        N
ATOM  8064 C   LYS A 527    -67.723  16.860  10.457  1.00 33.77        C
ATOM  8065 O   LYS A 527    -68.377  16.763   9.423  1.00 33.75        O
ATOM  8067 N   ARG A 528    -66.501  17.388  10.499  1.00 32.71        N
ATOM  8068 CA  ARG A 528    -65.840  17.929   9.310  1.00 31.79        C
ATOM  8070 CB  ARG A 528    -64.425  18.464   9.644  1.00 31.74        C
ATOM  8073 CG  ARG A 528    -64.419  19.844  10.330  1.00 30.90        C
ATOM  8076 CD  ARG A 528    -63.021  20.439  10.527  1.00 29.75        C
ATOM  8079 NE  ARG A 528    -63.098  21.745  11.190  1.00 29.55        N
ATOM  8081 CZ  ARG A 528    -62.056  22.513  11.528  1.00 29.96        C
ATOM  8082 NH1 ARG A 528    -60.801  22.145  11.284  1.00 29.74        N
ATOM  8085 NH2 ARG A 528    -62.269  23.677  12.130  1.00 30.71        N
ATOM  8088 C   ARG A 528    -65.796  16.904   8.172  1.00 30.99        C
ATOM  8089 O   ARG A 528    -66.226  17.206   7.068  1.00 30.97        O
ATOM  8091 N   VAL A 529    -65.313  15.694   8.450  1.00 30.12        N
ATOM  8092 CA  VAL A 529    -65.239  14.631   7.438  1.00 29.43        C
ATOM  8094 CB  VAL A 529    -64.557  13.354   7.972  1.00 29.39        C
ATOM  8096 CG1 VAL A 529    -64.785  12.187   7.023  1.00 28.89        C
ATOM  8100 CG2 VAL A 529    -63.062  13.589   8.186  1.00 29.44        C
ATOM  8104 C   VAL A 529    -66.609  14.243   6.887  1.00 28.95        C
ATOM  8105 O   VAL A 529    -66.755  14.016   5.690  1.00 29.09        O
ATOM  8107 N   LEU A 530    -67.615  14.153   7.744  1.00 28.18        N
ATOM  8108 CA  LEU A 530    -68.956  13.874   7.246  1.00 27.72        C
ATOM  8110 CB  LEU A 530    -69.971  13.715   8.395  1.00 27.75        C
ATOM  8113 CG  LEU A 530    -70.334  12.274   8.775  1.00 27.36        C
ATOM  8115 CD1 LEU A 530    -69.096  11.415   9.050  1.00 26.86        C
ATOM  8119 CD2 LEU A 530    -71.273  12.279   9.968  1.00 27.14        C
ATOM  8123 C   LEU A 530    -69.401  14.963   6.256  1.00 27.16        C
ATOM  8124 O   LEU A 530    -69.861  14.652   5.161  1.00 27.42        O
ATOM  8126 N   SER A 531    -69.230  16.229   6.635  1.00 26.21        N
ATOM  8127 CA  SER A 531    -69.730  17.359   5.853  1.00 25.12        C
ATOM  8129 CB  SER A 531    -69.519  18.657   6.618  1.00 25.01        C
ATOM  8132 OG  SER A 531    -68.167  18.791   6.985  1.00 23.94        O
ATOM  8134 C   SER A 531    -69.055  17.476   4.507  1.00 24.48        C
ATOM  8135 O   SER A 531    -69.687  17.886   3.538  1.00 24.14        O
ATOM  8137 N   VAL A 532    -67.774  17.115   4.461  1.00 23.89        N
ATOM  8138 CA  VAL A 532    -66.962  17.226   3.246  1.00 23.53        C
ATOM  8140 CB  VAL A 532    -65.470  17.437   3.575  1.00 23.09        C
ATOM  8142 CG1 VAL A 532    -64.633  17.355   2.348  1.00 22.32        C
ATOM  8146 CG2 VAL A 532    -65.268  18.773   4.198  1.00 23.07        C
ATOM  8150 C   VAL A 532    -67.100  16.028   2.316  1.00 23.67        C
ATOM  8151 O   VAL A 532    -67.137  16.209   1.099  1.00 23.58        O
ATOM  8153 N   ILE A 533    -67.187  14.824   2.886  1.00 23.85        N
ATOM  8154 CA  ILE A 533    -67.172  13.578   2.107  1.00 24.08        C
ATOM  8156 CB  ILE A 533    -66.172  12.555   2.691  1.00 24.10        C
ATOM  8158 CG1 ILE A 533    -64.745  13.079   2.631  1.00 23.47        C
ATOM  8161 CD1 ILE A 533    -64.178  13.083   1.255  1.00 23.42        C
ATOM  8165 CG2 ILE A 533    -66.254  11.231   1.932  1.00 24.56        C
ATOM  8169 C   ILE A 533    -68.522  12.859   1.990  1.00 24.27        C
ATOM  8170 O   ILE A 533    -68.991  12.620    .887  1.00 24.34        O
```

ATOM 8172 N THR A 534 -69.133 12.487 3.111 1.00 24.57 N
ATOM 8173 CA THR A 534 -70.279 11.564 3.072 1.00 24.92 C
ATOM 8175 CB THR A 534 -70.200 10.522 4.207 1.00 24.93 C
ATOM 8177 OG1 THR A 534 -70.491 11.149 5.458 1.00 25.28 O
ATOM 8179 CG2 THR A 534 -68.804 9.885 4.257 1.00 24.75 C
ATOM 8183 C THR A 534 -71.673 12.209 3.083 1.00 25.00 C
ATOM 8184 O THR A 534 -72.601 11.646 2.522 1.00 24.94 O
ATOM 8186 N GLU A 535 -71.821 13.374 3.708 1.00 25.26 N
ATOM 8187 CA GLU A 535 -73.132 14.024 3.833 1.00 25.34 C
ATOM 8189 CB GLU A 535 -73.333 14.523 5.255 1.00 25.44 C
ATOM 8192 CG GLU A 535 -73.753 13.424 6.196 1.00 25.80 C
ATOM 8195 CD GLU A 535 -74.307 13.963 7.468 1.00 25.72 C
ATOM 8196 OE1 GLU A 535 -75.375 13.487 7.881 1.00 24.50 O
ATOM 8197 OE2 GLU A 535 -73.678 14.877 8.039 1.00 27.03 O
ATOM 8198 C GLU A 535 -73.363 15.179 2.859 1.00 25.26 C
ATOM 8199 O GLU A 535 -72.686 16.206 2.939 1.00 25.02 O
ATOM 8201 N PRO A 536 -74.351 15.030 1.959 1.00 25.25 N
ATOM 8202 CA PRO A 536 -74.655 16.111 1.050 1.00 25.18 C
ATOM 8204 CB PRO A 536 -75.661 15.484 .076 1.00 25.15 C
ATOM 8207 CG PRO A 536 -75.825 14.077 .476 1.00 24.98 C
ATOM 8210 CD PRO A 536 -75.363 13.965 1.868 1.00 25.26 C
ATOM 8213 C PRO A 536 -75.289 17.265 1.801 1.00 25.30 C
ATOM 8214 O PRO A 536 -75.826 17.070 2.883 1.00 25.57 O
ATOM 8215 N ILE A 537 -75.213 18.458 1.230 1.00 25.36 N
ATOM 8216 CA ILE A 537 -75.807 19.638 1.827 1.00 25.34 C
ATOM 8218 CB ILE A 537 -75.201 20.918 1.221 1.00 25.14 C
ATOM 8220 CG1 ILE A 537 -73.787 21.131 1.744 1.00 24.32 C
ATOM 8223 CD1 ILE A 537 -73.228 22.472 1.406 1.00 23.22 C
ATOM 8227 CG2 ILE A 537 -76.030 22.131 1.569 1.00 25.54 C
ATOM 8231 C ILE A 537 -77.313 19.603 1.611 1.00 25.67 C
ATOM 8232 O ILE A 537 -77.786 19.132 .579 1.00 25.47 O
ATOM 8234 N LEU A 538 -78.071 20.088 2.586 1.00 26.22 N
ATOM 8235 CA LEU A 538 -79.514 20.051 2.467 1.00 26.65 C
ATOM 8237 CB LEU A 538 -80.213 20.525 3.749 1.00 26.78 C
ATOM 8240 CG LEU A 538 -80.162 19.609 4.989 1.00 26.64 C
ATOM 8242 CD1 LEU A 538 -81.218 20.033 6.007 1.00 26.16 C
ATOM 8246 CD2 LEU A 538 -80.346 18.138 4.633 1.00 26.12 C
ATOM 8250 C LEU A 538 -79.925 20.881 1.262 1.00 27.08 C
ATOM 8253 N PRO A 539 -80.786 20.306 .414 1.00 28.03 N
ATOM 8254 CA PRO A 539 -81.117 20.855 -.888 1.00 28.44 C
ATOM 8256 CB PRO A 539 -82.093 19.828 -1.449 1.00 28.40 C
ATOM 8259 CG PRO A 539 -82.793 19.328 -.253 1.00 28.30 C
ATOM 8262 CD PRO A 539 -81.720 19.228 .787 1.00 28.11 C
ATOM 8265 C PRO A 539 -81.813 22.194 -.804 1.00 28.89 C
ATOM 8266 O PRO A 539 -82.396 22.535 .226 1.00 28.97 O
ATOM 8267 N PHE A 540 -81.774 22.932 -1.906 1.00 29.32 N
ATOM 8268 CA PHE A 540 -82.380 24.245 -1.962 1.00 29.50 C
ATOM 8270 CB PHE A 540 -82.146 24.874 -3.326 1.00 29.56 C
ATOM 8273 CG PHE A 540 -82.757 26.227 -3.463 1.00 29.75 C
ATOM 8274 CD1 PHE A 540 -83.874 26.429 -4.255 1.00 29.47 C
ATOM 8276 CE1 PHE A 540 -84.441 27.681 -4.364 1.00 29.46 C
ATOM 8278 CZ PHE A 540 -83.901 28.743 -3.674 1.00 29.81 C
ATOM 8280 CE2 PHE A 540 -82.791 28.553 -2.877 1.00 30.21 C
ATOM 8282 CD2 PHE A 540 -82.229 27.300 -2.770 1.00 30.17 C
ATOM 8284 C PHE A 540 -83.865 24.129 -1.722 1.00 29.66 C
ATOM 8285 O PHE A 540 -84.568 23.551 -2.545 1.00 29.66 O
ATOM 8287 N GLU A 541 -84.337 24.673 -.601 1.00 29.90 N
ATOM 8288 CA GLU A 541 -85.761 24.605 -.233 1.00 30.06 C
ATOM 8290 CB GLU A 541 -85.951 23.724 1.017 1.00 30.15 C
ATOM 8293 CG GLU A 541 -87.411 23.361 1.367 1.00 30.64 C

ATOM 8296 CD GLU A 541 -88.091 24.351 2.322 1.00 31.35 C
ATOM 8297 OE1 GLU A 541 -87.468 25.370 2.680 1.00 32.67 O
ATOM 8298 OE2 GLU A 541 -89.254 24.114 2.719 1.00 30.48 O
ATOM 8299 C GLU A 541 -86.315 26.011 -.010 1.00 29.89 C
ATOM 8300 O GLU A 541 -86.835 26.636 -.936 1.00 29.71 O
ATOM 8302 N LEU B 17 -69.666 -25.325 2.227 1.00 33.20 N
ATOM 8303 CA LEU B 17 -69.356 -25.417 .755 1.00 33.49 C
ATOM 8305 CB LEU B 17 -70.240 -26.475 .048 1.00 33.44 C
ATOM 8308 CG LEU B 17 -70.077 -27.986 .328 1.00 33.60 C
ATOM 8310 CD1 LEU B 17 -71.285 -28.778 -.217 1.00 32.76 C
ATOM 8314 CD2 LEU B 17 -68.763 -28.553 -.230 1.00 33.21 C
ATOM 8318 C LEU B 17 -69.513 -24.044 .055 1.00 33.54 C
ATOM 8319 O LEU B 17 -70.550 -23.380 .195 1.00 33.77 O
ATOM 8323 N LEU B 18 -68.481 -23.637 -.696 1.00 33.44 N
ATOM 8324 CA LEU B 18 -68.476 -22.362 -1.454 1.00 33.07 C
ATOM 8326 CB LEU B 18 -67.029 -21.960 -1.840 1.00 33.21 C
ATOM 8329 CG LEU B 18 -66.065 -21.488 -.721 1.00 34.06 C
ATOM 8331 CD1 LEU B 18 -64.607 -21.351 -1.235 1.00 34.51 C
ATOM 8335 CD2 LEU B 18 -66.516 -20.164 -.061 1.00 33.43 C
ATOM 8339 C LEU B 18 -69.379 -22.400 -2.714 1.00 32.37 C
ATOM 8340 O LEU B 18 -69.710 -21.355 -3.274 1.00 32.29 O
ATOM 8342 N SER B 19 -69.765 -23.597 -3.153 1.00 31.62 N
ATOM 8343 CA SER B 19 -70.711 -23.749 -4.253 1.00 31.16 C
ATOM 8345 CB SER B 19 -70.443 -25.067 -5.033 1.00 31.09 C
ATOM 8348 OG SER B 19 -70.977 -26.243 -4.421 1.00 29.36 O
ATOM 8350 C SER B 19 -72.168 -23.663 -3.759 1.00 31.45 C
ATOM 8351 O SER B 19 -73.076 -23.432 -4.551 1.00 31.13 O
ATOM 8353 N SER B 20 -72.386 -23.824 -2.451 1.00 31.91 N
ATOM 8354 CA SER B 20 -73.749 -23.900 -1.879 1.00 32.34 C
ATOM 8356 CB SER B 20 -73.706 -24.122 -.357 1.00 32.35 C
ATOM 8359 OG SER B 20 -73.393 -25.473 -.055 1.00 32.34 O
ATOM 8361 C SER B 20 -74.601 -22.670 -2.204 1.00 32.69 C
ATOM 8362 O SER B 20 -74.072 -21.600 -2.487 1.00 32.89 O
ATOM 8364 N ASP B 21 -75.921 -22.831 -2.119 1.00 33.13 N
ATOM 8365 CA ASP B 21 -76.874 -21.901 -2.745 1.00 33.40 C
ATOM 8367 CB ASP B 21 -78.179 -22.628 -3.045 1.00 33.64 C
ATOM 8370 CG ASP B 21 -77.943 -23.883 -3.828 1.00 35.35 C
ATOM 8371 OD1 ASP B 21 -77.031 -23.866 -4.684 1.00 38.26 O
ATOM 8372 OD2 ASP B 21 -78.631 -24.890 -3.590 1.00 37.55 O
ATOM 8373 C ASP B 21 -77.141 -20.649 -1.940 1.00 33.23 C
ATOM 8374 O ASP B 21 -78.039 -20.616 -1.106 1.00 32.91 O
ATOM 8376 N THR B 22 -76.348 -19.621 -2.229 1.00 33.46 N
ATOM 8377 CA THR B 22 -76.443 -18.307 -1.593 1.00 33.79 C
ATOM 8379 CB THR B 22 -76.460 -18.378 -.016 1.00 33.74 C
ATOM 8381 OG1 THR B 22 -75.426 -19.250 .460 1.00 32.97 O
ATOM 8383 CG2 THR B 22 -77.805 -18.838 .535 1.00 33.55 C
ATOM 8387 C THR B 22 -75.217 -17.479 -2.018 1.00 34.24 C
ATOM 8388 O THR B 22 -74.102 -17.988 -1.892 1.00 33.95 O
ATOM 8390 N ASP B 23 -75.361 -16.248 -2.543 1.00 34.99 N
ATOM 8391 CA ASP B 23 -76.603 -15.620 -3.103 1.00 35.61 C
ATOM 8393 CB ASP B 23 -77.242 -16.538 -4.170 1.00 35.51 C
ATOM 8396 CG ASP B 23 -76.196 -17.236 -5.034 1.00 36.08 C
ATOM 8397 OD1 ASP B 23 -75.084 -16.685 -5.194 1.00 35.58 O
ATOM 8398 OD2 ASP B 23 -76.473 -18.344 -5.541 1.00 37.65 O
ATOM 8399 C ASP B 23 -77.662 -15.083 -2.097 1.00 36.10 C
ATOM 8400 O ASP B 23 -78.644 -15.770 -1.799 1.00 36.13 O
ATOM 8402 N GLU B 24 -77.487 -13.845 -1.616 1.00 36.74 N
ATOM 8403 CA GLU B 24 -78.358 -13.316 -.543 1.00 37.59 C
ATOM 8405 CB GLU B 24 -77.765 -13.666 .838 1.00 37.88 C
ATOM 8408 CG GLU B 24 -77.624 -15.173 1.120 1.00 38.51 C

ATOM 8411 CD GLU B 24 -77.314 -15.510 2.588 1.00 39.48 C
ATOM 8412 OE1 GLU B 24 -77.171 -14.581 3.434 1.00 39.60 O
ATOM 8413 OE2 GLU B 24 -77.221 -16.725 2.884 1.00 39.51 O
ATOM 8414 C GLU B 24 -78.730 -11.809 -.559 1.00 38.11 C
ATOM 8415 O GLU B 24 -79.840 -11.453 -.972 1.00 38.20 O
ATOM 8417 N SER B 25 -77.825 -10.941 -.089 1.00 38.70 N
ATOM 8418 CA SER B 25 -78.192 -9.560 .312 1.00 39.21 C
ATOM 8420 CB SER B 25 -76.995 -8.783 .916 1.00 39.29 C
ATOM 8423 OG SER B 25 -76.267 -8.037 -.056 1.00 39.40 O
ATOM 8425 C SER B 25 -78.853 -8.738 -.802 1.00 39.69 C
ATOM 8426 O SER B 25 -78.707 -9.050 -1.995 1.00 39.75 O
ATOM 8428 N ILE B 26 -79.544 -7.670 -.378 1.00 40.21 N
ATOM 8429 CA ILE B 26 -80.554 -6.962 -1.189 1.00 40.55 C
ATOM 8431 CB ILE B 26 -79.925 -6.082 -2.319 1.00 40.66 C
ATOM 8433 CG1 ILE B 26 -79.083 -4.951 -1.700 1.00 40.73 C
ATOM 8436 CD1 ILE B 26 -78.596 -3.877 -2.698 1.00 40.68 C
ATOM 8440 CG2 ILE B 26 -81.018 -5.475 -3.203 1.00 40.88 C
ATOM 8444 C ILE B 26 -81.575 -7.999 -1.714 1.00 40.72 C
ATOM 8445 O ILE B 26 -81.311 -8.710 -2.690 1.00 40.80 O
ATOM 8447 N GLU B 27 -82.729 -8.070 -1.037 1.00 40.86 N
ATOM 8448 CA GLU B 27 -83.694 -9.190 -1.160 1.00 40.88 C
ATOM 8450 CB GLU B 27 -84.782 -9.060 -.061 1.00 40.95 C
ATOM 8453 CG GLU B 27 -84.235 -9.257 1.379 1.00 41.28 C
ATOM 8456 CD GLU B 27 -85.123 -8.657 2.484 1.00 41.74 C
ATOM 8457 OE1 GLU B 27 -85.593 -7.504 2.344 1.00 41.14 O
ATOM 8458 OE2 GLU B 27 -85.332 -9.337 3.514 1.00 42.36 O
ATOM 8459 C GLU B 27 -84.290 -9.355 -2.587 1.00 40.75 C
ATOM 8460 O GLU B 27 -83.664 -8.936 -3.569 1.00 40.88 O
ATOM 8462 N VAL B 28 -85.461 -9.994 -2.712 1.00 40.40 N
ATOM 8463 CA VAL B 28 -86.033 -10.361 -4.027 1.00 39.97 C
ATOM 8465 CB VAL B 28 -86.034 -9.157 -5.053 1.00 40.03 C
ATOM 8467 CG1 VAL B 28 -86.494 -9.600 -6.444 1.00 39.63 C
ATOM 8471 CG2 VAL B 28 -86.900 -7.994 -4.525 1.00 39.86 C
ATOM 8475 C VAL B 28 -85.335 -11.600 -4.625 1.00 39.63 C
ATOM 8476 O VAL B 28 -85.858 -12.204 -5.567 1.00 39.63 O
ATOM 8478 N HIS B 29 -84.175 -11.980 -4.069 1.00 39.21 N
ATOM 8479 CA HIS B 29 -83.431 -13.177 -4.504 1.00 38.81 C
ATOM 8481 CB HIS B 29 -81.914 -12.913 -4.665 1.00 38.97 C
ATOM 8484 CG HIS B 29 -81.571 -11.721 -5.512 1.00 39.99 C
ATOM 8485 ND1 HIS B 29 -81.181 -11.825 -6.834 1.00 40.79 N
ATOM 8487 CE1 HIS B 29 -80.931 -10.615 -7.312 1.00 40.76 C
ATOM 8489 NE2 HIS B 29 -81.134 -9.734 -6.346 1.00 40.27 N
ATOM 8491 CD2 HIS B 29 -81.525 -10.400 -5.209 1.00 40.17 C
ATOM 8493 C HIS B 29 -83.611 -14.340 -3.523 1.00 38.05 C
ATOM 8494 O HIS B 29 -82.782 -15.259 -3.526 1.00 38.02 O
ATOM 8496 N LYS B 30 -84.667 -14.321 -2.694 1.00 37.06 N
ATOM 8497 CA LYS B 30 -85.107 -15.559 -2.022 1.00 36.33 C
ATOM 8499 CB LYS B 30 -86.056 -15.286 -.836 1.00 36.27 C
ATOM 8502 CG LYS B 30 -85.352 -14.818 .461 1.00 36.09 C
ATOM 8505 CD LYS B 30 -86.355 -14.599 1.612 1.00 36.03 C
ATOM 8508 CE LYS B 30 -85.811 -13.659 2.701 1.00 36.24 C
ATOM 8511 NZ LYS B 30 -86.802 -13.356 3.789 1.00 35.65 N
ATOM 8515 C LYS B 30 -85.710 -16.510 -3.094 1.00 35.69 C
ATOM 8516 O LYS B 30 -86.706 -17.205 -2.879 1.00 35.35 O
ATOM 8518 N ASP B 31 -85.075 -16.484 -4.268 1.00 35.13 N
ATOM 8519 CA ASP B 31 -85.145 -17.519 -5.282 1.00 34.64 C
ATOM 8521 CB ASP B 31 -84.592 -16.962 -6.623 1.00 34.60 C
ATOM 8524 CG ASP B 31 -84.419 -18.032 -7.725 1.00 34.24 C
ATOM 8525 OD1 ASP B 31 -84.914 -19.165 -7.570 1.00 34.58 O
ATOM 8526 OD2 ASP B 31 -83.776 -17.732 -8.761 1.00 31.56 O

ATOM 8527 C ASP B 31 -84.304 -18.675 -4.721 1.00 34.31 C
ATOM 8528 O ASP B 31 -83.122 -18.838 -5.038 1.00 34.03 O
ATOM 8530 N LYS B 32 -84.917 -19.429 -3.813 1.00 33.94 N
ATOM 8531 CA LYS B 32 -84.380 -20.710 -3.369 1.00 33.36 C
ATOM 8533 CB LYS B 32 -83.772 -20.607 -1.973 1.00 33.45 C
ATOM 8536 CG LYS B 32 -82.540 -19.693 -1.951 1.00 33.56 C
ATOM 8539 CD LYS B 32 -82.025 -19.455 -.532 1.00 34.17 C
ATOM 8542 CE LYS B 32 -81.671 -17.987 -.283 1.00 34.16 C
ATOM 8545 NZ LYS B 32 -80.746 -17.437 -1.311 1.00 34.07 N
ATOM 8549 C LYS B 32 -85.490 -21.764 -3.499 1.00 32.57 C
ATOM 8550 O LYS B 32 -85.908 -22.412 -2.538 1.00 32.10 O
ATOM 8552 N ALA B 33 -85.976 -21.859 -4.738 1.00 31.66 N
ATOM 8553 CA ALA B 33 -86.576 -23.055 -5.259 1.00 30.94 C
ATOM 8555 CB ALA B 33 -87.247 -22.773 -6.597 1.00 30.47 C
ATOM 8559 C ALA B 33 -85.442 -24.081 -5.403 1.00 30.55 C
ATOM 8560 O ALA B 33 -85.684 -25.230 -5.751 1.00 31.12 O
ATOM 8562 N LYS B 34 -84.200 -23.660 -5.161 1.00 29.73 N
ATOM 8563 CA LYS B 34 -83.107 -24.585 -4.839 1.00 29.09 C
ATOM 8565 CB LYS B 34 -81.776 -23.817 -4.865 1.00 29.30 C
ATOM 8568 CG LYS B 34 -80.678 -24.474 -5.726 1.00 29.76 C
ATOM 8571 CD LYS B 34 -79.633 -23.458 -6.283 1.00 28.74 C
ATOM 8574 CE LYS B 34 -78.417 -24.186 -6.890 1.00 27.56 C
ATOM 8577 NZ LYS B 34 -78.745 -25.174 -7.935 1.00 26.16 N
ATOM 8581 C LYS B 34 -83.376 -25.320 -3.472 1.00 28.37 C
ATOM 8582 O LYS B 34 -83.254 -24.755 -2.374 1.00 27.82 O
ATOM 8584 N LYS B 35 -83.635 -26.620 -3.604 1.00 27.53 N
ATOM 8585 CA LYS B 35 -84.629 -27.429 -2.851 1.00 26.77 C
ATOM 8587 CB LYS B 35 -85.729 -26.602 -2.170 1.00 26.81 C
ATOM 8590 CG LYS B 35 -87.089 -26.520 -2.907 1.00 27.05 C
ATOM 8593 CD LYS B 35 -88.096 -27.604 -2.452 1.00 27.41 C
ATOM 8596 CE LYS B 35 -89.394 -27.636 -3.300 1.00 27.21 C
ATOM 8599 NZ LYS B 35 -90.501 -26.792 -2.762 1.00 26.28 N
ATOM 8603 C LYS B 35 -85.257 -28.357 -3.920 1.00 26.03 C
ATOM 8604 O LYS B 35 -85.853 -29.386 -3.626 1.00 26.00 O
ATOM 8606 N LEU B 36 -85.171 -27.909 -5.168 1.00 24.98 N
ATOM 8607 CA LEU B 36 -85.095 -28.783 -6.319 1.00 24.02 C
ATOM 8609 CB LEU B 36 -85.004 -27.930 -7.594 1.00 23.83 C
ATOM 8612 CG LEU B 36 -86.208 -27.103 -8.062 1.00 22.23 C
ATOM 8614 CD1 LEU B 36 -85.762 -25.873 -8.802 1.00 19.93 C
ATOM 8618 CD2 LEU B 36 -87.092 -27.930 -8.951 1.00 22.11 C
ATOM 8622 C LEU B 36 -83.834 -29.659 -6.185 1.00 23.58 C
ATOM 8623 O LEU B 36 -83.840 -30.842 -6.508 1.00 23.38 O
ATOM 8625 N GLU B 37 -82.742 -29.046 -5.739 1.00 23.18 N
ATOM 8626 CA GLU B 37 -81.510 -29.753 -5.396 1.00 22.88 C
ATOM 8628 CB GLU B 37 -80.466 -28.766 -4.855 1.00 22.76 C
ATOM 8631 CG GLU B 37 -79.038 -29.297 -4.874 1.00 22.24 C
ATOM 8634 CD GLU B 37 -78.085 -28.505 -4.009 1.00 21.06 C
ATOM 8635 OE1 GLU B 37 -78.368 -27.331 -3.737 1.00 19.65 O
ATOM 8636 OE2 GLU B 37 -77.037 -29.059 -3.615 1.00 20.62 O
ATOM 8637 C GLU B 37 -81.748 -30.856 -4.364 1.00 22.95 C
ATOM 8638 O GLU B 37 -81.164 -31.933 -4.458 1.00 22.99 O
ATOM 8640 N ALA B 38 -82.591 -30.575 -3.372 1.00 23.02 N
ATOM 8641 CA ALA B 38 -82.973 -31.565 -2.364 1.00 22.93 C
ATOM 8643 CB ALA B 38 -83.966 -30.959 -1.374 1.00 22.73 C
ATOM 8647 C ALA B 38 -83.580 -32.778 -3.044 1.00 23.05 C
ATOM 8648 O ALA B 38 -83.170 -33.909 -2.813 1.00 22.52 O
ATOM 8650 N GLU B 39 -84.546 -32.506 -3.912 1.00 23.66 N
ATOM 8651 CA GLU B 39 -85.273 -33.534 -4.642 1.00 24.08 C
ATOM 8653 CB GLU B 39 -86.403 -32.891 -5.453 1.00 24.28 C
ATOM 8656 CG GLU B 39 -87.405 -33.869 -6.075 1.00 25.14 C

```
ATOM  8659 CD  GLU B  39    -88.773 -33.227  -6.341  1.00 26.43       C
ATOM  8660 OE1 GLU B  39    -89.232 -32.381  -5.519  1.00 25.90       O
ATOM  8661 OE2 GLU B  39    -89.387 -33.584  -7.375  1.00 26.99       O
ATOM  8662 C   GLU B  39    -84.362 -34.359  -5.545  1.00 24.18       C
ATOM  8663 O   GLU B  39    -84.483 -35.579  -5.575  1.00 24.32       O
ATOM  8665 N   VAL B  40    -83.450 -33.710  -6.269  1.00 24.43       N
ATOM  8666 CA  VAL B  40    -82.533 -34.437  -7.153  1.00 24.59       C
ATOM  8668 CB  VAL B  40    -81.734 -33.496  -8.087  1.00 24.65       C
ATOM  8670 CG1 VAL B  40    -80.611 -34.258  -8.792  1.00 24.14       C
ATOM  8674 CG2 VAL B  40    -82.662 -32.852  -9.106  1.00 23.89       C
ATOM  8678 C   VAL B  40    -81.592 -35.304  -6.328  1.00 24.99       C
ATOM  8679 O   VAL B  40    -81.265 -36.407  -6.717  1.00 24.77       O
ATOM  8681 N   ARG B  41    -81.184 -34.811  -5.171  1.00 25.79       N
ATOM  8682 CA  ARG B  41    -80.387 -35.613  -4.248  1.00 26.75       C
ATOM  8684 CB  ARG B  41    -80.032 -34.823  -2.998  1.00 27.38       C
ATOM  8687 CG  ARG B  41    -78.568 -34.777  -2.757  1.00 30.18       C
ATOM  8690 CD  ARG B  41    -78.281 -34.610  -1.273  1.00 34.43       C
ATOM  8693 NE  ARG B  41    -76.896 -34.198  -1.016  1.00 37.07       N
ATOM  8695 CZ  ARG B  41    -76.350 -33.045  -1.416  1.00 38.54       C
ATOM  8696 NH1 ARG B  41    -75.083 -32.797  -1.112  1.00 40.04       N
ATOM  8699 NH2 ARG B  41    -77.037 -32.145  -2.128  1.00 38.45       N
ATOM  8702 C   ARG B  41    -81.081 -36.860  -3.762  1.00 26.60       C
ATOM  8703 O   ARG B  41    -80.446 -37.894  -3.627  1.00 26.89       O
ATOM  8705 N   ARG B  42    -82.363 -36.733  -3.423  1.00 26.41       N
ATOM  8706 CA  ARG B  42    -83.159 -37.870  -3.002  1.00 26.09       C
ATOM  8708 CB  ARG B  42    -84.588 -37.452  -2.674  1.00 25.99       C
ATOM  8711 CG  ARG B  42    -85.426 -38.562  -2.049  1.00 25.45       C
ATOM  8714 CD  ARG B  42    -86.783 -38.078  -1.645  1.00 24.26       C
ATOM  8717 NE  ARG B  42    -87.549 -37.602  -2.794  1.00 23.73       N
ATOM  8719 CZ  ARG B  42    -88.547 -36.722  -2.717  1.00 24.51       C
ATOM  8720 NH1 ARG B  42    -88.912 -36.195  -1.545  1.00 24.99       N
ATOM  8723 NH2 ARG B  42    -89.185 -36.354  -3.816  1.00 24.46       N
ATOM  8726 C   ARG B  42    -83.167 -38.894  -4.118  1.00 26.28       C
ATOM  8727 O   ARG B  42    -82.864 -40.054  -3.888  1.00 26.39       O
ATOM  8729 N   GLU B  43    -83.476 -38.460  -5.334  1.00 26.52       N
ATOM  8730 CA  GLU B  43    -83.476 -39.370  -6.479  1.00 27.00       C
ATOM  8732 CB  GLU B  43    -83.982 -38.676  -7.753  1.00 27.50       C
ATOM  8735 CG  GLU B  43    -85.469 -38.275  -7.699  1.00 29.78       C
ATOM  8738 CD  GLU B  43    -86.342 -39.301  -6.974  1.00 32.52       C
ATOM  8739 OE1 GLU B  43    -86.388 -40.455  -7.445  1.00 35.06       O
ATOM  8740 OE2 GLU B  43    -86.966 -38.963  -5.936  1.00 33.80       O
ATOM  8741 C   GLU B  43    -82.147 -40.059  -6.769  1.00 26.37       C
ATOM  8742 O   GLU B  43    -82.162 -41.126  -7.355  1.00 26.63       O
ATOM  8744 N   ILE B  44    -81.018 -39.472  -6.373  1.00 25.85       N
ATOM  8745 CA  ILE B  44    -79.717 -40.126  -6.555  1.00 25.55       C
ATOM  8747 CB  ILE B  44    -78.547 -39.121  -6.692  1.00 25.26       C
ATOM  8749 CG1 ILE B  44    -78.706 -38.273  -7.953  1.00 24.47       C
ATOM  8752 CD1 ILE B  44    -77.690 -37.163  -8.114  1.00 23.21       C
ATOM  8756 CG2 ILE B  44    -77.207 -39.863  -6.778  1.00 25.35       C
ATOM  8760 C   ILE B  44    -79.404 -41.109  -5.428  1.00 25.84       C
ATOM  8761 O   ILE B  44    -78.925 -42.208  -5.698  1.00 25.97       O
ATOM  8763 N   ASN B  45    -79.663 -40.708  -4.177  1.00 26.25       N
ATOM  8764 CA  ASN B  45    -79.403 -41.542  -2.983  1.00 26.34       C
ATOM  8766 CB  ASN B  45    -79.284 -40.681  -1.719  1.00 26.01       C
ATOM  8769 CG  ASN B  45    -78.072 -39.789  -1.723  1.00 24.65       C
ATOM  8770 OD1 ASN B  45    -76.957 -40.226  -1.434  1.00 22.47       O
ATOM  8771 ND2 ASN B  45    -78.288 -38.516  -2.009  1.00 23.36       N
ATOM  8774 C   ASN B  45    -80.488 -42.586  -2.731  1.00 27.18       C
ATOM  8775 O   ASN B  45    -80.374 -43.390  -1.806  1.00 27.30       O
ATOM  8777 N   ASN B  46    -81.553 -42.541  -3.527  1.00 28.17       N
```

ATOM 8778 CA ASN B 46 -82.619 -43.536 -3.489 1.00 29.02 C
ATOM 8780 CB ASN B 46 -83.558 -43.289 -4.665 1.00 29.05 C
ATOM 8783 CG ASN B 46 -84.615 -44.345 -4.806 1.00 28.82 C
ATOM 8784 OD1 ASN B 46 -84.861 -45.132 -3.895 1.00 28.14 O
ATOM 8785 ND2 ASN B 46 -85.255 -44.369 -5.968 1.00 29.67 N
ATOM 8788 C ASN B 46 -82.076 -44.958 -3.549 1.00 30.14 C
ATOM 8789 O ASN B 46 -81.566 -45.408 -4.581 1.00 30.30 O
ATOM 8791 N GLU B 47 -82.218 -45.674 -2.446 1.00 31.36 N
ATOM 8792 CA GLU B 47 -81.575 -46.968 -2.295 1.00 32.61 C
ATOM 8794 CB GLU B 47 -81.617 -47.430 -.823 1.00 33.09 C
ATOM 8797 CG GLU B 47 -80.974 -46.466 .218 1.00 34.19 C
ATOM 8800 CD GLU B 47 -81.919 -45.337 .721 1.00 34.57 C
ATOM 8801 OE1 GLU B 47 -82.911 -45.012 .029 1.00 34.53 O
ATOM 8802 OE2 GLU B 47 -81.652 -44.762 1.805 1.00 34.30 O
ATOM 8803 C GLU B 47 -82.205 -48.046 -3.172 1.00 33.18 C
ATOM 8804 O GLU B 47 -81.604 -49.088 -3.370 1.00 33.44 O
ATOM 8806 N LYS B 48 -83.408 -47.808 -3.692 1.00 34.11 N
ATOM 8807 CA LYS B 48 -84.164 -48.853 -4.396 1.00 34.85 C
ATOM 8809 CB LYS B 48 -85.379 -49.254 -3.542 1.00 35.09 C
ATOM 8812 CG LYS B 48 -85.003 -49.723 -2.127 1.00 36.00 C
ATOM 8815 CD LYS B 48 -86.174 -50.338 -1.350 1.00 37.13 C
ATOM 8818 CE LYS B 48 -87.312 -49.340 -1.094 1.00 37.90 C
ATOM 8821 NZ LYS B 48 -86.908 -48.161 -.272 1.00 38.31 N
ATOM 8825 C LYS B 48 -84.586 -48.487 -5.835 1.00 35.13 C
ATOM 8826 O LYS B 48 -85.544 -49.030 -6.361 1.00 34.60 O
ATOM 8828 N ALA B 49 -83.858 -47.576 -6.474 1.00 36.09 N
ATOM 8829 CA ALA B 49 -84.093 -47.261 -7.886 1.00 36.87 C
ATOM 8831 CB ALA B 49 -83.550 -45.880 -8.238 1.00 36.73 C
ATOM 8835 C ALA B 49 -83.406 -48.325 -8.714 1.00 37.56 C
ATOM 8836 O ALA B 49 -82.315 -48.761 -8.363 1.00 37.62 O
ATOM 8838 N GLU B 50 -84.028 -48.754 -9.807 1.00 38.54 N
ATOM 8839 CA GLU B 50 -83.399 -49.772 -10.652 1.00 39.40 C
ATOM 8841 CB GLU B 50 -84.380 -50.384 -11.673 1.00 39.71 C
ATOM 8844 CG GLU B 50 -83.959 -51.808 -12.179 1.00 41.33 C
ATOM 8847 CD GLU B 50 -83.733 -52.860 -11.039 1.00 42.88 C
ATOM 8848 OE1 GLU B 50 -84.683 -53.628 -10.718 1.00 42.94 O
ATOM 8849 OE2 GLU B 50 -82.603 -52.921 -10.472 1.00 42.96 O
ATOM 8850 C GLU B 50 -82.171 -49.163 -11.330 1.00 39.43 C
ATOM 8851 O GLU B 50 -82.211 -48.017 -11.791 1.00 39.66 O
ATOM 8853 N PHE B 51 -81.084 -49.929 -11.376 1.00 39.32 N
ATOM 8854 CA PHE B 51 -79.763 -49.360 -11.636 1.00 39.32 C
ATOM 8856 CB PHE B 51 -78.675 -50.429 -11.476 1.00 39.62 C
ATOM 8859 CG PHE B 51 -78.470 -50.889 -10.032 1.00 41.82 C
ATOM 8860 CD1 PHE B 51 -78.093 -49.978 -9.032 1.00 42.93 C
ATOM 8862 CE1 PHE B 51 -77.892 -50.391 -7.705 1.00 43.30 C
ATOM 8864 CZ PHE B 51 -78.059 -51.729 -7.359 1.00 44.33 C
ATOM 8866 CE2 PHE B 51 -78.430 -52.659 -8.341 1.00 44.75 C
ATOM 8868 CD2 PHE B 51 -78.633 -52.234 -9.677 1.00 44.06 C
ATOM 8870 C PHE B 51 -79.646 -48.625 -12.976 1.00 38.57 C
ATOM 8871 O PHE B 51 -79.045 -47.564 -13.046 1.00 38.50 O
ATOM 8873 N LEU B 52 -80.262 -49.155 -14.024 1.00 37.99 N
ATOM 8874 CA LEU B 52 -80.176 -48.539 -15.351 1.00 37.42 C
ATOM 8876 CB LEU B 52 -80.774 -49.476 -16.399 1.00 37.66 C
ATOM 8879 CG LEU B 52 -80.502 -49.168 -17.876 1.00 38.39 C
ATOM 8881 CD1 LEU B 52 -80.171 -50.452 -18.652 1.00 38.46 C
ATOM 8885 CD2 LEU B 52 -81.703 -48.432 -18.500 1.00 39.23 C
ATOM 8889 C LEU B 52 -80.824 -47.143 -15.431 1.00 36.69 C
ATOM 8890 O LEU B 52 -80.383 -46.312 -16.224 1.00 36.59 O
ATOM 8892 N THR B 53 -81.859 -46.879 -14.625 1.00 35.87 N
ATOM 8893 CA THR B 53 -82.409 -45.510 -14.513 1.00 34.91 C

ATOM 8895 CB THR B 53 -83.784 -45.421 -13.805 1.00 34.72 C
ATOM 8897 OG1 THR B 53 -84.724 -46.269 -14.455 1.00 34.04 O
ATOM 8899 CG2 THR B 53 -84.316 -43.981 -13.855 1.00 34.81 C
ATOM 8903 C THR B 53 -81.454 -44.642 -13.722 1.00 34.05 C
ATOM 8904 O THR B 53 -81.170 -43.513 -14.121 1.00 34.16 O
ATOM 8906 N LEU B 54 -80.987 -45.167 -12.593 1.00 32.84 N
ATOM 8907 CA LEU B 54 -80.027 -44.461 -11.772 1.00 32.16 C
ATOM 8909 CB LEU B 54 -79.506 -45.354 -10.662 1.00 32.27 C
ATOM 8912 CG LEU B 54 -78.521 -44.702 -9.698 1.00 32.56 C
ATOM 8914 CD1 LEU B 54 -79.275 -43.760 -8.769 1.00 32.38 C
ATOM 8918 CD2 LEU B 54 -77.755 -45.789 -8.917 1.00 33.29 C
ATOM 8922 C LEU B 54 -78.870 -44.006 -12.634 1.00 31.50 C
ATOM 8923 O LEU B 54 -78.509 -42.840 -12.607 1.00 31.98 O
ATOM 8925 N LEU B 55 -78.297 -44.914 -13.418 1.00 30.43 N
ATOM 8926 CA LEU B 55 -77.220 -44.540 -14.333 1.00 29.36 C
ATOM 8928 CB LEU B 55 -76.765 -45.733 -15.173 1.00 29.23 C
ATOM 8931 CG LEU B 55 -76.157 -46.902 -14.391 1.00 28.60 C
ATOM 8933 CD1 LEU B 55 -75.697 -48.004 -15.348 1.00 27.60 C
ATOM 8937 CD2 LEU B 55 -75.020 -46.440 -13.469 1.00 27.20 C
ATOM 8941 C LEU B 55 -77.678 -43.406 -15.230 1.00 28.60 C
ATOM 8942 O LEU B 55 -77.063 -42.365 -15.267 1.00 28.17 O
ATOM 8944 N GLU B 56 -78.786 -43.594 -15.919 1.00 28.23 N
ATOM 8945 CA GLU B 56 -79.326 -42.530 -16.759 1.00 28.64 C
ATOM 8947 CB GLU B 56 -80.567 -43.031 -17.524 1.00 29.27 C
ATOM 8950 CG GLU B 56 -80.229 -43.783 -18.829 1.00 31.73 C
ATOM 8953 CD GLU B 56 -81.265 -44.860 -19.206 1.00 35.52 C
ATOM 8954 OE1 GLU B 56 -82.474 -44.693 -18.889 1.00 36.97 O
ATOM 8955 OE2 GLU B 56 -80.856 -45.877 -19.825 1.00 37.55 O
ATOM 8956 C GLU B 56 -79.632 -41.203 -15.995 1.00 27.77 C
ATOM 8957 O GLU B 56 -79.561 -40.103 -16.582 1.00 27.84 O
ATOM 8959 N LEU B 57 -79.976 -41.303 -14.710 1.00 26.29 N
ATOM 8960 CA LEU B 57 -80.158 -40.120 -13.895 1.00 25.06 C
ATOM 8962 CB LEU B 57 -80.724 -40.462 -12.514 1.00 24.83 C
ATOM 8965 CG LEU B 57 -80.952 -39.298 -11.544 1.00 23.72 C
ATOM 8967 CD1 LEU B 57 -81.909 -38.278 -12.117 1.00 21.43 C
ATOM 8971 CD2 LEU B 57 -81.477 -39.830 -10.227 1.00 22.41 C
ATOM 8975 C LEU B 57 -78.801 -39.459 -13.780 1.00 24.40 C
ATOM 8976 O LEU B 57 -78.591 -38.373 -14.306 1.00 24.70 O
ATOM 8978 N ILE B 58 -77.855 -40.133 -13.144 1.00 23.56 N
ATOM 8979 CA ILE B 58 -76.509 -39.574 -12.991 1.00 22.91 C
ATOM 8981 CB ILE B 58 -75.454 -40.635 -12.599 1.00 22.49 C
ATOM 8983 CG1 ILE B 58 -75.753 -41.251 -11.235 1.00 22.09 C
ATOM 8986 CD1 ILE B 58 -74.936 -42.464 -10.926 1.00 20.88 C
ATOM 8990 CG2 ILE B 58 -74.103 -39.992 -12.534 1.00 22.63 C
ATOM 8994 C ILE B 58 -76.062 -38.927 -14.302 1.00 22.64 C
ATOM 8995 O ILE B 58 -75.603 -37.796 -14.315 1.00 22.38 O
ATOM 8997 N ASP B 59 -76.228 -39.646 -15.404 1.00 22.56 N
ATOM 8998 CA ASP B 59 -75.715 -39.196 -16.684 1.00 22.76 C
ATOM 9000 CB ASP B 59 -75.926 -40.269 -17.757 1.00 22.93 C
ATOM 9003 CG ASP B 59 -75.274 -39.904 -19.088 1.00 24.58 C
ATOM 9004 OD1 ASP B 59 -74.157 -39.322 -19.081 1.00 25.70 O
ATOM 9005 OD2 ASP B 59 -75.897 -40.186 -20.142 1.00 27.51 O
ATOM 9006 C ASP B 59 -76.343 -37.863 -17.104 1.00 22.40 C
ATOM 9007 O ASP B 59 -75.634 -36.939 -17.520 1.00 22.40 O
ATOM 9009 N ASN B 60 -77.662 -37.767 -16.991 1.00 21.91 N
ATOM 9010 CA ASN B 60 -78.349 -36.500 -17.217 1.00 21.70 C
ATOM 9012 CB ASN B 60 -79.867 -36.674 -17.088 1.00 22.12 C
ATOM 9015 CG ASN B 60 -80.477 -37.390 -18.268 1.00 22.76 C
ATOM 9016 OD1 ASN B 60 -80.027 -37.233 -19.393 1.00 24.28 O
ATOM 9017 ND2 ASN B 60 -81.515 -38.172 -18.017 1.00 24.36 N

ATOM 9020 C ASN B 60 -77.898 -35.427 -16.234 1.00 21.17 C
ATOM 9021 O ASN B 60 -77.700 -34.273 -16.614 1.00 20.85 O
ATOM 9023 N VAL B 61 -77.745 -35.805 -14.968 1.00 20.60 N
ATOM 9024 CA VAL B 61 -77.382 -34.841 -13.942 1.00 20.48 C
ATOM 9026 CB VAL B 61 -77.277 -35.490 -12.551 1.00 20.26 C
ATOM 9028 CG1 VAL B 61 -76.585 -34.562 -11.565 1.00 19.92 C
ATOM 9032 CG2 VAL B 61 -78.668 -35.857 -12.049 1.00 20.66 C
ATOM 9036 C VAL B 61 -76.068 -34.208 -14.335 1.00 20.66 C
ATOM 9037 O VAL B 61 -75.871 -32.998 -14.182 1.00 20.74 O
ATOM 9039 N GLN B 62 -75.187 -35.048 -14.875 1.00 20.92 N
ATOM 9040 CA GLN B 62 -73.854 -34.636 -15.285 1.00 20.69 C
ATOM 9042 CB GLN B 62 -72.917 -35.847 -15.404 1.00 20.77 C
ATOM 9045 CG GLN B 62 -72.456 -36.369 -14.035 1.00 20.91 C
ATOM 9048 CD GLN B 62 -71.328 -37.383 -14.112 1.00 20.75 C
ATOM 9049 OE1 GLN B 62 -70.512 -37.498 -13.192 1.00 20.93 O
ATOM 9050 NE2 GLN B 62 -71.291 -38.135 -15.195 1.00 20.39 N
ATOM 9053 C GLN B 62 -73.900 -33.834 -16.567 1.00 20.32 C
ATOM 9054 O GLN B 62 -73.410 -32.712 -16.569 1.00 20.79 O
ATOM 9056 N ARG B 63 -74.512 -34.373 -17.625 1.00 19.87 N
ATOM 9057 CA ARG B 63 -74.520 -33.696 -18.940 1.00 19.81 C
ATOM 9059 CB ARG B 63 -75.240 -34.536 -20.013 1.00 19.75 C
ATOM 9062 CG ARG B 63 -74.492 -35.846 -20.345 1.00 21.69 C
ATOM 9065 CD ARG B 63 -75.158 -36.786 -21.368 1.00 24.89 C
ATOM 9068 NE ARG B 63 -74.674 -36.558 -22.741 1.00 29.32 N
ATOM 9070 CZ ARG B 63 -75.323 -35.878 -23.702 1.00 33.71 C
ATOM 9071 NH1 ARG B 63 -76.537 -35.345 -23.510 1.00 36.67 N
ATOM 9074 NH2 ARG B 63 -74.761 -35.736 -24.894 1.00 34.58 N
ATOM 9077 C ARG B 63 -75.099 -32.276 -18.822 1.00 19.39 C
ATOM 9078 O ARG B 63 -74.553 -31.310 -19.395 1.00 19.63 O
ATOM 9080 N LEU B 64 -76.155 -32.148 -18.017 1.00 18.62 N
ATOM 9081 CA LEU B 64 -76.811 -30.856 -17.753 1.00 17.96 C
ATOM 9083 CB LEU B 64 -78.136 -31.077 -17.008 1.00 17.97 C
ATOM 9086 CG LEU B 64 -79.264 -31.737 -17.809 1.00 17.08 C
ATOM 9088 CD1 LEU B 64 -80.276 -32.354 -16.879 1.00 15.15 C
ATOM 9092 CD2 LEU B 64 -79.904 -30.734 -18.737 1.00 15.30 C
ATOM 9096 C LEU B 64 -75.975 -29.847 -16.966 1.00 17.39 C
ATOM 9097 O LEU B 64 -76.370 -28.685 -16.825 1.00 17.38 O
ATOM 9099 N GLY B 65 -74.848 -30.286 -16.432 1.00 16.73 N
ATOM 9100 CA GLY B 65 -73.917 -29.374 -15.818 1.00 16.65 C
ATOM 9103 C GLY B 65 -74.077 -29.249 -14.319 1.00 16.68 C
ATOM 9104 O GLY B 65 -73.565 -28.302 -13.718 1.00 16.79 O
ATOM 9106 N LEU B 66 -74.758 -30.209 -13.702 1.00 16.60 N
ATOM 9107 CA LEU B 66 -74.978 -30.177 -12.264 1.00 16.58 C
ATOM 9109 CB LEU B 66 -76.465 -30.389 -11.957 1.00 16.35 C
ATOM 9112 CG LEU B 66 -77.363 -29.187 -12.234 1.00 15.57 C
ATOM 9114 CD1 LEU B 66 -78.828 -29.602 -12.163 1.00 15.26 C
ATOM 9118 CD2 LEU B 66 -77.063 -28.051 -11.270 1.00 13.66 C
ATOM 9122 C LEU B 66 -74.129 -31.203 -11.513 1.00 16.94 C
ATOM 9123 O LEU B 66 -74.152 -31.251 -10.279 1.00 17.50 O
ATOM 9125 N GLY B 67 -73.373 -32.017 -12.236 1.00 17.03 N
ATOM 9126 CA GLY B 67 -72.541 -33.036 -11.602 1.00 17.13 C
ATOM 9129 C GLY B 67 -71.642 -32.557 -10.461 1.00 17.08 C
ATOM 9130 O GLY B 67 -71.378 -33.317 -9.522 1.00 17.33 O
ATOM 9132 N TYR B 68 -71.159 -31.316 -10.541 1.00 16.83 N
ATOM 9133 CA TYR B 68 -70.217 -30.804 -9.552 1.00 16.64 C
ATOM 9135 CB TYR B 68 -69.654 -29.437 -9.951 1.00 16.25 C
ATOM 9138 CG TYR B 68 -70.609 -28.273 -9.802 1.00 13.51 C
ATOM 9139 CD1 TYR B 68 -70.521 -27.411 -8.738 1.00 10.49 C
ATOM 9141 CE1 TYR B 68 -71.407 -26.342 -8.608 1.00 10.25 C
ATOM 9143 CZ TYR B 68 -72.382 -26.135 -9.555 1.00 9.74 C

ATOM 9144 OH TYR B 68 -73.253 -25.086 -9.450 1.00 7.62 O
ATOM 9146 CE2 TYR B 68 -72.484 -26.978 -10.625 1.00 11.14 C
ATOM 9148 CD2 TYR B 68 -71.603 -28.037 -10.748 1.00 12.56 C
ATOM 9150 C TYR B 68 -70.828 -30.700 -8.172 1.00 17.79 C
ATOM 9151 O TYR B 68 -70.107 -30.811 -7.182 1.00 18.00 O
ATOM 9153 N ARG B 69 -72.146 -30.485 -8.090 1.00 18.85 N
ATOM 9154 CA ARG B 69 -72.784 -30.269 -6.789 1.00 19.46 C
ATOM 9156 CB ARG B 69 -73.708 -29.047 -6.819 1.00 19.23 C
ATOM 9159 CG ARG B 69 -75.030 -29.219 -7.509 1.00 18.83 C
ATOM 9162 CD ARG B 69 -76.053 -28.192 -6.985 1.00 17.73 C
ATOM 9165 NE ARG B 69 -75.642 -26.830 -7.297 1.00 16.01 N
ATOM 9167 CZ ARG B 69 -75.330 -25.889 -6.417 1.00 14.68 C
ATOM 9168 NH1 ARG B 69 -75.400 -26.093 -5.112 1.00 14.99 N
ATOM 9171 NH2 ARG B 69 -74.959 -24.707 -6.861 1.00 15.04 N
ATOM 9174 C ARG B 69 -73.490 -31.489 -6.234 1.00 20.50 C
ATOM 9175 O ARG B 69 -74.084 -31.418 -5.163 1.00 20.67 O
ATOM 9177 N PHE B 70 -73.416 -32.607 -6.959 1.00 22.04 N
ATOM 9178 CA PHE B 70 -73.853 -33.917 -6.450 1.00 23.03 C
ATOM 9180 CB PHE B 70 -75.081 -34.428 -7.211 1.00 22.94 C
ATOM 9183 CG PHE B 70 -76.236 -33.503 -7.157 1.00 21.78 C
ATOM 9184 CD1 PHE B 70 -77.024 -33.441 -6.028 1.00 20.54 C
ATOM 9186 CE1 PHE B 70 -78.076 -32.571 -5.959 1.00 20.32 C
ATOM 9188 CZ PHE B 70 -78.353 -31.752 -7.025 1.00 20.73 C
ATOM 9190 CE2 PHE B 70 -77.564 -31.796 -8.160 1.00 21.24 C
ATOM 9192 CD2 PHE B 70 -76.511 -32.665 -8.220 1.00 21.22 C
ATOM 9194 C PHE B 70 -72.765 -34.962 -6.570 1.00 24.33 C
ATOM 9195 O PHE B 70 -73.069 -36.142 -6.614 1.00 24.56 O
ATOM 9197 N GLU B 71 -71.500 -34.547 -6.624 1.00 26.01 N
ATOM 9198 CA GLU B 71 -70.413 -35.506 -6.804 1.00 27.04 C
ATOM 9200 CB GLU B 71 -69.042 -34.824 -6.885 1.00 27.48 C
ATOM 9203 CG GLU B 71 -67.851 -35.816 -6.794 1.00 28.94 C
ATOM 9206 CD GLU B 71 -66.491 -35.192 -7.081 1.00 30.38 C
ATOM 9207 OE1 GLU B 71 -66.398 -34.192 -7.835 1.00 30.52 O
ATOM 9208 OE2 GLU B 71 -65.501 -35.730 -6.544 1.00 32.16 O
ATOM 9209 C GLU B 71 -70.436 -36.531 -5.680 1.00 27.46 C
ATOM 9210 O GLU B 71 -70.449 -37.723 -5.937 1.00 27.67 O
ATOM 9212 N SER B 72 -70.464 -36.087 -4.435 1.00 28.04 N
ATOM 9213 CA SER B 72 -70.381 -37.044 -3.348 1.00 28.86 C
ATOM 9215 CB SER B 72 -70.388 -36.340 -1.983 1.00 29.09 C
ATOM 9218 OG SER B 72 -71.649 -35.751 -1.687 1.00 30.21 O
ATOM 9220 C SER B 72 -71.519 -38.058 -3.481 1.00 29.30 C
ATOM 9221 O SER B 72 -71.304 -39.265 -3.384 1.00 29.24 O
ATOM 9223 N ASP B 73 -72.719 -37.560 -3.756 1.00 30.03 N
ATOM 9224 CA ASP B 73 -73.897 -38.417 -3.874 1.00 30.63 C
ATOM 9226 CB ASP B 73 -75.184 -37.598 -4.116 1.00 30.74 C
ATOM 9229 CG ASP B 73 -75.419 -36.509 -3.052 1.00 31.84 C
ATOM 9230 OD1 ASP B 73 -75.562 -36.830 -1.841 1.00 31.70 O
ATOM 9231 OD2 ASP B 73 -75.473 -35.317 -3.443 1.00 33.81 O
ATOM 9232 C ASP B 73 -73.722 -39.443 -4.994 1.00 30.81 C
ATOM 9233 O ASP B 73 -74.130 -40.590 -4.835 1.00 31.39 O
ATOM 9235 N ILE B 74 -73.122 -39.031 -6.112 1.00 30.96 N
ATOM 9236 CA ILE B 74 -72.917 -39.912 -7.282 1.00 31.04 C
ATOM 9238 CB ILE B 74 -72.461 -39.114 -8.524 1.00 30.88 C
ATOM 9240 CG1 ILE B 74 -73.585 -38.213 -9.018 1.00 30.99 C
ATOM 9243 CD1 ILE B 74 -73.105 -37.120 -9.923 1.00 31.54 C
ATOM 9247 CG2 ILE B 74 -72.052 -40.035 -9.642 1.00 29.85 C
ATOM 9251 C ILE B 74 -71.885 -41.005 -6.999 1.00 31.45 C
ATOM 9252 O ILE B 74 -72.098 -42.165 -7.347 1.00 31.31 O
ATOM 9254 N ARG B 75 -70.768 -40.628 -6.380 1.00 31.93 N
ATOM 9255 CA ARG B 75 -69.778 -41.601 -5.947 1.00 32.38 C

ATOM 9257 CB ARG B 75 -68.629 -40.959 -5.137 1.00 32.87 C
ATOM 9260 CG ARG B 75 -67.310 -40.751 -5.915 1.00 35.01 C
ATOM 9263 CD ARG B 75 -66.089 -40.489 -5.003 1.00 37.62 C
ATOM 9266 NE ARG B 75 -65.260 -41.687 -4.783 1.00 41.03 N
ATOM 9268 CZ ARG B 75 -64.461 -42.253 -5.700 1.00 44.29 C
ATOM 9269 NH1 ARG B 75 -64.385 -41.751 -6.931 1.00 46.22 N
ATOM 9272 NH2 ARG B 75 -63.741 -43.341 -5.404 1.00 44.30 N
ATOM 9275 C ARG B 75 -70.478 -42.673 -5.126 1.00 32.18 C
ATOM 9276 O ARG B 75 -70.307 -43.849 -5.398 1.00 32.19 O
ATOM 9278 N ARG B 76 -71.280 -42.275 -4.143 1.00 32.21 N
ATOM 9279 CA ARG B 76 -71.975 -43.256 -3.307 1.00 32.61 C
ATOM 9281 CB ARG B 76 -72.737 -42.582 -2.162 1.00 32.75 C
ATOM 9284 CG ARG B 76 -71.880 -42.320 -.929 1.00 33.44 C
ATOM 9287 CD ARG B 76 -72.720 -42.046 .334 1.00 34.16 C
ATOM 9290 NE ARG B 76 -73.797 -41.074 .124 1.00 34.53 N
ATOM 9292 CZ ARG B 76 -73.627 -39.765 -.063 1.00 34.38 C
ATOM 9293 NH1 ARG B 76 -72.414 -39.219 -.092 1.00 34.34 N
ATOM 9296 NH2 ARG B 76 -74.689 -38.993 -.241 1.00 34.71 N
ATOM 9299 C ARG B 76 -72.918 -44.159 -4.112 1.00 32.81 C
ATOM 9300 O ARG B 76 -72.863 -45.379 -3.995 1.00 32.86 O
ATOM 9302 N ALA B 77 -73.780 -43.559 -4.923 1.00 33.10 N
ATOM 9303 CA ALA B 77 -74.655 -44.307 -5.813 1.00 33.27 C
ATOM 9305 CB ALA B 77 -75.321 -43.366 -6.770 1.00 33.26 C
ATOM 9309 C ALA B 77 -73.884 -45.370 -6.578 1.00 33.80 C
ATOM 9310 O ALA B 77 -74.235 -46.542 -6.559 1.00 33.75 O
ATOM 9312 N LEU B 78 -72.816 -44.952 -7.242 1.00 34.77 N
ATOM 9313 CA LEU B 78 -71.987 -45.868 -8.019 1.00 35.41 C
ATOM 9315 CB LEU B 78 -70.845 -45.109 -8.702 1.00 35.01 C
ATOM 9318 CG LEU B 78 -71.220 -44.092 -9.782 1.00 34.37 C
ATOM 9320 CD1 LEU B 78 -69.945 -43.502 -10.381 1.00 33.93 C
ATOM 9324 CD2 LEU B 78 -72.109 -44.692 -10.873 1.00 32.94 C
ATOM 9328 C LEU B 78 -71.409 -46.974 -7.142 1.00 36.50 C
ATOM 9329 O LEU B 78 -71.336 -48.124 -7.552 1.00 36.87 O
ATOM 9331 N ASP B 79 -71.005 -46.619 -5.931 1.00 37.74 N
ATOM 9332 CA ASP B 79 -70.308 -47.545 -5.056 1.00 38.74 C
ATOM 9334 CB ASP B 79 -69.787 -46.810 -3.819 1.00 38.99 C
ATOM 9337 CG ASP B 79 -68.499 -47.386 -3.313 1.00 40.08 C
ATOM 9338 OD1 ASP B 79 -68.494 -48.591 -2.976 1.00 42.32 O
ATOM 9339 OD2 ASP B 79 -67.494 -46.638 -3.261 1.00 41.24 O
ATOM 9340 C ASP B 79 -71.207 -48.705 -4.645 1.00 39.42 C
ATOM 9341 O ASP B 79 -70.736 -49.835 -4.505 1.00 39.58 O
ATOM 9343 N ARG B 80 -72.495 -48.424 -4.450 1.00 40.26 N
ATOM 9344 CA ARG B 80 -73.471 -49.470 -4.143 1.00 40.92 C
ATOM 9346 CB ARG B 80 -74.823 -48.881 -3.716 1.00 41.46 C
ATOM 9349 CG ARG B 80 -74.871 -48.247 -2.308 1.00 42.87 C
ATOM 9352 CD ARG B 80 -76.316 -47.826 -1.936 1.00 44.62 C
ATOM 9355 NE ARG B 80 -76.946 -46.968 -2.949 1.00 45.87 N
ATOM 9357 CZ ARG B 80 -76.741 -45.651 -3.089 1.00 46.82 C
ATOM 9358 NH1 ARG B 80 -75.905 -44.989 -2.282 1.00 46.27 N
ATOM 9361 NH2 ARG B 80 -77.378 -44.988 -4.059 1.00 47.22 N
ATOM 9364 C ARG B 80 -73.667 -50.341 -5.371 1.00 40.77 C
ATOM 9365 O ARG B 80 -73.642 -51.563 -5.275 1.00 41.06 O
ATOM 9367 N PHE B 81 -73.863 -49.705 -6.520 1.00 40.56 N
ATOM 9368 CA PHE B 81 -73.986 -50.418 -7.787 1.00 40.59 C
ATOM 9370 CB PHE B 81 -73.984 -49.426 -8.956 1.00 40.73 C
ATOM 9373 CG PHE B 81 -73.898 -50.063 -10.323 1.00 40.84 C
ATOM 9374 CD1 PHE B 81 -75.000 -50.668 -10.893 1.00 41.39 C
ATOM 9376 CE1 PHE B 81 -74.925 -51.236 -12.167 1.00 41.67 C
ATOM 9378 CZ PHE B 81 -73.741 -51.191 -12.877 1.00 41.33 C
ATOM 9380 CE2 PHE B 81 -72.638 -50.580 -12.326 1.00 41.19 C

ATOM 9382 CD2 PHE B 81 -72.720 -50.012 -11.057 1.00 41.39 C
ATOM 9384 C PHE B 81 -72.871 -51.441 -7.953 1.00 40.47 C
ATOM 9385 O PHE B 81 -73.134 -52.583 -8.311 1.00 40.85 O
ATOM 9387 N VAL B 82 -71.633 -51.051 -7.683 1.00 40.26 N
ATOM 9388 CA VAL B 82 -70.522 -51.986 -7.821 1.00 40.24 C
ATOM 9390 CB VAL B 82 -69.173 -51.386 -7.379 1.00 40.28 C
ATOM 9392 CG1 VAL B 82 -68.164 -52.493 -7.063 1.00 39.98 C
ATOM 9396 CG2 VAL B 82 -68.644 -50.462 -8.451 1.00 40.09 C
ATOM 9400 C VAL B 82 -70.788 -53.230 -7.005 1.00 40.16 C
ATOM 9401 O VAL B 82 -70.880 -54.313 -7.559 1.00 40.13 O
ATOM 9403 N SER B 83 -70.953 -53.056 -5.698 1.00 40.26 N
ATOM 9404 CA SER B 83 -71.070 -54.174 -4.749 1.00 40.43 C
ATOM 9406 CB SER B 83 -70.797 -53.666 -3.331 1.00 40.54 C
ATOM 9409 OG SER B 83 -71.256 -52.330 -3.191 1.00 40.89 O
ATOM 9411 C SER B 83 -72.415 -54.912 -4.831 1.00 40.34 C
ATOM 9412 O SER B 83 -73.137 -55.046 -3.845 1.00 39.99 O
ATOM 9414 N SER B 84 -72.698 -55.400 -6.038 1.00 40.57 N
ATOM 9415 CA SER B 84 -73.902 -56.154 -6.411 1.00 40.63 C
ATOM 9417 CB SER B 84 -75.154 -55.679 -5.651 1.00 40.56 C
ATOM 9420 OG SER B 84 -75.292 -54.268 -5.663 1.00 39.82 O
ATOM 9422 C SER B 84 -74.104 -56.026 -7.940 1.00 40.85 C
ATOM 9423 O SER B 84 -75.104 -55.462 -8.395 1.00 41.24 O
ATOM 9425 N GLY B 85 -73.136 -56.524 -8.720 1.00 40.75 N
ATOM 9426 CA GLY B 85 -73.201 -56.506 -10.191 1.00 40.64 C
ATOM 9429 C GLY B 85 -73.225 -55.120 -10.815 1.00 40.64 C
ATOM 9430 O GLY B 85 -74.133 -54.794 -11.590 1.00 40.32 O
ATOM 9432 N THR B 93 -74.847 -57.360 -18.759 1.00 36.30 N
ATOM 9433 CA THR B 93 -75.593 -58.129 -19.774 1.00 35.99 C
ATOM 9435 CB THR B 93 -76.251 -59.379 -19.152 1.00 35.87 C
ATOM 9437 OG1 THR B 93 -76.347 -60.389 -20.158 1.00 35.64 O
ATOM 9439 CG2 THR B 93 -77.646 -59.062 -18.548 1.00 34.95 C
ATOM 9443 C THR B 93 -76.625 -57.274 -20.583 1.00 35.90 C
ATOM 9444 O THR B 93 -77.764 -57.688 -20.843 1.00 35.74 O
ATOM 9446 N SER B 94 -76.175 -56.076 -20.963 1.00 35.58 N
ATOM 9447 CA SER B 94 -76.874 -55.150 -21.866 1.00 34.97 C
ATOM 9449 CB SER B 94 -78.074 -54.472 -21.190 1.00 35.06 C
ATOM 9452 OG SER B 94 -77.702 -53.260 -20.541 1.00 34.37 O
ATOM 9454 C SER B 94 -75.831 -54.097 -22.232 1.00 34.39 C
ATOM 9455 O SER B 94 -75.212 -53.518 -21.341 1.00 34.11 O
ATOM 9457 N LEU B 95 -75.619 -53.864 -23.522 1.00 33.77 N
ATOM 9458 CA LEU B 95 -74.490 -53.045 -23.952 1.00 33.33 C
ATOM 9460 CB LEU B 95 -74.373 -53.010 -25.475 1.00 33.30 C
ATOM 9463 CG LEU B 95 -73.154 -52.246 -26.006 1.00 33.27 C
ATOM 9465 CD1 LEU B 95 -71.909 -52.455 -25.137 1.00 32.89 C
ATOM 9469 CD2 LEU B 95 -72.864 -52.649 -27.438 1.00 33.19 C
ATOM 9473 C LEU B 95 -74.551 -51.623 -23.413 1.00 33.00 C
ATOM 9474 O LEU B 95 -73.588 -51.151 -22.809 1.00 32.83 O
ATOM 9476 N HIS B 96 -75.678 -50.949 -23.633 1.00 32.64 N
ATOM 9477 CA HIS B 96 -75.853 -49.576 -23.171 1.00 32.39 C
ATOM 9479 CB HIS B 96 -77.246 -49.069 -23.527 1.00 32.64 C
ATOM 9482 CG HIS B 96 -77.528 -47.689 -23.025 1.00 34.16 C
ATOM 9483 ND1 HIS B 96 -76.565 -46.703 -22.981 1.00 36.21 N
ATOM 9485 CE1 HIS B 96 -77.096 -45.594 -22.496 1.00 36.92 C
ATOM 9487 NE2 HIS B 96 -78.371 -45.827 -22.227 1.00 37.06 N
ATOM 9489 CD2 HIS B 96 -78.664 -47.130 -22.548 1.00 35.43 C
ATOM 9491 C HIS B 96 -75.612 -49.445 -21.665 1.00 31.78 C
ATOM 9492 O HIS B 96 -74.936 -48.523 -21.215 1.00 31.95 O
ATOM 9494 N GLY B 97 -76.156 -50.372 -20.887 1.00 31.10 N
ATOM 9495 CA GLY B 97 -75.907 -50.396 -19.446 1.00 30.52 C
ATOM 9498 C GLY B 97 -74.434 -50.532 -19.085 1.00 29.95 C

ATOM 9499 O GLY B 97 -73.936 -49.797 -18.241 1.00 30.21 O
ATOM 9501 N THR B 98 -73.740 -51.470 -19.726 1.00 29.15 N
ATOM 9502 CA THR B 98 -72.314 -51.690 -19.490 1.00 28.55 C
ATOM 9504 CB THR B 98 -71.803 -52.955 -20.248 1.00 28.48 C
ATOM 9506 OG1 THR B 98 -72.678 -54.066 -19.997 1.00 28.41 O
ATOM 9508 CG2 THR B 98 -70.405 -53.331 -19.816 1.00 27.74 C
ATOM 9512 C THR B 98 -71.492 -50.452 -19.894 1.00 28.31 C
ATOM 9513 O THR B 98 -70.658 -49.979 -19.127 1.00 28.13 O
ATOM 9515 N ALA B 99 -71.750 -49.910 -21.080 1.00 28.04 N
ATOM 9516 CA ALA B 99 -70.984 -48.758 -21.578 1.00 27.88 C
ATOM 9518 CB ALA B 99 -71.387 -48.406 -23.014 1.00 27.78 C
ATOM 9522 C ALA B 99 -71.127 -47.538 -20.684 1.00 27.62 C
ATOM 9523 O ALA B 99 -70.135 -46.885 -20.361 1.00 27.84 O
ATOM 9525 N LEU B 100 -72.357 -47.233 -20.290 1.00 27.20 N
ATOM 9526 CA LEU B 100 -72.613 -46.088 -19.422 1.00 27.08 C
ATOM 9528 CB LEU B 100 -74.122 -45.900 -19.230 1.00 26.95 C
ATOM 9531 CG LEU B 100 -74.560 -44.715 -18.367 1.00 26.27 C
ATOM 9533 CD1 LEU B 100 -73.753 -43.478 -18.734 1.00 26.19 C
ATOM 9537 CD2 LEU B 100 -76.052 -44.445 -18.504 1.00 25.20 C
ATOM 9541 C LEU B 100 -71.928 -46.221 -18.046 1.00 27.23 C
ATOM 9542 O LEU B 100 -71.368 -45.243 -17.523 1.00 27.16 O
ATOM 9544 N SER B 101 -71.980 -47.429 -17.472 1.00 27.00 N
ATOM 9545 CA SER B 101 -71.475 -47.682 -16.117 1.00 26.63 C
ATOM 9547 CB SER B 101 -72.039 -48.992 -15.568 1.00 26.49 C
ATOM 9550 OG SER B 101 -71.758 -50.063 -16.442 1.00 26.38 O
ATOM 9552 C SER B 101 -69.956 -47.740 -16.090 1.00 26.47 C
ATOM 9553 O SER B 101 -69.326 -47.324 -15.121 1.00 26.35 O
ATOM 9555 N PHE B 102 -69.381 -48.288 -17.154 1.00 26.29 N
ATOM 9556 CA PHE B 102 -67.934 -48.332 -17.322 1.00 25.91 C
ATOM 9558 CB PHE B 102 -67.588 -49.005 -18.652 1.00 25.96 C
ATOM 9561 CG PHE B 102 -66.133 -49.020 -18.958 1.00 25.81 C
ATOM 9562 CD1 PHE B 102 -65.360 -50.115 -18.633 1.00 25.96 C
ATOM 9564 CE1 PHE B 102 -63.999 -50.122 -18.909 1.00 26.94 C
ATOM 9566 CZ PHE B 102 -63.403 -49.026 -19.519 1.00 26.27 C
ATOM 9568 CE2 PHE B 102 -64.174 -47.930 -19.848 1.00 26.19 C
ATOM 9570 CD2 PHE B 102 -65.531 -47.933 -19.573 1.00 26.04 C
ATOM 9572 C PHE B 102 -67.416 -46.911 -17.315 1.00 25.56 C
ATOM 9573 O PHE B 102 -66.486 -46.564 -16.568 1.00 25.37 O
ATOM 9575 N ARG B 103 -68.050 -46.095 -18.152 1.00 25.20 N
ATOM 9576 CA ARG B 103 -67.663 -44.696 -18.322 1.00 25.09 C
ATOM 9578 CB ARG B 103 -68.510 -44.026 -19.400 1.00 25.12 C
ATOM 9581 CG ARG B 103 -68.194 -42.561 -19.572 1.00 25.41 C
ATOM 9584 CD ARG B 103 -68.744 -42.035 -20.889 1.00 26.68 C
ATOM 9587 NE ARG B 103 -70.197 -41.843 -20.877 1.00 27.49 N
ATOM 9589 CZ ARG B 103 -70.826 -40.851 -20.246 1.00 26.56 C
ATOM 9590 NH1 ARG B 103 -70.139 -39.963 -19.531 1.00 27.11 N
ATOM 9593 NH2 ARG B 103 -72.148 -40.759 -20.310 1.00 25.20 N
ATOM 9596 C ARG B 103 -67.785 -43.898 -17.033 1.00 24.61 C
ATOM 9597 O ARG B 103 -66.865 -43.168 -16.659 1.00 24.67 O
ATOM 9599 N LEU B 104 -68.927 -44.013 -16.371 1.00 23.79 N
ATOM 9600 CA LEU B 104 -69.125 -43.263 -15.148 1.00 23.23 C
ATOM 9602 CB LEU B 104 -70.591 -43.342 -14.693 1.00 23.01 C
ATOM 9605 CG LEU B 104 -71.607 -42.620 -15.584 1.00 21.36 C
ATOM 9607 CD1 LEU B 104 -73.002 -42.860 -15.067 1.00 19.31 C
ATOM 9611 CD2 LEU B 104 -71.310 -41.157 -15.633 1.00 19.57 C
ATOM 9615 C LEU B 104 -68.156 -43.781 -14.071 1.00 23.15 C
ATOM 9616 O LEU B 104 -67.445 -43.007 -13.423 1.00 23.40 O
ATOM 9618 N LEU B 105 -68.106 -45.091 -13.894 1.00 22.79 N
ATOM 9619 CA LEU B 105 -67.203 -45.659 -12.916 1.00 22.40 C
ATOM 9621 CB LEU B 105 -67.303 -47.178 -12.912 1.00 22.42 C

ATOM 9624 CG LEU B 105 -68.505 -47.709 -12.163 1.00 21.82 C
ATOM 9626 CD1 LEU B 105 -68.810 -49.120 -12.591 1.00 21.95 C
ATOM 9630 CD2 LEU B 105 -68.201 -47.648 -10.692 1.00 22.14 C
ATOM 9634 C LEU B 105 -65.767 -45.239 -13.196 1.00 22.33 C
ATOM 9635 O LEU B 105 -65.049 -44.823 -12.275 1.00 22.13 O
ATOM 9637 N ARG B 106 -65.331 -45.342 -14.451 1.00 22.08 N
ATOM 9638 CA ARG B 106 -63.953 -44.973 -14.730 1.00 22.20 C
ATOM 9640 CB ARG B 106 -63.521 -45.266 -16.151 1.00 22.33 C
ATOM 9643 CG ARG B 106 -62.075 -44.827 -16.329 1.00 23.60 C
ATOM 9646 CD ARG B 106 -61.383 -45.445 -17.513 1.00 24.71 C
ATOM 9649 NE ARG B 106 -61.078 -46.852 -17.319 1.00 24.66 N
ATOM 9651 CZ ARG B 106 -60.418 -47.582 -18.206 1.00 25.75 C
ATOM 9652 NH1 ARG B 106 -59.995 -47.028 -19.337 1.00 26.41 N
ATOM 9655 NH2 ARG B 106 -60.182 -48.866 -17.971 1.00 26.54 N
ATOM 9658 C ARG B 106 -63.732 -43.504 -14.438 1.00 21.75 C
ATOM 9659 O ARG B 106 -62.801 -43.145 -13.725 1.00 21.50 O
ATOM 9661 N GLN B 107 -64.609 -42.680 -15.003 1.00 21.69 N
ATOM 9662 CA GLN B 107 -64.630 -41.239 -14.794 1.00 21.64 C
ATOM 9664 CB GLN B 107 -65.964 -40.664 -15.261 1.00 21.71 C
ATOM 9667 CG GLN B 107 -66.169 -39.178 -14.929 1.00 21.97 C
ATOM 9670 CD GLN B 107 -67.588 -38.723 -15.172 1.00 21.54 C
ATOM 9671 OE1 GLN B 107 -68.355 -39.365 -15.906 1.00 20.08 O
ATOM 9672 NE2 GLN B 107 -67.948 -37.600 -14.556 1.00 21.45 N
ATOM 9675 C GLN B 107 -64.454 -40.850 -13.352 1.00 21.70 C
ATOM 9676 O GLN B 107 -63.776 -39.865 -13.078 1.00 22.14 O
ATOM 9678 N HIS B 108 -65.091 -41.599 -12.450 1.00 21.53 N
ATOM 9679 CA HIS B 108 -65.049 -41.326 -11.019 1.00 21.63 C
ATOM 9681 CB HIS B 108 -66.447 -41.535 -10.429 1.00 21.47 C
ATOM 9684 CG HIS B 108 -67.416 -40.445 -10.752 1.00 20.91 C
ATOM 9685 ND1 HIS B 108 -67.541 -39.315 -9.976 1.00 20.66 N
ATOM 9687 CE1 HIS B 108 -68.476 -38.535 -10.490 1.00 20.90 C
ATOM 9689 NE2 HIS B 108 -68.966 -39.118 -11.567 1.00 19.67 N
ATOM 9691 CD2 HIS B 108 -68.326 -40.320 -11.747 1.00 20.76 C
ATOM 9693 C HIS B 108 -64.024 -42.209 -10.269 1.00 22.22 C
ATOM 9694 O HIS B 108 -64.220 -42.553 -9.104 1.00 22.17 O
ATOM 9696 N GLY B 109 -62.950 -42.613 -10.933 1.00 22.91 N
ATOM 9697 CA GLY B 109 -61.846 -43.288 -10.245 1.00 23.85 C
ATOM 9700 C GLY B 109 -61.986 -44.748 -9.800 1.00 24.50 C
ATOM 9701 O GLY B 109 -61.053 -45.306 -9.189 1.00 24.12 O
ATOM 9703 N PHE B 110 -63.128 -45.371 -10.094 1.00 25.16 N
ATOM 9704 CA PHE B 110 -63.309 -46.791 -9.800 1.00 25.67 C
ATOM 9706 CB PHE B 110 -64.782 -47.187 -9.891 1.00 25.80 C
ATOM 9709 CG PHE B 110 -65.625 -46.656 -8.772 1.00 26.12 C
ATOM 9710 CD1 PHE B 110 -65.564 -47.230 -7.510 1.00 27.13 C
ATOM 9712 CE1 PHE B 110 -66.353 -46.751 -6.468 1.00 27.42 C
ATOM 9714 CZ PHE B 110 -67.215 -45.691 -6.692 1.00 26.93 C
ATOM 9716 CE2 PHE B 110 -67.284 -45.119 -7.954 1.00 26.49 C
ATOM 9718 CD2 PHE B 110 -66.494 -45.601 -8.981 1.00 25.96 C
ATOM 9720 C PHE B 110 -62.505 -47.615 -10.793 1.00 25.92 C
ATOM 9721 O PHE B 110 -62.232 -47.157 -11.898 1.00 26.41 O
ATOM 9723 N GLU B 111 -62.134 -48.832 -10.406 1.00 26.06 N
ATOM 9724 CA GLU B 111 -61.403 -49.724 -11.304 1.00 26.17 C
ATOM 9726 CB GLU B 111 -60.444 -50.609 -10.511 1.00 26.50 C
ATOM 9729 CG GLU B 111 -59.372 -51.272 -11.374 1.00 28.11 C
ATOM 9732 CD GLU B 111 -58.607 -52.377 -10.646 1.00 30.70 C
ATOM 9733 OE1 GLU B 111 -58.660 -52.436 -9.390 1.00 31.99 O
ATOM 9734 OE2 GLU B 111 -57.948 -53.190 -11.338 1.00 32.09 O
ATOM 9735 C GLU B 111 -62.355 -50.598 -12.130 1.00 25.60 C
ATOM 9736 O GLU B 111 -63.116 -51.388 -11.585 1.00 25.48 O
ATOM 9738 N VAL B 112 -62.314 -50.439 -13.447 1.00 25.24 N

ATOM 9739 CA VAL B 112 -63.026 -51.331 -14.357 1.00 24.90 C
ATOM 9741 CB VAL B 112 -64.308 -50.712 -14.908 1.00 24.92 C
ATOM 9743 CG1 VAL B 112 -65.268 -50.437 -13.771 1.00 25.26 C
ATOM 9747 CG2 VAL B 112 -63.999 -49.450 -15.706 1.00 24.77 C
ATOM 9751 C VAL B 112 -62.144 -51.701 -15.522 1.00 24.66 C
ATOM 9752 O VAL B 112 -61.217 -50.964 -15.862 1.00 23.80 O
ATOM 9754 N SER B 113 -62.467 -52.842 -16.132 1.00 24.88 N
ATOM 9755 CA SER B 113 -61.604 -53.494 -17.109 1.00 25.21 C
ATOM 9757 CB SER B 113 -61.286 -54.913 -16.654 1.00 24.94 C
ATOM 9760 OG SER B 113 -60.357 -55.523 -17.528 1.00 24.31 O
ATOM 9762 C SER B 113 -62.233 -53.532 -18.492 1.00 25.88 C
ATOM 9763 O SER B 113 -63.446 -53.651 -18.630 1.00 25.86 O
ATOM 9765 N GLN B 114 -61.406 -53.438 -19.526 1.00 26.92 N
ATOM 9766 CA GLN B 114 -61.928 -53.491 -20.880 1.00 27.83 C
ATOM 9768 CB GLN B 114 -60.846 -53.194 -21.917 1.00 27.75 C
ATOM 9771 CG GLN B 114 -59.559 -53.952 -21.726 1.00 28.05 C
ATOM 9774 CD GLN B 114 -58.739 -54.077 -23.007 1.00 28.39 C
ATOM 9775 OE1 GLN B 114 -59.086 -53.515 -24.051 1.00 29.05 O
ATOM 9776 NE2 GLN B 114 -57.637 -54.808 -22.925 1.00 27.62 N
ATOM 9779 C GLN B 114 -62.615 -54.827 -21.158 1.00 28.78 C
ATOM 9780 O GLN B 114 -63.484 -54.905 -22.022 1.00 29.10 O
ATOM 9782 N GLU B 115 -62.248 -55.861 -20.401 1.00 29.99 N
ATOM 9783 CA GLU B 115 -62.888 -57.181 -20.505 1.00 30.89 C
ATOM 9785 CB GLU B 115 -62.252 -58.202 -19.549 1.00 31.10 C
ATOM 9788 CG GLU B 115 -60.740 -58.394 -19.697 1.00 32.35 C
ATOM 9791 CD GLU B 115 -60.320 -58.796 -21.106 1.00 34.20 C
ATOM 9792 OE1 GLU B 115 -60.965 -59.699 -21.688 1.00 34.94 O
ATOM 9793 OE2 GLU B 115 -59.348 -58.201 -21.634 1.00 35.60 O
ATOM 9794 C GLU B 115 -64.380 -57.120 -20.224 1.00 31.26 C
ATOM 9795 O GLU B 115 -65.125 -57.971 -20.691 1.00 31.54 O
ATOM 9797 N ALA B 116 -64.825 -56.127 -19.465 1.00 31.91 N
ATOM 9798 CA ALA B 116 -66.255 -55.937 -19.259 1.00 32.69 C
ATOM 9800 CB ALA B 116 -66.521 -54.648 -18.513 1.00 32.62 C
ATOM 9804 C ALA B 116 -66.999 -55.950 -20.597 1.00 33.33 C
ATOM 9805 O ALA B 116 -68.156 -56.364 -20.668 1.00 33.26 O
ATOM 9807 N PHE B 117 -66.316 -55.521 -21.655 1.00 34.16 N
ATOM 9808 CA PHE B 117 -66.889 -55.498 -22.996 1.00 34.98 C
ATOM 9810 CB PHE B 117 -66.310 -54.314 -23.766 1.00 35.02 C
ATOM 9813 CG PHE B 117 -66.868 -52.997 -23.345 1.00 35.06 C
ATOM 9814 CD1 PHE B 117 -66.061 -52.046 -22.729 1.00 35.33 C
ATOM 9816 CE1 PHE B 117 -66.576 -50.825 -22.342 1.00 35.16 C
ATOM 9818 CZ PHE B 117 -67.907 -50.544 -22.570 1.00 35.37 C
ATOM 9820 CE2 PHE B 117 -68.723 -51.488 -23.187 1.00 35.28 C
ATOM 9822 CD2 PHE B 117 -68.201 -52.701 -23.571 1.00 34.68 C
ATOM 9824 C PHE B 117 -66.676 -56.766 -23.830 1.00 35.86 C
ATOM 9825 O PHE B 117 -66.934 -56.755 -25.037 1.00 35.91 O
ATOM 9827 N SER B 118 -66.215 -57.853 -23.212 1.00 36.98 N
ATOM 9828 CA SER B 118 -65.924 -59.086 -23.960 1.00 37.76 C
ATOM 9830 CB SER B 118 -64.836 -59.907 -23.262 1.00 37.73 C
ATOM 9833 OG SER B 118 -65.272 -60.346 -21.987 1.00 37.77 O
ATOM 9835 C SER B 118 -67.178 -59.939 -24.215 1.00 38.48 C
ATOM 9836 O SER B 118 -67.207 -60.724 -25.157 1.00 38.42 O
ATOM 9838 N GLY B 119 -68.221 -59.765 -23.407 1.00 39.51 N
ATOM 9839 CA GLY B 119 -69.481 -60.473 -23.629 1.00 40.51 C
ATOM 9842 C GLY B 119 -70.287 -60.034 -24.848 1.00 41.51 C
ATOM 9843 O GLY B 119 -71.444 -60.433 -25.002 1.00 41.53 O
ATOM 9845 N PHE B 120 -69.688 -59.210 -25.709 1.00 42.79 N
ATOM 9846 CA PHE B 120 -70.382 -58.621 -26.864 1.00 43.81 C
ATOM 9848 CB PHE B 120 -70.643 -57.121 -26.601 1.00 43.76 C
ATOM 9851 CG PHE B 120 -71.367 -56.853 -25.293 1.00 43.65 C

ATOM 9852 CD1 PHE B 120 -72.762 -56.874 -25.230 1.00 43.48 C
ATOM 9854 CE1 PHE B 120 -73.437 -56.650 -24.023 1.00 43.03 C
ATOM 9856 CZ PHE B 120 -72.717 -56.413 -22.865 1.00 43.09 C
ATOM 9858 CE2 PHE B 120 -71.323 -56.397 -22.909 1.00 43.38 C
ATOM 9860 CD2 PHE B 120 -70.655 -56.619 -24.120 1.00 43.41 C
ATOM 9862 C PHE B 120 -69.607 -58.832 -28.175 1.00 44.81 C
ATOM 9863 O PHE B 120 -69.930 -58.238 -29.205 1.00 44.65 O
ATOM 9865 N LYS B 121 -68.602 -59.705 -28.126 1.00 46.19 N
ATOM 9866 CA LYS B 121 -67.757 -60.004 -29.272 1.00 47.31 C
ATOM 9868 CB LYS B 121 -66.275 -59.928 -28.870 1.00 47.47 C
ATOM 9871 CG LYS B 121 -65.743 -58.495 -28.637 1.00 48.13 C
ATOM 9874 CD LYS B 121 -64.532 -58.439 -27.675 1.00 48.89 C
ATOM 9877 CE LYS B 121 -63.261 -59.094 -28.241 1.00 49.20 C
ATOM 9880 NZ LYS B 121 -62.541 -58.232 -29.218 1.00 49.04 N
ATOM 9884 C LYS B 121 -68.096 -61.400 -29.810 1.00 48.15 C
ATOM 9885 O LYS B 121 -68.199 -62.361 -29.043 1.00 48.36 O
ATOM 9887 N ASP B 122 -68.270 -61.510 -31.126 1.00 49.04 N
ATOM 9888 CA ASP B 122 -68.611 -62.788 -31.754 1.00 49.60 C
ATOM 9890 CB ASP B 122 -69.070 -62.596 -33.217 1.00 49.52 C
ATOM 9893 CG ASP B 122 -67.989 -62.015 -34.126 1.00 49.18 C
ATOM 9894 OD1 ASP B 122 -66.792 -62.306 -33.938 1.00 48.96 O
ATOM 9895 OD2 ASP B 122 -68.351 -61.268 -35.057 1.00 48.82 O
ATOM 9896 C ASP B 122 -67.455 -63.785 -31.651 1.00 50.31 C
ATOM 9897 O ASP B 122 -66.369 -63.441 -31.171 1.00 50.33 O
ATOM 9899 N GLN B 123 -67.705 -65.014 -32.098 1.00 51.05 N
ATOM 9900 CA GLN B 123 -66.716 -66.095 -32.057 1.00 51.61 C
ATOM 9902 CB GLN B 123 -67.263 -67.330 -32.785 1.00 51.82 C
ATOM 9905 CG GLN B 123 -68.483 -67.986 -32.117 1.00 52.32 C
ATOM 9908 CD GLN B 123 -68.117 -69.137 -31.184 1.00 52.64 C
ATOM 9909 OE1 GLN B 123 -67.146 -69.062 -30.432 1.00 53.02 O
ATOM 9910 NE2 GLN B 123 -68.904 -70.207 -31.230 1.00 52.04 N
ATOM 9913 C GLN B 123 -65.358 -65.694 -32.659 1.00 51.78 C
ATOM 9914 O GLN B 123 -64.309 -66.000 -32.090 1.00 51.67 O
ATOM 9916 N ASN B 124 -65.388 -65.004 -33.799 1.00 52.05 N
ATOM 9917 CA ASN B 124 -64.166 -64.547 -34.473 1.00 52.25 C
ATOM 9919 CB ASN B 124 -64.486 -64.042 -35.884 1.00 52.25 C
ATOM 9922 CG ASN B 124 -64.911 -65.158 -36.819 1.00 51.88 C
ATOM 9923 OD1 ASN B 124 -65.918 -65.825 -36.592 1.00 51.43 O
ATOM 9924 ND2 ASN B 124 -64.144 -65.364 -37.880 1.00 51.23 N
ATOM 9927 C ASN B 124 -63.382 -63.466 -33.716 1.00 52.43 C
ATOM 9928 O ASN B 124 -62.189 -63.287 -33.959 1.00 52.33 O
ATOM 9930 N GLY B 125 -64.051 -62.747 -32.815 1.00 52.66 N
ATOM 9931 CA GLY B 125 -63.396 -61.745 -31.968 1.00 52.68 C
ATOM 9934 C GLY B 125 -63.916 -60.329 -32.135 1.00 52.63 C
ATOM 9935 O GLY B 125 -63.539 -59.447 -31.367 1.00 52.57 O
ATOM 9937 N ASN B 126 -64.782 -60.117 -33.129 1.00 52.54 N
ATOM 9938 CA ASN B 126 -65.343 -58.793 -33.443 1.00 52.41 C
ATOM 9940 CB ASN B 126 -65.575 -58.671 -34.949 1.00 52.40 C
ATOM 9943 CG ASN B 126 -64.322 -58.951 -35.751 1.00 52.64 C
ATOM 9944 OD1 ASN B 126 -63.426 -59.665 -35.297 1.00 52.77 O
ATOM 9945 ND2 ASN B 126 -64.249 -58.390 -36.952 1.00 53.00 N
ATOM 9948 C ASN B 126 -66.656 -58.524 -32.712 1.00 52.10 C
ATOM 9949 O ASN B 126 -67.253 -59.432 -32.153 1.00 52.27 O
ATOM 9951 N PHE B 127 -67.111 -57.279 -32.724 1.00 51.61 N
ATOM 9952 CA PHE B 127 -68.362 -56.936 -32.055 1.00 51.23 C
ATOM 9954 CB PHE B 127 -68.506 -55.416 -31.905 1.00 51.21 C
ATOM 9957 CG PHE B 127 -67.702 -54.848 -30.770 1.00 50.58 C
ATOM 9958 CD1 PHE B 127 -66.513 -54.192 -31.003 1.00 50.15 C
ATOM 9960 CE1 PHE B 127 -65.777 -53.686 -29.948 1.00 50.15 C
ATOM 9962 CZ PHE B 127 -66.225 -53.839 -28.647 1.00 49.71 C

ATOM 9964 CE2 PHE B 127 -67.399 -54.496 -28.405 1.00 49.50 C
ATOM 9966 CD2 PHE B 127 -68.132 -54.999 -29.459 1.00 49.99 C
ATOM 9968 C PHE B 127 -69.537 -57.505 -32.821 1.00 50.99 C
ATOM 9969 O PHE B 127 -69.468 -57.641 -34.040 1.00 50.92 O
ATOM 9971 N LEU B 128 -70.609 -57.840 -32.106 1.00 50.83 N
ATOM 9972 CA LEU B 128 -71.799 -58.422 -32.731 1.00 50.76 C
ATOM 9974 CB LEU B 128 -72.780 -58.953 -31.669 1.00 50.80 C
ATOM 9977 CG LEU B 128 -72.341 -60.098 -30.734 1.00 50.91 C
ATOM 9979 CD1 LEU B 128 -73.483 -60.532 -29.813 1.00 50.61 C
ATOM 9983 CD2 LEU B 128 -71.818 -61.303 -31.497 1.00 50.79 C
ATOM 9987 C LEU B 128 -72.500 -57.407 -33.646 1.00 50.55 C
ATOM 9988 O LEU B 128 -73.105 -56.455 -33.171 1.00 50.34 O
ATOM 9990 N GLU B 129 -72.402 -57.628 -34.957 1.00 50.50 N
ATOM 9991 CA GLU B 129 -73.038 -56.783 -35.982 1.00 50.48 C
ATOM 9993 CB GLU B 129 -73.150 -57.551 -37.310 1.00 50.68 C
ATOM 9996 CG GLU B 129 -72.262 -57.024 -38.434 1.00 51.36 C
ATOM 9999 CD GLU B 129 -72.799 -55.745 -39.060 1.00 51.88 C
ATOM 10000 OE1 GLU B 129 -72.110 -54.707 -38.961 1.00 52.72 O
ATOM 10001 OE2 GLU B 129 -73.906 -55.773 -39.643 1.00 51.58 O
ATOM 10002 C GLU B 129 -74.428 -56.264 -35.629 1.00 50.25 C
ATOM 10003 O GLU B 129 -74.737 -55.110 -35.899 1.00 50.18 O
ATOM 10005 N ASN B 130 -75.263 -57.125 -35.047 1.00 50.06 N
ATOM 10006 CA ASN B 130 -76.678 -56.806 -34.785 1.00 49.71 C
ATOM 10008 CB ASN B 130 -77.477 -58.100 -34.550 1.00 49.69 C
ATOM 10011 CG ASN B 130 -77.053 -58.837 -33.291 1.00 49.39 C
ATOM 10012 OD1 ASN B 130 -76.357 -59.848 -33.361 1.00 48.74 O
ATOM 10013 ND2 ASN B 130 -77.468 -58.329 -32.134 1.00 48.99 N
ATOM 10016 C ASN B 130 -76.934 -55.800 -33.646 1.00 49.37 C
ATOM 10017 O ASN B 130 -78.083 -55.456 -33.366 1.00 49.29 O
ATOM 10019 N LEU B 131 -75.868 -55.336 -32.996 1.00 48.98 N
ATOM 10020 CA LEU B 131 -75.957 -54.279 -31.988 1.00 48.56 C
ATOM 10022 CB LEU B 131 -74.797 -54.392 -30.991 1.00 48.44 C
ATOM 10025 CG LEU B 131 -74.759 -55.671 -30.148 1.00 48.19 C
ATOM 10027 CD1 LEU B 131 -73.382 -55.852 -29.523 1.00 47.23 C
ATOM 10031 CD2 LEU B 131 -75.861 -55.670 -29.083 1.00 47.77 C
ATOM 10035 C LEU B 131 -75.968 -52.875 -32.604 1.00 48.29 C
ATOM 10036 O LEU B 131 -76.022 -51.895 -31.874 1.00 48.44 O
ATOM 10038 N LYS B 132 -75.927 -52.771 -33.934 1.00 47.95 N
ATOM 10039 CA LYS B 132 -76.020 -51.471 -34.621 1.00 47.64 C
ATOM 10041 CB LYS B 132 -75.548 -51.590 -36.080 1.00 47.63 C
ATOM 10044 CG LYS B 132 -76.595 -52.235 -36.998 1.00 48.19 C
ATOM 10047 CD LYS B 132 -76.111 -52.483 -38.429 1.00 48.16 C
ATOM 10050 CE LYS B 132 -77.239 -53.040 -39.290 1.00 47.23 C
ATOM 10053 NZ LYS B 132 -76.725 -53.936 -40.331 1.00 47.01 N
ATOM 10057 C LYS B 132 -77.449 -50.907 -34.597 1.00 47.13 C
ATOM 10058 O LYS B 132 -77.683 -49.772 -35.005 1.00 46.87 O
ATOM 10060 N GLU B 133 -78.403 -51.716 -34.149 1.00 46.77 N
ATOM 10061 CA GLU B 133 -79.806 -51.315 -34.107 1.00 46.49 C
ATOM 10063 CB GLU B 133 -80.691 -52.458 -34.622 1.00 46.56 C
ATOM 10066 CG GLU B 133 -80.732 -52.515 -36.155 1.00 47.01 C
ATOM 10069 CD GLU B 133 -80.737 -53.926 -36.715 1.00 47.40 C
ATOM 10070 OE1 GLU B 133 -81.500 -54.775 -36.206 1.00 47.97 O
ATOM 10071 OE2 GLU B 133 -79.983 -54.177 -37.679 1.00 47.22 O
ATOM 10072 C GLU B 133 -80.260 -50.830 -32.723 1.00 45.92 C
ATOM 10073 O GLU B 133 -81.369 -50.308 -32.600 1.00 46.14 O
ATOM 10075 N ASP B 134 -79.424 -51.002 -31.691 1.00 44.98 N
ATOM 10076 CA ASP B 134 -79.611 -50.277 -30.428 1.00 44.14 C
ATOM 10078 CB ASP B 134 -79.375 -51.162 -29.197 1.00 43.95 C
ATOM 10081 CG ASP B 134 -79.646 -50.419 -27.883 1.00 43.57 C
ATOM 10082 OD1 ASP B 134 -80.014 -49.230 -27.919 1.00 42.21 O

ATOM 10083 OD2 ASP B 134 -79.488 -51.011 -26.802 1.00 43.69 O
ATOM 10084 C ASP B 134 -78.662 -49.073 -30.426 1.00 43.47 C
ATOM 10085 O ASP B 134 -77.478 -49.196 -30.104 1.00 43.55 O
ATOM 10087 N ILE B 135 -79.198 -47.908 -30.776 1.00 42.47 N
ATOM 10088 CA ILE B 135 -78.375 -46.739 -31.033 1.00 41.65 C
ATOM 10090 CB ILE B 135 -79.080 -45.783 -32.012 1.00 41.45 C
ATOM 10092 CG1 ILE B 135 -78.877 -46.313 -33.434 1.00 41.74 C
ATOM 10095 CD1 ILE B 135 -79.174 -45.331 -34.540 1.00 42.77 C
ATOM 10099 CG2 ILE B 135 -78.533 -44.391 -31.905 1.00 41.68 C
ATOM 10103 C ILE B 135 -77.901 -46.059 -29.746 1.00 41.14 C
ATOM 10104 O ILE B 135 -76.752 -45.624 -29.676 1.00 41.11 O
ATOM 10106 N LYS B 136 -78.742 -45.998 -28.714 1.00 40.53 N
ATOM 10107 CA LYS B 136 -78.281 -45.480 -27.409 1.00 40.10 C
ATOM 10109 CB LYS B 136 -79.431 -45.361 -26.375 1.00 40.40 C
ATOM 10112 CG LYS B 136 -79.910 -46.697 -25.786 1.00 42.49 C
ATOM 10115 CD LYS B 136 -81.002 -46.574 -24.698 1.00 44.79 C
ATOM 10118 CE LYS B 136 -81.599 -47.994 -24.363 1.00 46.03 C
ATOM 10121 NZ LYS B 136 -82.231 -48.149 -22.994 1.00 46.23 N
ATOM 10125 C LYS B 136 -77.104 -46.327 -26.863 1.00 38.85 C
ATOM 10126 O LYS B 136 -76.246 -45.806 -26.143 1.00 38.91 O
ATOM 10128 N ALA B 137 -77.062 -47.617 -27.219 1.00 37.27 N
ATOM 10129 CA ALA B 137 -75.935 -48.486 -26.864 1.00 35.88 C
ATOM 10131 CB ALA B 137 -76.255 -49.952 -27.116 1.00 35.69 C
ATOM 10135 C ALA B 137 -74.708 -48.085 -27.645 1.00 34.63 C
ATOM 10136 O ALA B 137 -73.647 -47.894 -27.055 1.00 34.70 O
ATOM 10138 N ILE B 138 -74.845 -47.946 -28.965 1.00 33.12 N
ATOM 10139 CA ILE B 138 -73.693 -47.597 -29.805 1.00 31.97 C
ATOM 10141 CB ILE B 138 -74.020 -47.572 -31.296 1.00 31.50 C
ATOM 10143 CG1 ILE B 138 -74.433 -48.955 -31.774 1.00 31.28 C
ATOM 10146 CD1 ILE B 138 -73.460 -50.052 -31.417 1.00 30.86 C
ATOM 10150 CG2 ILE B 138 -72.819 -47.138 -32.073 1.00 30.61 C
ATOM 10154 C ILE B 138 -73.124 -46.245 -29.413 1.00 31.57 C
ATOM 10155 O ILE B 138 -71.909 -46.090 -29.305 1.00 31.77 O
ATOM 10157 N LEU B 139 -73.997 -45.268 -29.192 1.00 30.92 N
ATOM 10158 CA LEU B 139 -73.555 -43.962 -28.713 1.00 30.29 C
ATOM 10160 CB LEU B 139 -74.732 -43.000 -28.530 1.00 30.13 C
ATOM 10163 CG LEU B 139 -74.778 -41.890 -29.574 1.00 29.96 C
ATOM 10165 CD1 LEU B 139 -73.496 -41.060 -29.508 1.00 28.26 C
ATOM 10169 CD2 LEU B 139 -76.022 -41.019 -29.397 1.00 29.48 C
ATOM 10173 C LEU B 139 -72.835 -44.136 -27.397 1.00 29.95 C
ATOM 10174 O LEU B 139 -71.709 -43.687 -27.232 1.00 30.45 O
ATOM 10176 N SER B 140 -73.492 -44.807 -26.463 1.00 29.33 N
ATOM 10177 CA SER B 140 -72.916 -45.061 -25.150 1.00 28.84 C
ATOM 10179 CB SER B 140 -73.900 -45.878 -24.298 1.00 28.93 C
ATOM 10182 OG SER B 140 -73.527 -45.870 -22.930 1.00 30.33 O
ATOM 10184 C SER B 140 -71.555 -45.770 -25.243 1.00 27.78 C
ATOM 10185 O SER B 140 -70.637 -45.454 -24.489 1.00 27.46 O
ATOM 10187 N LEU B 141 -71.432 -46.719 -26.167 1.00 26.82 N
ATOM 10188 CA LEU B 141 -70.178 -47.433 -26.348 1.00 26.34 C
ATOM 10190 CB LEU B 141 -70.366 -48.658 -27.256 1.00 26.16 C
ATOM 10193 CG LEU B 141 -69.098 -49.472 -27.584 1.00 26.09 C
ATOM 10195 CD1 LEU B 141 -68.355 -49.960 -26.330 1.00 24.64 C
ATOM 10199 CD2 LEU B 141 -69.455 -50.643 -28.481 1.00 25.94 C
ATOM 10203 C LEU B 141 -69.124 -46.476 -26.914 1.00 25.89 C
ATOM 10204 O LEU B 141 -68.025 -46.346 -26.366 1.00 25.77 O
ATOM 10206 N TYR B 142 -69.471 -45.809 -28.008 1.00 25.41 N
ATOM 10207 CA TYR B 142 -68.609 -44.804 -28.610 1.00 25.03 C
ATOM 10209 CB TYR B 142 -69.399 -43.982 -29.617 1.00 24.80 C
ATOM 10212 CG TYR B 142 -68.736 -42.695 -30.043 1.00 24.47 C
ATOM 10213 CD1 TYR B 142 -67.761 -42.686 -31.029 1.00 24.18 C

ATOM 10215 CE1 TYR B 142 -67.166 -41.516 -31.438 1.00 24.70 C
ATOM 10217 CZ TYR B 142 -67.548 -40.315 -30.871 1.00 25.80 C
ATOM 10218 OH TYR B 142 -66.940 -39.129 -31.279 1.00 27.63 O
ATOM 10220 CE2 TYR B 142 -68.522 -40.299 -29.890 1.00 25.57 C
ATOM 10222 CD2 TYR B 142 -69.110 -41.485 -29.485 1.00 24.73 C
ATOM 10224 C TYR B 142 -68.095 -43.883 -27.537 1.00 25.17 C
ATOM 10225 O TYR B 142 -66.886 -43.732 -27.360 1.00 25.40 O
ATOM 10227 N GLU B 143 -69.038 -43.293 -26.807 1.00 25.12 N
ATOM 10228 CA GLU B 143 -68.744 -42.256 -25.828 1.00 25.10 C
ATOM 10230 CB GLU B 143 -70.046 -41.726 -25.226 1.00 25.33 C
ATOM 10233 CG GLU B 143 -70.006 -40.244 -24.849 1.00 27.57 C
ATOM 10236 CD GLU B 143 -70.321 -39.313 -26.023 1.00 30.43 C
ATOM 10237 OE1 GLU B 143 -69.343 -38.764 -26.583 1.00 32.89 O
ATOM 10238 OE2 GLU B 143 -71.526 -39.130 -26.377 1.00 30.86 O
ATOM 10239 C GLU B 143 -67.794 -42.746 -24.729 1.00 24.43 C
ATOM 10240 O GLU B 143 -67.026 -41.959 -24.179 1.00 24.06 O
ATOM 10242 N ALA B 144 -67.840 -44.050 -24.449 1.00 24.01 N
ATOM 10243 CA ALA B 144 -67.033 -44.681 -23.399 1.00 23.74 C
ATOM 10245 CB ALA B 144 -67.726 -45.943 -22.883 1.00 23.48 C
ATOM 10249 C ALA B 144 -65.631 -45.025 -23.864 1.00 23.57 C
ATOM 10250 O ALA B 144 -64.720 -45.171 -23.060 1.00 23.69 O
ATOM 10252 N SER B 145 -65.455 -45.168 -25.165 1.00 23.45 N
ATOM 10253 CA SER B 145 -64.168 -45.568 -25.701 1.00 23.44 C
ATOM 10255 CB SER B 145 -64.300 -45.856 -27.214 1.00 23.63 C
ATOM 10258 OG SER B 145 -64.822 -44.748 -27.952 1.00 24.24 O
ATOM 10260 C SER B 145 -63.065 -44.520 -25.416 1.00 23.24 C
ATOM 10261 O SER B 145 -61.877 -44.848 -25.288 1.00 23.25 O
ATOM 10263 N PHE B 146 -63.454 -43.257 -25.285 1.00 22.92 N
ATOM 10264 CA PHE B 146 -62.464 -42.189 -25.170 1.00 22.35 C
ATOM 10266 CB PHE B 146 -63.090 -40.837 -25.478 1.00 22.09 C
ATOM 10269 CG PHE B 146 -63.505 -40.717 -26.911 1.00 22.40 C
ATOM 10270 CD1 PHE B 146 -62.619 -40.229 -27.868 1.00 21.98 C
ATOM 10272 CE1 PHE B 146 -62.985 -40.156 -29.201 1.00 21.80 C
ATOM 10274 CZ PHE B 146 -64.241 -40.579 -29.594 1.00 21.91 C
ATOM 10276 CE2 PHE B 146 -65.123 -41.098 -28.649 1.00 22.29 C
ATOM 10278 CD2 PHE B 146 -64.751 -41.170 -27.323 1.00 22.34 C
ATOM 10280 C PHE B 146 -61.762 -42.208 -23.837 1.00 21.91 C
ATOM 10281 O PHE B 146 -60.669 -41.683 -23.733 1.00 22.30 O
ATOM 10283 N LEU B 147 -62.361 -42.864 -22.841 1.00 21.27 N
ATOM 10284 CA LEU B 147 -61.727 -43.050 -21.535 1.00 20.49 C
ATOM 10286 CB LEU B 147 -62.791 -43.333 -20.478 1.00 20.14 C
ATOM 10289 CG LEU B 147 -63.609 -42.109 -20.102 1.00 18.87 C
ATOM 10291 CD1 LEU B 147 -64.813 -42.020 -20.959 1.00 15.94 C
ATOM 10295 CD2 LEU B 147 -63.988 -42.189 -18.642 1.00 18.62 C
ATOM 10299 C LEU B 147 -60.678 -44.163 -21.498 1.00 20.41 C
ATOM 10300 O LEU B 147 -60.243 -44.552 -20.415 1.00 20.44 O
ATOM 10302 N ALA B 148 -60.268 -44.664 -22.662 1.00 20.28 N
ATOM 10303 CA ALA B 148 -59.330 -45.784 -22.745 1.00 20.33 C
ATOM 10305 CB ALA B 148 -59.188 -46.231 -24.194 1.00 20.15 C
ATOM 10309 C ALA B 148 -57.952 -45.462 -22.170 1.00 20.54 C
ATOM 10310 O ALA B 148 -57.435 -44.366 -22.341 1.00 20.23 O
ATOM 10312 N LEU B 149 -57.366 -46.435 -21.486 1.00 21.19 N
ATOM 10313 CA LEU B 149 -55.969 -46.354 -21.067 1.00 22.02 C
ATOM 10315 CB LEU B 149 -55.768 -47.073 -19.725 1.00 21.90 C
ATOM 10318 CG LEU B 149 -56.541 -46.496 -18.523 1.00 21.50 C
ATOM 10320 CD1 LEU B 149 -55.979 -47.006 -17.223 1.00 20.96 C
ATOM 10324 CD2 LEU B 149 -56.520 -44.974 -18.505 1.00 20.95 C
ATOM 10328 C LEU B 149 -55.054 -46.930 -22.159 1.00 22.84 C
ATOM 10329 O LEU B 149 -55.507 -47.678 -23.017 1.00 22.91 O
ATOM 10331 N GLU B 150 -53.781 -46.550 -22.163 1.00 23.93 N

ATOM 10332 CA GLU B 150 -52.858 -47.071 -23.174 1.00 25.03 C
ATOM 10334 CB GLU B 150 -51.472 -46.431 -23.012 1.00 25.41 C
ATOM 10337 CG GLU B 150 -50.530 -46.608 -24.213 1.00 27.44 C
ATOM 10340 CD GLU B 150 -49.132 -45.987 -23.992 1.00 30.04 C
ATOM 10341 OE1 GLU B 150 -48.925 -45.330 -22.943 1.00 31.41 O
ATOM 10342 OE2 GLU B 150 -48.242 -46.161 -24.867 1.00 30.34 O
ATOM 10343 C GLU B 150 -52.787 -48.600 -23.024 1.00 25.36 C
ATOM 10344 O GLU B 150 -52.613 -49.098 -21.911 1.00 25.58 O
ATOM 10346 N GLY B 151 -52.968 -49.337 -24.122 1.00 25.79 N
ATOM 10347 CA GLY B 151 -52.959 -50.816 -24.086 1.00 26.11 C
ATOM 10350 C GLY B 151 -54.323 -51.522 -24.047 1.00 26.44 C
ATOM 10351 O GLY B 151 -54.393 -52.747 -24.135 1.00 26.91 O
ATOM 10353 N GLU B 152 -55.407 -50.768 -23.899 1.00 26.58 N
ATOM 10354 CA GLU B 152 -56.757 -51.319 -23.971 1.00 26.57 C
ATOM 10356 CB GLU B 152 -57.697 -50.531 -23.065 1.00 26.74 C
ATOM 10359 CG GLU B 152 -57.291 -50.595 -21.596 1.00 27.63 C
ATOM 10362 CD GLU B 152 -58.271 -49.893 -20.668 1.00 28.86 C
ATOM 10363 OE1 GLU B 152 -58.239 -50.192 -19.449 1.00 28.80 O
ATOM 10364 OE2 GLU B 152 -59.066 -49.044 -21.154 1.00 29.26 O
ATOM 10365 C GLU B 152 -57.254 -51.303 -25.415 1.00 26.53 C
ATOM 10366 O GLU B 152 -57.937 -50.381 -25.869 1.00 26.00 O
ATOM 10368 N ASN B 153 -56.888 -52.354 -26.127 1.00 26.77 N
ATOM 10369 CA ASN B 153 -57.189 -52.498 -27.545 1.00 27.05 C
ATOM 10371 CB ASN B 153 -56.345 -53.640 -28.104 1.00 27.12 C
ATOM 10374 CG ASN B 153 -56.770 -54.992 -27.549 1.00 27.81 C
ATOM 10375 OD1 ASN B 153 -56.540 -55.307 -26.379 1.00 27.65 O
ATOM 10376 ND2 ASN B 153 -57.426 -55.782 -28.382 1.00 29.43 N
ATOM 10379 C ASN B 153 -58.659 -52.788 -27.873 1.00 27.09 C
ATOM 10380 O ASN B 153 -59.053 -52.658 -29.029 1.00 27.11 O
ATOM 10382 N ILE B 154 -59.448 -53.223 -26.884 1.00 27.17 N
ATOM 10383 CA ILE B 154 -60.865 -53.544 -27.100 1.00 27.11 C
ATOM 10385 CB ILE B 154 -61.454 -54.369 -25.956 1.00 26.99 C
ATOM 10387 CG1 ILE B 154 -60.811 -55.750 -25.907 1.00 27.16 C
ATOM 10390 CD1 ILE B 154 -61.309 -56.622 -24.746 1.00 27.41 C
ATOM 10394 CG2 ILE B 154 -62.953 -54.519 -26.124 1.00 26.65 C
ATOM 10398 C ILE B 154 -61.704 -52.284 -27.229 1.00 27.43 C
ATOM 10399 O ILE B 154 -62.718 -52.279 -27.939 1.00 27.39 O
ATOM 10401 N LEU B 155 -61.296 -51.226 -26.522 1.00 27.76 N
ATOM 10402 CA LEU B 155 -61.964 -49.918 -26.609 1.00 27.75 C
ATOM 10404 CB LEU B 155 -61.578 -49.024 -25.430 1.00 27.31 C
ATOM 10407 CG LEU B 155 -61.968 -49.544 -24.052 1.00 26.64 C
ATOM 10409 CD1 LEU B 155 -61.444 -48.631 -22.981 1.00 25.82 C
ATOM 10413 CD2 LEU B 155 -63.465 -49.674 -23.944 1.00 26.45 C
ATOM 10417 C LEU B 155 -61.620 -49.226 -27.924 1.00 28.32 C
ATOM 10418 O LEU B 155 -62.499 -48.672 -28.583 1.00 28.72 O
ATOM 10420 N ASP B 156 -60.348 -49.264 -28.309 1.00 28.84 N
ATOM 10421 CA ASP B 156 -59.934 -48.737 -29.601 1.00 29.43 C
ATOM 10423 CB ASP B 156 -58.423 -48.928 -29.823 1.00 29.92 C
ATOM 10426 CG ASP B 156 -57.566 -47.912 -29.045 1.00 31.35 C
ATOM 10427 OD1 ASP B 156 -57.803 -46.680 -29.162 1.00 33.23 O
ATOM 10428 OD2 ASP B 156 -56.640 -48.351 -28.324 1.00 33.08 O
ATOM 10429 C ASP B 156 -60.719 -49.411 -30.717 1.00 29.36 C
ATOM 10430 O ASP B 156 -61.075 -48.768 -31.697 1.00 29.33 O
ATOM 10432 N GLU B 157 -60.981 -50.705 -30.558 1.00 29.63 N
ATOM 10433 CA GLU B 157 -61.845 -51.457 -31.479 1.00 29.98 C
ATOM 10435 CB GLU B 157 -61.729 -52.971 -31.234 1.00 30.30 C
ATOM 10438 CG GLU B 157 -60.664 -53.647 -32.087 1.00 31.79 C
ATOM 10441 CD GLU B 157 -60.075 -54.901 -31.439 1.00 33.87 C
ATOM 10442 OE1 GLU B 157 -60.793 -55.560 -30.640 1.00 35.07 O
ATOM 10443 OE2 GLU B 157 -58.894 -55.223 -31.743 1.00 33.70 O

ATOM 10444 C GLU B 157 -63.304 -51.030 -31.349 1.00 29.53 C
ATOM 10445 O GLU B 157 -63.999 -50.878 -32.351 1.00 29.53 O
ATOM 10447 N ALA B 158 -63.758 -50.853 -30.112 1.00 29.11 N
ATOM 10448 CA ALA B 158 -65.104 -50.370 -29.840 1.00 28.87 C
ATOM 10450 CB ALA B 158 -65.307 -50.195 -28.351 1.00 28.82 C
ATOM 10454 C ALA B 158 -65.383 -49.065 -30.567 1.00 28.73 C
ATOM 10455 O ALA B 158 -66.485 -48.857 -31.065 1.00 28.80 O
ATOM 10457 N LYS B 159 -64.385 -48.197 -30.642 1.00 28.65 N
ATOM 10458 CA LYS B 159 -64.553 -46.910 -31.296 1.00 28.98 C
ATOM 10460 CB LYS B 159 -63.439 -45.950 -30.857 1.00 29.16 C
ATOM 10463 CG LYS B 159 -63.558 -44.536 -31.426 1.00 29.82 C
ATOM 10466 CD LYS B 159 -62.812 -43.493 -30.592 1.00 30.96 C
ATOM 10469 CE LYS B 159 -61.295 -43.610 -30.691 1.00 31.57 C
ATOM 10472 NZ LYS B 159 -60.630 -42.426 -30.079 1.00 31.49 N
ATOM 10476 C LYS B 159 -64.594 -47.041 -32.826 1.00 29.08 C
ATOM 10477 O LYS B 159 -65.385 -46.372 -33.486 1.00 28.73 O
ATOM 10479 N VAL B 160 -63.736 -47.891 -33.386 1.00 29.53 N
ATOM 10480 CA VAL B 160 -63.686 -48.087 -34.836 1.00 29.89 C
ATOM 10482 CB VAL B 160 -62.466 -48.971 -35.282 1.00 29.93 C
ATOM 10484 CG1 VAL B 160 -62.576 -49.375 -36.756 1.00 29.58 C
ATOM 10488 CG2 VAL B 160 -61.152 -48.244 -35.040 1.00 29.41 C
ATOM 10492 C VAL B 160 -65.001 -48.723 -35.263 1.00 30.32 C
ATOM 10493 O VAL B 160 -65.507 -48.459 -36.362 1.00 30.41 O
ATOM 10495 N PHE B 161 -65.558 -49.540 -34.371 1.00 30.83 N
ATOM 10496 CA PHE B 161 -66.854 -50.178 -34.599 1.00 31.34 C
ATOM 10498 CB PHE B 161 -67.090 -51.321 -33.599 1.00 31.34 C
ATOM 10501 CG PHE B 161 -68.492 -51.834 -33.603 1.00 31.09 C
ATOM 10502 CD1 PHE B 161 -68.940 -52.636 -34.633 1.00 31.61 C
ATOM 10504 CE1 PHE B 161 -70.249 -53.098 -34.649 1.00 31.48 C
ATOM 10506 CZ PHE B 161 -71.114 -52.748 -33.628 1.00 30.76 C
ATOM 10508 CE2 PHE B 161 -70.677 -51.944 -32.606 1.00 30.19 C
ATOM 10510 CD2 PHE B 161 -69.378 -51.486 -32.597 1.00 30.70 C
ATOM 10512 C PHE B 161 -67.992 -49.173 -34.504 1.00 31.65 C
ATOM 10513 O PHE B 161 -68.785 -49.038 -35.432 1.00 31.62 O
ATOM 10515 N ALA B 162 -68.068 -48.483 -33.373 1.00 32.26 N
ATOM 10516 CA ALA B 162 -69.135 -47.519 -33.129 1.00 32.84 C
ATOM 10518 CB ALA B 162 -68.948 -46.854 -31.778 1.00 32.66 C
ATOM 10522 C ALA B 162 -69.224 -46.474 -34.245 1.00 33.40 C
ATOM 10523 O ALA B 162 -70.229 -46.408 -34.937 1.00 33.45 O
ATOM 10525 N ILE B 163 -68.164 -45.697 -34.444 1.00 34.38 N
ATOM 10526 CA ILE B 163 -68.166 -44.610 -35.439 1.00 35.23 C
ATOM 10528 CB ILE B 163 -66.734 -44.062 -35.733 1.00 35.18 C
ATOM 10530 CG1 ILE B 163 -66.092 -43.457 -34.488 1.00 35.21 C
ATOM 10533 CD1 ILE B 163 -64.620 -43.171 -34.663 1.00 35.96 C
ATOM 10537 CG2 ILE B 163 -66.778 -42.977 -36.799 1.00 34.72 C
ATOM 10541 C ILE B 163 -68.778 -45.052 -36.766 1.00 36.18 C
ATOM 10542 O ILE B 163 -69.588 -44.335 -37.360 1.00 35.87 O
ATOM 10544 N SER B 164 -68.379 -46.240 -37.217 1.00 37.67 N
ATOM 10545 CA SER B 164 -68.761 -46.752 -38.539 1.00 38.74 C
ATOM 10547 CB SER B 164 -68.104 -48.117 -38.815 1.00 38.80 C
ATOM 10550 OG SER B 164 -68.733 -49.158 -38.077 1.00 39.07 O
ATOM 10552 C SER B 164 -70.277 -46.861 -38.699 1.00 39.51 C
ATOM 10553 O SER B 164 -70.820 -46.494 -39.737 1.00 39.96 O
ATOM 10555 N HIS B 165 -70.962 -47.363 -37.680 1.00 40.28 N
ATOM 10556 CA HIS B 165 -72.410 -47.485 -37.767 1.00 41.07 C
ATOM 10558 CB HIS B 165 -72.911 -48.686 -36.957 1.00 41.38 C
ATOM 10561 CG HIS B 165 -72.571 -50.005 -37.587 1.00 42.65 C
ATOM 10562 ND1 HIS B 165 -71.647 -50.875 -37.046 1.00 43.54 N
ATOM 10564 CE1 HIS B 165 -71.535 -51.938 -37.825 1.00 43.54 C
ATOM 10566 NE2 HIS B 165 -72.346 -51.785 -38.858 1.00 43.25 N

ATOM 10568 CD2 HIS B 165 -73.001 -50.582 -38.737 1.00 43.31 C
ATOM 10570 C HIS B 165 -73.125 -46.193 -37.380 1.00 41.21 C
ATOM 10571 O HIS B 165 -74.257 -45.980 -37.805 1.00 41.53 O
ATOM 10573 N LEU B 166 -72.459 -45.326 -36.614 1.00 41.32 N
ATOM 10574 CA LEU B 166 -73.042 -44.039 -36.201 1.00 41.31 C
ATOM 10576 CB LEU B 166 -72.317 -43.460 -34.973 1.00 41.14 C
ATOM 10579 CG LEU B 166 -72.732 -43.975 -33.589 1.00 40.03 C
ATOM 10581 CD1 LEU B 166 -71.673 -43.634 -32.579 1.00 38.86 C
ATOM 10585 CD2 LEU B 166 -74.077 -43.421 -33.151 1.00 38.52 C
ATOM 10589 C LEU B 166 -73.045 -42.992 -37.313 1.00 41.80 C
ATOM 10590 O LEU B 166 -74.006 -42.230 -37.442 1.00 41.73 O
ATOM 10592 N LYS B 167 -71.982 -42.947 -38.116 1.00 42.47 N
ATOM 10593 CA LYS B 167 -71.847 -41.891 -39.137 1.00 43.00 C
ATOM 10595 CB LYS B 167 -70.416 -41.822 -39.702 1.00 43.12 C
ATOM 10598 CG LYS B 167 -69.937 -43.068 -40.450 1.00 44.12 C
ATOM 10601 CD LYS B 167 -69.138 -42.725 -41.736 1.00 45.36 C
ATOM 10604 CE LYS B 167 -67.898 -41.842 -41.483 1.00 45.65 C
ATOM 10607 NZ LYS B 167 -67.267 -41.400 -42.762 1.00 44.94 N
ATOM 10611 C LYS B 167 -72.873 -41.950 -40.283 1.00 42.99 C
ATOM 10612 O LYS B 167 -72.826 -41.124 -41.182 1.00 42.95 O
ATOM 10614 N GLU B 168 -73.791 -42.912 -40.244 1.00 43.23 N
ATOM 10615 CA GLU B 168 -74.928 -42.940 -41.167 1.00 43.44 C
ATOM 10617 CB GLU B 168 -74.652 -43.969 -42.272 1.00 43.58 C
ATOM 10620 CG GLU B 168 -73.918 -43.363 -43.501 1.00 44.36 C
ATOM 10623 CD GLU B 168 -72.618 -44.082 -43.895 1.00 44.53 C
ATOM 10624 OE1 GLU B 168 -71.853 -44.494 -42.992 1.00 44.71 O
ATOM 10625 OE2 GLU B 168 -72.351 -44.197 -45.115 1.00 43.31 O
ATOM 10626 C GLU B 168 -76.263 -43.214 -40.442 1.00 43.24 C
ATOM 10627 O GLU B 168 -76.932 -42.291 -39.942 1.00 42.54 O
ATOM 10629 N GLY B 175 -83.548 -42.037 -36.239 1.00 49.43 N
ATOM 10630 CA GLY B 175 -84.473 -41.266 -35.416 1.00 49.54 C
ATOM 10633 C GLY B 175 -84.709 -39.884 -36.001 1.00 49.76 C
ATOM 10634 O GLY B 175 -84.828 -39.741 -37.220 1.00 49.70 O
ATOM 10636 N LYS B 176 -84.766 -38.870 -35.131 1.00 49.95 N
ATOM 10637 CA LYS B 176 -85.014 -37.468 -35.534 1.00 50.05 C
ATOM 10639 CB LYS B 176 -86.522 -37.225 -35.730 1.00 50.27 C
ATOM 10642 CG LYS B 176 -87.301 -36.813 -34.460 1.00 51.33 C
ATOM 10645 CD LYS B 176 -88.553 -37.658 -34.202 1.00 52.21 C
ATOM 10648 CE LYS B 176 -88.841 -37.754 -32.695 1.00 52.36 C
ATOM 10651 NZ LYS B 176 -90.029 -38.607 -32.422 1.00 52.15 N
ATOM 10655 C LYS B 176 -84.427 -36.432 -34.554 1.00 49.75 C
ATOM 10656 O LYS B 176 -83.990 -35.370 -34.972 1.00 49.88 O
ATOM 10658 N GLU B 177 -84.473 -36.729 -33.254 1.00 49.46 N
ATOM 10659 CA GLU B 177 -83.769 -35.959 -32.221 1.00 48.92 C
ATOM 10661 CB GLU B 177 -84.628 -35.813 -30.946 1.00 49.03 C
ATOM 10664 CG GLU B 177 -84.196 -36.691 -29.732 1.00 49.60 C
ATOM 10667 CD GLU B 177 -85.278 -36.871 -28.662 1.00 50.10 C
ATOM 10668 OE1 GLU B 177 -84.998 -37.576 -27.670 1.00 49.78 O
ATOM 10669 OE2 GLU B 177 -86.401 -36.336 -28.808 1.00 50.78 O
ATOM 10670 C GLU B 177 -82.469 -36.703 -31.924 1.00 48.19 C
ATOM 10671 O GLU B 177 -81.421 -36.085 -31.721 1.00 48.68 O
ATOM 10673 N LEU B 178 -82.557 -38.037 -31.900 1.00 46.98 N
ATOM 10674 CA LEU B 178 -81.398 -38.924 -31.817 1.00 45.91 C
ATOM 10676 CB LEU B 178 -81.838 -40.387 -31.945 1.00 45.70 C
ATOM 10679 CG LEU B 178 -81.111 -41.408 -31.074 1.00 45.24 C
ATOM 10681 CD1 LEU B 178 -81.498 -41.225 -29.609 1.00 44.88 C
ATOM 10685 CD2 LEU B 178 -81.413 -42.826 -31.539 1.00 44.19 C
ATOM 10689 C LEU B 178 -80.423 -38.571 -32.934 1.00 45.27 C
ATOM 10690 O LEU B 178 -79.211 -38.624 -32.759 1.00 44.99 O
ATOM 10692 N ALA B 179 -80.970 -38.203 -34.088 1.00 44.75 N

ATOM 10693 CA ALA B 179 -80.174 -37.661 -35.181 1.00 44.24 C
ATOM 10695 CB ALA B 179 -81.088 -37.069 -36.231 1.00 44.30 C
ATOM 10699 C ALA B 179 -79.192 -36.602 -34.683 1.00 43.65 C
ATOM 10700 O ALA B 179 -78.028 -36.604 -35.061 1.00 43.56 O
ATOM 10702 N GLU B 180 -79.675 -35.707 -33.827 1.00 43.01 N
ATOM 10703 CA GLU B 180 -78.863 -34.610 -33.311 1.00 42.49 C
ATOM 10705 CB GLU B 180 -79.749 -33.477 -32.789 1.00 42.85 C
ATOM 10708 CG GLU B 180 -80.574 -32.800 -33.881 1.00 44.23 C
ATOM 10711 CD GLU B 180 -80.991 -31.382 -33.519 1.00 45.80 C
ATOM 10712 OE1 GLU B 180 -80.098 -30.580 -33.156 1.00 46.69 O
ATOM 10713 OE2 GLU B 180 -82.203 -31.065 -33.610 1.00 46.71 O
ATOM 10714 C GLU B 180 -77.944 -35.075 -32.210 1.00 41.39 C
ATOM 10715 O GLU B 180 -76.843 -34.562 -32.071 1.00 41.27 O
ATOM 10717 N GLN B 181 -78.404 -36.035 -31.419 1.00 40.20 N
ATOM 10718 CA GLN B 181 -77.570 -36.632 -30.394 1.00 39.45 C
ATOM 10720 CB GLN B 181 -78.280 -37.809 -29.736 1.00 39.88 C
ATOM 10723 CG GLN B 181 -78.005 -37.959 -28.249 1.00 41.64 C
ATOM 10726 CD GLN B 181 -78.873 -37.036 -27.404 1.00 44.00 C
ATOM 10727 OE1 GLN B 181 -80.109 -36.992 -27.581 1.00 45.65 O
ATOM 10728 NE2 GLN B 181 -78.235 -36.291 -26.474 1.00 43.41 N
ATOM 10731 C GLN B 181 -76.270 -37.120 -31.003 1.00 38.28 C
ATOM 10732 O GLN B 181 -75.203 -36.767 -30.523 1.00 38.27 O
ATOM 10734 N VAL B 182 -76.358 -37.911 -32.072 1.00 37.05 N
ATOM 10735 CA VAL B 182 -75.160 -38.515 -32.675 1.00 36.20 C
ATOM 10737 CB VAL B 182 -75.486 -39.661 -33.681 1.00 36.11 C
ATOM 10739 CG1 VAL B 182 -76.493 -40.641 -33.080 1.00 36.13 C
ATOM 10743 CG2 VAL B 182 -75.977 -39.106 -35.004 1.00 36.06 C
ATOM 10747 C VAL B 182 -74.238 -37.495 -33.364 1.00 35.44 C
ATOM 10748 O VAL B 182 -73.012 -37.682 -33.375 1.00 35.19 O
ATOM 10750 N SER B 183 -74.811 -36.432 -33.936 1.00 34.41 N
ATOM 10751 CA SER B 183 -73.998 -35.416 -34.630 1.00 33.74 C
ATOM 10753 CB SER B 183 -74.858 -34.438 -35.422 1.00 33.58 C
ATOM 10756 OG SER B 183 -76.003 -35.085 -35.925 1.00 34.52 O
ATOM 10758 C SER B 183 -73.184 -34.644 -33.625 1.00 32.88 C
ATOM 10759 O SER B 183 -72.055 -34.251 -33.906 1.00 33.25 O
ATOM 10761 N HIS B 184 -73.788 -34.427 -32.461 1.00 31.83 N
ATOM 10762 CA HIS B 184 -73.150 -33.787 -31.326 1.00 30.98 C
ATOM 10764 CB HIS B 184 -74.188 -33.627 -30.212 1.00 31.14 C
ATOM 10767 CG HIS B 184 -73.710 -32.849 -29.030 1.00 31.91 C
ATOM 10768 ND1 HIS B 184 -73.326 -31.527 -29.114 1.00 33.18 N
ATOM 10770 CE1 HIS B 184 -72.960 -31.107 -27.914 1.00 33.10 C
ATOM 10772 NE2 HIS B 184 -73.106 -32.102 -27.056 1.00 31.85 N
ATOM 10774 CD2 HIS B 184 -73.583 -33.200 -27.727 1.00 31.86 C
ATOM 10776 C HIS B 184 -71.968 -34.632 -30.865 1.00 30.13 C
ATOM 10777 O HIS B 184 -70.863 -34.122 -30.709 1.00 29.95 O
ATOM 10779 N ALA B 185 -72.194 -35.931 -30.683 1.00 29.27 N
ATOM 10780 CA ALA B 185 -71.123 -36.856 -30.281 1.00 28.64 C
ATOM 10782 CB ALA B 185 -71.689 -38.233 -29.986 1.00 28.44 C
ATOM 10786 C ALA B 185 -70.017 -36.965 -31.330 1.00 28.08 C
ATOM 10787 O ALA B 185 -68.839 -37.043 -30.992 1.00 28.26 O
ATOM 10789 N LEU B 186 -70.394 -36.984 -32.602 1.00 27.40 N
ATOM 10790 CA LEU B 186 -69.412 -37.101 -33.674 1.00 26.84 C
ATOM 10792 CB LEU B 186 -70.088 -37.481 -35.000 1.00 26.75 C
ATOM 10795 CG LEU B 186 -70.085 -38.983 -35.320 1.00 26.70 C
ATOM 10797 CD1 LEU B 186 -70.214 -39.868 -34.075 1.00 27.07 C
ATOM 10801 CD2 LEU B 186 -71.179 -39.306 -36.303 1.00 26.29 C
ATOM 10805 C LEU B 186 -68.594 -35.822 -33.815 1.00 26.45 C
ATOM 10806 O LEU B 186 -67.449 -35.875 -34.237 1.00 26.48 O
ATOM 10808 N GLU B 187 -69.186 -34.685 -33.454 1.00 25.93 N
ATOM 10809 CA GLU B 187 -68.479 -33.406 -33.403 1.00 25.57 C

ATOM 10811 CB GLU B 187 -69.447 -32.310 -32.962 1.00 25.61 C
ATOM 10814 CG GLU B 187 -69.035 -30.899 -33.325 1.00 26.29 C
ATOM 10817 CD GLU B 187 -69.930 -29.857 -32.671 1.00 27.10 C
ATOM 10818 OE1 GLU B 187 -70.312 -30.057 -31.487 1.00 26.51 O
ATOM 10819 OE2 GLU B 187 -70.251 -28.846 -33.344 1.00 27.54 O
ATOM 10820 C GLU B 187 -67.307 -33.490 -32.418 1.00 25.13 C
ATOM 10821 O GLU B 187 -66.155 -33.165 -32.749 1.00 24.85 O
ATOM 10823 N LEU B 188 -67.625 -33.938 -31.204 1.00 24.58 N
ATOM 10824 CA LEU B 188 -66.644 -34.137 -30.148 1.00 24.06 C
ATOM 10826 CB LEU B 188 -66.343 -32.817 -29.451 1.00 24.12 C
ATOM 10829 CG LEU B 188 -65.042 -32.714 -28.670 1.00 23.61 C
ATOM 10831 CD1 LEU B 188 -63.895 -32.872 -29.629 1.00 23.12 C
ATOM 10835 CD2 LEU B 188 -64.976 -31.368 -27.964 1.00 23.18 C
ATOM 10839 C LEU B 188 -67.248 -35.087 -29.140 1.00 23.70 C
ATOM 10840 O LEU B 188 -68.392 -34.901 -28.743 1.00 23.68 O
ATOM 10842 N PRO B 189 -66.493 -36.106 -28.713 1.00 23.34 N
ATOM 10843 CA PRO B 189 -67.031 -36.983 -27.692 1.00 23.08 C
ATOM 10845 CB PRO B 189 -66.018 -38.115 -27.638 1.00 22.96 C
ATOM 10848 CG PRO B 189 -64.743 -37.452 -27.940 1.00 23.22 C
ATOM 10851 CD PRO B 189 -65.059 -36.350 -28.929 1.00 23.54 C
ATOM 10854 C PRO B 189 -67.053 -36.229 -26.387 1.00 22.86 C
ATOM 10855 O PRO B 189 -66.284 -35.285 -26.215 1.00 23.03 O
ATOM 10856 N LEU B 190 -67.912 -36.628 -25.465 1.00 22.56 N
ATOM 10857 CA LEU B 190 -68.152 -35.773 -24.323 1.00 22.41 C
ATOM 10859 CB LEU B 190 -69.567 -35.970 -23.766 1.00 23.04 C
ATOM 10862 CG LEU B 190 -69.853 -37.136 -22.848 1.00 23.41 C
ATOM 10864 CD1 LEU B 190 -69.303 -36.733 -21.481 1.00 25.02 C
ATOM 10868 CD2 LEU B 190 -71.342 -37.411 -22.820 1.00 21.69 C
ATOM 10872 C LEU B 190 -67.065 -35.899 -23.266 1.00 21.56 C
ATOM 10873 O LEU B 190 -66.860 -34.976 -22.477 1.00 21.67 O
ATOM 10875 N HIS B 191 -66.320 -36.998 -23.283 1.00 20.39 N
ATOM 10876 CA HIS B 191 -65.089 -37.037 -22.490 1.00 19.40 C
ATOM 10878 CB HIS B 191 -64.399 -38.393 -22.597 1.00 19.19 C
ATOM 10881 CG HIS B 191 -63.222 -38.530 -21.689 1.00 19.32 C
ATOM 10882 ND1 HIS B 191 -63.347 -38.562 -20.317 1.00 20.95 N
ATOM 10884 CE1 HIS B 191 -62.145 -38.659 -19.771 1.00 21.15 C
ATOM 10886 NE2 HIS B 191 -61.245 -38.689 -20.741 1.00 19.36 N
ATOM 10888 CD2 HIS B 191 -61.893 -38.604 -21.948 1.00 19.49 C
ATOM 10890 C HIS B 191 -64.094 -35.913 -22.841 1.00 18.62 C
ATOM 10891 O HIS B 191 -63.150 -35.677 -22.085 1.00 18.59 O
ATOM 10893 N ARG B 192 -64.307 -35.216 -23.957 1.00 17.72 N
ATOM 10894 CA ARG B 192 -63.394 -34.150 -24.394 1.00 17.57 C
ATOM 10896 CB ARG B 192 -62.838 -34.504 -25.773 1.00 17.81 C
ATOM 10899 CG ARG B 192 -61.971 -35.736 -25.781 1.00 18.59 C
ATOM 10902 CD ARG B 192 -61.484 -36.067 -27.181 1.00 20.10 C
ATOM 10905 NE ARG B 192 -60.462 -37.116 -27.165 1.00 21.62 N
ATOM 10907 CZ ARG B 192 -59.919 -37.648 -28.254 1.00 22.77 C
ATOM 10908 NH1 ARG B 192 -60.304 -37.248 -29.454 1.00 24.20 N
ATOM 10911 NH2 ARG B 192 -58.987 -38.581 -28.149 1.00 23.37 N
ATOM 10914 C ARG B 192 -63.983 -32.726 -24.440 1.00 17.01 C
ATOM 10915 O ARG B 192 -63.242 -31.739 -24.526 1.00 15.78 O
ATOM 10917 N ARG B 193 -65.309 -32.634 -24.392 1.00 17.01 N
ATOM 10918 CA ARG B 193 -66.015 -31.350 -24.453 1.00 16.99 C
ATOM 10920 CB ARG B 193 -67.476 -31.582 -24.892 1.00 17.29 C
ATOM 10923 CG ARG B 193 -68.192 -30.318 -25.377 1.00 18.42 C
ATOM 10926 CD ARG B 193 -69.664 -30.559 -25.646 1.00 19.63 C
ATOM 10929 NE ARG B 193 -69.912 -31.592 -26.648 1.00 21.16 N
ATOM 10931 CZ ARG B 193 -69.868 -31.398 -27.971 1.00 23.56 C
ATOM 10932 NH1 ARG B 193 -69.575 -30.210 -28.496 1.00 23.37 N
ATOM 10935 NH2 ARG B 193 -70.112 -32.413 -28.789 1.00 25.37 N

ATOM 10938 C ARG B 193 -65.974 -30.658 -23.087 1.00 16.46 C
ATOM 10939 O ARG B 193 -66.040 -31.323 -22.034 1.00 16.47 O
ATOM 10941 N THR B 194 -65.864 -29.335 -23.078 1.00 15.84 N
ATOM 10942 CA THR B 194 -65.886 -28.629 -21.799 1.00 15.67 C
ATOM 10944 CB THR B 194 -65.354 -27.199 -21.884 1.00 15.48 C
ATOM 10946 OG1 THR B 194 -66.077 -26.478 -22.882 1.00 15.55 O
ATOM 10948 CG2 THR B 194 -63.877 -27.189 -22.211 1.00 14.65 C
ATOM 10952 C THR B 194 -67.310 -28.613 -21.270 1.00 15.79 C
ATOM 10953 O THR B 194 -68.264 -28.652 -22.030 1.00 15.73 O
ATOM 10955 N GLN B 195 -67.444 -28.557 -19.957 1.00 16.20 N
ATOM 10956 CA GLN B 195 -68.737 -28.711 -19.328 1.00 16.84 C
ATOM 10958 CB GLN B 195 -68.601 -28.781 -17.816 1.00 17.07 C
ATOM 10961 CG GLN B 195 -69.921 -28.440 -17.153 1.00 18.86 C
ATOM 10964 CD GLN B 195 -69.999 -28.875 -15.746 1.00 20.95 C
ATOM 10965 OE1 GLN B 195 -69.099 -29.511 -15.245 1.00 24.63 O
ATOM 10966 NE2 GLN B 195 -71.071 -28.529 -15.082 1.00 22.36 N
ATOM 10969 C GLN B 195 -69.757 -27.623 -19.669 1.00 16.93 C
ATOM 10970 O GLN B 195 -70.858 -27.931 -20.136 1.00 16.98 O
ATOM 10972 N ARG B 196 -69.430 -26.366 -19.386 1.00 16.92 N
ATOM 10973 CA ARG B 196 -70.358 -25.301 -19.685 1.00 17.06 C
ATOM 10975 CB ARG B 196 -69.719 -23.932 -19.459 1.00 17.00 C
ATOM 10978 CG ARG B 196 -70.095 -23.289 -18.120 1.00 17.09 C
ATOM 10981 CD ARG B 196 -70.283 -24.320 -16.995 1.00 17.56 C
ATOM 10984 NE ARG B 196 -71.452 -24.043 -16.146 1.00 17.64 N
ATOM 10986 CZ ARG B 196 -72.289 -24.965 -15.664 1.00 17.93 C
ATOM 10987 NH1 ARG B 196 -72.136 -26.244 -15.966 1.00 17.72 N
ATOM 10990 NH2 ARG B 196 -73.305 -24.611 -14.878 1.00 18.27 N
ATOM 10993 C ARG B 196 -70.881 -25.481 -21.098 1.00 17.42 C
ATOM 10994 O ARG B 196 -72.079 -25.519 -21.317 1.00 17.66 O
ATOM 10996 N LEU B 197 -69.984 -25.676 -22.044 1.00 18.04 N
ATOM 10997 CA LEU B 197 -70.379 -25.925 -23.425 1.00 18.51 C
ATOM 10999 CB LEU B 197 -69.133 -26.085 -24.289 1.00 18.52 C
ATOM 11002 CG LEU B 197 -68.998 -25.185 -25.508 1.00 18.06 C
ATOM 11004 CD1 LEU B 197 -68.209 -23.932 -25.205 1.00 15.52 C
ATOM 11008 CD2 LEU B 197 -68.293 -26.002 -26.574 1.00 20.21 C
ATOM 11012 C LEU B 197 -71.290 -27.163 -23.580 1.00 19.14 C
ATOM 11013 O LEU B 197 -72.226 -27.150 -24.372 1.00 19.52 O
ATOM 11015 N GLU B 198 -71.030 -28.235 -22.842 1.00 19.72 N
ATOM 11016 CA GLU B 198 -71.918 -29.396 -22.909 1.00 20.43 C
ATOM 11018 CB GLU B 198 -71.272 -30.631 -22.270 1.00 20.65 C
ATOM 11021 CG GLU B 198 -72.176 -31.880 -22.172 1.00 22.51 C
ATOM 11024 CD GLU B 198 -72.635 -32.460 -23.522 1.00 25.57 C
ATOM 11025 OE1 GLU B 198 -72.315 -31.896 -24.581 1.00 28.90 O
ATOM 11026 OE2 GLU B 198 -73.326 -33.506 -23.540 1.00 28.09 O
ATOM 11027 C GLU B 198 -73.271 -29.101 -22.259 1.00 20.72 C
ATOM 11028 O GLU B 198 -74.281 -29.693 -22.644 1.00 20.82 O
ATOM 11030 N ALA B 199 -73.282 -28.199 -21.270 1.00 20.86 N
ATOM 11031 CA ALA B 199 -74.508 -27.814 -20.565 1.00 20.66 C
ATOM 11033 CB ALA B 199 -74.176 -27.013 -19.326 1.00 20.36 C
ATOM 11037 C ALA B 199 -75.472 -27.033 -21.461 1.00 20.84 C
ATOM 11038 O ALA B 199 -76.644 -27.404 -21.590 1.00 20.84 O
ATOM 11040 N VAL B 200 -75.002 -25.961 -22.092 1.00 21.12 N
ATOM 11041 CA VAL B 200 -75.903 -25.177 -22.942 1.00 21.60 C
ATOM 11043 CB VAL B 200 -75.215 -24.042 -23.701 1.00 21.30 C
ATOM 11045 CG1 VAL B 200 -74.660 -23.055 -22.738 1.00 21.26 C
ATOM 11049 CG2 VAL B 200 -74.135 -24.575 -24.626 1.00 21.28 C
ATOM 11053 C VAL B 200 -76.603 -26.077 -23.944 1.00 22.32 C
ATOM 11054 O VAL B 200 -77.791 -25.908 -24.218 1.00 22.32 O
ATOM 11056 N TRP B 201 -75.872 -27.047 -24.472 1.00 23.16 N
ATOM 11057 CA TRP B 201 -76.441 -27.946 -25.454 1.00 24.02 C

ATOM 11059 CB TRP B 201 -75.348 -28.718 -26.195 1.00 24.36 C
ATOM 11062 CG TRP B 201 -75.898 -29.510 -27.331 1.00 24.84 C
ATOM 11063 CD1 TRP B 201 -76.060 -29.092 -28.613 1.00 25.41 C
ATOM 11065 NE1 TRP B 201 -76.599 -30.094 -29.374 1.00 25.61 N
ATOM 11067 CE2 TRP B 201 -76.807 -31.184 -28.579 1.00 25.34 C
ATOM 11068 CD2 TRP B 201 -76.374 -30.847 -27.279 1.00 25.56 C
ATOM 11069 CE3 TRP B 201 -76.466 -31.800 -26.264 1.00 27.13 C
ATOM 11071 CZ3 TRP B 201 -76.989 -33.046 -26.574 1.00 28.66 C
ATOM 11073 CH2 TRP B 201 -77.419 -33.347 -27.885 1.00 28.01 C
ATOM 11075 CZ2 TRP B 201 -77.332 -32.425 -28.894 1.00 26.09 C
ATOM 11077 C TRP B 201 -77.411 -28.938 -24.833 1.00 24.22 C
ATOM 11078 O TRP B 201 -78.473 -29.172 -25.383 1.00 24.83 O
ATOM 11080 N SER B 202 -77.034 -29.541 -23.715 1.00 24.39 N
ATOM 11081 CA SER B 202 -77.818 -30.626 -23.144 1.00 24.50 C
ATOM 11083 CB SER B 202 -76.968 -31.455 -22.184 1.00 24.42 C
ATOM 11086 OG SER B 202 -75.848 -32.021 -22.848 1.00 23.80 O
ATOM 11088 C SER B 202 -79.067 -30.099 -22.441 1.00 24.98 C
ATOM 11089 O SER B 202 -80.057 -30.816 -22.324 1.00 24.73 O
ATOM 11091 N ILE B 203 -79.032 -28.849 -21.982 1.00 25.60 N
ATOM 11092 CA ILE B 203 -80.219 -28.255 -21.372 1.00 25.98 C
ATOM 11094 CB ILE B 203 -79.908 -26.967 -20.591 1.00 25.85 C
ATOM 11096 CG1 ILE B 203 -79.086 -27.326 -19.348 1.00 25.76 C
ATOM 11099 CD1 ILE B 203 -78.779 -26.159 -18.431 1.00 26.28 C
ATOM 11103 CG2 ILE B 203 -81.212 -26.253 -20.206 1.00 24.51 C
ATOM 11107 C ILE B 203 -81.280 -28.016 -22.443 1.00 26.67 C
ATOM 11108 O ILE B 203 -82.428 -28.398 -22.260 1.00 26.96 O
ATOM 11110 N GLU B 204 -80.879 -27.412 -23.563 1.00 27.30 N
ATOM 11111 CA GLU B 204 -81.758 -27.205 -24.720 1.00 27.49 C
ATOM 11113 CB GLU B 204 -81.036 -26.384 -25.804 1.00 27.67 C
ATOM 11116 CG GLU B 204 -81.849 -26.077 -27.073 1.00 28.50 C
ATOM 11119 CD GLU B 204 -82.987 -25.072 -26.855 1.00 29.81 C
ATOM 11120 OE1 GLU B 204 -83.158 -24.600 -25.711 1.00 31.40 O
ATOM 11121 OE2 GLU B 204 -83.710 -24.750 -27.832 1.00 29.57 O
ATOM 11122 C GLU B 204 -82.201 -28.542 -25.287 1.00 27.52 C
ATOM 11123 O GLU B 204 -83.321 -28.667 -25.738 1.00 27.67 O
ATOM 11125 N ALA B 205 -81.326 -29.539 -25.266 1.00 27.74 N
ATOM 11126 CA ALA B 205 -81.684 -30.872 -25.728 1.00 28.09 C
ATOM 11128 CB ALA B 205 -80.472 -31.789 -25.726 1.00 27.75 C
ATOM 11132 C ALA B 205 -82.771 -31.448 -24.839 1.00 28.81 C
ATOM 11133 O ALA B 205 -83.811 -31.877 -25.325 1.00 28.90 O
ATOM 11135 N TYR B 206 -82.517 -31.433 -23.531 1.00 29.72 N
ATOM 11136 CA TYR B 206 -83.408 -32.020 -22.527 1.00 30.30 C
ATOM 11138 CB TYR B 206 -82.760 -31.915 -21.149 1.00 30.24 C
ATOM 11141 CG TYR B 206 -83.276 -32.889 -20.127 1.00 29.79 C
ATOM 11142 CD1 TYR B 206 -83.055 -34.245 -20.286 1.00 30.71 C
ATOM 11144 CE1 TYR B 206 -83.498 -35.161 -19.360 1.00 30.78 C
ATOM 11146 CZ TYR B 206 -84.159 -34.731 -18.238 1.00 30.03 C
ATOM 11147 OH TYR B 206 -84.582 -35.684 -17.343 1.00 30.51 O
ATOM 11149 CE2 TYR B 206 -84.394 -33.379 -18.042 1.00 29.42 C
ATOM 11151 CD2 TYR B 206 -83.945 -32.463 -18.989 1.00 29.05 C
ATOM 11153 C TYR B 206 -84.744 -31.308 -22.467 1.00 31.19 C
ATOM 11154 O TYR B 206 -85.790 -31.930 -22.311 1.00 31.44 O
ATOM 11156 N ARG B 207 -84.683 -29.988 -22.558 1.00 32.21 N
ATOM 11157 CA ARG B 207 -85.853 -29.128 -22.521 1.00 33.04 C
ATOM 11159 CB ARG B 207 -85.394 -27.700 -22.843 1.00 32.86 C
ATOM 11162 CG ARG B 207 -86.441 -26.637 -22.846 1.00 32.82 C
ATOM 11165 CD ARG B 207 -85.905 -25.360 -23.462 1.00 32.76 C
ATOM 11168 NE ARG B 207 -85.148 -24.561 -22.504 1.00 32.80 N
ATOM 11170 CZ ARG B 207 -85.676 -23.709 -21.628 1.00 33.40 C
ATOM 11171 NH1 ARG B 207 -86.989 -23.526 -21.555 1.00 34.29 N

ATOM 11174 NH2 ARG B 207 -84.884 -23.030 -20.808 1.00 33.89 N
ATOM 11177 C ARG B 207 -86.971 -29.606 -23.478 1.00 34.14 C
ATOM 11178 O ARG B 207 -88.144 -29.521 -23.128 1.00 34.34 O
ATOM 11180 N LYS B 208 -86.607 -30.137 -24.652 1.00 35.32 N
ATOM 11181 CA LYS B 208 -87.581 -30.535 -25.688 1.00 36.16 C
ATOM 11183 CB LYS B 208 -86.960 -30.468 -27.090 1.00 36.01 C
ATOM 11186 CG LYS B 208 -86.126 -29.234 -27.368 1.00 35.85 C
ATOM 11189 CD LYS B 208 -85.934 -29.023 -28.861 1.00 35.98 C
ATOM 11192 CE LYS B 208 -84.774 -28.086 -29.186 1.00 35.63 C
ATOM 11195 NZ LYS B 208 -83.566 -28.843 -29.596 1.00 35.17 N
ATOM 11199 C LYS B 208 -88.166 -31.937 -25.490 1.00 37.25 C
ATOM 11200 O LYS B 208 -89.212 -32.250 -26.054 1.00 37.50 O
ATOM 11202 N LYS B 209 -87.484 -32.788 -24.730 1.00 38.58 N
ATOM 11203 CA LYS B 209 -88.026 -34.106 -24.383 1.00 39.89 C
ATOM 11205 CB LYS B 209 -87.013 -34.923 -23.578 1.00 40.23 C
ATOM 11208 CG LYS B 209 -85.914 -35.604 -24.373 1.00 41.47 C
ATOM 11211 CD LYS B 209 -84.858 -36.178 -23.417 1.00 43.71 C
ATOM 11214 CE LYS B 209 -84.448 -37.612 -23.764 1.00 45.15 C
ATOM 11217 NZ LYS B 209 -85.390 -38.621 -23.163 1.00 45.73 N
ATOM 11221 C LYS B 209 -89.288 -33.950 -23.530 1.00 40.51 C
ATOM 11222 O LYS B 209 -89.230 -33.367 -22.441 1.00 40.84 O
ATOM 11224 N GLU B 210 -90.418 -34.477 -24.000 1.00 40.92 N
ATOM 11225 CA GLU B 210 -91.652 -34.386 -23.223 1.00 41.27 C
ATOM 11227 CB GLU B 210 -92.855 -34.935 -23.998 1.00 41.77 C
ATOM 11230 CG GLU B 210 -92.822 -36.446 -24.265 1.00 43.47 C
ATOM 11233 CD GLU B 210 -94.049 -36.922 -25.032 1.00 45.23 C
ATOM 11234 OE1 GLU B 210 -95.188 -36.590 -24.612 1.00 45.02 O
ATOM 11235 OE2 GLU B 210 -93.863 -37.629 -26.053 1.00 46.74 O
ATOM 11236 C GLU B 210 -91.494 -35.121 -21.895 1.00 40.71 C
ATOM 11237 O GLU B 210 -91.996 -34.667 -20.864 1.00 40.99 O
ATOM 11239 N ASP B 211 -90.773 -36.240 -21.924 1.00 39.76 N
ATOM 11240 CA ASP B 211 -90.533 -37.050 -20.721 1.00 38.96 C
ATOM 11242 CB ASP B 211 -90.151 -38.476 -21.123 1.00 39.10 C
ATOM 11245 CG ASP B 211 -89.101 -38.499 -22.212 1.00 40.26 C
ATOM 11246 OD1 ASP B 211 -89.327 -37.827 -23.254 1.00 41.25 O
ATOM 11247 OD2 ASP B 211 -88.055 -39.160 -22.020 1.00 41.66 O
ATOM 11248 C ASP B 211 -89.440 -36.468 -19.826 1.00 37.75 C
ATOM 11249 O ASP B 211 -89.009 -37.131 -18.892 1.00 37.62 O
ATOM 11251 N ALA B 212 -88.989 -35.245 -20.115 1.00 36.47 N
ATOM 11252 CA ALA B 212 -87.941 -34.587 -19.335 1.00 35.36 C
ATOM 11254 CB ALA B 212 -87.516 -33.294 -20.011 1.00 35.23 C
ATOM 11258 C ALA B 212 -88.423 -34.307 -17.920 1.00 34.40 C
ATOM 11259 O ALA B 212 -89.559 -33.870 -17.728 1.00 34.42 O
ATOM 11261 N ASN B 213 -87.565 -34.574 -16.937 1.00 33.24 N
ATOM 11262 CA ASN B 213 -87.890 -34.333 -15.533 1.00 32.67 C
ATOM 11264 CB ASN B 213 -86.840 -34.986 -14.623 1.00 32.58 C
ATOM 11267 CG ASN B 213 -87.204 -34.912 -13.152 1.00 32.67 C
ATOM 11268 OD1 ASN B 213 -87.891 -33.994 -12.722 1.00 32.62 O
ATOM 11269 ND2 ASN B 213 -86.734 -35.882 -12.371 1.00 33.18 N
ATOM 11272 C ASN B 213 -87.990 -32.825 -15.266 1.00 32.19 C
ATOM 11273 O ASN B 213 -87.010 -32.092 -15.376 1.00 32.38 O
ATOM 11275 N GLN B 214 -89.182 -32.356 -14.923 1.00 31.48 N
ATOM 11276 CA GLN B 214 -89.389 -30.924 -14.756 1.00 30.85 C
ATOM 11278 CB GLN B 214 -90.889 -30.581 -14.693 1.00 30.82 C
ATOM 11281 CG GLN B 214 -91.684 -30.869 -16.002 1.00 30.80 C
ATOM 11284 CD GLN B 214 -90.990 -30.378 -17.291 1.00 29.69 C
ATOM 11285 OE1 GLN B 214 -90.893 -29.174 -17.543 1.00 29.07 O
ATOM 11286 NE2 GLN B 214 -90.526 -31.321 -18.113 1.00 27.71 N
ATOM 11289 C GLN B 214 -88.638 -30.369 -13.543 1.00 30.37 C
ATOM 11290 O GLN B 214 -88.263 -29.200 -13.533 1.00 30.80 O

ATOM 11292 N VAL B 215 -88.393 -31.200 -12.532 1.00 29.54 N
ATOM 11293 CA VAL B 215 -87.566 -30.779 -11.395 1.00 28.56 C
ATOM 11295 CB VAL B 215 -87.564 -31.818 -10.260 1.00 28.64 C
ATOM 11297 CG1 VAL B 215 -86.758 -31.299 -9.075 1.00 27.94 C
ATOM 11301 CG2 VAL B 215 -88.999 -32.167 -9.856 1.00 28.26 C
ATOM 11305 C VAL B 215 -86.124 -30.545 -11.845 1.00 27.63 C
ATOM 11306 O VAL B 215 -85.566 -29.472 -11.615 1.00 27.58 O
ATOM 11308 N LEU B 216 -85.546 -31.548 -12.504 1.00 26.37 N
ATOM 11309 CA LEU B 216 -84.143 -31.509 -12.930 1.00 25.47 C
ATOM 11311 CB LEU B 216 -83.714 -32.866 -13.490 1.00 25.46 C
ATOM 11314 CG LEU B 216 -82.274 -32.995 -13.979 1.00 24.97 C
ATOM 11316 CD1 LEU B 216 -81.289 -32.640 -12.883 1.00 24.62 C
ATOM 11320 CD2 LEU B 216 -82.042 -34.407 -14.472 1.00 24.55 C
ATOM 11324 C LEU B 216 -83.861 -30.447 -13.972 1.00 24.68 C
ATOM 11325 O LEU B 216 -82.819 -29.820 -13.929 1.00 24.91 O
ATOM 11327 N LEU B 217 -84.776 -30.269 -14.916 1.00 23.79 N
ATOM 11328 CA LEU B 217 -84.625 -29.260 -15.960 1.00 23.13 C
ATOM 11330 CB LEU B 217 -85.765 -29.384 -16.972 1.00 23.36 C
ATOM 11333 CG LEU B 217 -85.808 -28.374 -18.123 1.00 23.18 C
ATOM 11335 CD1 LEU B 217 -84.462 -28.268 -18.796 1.00 22.69 C
ATOM 11339 CD2 LEU B 217 -86.861 -28.786 -19.126 1.00 23.38 C
ATOM 11343 C LEU B 217 -84.631 -27.853 -15.383 1.00 22.51 C
ATOM 11344 O LEU B 217 -83.903 -26.973 -15.855 1.00 22.08 O
ATOM 11346 N GLU B 218 -85.481 -27.647 -14.375 1.00 21.84 N
ATOM 11347 CA GLU B 218 -85.619 -26.339 -13.725 1.00 21.26 C
ATOM 11349 CB GLU B 218 -86.813 -26.341 -12.768 1.00 21.27 C
ATOM 11352 CG GLU B 218 -87.206 -24.956 -12.246 1.00 21.35 C
ATOM 11355 CD GLU B 218 -88.501 -24.964 -11.441 1.00 20.89 C
ATOM 11356 OE1 GLU B 218 -89.097 -26.052 -11.263 1.00 20.47 O
ATOM 11357 OE2 GLU B 218 -88.915 -23.874 -10.986 1.00 20.15 O
ATOM 11358 C GLU B 218 -84.348 -26.001 -12.969 1.00 20.58 C
ATOM 11359 O GLU B 218 -83.877 -24.865 -12.982 1.00 20.31 O
ATOM 11361 N LEU B 219 -83.802 -27.015 -12.312 1.00 19.87 N
ATOM 11362 CA LEU B 219 -82.559 -26.885 -11.592 1.00 19.12 C
ATOM 11364 CB LEU B 219 -82.310 -28.132 -10.746 1.00 18.58 C
ATOM 11367 CG LEU B 219 -81.159 -28.054 -9.762 1.00 17.07 C
ATOM 11369 CD1 LEU B 219 -81.321 -26.847 -8.872 1.00 16.10 C
ATOM 11373 CD2 LEU B 219 -81.107 -29.311 -8.954 1.00 15.22 C
ATOM 11377 C LEU B 219 -81.443 -26.675 -12.599 1.00 19.16 C
ATOM 11378 O LEU B 219 -80.684 -25.721 -12.478 1.00 19.42 O
ATOM 11380 N ALA B 220 -81.368 -27.546 -13.606 1.00 19.04 N
ATOM 11381 CA ALA B 220 -80.356 -27.431 -14.669 1.00 19.04 C
ATOM 11383 CB ALA B 220 -80.648 -28.398 -15.817 1.00 18.64 C
ATOM 11387 C ALA B 220 -80.257 -26.004 -15.196 1.00 19.06 C
ATOM 11388 O ALA B 220 -79.159 -25.472 -15.321 1.00 19.08 O
ATOM 11390 N ILE B 221 -81.410 -25.393 -15.475 1.00 19.19 N
ATOM 11391 CA ILE B 221 -81.473 -24.016 -15.963 1.00 19.22 C
ATOM 11393 CB ILE B 221 -82.898 -23.638 -16.423 1.00 19.03 C
ATOM 11395 CG1 ILE B 221 -83.229 -24.323 -17.755 1.00 18.52 C
ATOM 11398 CD1 ILE B 221 -84.687 -24.645 -17.928 1.00 17.52 C
ATOM 11402 CG2 ILE B 221 -83.024 -22.121 -16.564 1.00 18.03 C
ATOM 11406 C ILE B 221 -81.030 -23.013 -14.906 1.00 19.62 C
ATOM 11407 O ILE B 221 -80.137 -22.190 -15.136 1.00 19.53 O
ATOM 11409 N LEU B 222 -81.666 -23.096 -13.745 1.00 20.27 N
ATOM 11410 CA LEU B 222 -81.412 -22.161 -12.654 1.00 20.63 C
ATOM 11412 CB LEU B 222 -82.203 -22.561 -11.412 1.00 20.50 C
ATOM 11415 CG LEU B 222 -82.195 -21.523 -10.296 1.00 20.76 C
ATOM 11417 CD1 LEU B 222 -83.439 -21.675 -9.431 1.00 21.02 C
ATOM 11421 CD2 LEU B 222 -80.924 -21.625 -9.453 1.00 20.21 C
ATOM 11425 C LEU B 222 -79.925 -22.089 -12.341 1.00 20.98 C

ATOM 11426 O LEU B 222 -79.337 -21.011 -12.381 1.00 21.40 O
ATOM 11428 N ASP B 223 -79.319 -23.240 -12.064 1.00 21.24 N
ATOM 11429 CA ASP B 223 -77.907 -23.298 -11.709 1.00 21.48 C
ATOM 11431 CB ASP B 223 -77.509 -24.724 -11.314 1.00 21.66 C
ATOM 11434 CG ASP B 223 -76.168 -24.792 -10.589 1.00 22.70 C
ATOM 11435 OD1 ASP B 223 -75.095 -24.775 -11.244 1.00 24.25 O
ATOM 11436 OD2 ASP B 223 -76.190 -24.893 -9.349 1.00 24.85 O
ATOM 11437 C ASP B 223 -77.017 -22.768 -12.835 1.00 21.64 C
ATOM 11438 O ASP B 223 -76.035 -22.104 -12.548 1.00 21.66 O
ATOM 11440 N TYR B 224 -77.361 -23.023 -14.100 1.00 22.07 N
ATOM 11441 CA TYR B 224 -76.517 -22.561 -15.218 1.00 22.47 C
ATOM 11443 CB TYR B 224 -76.980 -23.111 -16.589 1.00 22.35 C
ATOM 11446 CG TYR B 224 -76.032 -22.733 -17.724 1.00 22.25 C
ATOM 11447 CD1 TYR B 224 -75.002 -23.576 -18.116 1.00 21.46 C
ATOM 11449 CE1 TYR B 224 -74.126 -23.216 -19.135 1.00 21.43 C
ATOM 11451 CZ TYR B 224 -74.260 -21.991 -19.761 1.00 21.62 C
ATOM 11452 OH TYR B 224 -73.387 -21.618 -20.760 1.00 20.46 O
ATOM 11454 CE2 TYR B 224 -75.270 -21.132 -19.387 1.00 22.04 C
ATOM 11456 CD2 TYR B 224 -76.144 -21.500 -18.373 1.00 22.73 C
ATOM 11458 C TYR B 224 -76.414 -21.023 -15.262 1.00 23.06 C
ATOM 11459 O TYR B 224 -75.323 -20.467 -15.507 1.00 22.89 O
ATOM 11461 N ASN B 225 -77.543 -20.350 -15.027 1.00 23.66 N
ATOM 11462 CA ASN B 225 -77.593 -18.884 -15.072 1.00 24.16 C
ATOM 11464 CB ASN B 225 -79.040 -18.367 -15.107 1.00 24.12 C
ATOM 11467 CG ASN B 225 -79.778 -18.761 -16.365 1.00 23.89 C
ATOM 11468 OD1 ASN B 225 -79.182 -18.877 -17.437 1.00 24.33 O
ATOM 11469 ND2 ASN B 225 -81.088 -18.965 -16.244 1.00 22.05 N
ATOM 11472 C ASN B 225 -76.880 -18.265 -13.881 1.00 24.73 C
ATOM 11473 O ASN B 225 -76.195 -17.247 -14.027 1.00 25.09 O
ATOM 11475 N MET B 226 -77.067 -18.864 -12.703 1.00 25.15 N
ATOM 11476 CA MET B 226 -76.423 -18.390 -11.479 1.00 25.53 C
ATOM 11478 CB MET B 226 -76.806 -19.278 -10.282 1.00 26.11 C
ATOM 11481 CG MET B 226 -75.905 -19.169 -9.023 1.00 27.59 C
ATOM 11484 SD MET B 226 -75.676 -20.788 -8.214 1.00 30.67 S
ATOM 11485 CE MET B 226 -77.308 -21.005 -7.476 1.00 29.78 C
ATOM 11489 C MET B 226 -74.920 -18.380 -11.692 1.00 25.16 C
ATOM 11490 O MET B 226 -74.258 -17.387 -11.391 1.00 25.10 O
ATOM 11492 N ILE B 227 -74.388 -19.473 -12.239 1.00 24.88 N
ATOM 11493 CA ILE B 227 -72.944 -19.564 -12.501 1.00 24.70 C
ATOM 11495 CB ILE B 227 -72.476 -20.994 -12.882 1.00 24.45 C
ATOM 11497 CG1 ILE B 227 -72.656 -21.947 -11.695 1.00 23.80 C
ATOM 11500 CD1 ILE B 227 -72.094 -23.332 -11.885 1.00 21.97 C
ATOM 11504 CG2 ILE B 227 -71.030 -20.969 -13.266 1.00 24.90 C
ATOM 11508 C ILE B 227 -72.529 -18.550 -13.566 1.00 24.45 C
ATOM 11509 O ILE B 227 -71.578 -17.810 -13.373 1.00 24.42 O
ATOM 11511 N GLN B 228 -73.264 -18.484 -14.668 1.00 24.31 N
ATOM 11512 CA GLN B 228 -73.038 -17.414 -15.639 1.00 24.19 C
ATOM 11514 CB GLN B 228 -74.143 -17.363 -16.688 1.00 24.02 C
ATOM 11517 CG GLN B 228 -73.788 -16.488 -17.864 1.00 23.42 C
ATOM 11520 CD GLN B 228 -74.807 -16.567 -18.983 1.00 23.70 C
ATOM 11521 OE1 GLN B 228 -75.790 -15.813 -19.015 1.00 24.07 O
ATOM 11522 NE2 GLN B 228 -74.564 -17.465 -19.927 1.00 23.49 N
ATOM 11525 C GLN B 228 -72.913 -16.037 -14.987 1.00 24.37 C
ATOM 11526 O GLN B 228 -72.145 -15.210 -15.470 1.00 24.45 O
ATOM 11528 N SER B 229 -73.653 -15.776 -13.909 1.00 24.45 N
ATOM 11529 CA SER B 229 -73.578 -14.459 -13.264 1.00 24.76 C
ATOM 11531 CB SER B 229 -74.815 -14.163 -12.397 1.00 24.84 C
ATOM 11534 OG SER B 229 -74.711 -14.718 -11.096 1.00 25.81 O
ATOM 11536 C SER B 229 -72.270 -14.279 -12.469 1.00 24.64 C
ATOM 11537 O SER B 229 -71.726 -13.172 -12.408 1.00 24.95 O

ATOM 11539 N VAL B 230 -71.751 -15.350 -11.878 1.00 24.20 N
ATOM 11540 CA VAL B 230 -70.415 -15.277 -11.299 1.00 23.99 C
ATOM 11542 CB VAL B 230 -70.006 -16.581 -10.574 1.00 23.92 C
ATOM 11544 CG1 VAL B 230 -68.546 -16.510 -10.105 1.00 23.71 C
ATOM 11548 CG2 VAL B 230 -70.923 -16.853 -9.409 1.00 23.52 C
ATOM 11552 C VAL B 230 -69.386 -14.966 -12.400 1.00 24.12 C
ATOM 11553 O VAL B 230 -68.397 -14.291 -12.136 1.00 24.01 O
ATOM 11555 N TYR B 231 -69.612 -15.461 -13.621 1.00 24.30 N
ATOM 11556 CA TYR B 231 -68.672 -15.235 -14.728 1.00 24.53 C
ATOM 11558 CB TYR B 231 -68.997 -16.104 -15.946 1.00 24.08 C
ATOM 11561 CG TYR B 231 -68.892 -17.605 -15.754 1.00 23.29 C
ATOM 11562 CD1 TYR B 231 -68.173 -18.168 -14.706 1.00 23.08 C
ATOM 11564 CE1 TYR B 231 -68.073 -19.547 -14.565 1.00 22.01 C
ATOM 11566 CZ TYR B 231 -68.685 -20.369 -15.479 1.00 21.16 C
ATOM 11567 OH TYR B 231 -68.607 -21.746 -15.353 1.00 20.18 O
ATOM 11569 CE2 TYR B 231 -69.387 -19.825 -16.523 1.00 21.64 C
ATOM 11571 CD2 TYR B 231 -69.476 -18.464 -16.662 1.00 22.15 C
ATOM 11573 C TYR B 231 -68.658 -13.772 -15.166 1.00 25.37 C
ATOM 11574 O TYR B 231 -67.602 -13.221 -15.528 1.00 25.25 O
ATOM 11576 N GLN B 232 -69.832 -13.148 -15.129 1.00 26.11 N
ATOM 11577 CA GLN B 232 -69.978 -11.797 -15.622 1.00 26.68 C
ATOM 11579 CB GLN B 232 -71.430 -11.541 -15.995 1.00 26.45 C
ATOM 11582 CG GLN B 232 -71.883 -12.385 -17.176 1.00 25.67 C
ATOM 11585 CD GLN B 232 -73.388 -12.394 -17.381 1.00 24.91 C
ATOM 11586 OE1 GLN B 232 -74.140 -11.761 -16.637 1.00 24.81 O
ATOM 11587 NE2 GLN B 232 -73.834 -13.113 -18.407 1.00 23.39 N
ATOM 11590 C GLN B 232 -69.445 -10.802 -14.593 1.00 27.90 C
ATOM 11591 O GLN B 232 -68.909 -9.752 -14.958 1.00 27.96 O
ATOM 11593 N ARG B 233 -69.572 -11.145 -13.312 1.00 29.35 N
ATOM 11594 CA ARG B 233 -68.908 -10.396 -12.241 1.00 30.59 C
ATOM 11596 CB ARG B 233 -69.490 -10.775 -10.867 1.00 30.99 C
ATOM 11599 CG ARG B 233 -68.824 -10.114 -9.661 1.00 32.72 C
ATOM 11602 CD ARG B 233 -69.695 -10.210 -8.391 1.00 35.70 C
ATOM 11605 NE ARG B 233 -70.162 -11.578 -8.086 1.00 38.29 N
ATOM 11607 CZ ARG B 233 -71.403 -12.053 -8.276 1.00 39.65 C
ATOM 11608 NH1 ARG B 233 -72.367 -11.287 -8.787 1.00 40.23 N
ATOM 11611 NH2 ARG B 233 -71.687 -13.320 -7.949 1.00 39.61 N
ATOM 11614 C ARG B 233 -67.390 -10.632 -12.303 1.00 31.10 C
ATOM 11615 O ARG B 233 -66.615 -9.693 -12.181 1.00 31.19 O
ATOM 11617 N ASP B 234 -66.954 -11.868 -12.517 1.00 31.91 N
ATOM 11618 CA ASP B 234 -65.530 -12.102 -12.750 1.00 32.63 C
ATOM 11620 CB ASP B 234 -65.220 -13.566 -13.090 1.00 32.53 C
ATOM 11623 CG ASP B 234 -65.336 -14.493 -11.894 1.00 32.90 C
ATOM 11624 OD1 ASP B 234 -65.477 -14.028 -10.746 1.00 33.06 O
ATOM 11625 OD2 ASP B 234 -65.293 -15.713 -12.107 1.00 34.22 O
ATOM 11626 C ASP B 234 -65.058 -11.206 -13.886 1.00 33.10 C
ATOM 11627 O ASP B 234 -64.097 -10.458 -13.723 1.00 33.55 O
ATOM 11629 N LEU B 235 -65.753 -11.256 -15.017 1.00 33.49 N
ATOM 11630 CA LEU B 235 -65.311 -10.550 -16.216 1.00 34.06 C
ATOM 11632 CB LEU B 235 -66.139 -10.996 -17.422 1.00 33.80 C
ATOM 11635 CG LEU B 235 -65.769 -10.403 -18.775 1.00 32.13 C
ATOM 11637 CD1 LEU B 235 -64.303 -10.679 -19.050 1.00 30.94 C
ATOM 11641 CD2 LEU B 235 -66.670 -10.959 -19.870 1.00 29.93 C
ATOM 11645 C LEU B 235 -65.345 -9.023 -16.103 1.00 35.40 C
ATOM 11646 O LEU B 235 -64.500 -8.352 -16.682 1.00 35.61 O
ATOM 11648 N ARG B 236 -66.327 -8.473 -15.386 1.00 36.92 N
ATOM 11649 CA ARG B 236 -66.380 -7.019 -15.137 1.00 38.06 C
ATOM 11651 CB ARG B 236 -67.650 -6.607 -14.367 1.00 38.43 C
ATOM 11654 CG ARG B 236 -68.882 -6.321 -15.230 1.00 39.58 C
ATOM 11657 CD ARG B 236 -69.958 -5.520 -14.459 1.00 40.93 C

ATOM 11660 NE ARG B 236 -70.383 -6.149 -13.199 1.00 41.74 N
ATOM 11662 CZ ARG B 236 -71.208 -7.195 -13.095 1.00 42.20 C
ATOM 11663 NH1 ARG B 236 -71.719 -7.784 -14.175 1.00 41.61 N
ATOM 11666 NH2 ARG B 236 -71.517 -7.672 -11.892 1.00 42.99 N
ATOM 11669 C ARG B 236 -65.170 -6.550 -14.343 1.00 38.57 C
ATOM 11670 O ARG B 236 -64.593 -5.524 -14.665 1.00 38.61 O
ATOM 11672 N GLU B 237 -64.822 -7.292 -13.291 1.00 39.42 N
ATOM 11673 CA GLU B 237 -63.625 -7.017 -12.480 1.00 40.18 C
ATOM 11675 CB GLU B 237 -63.471 -8.033 -11.317 1.00 40.67 C
ATOM 11678 CG GLU B 237 -64.336 -7.750 -10.057 1.00 42.61 C
ATOM 11681 CD GLU B 237 -64.258 -8.858 -8.961 1.00 45.07 C
ATOM 11682 OE1 GLU B 237 -64.051 -10.066 -9.282 1.00 46.74 O
ATOM 11683 OE2 GLU B 237 -64.436 -8.511 -7.764 1.00 45.87 O
ATOM 11684 C GLU B 237 -62.352 -7.024 -13.344 1.00 39.93 C
ATOM 11685 O GLU B 237 -61.593 -6.050 -13.332 1.00 39.96 O
ATOM 11687 N THR B 238 -62.123 -8.104 -14.095 1.00 39.56 N
ATOM 11688 CA THR B 238 -60.900 -8.200 -14.895 1.00 39.42 C
ATOM 11690 CB THR B 238 -60.492 -9.666 -15.268 1.00 39.39 C
ATOM 11692 OG1 THR B 238 -61.222 -10.123 -16.413 1.00 39.37 O
ATOM 11694 CG2 THR B 238 -60.683 -10.612 -14.095 1.00 38.73 C
ATOM 11698 C THR B 238 -60.961 -7.326 -16.156 1.00 39.48 C
ATOM 11699 O THR B 238 -59.930 -7.062 -16.761 1.00 39.48 O
ATOM 11701 N SER B 239 -62.149 -6.871 -16.549 1.00 39.62 N
ATOM 11702 CA SER B 239 -62.264 -5.882 -17.631 1.00 39.63 C
ATOM 11704 CB SER B 239 -63.689 -5.810 -18.172 1.00 39.56 C
ATOM 11707 OG SER B 239 -63.945 -6.917 -19.010 1.00 38.96 O
ATOM 11709 C SER B 239 -61.796 -4.496 -17.181 1.00 39.99 C
ATOM 11710 O SER B 239 -61.108 -3.807 -17.933 1.00 40.10 O
ATOM 11712 N ARG B 240 -62.168 -4.088 -15.965 1.00 40.35 N
ATOM 11713 CA ARG B 240 -61.624 -2.864 -15.363 1.00 40.68 C
ATOM 11715 CB ARG B 240 -62.025 -2.712 -13.881 1.00 41.26 C
ATOM 11718 CG ARG B 240 -63.231 -1.782 -13.621 1.00 43.86 C
ATOM 11721 CD ARG B 240 -63.334 -1.375 -12.130 1.00 47.07 C
ATOM 11724 NE ARG B 240 -63.365 -2.537 -11.222 1.00 50.14 N
ATOM 11726 CZ ARG B 240 -64.462 -3.077 -10.671 1.00 52.32 C
ATOM 11727 NH1 ARG B 240 -64.342 -4.141 -9.875 1.00 53.16 N
ATOM 11730 NH2 ARG B 240 -65.677 -2.577 -10.899 1.00 53.18 N
ATOM 11733 C ARG B 240 -60.113 -2.914 -15.464 1.00 39.91 C
ATOM 11734 O ARG B 240 -59.490 -2.000 -15.988 1.00 39.86 O
ATOM 11736 N TRP B 241 -59.541 -4.002 -14.962 1.00 39.14 N
ATOM 11737 CA TRP B 241 -58.105 -4.217 -15.004 1.00 38.37 C
ATOM 11739 CB TRP B 241 -57.773 -5.635 -14.521 1.00 38.17 C
ATOM 11742 CG TRP B 241 -56.373 -6.005 -14.773 1.00 36.58 C
ATOM 11743 CD1 TRP B 241 -55.290 -5.668 -14.022 1.00 36.32 C
ATOM 11745 NE1 TRP B 241 -54.152 -6.176 -14.587 1.00 35.63 N
ATOM 11747 CE2 TRP B 241 -54.494 -6.846 -15.731 1.00 34.31 C
ATOM 11748 CD2 TRP B 241 -55.883 -6.757 -15.874 1.00 33.99 C
ATOM 11749 CE3 TRP B 241 -56.484 -7.357 -16.977 1.00 33.28 C
ATOM 11751 CZ3 TRP B 241 -55.691 -8.034 -17.883 1.00 32.79 C
ATOM 11753 CH2 TRP B 241 -54.313 -8.101 -17.720 1.00 33.06 C
ATOM 11755 CZ2 TRP B 241 -53.697 -7.515 -16.648 1.00 34.16 C
ATOM 11757 C TRP B 241 -57.561 -3.999 -16.409 1.00 38.25 C
ATOM 11758 O TRP B 241 -56.607 -3.252 -16.603 1.00 38.13 O
ATOM 11760 N TRP B 242 -58.186 -4.644 -17.386 1.00 38.21 N
ATOM 11761 CA TRP B 242 -57.695 -4.628 -18.765 1.00 38.27 C
ATOM 11763 CB TRP B 242 -58.479 -5.640 -19.609 1.00 38.31 C
ATOM 11766 CG TRP B 242 -57.948 -5.872 -20.990 1.00 38.61 C
ATOM 11767 CD1 TRP B 242 -58.642 -5.754 -22.156 1.00 39.11 C
ATOM 11769 NE1 TRP B 242 -57.828 -6.046 -23.224 1.00 39.31 N
ATOM 11771 CE2 TRP B 242 -56.582 -6.363 -22.759 1.00 38.95 C

ATOM 11772 CD2 TRP B 242 -56.617 -6.263 -21.356 1.00 38.66 C
ATOM 11773 CE3 TRP B 242 -55.454 -6.528 -20.637 1.00 38.98 C
ATOM 11775 CZ3 TRP B 242 -54.314 -6.886 -21.326 1.00 39.20 C
ATOM 11777 CH2 TRP B 242 -54.313 -6.985 -22.716 1.00 39.12 C
ATOM 11779 CZ2 TRP B 242 -55.434 -6.724 -23.451 1.00 39.22 C
ATOM 11781 C TRP B 242 -57.739 -3.241 -19.400 1.00 38.27 C
ATOM 11782 O TRP B 242 -56.814 -2.873 -20.108 1.00 37.81 O
ATOM 11784 N ARG B 243 -58.809 -2.489 -19.140 1.00 38.79 N
ATOM 11785 CA ARG B 243 -58.936 -1.097 -19.607 1.00 39.37 C
ATOM 11787 CB ARG B 243 -60.351 -.552 -19.346 1.00 39.66 C
ATOM 11790 CG ARG B 243 -61.324 -.792 -20.520 1.00 41.96 C
ATOM 11793 CD ARG B 243 -62.687 -1.338 -20.085 1.00 44.82 C
ATOM 11796 NE ARG B 243 -63.461 -.380 -19.296 1.00 47.15 N
ATOM 11798 CZ ARG B 243 -64.389 -.704 -18.386 1.00 49.26 C
ATOM 11799 NH1 ARG B 243 -64.685 -1.976 -18.109 1.00 49.18 N
ATOM 11802 NH2 ARG B 243 -65.028 .262 -17.729 1.00 50.40 N
ATOM 11805 C ARG B 243 -57.890 -.183 -18.980 1.00 39.28 C
ATOM 11806 O ARG B 243 -57.246 .577 -19.681 1.00 39.40 O
ATOM 11808 N ARG B 244 -57.724 -.282 -17.665 1.00 39.52 N
ATOM 11809 CA ARG B 244 -56.734 .489 -16.888 1.00 39.61 C
ATOM 11811 CB ARG B 244 -56.774 .041 -15.409 1.00 40.25 C
ATOM 11814 CG ARG B 244 -56.115 .971 -14.383 1.00 42.01 C
ATOM 11817 CD ARG B 244 -57.029 2.154 -14.017 1.00 44.39 C
ATOM 11820 NE ARG B 244 -56.391 3.115 -13.103 1.00 46.36 N
ATOM 11822 CZ ARG B 244 -55.434 3.984 -13.441 1.00 48.06 C
ATOM 11823 NH1 ARG B 244 -54.951 4.043 -14.686 1.00 48.90 N
ATOM 11826 NH2 ARG B 244 -54.947 4.805 -12.519 1.00 48.82 N
ATOM 11829 C ARG B 244 -55.323 .322 -17.437 1.00 38.83 C
ATOM 11830 O ARG B 244 -54.594 1.300 -17.567 1.00 38.39 O
ATOM 11832 N VAL B 245 -54.953 -.922 -17.738 1.00 38.52 N
ATOM 11833 CA VAL B 245 -53.694 -1.241 -18.437 1.00 38.43 C
ATOM 11835 CB VAL B 245 -53.491 -2.760 -18.614 1.00 38.31 C
ATOM 11837 CG1 VAL B 245 -53.247 -3.426 -17.283 1.00 37.77 C
ATOM 11841 CG2 VAL B 245 -52.344 -3.036 -19.561 1.00 37.66 C
ATOM 11845 C VAL B 245 -53.650 -.638 -19.832 1.00 38.68 C
ATOM 11846 O VAL B 245 -52.615 -.153 -20.247 1.00 38.57 O
ATOM 11848 N GLY B 246 -54.765 -.724 -20.559 1.00 39.26 N
ATOM 11849 CA GLY B 246 -54.974 -.012 -21.834 1.00 39.62 C
ATOM 11852 C GLY B 246 -53.962 -.262 -22.942 1.00 40.08 C
ATOM 11853 O GLY B 246 -53.617 .650 -23.700 1.00 39.89 O
ATOM 11855 N LEU B 247 -53.502 -1.500 -23.062 1.00 40.75 N
ATOM 11856 CA LEU B 247 -52.347 -1.778 -23.905 1.00 41.34 C
ATOM 11858 CB LEU B 247 -51.655 -3.065 -23.459 1.00 41.15 C
ATOM 11861 CG LEU B 247 -50.132 -3.026 -23.298 1.00 40.49 C
ATOM 11863 CD1 LEU B 247 -49.622 -1.769 -22.605 1.00 39.50 C
ATOM 11867 CD2 LEU B 247 -49.695 -4.242 -22.526 1.00 39.98 C
ATOM 11871 C LEU B 247 -52.744 -1.836 -25.370 1.00 42.50 C
ATOM 11872 O LEU B 247 -52.005 -1.358 -26.225 1.00 42.33 O
ATOM 11874 N ALA B 248 -53.925 -2.390 -25.654 1.00 44.14 N
ATOM 11875 CA ALA B 248 -54.439 -2.494 -27.041 1.00 45.16 C
ATOM 11877 CB ALA B 248 -55.705 -3.347 -27.087 1.00 45.15 C
ATOM 11881 C ALA B 248 -54.692 -1.140 -27.739 1.00 45.98 C
ATOM 11882 O ALA B 248 -54.604 -1.053 -28.971 1.00 46.37 O
ATOM 11884 N THR B 249 -55.004 -.095 -26.975 1.00 46.64 N
ATOM 11885 CA THR B 249 -55.142 1.234 -27.570 1.00 47.25 C
ATOM 11887 CB THR B 249 -55.905 2.253 -26.655 1.00 47.44 C
ATOM 11889 OG1 THR B 249 -55.001 2.845 -25.706 1.00 47.52 O
ATOM 11891 CG2 THR B 249 -57.104 1.592 -25.928 1.00 47.44 C
ATOM 11895 C THR B 249 -53.756 1.793 -27.931 1.00 47.59 C
ATOM 11896 O THR B 249 -53.553 2.279 -29.049 1.00 48.07 O

ATOM 11898 N LYS B 250 -52.808 1.710 -26.995 1.00 47.67 N
ATOM 11899 CA LYS B 250 -51.469 2.299 -27.185 1.00 47.68 C
ATOM 11901 CB LYS B 250 -50.793 2.553 -25.833 1.00 47.68 C
ATOM 11904 CG LYS B 250 -51.428 3.673 -24.999 1.00 47.77 C
ATOM 11907 CD LYS B 250 -51.142 5.086 -25.552 1.00 47.59 C
ATOM 11910 CE LYS B 250 -49.676 5.496 -25.441 1.00 46.75 C
ATOM 11913 NZ LYS B 250 -49.479 6.878 -25.948 1.00 46.49 N
ATOM 11917 C LYS B 250 -50.541 1.465 -28.082 1.00 47.72 C
ATOM 11918 O LYS B 250 -49.591 1.988 -28.663 1.00 47.54 O
ATOM 11920 N LEU B 251 -50.804 .169 -28.184 1.00 47.82 N
ATOM 11921 CA LEU B 251 -50.072 -.675 -29.118 1.00 47.96 C
ATOM 11923 CB LEU B 251 -49.584 -1.970 -28.447 1.00 48.04 C
ATOM 11926 CG LEU B 251 -48.109 -2.064 -28.033 1.00 47.39 C
ATOM 11928 CD1 LEU B 251 -47.659 -.881 -27.186 1.00 46.47 C
ATOM 11932 CD2 LEU B 251 -47.894 -3.376 -27.304 1.00 46.78 C
ATOM 11936 C LEU B 251 -50.985 -.964 -30.306 1.00 48.19 C
ATOM 11937 O LEU B 251 -51.975 -1.693 -30.194 1.00 48.38 O
ATOM 11939 N HIS B 252 -50.627 -.396 -31.449 1.00 48.42 N
ATOM 11940 CA HIS B 252 -51.521 -.329 -32.601 1.00 48.62 C
ATOM 11942 CB HIS B 252 -51.110 .850 -33.492 1.00 48.99 C
ATOM 11945 CG HIS B 252 -51.000 2.145 -32.742 1.00 50.56 C
ATOM 11946 ND1 HIS B 252 -52.095 2.935 -32.453 1.00 52.11 N
ATOM 11948 CE1 HIS B 252 -51.704 3.993 -31.766 1.00 52.68 C
ATOM 11950 NE2 HIS B 252 -50.397 3.912 -31.585 1.00 52.86 N
ATOM 11952 CD2 HIS B 252 -49.932 2.764 -32.181 1.00 51.68 C
ATOM 11954 C HIS B 252 -51.582 -1.636 -33.383 1.00 48.14 C
ATOM 11955 O HIS B 252 -52.615 -1.975 -33.935 1.00 48.02 O
ATOM 11957 N PHE B 253 -50.481 -2.372 -33.405 1.00 48.10 N
ATOM 11958 CA PHE B 253 -50.422 -3.702 -34.044 1.00 48.18 C
ATOM 11960 CB PHE B 253 -48.965 -4.070 -34.375 1.00 48.16 C
ATOM 11963 CG PHE B 253 -48.119 -4.311 -33.163 1.00 47.85 C
ATOM 11964 CD1 PHE B 253 -47.900 -5.596 -32.702 1.00 48.56 C
ATOM 11966 CE1 PHE B 253 -47.140 -5.812 -31.576 1.00 48.98 C
ATOM 11968 CZ PHE B 253 -46.602 -4.729 -30.895 1.00 48.50 C
ATOM 11970 CE2 PHE B 253 -46.817 -3.454 -31.349 1.00 47.40 C
ATOM 11972 CD2 PHE B 253 -47.569 -3.249 -32.465 1.00 47.22 C
ATOM 11974 C PHE B 253 -51.038 -4.819 -33.185 1.00 48.30 C
ATOM 11975 O PHE B 253 -51.344 -5.903 -33.691 1.00 47.63 O
ATOM 11977 N ALA B 254 -51.204 -4.541 -31.888 1.00 48.86 N
ATOM 11978 CA ALA B 254 -51.653 -5.531 -30.903 1.00 49.13 C
ATOM 11980 CB ALA B 254 -51.290 -5.071 -29.494 1.00 49.02 C
ATOM 11984 C ALA B 254 -53.153 -5.806 -30.982 1.00 49.46 C
ATOM 11985 O ALA B 254 -53.967 -4.870 -31.011 1.00 49.50 O
ATOM 11987 N ARG B 255 -53.501 -7.097 -31.006 1.00 49.75 N
ATOM 11988 CA ARG B 255 -54.896 -7.549 -30.918 1.00 49.89 C
ATOM 11990 CB ARG B 255 -55.028 -9.051 -31.245 1.00 49.94 C
ATOM 11993 CG ARG B 255 -54.839 -9.439 -32.724 1.00 49.93 C
ATOM 11996 CD ARG B 255 -54.709 -10.967 -32.904 1.00 49.79 C
ATOM 11999 NE ARG B 255 -53.527 -11.505 -32.219 1.00 50.11 N
ATOM 12001 CZ ARG B 255 -53.276 -12.801 -32.010 1.00 50.54 C
ATOM 12002 NH1 ARG B 255 -54.117 -13.736 -32.439 1.00 51.36 N
ATOM 12005 NH2 ARG B 255 -52.175 -13.172 -31.360 1.00 50.21 N
ATOM 12008 C ARG B 255 -55.425 -7.308 -29.511 1.00 49.83 C
ATOM 12009 O ARG B 255 -54.666 -6.975 -28.599 1.00 49.95 O
ATOM 12011 N ASP B 256 -56.736 -7.463 -29.350 1.00 49.72 N
ATOM 12012 CA ASP B 256 -57.360 -7.483 -28.034 1.00 49.55 C
ATOM 12014 CB ASP B 256 -58.183 -6.222 -27.812 1.00 49.52 C
ATOM 12017 CG ASP B 256 -59.134 -6.362 -26.654 1.00 50.30 C
ATOM 12018 OD1 ASP B 256 -60.310 -5.944 -26.780 1.00 50.45 O
ATOM 12019 OD2 ASP B 256 -58.702 -6.926 -25.622 1.00 51.68 O

ATOM 12020 C ASP B 256 -58.254 -8.721 -27.931 1.00 49.15 C
ATOM 12021 O ASP B 256 -59.159 -8.901 -28.737 1.00 49.28 O
ATOM 12023 N ARG B 257 -57.998 -9.565 -26.937 1.00 48.61 N
ATOM 12024 CA ARG B 257 -58.743 -10.809 -26.765 1.00 48.20 C
ATOM 12026 CB ARG B 257 -57.949 -11.984 -27.373 1.00 48.41 C
ATOM 12029 CG ARG B 257 -57.505 -11.799 -28.821 1.00 49.37 C
ATOM 12032 CD ARG B 257 -58.693 -11.636 -29.784 1.00 50.80 C
ATOM 12035 NE ARG B 257 -58.908 -12.814 -30.627 1.00 52.11 N
ATOM 12037 CZ ARG B 257 -58.678 -12.876 -31.944 1.00 52.99 C
ATOM 12038 NH1 ARG B 257 -58.214 -11.820 -32.623 1.00 52.37 N
ATOM 12041 NH2 ARG B 257 -58.918 -14.016 -32.596 1.00 52.97 N
ATOM 12044 C ARG B 257 -59.032 -11.089 -25.280 1.00 47.32 C
ATOM 12045 O ARG B 257 -58.579 -12.101 -24.735 1.00 47.46 O
ATOM 12047 N LEU B 258 -59.770 -10.201 -24.616 1.00 45.94 N
ATOM 12048 CA LEU B 258 -60.108 -10.430 -23.205 1.00 44.67 C
ATOM 12050 CB LEU B 258 -60.332 -9.130 -22.438 1.00 44.61 C
ATOM 12053 CG LEU B 258 -60.422 -9.323 -20.920 1.00 43.83 C
ATOM 12055 CD1 LEU B 258 -59.045 -9.552 -20.339 1.00 43.48 C
ATOM 12059 CD2 LEU B 258 -61.073 -8.139 -20.262 1.00 43.85 C
ATOM 12063 C LEU B 258 -61.347 -11.286 -23.090 1.00 43.49 C
ATOM 12064 O LEU B 258 -61.375 -12.220 -22.295 1.00 43.84 O
ATOM 12066 N ILE B 259 -62.364 -10.968 -23.883 1.00 41.92 N
ATOM 12067 CA ILE B 259 -63.617 -11.711 -23.841 1.00 40.80 C
ATOM 12069 CB ILE B 259 -64.718 -11.132 -24.783 1.00 41.05 C
ATOM 12071 CG1 ILE B 259 -64.852 -9.598 -24.653 1.00 41.61 C
ATOM 12074 CD1 ILE B 259 -65.200 -8.874 -25.985 1.00 42.16 C
ATOM 12078 CG2 ILE B 259 -66.065 -11.816 -24.496 1.00 40.46 C
ATOM 12082 C ILE B 259 -63.319 -13.151 -24.250 1.00 39.50 C
ATOM 12083 O ILE B 259 -63.782 -14.082 -23.598 1.00 39.30 O
ATOM 12085 N GLU B 260 -62.524 -13.318 -25.316 1.00 37.99 N
ATOM 12086 CA GLU B 260 -62.120 -14.652 -25.812 1.00 36.60 C
ATOM 12088 CB GLU B 260 -61.329 -14.574 -27.142 1.00 36.75 C
ATOM 12091 CG GLU B 260 -62.167 -14.319 -28.425 1.00 37.79 C
ATOM 12094 CD GLU B 260 -62.134 -12.851 -28.905 1.00 39.47 C
ATOM 12095 OE1 GLU B 260 -62.207 -11.923 -28.055 1.00 39.97 O
ATOM 12096 OE2 GLU B 260 -62.033 -12.628 -30.139 1.00 40.31 O
ATOM 12097 C GLU B 260 -61.282 -15.381 -24.770 1.00 34.83 C
ATOM 12098 O GLU B 260 -61.465 -16.568 -24.544 1.00 34.69 O
ATOM 12100 N SER B 261 -60.365 -14.669 -24.131 1.00 32.89 N
ATOM 12101 CA SER B 261 -59.508 -15.292 -23.139 1.00 31.48 C
ATOM 12103 CB SER B 261 -58.341 -14.376 -22.768 1.00 31.55 C
ATOM 12106 OG SER B 261 -57.298 -14.493 -23.728 1.00 31.75 O
ATOM 12108 C SER B 261 -60.294 -15.716 -21.900 1.00 30.04 C
ATOM 12109 O SER B 261 -59.921 -16.674 -21.208 1.00 29.70 O
ATOM 12111 N PHE B 262 -61.389 -15.021 -21.618 1.00 28.25 N
ATOM 12112 CA PHE B 262 -62.203 -15.404 -20.480 1.00 26.75 C
ATOM 12114 CB PHE B 262 -63.111 -14.278 -20.009 1.00 26.36 C
ATOM 12117 CG PHE B 262 -63.532 -14.453 -18.603 1.00 24.33 C
ATOM 12118 CD1 PHE B 262 -62.697 -14.092 -17.584 1.00 22.66 C
ATOM 12120 CE1 PHE B 262 -63.047 -14.283 -16.301 1.00 22.65 C
ATOM 12122 CZ PHE B 262 -64.245 -14.873 -16.007 1.00 23.93 C
ATOM 12124 CE2 PHE B 262 -65.076 -15.267 -17.010 1.00 24.08 C
ATOM 12126 CD2 PHE B 262 -64.711 -15.067 -18.304 1.00 23.96 C
ATOM 12128 C PHE B 262 -63.017 -16.660 -20.751 1.00 26.02 C
ATOM 12129 O PHE B 262 -63.074 -17.546 -19.909 1.00 26.32 O
ATOM 12131 N TYR B 263 -63.652 -16.732 -21.915 1.00 24.98 N
ATOM 12132 CA TYR B 263 -64.299 -17.969 -22.396 1.00 24.14 C
ATOM 12134 CB TYR B 263 -64.701 -17.756 -23.853 1.00 24.00 C
ATOM 12137 CG TYR B 263 -65.080 -18.961 -24.667 1.00 24.32 C
ATOM 12138 CD1 TYR B 263 -66.302 -19.604 -24.489 1.00 25.03 C

ATOM 12140 CE1 TYR B 263 -66.666 -20.694 -25.285 1.00 25.81 C
ATOM 12142 CZ TYR B 263 -65.798 -21.132 -26.287 1.00 27.06 C
ATOM 12143 OH TYR B 263 -66.106 -22.191 -27.123 1.00 27.14 O
ATOM 12145 CE2 TYR B 263 -64.590 -20.489 -26.479 1.00 26.80 C
ATOM 12147 CD2 TYR B 263 -64.250 -19.404 -25.680 1.00 25.65 C
ATOM 12149 C TYR B 263 -63.351 -19.162 -22.256 1.00 23.35 C
ATOM 12150 O TYR B 263 -63.712 -20.219 -21.740 1.00 22.80 O
ATOM 12152 N TRP B 264 -62.119 -18.955 -22.702 1.00 22.64 N
ATOM 12153 CA TRP B 264 -61.047 -19.918 -22.523 1.00 21.95 C
ATOM 12155 CB TRP B 264 -59.737 -19.334 -23.061 1.00 21.84 C
ATOM 12158 CG TRP B 264 -58.603 -20.278 -22.964 1.00 22.90 C
ATOM 12159 CD1 TRP B 264 -57.700 -20.387 -21.943 1.00 23.98 C
ATOM 12161 NE1 TRP B 264 -56.800 -21.386 -22.214 1.00 23.95 N
ATOM 12163 CE2 TRP B 264 -57.124 -21.949 -23.417 1.00 23.51 C
ATOM 12164 CD2 TRP B 264 -58.252 -21.273 -23.915 1.00 23.40 C
ATOM 12165 CE3 TRP B 264 -58.776 -21.652 -25.147 1.00 23.68 C
ATOM 12167 CZ3 TRP B 264 -58.178 -22.669 -25.826 1.00 24.44 C
ATOM 12169 CH2 TRP B 264 -57.060 -23.324 -25.310 1.00 24.97 C
ATOM 12171 CZ2 TRP B 264 -56.521 -22.978 -24.103 1.00 24.44 C
ATOM 12173 C TRP B 264 -60.897 -20.326 -21.050 1.00 21.11 C
ATOM 12174 O TRP B 264 -60.768 -21.511 -20.748 1.00 20.98 O
ATOM 12176 N ALA B 265 -60.916 -19.344 -20.147 1.00 20.17 N
ATOM 12177 CA ALA B 265 -60.774 -19.602 -18.712 1.00 19.36 C
ATOM 12179 CB ALA B 265 -60.621 -18.305 -17.944 1.00 19.30 C
ATOM 12183 C ALA B 265 -61.947 -20.397 -18.171 1.00 18.63 C
ATOM 12184 O ALA B 265 -61.763 -21.349 -17.434 1.00 18.64 O
ATOM 12186 N VAL B 266 -63.159 -20.034 -18.557 1.00 18.11 N
ATOM 12187 CA VAL B 266 -64.335 -20.758 -18.075 1.00 17.60 C
ATOM 12189 CB VAL B 266 -65.652 -20.221 -18.675 1.00 17.38 C
ATOM 12191 CG1 VAL B 266 -65.902 -18.803 -18.199 1.00 17.09 C
ATOM 12195 CG2 VAL B 266 -66.817 -21.120 -18.312 1.00 15.40 C
ATOM 12199 C VAL B 266 -64.221 -22.246 -18.376 1.00 17.67 C
ATOM 12200 O VAL B 266 -64.766 -23.058 -17.647 1.00 18.27 O
ATOM 12202 N GLY B 267 -63.516 -22.607 -19.444 1.00 17.43 N
ATOM 12203 CA GLY B 267 -63.316 -24.013 -19.789 1.00 16.98 C
ATOM 12206 C GLY B 267 -62.253 -24.683 -18.947 1.00 16.55 C
ATOM 12207 O GLY B 267 -62.360 -25.859 -18.609 1.00 16.37 O
ATOM 12209 N VAL B 268 -61.215 -23.939 -18.608 1.00 16.30 N
ATOM 12210 CA VAL B 268 -60.160 -24.500 -17.794 1.00 16.23 C
ATOM 12212 CB VAL B 268 -58.893 -23.651 -17.840 1.00 15.68 C
ATOM 12214 CG1 VAL B 268 -57.857 -24.194 -16.894 1.00 15.01 C
ATOM 12218 CG2 VAL B 268 -58.361 -23.674 -19.235 1.00 15.01 C
ATOM 12222 C VAL B 268 -60.654 -24.718 -16.374 1.00 16.86 C
ATOM 12223 O VAL B 268 -60.421 -25.784 -15.813 1.00 16.93 O
ATOM 12225 N ALA B 269 -61.362 -23.733 -15.817 1.00 17.64 N
ATOM 12226 CA ALA B 269 -61.911 -23.838 -14.461 1.00 18.46 C
ATOM 12228 CB ALA B 269 -60.958 -23.215 -13.472 1.00 18.15 C
ATOM 12232 C ALA B 269 -63.312 -23.213 -14.340 1.00 19.34 C
ATOM 12233 O ALA B 269 -63.448 -22.030 -14.047 1.00 19.78 O
ATOM 12235 N PHE B 270 -64.347 -24.028 -14.529 1.00 20.34 N
ATOM 12236 CA PHE B 270 -65.724 -23.535 -14.631 1.00 21.21 C
ATOM 12238 CB PHE B 270 -66.564 -24.483 -15.482 1.00 21.34 C
ATOM 12241 CG PHE B 270 -67.083 -25.667 -14.718 1.00 22.46 C
ATOM 12242 CD1 PHE B 270 -68.294 -25.596 -14.039 1.00 23.19 C
ATOM 12244 CE1 PHE B 270 -68.756 -26.672 -13.315 1.00 23.27 C
ATOM 12246 CZ PHE B 270 -68.003 -27.836 -13.258 1.00 23.35 C
ATOM 12248 CE2 PHE B 270 -66.794 -27.918 -13.932 1.00 22.73 C
ATOM 12250 CD2 PHE B 270 -66.340 -26.843 -14.646 1.00 22.88 C
ATOM 12252 C PHE B 270 -66.464 -23.366 -13.316 1.00 21.98 C
ATOM 12253 O PHE B 270 -67.408 -22.583 -13.268 1.00 21.93 O

ATOM 12255 N GLU B 271 -66.102 -24.126 -12.275 1.00 23.01 N
ATOM 12256 CA GLU B 271 -66.929 -24.142 -11.037 1.00 23.99 C
ATOM 12258 CB GLU B 271 -66.679 -25.353 -10.113 1.00 24.25 C
ATOM 12261 CG GLU B 271 -65.286 -25.877 -10.092 1.00 26.22 C
ATOM 12264 CD GLU B 271 -65.013 -26.914 -11.183 1.00 29.01 C
ATOM 12265 OE1 GLU B 271 -65.563 -28.032 -11.090 1.00 31.36 O
ATOM 12266 OE2 GLU B 271 -64.232 -26.622 -12.121 1.00 30.98 O
ATOM 12267 C GLU B 271 -66.795 -22.831 -10.281 1.00 23.90 C
ATOM 12268 O GLU B 271 -65.702 -22.296 -10.181 1.00 24.29 O
ATOM 12270 N PRO B 272 -67.913 -22.316 -9.745 1.00 24.09 N
ATOM 12271 CA PRO B 272 -68.005 -20.885 -9.428 1.00 24.11 C
ATOM 12273 CB PRO B 272 -69.380 -20.751 -8.751 1.00 24.03 C
ATOM 12276 CG PRO B 272 -70.083 -22.069 -8.997 1.00 24.12 C
ATOM 12279 CD PRO B 272 -69.013 -23.083 -9.132 1.00 23.99 C
ATOM 12282 C PRO B 272 -66.900 -20.386 -8.501 1.00 24.28 C
ATOM 12283 O PRO B 272 -66.421 -19.261 -8.676 1.00 24.40 O
ATOM 12284 N GLN B 273 -66.480 -21.222 -7.547 1.00 24.20 N
ATOM 12285 CA GLN B 273 -65.500 -20.809 -6.551 1.00 24.20 C
ATOM 12287 CB GLN B 273 -65.437 -21.840 -5.426 1.00 24.42 C
ATOM 12290 CG GLN B 273 -64.750 -23.176 -5.775 1.00 25.17 C
ATOM 12293 CD GLN B 273 -65.717 -24.334 -6.007 1.00 26.13 C
ATOM 12294 OE1 GLN B 273 -66.857 -24.141 -6.453 1.00 27.46 O
ATOM 12295 NE2 GLN B 273 -65.251 -25.554 -5.721 1.00 25.05 N
ATOM 12298 C GLN B 273 -64.086 -20.546 -7.088 1.00 24.27 C
ATOM 12299 O GLN B 273 -63.221 -20.151 -6.329 1.00 24.32 O
ATOM 12301 N TYR B 274 -63.842 -20.759 -8.380 1.00 24.59 N
ATOM 12302 CA TYR B 274 -62.509 -20.551 -8.962 1.00 24.85 C
ATOM 12304 CB TYR B 274 -62.129 -21.724 -9.880 1.00 24.62 C
ATOM 12307 CG TYR B 274 -62.009 -23.054 -9.184 1.00 24.35 C
ATOM 12308 CD1 TYR B 274 -61.395 -23.169 -7.946 1.00 24.62 C
ATOM 12310 CE1 TYR B 274 -61.280 -24.391 -7.314 1.00 25.10 C
ATOM 12312 CZ TYR B 274 -61.771 -25.525 -7.920 1.00 24.92 C
ATOM 12313 OH TYR B 274 -61.661 -26.748 -7.299 1.00 24.73 O
ATOM 12315 CE2 TYR B 274 -62.366 -25.437 -9.150 1.00 24.76 C
ATOM 12317 CD2 TYR B 274 -62.477 -24.203 -9.779 1.00 24.70 C
ATOM 12319 C TYR B 274 -62.409 -19.235 -9.745 1.00 25.27 C
ATOM 12320 O TYR B 274 -61.956 -19.210 -10.895 1.00 25.42 O
ATOM 12322 N SER B 275 -62.808 -18.134 -9.121 1.00 25.40 N
ATOM 12323 CA SER B 275 -62.755 -16.849 -9.802 1.00 25.43 C
ATOM 12325 CB SER B 275 -63.615 -15.814 -9.071 1.00 25.53 C
ATOM 12328 OG SER B 275 -65.006 -16.068 -9.291 1.00 25.52 O
ATOM 12330 C SER B 275 -61.300 -16.403 -9.948 1.00 25.36 C
ATOM 12331 O SER B 275 -60.885 -15.903 -10.996 1.00 25.17 O
ATOM 12333 N ASP B 276 -60.517 -16.617 -8.901 1.00 25.41 N
ATOM 12334 CA ASP B 276 -59.095 -16.353 -8.979 1.00 25.42 C
ATOM 12336 CB ASP B 276 -58.390 -16.794 -7.712 1.00 25.44 C
ATOM 12339 CG ASP B 276 -58.728 -15.925 -6.558 1.00 26.32 C
ATOM 12340 OD1 ASP B 276 -59.302 -14.857 -6.818 1.00 27.50 O
ATOM 12341 OD2 ASP B 276 -58.442 -16.299 -5.398 1.00 30.16 O
ATOM 12342 C ASP B 276 -58.495 -17.069 -10.157 1.00 25.20 C
ATOM 12343 O ASP B 276 -57.745 -16.461 -10.929 1.00 25.66 O
ATOM 12345 N CYS B 277 -58.814 -18.353 -10.305 1.00 24.60 N
ATOM 12346 CA CYS B 277 -58.228 -19.110 -11.391 1.00 24.30 C
ATOM 12348 CB CYS B 277 -58.684 -20.561 -11.392 1.00 24.28 C
ATOM 12351 SG CYS B 277 -57.737 -21.574 -12.569 1.00 23.82 S
ATOM 12353 C CYS B 277 -58.593 -18.448 -12.698 1.00 24.09 C
ATOM 12354 O CYS B 277 -57.727 -18.013 -13.450 1.00 23.87 O
ATOM 12356 N ARG B 278 -59.893 -18.329 -12.933 1.00 24.22 N
ATOM 12357 CA ARG B 278 -60.400 -17.746 -14.171 1.00 23.98 C
ATOM 12359 CB ARG B 278 -61.917 -17.556 -14.123 1.00 23.93 C

ATOM 12362 CG ARG B 278 -62.662 -18.871 -14.283 1.00 24.07 C
ATOM 12365 CD ARG B 278 -64.132 -18.670 -14.607 1.00 24.48 C
ATOM 12368 NE ARG B 278 -64.874 -18.141 -13.472 1.00 23.75 N
ATOM 12370 CZ ARG B 278 -65.254 -18.856 -12.419 1.00 23.72 C
ATOM 12371 NH1 ARG B 278 -64.973 -20.149 -12.326 1.00 22.86 N
ATOM 12374 NH2 ARG B 278 -65.927 -18.262 -11.443 1.00 25.08 N
ATOM 12377 C ARG B 278 -59.701 -16.453 -14.491 1.00 23.56 C
ATOM 12378 O ARG B 278 -59.296 -16.265 -15.628 1.00 23.87 O
ATOM 12380 N ASN B 279 -59.512 -15.593 -13.495 1.00 23.24 N
ATOM 12381 CA ASN B 279 -58.854 -14.301 -13.734 1.00 23.48 C
ATOM 12383 CB ASN B 279 -59.055 -13.340 -12.574 1.00 24.05 C
ATOM 12386 CG ASN B 279 -60.510 -13.017 -12.346 1.00 26.58 C
ATOM 12387 OD1 ASN B 279 -61.378 -13.310 -13.189 1.00 28.96 O
ATOM 12388 ND2 ASN B 279 -60.799 -12.416 -11.194 1.00 30.30 N
ATOM 12391 C ASN B 279 -57.376 -14.404 -14.027 1.00 22.58 C
ATOM 12392 O ASN B 279 -56.903 -13.749 -14.941 1.00 22.73 O
ATOM 12394 N SER B 280 -56.648 -15.205 -13.251 1.00 21.62 N
ATOM 12395 CA SER B 280 -55.243 -15.483 -13.550 1.00 20.73 C
ATOM 12397 CB SER B 280 -54.696 -16.597 -12.659 1.00 20.85 C
ATOM 12400 OG SER B 280 -53.805 -16.099 -11.683 1.00 21.55 O
ATOM 12402 C SER B 280 -55.091 -15.896 -15.004 1.00 20.04 C
ATOM 12403 O SER B 280 -54.293 -15.312 -15.738 1.00 19.87 O
ATOM 12405 N VAL B 281 -55.875 -16.893 -15.413 1.00 19.24 N
ATOM 12406 CA VAL B 281 -55.720 -17.491 -16.720 1.00 18.77 C
ATOM 12408 CB VAL B 281 -56.482 -18.834 -16.815 1.00 18.74 C
ATOM 12410 CG1 VAL B 281 -56.467 -19.404 -18.251 1.00 18.34 C
ATOM 12414 CG2 VAL B 281 -55.863 -19.844 -15.848 1.00 18.13 C
ATOM 12418 C VAL B 281 -56.142 -16.486 -17.787 1.00 18.89 C
ATOM 12419 O VAL B 281 -55.483 -16.364 -18.832 1.00 18.75 O
ATOM 12421 N ALA B 282 -57.210 -15.739 -17.505 1.00 18.85 N
ATOM 12422 CA ALA B 282 -57.709 -14.723 -18.439 1.00 18.80 C
ATOM 12424 CB ALA B 282 -59.051 -14.191 -17.991 1.00 18.32 C
ATOM 12428 C ALA B 282 -56.718 -13.576 -18.615 1.00 18.94 C
ATOM 12429 O ALA B 282 -56.582 -13.021 -19.700 1.00 19.16 O
ATOM 12431 N LYS B 283 -56.022 -13.211 -17.553 1.00 19.24 N
ATOM 12432 CA LYS B 283 -55.037 -12.145 -17.658 1.00 19.62 C
ATOM 12434 CB LYS B 283 -54.649 -11.615 -16.276 1.00 19.68 C
ATOM 12437 CG LYS B 283 -55.779 -10.923 -15.518 1.00 19.95 C
ATOM 12440 CD LYS B 283 -55.265 -10.398 -14.196 1.00 21.72 C
ATOM 12443 CE LYS B 283 -56.364 -10.236 -13.164 1.00 23.83 C
ATOM 12446 NZ LYS B 283 -56.129 -9.003 -12.351 1.00 24.72 N
ATOM 12450 C LYS B 283 -53.802 -12.643 -18.396 1.00 19.77 C
ATOM 12451 O LYS B 283 -53.237 -11.929 -19.208 1.00 20.05 O
ATOM 12453 N MET B 284 -53.387 -13.871 -18.117 1.00 19.88 N
ATOM 12454 CA MET B 284 -52.136 -14.367 -18.652 1.00 19.90 C
ATOM 12456 CB MET B 284 -51.719 -15.676 -17.960 1.00 20.08 C
ATOM 12459 CG MET B 284 -51.125 -15.505 -16.560 1.00 20.62 C
ATOM 12462 SD MET B 284 -49.782 -14.295 -16.485 1.00 23.69 S
ATOM 12463 CE MET B 284 -50.600 -12.872 -15.754 1.00 23.82 C
ATOM 12467 C MET B 284 -52.257 -14.572 -20.145 1.00 19.82 C
ATOM 12468 O MET B 284 -51.326 -14.269 -20.889 1.00 20.21 O
ATOM 12470 N PHE B 285 -53.401 -15.088 -20.579 1.00 19.72 N
ATOM 12471 CA PHE B 285 -53.620 -15.428 -21.986 1.00 19.66 C
ATOM 12473 CB PHE B 285 -54.863 -16.324 -22.114 1.00 20.09 C
ATOM 12476 CG PHE B 285 -54.986 -17.077 -23.427 1.00 21.18 C
ATOM 12477 CD1 PHE B 285 -53.877 -17.362 -24.232 1.00 22.86 C
ATOM 12479 CE1 PHE B 285 -54.013 -18.070 -25.424 1.00 22.58 C
ATOM 12481 CZ PHE B 285 -55.254 -18.518 -25.806 1.00 23.49 C
ATOM 12483 CE2 PHE B 285 -56.365 -18.254 -25.002 1.00 23.36 C
ATOM 12485 CD2 PHE B 285 -56.222 -17.551 -23.823 1.00 21.76 C

ATOM 12487 C PHE B 285 -53.781 -14.148 -22.781 1.00 19.18 C
ATOM 12488 O PHE B 285 -53.333 -14.046 -23.914 1.00 18.98 O
ATOM 12490 N SER B 286 -54.410 -13.161 -22.164 1.00 18.92 N
ATOM 12491 CA SER B 286 -54.488 -11.843 -22.753 1.00 19.15 C
ATOM 12493 CB SER B 286 -55.292 -10.894 -21.863 1.00 19.38 C
ATOM 12496 OG SER B 286 -56.684 -11.180 -21.957 1.00 20.24 O
ATOM 12498 C SER B 286 -53.106 -11.267 -23.032 1.00 18.91 C
ATOM 12499 O SER B 286 -52.894 -10.668 -24.087 1.00 19.48 O
ATOM 12501 N PHE B 287 -52.172 -11.446 -22.102 1.00 18.48 N
ATOM 12502 CA PHE B 287 -50.768 -11.065 -22.339 1.00 18.30 C
ATOM 12504 CB PHE B 287 -49.958 -11.035 -21.044 1.00 18.27 C
ATOM 12507 CG PHE B 287 -50.040 -9.740 -20.324 1.00 18.59 C
ATOM 12508 CD1 PHE B 287 -49.375 -8.624 -20.813 1.00 20.02 C
ATOM 12510 CE1 PHE B 287 -49.456 -7.410 -20.152 1.00 20.57 C
ATOM 12512 CZ PHE B 287 -50.208 -7.308 -18.985 1.00 20.02 C
ATOM 12514 CE2 PHE B 287 -50.869 -8.417 -18.503 1.00 19.78 C
ATOM 12516 CD2 PHE B 287 -50.781 -9.623 -19.164 1.00 19.05 C
ATOM 12518 C PHE B 287 -50.067 -11.978 -23.339 1.00 18.01 C
ATOM 12519 O PHE B 287 -49.374 -11.498 -24.229 1.00 18.00 O
ATOM 12521 N VAL B 288 -50.236 -13.286 -23.194 1.00 17.69 N
ATOM 12522 CA VAL B 288 -49.720 -14.206 -24.197 1.00 17.66 C
ATOM 12524 CB VAL B 288 -50.168 -15.649 -23.930 1.00 17.37 C
ATOM 12526 CG1 VAL B 288 -49.937 -16.529 -25.134 1.00 16.24 C
ATOM 12530 CG2 VAL B 288 -49.414 -16.185 -22.758 1.00 17.21 C
ATOM 12534 C VAL B 288 -50.081 -13.761 -25.633 1.00 18.08 C
ATOM 12535 O VAL B 288 -49.207 -13.710 -26.492 1.00 18.08 O
ATOM 12537 N THR B 289 -51.327 -13.396 -25.895 1.00 18.42 N
ATOM 12538 CA THR B 289 -51.683 -13.001 -27.256 1.00 19.33 C
ATOM 12540 CB THR B 289 -53.171 -12.736 -27.401 1.00 19.35 C
ATOM 12542 OG1 THR B 289 -53.573 -11.895 -26.321 1.00 21.59 O
ATOM 12544 CG2 THR B 289 -53.973 -14.046 -27.350 1.00 19.09 C
ATOM 12548 C THR B 289 -50.901 -11.766 -27.723 1.00 19.71 C
ATOM 12549 O THR B 289 -50.469 -11.707 -28.891 1.00 19.88 O
ATOM 12551 N ILE B 290 -50.689 -10.796 -26.829 1.00 19.94 N
ATOM 12552 CA ILE B 290 -49.943 -9.585 -27.225 1.00 20.39 C
ATOM 12554 CB ILE B 290 -50.069 -8.410 -26.221 1.00 20.50 C
ATOM 12556 CG1 ILE B 290 -51.510 -8.137 -25.823 1.00 21.25 C
ATOM 12559 CD1 ILE B 290 -51.650 -6.854 -25.002 1.00 21.58 C
ATOM 12563 CG2 ILE B 290 -49.546 -7.134 -26.853 1.00 20.39 C
ATOM 12567 C ILE B 290 -48.434 -9.840 -27.438 1.00 20.45 C
ATOM 12568 O ILE B 290 -47.853 -9.317 -28.393 1.00 20.76 O
ATOM 12570 N ILE B 291 -47.808 -10.616 -26.546 1.00 20.21 N
ATOM 12571 CA ILE B 291 -46.375 -10.869 -26.618 1.00 19.87 C
ATOM 12573 CB ILE B 291 -45.840 -11.603 -25.407 1.00 19.79 C
ATOM 12575 CG1 ILE B 291 -46.205 -10.879 -24.102 1.00 19.71 C
ATOM 12578 CD1 ILE B 291 -45.326 -9.734 -23.748 1.00 19.77 C
ATOM 12582 CG2 ILE B 291 -44.336 -11.747 -25.516 1.00 18.91 C
ATOM 12586 C ILE B 291 -46.134 -11.735 -27.825 1.00 20.44 C
ATOM 12587 O ILE B 291 -45.233 -11.481 -28.600 1.00 20.35 O
ATOM 12589 N ASP B 292 -46.965 -12.751 -28.005 1.00 21.33 N
ATOM 12590 CA ASP B 292 -46.915 -13.563 -29.228 1.00 22.13 C
ATOM 12592 CB ASP B 292 -48.120 -14.508 -29.316 1.00 22.40 C
ATOM 12595 CG ASP B 292 -47.847 -15.741 -30.160 1.00 23.47 C
ATOM 12596 OD1 ASP B 292 -46.852 -15.765 -30.923 1.00 24.83 O
ATOM 12597 OD2 ASP B 292 -48.637 -16.707 -30.038 1.00 25.22 O
ATOM 12598 C ASP B 292 -46.856 -12.716 -30.507 1.00 22.28 C
ATOM 12599 O ASP B 292 -46.088 -13.033 -31.399 1.00 22.73 O
ATOM 12601 N ASP B 293 -47.656 -11.658 -30.611 1.00 22.22 N
ATOM 12602 CA ASP B 293 -47.630 -10.828 -31.822 1.00 22.43 C
ATOM 12604 CB ASP B 293 -48.840 -9.894 -31.885 1.00 23.03 C

ATOM 12607 CG ASP B 293 -50.157 -10.644 -31.959 1.00 24.69 C
ATOM 12608 OD1 ASP B 293 -50.113 -11.900 -32.025 1.00 28.66 O
ATOM 12609 OD2 ASP B 293 -51.231 -9.986 -31.930 1.00 23.57 O
ATOM 12610 C ASP B 293 -46.354 -9.997 -31.921 1.00 21.94 C
ATOM 12611 O ASP B 293 -45.898 -9.674 -33.019 1.00 22.31 O
ATOM 12613 N ILE B 294 -45.783 -9.643 -30.780 1.00 21.05 N
ATOM 12614 CA ILE B 294 -44.513 -8.941 -30.770 1.00 20.53 C
ATOM 12616 CB ILE B 294 -44.166 -8.448 -29.344 1.00 20.42 C
ATOM 12618 CG1 ILE B 294 -45.150 -7.349 -28.945 1.00 19.66 C
ATOM 12621 CD1 ILE B 294 -45.057 -6.956 -27.536 1.00 18.81 C
ATOM 12625 CG2 ILE B 294 -42.726 -7.924 -29.253 1.00 19.99 C
ATOM 12629 C ILE B 294 -43.416 -9.845 -31.343 1.00 20.44 C
ATOM 12630 O ILE B 294 -42.650 -9.431 -32.205 1.00 20.17 O
ATOM 12632 N TYR B 295 -43.355 -11.088 -30.886 1.00 20.65 N
ATOM 12633 CA TYR B 295 -42.313 -12.008 -31.353 1.00 20.76 C
ATOM 12635 CB TYR B 295 -42.145 -13.198 -30.412 1.00 20.29 C
ATOM 12638 CG TYR B 295 -41.393 -12.926 -29.129 1.00 17.92 C
ATOM 12639 CD1 TYR B 295 -40.117 -13.409 -28.936 1.00 17.62 C
ATOM 12641 CE1 TYR B 295 -39.427 -13.195 -27.747 1.00 17.12 C
ATOM 12643 CZ TYR B 295 -40.022 -12.493 -26.730 1.00 16.61 C
ATOM 12644 OH TYR B 295 -39.357 -12.281 -25.528 1.00 14.46 O
ATOM 12646 CE2 TYR B 295 -41.296 -12.008 -26.911 1.00 16.82 C
ATOM 12648 CD2 TYR B 295 -41.972 -12.235 -28.102 1.00 16.39 C
ATOM 12650 C TYR B 295 -42.619 -12.519 -32.749 1.00 21.65 C
ATOM 12651 O TYR B 295 -41.698 -12.751 -33.540 1.00 22.13 O
ATOM 12653 N ASP B 296 -43.905 -12.677 -33.049 1.00 22.47 N
ATOM 12654 CA ASP B 296 -44.327 -13.316 -34.285 1.00 23.52 C
ATOM 12656 CB ASP B 296 -45.761 -13.851 -34.185 1.00 23.99 C
ATOM 12659 CG ASP B 296 -46.134 -14.744 -35.369 1.00 26.22 C
ATOM 12660 OD1 ASP B 296 -45.508 -15.832 -35.538 1.00 27.70 O
ATOM 12661 OD2 ASP B 296 -47.052 -14.348 -36.128 1.00 28.78 O
ATOM 12662 C ASP B 296 -44.228 -12.392 -35.478 1.00 23.68 C
ATOM 12663 O ASP B 296 -43.673 -12.784 -36.502 1.00 24.01 O
ATOM 12665 N VAL B 297 -44.765 -11.178 -35.364 1.00 23.90 N
ATOM 12666 CA VAL B 297 -44.801 -10.273 -36.524 1.00 23.99 C
ATOM 12668 CB VAL B 297 -46.251 -10.003 -36.973 1.00 23.87 C
ATOM 12670 CG1 VAL B 297 -46.949 -11.310 -37.197 1.00 23.75 C
ATOM 12674 CG2 VAL B 297 -47.002 -9.136 -35.966 1.00 23.05 C
ATOM 12678 C VAL B 297 -44.060 -8.940 -36.383 1.00 24.27 C
ATOM 12679 O VAL B 297 -43.485 -8.465 -37.342 1.00 23.84 O
ATOM 12681 N TYR B 298 -44.058 -8.347 -35.199 1.00 24.87 N
ATOM 12682 CA TYR B 298 -43.760 -6.926 -35.078 1.00 25.67 C
ATOM 12684 CB TYR B 298 -44.656 -6.294 -34.010 1.00 26.06 C
ATOM 12687 CG TYR B 298 -44.520 -4.789 -33.932 1.00 27.95 C
ATOM 12688 CD1 TYR B 298 -45.097 -3.968 -34.901 1.00 29.74 C
ATOM 12690 CE1 TYR B 298 -44.982 -2.574 -34.843 1.00 29.93 C
ATOM 12692 CZ TYR B 298 -44.282 -1.991 -33.806 1.00 29.96 C
ATOM 12693 OH TYR B 298 -44.165 -.631 -33.746 1.00 30.01 O
ATOM 12695 CE2 TYR B 298 -43.697 -2.777 -32.829 1.00 30.39 C
ATOM 12697 CD2 TYR B 298 -43.811 -4.181 -32.899 1.00 29.96 C
ATOM 12699 C TYR B 298 -42.318 -6.592 -34.755 1.00 25.76 C
ATOM 12700 O TYR B 298 -41.696 -5.830 -35.470 1.00 26.54 O
ATOM 12702 N GLY B 299 -41.798 -7.111 -33.653 1.00 25.89 N
ATOM 12703 CA GLY B 299 -40.473 -6.706 -33.167 1.00 25.78 C
ATOM 12706 C GLY B 299 -39.346 -7.341 -33.951 1.00 25.52 C
ATOM 12707 O GLY B 299 -39.513 -8.410 -34.525 1.00 26.04 O
ATOM 12709 N THR B 300 -38.196 -6.685 -33.990 1.00 25.32 N
ATOM 12710 CA THR B 300 -37.063 -7.237 -34.716 1.00 25.16 C
ATOM 12712 CB THR B 300 -36.088 -6.164 -35.295 1.00 25.08 C
ATOM 12714 OG1 THR B 300 -35.191 -5.710 -34.281 1.00 25.07 O

ATOM 12716 CG2 THR B 300 -36.833 -4.978 -35.875 1.00 25.08 C
ATOM 12720 C THR B 300 -36.324 -8.139 -33.771 1.00 25.13 C
ATOM 12721 O THR B 300 -36.335 -7.950 -32.570 1.00 25.28 O
ATOM 12723 N LEU B 301 -35.662 -9.129 -34.332 1.00 25.50 N
ATOM 12724 CA LEU B 301 -34.918 -10.093 -33.538 1.00 25.42 C
ATOM 12726 CB LEU B 301 -34.148 -11.020 -34.479 1.00 25.17 C
ATOM 12729 CG LEU B 301 -33.624 -12.338 -33.941 1.00 24.95 C
ATOM 12731 CD1 LEU B 301 -34.715 -13.233 -33.437 1.00 24.42 C
ATOM 12735 CD2 LEU B 301 -32.900 -12.998 -35.080 1.00 26.50 C
ATOM 12739 C LEU B 301 -33.995 -9.425 -32.485 1.00 25.54 C
ATOM 12740 O LEU B 301 -33.843 -9.959 -31.394 1.00 25.35 O
ATOM 12742 N ASP B 302 -33.417 -8.257 -32.782 1.00 25.68 N
ATOM 12743 CA ASP B 302 -32.598 -7.550 -31.774 1.00 26.02 C
ATOM 12745 CB ASP B 302 -31.800 -6.377 -32.378 1.00 26.37 C
ATOM 12748 CG ASP B 302 -30.563 -6.833 -33.167 1.00 28.27 C
ATOM 12749 OD1 ASP B 302 -29.508 -6.156 -33.048 1.00 29.05 O
ATOM 12750 OD2 ASP B 302 -30.652 -7.852 -33.910 1.00 31.04 O
ATOM 12751 C ASP B 302 -33.472 -7.037 -30.630 1.00 25.69 C
ATOM 12752 O ASP B 302 -33.110 -7.142 -29.447 1.00 25.90 O
ATOM 12754 N GLU B 303 -34.622 -6.473 -30.993 1.00 25.04 N
ATOM 12755 CA GLU B 303 -35.600 -6.029 -30.011 1.00 24.33 C
ATOM 12757 CB GLU B 303 -36.783 -5.346 -30.697 1.00 24.20 C
ATOM 12760 CG GLU B 303 -36.399 -4.109 -31.466 1.00 24.23 C
ATOM 12763 CD GLU B 303 -37.589 -3.382 -32.063 1.00 24.23 C
ATOM 12764 OE1 GLU B 303 -38.496 -4.065 -32.604 1.00 22.66 O
ATOM 12765 OE2 GLU B 303 -37.592 -2.121 -31.995 1.00 23.93 O
ATOM 12766 C GLU B 303 -36.103 -7.212 -29.193 1.00 23.87 C
ATOM 12767 O GLU B 303 -36.396 -7.058 -28.011 1.00 23.59 O
ATOM 12769 N LEU B 304 -36.204 -8.383 -29.825 1.00 23.39 N
ATOM 12770 CA LEU B 304 -36.766 -9.570 -29.166 1.00 23.23 C
ATOM 12772 CB LEU B 304 -37.180 -10.624 -30.208 1.00 22.83 C
ATOM 12775 CG LEU B 304 -38.381 -10.217 -31.074 1.00 22.06 C
ATOM 12777 CD1 LEU B 304 -38.822 -11.321 -32.037 1.00 20.11 C
ATOM 12781 CD2 LEU B 304 -39.551 -9.800 -30.163 1.00 21.94 C
ATOM 12785 C LEU B 304 -35.810 -10.147 -28.106 1.00 23.37 C
ATOM 12786 O LEU B 304 -36.248 -10.785 -27.141 1.00 23.22 O
ATOM 12788 N GLU B 305 -34.514 -9.892 -28.283 1.00 23.30 N
ATOM 12789 CA GLU B 305 -33.512 -10.308 -27.324 1.00 23.18 C
ATOM 12791 CB GLU B 305 -32.114 -10.176 -27.899 1.00 23.58 C
ATOM 12794 CG GLU B 305 -31.832 -11.142 -29.047 1.00 25.27 C
ATOM 12797 CD GLU B 305 -31.306 -12.488 -28.585 1.00 27.91 C
ATOM 12798 OE1 GLU B 305 -30.946 -13.303 -29.470 1.00 29.87 O
ATOM 12799 OE2 GLU B 305 -31.244 -12.728 -27.351 1.00 29.28 O
ATOM 12800 C GLU B 305 -33.633 -9.440 -26.104 1.00 22.52 C
ATOM 12801 O GLU B 305 -33.793 -9.956 -25.005 1.00 23.39 O
ATOM 12803 N LEU B 306 -33.576 -8.124 -26.274 1.00 21.51 N
ATOM 12804 CA LEU B 306 -33.715 -7.224 -25.114 1.00 20.70 C
ATOM 12806 CB LEU B 306 -33.899 -5.764 -25.544 1.00 20.59 C
ATOM 12809 CG LEU B 306 -32.769 -5.065 -26.293 1.00 20.12 C
ATOM 12811 CD1 LEU B 306 -32.992 -3.576 -26.203 1.00 19.89 C
ATOM 12815 CD2 LEU B 306 -31.402 -5.437 -25.739 1.00 19.81 C
ATOM 12819 C LEU B 306 -34.896 -7.645 -24.237 1.00 19.91 C
ATOM 12820 O LEU B 306 -34.771 -7.778 -23.031 1.00 19.53 O
ATOM 12822 N PHE B 307 -36.030 -7.883 -24.872 1.00 19.48 N
ATOM 12823 CA PHE B 307 -37.231 -8.267 -24.170 1.00 19.36 C
ATOM 12825 CB PHE B 307 -38.400 -8.406 -25.138 1.00 19.54 C
ATOM 12828 CG PHE B 307 -39.729 -8.296 -24.482 1.00 19.66 C
ATOM 12829 CD1 PHE B 307 -40.365 -7.079 -24.400 1.00 21.03 C
ATOM 12831 CE1 PHE B 307 -41.590 -6.968 -23.787 1.00 21.62 C
ATOM 12833 CZ PHE B 307 -42.182 -8.072 -23.248 1.00 20.25 C

ATOM 12835 CE2 PHE B 307 -41.553 -9.292 -23.329 1.00 20.07 C
ATOM 12837 CD2 PHE B 307 -40.338 -9.400 -23.939 1.00 19.62 C
ATOM 12839 C PHE B 307 -37.039 -9.577 -23.443 1.00 19.22 C
ATOM 12840 O PHE B 307 -37.354 -9.684 -22.260 1.00 19.50 O
ATOM 12842 N THR B 308 -36.532 -10.583 -24.143 1.00 18.96 N
ATOM 12843 CA THR B 308 -36.321 -11.874 -23.511 1.00 18.84 C
ATOM 12845 CB THR B 308 -35.774 -12.879 -24.490 1.00 18.62 C
ATOM 12847 OG1 THR B 308 -36.687 -12.988 -25.579 1.00 18.88 O
ATOM 12849 CG2 THR B 308 -35.626 -14.228 -23.833 1.00 18.74 C
ATOM 12853 C THR B 308 -35.384 -11.737 -22.317 1.00 19.04 C
ATOM 12854 O THR B 308 -35.686 -12.244 -21.233 1.00 18.69 O
ATOM 12856 N ASP B 309 -34.264 -11.031 -22.511 1.00 19.36 N
ATOM 12857 CA ASP B 309 -33.335 -10.751 -21.421 1.00 19.65 C
ATOM 12859 CB ASP B 309 -32.121 -9.983 -21.942 1.00 19.92 C
ATOM 12862 CG ASP B 309 -31.171 -9.536 -20.814 1.00 23.51 C
ATOM 12863 OD1 ASP B 309 -30.520 -10.412 -20.175 1.00 27.27 O
ATOM 12864 OD2 ASP B 309 -31.076 -8.299 -20.561 1.00 27.40 O
ATOM 12865 C ASP B 309 -34.048 -9.977 -20.295 1.00 19.08 C
ATOM 12866 O ASP B 309 -33.912 -10.308 -19.124 1.00 18.55 O
ATOM 12868 N ALA B 310 -34.836 -8.975 -20.665 1.00 18.93 N
ATOM 12869 CA ALA B 310 -35.546 -8.151 -19.688 1.00 19.12 C
ATOM 12871 CB ALA B 310 -36.346 -7.062 -20.380 1.00 18.79 C
ATOM 12875 C ALA B 310 -36.462 -8.965 -18.784 1.00 19.36 C
ATOM 12876 O ALA B 310 -36.560 -8.696 -17.577 1.00 19.58 O
ATOM 12878 N VAL B 311 -37.143 -9.942 -19.370 1.00 19.61 N
ATOM 12879 CA VAL B 311 -37.996 -10.845 -18.611 1.00 19.68 C
ATOM 12881 CB VAL B 311 -38.867 -11.682 -19.555 1.00 19.46 C
ATOM 12883 CG1 VAL B 311 -39.948 -10.825 -20.123 1.00 18.49 C
ATOM 12887 CG2 VAL B 311 -39.469 -12.863 -18.843 1.00 19.31 C
ATOM 12891 C VAL B 311 -37.161 -11.726 -17.673 1.00 20.46 C
ATOM 12892 O VAL B 311 -37.479 -11.843 -16.494 1.00 20.25 O
ATOM 12894 N GLU B 312 -36.085 -12.317 -18.189 1.00 21.67 N
ATOM 12895 CA GLU B 312 -35.198 -13.168 -17.384 1.00 22.65 C
ATOM 12897 CB GLU B 312 -34.056 -13.708 -18.239 1.00 23.03 C
ATOM 12900 CG GLU B 312 -34.454 -14.764 -19.261 1.00 24.88 C
ATOM 12903 CD GLU B 312 -33.335 -15.077 -20.267 1.00 27.34 C
ATOM 12904 OE1 GLU B 312 -33.485 -16.057 -21.028 1.00 29.07 O
ATOM 12905 OE2 GLU B 312 -32.316 -14.342 -20.313 1.00 28.63 O
ATOM 12906 C GLU B 312 -34.598 -12.443 -16.167 1.00 23.09 C
ATOM 12907 O GLU B 312 -34.506 -13.007 -15.082 1.00 23.04 O
ATOM 12909 N ARG B 313 -34.186 -11.199 -16.335 1.00 23.67 N
ATOM 12910 CA ARG B 313 -33.590 -10.486 -15.222 1.00 24.60 C
ATOM 12912 CB ARG B 313 -32.609 -9.436 -15.735 1.00 25.26 C
ATOM 12915 CG ARG B 313 -31.333 -10.030 -16.398 1.00 27.83 C
ATOM 12918 CD ARG B 313 -30.289 -8.943 -16.754 1.00 31.87 C
ATOM 12921 NE ARG B 313 -30.922 -7.793 -17.430 1.00 35.71 N
ATOM 12923 CZ ARG B 313 -31.341 -6.661 -16.837 1.00 38.42 C
ATOM 12924 NH1 ARG B 313 -31.189 -6.452 -15.522 1.00 39.15 N
ATOM 12927 NH2 ARG B 313 -31.919 -5.711 -17.576 1.00 39.25 N
ATOM 12930 C ARG B 313 -34.638 -9.879 -14.280 1.00 24.67 C
ATOM 12931 O ARG B 313 -34.359 -9.645 -13.117 1.00 24.09 O
ATOM 12933 N TRP B 314 -35.843 -9.635 -14.781 1.00 25.60 N
ATOM 12934 CA TRP B 314 -36.971 -9.180 -13.951 1.00 26.20 C
ATOM 12936 CB TRP B 314 -37.488 -10.339 -13.097 1.00 25.90 C
ATOM 12939 CG TRP B 314 -38.912 -10.184 -12.662 1.00 23.93 C
ATOM 12940 CD1 TRP B 314 -39.355 -9.854 -11.424 1.00 22.76 C
ATOM 12942 NE1 TRP B 314 -40.727 -9.804 -11.412 1.00 21.93 N
ATOM 12944 CE2 TRP B 314 -41.189 -10.107 -12.659 1.00 20.38 C
ATOM 12945 CD2 TRP B 314 -40.074 -10.352 -13.473 1.00 21.17 C
ATOM 12946 CE3 TRP B 314 -40.277 -10.684 -14.811 1.00 20.19 C

ATOM 12948 CZ3 TRP B 314 -41.549 -10.766 -15.280 1.00 19.79 C
ATOM 12950 CH2 TRP B 314 -42.640 -10.512 -14.445 1.00 21.00 C
ATOM 12952 CZ2 TRP B 314 -42.474 -10.179 -13.130 1.00 20.60 C
ATOM 12954 C TRP B 314 -36.620 -7.966 -13.076 1.00 27.57 C
ATOM 12955 O TRP B 314 -36.890 -7.935 -11.870 1.00 27.56 O
ATOM 12957 N ASP B 315 -36.039 -6.959 -13.718 1.00 29.12 N
ATOM 12958 CA ASP B 315 -35.452 -5.822 -13.027 1.00 30.46 C
ATOM 12960 CB ASP B 315 -33.935 -5.796 -13.315 1.00 30.84 C
ATOM 12963 CG ASP B 315 -33.227 -4.551 -12.772 1.00 32.75 C
ATOM 12964 OD1 ASP B 315 -33.747 -3.904 -11.830 1.00 35.67 O
ATOM 12965 OD2 ASP B 315 -32.128 -4.222 -13.295 1.00 34.91 O
ATOM 12966 C ASP B 315 -36.157 -4.592 -13.557 1.00 31.10 C
ATOM 12967 O ASP B 315 -35.888 -4.157 -14.674 1.00 31.35 O
ATOM 12969 N VAL B 316 -37.088 -4.044 -12.781 1.00 32.06 N
ATOM 12970 CA VAL B 316 -37.864 -2.896 -13.262 1.00 32.65 C
ATOM 12972 CB VAL B 316 -39.016 -2.510 -12.334 1.00 32.45 C
ATOM 12974 CG1 VAL B 316 -39.911 -1.499 -13.012 1.00 32.15 C
ATOM 12978 CG2 VAL B 316 -38.490 -1.960 -11.040 1.00 32.91 C
ATOM 12982 C VAL B 316 -36.964 -1.692 -13.442 1.00 33.43 C
ATOM 12983 O VAL B 316 -37.228 -.854 -14.294 1.00 33.74 O
ATOM 12985 N ASN B 317 -35.881 -1.628 -12.663 1.00 34.29 N
ATOM 12986 CA ASN B 317 -34.937 -.510 -12.730 1.00 34.63 C
ATOM 12988 CB ASN B 317 -33.995 -.526 -11.505 1.00 34.50 C
ATOM 12991 CG ASN B 317 -34.692 -.084 -10.201 1.00 34.08 C
ATOM 12992 OD1 ASN B 317 -35.198 1.042 -10.104 1.00 33.72 O
ATOM 12993 ND2 ASN B 317 -34.690 -.961 -9.193 1.00 31.22 N
ATOM 12996 C ASN B 317 -34.124 -.481 -14.029 1.00 35.21 C
ATOM 12997 O ASN B 317 -33.196 .296 -14.127 1.00 35.52 O
ATOM 12999 N ALA B 318 -34.470 -1.318 -15.013 1.00 35.89 N
ATOM 13000 CA ALA B 318 -33.757 -1.382 -16.299 1.00 36.48 C
ATOM 13002 CB ALA B 318 -32.727 -2.508 -16.253 1.00 36.49 C
ATOM 13006 C ALA B 318 -34.695 -1.525 -17.534 1.00 37.02 C
ATOM 13007 O ALA B 318 -34.297 -1.984 -18.616 1.00 36.52 O
ATOM 13009 N ILE B 319 -35.952 -1.137 -17.339 1.00 37.76 N
ATOM 13010 CA ILE B 319 -36.848 -.733 -18.424 1.00 38.08 C
ATOM 13012 CB ILE B 319 -37.926 .247 -17.893 1.00 38.11 C
ATOM 13014 CG1 ILE B 319 -39.110 -.495 -17.293 1.00 38.08 C
ATOM 13017 CD1 ILE B 319 -40.068 .451 -16.596 1.00 38.27 C
ATOM 13021 CG2 ILE B 319 -38.408 1.189 -18.996 1.00 37.84 C
ATOM 13025 C ILE B 319 -36.134 .053 -19.516 1.00 38.29 C
ATOM 13026 O ILE B 319 -36.192 -.324 -20.677 1.00 38.68 O
ATOM 13028 N ASN B 320 -35.460 1.141 -19.125 1.00 38.36 N
ATOM 13029 CA ASN B 320 -34.977 2.168 -20.074 1.00 38.17 C
ATOM 13031 CB ASN B 320 -34.278 3.331 -19.331 1.00 38.16 C
ATOM 13034 CG ASN B 320 -35.258 4.207 -18.514 1.00 37.87 C
ATOM 13035 OD1 ASN B 320 -36.366 4.542 -18.955 1.00 36.50 O
ATOM 13036 ND2 ASN B 320 -34.827 4.589 -17.322 1.00 38.12 N
ATOM 13039 C ASN B 320 -34.082 1.643 -21.206 1.00 37.78 C
ATOM 13040 O ASN B 320 -33.856 2.332 -22.181 1.00 37.76 O
ATOM 13042 N ASP B 321 -33.600 .416 -21.083 1.00 37.46 N
ATOM 13043 CA ASP B 321 -32.852 -.224 -22.162 1.00 37.25 C
ATOM 13045 CB ASP B 321 -32.091 -1.467 -21.629 1.00 37.83 C
ATOM 13048 CG ASP B 321 -31.351 -1.207 -20.285 1.00 39.33 C
ATOM 13049 OD1 ASP B 321 -31.247 -.021 -19.871 1.00 40.72 O
ATOM 13050 OD2 ASP B 321 -30.887 -2.199 -19.648 1.00 39.62 O
ATOM 13051 C ASP B 321 -33.764 -.636 -23.339 1.00 35.99 C
ATOM 13052 O ASP B 321 -33.273 -.904 -24.436 1.00 35.87 O
ATOM 13054 N LEU B 322 -35.076 -.674 -23.111 1.00 34.66 N
ATOM 13055 CA LEU B 322 -36.024 -1.263 -24.061 1.00 33.77 C
ATOM 13057 CB LEU B 322 -37.180 -1.961 -23.327 1.00 33.65 C

ATOM 13060 CG LEU B 322 -36.994 -3.260 -22.544 1.00 32.41 C
ATOM 13062 CD1 LEU B 322 -38.223 -3.482 -21.693 1.00 31.54 C
ATOM 13066 CD2 LEU B 322 -36.769 -4.432 -23.460 1.00 30.73 C
ATOM 13070 C LEU B 322 -36.670 -.243 -24.982 1.00 33.32 C
ATOM 13071 O LEU B 322 -36.910 .893 -24.570 1.00 33.37 O
ATOM 13073 N PRO B 323 -37.005 -.667 -26.218 1.00 32.72 N
ATOM 13074 CA PRO B 323 -37.856 .068 -27.126 1.00 32.42 C
ATOM 13076 CB PRO B 323 -38.239 -.985 -28.158 1.00 32.28 C
ATOM 13079 CG PRO B 323 -37.098 -1.849 -28.231 1.00 32.46 C
ATOM 13082 CD PRO B 323 -36.498 -1.891 -26.857 1.00 32.79 C
ATOM 13085 C PRO B 323 -39.115 .576 -26.453 1.00 32.50 C
ATOM 13086 O PRO B 323 -39.655 -.083 -25.550 1.00 32.46 O
ATOM 13087 N ASP B 324 -39.590 1.725 -26.923 1.00 32.44 N
ATOM 13088 CA ASP B 324 -40.729 2.387 -26.318 1.00 32.44 C
ATOM 13090 CB ASP B 324 -41.059 3.678 -27.071 1.00 32.91 C
ATOM 13093 CG ASP B 324 -40.241 4.873 -26.576 1.00 34.17 C
ATOM 13094 OD1 ASP B 324 -39.507 4.728 -25.562 1.00 35.83 O
ATOM 13095 OD2 ASP B 324 -40.351 5.960 -27.196 1.00 35.42 O
ATOM 13096 C ASP B 324 -41.967 1.504 -26.186 1.00 31.78 C
ATOM 13097 O ASP B 324 -42.546 1.440 -25.102 1.00 31.77 O
ATOM 13099 N TYR B 325 -42.368 .821 -27.258 1.00 30.99 N
ATOM 13100 CA TYR B 325 -43.519 -.086 -27.167 1.00 30.49 C
ATOM 13102 CB TYR B 325 -43.941 -.640 -28.536 1.00 30.28 C
ATOM 13105 CG TYR B 325 -43.027 -1.688 -29.134 1.00 30.25 C
ATOM 13106 CD1 TYR B 325 -41.917 -1.332 -29.893 1.00 29.81 C
ATOM 13108 CE1 TYR B 325 -41.089 -2.300 -30.449 1.00 29.74 C
ATOM 13110 CZ TYR B 325 -41.371 -3.643 -30.258 1.00 30.22 C
ATOM 13111 OH TYR B 325 -40.565 -4.625 -30.805 1.00 31.28 O
ATOM 13113 CE2 TYR B 325 -42.466 -4.015 -29.519 1.00 30.23 C
ATOM 13115 CD2 TYR B 325 -43.288 -3.038 -28.963 1.00 30.49 C
ATOM 13117 C TYR B 325 -43.284 -1.221 -26.168 1.00 30.14 C
ATOM 13118 O TYR B 325 -44.219 -1.638 -25.483 1.00 30.19 O
ATOM 13120 N MET B 326 -42.048 -1.700 -26.060 1.00 29.74 N
ATOM 13121 CA MET B 326 -41.755 -2.820 -25.155 1.00 29.82 C
ATOM 13123 CB MET B 326 -40.461 -3.541 -25.549 1.00 29.69 C
ATOM 13126 CG MET B 326 -40.650 -4.510 -26.686 1.00 28.83 C
ATOM 13129 SD MET B 326 -39.123 -5.272 -27.204 1.00 26.99 S
ATOM 13130 CE MET B 326 -39.761 -6.499 -28.328 1.00 29.13 C
ATOM 13134 C MET B 326 -41.696 -2.402 -23.683 1.00 29.92 C
ATOM 13135 O MET B 326 -42.032 -3.204 -22.801 1.00 29.75 O
ATOM 13137 N LYS B 327 -41.251 -1.166 -23.429 1.00 29.68 N
ATOM 13138 CA LYS B 327 -41.318 -.578 -22.088 1.00 29.46 C
ATOM 13140 CB LYS B 327 -41.016 .921 -22.114 1.00 29.93 C
ATOM 13143 CG LYS B 327 -39.572 1.305 -21.951 1.00 31.63 C
ATOM 13146 CD LYS B 327 -39.410 2.803 -22.249 1.00 34.93 C
ATOM 13149 CE LYS B 327 -37.986 3.291 -22.021 1.00 36.86 C
ATOM 13152 NZ LYS B 327 -37.642 4.436 -22.917 1.00 37.83 N
ATOM 13156 C LYS B 327 -42.708 -.752 -21.531 1.00 28.46 C
ATOM 13157 O LYS B 327 -42.879 -1.314 -20.461 1.00 28.54 O
ATOM 13159 N LEU B 328 -43.696 -.258 -22.268 1.00 27.39 N
ATOM 13160 CA LEU B 328 -45.056 -.216 -21.785 1.00 26.79 C
ATOM 13162 CB LEU B 328 -45.946 .519 -22.773 1.00 26.68 C
ATOM 13165 CG LEU B 328 -47.265 1.034 -22.212 1.00 26.00 C
ATOM 13167 CD1 LEU B 328 -47.010 1.964 -21.036 1.00 24.88 C
ATOM 13171 CD2 LEU B 328 -48.051 1.740 -23.308 1.00 24.55 C
ATOM 13175 C LEU B 328 -45.560 -1.628 -21.587 1.00 26.70 C
ATOM 13176 O LEU B 328 -46.110 -1.983 -20.543 1.00 27.03 O
ATOM 13178 N CYS B 329 -45.341 -2.453 -22.591 1.00 26.39 N
ATOM 13179 CA CYS B 329 -45.750 -3.843 -22.524 1.00 26.12 C
ATOM 13181 CB CYS B 329 -45.382 -4.526 -23.838 1.00 26.47 C

ATOM 13184 SG CYS B 329 -45.857 -6.236 -23.880 1.00 30.60 S
ATOM 13186 C CYS B 329 -45.124 -4.568 -21.319 1.00 24.45 C
ATOM 13187 O CYS B 329 -45.829 -5.105 -20.486 1.00 23.93 O
ATOM 13189 N PHE B 330 -43.801 -4.553 -21.228 1.00 23.30 N
ATOM 13190 CA PHE B 330 -43.087 -5.220 -20.141 1.00 22.47 C
ATOM 13192 CB PHE B 330 -41.575 -5.019 -20.267 1.00 22.42 C
ATOM 13195 CG PHE B 330 -40.800 -5.518 -19.076 1.00 22.37 C
ATOM 13196 CD1 PHE B 330 -40.502 -6.864 -18.940 1.00 22.47 C
ATOM 13198 CE1 PHE B 330 -39.799 -7.339 -17.836 1.00 21.64 C
ATOM 13200 CZ PHE B 330 -39.379 -6.472 -16.866 1.00 21.50 C
ATOM 13202 CE2 PHE B 330 -39.659 -5.122 -16.983 1.00 21.92 C
ATOM 13204 CD2 PHE B 330 -40.374 -4.648 -18.084 1.00 22.29 C
ATOM 13206 C PHE B 330 -43.524 -4.739 -18.765 1.00 21.87 C
ATOM 13207 O PHE B 330 -43.779 -5.552 -17.875 1.00 21.98 O
ATOM 13209 N LEU B 331 -43.594 -3.427 -18.573 1.00 20.88 N
ATOM 13210 CA LEU B 331 -43.997 -2.894 -17.276 1.00 20.25 C
ATOM 13212 CB LEU B 331 -43.927 -1.354 -17.257 1.00 20.06 C
ATOM 13215 CG LEU B 331 -44.124 -.628 -15.912 1.00 19.21 C
ATOM 13217 CD1 LEU B 331 -43.542 -1.408 -14.737 1.00 18.78 C
ATOM 13221 CD2 LEU B 331 -43.555 .770 -15.957 1.00 15.75 C
ATOM 13225 C LEU B 331 -45.398 -3.408 -16.902 1.00 19.99 C
ATOM 13226 O LEU B 331 -45.606 -3.860 -15.771 1.00 19.67 O
ATOM 13228 N ALA B 332 -46.336 -3.373 -17.860 1.00 19.56 N
ATOM 13229 CA ALA B 332 -47.695 -3.882 -17.629 1.00 19.24 C
ATOM 13231 CB ALA B 332 -48.528 -3.802 -18.891 1.00 18.58 C
ATOM 13235 C ALA B 332 -47.637 -5.321 -17.108 1.00 19.23 C
ATOM 13236 O ALA B 332 -48.235 -5.650 -16.079 1.00 19.18 O
ATOM 13238 N LEU B 333 -46.891 -6.162 -17.816 1.00 19.16 N
ATOM 13239 CA LEU B 333 -46.727 -7.554 -17.438 1.00 19.08 C
ATOM 13241 CB LEU B 333 -45.830 -8.260 -18.462 1.00 18.97 C
ATOM 13244 CG LEU B 333 -45.511 -9.758 -18.307 1.00 19.18 C
ATOM 13246 CD1 LEU B 333 -46.779 -10.611 -18.121 1.00 18.09 C
ATOM 13250 CD2 LEU B 333 -44.676 -10.262 -19.499 1.00 17.17 C
ATOM 13254 C LEU B 333 -46.111 -7.616 -16.042 1.00 19.16 C
ATOM 13255 O LEU B 333 -46.629 -8.279 -15.137 1.00 18.97 O
ATOM 13257 N TYR B 334 -45.013 -6.887 -15.884 1.00 19.23 N
ATOM 13258 CA TYR B 334 -44.212 -6.906 -14.664 1.00 19.33 C
ATOM 13260 CB TYR B 334 -43.092 -5.873 -14.785 1.00 19.43 C
ATOM 13263 CG TYR B 334 -42.190 -5.748 -13.596 1.00 19.44 C
ATOM 13264 CD1 TYR B 334 -41.006 -6.464 -13.524 1.00 20.60 C
ATOM 13266 CE1 TYR B 334 -40.148 -6.347 -12.442 1.00 20.77 C
ATOM 13268 CZ TYR B 334 -40.474 -5.503 -11.417 1.00 21.51 C
ATOM 13269 OH TYR B 334 -39.628 -5.387 -10.353 1.00 21.42 O
ATOM 13271 CE2 TYR B 334 -41.646 -4.768 -11.466 1.00 22.15 C
ATOM 13273 CD2 TYR B 334 -42.495 -4.892 -12.565 1.00 20.55 C
ATOM 13275 C TYR B 334 -45.065 -6.614 -13.443 1.00 19.37 C
ATOM 13276 O TYR B 334 -44.980 -7.337 -12.441 1.00 19.94 O
ATOM 13278 N ASN B 335 -45.888 -5.565 -13.527 1.00 18.83 N
ATOM 13279 CA ASN B 335 -46.784 -5.236 -12.443 1.00 18.37 C
ATOM 13281 CB ASN B 335 -47.452 -3.896 -12.675 1.00 18.52 C
ATOM 13284 CG ASN B 335 -46.493 -2.742 -12.518 1.00 19.27 C
ATOM 13285 OD1 ASN B 335 -45.421 -2.906 -11.953 1.00 21.25 O
ATOM 13286 ND2 ASN B 335 -46.872 -1.566 -13.022 1.00 19.24 N
ATOM 13289 C ASN B 335 -47.812 -6.333 -12.291 1.00 18.22 C
ATOM 13290 O ASN B 335 -47.966 -6.891 -11.207 1.00 18.53 O
ATOM 13292 N THR B 336 -48.481 -6.697 -13.379 1.00 17.95 N
ATOM 13293 CA THR B 336 -49.525 -7.728 -13.301 1.00 17.61 C
ATOM 13295 CB THR B 336 -49.980 -8.204 -14.676 1.00 17.36 C
ATOM 13297 OG1 THR B 336 -50.249 -7.065 -15.500 1.00 17.02 O
ATOM 13299 CG2 THR B 336 -51.228 -9.044 -14.551 1.00 16.07 C

ATOM 13303 C THR B 336 -49.065 -8.941 -12.501 1.00 17.75 C
ATOM 13304 O THR B 336 -49.788 -9.429 -11.621 1.00 18.09 O
ATOM 13306 N ILE B 337 -47.859 -9.411 -12.785 1.00 17.69 N
ATOM 13307 CA ILE B 337 -47.384 -10.630 -12.165 1.00 17.74 C
ATOM 13309 CB ILE B 337 -46.228 -11.245 -12.949 1.00 17.40 C
ATOM 13311 CG1 ILE B 337 -46.795 -11.865 -14.227 1.00 18.44 C
ATOM 13314 CD1 ILE B 337 -45.767 -12.192 -15.300 1.00 19.26 C
ATOM 13318 CG2 ILE B 337 -45.568 -12.320 -12.152 1.00 16.25 C
ATOM 13322 C ILE B 337 -47.053 -10.395 -10.699 1.00 18.32 C
ATOM 13323 O ILE B 337 -47.497 -11.175 -9.838 1.00 18.06 O
ATOM 13325 N ASN B 338 -46.321 -9.311 -10.404 1.00 18.89 N
ATOM 13326 CA ASN B 338 -45.985 -8.978 -9.007 1.00 19.49 C
ATOM 13328 CB ASN B 338 -45.189 -7.690 -8.917 1.00 19.43 C
ATOM 13331 CG ASN B 338 -43.789 -7.836 -9.444 1.00 20.83 C
ATOM 13332 OD1 ASN B 338 -43.292 -8.954 -9.634 1.00 21.52 O
ATOM 13333 ND2 ASN B 338 -43.124 -6.697 -9.676 1.00 22.32 N
ATOM 13336 C ASN B 338 -47.229 -8.835 -8.146 1.00 20.05 C
ATOM 13337 O ASN B 338 -47.182 -9.055 -6.953 1.00 19.81 O
ATOM 13339 N GLU B 339 -48.337 -8.459 -8.770 1.00 20.81 N
ATOM 13340 CA GLU B 339 -49.589 -8.347 -8.086 1.00 21.81 C
ATOM 13342 CB GLU B 339 -50.563 -7.544 -8.933 1.00 22.69 C
ATOM 13345 CG GLU B 339 -51.240 -6.422 -8.148 1.00 27.28 C
ATOM 13348 CD GLU B 339 -52.571 -5.959 -8.768 1.00 32.79 C
ATOM 13349 OE1 GLU B 339 -52.761 -4.713 -8.897 1.00 36.20 O
ATOM 13350 OE2 GLU B 339 -53.416 -6.837 -9.114 1.00 34.35 O
ATOM 13351 C GLU B 339 -50.170 -9.732 -7.762 1.00 21.59 C
ATOM 13352 O GLU B 339 -50.690 -9.946 -6.666 1.00 21.38 O
ATOM 13354 N ILE B 340 -50.094 -10.676 -8.700 1.00 21.48 N
ATOM 13355 CA ILE B 340 -50.486 -12.049 -8.384 1.00 21.27 C
ATOM 13357 CB ILE B 340 -50.437 -12.990 -9.603 1.00 21.17 C
ATOM 13359 CG1 ILE B 340 -51.478 -12.589 -10.643 1.00 20.99 C
ATOM 13362 CD1 ILE B 340 -51.245 -13.202 -12.017 1.00 19.72 C
ATOM 13366 CG2 ILE B 340 -50.702 -14.444 -9.177 1.00 21.09 C
ATOM 13370 C ILE B 340 -49.557 -12.585 -7.278 1.00 21.40 C
ATOM 13371 O ILE B 340 -50.023 -13.238 -6.334 1.00 21.74 O
ATOM 13373 N ALA B 341 -48.256 -12.301 -7.380 1.00 20.90 N
ATOM 13374 CA ALA B 341 -47.312 -12.721 -6.349 1.00 20.62 C
ATOM 13376 CB ALA B 341 -45.922 -12.260 -6.694 1.00 20.53 C
ATOM 13380 C ALA B 341 -47.720 -12.195 -4.969 1.00 20.59 C
ATOM 13381 O ALA B 341 -47.606 -12.901 -3.950 1.00 20.57 O
ATOM 13383 N TYR B 342 -48.208 -10.958 -4.949 1.00 20.62 N
ATOM 13384 CA TYR B 342 -48.600 -10.303 -3.707 1.00 20.59 C
ATOM 13386 CB TYR B 342 -48.790 -8.792 -3.907 1.00 20.05 C
ATOM 13389 CG TYR B 342 -49.309 -8.143 -2.674 1.00 18.29 C
ATOM 13390 CD1 TYR B 342 -48.443 -7.683 -1.698 1.00 17.62 C
ATOM 13392 CE1 TYR B 342 -48.914 -7.111 -.518 1.00 17.91 C
ATOM 13394 CZ TYR B 342 -50.285 -7.005 -.298 1.00 18.18 C
ATOM 13395 OH TYR B 342 -50.763 -6.433 .877 1.00 16.00 O
ATOM 13397 CE2 TYR B 342 -51.169 -7.467 -1.275 1.00 18.10 C
ATOM 13399 CD2 TYR B 342 -50.670 -8.037 -2.450 1.00 17.67 C
ATOM 13401 C TYR B 342 -49.863 -10.928 -3.118 1.00 21.48 C
ATOM 13402 O TYR B 342 -49.960 -11.089 -1.913 1.00 20.91 O
ATOM 13404 N ASP B 343 -50.832 -11.273 -3.959 1.00 22.93 N
ATOM 13405 CA ASP B 343 -52.048 -11.925 -3.470 1.00 24.30 C
ATOM 13407 CB ASP B 343 -53.010 -12.282 -4.608 1.00 24.59 C
ATOM 13410 CG ASP B 343 -53.577 -11.060 -5.334 1.00 26.66 C
ATOM 13411 OD1 ASP B 343 -53.619 -9.936 -4.756 1.00 28.24 O
ATOM 13412 OD2 ASP B 343 -54.004 -11.247 -6.506 1.00 29.56 O
ATOM 13413 C ASP B 343 -51.660 -13.208 -2.761 1.00 24.97 C
ATOM 13414 O ASP B 343 -52.128 -13.495 -1.658 1.00 24.95 O

ATOM 13416 N ASN B 344 -50.792 -13.973 -3.413 1.00 25.90 N
ATOM 13417 CA ASN B 344 -50.322 -15.252 -2.884 1.00 26.59 C
ATOM 13419 CB ASN B 344 -49.623 -16.043 -3.978 1.00 26.74 C
ATOM 13422 CG ASN B 344 -50.594 -16.639 -4.933 1.00 28.21 C
ATOM 13423 OD1 ASN B 344 -51.080 -17.737 -4.688 1.00 32.10 O
ATOM 13424 ND2 ASN B 344 -50.923 -15.916 -6.016 1.00 28.40 N
ATOM 13427 C ASN B 344 -49.421 -15.146 -1.655 1.00 26.78 C
ATOM 13428 O ASN B 344 -49.424 -16.053 -.821 1.00 27.06 O
ATOM 13430 N LEU B 345 -48.647 -14.067 -1.533 1.00 26.74 N
ATOM 13431 CA LEU B 345 -47.970 -13.793 -.261 1.00 26.59 C
ATOM 13433 CB LEU B 345 -47.005 -12.618 -.396 1.00 26.25 C
ATOM 13436 CG LEU B 345 -46.046 -12.376 .764 1.00 24.65 C
ATOM 13438 CD1 LEU B 345 -45.258 -13.621 1.115 1.00 22.50 C
ATOM 13442 CD2 LEU B 345 -45.119 -11.251 .387 1.00 23.54 C
ATOM 13446 C LEU B 345 -49.004 -13.503 .840 1.00 27.00 C
ATOM 13447 O LEU B 345 -48.903 -14.014 1.947 1.00 26.93 O
ATOM 13449 N LYS B 346 -50.008 -12.697 .518 1.00 27.54 N
ATOM 13450 CA LYS B 346 -51.012 -12.300 1.491 1.00 27.96 C
ATOM 13452 CB LYS B 346 -51.998 -11.288 .889 1.00 28.13 C
ATOM 13455 CG LYS B 346 -52.822 -10.527 1.926 1.00 28.70 C
ATOM 13458 CD LYS B 346 -53.781 -9.526 1.281 1.00 29.73 C
ATOM 13461 CE LYS B 346 -55.205 -10.063 1.133 1.00 31.17 C
ATOM 13464 NZ LYS B 346 -55.839 -9.661 -.171 1.00 32.83 N
ATOM 13468 C LYS B 346 -51.788 -13.498 1.984 1.00 28.31 C
ATOM 13469 O LYS B 346 -52.074 -13.600 3.177 1.00 28.52 O
ATOM 13471 N ASP B 347 -52.149 -14.396 1.075 1.00 28.56 N
ATOM 13472 CA ASP B 347 -53.102 -15.441 1.427 1.00 29.11 C
ATOM 13474 CB ASP B 347 -54.068 -15.736 .268 1.00 29.50 C
ATOM 13477 CG ASP B 347 -54.902 -14.500 -.150 1.00 31.04 C
ATOM 13478 OD1 ASP B 347 -54.961 -13.500 .616 1.00 31.35 O
ATOM 13479 OD2 ASP B 347 -55.496 -14.534 -1.261 1.00 33.39 O
ATOM 13480 C ASP B 347 -52.403 -16.699 1.891 1.00 28.79 C
ATOM 13481 O ASP B 347 -52.824 -17.321 2.854 1.00 29.02 O
ATOM 13483 N LYS B 348 -51.326 -17.068 1.222 1.00 28.74 N
ATOM 13484 CA LYS B 348 -50.612 -18.293 1.564 1.00 28.84 C
ATOM 13486 CB LYS B 348 -50.290 -19.101 .299 1.00 29.24 C
ATOM 13489 CG LYS B 348 -51.513 -19.470 -.576 1.00 30.97 C
ATOM 13492 CD LYS B 348 -51.051 -20.300 -1.803 1.00 33.66 C
ATOM 13495 CE LYS B 348 -52.033 -20.244 -2.989 1.00 34.52 C
ATOM 13498 NZ LYS B 348 -53.445 -20.542 -2.607 1.00 35.61 N
ATOM 13502 C LYS B 348 -49.330 -18.029 2.358 1.00 27.97 C
ATOM 13503 O LYS B 348 -48.763 -18.948 2.925 1.00 27.88 O
ATOM 13505 N GLY B 349 -48.874 -16.785 2.403 1.00 27.21 N
ATOM 13506 CA GLY B 349 -47.625 -16.473 3.075 1.00 26.87 C
ATOM 13509 C GLY B 349 -46.437 -17.227 2.514 1.00 26.71 C
ATOM 13510 O GLY B 349 -45.576 -17.669 3.271 1.00 26.65 O
ATOM 13512 N GLU B 350 -46.409 -17.390 1.191 1.00 26.61 N
ATOM 13513 CA GLU B 350 -45.263 -17.953 .470 1.00 26.43 C
ATOM 13515 CB GLU B 350 -45.624 -19.310 -.128 1.00 26.85 C
ATOM 13518 CG GLU B 350 -45.685 -20.453 .888 1.00 29.63 C
ATOM 13521 CD GLU B 350 -44.304 -21.036 1.227 1.00 34.21 C
ATOM 13522 OE1 GLU B 350 -43.417 -21.045 .328 1.00 36.93 O
ATOM 13523 OE2 GLU B 350 -44.106 -21.498 2.384 1.00 35.89 O
ATOM 13524 C GLU B 350 -44.900 -16.981 -.637 1.00 25.49 C
ATOM 13525 O GLU B 350 -45.774 -16.312 -1.181 1.00 25.35 O
ATOM 13527 N ASN B 351 -43.616 -16.866 -.955 1.00 24.74 N
ATOM 13528 CA ASN B 351 -43.206 -16.046 -2.090 1.00 24.47 C
ATOM 13530 CB ASN B 351 -41.851 -15.369 -1.867 1.00 24.94 C
ATOM 13533 CG ASN B 351 -41.428 -14.489 -3.062 1.00 26.98 C
ATOM 13534 OD1 ASN B 351 -41.976 -14.605 -4.170 1.00 28.96 O

ATOM 13535 ND2 ASN B 351 -40.457 -13.601 -2.834 1.00 29.55 N
ATOM 13538 C ASN B 351 -43.095 -16.918 -3.303 1.00 23.33 C
ATOM 13539 O ASN B 351 -42.120 -17.641 -3.429 1.00 23.47 O
ATOM 13541 N ILE B 352 -44.060 -16.823 -4.208 1.00 22.09 N
ATOM 13542 CA ILE B 352 -44.048 -17.644 -5.410 1.00 21.22 C
ATOM 13544 CB ILE B 352 -45.452 -18.213 -5.675 1.00 21.23 C
ATOM 13546 CG1 ILE B 352 -46.464 -17.080 -5.913 1.00 21.11 C
ATOM 13549 CD1 ILE B 352 -47.346 -17.305 -7.126 1.00 20.33 C
ATOM 13553 CG2 ILE B 352 -45.875 -19.116 -4.519 1.00 19.79 C
ATOM 13557 C ILE B 352 -43.508 -16.947 -6.689 1.00 20.88 C
ATOM 13558 O ILE B 352 -43.486 -17.553 -7.758 1.00 20.76 O
ATOM 13560 N LEU B 353 -43.030 -15.705 -6.574 1.00 20.44 N
ATOM 13561 CA LEU B 353 -42.603 -14.907 -7.750 1.00 19.84 C
ATOM 13563 CB LEU B 353 -42.055 -13.527 -7.325 1.00 19.67 C
ATOM 13566 CG LEU B 353 -42.003 -12.339 -8.311 1.00 18.47 C
ATOM 13568 CD1 LEU B 353 -43.306 -12.083 -9.008 1.00 17.03 C
ATOM 13572 CD2 LEU B 353 -41.604 -11.064 -7.597 1.00 17.08 C
ATOM 13576 C LEU B 353 -41.587 -15.628 -8.633 1.00 19.81 C
ATOM 13577 O LEU B 353 -41.720 -15.596 -9.851 1.00 19.55 O
ATOM 13579 N PRO B 354 -40.578 -16.299 -8.024 1.00 20.01 N
ATOM 13580 CA PRO B 354 -39.571 -17.010 -8.822 1.00 19.73 C
ATOM 13582 CB PRO B 354 -38.781 -17.796 -7.779 1.00 19.55 C
ATOM 13585 CG PRO B 354 -38.928 -17.037 -6.542 1.00 19.61 C
ATOM 13588 CD PRO B 354 -40.289 -16.413 -6.578 1.00 19.90 C
ATOM 13591 C PRO B 354 -40.187 -17.971 -9.804 1.00 19.87 C
ATOM 13592 O PRO B 354 -39.693 -18.103 -10.918 1.00 20.08 O
ATOM 13593 N TYR B 355 -41.264 -18.636 -9.387 1.00 20.14 N
ATOM 13594 CA TYR B 355 -41.909 -19.665 -10.216 1.00 20.24 C
ATOM 13596 CB TYR B 355 -42.878 -20.520 -9.394 1.00 20.40 C
ATOM 13599 CG TYR B 355 -42.189 -21.153 -8.214 1.00 21.82 C
ATOM 13600 CD1 TYR B 355 -41.119 -21.999 -8.412 1.00 22.86 C
ATOM 13602 CE1 TYR B 355 -40.457 -22.564 -7.353 1.00 25.07 C
ATOM 13604 CZ TYR B 355 -40.850 -22.285 -6.053 1.00 25.58 C
ATOM 13605 OH TYR B 355 -40.153 -22.887 -5.020 1.00 27.33 O
ATOM 13607 CE2 TYR B 355 -41.918 -21.433 -5.815 1.00 23.93 C
ATOM 13609 CD2 TYR B 355 -42.577 -20.867 -6.900 1.00 23.10 C
ATOM 13611 C TYR B 355 -42.625 -19.001 -11.361 1.00 19.67 C
ATOM 13612 O TYR B 355 -42.455 -19.405 -12.510 1.00 19.75 O
ATOM 13614 N LEU B 356 -43.385 -17.954 -11.030 1.00 18.97 N
ATOM 13615 CA LEU B 356 -44.180 -17.205 -12.004 1.00 18.26 C
ATOM 13617 CB LEU B 356 -45.039 -16.157 -11.293 1.00 18.03 C
ATOM 13620 CG LEU B 356 -46.056 -16.727 -10.312 1.00 18.13 C
ATOM 13622 CD1 LEU B 356 -46.691 -15.613 -9.500 1.00 19.37 C
ATOM 13626 CD2 LEU B 356 -47.106 -17.521 -11.046 1.00 17.93 C
ATOM 13630 C LEU B 356 -43.298 -16.536 -13.056 1.00 17.76 C
ATOM 13631 O LEU B 356 -43.598 -16.567 -14.259 1.00 16.93 O
ATOM 13633 N THR B 357 -42.201 -15.949 -12.600 1.00 17.56 N
ATOM 13634 CA THR B 357 -41.335 -15.215 -13.501 1.00 17.63 C
ATOM 13636 CB THR B 357 -40.438 -14.236 -12.759 1.00 17.69 C
ATOM 13638 OG1 THR B 357 -39.530 -14.974 -11.934 1.00 18.39 O
ATOM 13640 CG2 THR B 357 -41.288 -13.242 -11.927 1.00 16.47 C
ATOM 13644 C THR B 357 -40.477 -16.145 -14.356 1.00 17.55 C
ATOM 13645 O THR B 357 -40.154 -15.793 -15.498 1.00 17.17 O
ATOM 13647 N LYS B 358 -40.127 -17.321 -13.824 1.00 17.37 N
ATOM 13648 CA LYS B 358 -39.462 -18.337 -14.649 1.00 17.55 C
ATOM 13650 CB LYS B 358 -39.030 -19.542 -13.827 1.00 17.87 C
ATOM 13653 CG LYS B 358 -38.450 -20.718 -14.640 1.00 18.75 C
ATOM 13656 CD LYS B 358 -37.013 -20.497 -15.112 1.00 20.18 C
ATOM 13659 CE LYS B 358 -36.361 -21.843 -15.457 1.00 21.49 C
ATOM 13662 NZ LYS B 358 -35.189 -21.702 -16.361 1.00 22.89 N

ATOM 13666 C LYS B 358 -40.403 -18.777 -15.754 1.00 17.43 C
ATOM 13667 O LYS B 358 -40.031 -18.775 -16.926 1.00 17.52 O
ATOM 13669 N ALA B 359 -41.633 -19.120 -15.384 1.00 17.42 N
ATOM 13670 CA ALA B 359 -42.654 -19.471 -16.359 1.00 17.52 C
ATOM 13672 CB ALA B 359 -44.011 -19.434 -15.738 1.00 17.16 C
ATOM 13676 C ALA B 359 -42.585 -18.521 -17.531 1.00 18.18 C
ATOM 13677 O ALA B 359 -42.513 -18.956 -18.675 1.00 18.50 O
ATOM 13679 N TRP B 360 -42.556 -17.223 -17.245 1.00 19.14 N
ATOM 13680 CA TRP B 360 -42.526 -16.206 -18.301 1.00 19.77 C
ATOM 13682 CB TRP B 360 -42.922 -14.837 -17.746 1.00 20.15 C
ATOM 13685 CG TRP B 360 -44.377 -14.653 -17.813 1.00 20.50 C
ATOM 13686 CD1 TRP B 360 -45.259 -14.729 -16.788 1.00 22.15 C
ATOM 13688 NE1 TRP B 360 -46.536 -14.533 -17.248 1.00 22.84 N
ATOM 13690 CE2 TRP B 360 -46.487 -14.348 -18.603 1.00 21.68 C
ATOM 13691 CD2 TRP B 360 -45.134 -14.418 -18.987 1.00 20.85 C
ATOM 13692 CE3 TRP B 360 -44.802 -14.253 -20.334 1.00 21.21 C
ATOM 13694 CZ3 TRP B 360 -45.821 -14.025 -21.245 1.00 20.75 C
ATOM 13696 CH2 TRP B 360 -47.166 -13.961 -20.827 1.00 21.21 C
ATOM 13698 CZ2 TRP B 360 -47.515 -14.123 -19.516 1.00 20.97 C
ATOM 13700 C TRP B 360 -41.215 -16.110 -19.081 1.00 19.96 C
ATOM 13701 O TRP B 360 -41.242 -15.791 -20.271 1.00 19.94 O
ATOM 13703 N ALA B 361 -40.089 -16.368 -18.420 1.00 20.14 N
ATOM 13704 CA ALA B 361 -38.790 -16.437 -19.102 1.00 20.41 C
ATOM 13706 CB ALA B 361 -37.676 -16.581 -18.102 1.00 20.67 C
ATOM 13710 C ALA B 361 -38.763 -17.618 -20.041 1.00 20.55 C
ATOM 13711 O ALA B 361 -38.330 -17.510 -21.187 1.00 20.76 O
ATOM 13713 N ASP B 362 -39.230 -18.749 -19.534 1.00 20.57 N
ATOM 13714 CA ASP B 362 -39.360 -19.965 -20.326 1.00 20.97 C
ATOM 13716 CB ASP B 362 -39.984 -21.082 -19.470 1.00 21.39 C
ATOM 13719 CG ASP B 362 -38.938 -21.902 -18.693 1.00 22.80 C
ATOM 13720 OD1 ASP B 362 -38.836 -23.109 -18.970 1.00 28.57 O
ATOM 13721 OD2 ASP B 362 -38.210 -21.384 -17.825 1.00 22.78 O
ATOM 13722 C ASP B 362 -40.179 -19.748 -21.618 1.00 20.66 C
ATOM 13723 O ASP B 362 -39.740 -20.141 -22.701 1.00 20.69 O
ATOM 13725 N LEU B 363 -41.346 -19.110 -21.501 1.00 20.22 N
ATOM 13726 CA LEU B 363 -42.245 -18.885 -22.648 1.00 19.82 C
ATOM 13728 CB LEU B 363 -43.592 -18.327 -22.164 1.00 19.11 C
ATOM 13731 CG LEU B 363 -44.644 -17.945 -23.209 1.00 17.02 C
ATOM 13733 CD1 LEU B 363 -44.829 -19.033 -24.214 1.00 16.20 C
ATOM 13737 CD2 LEU B 363 -45.979 -17.618 -22.586 1.00 14.21 C
ATOM 13741 C LEU B 363 -41.633 -17.950 -23.706 1.00 20.76 C
ATOM 13742 O LEU B 363 -41.656 -18.235 -24.910 1.00 21.00 O
ATOM 13744 N CYS B 364 -41.088 -16.826 -23.253 1.00 21.42 N
ATOM 13745 CA CYS B 364 -40.427 -15.884 -24.147 1.00 21.67 C
ATOM 13747 CB CYS B 364 -39.969 -14.639 -23.376 1.00 21.86 C
ATOM 13750 SG CYS B 364 -41.327 -13.638 -22.722 1.00 23.36 S
ATOM 13752 C CYS B 364 -39.229 -16.547 -24.835 1.00 21.52 C
ATOM 13753 O CYS B 364 -39.010 -16.323 -26.037 1.00 21.67 O
ATOM 13755 N ASN B 365 -38.454 -17.352 -24.095 1.00 20.83 N
ATOM 13756 CA ASN B 365 -37.306 -18.025 -24.713 1.00 20.65 C
ATOM 13758 CB ASN B 365 -36.425 -18.756 -23.691 1.00 20.74 C
ATOM 13761 CG ASN B 365 -35.330 -17.865 -23.100 1.00 20.53 C
ATOM 13762 OD1 ASN B 365 -34.553 -17.229 -23.830 1.00 18.26 O
ATOM 13763 ND2 ASN B 365 -35.252 -17.841 -21.763 1.00 20.69 N
ATOM 13766 C ASN B 365 -37.756 -18.987 -25.811 1.00 20.43 C
ATOM 13767 O ASN B 365 -36.998 -19.253 -26.759 1.00 20.11 O
ATOM 13769 N ALA B 366 -38.987 -19.492 -25.667 1.00 20.01 N
ATOM 13770 CA ALA B 366 -39.618 -20.340 -26.665 1.00 19.70 C
ATOM 13772 CB ALA B 366 -40.766 -21.113 -26.045 1.00 19.53 C
ATOM 13776 C ALA B 366 -40.099 -19.494 -27.838 1.00 19.74 C

ATOM 13777 O ALA B 366 -39.846 -19.824 -28.989 1.00 19.61 O
ATOM 13779 N PHE B 367 -40.791 -18.399 -27.553 1.00 19.99 N
ATOM 13780 CA PHE B 367 -41.138 -17.446 -28.606 1.00 20.36 C
ATOM 13782 CB PHE B 367 -41.805 -16.194 -28.026 1.00 20.62 C
ATOM 13785 CG PHE B 367 -43.200 -16.403 -27.537 1.00 21.75 C
ATOM 13786 CD1 PHE B 367 -44.136 -17.071 -28.315 1.00 23.00 C
ATOM 13788 CE1 PHE B 367 -45.435 -17.242 -27.874 1.00 23.60 C
ATOM 13790 CZ PHE B 367 -45.819 -16.731 -26.648 1.00 23.64 C
ATOM 13792 CE2 PHE B 367 -44.901 -16.049 -25.871 1.00 23.56 C
ATOM 13794 CD2 PHE B 367 -43.599 -15.883 -26.316 1.00 22.91 C
ATOM 13796 C PHE B 367 -39.906 -16.986 -29.393 1.00 20.19 C
ATOM 13797 O PHE B 367 -39.934 -16.903 -30.615 1.00 19.98 O
ATOM 13799 N LEU B 368 -38.839 -16.659 -28.675 1.00 20.24 N
ATOM 13800 CA LEU B 368 -37.629 -16.161 -29.298 1.00 20.31 C
ATOM 13802 CB LEU B 368 -36.569 -15.900 -28.232 1.00 20.27 C
ATOM 13805 CG LEU B 368 -35.235 -15.313 -28.694 1.00 20.12 C
ATOM 13807 CD1 LEU B 368 -35.417 -14.069 -29.592 1.00 20.05 C
ATOM 13811 CD2 LEU B 368 -34.409 -14.987 -27.465 1.00 18.60 C
ATOM 13815 C LEU B 368 -37.122 -17.179 -30.295 1.00 20.53 C
ATOM 13816 O LEU B 368 -36.844 -16.844 -31.446 1.00 20.49 O
ATOM 13818 N GLN B 369 -37.032 -18.426 -29.832 1.00 20.80 N
ATOM 13819 CA GLN B 369 -36.565 -19.557 -30.638 1.00 20.90 C
ATOM 13821 CB GLN B 369 -36.614 -20.857 -29.815 1.00 20.98 C
ATOM 13824 CG GLN B 369 -36.343 -22.159 -30.576 1.00 20.75 C
ATOM 13827 CD GLN B 369 -34.946 -22.238 -31.126 1.00 20.29 C
ATOM 13828 OE1 GLN B 369 -34.718 -21.984 -32.305 1.00 20.17 O
ATOM 13829 NE2 GLN B 369 -33.996 -22.581 -30.272 1.00 20.33 N
ATOM 13832 C GLN B 369 -37.365 -19.718 -31.910 1.00 21.04 C
ATOM 13833 O GLN B 369 -36.803 -20.097 -32.929 1.00 20.82 O
ATOM 13835 N GLU B 370 -38.668 -19.453 -31.863 1.00 21.80 N
ATOM 13836 CA GLU B 370 -39.480 -19.512 -33.087 1.00 22.73 C
ATOM 13838 CB GLU B 370 -40.996 -19.518 -32.801 1.00 23.18 C
ATOM 13841 CG GLU B 370 -41.449 -20.608 -31.809 1.00 25.92 C
ATOM 13844 CD GLU B 370 -42.927 -21.064 -31.957 1.00 29.74 C
ATOM 13845 OE1 GLU B 370 -43.840 -20.191 -32.101 1.00 30.13 O
ATOM 13846 OE2 GLU B 370 -43.156 -22.316 -31.892 1.00 31.94 O
ATOM 13847 C GLU B 370 -39.079 -18.358 -34.016 1.00 22.62 C
ATOM 13848 O GLU B 370 -38.933 -18.565 -35.221 1.00 22.53 O
ATOM 13850 N ALA B 371 -38.864 -17.166 -33.456 1.00 22.65 N
ATOM 13851 CA ALA B 371 -38.427 -16.023 -34.254 1.00 22.95 C
ATOM 13853 CB ALA B 371 -38.375 -14.753 -33.424 1.00 22.97 C
ATOM 13857 C ALA B 371 -37.070 -16.296 -34.891 1.00 23.13 C
ATOM 13858 O ALA B 371 -36.900 -16.063 -36.091 1.00 23.38 O
ATOM 13860 N LYS B 372 -36.113 -16.804 -34.107 1.00 23.15 N
ATOM 13861 CA LYS B 372 -34.776 -17.102 -34.640 1.00 23.10 C
ATOM 13863 CB LYS B 372 -33.808 -17.633 -33.575 1.00 22.85 C
ATOM 13866 CG LYS B 372 -33.414 -16.616 -32.514 1.00 24.28 C
ATOM 13869 CD LYS B 372 -31.973 -16.806 -31.969 1.00 26.34 C
ATOM 13872 CE LYS B 372 -31.919 -17.407 -30.544 1.00 27.84 C
ATOM 13875 NZ LYS B 372 -31.673 -16.405 -29.458 1.00 27.93 N
ATOM 13879 C LYS B 372 -34.887 -18.093 -35.790 1.00 23.16 C
ATOM 13880 O LYS B 372 -34.231 -17.920 -36.804 1.00 23.73 O
ATOM 13882 N TRP B 373 -35.720 -19.122 -35.658 1.00 23.11 N
ATOM 13883 CA TRP B 373 -35.844 -20.094 -36.742 1.00 22.99 C
ATOM 13885 CB TRP B 373 -36.746 -21.274 -36.370 1.00 22.71 C
ATOM 13888 CG TRP B 373 -36.081 -22.343 -35.562 1.00 20.71 C
ATOM 13889 CD1 TRP B 373 -34.770 -22.740 -35.623 1.00 19.89 C
ATOM 13891 NE1 TRP B 373 -34.540 -23.757 -34.734 1.00 19.05 N
ATOM 13893 CE2 TRP B 373 -35.715 -24.050 -34.090 1.00 18.91 C
ATOM 13894 CD2 TRP B 373 -36.707 -23.184 -34.599 1.00 18.41 C

ATOM 13895 CE3 TRP B 373 -38.007 -23.288 -34.105 1.00 15.66 C
ATOM 13897 CZ3 TRP B 373 -38.271 -24.216 -33.130 1.00 15.41 C
ATOM 13899 CH2 TRP B 373 -37.276 -25.069 -32.647 1.00 16.33 C
ATOM 13901 CZ2 TRP B 373 -35.994 -25.005 -33.112 1.00 17.53 C
ATOM 13903 C TRP B 373 -36.374 -19.416 -37.991 1.00 23.59 C
ATOM 13904 O TRP B 373 -35.878 -19.653 -39.096 1.00 23.60 O
ATOM 13906 N LEU B 374 -37.374 -18.559 -37.801 1.00 24.32 N
ATOM 13907 CA LEU B 374 -38.008 -17.859 -38.915 1.00 24.66 C
ATOM 13909 CB LEU B 374 -39.181 -17.019 -38.428 1.00 24.85 C
ATOM 13912 CG LEU B 374 -40.112 -16.449 -39.496 1.00 25.45 C
ATOM 13914 CD1 LEU B 374 -41.002 -17.535 -40.070 1.00 24.83 C
ATOM 13918 CD2 LEU B 374 -40.959 -15.293 -38.885 1.00 26.92 C
ATOM 13922 C LEU B 374 -37.009 -16.975 -39.618 1.00 24.64 C
ATOM 13923 O LEU B 374 -36.934 -16.992 -40.830 1.00 24.33 O
ATOM 13925 N TYR B 375 -36.232 -16.220 -38.850 1.00 25.09 N
ATOM 13926 CA TYR B 375 -35.283 -15.274 -39.433 1.00 25.71 C
ATOM 13928 CB TYR B 375 -34.534 -14.479 -38.349 1.00 25.91 C
ATOM 13931 CG TYR B 375 -33.536 -13.468 -38.892 1.00 27.11 C
ATOM 13932 CD1 TYR B 375 -33.950 -12.200 -39.305 1.00 27.98 C
ATOM 13934 CE1 TYR B 375 -33.039 -11.271 -39.811 1.00 28.61 C
ATOM 13936 CZ TYR B 375 -31.693 -11.605 -39.904 1.00 29.13 C
ATOM 13937 OH TYR B 375 -30.790 -10.685 -40.397 1.00 29.83 O
ATOM 13939 CE2 TYR B 375 -31.256 -12.863 -39.501 1.00 28.79 C
ATOM 13941 CD2 TYR B 375 -32.177 -13.783 -38.995 1.00 28.03 C
ATOM 13943 C TYR B 375 -34.305 -16.036 -40.301 1.00 25.64 C
ATOM 13944 O TYR B 375 -34.201 -15.788 -41.503 1.00 25.74 O
ATOM 13946 N ASN B 376 -33.635 -17.000 -39.685 1.00 25.73 N
ATOM 13947 CA ASN B 376 -32.599 -17.777 -40.346 1.00 25.78 C
ATOM 13949 CB ASN B 376 -31.739 -18.497 -39.303 1.00 25.73 C
ATOM 13952 CG ASN B 376 -31.155 -17.565 -38.273 1.00 25.13 C
ATOM 13953 OD1 ASN B 376 -30.491 -16.590 -38.601 1.00 25.53 O
ATOM 13954 ND2 ASN B 376 -31.389 -17.874 -37.013 1.00 24.64 N
ATOM 13957 C ASN B 376 -33.126 -18.824 -41.332 1.00 26.04 C
ATOM 13958 O ASN B 376 -32.343 -19.644 -41.807 1.00 26.36 O
ATOM 13960 N LYS B 377 -34.428 -18.824 -41.632 1.00 26.16 N
ATOM 13961 CA LYS B 377 -35.012 -19.811 -42.552 1.00 26.27 C
ATOM 13963 CB LYS B 377 -34.575 -19.538 -44.010 1.00 26.51 C
ATOM 13966 CG LYS B 377 -35.470 -18.561 -44.802 1.00 28.01 C
ATOM 13969 CD LYS B 377 -34.629 -17.592 -45.667 1.00 29.99 C
ATOM 13972 CE LYS B 377 -35.493 -16.605 -46.465 1.00 31.02 C
ATOM 13975 NZ LYS B 377 -36.420 -15.819 -45.589 1.00 32.17 N
ATOM 13979 C LYS B 377 -34.647 -21.243 -42.150 1.00 25.93 C
ATOM 13980 O LYS B 377 -34.380 -22.084 -43.003 1.00 25.82 O
ATOM 13982 N SER B 378 -34.637 -21.522 -40.852 1.00 25.65 N
ATOM 13983 CA SER B 378 -34.324 -22.860 -40.385 1.00 25.54 C
ATOM 13985 CB SER B 378 -34.132 -22.877 -38.882 1.00 25.41 C
ATOM 13988 OG SER B 378 -32.905 -22.269 -38.570 1.00 25.67 O
ATOM 13990 C SER B 378 -35.412 -23.838 -40.790 1.00 25.62 C
ATOM 13991 O SER B 378 -36.495 -23.435 -41.199 1.00 25.70 O
ATOM 13993 N THR B 379 -35.108 -25.129 -40.690 1.00 25.66 N
ATOM 13994 CA THR B 379 -36.038 -26.175 -41.097 1.00 25.55 C
ATOM 13996 CB THR B 379 -35.788 -26.635 -42.546 1.00 25.59 C
ATOM 13998 OG1 THR B 379 -34.391 -26.899 -42.736 1.00 25.46 O
ATOM 14000 CG2 THR B 379 -36.255 -25.574 -43.528 1.00 25.88 C
ATOM 14004 C THR B 379 -35.886 -27.348 -40.160 1.00 25.45 C
ATOM 14005 O THR B 379 -35.372 -28.393 -40.548 1.00 25.70 O
ATOM 14007 N PRO B 380 -36.335 -27.179 -38.915 1.00 25.37 N
ATOM 14008 CA PRO B 380 -36.144 -28.182 -37.876 1.00 25.22 C
ATOM 14010 CB PRO B 380 -36.500 -27.437 -36.583 1.00 25.19 C
ATOM 14013 CG PRO B 380 -36.643 -26.021 -36.955 1.00 25.83 C

ATOM 14016 CD PRO B 380 -37.025 -25.998 -38.390 1.00 25.71 C
ATOM 14019 C PRO B 380 -37.052 -29.379 -38.009 1.00 24.82 C
ATOM 14020 O PRO B 380 -38.143 -29.280 -38.575 1.00 24.84 O
ATOM 14021 N THR B 381 -36.607 -30.493 -37.436 1.00 24.42 N
ATOM 14022 CA THR B 381 -37.386 -31.712 -37.429 1.00 23.99 C
ATOM 14024 CB THR B 381 -36.614 -32.873 -36.789 1.00 23.99 C
ATOM 14026 OG1 THR B 381 -36.339 -32.575 -35.418 1.00 24.02 O
ATOM 14028 CG2 THR B 381 -35.302 -33.117 -37.524 1.00 23.76 C
ATOM 14032 C THR B 381 -38.649 -31.461 -36.636 1.00 23.78 C
ATOM 14033 O THR B 381 -38.700 -30.548 -35.813 1.00 23.89 O
ATOM 14035 N PHE B 382 -39.672 -32.267 -36.889 1.00 23.53 N
ATOM 14036 CA PHE B 382 -40.905 -32.204 -36.105 1.00 22.97 C
ATOM 14038 CB PHE B 382 -41.870 -33.305 -36.527 1.00 22.89 C
ATOM 14041 CG PHE B 382 -43.079 -33.394 -35.655 1.00 22.26 C
ATOM 14042 CD1 PHE B 382 -44.189 -32.601 -35.910 1.00 21.65 C
ATOM 14044 CE1 PHE B 382 -45.300 -32.672 -35.099 1.00 20.87 C
ATOM 14046 CZ PHE B 382 -45.310 -33.534 -34.016 1.00 20.36 C
ATOM 14048 CE2 PHE B 382 -44.204 -34.317 -33.744 1.00 20.52 C
ATOM 14050 CD2 PHE B 382 -43.098 -34.243 -34.556 1.00 21.17 C
ATOM 14052 C PHE B 382 -40.677 -32.329 -34.605 1.00 22.69 C
ATOM 14053 O PHE B 382 -41.341 -31.657 -33.834 1.00 22.44 O
ATOM 14055 N ASP B 383 -39.764 -33.205 -34.191 1.00 22.52 N
ATOM 14056 CA ASP B 383 -39.491 -33.375 -32.765 1.00 22.50 C
ATOM 14058 CB ASP B 383 -38.531 -34.525 -32.527 1.00 22.43 C
ATOM 14061 CG ASP B 383 -39.174 -35.863 -32.711 1.00 22.71 C
ATOM 14062 OD1 ASP B 383 -40.359 -35.945 -33.074 1.00 22.89 O
ATOM 14063 OD2 ASP B 383 -38.470 -36.856 -32.492 1.00 25.17 O
ATOM 14064 C ASP B 383 -38.954 -32.116 -32.091 1.00 22.43 C
ATOM 14065 O ASP B 383 -39.438 -31.758 -31.014 1.00 22.40 O
ATOM 14067 N ASP B 384 -37.966 -31.464 -32.713 1.00 22.37 N
ATOM 14068 CA ASP B 384 -37.422 -30.191 -32.213 1.00 22.61 C
ATOM 14070 CB ASP B 384 -36.317 -29.648 -33.124 1.00 22.82 C
ATOM 14073 CG ASP B 384 -34.963 -30.208 -32.807 1.00 23.40 C
ATOM 14074 OD1 ASP B 384 -34.847 -30.973 -31.832 1.00 25.33 O
ATOM 14075 OD2 ASP B 384 -34.009 -29.891 -33.545 1.00 24.26 O
ATOM 14076 C ASP B 384 -38.482 -29.113 -32.130 1.00 22.56 C
ATOM 14077 O ASP B 384 -38.598 -28.429 -31.108 1.00 22.48 O
ATOM 14079 N TYR B 385 -39.227 -28.963 -33.227 1.00 22.36 N
ATOM 14080 CA TYR B 385 -40.170 -27.870 -33.402 1.00 22.18 C
ATOM 14082 CB TYR B 385 -40.738 -27.867 -34.812 1.00 22.05 C
ATOM 14085 CG TYR B 385 -41.818 -26.834 -35.019 1.00 22.60 C
ATOM 14086 CD1 TYR B 385 -41.493 -25.553 -35.437 1.00 23.64 C
ATOM 14088 CE1 TYR B 385 -42.462 -24.580 -35.630 1.00 25.00 C
ATOM 14090 CZ TYR B 385 -43.788 -24.882 -35.410 1.00 26.86 C
ATOM 14091 OH TYR B 385 -44.734 -23.883 -35.622 1.00 28.48 O
ATOM 14093 CE2 TYR B 385 -44.149 -26.171 -34.980 1.00 25.95 C
ATOM 14095 CD2 TYR B 385 -43.158 -27.133 -34.790 1.00 23.94 C
ATOM 14097 C TYR B 385 -41.319 -27.986 -32.446 1.00 22.13 C
ATOM 14098 O TYR B 385 -41.703 -27.017 -31.808 1.00 22.95 O
ATOM 14100 N PHE B 386 -41.899 -29.169 -32.380 1.00 21.80 N
ATOM 14101 CA PHE B 386 -43.048 -29.394 -31.525 1.00 21.62 C
ATOM 14103 CB PHE B 386 -43.624 -30.795 -31.768 1.00 21.73 C
ATOM 14106 CG PHE B 386 -44.834 -31.104 -30.952 1.00 21.27 C
ATOM 14107 CD1 PHE B 386 -46.034 -30.447 -31.196 1.00 22.55 C
ATOM 14109 CE1 PHE B 386 -47.164 -30.732 -30.448 1.00 23.14 C
ATOM 14111 CZ PHE B 386 -47.095 -31.699 -29.446 1.00 23.20 C
ATOM 14113 CE2 PHE B 386 -45.896 -32.358 -29.208 1.00 21.57 C
ATOM 14115 CD2 PHE B 386 -44.781 -32.057 -29.959 1.00 20.29 C
ATOM 14117 C PHE B 386 -42.630 -29.226 -30.073 1.00 21.34 C
ATOM 14118 O PHE B 386 -43.353 -28.639 -29.284 1.00 21.44 O

ATOM 14120 N GLY B 387 -41.447 -29.725 -29.736 1.00 20.84 N
ATOM 14121 CA GLY B 387 -40.935 -29.618 -28.387 1.00 20.57 C
ATOM 14124 C GLY B 387 -40.854 -28.186 -27.916 1.00 20.26 C
ATOM 14125 O GLY B 387 -40.930 -27.908 -26.724 1.00 20.86 O
ATOM 14127 N ASN B 388 -40.691 -27.268 -28.852 1.00 19.81 N
ATOM 14128 CA ASN B 388 -40.758 -25.853 -28.536 1.00 19.51 C
ATOM 14130 CB ASN B 388 -39.877 -25.086 -29.508 1.00 19.42 C
ATOM 14133 CG ASN B 388 -39.593 -23.700 -29.045 1.00 19.26 C
ATOM 14134 OD1 ASN B 388 -38.916 -23.513 -28.038 1.00 18.93 O
ATOM 14135 ND2 ASN B 388 -40.105 -22.709 -29.774 1.00 17.99 N
ATOM 14138 C ASN B 388 -42.200 -25.320 -28.604 1.00 19.41 C
ATOM 14139 O ASN B 388 -42.591 -24.447 -27.833 1.00 19.58 O
ATOM 14141 N ALA B 389 -42.989 -25.848 -29.532 1.00 19.11 N
ATOM 14142 CA ALA B 389 -44.313 -25.307 -29.808 1.00 18.87 C
ATOM 14144 CB ALA B 389 -44.897 -25.949 -31.060 1.00 18.87 C
ATOM 14148 C ALA B 389 -45.264 -25.460 -28.634 1.00 18.51 C
ATOM 14149 O ALA B 389 -45.916 -24.511 -28.262 1.00 18.33 O
ATOM 14151 N TRP B 390 -45.344 -26.652 -28.054 1.00 18.73 N
ATOM 14152 CA TRP B 390 -46.258 -26.887 -26.935 1.00 18.74 C
ATOM 14154 CB TRP B 390 -46.389 -28.377 -26.569 1.00 18.75 C
ATOM 14157 CG TRP B 390 -45.166 -29.122 -26.019 1.00 18.46 C
ATOM 14158 CD1 TRP B 390 -44.390 -30.001 -26.705 1.00 18.75 C
ATOM 14160 NE1 TRP B 390 -43.417 -30.519 -25.897 1.00 17.56 N
ATOM 14162 CE2 TRP B 390 -43.559 -30.005 -24.642 1.00 16.67 C
ATOM 14163 CD2 TRP B 390 -44.661 -29.124 -24.674 1.00 17.50 C
ATOM 14164 CE3 TRP B 390 -45.008 -28.448 -23.505 1.00 18.38 C
ATOM 14166 CZ3 TRP B 390 -44.251 -28.685 -22.347 1.00 18.34 C
ATOM 14168 CH2 TRP B 390 -43.164 -29.573 -22.361 1.00 16.75 C
ATOM 14170 CZ2 TRP B 390 -42.805 -30.234 -23.495 1.00 15.75 C
ATOM 14172 C TRP B 390 -45.861 -26.066 -25.727 1.00 18.91 C
ATOM 14173 O TRP B 390 -46.707 -25.691 -24.919 1.00 19.02 O
ATOM 14175 N LYS B 391 -44.570 -25.787 -25.612 1.00 18.95 N
ATOM 14176 CA LYS B 391 -44.085 -24.810 -24.643 1.00 18.85 C
ATOM 14178 CB LYS B 391 -42.544 -24.888 -24.508 1.00 19.52 C
ATOM 14181 CG LYS B 391 -42.023 -25.373 -23.143 1.00 21.17 C
ATOM 14184 CD LYS B 391 -40.516 -25.689 -23.191 1.00 22.87 C
ATOM 14187 CE LYS B 391 -40.251 -27.159 -23.508 1.00 23.91 C
ATOM 14190 NZ LYS B 391 -38.938 -27.354 -24.191 1.00 25.44 N
ATOM 14194 C LYS B 391 -44.537 -23.400 -25.032 1.00 17.57 C
ATOM 14195 O LYS B 391 -44.937 -22.629 -24.180 1.00 17.66 O
ATOM 14197 N SER B 392 -44.490 -23.068 -26.314 1.00 16.65 N
ATOM 14198 CA SER B 392 -44.879 -21.718 -26.764 1.00 16.27 C
ATOM 14200 CB SER B 392 -44.241 -21.375 -28.119 1.00 16.22 C
ATOM 14203 OG SER B 392 -44.937 -21.969 -29.207 1.00 15.94 O
ATOM 14205 C SER B 392 -46.384 -21.504 -26.866 1.00 15.87 C
ATOM 14206 O SER B 392 -46.825 -20.395 -27.093 1.00 15.56 O
ATOM 14208 N SER B 393 -47.167 -22.568 -26.724 1.00 15.92 N
ATOM 14209 CA SER B 393 -48.629 -22.474 -26.718 1.00 15.80 C
ATOM 14211 CB SER B 393 -49.240 -23.867 -26.630 1.00 15.78 C
ATOM 14214 OG SER B 393 -49.025 -24.426 -25.348 1.00 15.00 O
ATOM 14216 C SER B 393 -49.097 -21.646 -25.533 1.00 15.94 C
ATOM 14217 O SER B 393 -50.115 -20.948 -25.599 1.00 15.60 O
ATOM 14219 N SER B 394 -48.296 -21.740 -24.471 1.00 16.14 N
ATOM 14220 CA SER B 394 -48.487 -21.091 -23.177 1.00 16.31 C
ATOM 14222 CB SER B 394 -49.062 -19.662 -23.271 1.00 16.18 C
ATOM 14225 OG SER B 394 -50.472 -19.649 -23.358 1.00 16.57 O
ATOM 14227 C SER B 394 -49.316 -22.006 -22.297 1.00 16.34 C
ATOM 14228 O SER B 394 -49.822 -21.595 -21.261 1.00 16.47 O
ATOM 14230 N GLY B 395 -49.403 -23.268 -22.702 1.00 16.55 N
ATOM 14231 CA GLY B 395 -50.103 -24.282 -21.927 1.00 16.79 C

ATOM 14234 C GLY B 395 -49.543 -24.391 -20.534 1.00 16.80 C
ATOM 14235 O GLY B 395 -50.222 -24.083 -19.556 1.00 16.74 O
ATOM 14237 N PRO B 396 -48.291 -24.824 -20.430 1.00 17.07 N
ATOM 14238 CA PRO B 396 -47.698 -24.930 -19.103 1.00 17.18 C
ATOM 14240 CB PRO B 396 -46.273 -25.399 -19.386 1.00 17.09 C
ATOM 14243 CG PRO B 396 -46.087 -25.237 -20.874 1.00 17.77 C
ATOM 14246 CD PRO B 396 -47.424 -25.390 -21.470 1.00 17.20 C
ATOM 14249 C PRO B 396 -47.707 -23.615 -18.313 1.00 17.17 C
ATOM 14250 O PRO B 396 -47.921 -23.644 -17.089 1.00 17.10 O
ATOM 14251 N LEU B 397 -47.499 -22.475 -18.983 1.00 17.04 N
ATOM 14252 CA LEU B 397 -47.513 -21.183 -18.261 1.00 16.77 C
ATOM 14254 CB LEU B 397 -47.116 -19.969 -19.135 1.00 16.84 C
ATOM 14257 CG LEU B 397 -47.145 -18.576 -18.458 1.00 16.91 C
ATOM 14259 CD1 LEU B 397 -46.577 -18.641 -17.096 1.00 18.36 C
ATOM 14263 CD2 LEU B 397 -46.373 -17.515 -19.196 1.00 16.88 C
ATOM 14267 C LEU B 397 -48.894 -20.988 -17.682 1.00 16.24 C
ATOM 14268 O LEU B 397 -49.051 -20.710 -16.494 1.00 16.09 O
ATOM 14270 N GLN B 398 -49.902 -21.173 -18.515 1.00 15.72 N
ATOM 14271 CA GLN B 398 -51.262 -21.093 -18.024 1.00 15.49 C
ATOM 14273 CB GLN B 398 -52.267 -21.387 -19.120 1.00 15.51 C
ATOM 14276 CG GLN B 398 -52.371 -20.275 -20.118 1.00 16.12 C
ATOM 14279 CD GLN B 398 -53.436 -20.545 -21.114 1.00 17.86 C
ATOM 14280 OE1 GLN B 398 -54.509 -21.028 -20.757 1.00 20.99 O
ATOM 14281 NE2 GLN B 398 -53.170 -20.239 -22.374 1.00 18.31 N
ATOM 14284 C GLN B 398 -51.471 -22.040 -16.873 1.00 15.03 C
ATOM 14285 O GLN B 398 -51.974 -21.638 -15.843 1.00 15.21 O
ATOM 14287 N LEU B 399 -51.065 -23.291 -17.022 1.00 14.72 N
ATOM 14288 CA LEU B 399 -51.361 -24.254 -15.978 1.00 14.65 C
ATOM 14290 CB LEU B 399 -51.201 -25.688 -16.475 1.00 14.44 C
ATOM 14293 CG LEU B 399 -52.250 -26.191 -17.478 1.00 14.28 C
ATOM 14295 CD1 LEU B 399 -51.907 -27.633 -17.846 1.00 15.50 C
ATOM 14299 CD2 LEU B 399 -53.713 -26.077 -16.986 1.00 10.96 C
ATOM 14303 C LEU B 399 -50.554 -23.995 -14.704 1.00 14.88 C
ATOM 14304 O LEU B 399 -51.100 -24.161 -13.618 1.00 15.21 O
ATOM 14306 N ILE B 400 -49.291 -23.562 -14.810 1.00 14.91 N
ATOM 14307 CA ILE B 400 -48.532 -23.174 -13.607 1.00 14.89 C
ATOM 14309 CB ILE B 400 -47.158 -22.574 -13.907 1.00 15.19 C
ATOM 14311 CG1 ILE B 400 -46.189 -23.674 -14.353 1.00 16.76 C
ATOM 14314 CD1 ILE B 400 -44.777 -23.162 -14.716 1.00 18.19 C
ATOM 14318 CG2 ILE B 400 -46.603 -21.906 -12.665 1.00 13.65 C
ATOM 14322 C ILE B 400 -49.288 -22.137 -12.819 1.00 14.77 C
ATOM 14323 O ILE B 400 -49.485 -22.302 -11.632 1.00 15.36 O
ATOM 14325 N PHE B 401 -49.717 -21.071 -13.486 1.00 14.59 N
ATOM 14326 CA PHE B 401 -50.491 -20.001 -12.844 1.00 14.22 C
ATOM 14328 CB PHE B 401 -50.825 -18.900 -13.845 1.00 14.12 C
ATOM 14331 CG PHE B 401 -49.803 -17.790 -13.872 1.00 13.83 C
ATOM 14332 CD1 PHE B 401 -50.012 -16.623 -13.173 1.00 12.77 C
ATOM 14334 CE1 PHE B 401 -49.074 -15.629 -13.189 1.00 13.09 C
ATOM 14336 CZ PHE B 401 -47.906 -15.781 -13.902 1.00 12.96 C
ATOM 14338 CE2 PHE B 401 -47.684 -16.928 -14.592 1.00 12.86 C
ATOM 14340 CD2 PHE B 401 -48.622 -17.932 -14.574 1.00 13.30 C
ATOM 14342 C PHE B 401 -51.765 -20.478 -12.212 1.00 14.26 C
ATOM 14343 O PHE B 401 -52.184 -19.944 -11.207 1.00 13.90 O
ATOM 14345 N ALA B 402 -52.377 -21.480 -12.828 1.00 15.09 N
ATOM 14346 CA ALA B 402 -53.641 -22.054 -12.364 1.00 15.76 C
ATOM 14348 CB ALA B 402 -54.264 -22.899 -13.454 1.00 15.57 C
ATOM 14352 C ALA B 402 -53.417 -22.896 -11.129 1.00 16.63 C
ATOM 14353 O ALA B 402 -54.284 -22.970 -10.259 1.00 17.00 O
ATOM 14355 N TYR B 403 -52.253 -23.544 -11.060 1.00 17.50 N
ATOM 14356 CA TYR B 403 -51.885 -24.317 -9.894 1.00 17.86 C

ATOM 14358 CB TYR B 403 -50.486 -24.911 -10.038 1.00 17.73 C
ATOM 14361 CG TYR B 403 -50.006 -25.576 -8.764 1.00 18.24 C
ATOM 14362 CD1 TYR B 403 -50.401 -26.867 -8.436 1.00 18.12 C
ATOM 14364 CE1 TYR B 403 -49.971 -27.476 -7.273 1.00 18.07 C
ATOM 14366 CZ TYR B 403 -49.145 -26.790 -6.409 1.00 18.62 C
ATOM 14367 OH TYR B 403 -48.727 -27.383 -5.244 1.00 17.70 O
ATOM 14369 CE2 TYR B 403 -48.748 -25.499 -6.703 1.00 18.93 C
ATOM 14371 CD2 TYR B 403 -49.177 -24.901 -7.876 1.00 18.88 C
ATOM 14373 C TYR B 403 -51.966 -23.461 -8.630 1.00 18.48 C
ATOM 14374 O TYR B 403 -52.494 -23.908 -7.616 1.00 18.66 O
ATOM 14376 N PHE B 404 -51.468 -22.232 -8.682 1.00 18.91 N
ATOM 14377 CA PHE B 404 -51.400 -21.430 -7.468 1.00 19.53 C
ATOM 14379 CB PHE B 404 -50.395 -20.325 -7.644 1.00 19.35 C
ATOM 14382 CG PHE B 404 -49.014 -20.808 -7.799 1.00 18.79 C
ATOM 14383 CD1 PHE B 404 -48.311 -21.246 -6.701 1.00 17.67 C
ATOM 14385 CE1 PHE B 404 -47.001 -21.683 -6.832 1.00 18.44 C
ATOM 14387 CZ PHE B 404 -46.384 -21.688 -8.078 1.00 18.44 C
ATOM 14389 CE2 PHE B 404 -47.083 -21.245 -9.190 1.00 18.79 C
ATOM 14391 CD2 PHE B 404 -48.396 -20.805 -9.047 1.00 18.90 C
ATOM 14393 C PHE B 404 -52.733 -20.817 -7.072 1.00 20.49 C
ATOM 14394 O PHE B 404 -52.925 -20.389 -5.924 1.00 19.95 O
ATOM 14396 N ALA B 405 -53.636 -20.756 -8.043 1.00 21.92 N
ATOM 14397 CA ALA B 405 -54.918 -20.106 -7.872 1.00 23.09 C
ATOM 14399 CB ALA B 405 -55.333 -19.426 -9.167 1.00 23.15 C
ATOM 14403 C ALA B 405 -55.959 -21.113 -7.446 1.00 24.23 C
ATOM 14404 O ALA B 405 -57.003 -20.726 -6.925 1.00 24.33 O
ATOM 14406 N VAL B 406 -55.657 -22.399 -7.662 1.00 25.80 N
ATOM 14407 CA VAL B 406 -56.569 -23.511 -7.355 1.00 26.88 C
ATOM 14409 CB VAL B 406 -56.640 -24.514 -8.512 1.00 26.64 C
ATOM 14411 CG1 VAL B 406 -57.132 -25.854 -8.012 1.00 27.24 C
ATOM 14415 CG2 VAL B 406 -57.547 -23.986 -9.593 1.00 26.45 C
ATOM 14419 C VAL B 406 -56.161 -24.266 -6.094 1.00 27.91 C
ATOM 14420 O VAL B 406 -56.932 -24.345 -5.155 1.00 28.28 O
ATOM 14422 N VAL B 407 -54.954 -24.825 -6.087 1.00 29.25 N
ATOM 14423 CA VAL B 407 -54.443 -25.573 -4.941 1.00 30.16 C
ATOM 14425 CB VAL B 407 -53.128 -26.276 -5.279 1.00 30.04 C
ATOM 14427 CG1 VAL B 407 -52.482 -26.831 -4.032 1.00 30.42 C
ATOM 14431 CG2 VAL B 407 -53.378 -27.376 -6.280 1.00 30.14 C
ATOM 14435 C VAL B 407 -54.208 -24.646 -3.755 1.00 31.34 C
ATOM 14436 O VAL B 407 -53.535 -23.618 -3.876 1.00 31.46 O
ATOM 14438 N GLN B 408 -54.753 -25.032 -2.604 1.00 32.63 N
ATOM 14439 CA GLN B 408 -54.727 -24.191 -1.417 1.00 33.51 C
ATOM 14441 CB GLN B 408 -55.891 -24.572 -.514 1.00 33.84 C
ATOM 14444 CG GLN B 408 -56.161 -23.548 .577 1.00 35.49 C
ATOM 14447 CD GLN B 408 -57.623 -23.161 .656 1.00 37.61 C
ATOM 14448 OE1 GLN B 408 -58.519 -24.006 .501 1.00 38.23 O
ATOM 14449 NE2 GLN B 408 -57.876 -21.874 .893 1.00 38.64 N
ATOM 14452 C GLN B 408 -53.399 -24.274 -.647 1.00 33.72 C
ATOM 14453 O GLN B 408 -52.852 -23.253 -.204 1.00 33.52 O
ATOM 14455 N ASN B 409 -52.889 -25.491 -.490 1.00 33.95 N
ATOM 14456 CA ASN B 409 -51.642 -25.707 .226 1.00 34.16 C
ATOM 14458 CB ASN B 409 -51.865 -26.665 1.391 1.00 34.25 C
ATOM 14461 CG ASN B 409 -52.756 -26.069 2.459 1.00 34.39 C
ATOM 14462 OD1 ASN B 409 -52.269 -25.577 3.480 1.00 34.40 O
ATOM 14463 ND2 ASN B 409 -54.070 -26.089 2.222 1.00 34.12 N
ATOM 14466 C ASN B 409 -50.582 -26.244 -.709 1.00 34.12 C
ATOM 14467 O ASN B 409 -50.578 -27.422 -1.046 1.00 34.41 O
ATOM 14469 N ILE B 410 -49.681 -25.369 -1.127 1.00 34.07 N
ATOM 14470 CA ILE B 410 -48.699 -25.718 -2.138 1.00 34.08 C
ATOM 14472 CB ILE B 410 -48.138 -24.455 -2.840 1.00 34.15 C

ATOM 14474 CG1 ILE B 410 -47.274 -23.610 -1.891 1.00 34.26 C
ATOM 14477 CD1 ILE B 410 -47.216 -22.139 -2.249 1.00 34.10 C
ATOM 14481 CG2 ILE B 410 -49.290 -23.634 -3.404 1.00 34.49 C
ATOM 14485 C ILE B 410 -47.586 -26.553 -1.533 1.00 33.93 C
ATOM 14486 O ILE B 410 -47.181 -26.317 -.405 1.00 33.80 O
ATOM 14488 N LYS B 411 -47.123 -27.546 -2.285 1.00 34.12 N
ATOM 14489 CA LYS B 411 -46.012 -28.395 -1.874 1.00 34.45 C
ATOM 14491 CB LYS B 411 -46.414 -29.873 -1.907 1.00 34.67 C
ATOM 14494 CG LYS B 411 -47.850 -30.130 -1.460 1.00 35.79 C
ATOM 14497 CD LYS B 411 -48.102 -31.586 -1.052 1.00 37.60 C
ATOM 14500 CE LYS B 411 -49.450 -31.728 -.309 1.00 38.80 C
ATOM 14503 NZ LYS B 411 -49.568 -32.992 .488 1.00 39.20 N
ATOM 14507 C LYS B 411 -44.843 -28.132 -2.810 1.00 34.33 C
ATOM 14508 O LYS B 411 -45.038 -27.956 -4.006 1.00 34.14 O
ATOM 14510 N LYS B 412 -43.631 -28.102 -2.265 1.00 34.50 N
ATOM 14511 CA LYS B 412 -42.460 -27.688 -3.042 1.00 34.69 C
ATOM 14513 CB LYS B 412 -41.242 -27.398 -2.154 1.00 35.13 C
ATOM 14516 CG LYS B 412 -41.205 -25.960 -1.613 1.00 36.90 C
ATOM 14519 CD LYS B 412 -40.079 -25.749 -.588 1.00 38.57 C
ATOM 14522 CE LYS B 412 -40.546 -24.852 .555 1.00 39.55 C
ATOM 14525 NZ LYS B 412 -39.491 -24.644 1.587 1.00 40.83 N
ATOM 14529 C LYS B 412 -42.075 -28.687 -4.103 1.00 34.13 C
ATOM 14530 O LYS B 412 -41.468 -28.308 -5.093 1.00 34.21 O
ATOM 14532 N GLU B 413 -42.408 -29.958 -3.910 1.00 33.54 N
ATOM 14533 CA GLU B 413 -42.095 -30.949 -4.933 1.00 33.19 C
ATOM 14535 CB GLU B 413 -41.886 -32.335 -4.330 1.00 33.44 C
ATOM 14538 CG GLU B 413 -43.127 -33.037 -3.807 1.00 34.37 C
ATOM 14541 CD GLU B 413 -42.834 -34.490 -3.499 1.00 35.56 C
ATOM 14542 OE1 GLU B 413 -42.662 -35.264 -4.471 1.00 35.30 O
ATOM 14543 OE2 GLU B 413 -42.751 -34.847 -2.297 1.00 36.69 O
ATOM 14544 C GLU B 413 -43.157 -30.965 -6.029 1.00 32.47 C
ATOM 14545 O GLU B 413 -42.846 -31.232 -7.193 1.00 32.28 O
ATOM 14547 N GLU B 414 -44.403 -30.676 -5.652 1.00 31.58 N
ATOM 14548 CA GLU B 414 -45.482 -30.512 -6.614 1.00 30.99 C
ATOM 14550 CB GLU B 414 -46.781 -30.101 -5.927 1.00 30.98 C
ATOM 14553 CG GLU B 414 -47.732 -31.245 -5.642 1.00 31.82 C
ATOM 14556 CD GLU B 414 -49.100 -30.774 -5.138 1.00 34.29 C
ATOM 14557 OE1 GLU B 414 -49.258 -29.581 -4.777 1.00 35.53 O
ATOM 14558 OE2 GLU B 414 -50.036 -31.603 -5.101 1.00 36.44 O
ATOM 14559 C GLU B 414 -45.104 -29.455 -7.628 1.00 30.59 C
ATOM 14560 O GLU B 414 -45.169 -29.687 -8.828 1.00 30.37 O
ATOM 14562 N ILE B 415 -44.684 -28.295 -7.140 1.00 30.49 N
ATOM 14563 CA ILE B 415 -44.367 -27.177 -8.028 1.00 30.40 C
ATOM 14565 CB ILE B 415 -44.412 -25.797 -7.320 1.00 30.40 C
ATOM 14567 CG1 ILE B 415 -43.235 -25.589 -6.388 1.00 30.36 C
ATOM 14570 CD1 ILE B 415 -43.373 -24.313 -5.611 1.00 31.01 C
ATOM 14574 CG2 ILE B 415 -45.686 -25.644 -6.523 1.00 30.85 C
ATOM 14578 C ILE B 415 -43.037 -27.347 -8.730 1.00 30.12 C
ATOM 14579 O ILE B 415 -42.870 -26.865 -9.840 1.00 30.42 O
ATOM 14581 N GLU B 416 -42.095 -28.030 -8.099 1.00 29.75 N
ATOM 14582 CA GLU B 416 -40.799 -28.249 -8.719 1.00 29.70 C
ATOM 14584 CB GLU B 416 -39.825 -28.777 -7.690 1.00 30.02 C
ATOM 14587 CG GLU B 416 -38.386 -28.426 -7.948 1.00 31.20 C
ATOM 14590 CD GLU B 416 -37.523 -28.839 -6.776 1.00 32.91 C
ATOM 14591 OE1 GLU B 416 -38.008 -28.723 -5.632 1.00 32.37 O
ATOM 14592 OE2 GLU B 416 -36.377 -29.294 -6.994 1.00 35.31 O
ATOM 14593 C GLU B 416 -40.917 -29.222 -9.890 1.00 29.24 C
ATOM 14594 O GLU B 416 -40.121 -29.177 -10.835 1.00 28.86 O
ATOM 14596 N ASN B 417 -41.915 -30.097 -9.819 1.00 28.81 N
ATOM 14597 CA ASN B 417 -42.252 -30.960 -10.941 1.00 28.66 C

ATOM 14599 CB ASN B 417 -43.165 -32.105 -10.503 1.00 28.72 C
ATOM 14602 CG ASN B 417 -42.379 -33.285 -9.973 1.00 29.78 C
ATOM 14603 OD1 ASN B 417 -41.887 -34.108 -10.744 1.00 30.39 O
ATOM 14604 ND2 ASN B 417 -42.223 -33.358 -8.653 1.00 31.45 N
ATOM 14607 C ASN B 417 -42.888 -30.183 -12.067 1.00 28.32 C
ATOM 14608 O ASN B 417 -42.611 -30.456 -13.232 1.00 27.95 O
ATOM 14610 N LEU B 418 -43.740 -29.217 -11.713 1.00 28.23 N
ATOM 14611 CA LEU B 418 -44.349 -28.313 -12.697 1.00 27.92 C
ATOM 14613 CB LEU B 418 -45.298 -27.320 -12.023 1.00 27.48 C
ATOM 14616 CG LEU B 418 -46.636 -27.896 -11.553 1.00 27.02 C
ATOM 14618 CD1 LEU B 418 -47.393 -26.882 -10.691 1.00 26.70 C
ATOM 14622 CD2 LEU B 418 -47.499 -28.355 -12.720 1.00 25.90 C
ATOM 14626 C LEU B 418 -43.275 -27.567 -13.491 1.00 28.20 C
ATOM 14627 O LEU B 418 -43.310 -27.541 -14.733 1.00 27.90 O
ATOM 14629 N GLN B 419 -42.308 -26.995 -12.770 1.00 28.43 N
ATOM 14630 CA GLN B 419 -41.170 -26.315 -13.395 1.00 28.72 C
ATOM 14632 CB GLN B 419 -40.223 -25.746 -12.347 1.00 28.81 C
ATOM 14635 CG GLN B 419 -40.592 -24.332 -11.946 1.00 30.14 C
ATOM 14638 CD GLN B 419 -39.535 -23.671 -11.092 1.00 32.05 C
ATOM 14639 OE1 GLN B 419 -39.246 -22.477 -11.257 1.00 33.88 O
ATOM 14640 NE2 GLN B 419 -38.948 -24.437 -10.170 1.00 31.84 N
ATOM 14643 C GLN B 419 -40.390 -27.179 -14.370 1.00 28.83 C
ATOM 14644 O GLN B 419 -39.922 -26.668 -15.386 1.00 28.72 O
ATOM 14646 N LYS B 420 -40.265 -28.475 -14.067 1.00 29.21 N
ATOM 14647 CA LYS B 420 -39.613 -29.451 -14.968 1.00 29.26 C
ATOM 14649 CB LYS B 420 -38.924 -30.555 -14.143 1.00 29.42 C
ATOM 14652 CG LYS B 420 -37.800 -30.052 -13.207 1.00 30.58 C
ATOM 14655 CD LYS B 420 -37.373 -31.113 -12.151 1.00 32.35 C
ATOM 14658 CE LYS B 420 -36.572 -30.506 -10.955 1.00 33.05 C
ATOM 14661 NZ LYS B 420 -36.520 -31.368 -9.702 1.00 32.62 N
ATOM 14665 C LYS B 420 -40.579 -30.057 -16.021 1.00 28.96 C
ATOM 14666 O LYS B 420 -40.216 -30.965 -16.753 1.00 28.66 O
ATOM 14668 N TYR B 421 -41.804 -29.543 -16.088 1.00 29.01 N
ATOM 14669 CA TYR B 421 -42.777 -29.893 -17.134 1.00 29.16 C
ATOM 14671 CB TYR B 421 -42.209 -29.602 -18.534 1.00 29.48 C
ATOM 14674 CG TYR B 421 -41.968 -28.127 -18.773 1.00 31.04 C
ATOM 14675 CD1 TYR B 421 -43.018 -27.219 -18.716 1.00 32.54 C
ATOM 14677 CE1 TYR B 421 -42.815 -25.878 -18.914 1.00 33.35 C
ATOM 14679 CZ TYR B 421 -41.556 -25.413 -19.193 1.00 34.56 C
ATOM 14680 OH TYR B 421 -41.377 -24.066 -19.384 1.00 37.99 O
ATOM 14682 CE2 TYR B 421 -40.490 -26.278 -19.267 1.00 33.56 C
ATOM 14684 CD2 TYR B 421 -40.702 -27.638 -19.051 1.00 32.75 C
ATOM 14686 C TYR B 421 -43.345 -31.311 -17.042 1.00 28.60 C
ATOM 14687 O TYR B 421 -43.395 -32.046 -18.025 1.00 28.49 O
ATOM 14689 N HIS B 422 -43.808 -31.662 -15.846 1.00 28.18 N
ATOM 14690 CA HIS B 422 -44.507 -32.919 -15.594 1.00 27.66 C
ATOM 14692 CB HIS B 422 -45.082 -32.914 -14.180 1.00 27.73 C
ATOM 14695 CG HIS B 422 -45.500 -34.264 -13.685 1.00 28.14 C
ATOM 14696 ND1 HIS B 422 -44.597 -35.195 -13.217 1.00 29.15 N
ATOM 14698 CE1 HIS B 422 -45.247 -36.277 -12.829 1.00 29.50 C
ATOM 14700 NE2 HIS B 422 -46.539 -36.078 -13.022 1.00 28.69 N
ATOM 14702 CD2 HIS B 422 -46.724 -34.827 -13.552 1.00 27.24 C
ATOM 14704 C HIS B 422 -45.650 -33.164 -16.575 1.00 27.29 C
ATOM 14705 O HIS B 422 -46.463 -32.269 -16.853 1.00 26.86 O
ATOM 14707 N ASP B 423 -45.712 -34.402 -17.060 1.00 26.96 N
ATOM 14708 CA ASP B 423 -46.772 -34.883 -17.952 1.00 26.78 C
ATOM 14710 CB ASP B 423 -46.792 -36.413 -17.939 1.00 27.01 C
ATOM 14713 CG ASP B 423 -45.594 -37.018 -18.646 1.00 28.21 C
ATOM 14714 OD1 ASP B 423 -45.100 -36.378 -19.602 1.00 31.33 O
ATOM 14715 OD2 ASP B 423 -45.153 -38.130 -18.262 1.00 28.39 O

ATOM 14716 C ASP B 423 -48.187 -34.383 -17.651 1.00 26.21 C
ATOM 14717 O ASP B 423 -49.015 -34.336 -18.556 1.00 26.75 O
ATOM 14719 N ILE B 424 -48.463 -34.042 -16.391 1.00 25.11 N
ATOM 14720 CA ILE B 424 -49.773 -33.553 -15.956 1.00 23.82 C
ATOM 14722 CB ILE B 424 -49.798 -33.310 -14.439 1.00 23.67 C
ATOM 14724 CG1 ILE B 424 -51.196 -32.990 -13.938 1.00 22.97 C
ATOM 14727 CD1 ILE B 424 -51.220 -32.693 -12.465 1.00 22.06 C
ATOM 14731 CG2 ILE B 424 -48.859 -32.171 -14.065 1.00 24.35 C
ATOM 14735 C ILE B 424 -50.102 -32.265 -16.669 1.00 23.08 C
ATOM 14736 O ILE B 424 -51.265 -32.025 -17.023 1.00 22.99 O
ATOM 14738 N ILE B 425 -49.082 -31.436 -16.886 1.00 22.22 N
ATOM 14739 CA ILE B 425 -49.282 -30.199 -17.633 1.00 21.61 C
ATOM 14741 CB ILE B 425 -48.796 -28.959 -16.848 1.00 21.18 C
ATOM 14743 CG1 ILE B 425 -47.279 -28.853 -16.804 1.00 19.47 C
ATOM 14746 CD1 ILE B 425 -46.850 -27.581 -16.140 1.00 18.00 C
ATOM 14750 CG2 ILE B 425 -49.357 -28.977 -15.428 1.00 20.75 C
ATOM 14754 C ILE B 425 -48.665 -30.255 -19.033 1.00 21.73 C
ATOM 14755 O ILE B 425 -49.100 -29.523 -19.912 1.00 21.75 O
ATOM 14757 N SER B 426 -47.686 -31.134 -19.258 1.00 21.74 N
ATOM 14758 CA SER B 426 -47.016 -31.174 -20.560 1.00 21.53 C
ATOM 14760 CB SER B 426 -45.639 -31.876 -20.516 1.00 21.66 C
ATOM 14763 OG SER B 426 -45.724 -33.281 -20.405 1.00 22.19 O
ATOM 14765 C SER B 426 -47.922 -31.798 -21.582 1.00 21.19 C
ATOM 14766 O SER B 426 -47.950 -31.358 -22.721 1.00 21.37 O
ATOM 14768 N ARG B 427 -48.692 -32.800 -21.177 1.00 20.91 N
ATOM 14769 CA ARG B 427 -49.532 -33.504 -22.143 1.00 20.78 C
ATOM 14771 CB ARG B 427 -50.038 -34.840 -21.616 1.00 20.94 C
ATOM 14774 CG ARG B 427 -49.006 -35.887 -21.874 1.00 22.76 C
ATOM 14777 CD ARG B 427 -49.158 -37.101 -21.025 1.00 26.75 C
ATOM 14780 NE ARG B 427 -47.960 -37.927 -21.185 1.00 29.36 N
ATOM 14782 CZ ARG B 427 -47.574 -38.887 -20.352 1.00 30.25 C
ATOM 14783 NH1 ARG B 427 -48.293 -39.179 -19.266 1.00 30.27 N
ATOM 14786 NH2 ARG B 427 -46.447 -39.547 -20.611 1.00 31.25 N
ATOM 14789 C ARG B 427 -50.646 -32.650 -22.668 1.00 20.07 C
ATOM 14790 O ARG B 427 -50.724 -32.466 -23.866 1.00 20.13 O
ATOM 14792 N PRO B 428 -51.482 -32.091 -21.786 1.00 19.38 N
ATOM 14793 CA PRO B 428 -52.533 -31.202 -22.264 1.00 19.05 C
ATOM 14795 CB PRO B 428 -53.046 -30.547 -20.990 1.00 19.13 C
ATOM 14798 CG PRO B 428 -52.696 -31.476 -19.918 1.00 19.55 C
ATOM 14801 CD PRO B 428 -51.443 -32.161 -20.319 1.00 19.20 C
ATOM 14804 C PRO B 428 -52.016 -30.135 -23.227 1.00 18.84 C
ATOM 14805 O PRO B 428 -52.688 -29.802 -24.205 1.00 18.73 O
ATOM 14806 N SER B 429 -50.828 -29.608 -22.964 1.00 18.57 N
ATOM 14807 CA SER B 429 -50.208 -28.679 -23.899 1.00 18.64 C
ATOM 14809 CB SER B 429 -48.960 -28.086 -23.291 1.00 18.46 C
ATOM 14812 OG SER B 429 -49.141 -27.980 -21.911 1.00 19.08 O
ATOM 14814 C SER B 429 -49.877 -29.315 -25.260 1.00 18.52 C
ATOM 14815 O SER B 429 -49.886 -28.633 -26.276 1.00 19.02 O
ATOM 14817 N HIS B 430 -49.579 -30.606 -25.297 1.00 18.29 N
ATOM 14818 CA HIS B 430 -49.457 -31.273 -26.583 1.00 18.25 C
ATOM 14820 CB HIS B 430 -49.085 -32.765 -26.467 1.00 18.40 C
ATOM 14823 CG HIS B 430 -47.753 -33.024 -25.806 1.00 19.41 C
ATOM 14824 ND1 HIS B 430 -46.776 -32.055 -25.657 1.00 19.55 N
ATOM 14826 CE1 HIS B 430 -45.729 -32.576 -25.043 1.00 17.77 C
ATOM 14828 NE2 HIS B 430 -45.981 -33.849 -24.800 1.00 18.52 N
ATOM 14830 CD2 HIS B 430 -47.232 -34.160 -25.277 1.00 19.19 C
ATOM 14832 C HIS B 430 -50.789 -31.105 -27.306 1.00 17.93 C
ATOM 14833 O HIS B 430 -50.816 -30.599 -28.417 1.00 18.54 O
ATOM 14835 N ILE B 431 -51.897 -31.479 -26.665 1.00 17.34 N
ATOM 14836 CA ILE B 431 -53.217 -31.372 -27.301 1.00 16.58 C

ATOM 14838 CB ILE B 431 -54.400 -31.738 -26.375 1.00 16.53 C
ATOM 14840 CG1 ILE B 431 -54.225 -33.123 -25.728 1.00 16.06 C
ATOM 14843 CD1 ILE B 431 -54.069 -34.212 -26.698 1.00 16.05 C
ATOM 14847 CG2 ILE B 431 -55.701 -31.666 -27.149 1.00 15.49 C
ATOM 14851 C ILE B 431 -53.431 -29.949 -27.748 1.00 16.35 C
ATOM 14852 O ILE B 431 -53.856 -29.712 -28.860 1.00 16.74 O
ATOM 14854 N PHE B 432 -53.110 -29.003 -26.881 1.00 16.15 N
ATOM 14855 CA PHE B 432 -53.353 -27.577 -27.145 1.00 16.19 C
ATOM 14857 CB PHE B 432 -52.811 -26.776 -25.956 1.00 16.36 C
ATOM 14860 CG PHE B 432 -53.007 -25.295 -26.043 1.00 16.54 C
ATOM 14861 CD1 PHE B 432 -53.869 -24.708 -26.946 1.00 16.55 C
ATOM 14863 CE1 PHE B 432 -54.007 -23.334 -26.974 1.00 17.89 C
ATOM 14865 CZ PHE B 432 -53.305 -22.538 -26.080 1.00 17.96 C
ATOM 14867 CE2 PHE B 432 -52.461 -23.114 -25.169 1.00 17.30 C
ATOM 14869 CD2 PHE B 432 -52.323 -24.482 -25.151 1.00 17.54 C
ATOM 14871 C PHE B 432 -52.726 -27.104 -28.452 1.00 15.93 C
ATOM 14872 O PHE B 432 -53.398 -26.525 -29.303 1.00 15.63 O
ATOM 14874 N ARG B 433 -51.438 -27.387 -28.594 1.00 15.79 N
ATOM 14875 CA ARG B 433 -50.674 -27.044 -29.778 1.00 15.74 C
ATOM 14877 CB ARG B 433 -49.196 -27.279 -29.470 1.00 15.68 C
ATOM 14880 CG ARG B 433 -48.259 -27.218 -30.665 1.00 16.39 C
ATOM 14883 CD ARG B 433 -48.348 -25.919 -31.388 1.00 16.27 C
ATOM 14886 NE ARG B 433 -47.969 -24.850 -30.492 1.00 17.34 N
ATOM 14888 CZ ARG B 433 -48.210 -23.565 -30.703 1.00 17.89 C
ATOM 14889 NH1 ARG B 433 -48.834 -23.142 -31.803 1.00 16.79 N
ATOM 14892 NH2 ARG B 433 -47.805 -22.701 -29.792 1.00 18.53 N
ATOM 14895 C ARG B 433 -51.114 -27.852 -31.011 1.00 15.85 C
ATOM 14896 O ARG B 433 -51.197 -27.328 -32.120 1.00 15.40 O
ATOM 14898 N LEU B 434 -51.381 -29.134 -30.813 1.00 16.18 N
ATOM 14899 CA LEU B 434 -51.794 -29.986 -31.902 1.00 16.58 C
ATOM 14901 CB LEU B 434 -51.802 -31.453 -31.468 1.00 16.79 C
ATOM 14904 CG LEU B 434 -50.408 -32.055 -31.232 1.00 17.49 C
ATOM 14906 CD1 LEU B 434 -50.486 -33.548 -30.864 1.00 16.63 C
ATOM 14910 CD2 LEU B 434 -49.511 -31.836 -32.467 1.00 18.00 C
ATOM 14914 C LEU B 434 -53.158 -29.559 -32.423 1.00 17.07 C
ATOM 14915 O LEU B 434 -53.333 -29.442 -33.633 1.00 17.44 O
ATOM 14917 N CYS B 435 -54.118 -29.308 -31.532 1.00 17.23 N
ATOM 14918 CA CYS B 435 -55.419 -28.778 -31.947 1.00 17.44 C
ATOM 14920 CB CYS B 435 -56.301 -28.529 -30.746 1.00 17.38 C
ATOM 14923 SG CYS B 435 -56.825 -29.993 -29.971 1.00 17.90 S
ATOM 14925 C CYS B 435 -55.295 -27.460 -32.696 1.00 17.78 C
ATOM 14926 O CYS B 435 -55.978 -27.232 -33.701 1.00 17.44 O
ATOM 14928 N ASN B 436 -54.442 -26.585 -32.178 1.00 18.31 N
ATOM 14929 CA ASN B 436 -54.248 -25.267 -32.769 1.00 19.14 C
ATOM 14931 CB ASN B 436 -53.392 -24.394 -31.844 1.00 19.31 C
ATOM 14934 CG ASN B 436 -52.984 -23.068 -32.478 1.00 20.07 C
ATOM 14935 OD1 ASN B 436 -53.456 -22.686 -33.555 1.00 22.72 O
ATOM 14936 ND2 ASN B 436 -52.099 -22.356 -31.800 1.00 20.90 N
ATOM 14939 C ASN B 436 -53.615 -25.345 -34.157 1.00 19.51 C
ATOM 14940 O ASN B 436 -54.173 -24.840 -35.131 1.00 19.79 O
ATOM 14942 N ASP B 437 -52.446 -25.965 -34.245 1.00 19.85 N
ATOM 14943 CA ASP B 437 -51.754 -26.058 -35.517 1.00 20.01 C
ATOM 14945 CB ASP B 437 -50.340 -26.638 -35.331 1.00 20.00 C
ATOM 14948 CG ASP B 437 -49.397 -25.675 -34.557 1.00 21.23 C
ATOM 14949 OD1 ASP B 437 -49.902 -24.749 -33.877 1.00 22.90 O
ATOM 14950 OD2 ASP B 437 -48.149 -25.821 -34.632 1.00 22.18 O
ATOM 14951 C ASP B 437 -52.629 -26.838 -36.512 1.00 20.00 C
ATOM 14952 O ASP B 437 -52.678 -26.491 -37.695 1.00 20.02 O
ATOM 14954 N LEU B 438 -53.372 -27.836 -36.021 1.00 20.02 N
ATOM 14955 CA LEU B 438 -54.352 -28.558 -36.858 1.00 20.18 C

ATOM 14957 CB LEU B 438 -55.144 -29.593 -36.049 1.00 19.88 C
ATOM 14960 CG LEU B 438 -54.699 -31.050 -36.142 1.00 18.97 C
ATOM 14962 CD1 LEU B 438 -55.537 -31.869 -35.200 1.00 18.86 C
ATOM 14966 CD2 LEU B 438 -54.818 -31.585 -37.550 1.00 16.23 C
ATOM 14970 C LEU B 438 -55.358 -27.644 -37.564 1.00 20.60 C
ATOM 14971 O LEU B 438 -55.717 -27.889 -38.712 1.00 20.30 O
ATOM 14973 N ALA B 439 -55.825 -26.620 -36.853 1.00 21.39 N
ATOM 14974 CA ALA B 439 -56.802 -25.654 -37.377 1.00 21.96 C
ATOM 14976 CB ALA B 439 -57.306 -24.741 -36.242 1.00 21.77 C
ATOM 14980 C ALA B 439 -56.214 -24.805 -38.494 1.00 22.47 C
ATOM 14981 O ALA B 439 -56.850 -24.559 -39.517 1.00 22.13 O
ATOM 14983 N SER B 440 -54.983 -24.370 -38.282 1.00 23.40 N
ATOM 14984 CA SER B 440 -54.337 -23.428 -39.169 1.00 24.40 C
ATOM 14986 CB SER B 440 -53.423 -22.529 -38.342 1.00 24.44 C
ATOM 14989 OG SER B 440 -52.994 -23.206 -37.166 1.00 25.19 O
ATOM 14991 C SER B 440 -53.544 -24.103 -40.289 1.00 25.15 C
ATOM 14992 O SER B 440 -53.093 -23.424 -41.210 1.00 25.24 O
ATOM 14994 N ALA B 441 -53.392 -25.428 -40.222 1.00 25.99 N
ATOM 14995 CA ALA B 441 -52.488 -26.160 -41.119 1.00 26.53 C
ATOM 14997 CB ALA B 441 -52.532 -27.655 -40.830 1.00 26.26 C
ATOM 15001 C ALA B 441 -52.726 -25.903 -42.608 1.00 27.31 C
ATOM 15002 O ALA B 441 -51.811 -25.489 -43.310 1.00 27.26 O
ATOM 15004 N SER B 442 -53.940 -26.134 -43.098 1.00 28.45 N
ATOM 15005 CA SER B 442 -54.138 -26.138 -44.545 1.00 29.47 C
ATOM 15007 CB SER B 442 -55.477 -26.769 -44.936 1.00 29.40 C
ATOM 15010 OG SER B 442 -56.454 -25.784 -45.181 1.00 30.36 O
ATOM 15012 C SER B 442 -53.966 -24.731 -45.125 1.00 30.22 C
ATOM 15013 O SER B 442 -53.304 -24.562 -46.139 1.00 30.26 O
ATOM 15015 N ALA B 443 -54.537 -23.729 -44.467 1.00 31.38 N
ATOM 15016 CA ALA B 443 -54.308 -22.333 -44.835 1.00 32.22 C
ATOM 15018 CB ALA B 443 -55.057 -21.410 -43.893 1.00 32.28 C
ATOM 15022 C ALA B 443 -52.820 -21.992 -44.818 1.00 33.12 C
ATOM 15023 O ALA B 443 -52.302 -21.419 -45.766 1.00 33.24 O
ATOM 15025 N GLU B 444 -52.136 -22.351 -43.736 1.00 34.43 N
ATOM 15026 CA GLU B 444 -50.711 -22.033 -43.582 1.00 35.35 C
ATOM 15028 CB GLU B 444 -50.237 -22.271 -42.134 1.00 35.46 C
ATOM 15031 CG GLU B 444 -50.757 -21.227 -41.126 1.00 36.42 C
ATOM 15034 CD GLU B 444 -50.178 -21.376 -39.708 1.00 37.82 C
ATOM 15035 OE1 GLU B 444 -49.965 -22.506 -39.224 1.00 37.92 O
ATOM 15036 OE2 GLU B 444 -49.955 -20.344 -39.049 1.00 40.09 O
ATOM 15037 C GLU B 444 -49.840 -22.794 -44.594 1.00 35.87 C
ATOM 15038 O GLU B 444 -48.870 -22.239 -45.107 1.00 35.85 O
ATOM 15040 N ILE B 445 -50.193 -24.048 -44.883 1.00 36.63 N
ATOM 15041 CA ILE B 445 -49.517 -24.837 -45.928 1.00 37.21 C
ATOM 15043 CB ILE B 445 -49.854 -26.366 -45.832 1.00 37.15 C
ATOM 15045 CG1 ILE B 445 -49.181 -26.991 -44.609 1.00 36.85 C
ATOM 15048 CD1 ILE B 445 -49.867 -28.244 -44.102 1.00 36.62 C
ATOM 15052 CG2 ILE B 445 -49.416 -27.120 -47.093 1.00 36.66 C
ATOM 15056 C ILE B 445 -49.933 -24.289 -47.290 1.00 37.88 C
ATOM 15057 O ILE B 445 -50.926 -24.733 -47.874 1.00 38.20 O
ATOM 15059 N ALA B 446 -49.175 -23.314 -47.785 1.00 38.56 N
ATOM 15060 CA ALA B 446 -49.544 -22.575 -48.992 1.00 39.03 C
ATOM 15062 CB ALA B 446 -49.833 -23.522 -50.169 1.00 39.19 C
ATOM 15066 C ALA B 446 -50.768 -21.740 -48.685 1.00 39.42 C
ATOM 15067 O ALA B 446 -51.866 -22.288 -48.742 1.00 39.26 O
ATOM 15069 N ARG B 447 -50.650 -20.443 -48.361 1.00 40.06 N
ATOM 15070 CA ARG B 447 -49.426 -19.589 -48.361 1.00 40.54 C
ATOM 15072 CB ARG B 447 -49.276 -18.901 -46.986 1.00 40.70 C
ATOM 15075 CG ARG B 447 -50.121 -17.634 -46.836 1.00 41.82 C
ATOM 15078 CD ARG B 447 -50.292 -17.234 -45.377 1.00 42.99 C

ATOM 15081 NE ARG B 447 -51.628 -17.546 -44.864 1.00 44.22 N
ATOM 15083 CZ ARG B 447 -51.924 -17.766 -43.580 1.00 46.00 C
ATOM 15084 NH1 ARG B 447 -50.977 -17.730 -42.633 1.00 46.34 N
ATOM 15087 NH2 ARG B 447 -53.184 -18.039 -43.236 1.00 46.39 N
ATOM 15090 C ARG B 447 -48.095 -20.208 -48.837 1.00 40.35 C
ATOM 15091 O ARG B 447 -47.897 -20.403 -50.038 1.00 40.95 O
ATOM 15093 N GLY B 448 -47.170 -20.442 -47.918 1.00 39.87 N
ATOM 15094 CA GLY B 448 -46.020 -21.306 -48.162 1.00 39.52 C
ATOM 15097 C GLY B 448 -45.258 -21.517 -46.865 1.00 39.26 C
ATOM 15098 O GLY B 448 -44.071 -21.842 -46.885 1.00 39.15 O
ATOM 15100 N GLU B 449 -45.966 -21.344 -45.742 1.00 38.85 N
ATOM 15101 CA GLU B 449 -45.365 -21.215 -44.426 1.00 38.45 C
ATOM 15103 CB GLU B 449 -46.288 -20.472 -43.444 1.00 38.76 C
ATOM 15106 CG GLU B 449 -46.346 -18.943 -43.636 1.00 40.34 C
ATOM 15109 CD GLU B 449 -47.486 -18.257 -42.839 1.00 42.09 C
ATOM 15110 OE1 GLU B 449 -47.897 -18.787 -41.780 1.00 43.23 O
ATOM 15111 OE2 GLU B 449 -47.972 -17.184 -43.274 1.00 42.13 O
ATOM 15112 C GLU B 449 -45.073 -22.600 -43.906 1.00 37.54 C
ATOM 15113 O GLU B 449 -45.810 -23.553 -44.167 1.00 37.34 O
ATOM 15115 N THR B 450 -43.986 -22.688 -43.159 1.00 36.47 N
ATOM 15116 CA THR B 450 -43.459 -23.950 -42.702 1.00 35.65 C
ATOM 15118 CB THR B 450 -42.017 -24.105 -43.245 1.00 35.81 C
ATOM 15120 OG1 THR B 450 -41.593 -25.465 -43.109 1.00 37.67 O
ATOM 15122 CG2 THR B 450 -41.029 -23.152 -42.538 1.00 36.21 C
ATOM 15126 C THR B 450 -43.528 -24.084 -41.166 1.00 34.22 C
ATOM 15127 O THR B 450 -43.165 -25.127 -40.619 1.00 34.00 O
ATOM 15129 N ALA B 451 -44.024 -23.034 -40.495 1.00 32.69 N
ATOM 15130 CA ALA B 451 -44.144 -22.974 -39.026 1.00 31.28 C
ATOM 15132 CB ALA B 451 -43.952 -21.546 -38.545 1.00 31.06 C
ATOM 15136 C ALA B 451 -45.495 -23.500 -38.547 1.00 29.97 C
ATOM 15137 O ALA B 451 -46.337 -22.735 -38.082 1.00 30.08 O
ATOM 15139 N ASN B 452 -45.690 -24.809 -38.656 1.00 28.19 N
ATOM 15140 CA ASN B 452 -46.935 -25.444 -38.272 1.00 26.73 C
ATOM 15142 CB ASN B 452 -47.929 -25.339 -39.422 1.00 26.45 C
ATOM 15145 CG ASN B 452 -49.311 -25.832 -39.057 1.00 25.38 C
ATOM 15146 OD1 ASN B 452 -49.608 -27.004 -39.195 1.00 24.57 O
ATOM 15147 ND2 ASN B 452 -50.171 -24.928 -38.618 1.00 24.44 N
ATOM 15150 C ASN B 452 -46.631 -26.889 -37.952 1.00 26.05 C
ATOM 15151 O ASN B 452 -45.930 -27.544 -38.695 1.00 26.21 O
ATOM 15153 N SER B 453 -47.131 -27.388 -36.834 1.00 25.30 N
ATOM 15154 CA SER B 453 -46.843 -28.760 -36.432 1.00 24.72 C
ATOM 15156 CB SER B 453 -47.638 -29.139 -35.174 1.00 24.81 C
ATOM 15159 OG SER B 453 -47.143 -28.455 -34.031 1.00 24.36 O
ATOM 15161 C SER B 453 -47.111 -29.770 -37.543 1.00 24.12 C
ATOM 15162 O SER B 453 -46.325 -30.679 -37.743 1.00 24.33 O
ATOM 15164 N VAL B 454 -48.202 -29.606 -38.272 1.00 23.57 N
ATOM 15165 CA VAL B 454 -48.546 -30.541 -39.328 1.00 23.27 C
ATOM 15167 CB VAL B 454 -50.001 -30.361 -39.795 1.00 23.06 C
ATOM 15169 CG1 VAL B 454 -50.363 -31.385 -40.829 1.00 22.41 C
ATOM 15173 CG2 VAL B 454 -50.946 -30.489 -38.622 1.00 22.80 C
ATOM 15177 C VAL B 454 -47.581 -30.473 -40.521 1.00 23.83 C
ATOM 15178 O VAL B 454 -47.370 -31.493 -41.175 1.00 24.48 O
ATOM 15180 N SER B 455 -46.981 -29.309 -40.803 1.00 23.99 N
ATOM 15181 CA SER B 455 -45.978 -29.198 -41.881 1.00 24.22 C
ATOM 15183 CB SER B 455 -45.577 -27.767 -42.111 1.00 24.02 C
ATOM 15186 OG SER B 455 -46.655 -27.098 -42.689 1.00 25.57 O
ATOM 15188 C SER B 455 -44.708 -29.949 -41.582 1.00 24.65 C
ATOM 15189 O SER B 455 -44.211 -30.700 -42.417 1.00 25.23 O
ATOM 15191 N CYS B 456 -44.151 -29.700 -40.405 1.00 24.82 N
ATOM 15192 CA CYS B 456 -43.024 -30.462 -39.935 1.00 24.81 C

ATOM 15194 CB CYS B 456 -42.765 -30.170 -38.470 1.00 24.92 C
ATOM 15197 SG CYS B 456 -42.139 -28.541 -38.190 1.00 25.18 S
ATOM 15199 C CYS B 456 -43.304 -31.938 -40.124 1.00 24.84 C
ATOM 15200 O CYS B 456 -42.507 -32.634 -40.728 1.00 25.34 O
ATOM 15202 N TYR B 457 -44.442 -32.421 -39.644 1.00 24.75 N
ATOM 15203 CA TYR B 457 -44.735 -33.838 -39.778 1.00 24.85 C
ATOM 15205 CB TYR B 457 -46.069 -34.197 -39.142 1.00 24.64 C
ATOM 15208 CG TYR B 457 -46.057 -35.537 -38.451 1.00 24.00 C
ATOM 15209 CD1 TYR B 457 -45.846 -35.635 -37.083 1.00 24.19 C
ATOM 15211 CE1 TYR B 457 -45.848 -36.873 -36.436 1.00 23.72 C
ATOM 15213 CZ TYR B 457 -46.059 -38.025 -37.170 1.00 23.27 C
ATOM 15214 OH TYR B 457 -46.063 -39.244 -36.554 1.00 22.94 O
ATOM 15216 CE2 TYR B 457 -46.268 -37.961 -38.528 1.00 23.68 C
ATOM 15218 CD2 TYR B 457 -46.265 -36.711 -39.163 1.00 24.16 C
ATOM 15220 C TYR B 457 -44.676 -34.267 -41.251 1.00 25.30 C
ATOM 15221 O TYR B 457 -43.965 -35.208 -41.584 1.00 24.94 O
ATOM 15223 N MET B 458 -45.388 -33.569 -42.134 1.00 26.02 N
ATOM 15224 CA MET B 458 -45.207 -33.775 -43.585 1.00 26.76 C
ATOM 15226 CB MET B 458 -45.913 -32.685 -44.407 1.00 26.84 C
ATOM 15229 CG MET B 458 -47.419 -32.720 -44.429 1.00 27.32 C
ATOM 15232 SD MET B 458 -48.092 -31.238 -45.229 1.00 27.76 S
ATOM 15233 CE MET B 458 -47.283 -31.311 -46.830 1.00 26.95 C
ATOM 15237 C MET B 458 -43.723 -33.759 -43.996 1.00 27.06 C
ATOM 15238 O MET B 458 -43.192 -34.746 -44.485 1.00 26.94 O
ATOM 15240 N ARG B 459 -43.069 -32.624 -43.800 1.00 27.58 N
ATOM 15241 CA ARG B 459 -41.720 -32.419 -44.289 1.00 28.38 C
ATOM 15243 CB ARG B 459 -41.313 -30.965 -44.041 1.00 28.96 C
ATOM 15246 CG ARG B 459 -39.862 -30.642 -44.328 1.00 31.93 C
ATOM 15249 CD ARG B 459 -39.656 -29.139 -44.480 1.00 36.88 C
ATOM 15252 NE ARG B 459 -40.318 -28.349 -43.427 1.00 41.70 N
ATOM 15254 CZ ARG B 459 -39.890 -28.241 -42.161 1.00 45.68 C
ATOM 15255 NH1 ARG B 459 -38.795 -28.899 -41.751 1.00 48.08 N
ATOM 15258 NH2 ARG B 459 -40.566 -27.489 -41.284 1.00 45.92 N
ATOM 15261 C ARG B 459 -40.717 -33.401 -43.672 1.00 28.03 C
ATOM 15262 O ARG B 459 -39.829 -33.881 -44.356 1.00 28.13 O
ATOM 15264 N THR B 460 -40.882 -33.711 -42.393 1.00 27.88 N
ATOM 15265 CA THR B 460 -40.002 -34.635 -41.664 1.00 27.75 C
ATOM 15267 CB THR B 460 -40.240 -34.502 -40.134 1.00 27.79 C
ATOM 15269 OG1 THR B 460 -39.805 -33.209 -39.689 1.00 27.98 O
ATOM 15271 CG2 THR B 460 -39.519 -35.589 -39.356 1.00 27.46 C
ATOM 15275 C THR B 460 -40.171 -36.114 -42.045 1.00 27.72 C
ATOM 15276 O THR B 460 -39.211 -36.857 -42.069 1.00 27.60 O
ATOM 15278 N LYS B 461 -41.398 -36.538 -42.313 1.00 28.05 N
ATOM 15279 CA LYS B 461 -41.701 -37.929 -42.649 1.00 28.25 C
ATOM 15281 CB LYS B 461 -42.972 -38.381 -41.914 1.00 28.32 C
ATOM 15284 CG LYS B 461 -42.767 -38.763 -40.453 1.00 28.57 C
ATOM 15287 CD LYS B 461 -42.569 -40.271 -40.299 1.00 29.79 C
ATOM 15290 CE LYS B 461 -41.913 -40.651 -38.970 1.00 30.32 C
ATOM 15293 NZ LYS B 461 -42.651 -40.184 -37.749 1.00 30.60 N
ATOM 15297 C LYS B 461 -41.876 -38.139 -44.155 1.00 28.50 C
ATOM 15298 O LYS B 461 -42.071 -39.269 -44.598 1.00 28.58 O
ATOM 15300 N GLY B 462 -41.818 -37.057 -44.933 1.00 28.79 N
ATOM 15301 CA GLY B 462 -41.978 -37.114 -46.385 1.00 29.04 C
ATOM 15304 C GLY B 462 -43.333 -37.610 -46.853 1.00 29.39 C
ATOM 15305 O GLY B 462 -43.410 -38.452 -47.738 1.00 29.53 O
ATOM 15307 N ILE B 463 -44.406 -37.081 -46.270 1.00 29.91 N
ATOM 15308 CA ILE B 463 -45.764 -37.552 -46.572 1.00 30.27 C
ATOM 15310 CB ILE B 463 -46.333 -38.444 -45.433 1.00 30.13 C
ATOM 15312 CG1 ILE B 463 -46.308 -37.706 -44.092 1.00 30.22 C
ATOM 15315 CD1 ILE B 463 -46.983 -38.462 -42.965 1.00 30.14 C

ATOM 15319 CG2 ILE B 463 -45.558 -39.740 -45.340 1.00 29.85 C
ATOM 15323 C ILE B 463 -46.775 -36.429 -46.881 1.00 30.75 C
ATOM 15324 O ILE B 463 -46.595 -35.270 -46.495 1.00 30.52 O
ATOM 15326 N SER B 464 -47.842 -36.822 -47.581 1.00 31.33 N
ATOM 15327 CA SER B 464 -48.951 -35.944 -47.952 1.00 31.68 C
ATOM 15329 CB SER B 464 -49.948 -36.709 -48.830 1.00 32.02 C
ATOM 15332 OG SER B 464 -50.547 -37.793 -48.123 1.00 32.84 O
ATOM 15334 C SER B 464 -49.705 -35.396 -46.747 1.00 31.62 C
ATOM 15335 O SER B 464 -49.897 -36.097 -45.747 1.00 31.69 O
ATOM 15337 N GLU B 465 -50.165 -34.153 -46.874 1.00 31.42 N
ATOM 15338 CA GLU B 465 -50.881 -33.466 -45.803 1.00 31.20 C
ATOM 15340 CB GLU B 465 -51.465 -32.141 -46.324 1.00 31.33 C
ATOM 15343 CG GLU B 465 -52.441 -31.455 -45.359 1.00 31.42 C
ATOM 15346 CD GLU B 465 -52.768 -30.006 -45.712 1.00 31.30 C
ATOM 15347 OE1 GLU B 465 -52.325 -29.490 -46.765 1.00 30.56 O
ATOM 15348 OE2 GLU B 465 -53.487 -29.380 -44.906 1.00 31.84 O
ATOM 15349 C GLU B 465 -51.985 -34.325 -45.202 1.00 30.97 C
ATOM 15350 O GLU B 465 -52.175 -34.327 -43.992 1.00 30.72 O
ATOM 15352 N GLU B 466 -52.709 -35.052 -46.055 1.00 30.98 N
ATOM 15353 CA GLU B 466 -53.865 -35.833 -45.618 1.00 30.65 C
ATOM 15355 CB GLU B 466 -54.553 -36.541 -46.788 1.00 30.62 C
ATOM 15358 CG GLU B 466 -55.733 -37.401 -46.336 1.00 31.50 C
ATOM 15361 CD GLU B 466 -56.353 -38.240 -47.446 1.00 33.14 C
ATOM 15362 OE1 GLU B 466 -56.512 -37.736 -48.581 1.00 34.40 O
ATOM 15363 OE2 GLU B 466 -56.699 -39.413 -47.173 1.00 33.21 O
ATOM 15364 C GLU B 466 -53.477 -36.851 -44.564 1.00 30.17 C
ATOM 15365 O GLU B 466 -54.215 -37.049 -43.606 1.00 30.46 O
ATOM 15367 N LEU B 467 -52.333 -37.506 -44.726 1.00 29.59 N
ATOM 15368 CA LEU B 467 -51.953 -38.540 -43.769 1.00 29.19 C
ATOM 15370 CB LEU B 467 -51.640 -39.869 -44.476 1.00 29.27 C
ATOM 15373 CG LEU B 467 -50.356 -40.081 -45.268 1.00 29.84 C
ATOM 15375 CD1 LEU B 467 -49.341 -40.761 -44.357 1.00 31.06 C
ATOM 15379 CD2 LEU B 467 -50.589 -40.920 -46.523 1.00 29.47 C
ATOM 15383 C LEU B 467 -50.865 -38.092 -42.794 1.00 28.54 C
ATOM 15384 O LEU B 467 -50.490 -38.834 -41.894 1.00 28.28 O
ATOM 15386 N ALA B 468 -50.388 -36.862 -42.962 1.00 28.04 N
ATOM 15387 CA ALA B 468 -49.682 -36.158 -41.893 1.00 27.54 C
ATOM 15389 CB ALA B 468 -48.922 -34.970 -42.435 1.00 27.34 C
ATOM 15393 C ALA B 468 -50.711 -35.698 -40.865 1.00 27.17 C
ATOM 15394 O ALA B 468 -50.482 -35.801 -39.662 1.00 27.40 O
ATOM 15396 N THR B 469 -51.841 -35.182 -41.349 1.00 26.57 N
ATOM 15397 CA THR B 469 -52.957 -34.795 -40.490 1.00 25.87 C
ATOM 15399 CB THR B 469 -54.130 -34.297 -41.328 1.00 25.53 C
ATOM 15401 OG1 THR B 469 -53.737 -33.111 -42.025 1.00 24.99 O
ATOM 15403 CG2 THR B 469 -55.316 -33.993 -40.453 1.00 24.62 C
ATOM 15407 C THR B 469 -53.412 -35.988 -39.669 1.00 25.95 C
ATOM 15408 O THR B 469 -53.551 -35.925 -38.450 1.00 25.80 O
ATOM 15410 N GLU B 470 -53.618 -37.091 -40.367 1.00 26.06 N
ATOM 15411 CA GLU B 470 -54.043 -38.344 -39.756 1.00 26.10 C
ATOM 15413 CB GLU B 470 -54.057 -39.436 -40.848 1.00 26.60 C
ATOM 15416 CG GLU B 470 -55.038 -40.587 -40.646 1.00 28.01 C
ATOM 15419 CD GLU B 470 -54.553 -41.897 -41.286 1.00 29.05 C
ATOM 15420 OE1 GLU B 470 -54.298 -41.930 -42.515 1.00 27.96 O
ATOM 15421 OE2 GLU B 470 -54.435 -42.892 -40.536 1.00 30.42 O
ATOM 15422 C GLU B 470 -53.148 -38.746 -38.557 1.00 25.28 C
ATOM 15423 O GLU B 470 -53.629 -39.266 -37.556 1.00 25.08 O
ATOM 15425 N SER B 471 -51.850 -38.497 -38.654 1.00 24.70 N
ATOM 15426 CA SER B 471 -50.930 -38.906 -37.599 1.00 24.26 C
ATOM 15428 CB SER B 471 -49.494 -38.842 -38.085 1.00 24.11 C
ATOM 15431 OG SER B 471 -49.315 -39.693 -39.186 1.00 23.98 O

ATOM 15433 C SER B 471 -51.085 -38.029 -36.377 1.00 23.92 C
ATOM 15434 O SER B 471 -51.240 -38.530 -35.270 1.00 24.09 O
ATOM 15436 N VAL B 472 -51.032 -36.719 -36.582 1.00 23.48 N
ATOM 15437 CA VAL B 472 -51.279 -35.774 -35.510 1.00 23.15 C
ATOM 15439 CB VAL B 472 -51.377 -34.332 -36.045 1.00 23.03 C
ATOM 15441 CG1 VAL B 472 -51.739 -33.347 -34.929 1.00 21.74 C
ATOM 15445 CG2 VAL B 472 -50.067 -33.945 -36.728 1.00 22.27 C
ATOM 15449 C VAL B 472 -52.572 -36.192 -34.830 1.00 23.49 C
ATOM 15450 O VAL B 472 -52.663 -36.276 -33.614 1.00 23.29 O
ATOM 15452 N MET B 473 -53.573 -36.508 -35.626 1.00 24.34 N
ATOM 15453 CA MET B 473 -54.850 -36.901 -35.070 1.00 24.93 C
ATOM 15455 CB MET B 473 -55.816 -37.266 -36.190 1.00 25.09 C
ATOM 15458 CG MET B 473 -57.191 -36.788 -35.912 1.00 26.94 C
ATOM 15461 SD MET B 473 -57.328 -35.035 -36.251 1.00 29.69 S
ATOM 15462 CE MET B 473 -58.316 -35.080 -37.775 1.00 29.12 C
ATOM 15466 C MET B 473 -54.668 -38.072 -34.100 1.00 25.00 C
ATOM 15467 O MET B 473 -55.135 -38.018 -32.963 1.00 24.78 O
ATOM 15469 N ASN B 474 -53.965 -39.110 -34.556 1.00 25.30 N
ATOM 15470 CA ASN B 474 -53.681 -40.293 -33.738 1.00 25.55 C
ATOM 15472 CB ASN B 474 -53.143 -41.439 -34.601 1.00 25.82 C
ATOM 15475 CG ASN B 474 -54.243 -42.137 -35.402 1.00 27.62 C
ATOM 15476 OD1 ASN B 474 -54.238 -42.102 -36.638 1.00 29.33 O
ATOM 15477 ND2 ASN B 474 -55.196 -42.780 -34.697 1.00 28.58 N
ATOM 15480 C ASN B 474 -52.711 -40.034 -32.592 1.00 25.20 C
ATOM 15481 O ASN B 474 -52.711 -40.773 -31.621 1.00 25.71 O
ATOM 15483 N LEU B 475 -51.883 -38.999 -32.704 1.00 24.65 N
ATOM 15484 CA LEU B 475 -50.987 -38.595 -31.614 1.00 24.04 C
ATOM 15486 CB LEU B 475 -49.939 -37.626 -32.142 1.00 23.88 C
ATOM 15489 CG LEU B 475 -48.837 -37.285 -31.164 1.00 23.70 C
ATOM 15491 CD1 LEU B 475 -47.936 -38.471 -31.004 1.00 23.97 C
ATOM 15495 CD2 LEU B 475 -48.088 -36.104 -31.679 1.00 23.99 C
ATOM 15499 C LEU B 475 -51.747 -37.940 -30.453 1.00 23.65 C
ATOM 15500 O LEU B 475 -51.323 -38.014 -29.299 1.00 23.74 O
ATOM 15502 N ILE B 476 -52.858 -37.282 -30.766 1.00 23.15 N
ATOM 15503 CA ILE B 476 -53.728 -36.711 -29.742 1.00 22.50 C
ATOM 15505 CB ILE B 476 -54.779 -35.755 -30.359 1.00 22.27 C
ATOM 15507 CG1 ILE B 476 -54.099 -34.508 -30.910 1.00 20.55 C
ATOM 15510 CD1 ILE B 476 -55.000 -33.671 -31.693 1.00 19.19 C
ATOM 15514 CG2 ILE B 476 -55.817 -35.363 -29.336 1.00 22.15 C
ATOM 15518 C ILE B 476 -54.398 -37.849 -28.985 1.00 22.40 C
ATOM 15519 O ILE B 476 -54.316 -37.900 -27.767 1.00 22.32 O
ATOM 15521 N ASP B 477 -55.023 -38.777 -29.708 1.00 22.37 N
ATOM 15522 CA ASP B 477 -55.616 -39.975 -29.090 1.00 22.55 C
ATOM 15524 CB ASP B 477 -55.996 -41.007 -30.151 1.00 22.67 C
ATOM 15527 CG ASP B 477 -57.262 -40.636 -30.892 1.00 24.93 C
ATOM 15528 OD1 ASP B 477 -57.690 -39.458 -30.818 1.00 28.87 O
ATOM 15529 OD2 ASP B 477 -57.847 -41.523 -31.549 1.00 27.92 O
ATOM 15530 C ASP B 477 -54.675 -40.622 -28.083 1.00 22.10 C
ATOM 15531 O ASP B 477 -55.048 -40.877 -26.938 1.00 21.83 O
ATOM 15533 N GLU B 478 -53.444 -40.867 -28.510 1.00 21.73 N
ATOM 15534 CA GLU B 478 -52.472 -41.506 -27.645 1.00 21.69 C
ATOM 15536 CB GLU B 478 -51.233 -41.920 -28.437 1.00 21.97 C
ATOM 15539 CG GLU B 478 -50.786 -43.360 -28.150 1.00 24.18 C
ATOM 15542 CD GLU B 478 -51.793 -44.429 -28.618 1.00 27.03 C
ATOM 15543 OE1 GLU B 478 -51.599 -45.627 -28.285 1.00 29.15 O
ATOM 15544 OE2 GLU B 478 -52.770 -44.080 -29.323 1.00 28.37 O
ATOM 15545 C GLU B 478 -52.107 -40.608 -26.449 1.00 20.97 C
ATOM 15546 O GLU B 478 -51.928 -41.110 -25.316 1.00 21.15 O
ATOM 15548 N THR B 479 -52.031 -39.291 -26.687 1.00 19.82 N
ATOM 15549 CA THR B 479 -51.787 -38.319 -25.604 1.00 18.59 C

ATOM 15551 CB THR B 479 -51.587 -36.897 -26.129 1.00 17.95 C
ATOM 15553 OG1 THR B 479 -50.291 -36.779 -26.712 1.00 17.43 O
ATOM 15555 CG2 THR B 479 -51.654 -35.938 -25.009 1.00 17.90 C
ATOM 15559 C THR B 479 -52.927 -38.342 -24.580 1.00 18.16 C
ATOM 15560 O THR B 479 -52.695 -38.339 -23.383 1.00 18.06 O
ATOM 15562 N TRP B 480 -54.160 -38.390 -25.057 1.00 17.77 N
ATOM 15563 CA TRP B 480 -55.301 -38.493 -24.169 1.00 17.54 C
ATOM 15565 CB TRP B 480 -56.605 -38.464 -24.970 1.00 17.49 C
ATOM 15568 CG TRP B 480 -57.239 -37.099 -25.028 1.00 17.53 C
ATOM 15569 CD1 TRP B 480 -57.150 -36.186 -26.041 1.00 17.04 C
ATOM 15571 NE1 TRP B 480 -57.857 -35.067 -25.721 1.00 16.57 N
ATOM 15573 CE2 TRP B 480 -58.423 -35.236 -24.484 1.00 16.41 C
ATOM 15574 CD2 TRP B 480 -58.055 -36.498 -24.020 1.00 16.68 C
ATOM 15575 CE3 TRP B 480 -58.507 -36.914 -22.765 1.00 16.92 C
ATOM 15577 CZ3 TRP B 480 -59.300 -36.076 -22.039 1.00 16.97 C
ATOM 15579 CH2 TRP B 480 -59.654 -34.823 -22.524 1.00 16.91 C
ATOM 15581 CZ2 TRP B 480 -59.223 -34.383 -23.742 1.00 16.89 C
ATOM 15583 C TRP B 480 -55.232 -39.760 -23.334 1.00 17.75 C
ATOM 15584 O TRP B 480 -55.582 -39.747 -22.164 1.00 17.74 O
ATOM 15586 N LYS B 481 -54.784 -40.861 -23.933 1.00 18.09 N
ATOM 15587 CA LYS B 481 -54.721 -42.124 -23.210 1.00 18.10 C
ATOM 15589 CB LYS B 481 -54.277 -43.282 -24.115 1.00 18.01 C
ATOM 15592 CG LYS B 481 -55.311 -43.803 -25.114 1.00 16.89 C
ATOM 15595 CD LYS B 481 -54.613 -44.663 -26.199 1.00 15.83 C
ATOM 15598 CE LYS B 481 -55.587 -45.500 -27.025 1.00 14.74 C
ATOM 15601 NZ LYS B 481 -55.119 -45.725 -28.413 1.00 12.34 N
ATOM 15605 C LYS B 481 -53.750 -41.970 -22.054 1.00 18.46 C
ATOM 15606 O LYS B 481 -53.976 -42.494 -20.969 1.00 18.44 O
ATOM 15608 N LYS B 482 -52.662 -41.252 -22.279 1.00 18.80 N
ATOM 15609 CA LYS B 482 -51.727 -41.019 -21.192 1.00 19.58 C
ATOM 15611 CB LYS B 482 -50.425 -40.424 -21.727 1.00 20.03 C
ATOM 15614 CG LYS B 482 -49.499 -41.500 -22.277 1.00 22.03 C
ATOM 15617 CD LYS B 482 -48.706 -41.063 -23.506 1.00 24.87 C
ATOM 15620 CE LYS B 482 -47.908 -42.268 -24.066 1.00 26.65 C
ATOM 15623 NZ LYS B 482 -47.287 -41.996 -25.408 1.00 28.80 N
ATOM 15627 C LYS B 482 -52.363 -40.156 -20.096 1.00 19.56 C
ATOM 15628 O LYS B 482 -52.367 -40.537 -18.926 1.00 19.19 O
ATOM 15630 N MET B 483 -52.922 -39.013 -20.483 1.00 20.00 N
ATOM 15631 CA MET B 483 -53.677 -38.165 -19.552 1.00 20.37 C
ATOM 15633 CB MET B 483 -54.426 -37.057 -20.295 1.00 20.25 C
ATOM 15636 CG MET B 483 -53.529 -35.951 -20.807 1.00 20.52 C
ATOM 15639 SD MET B 483 -54.461 -34.483 -21.225 1.00 20.47 S
ATOM 15640 CE MET B 483 -55.361 -35.084 -22.649 1.00 22.07 C
ATOM 15644 C MET B 483 -54.668 -38.981 -18.741 1.00 20.72 C
ATOM 15645 O MET B 483 -54.809 -38.779 -17.543 1.00 20.37 O
ATOM 15647 N ASN B 484 -55.345 -39.910 -19.403 1.00 21.57 N
ATOM 15648 CA ASN B 484 -56.339 -40.731 -18.744 1.00 22.46 C
ATOM 15650 CB ASN B 484 -57.042 -41.631 -19.765 1.00 22.23 C
ATOM 15653 CG ASN B 484 -58.118 -40.900 -20.576 1.00 21.61 C
ATOM 15654 OD1 ASN B 484 -58.412 -39.722 -20.362 1.00 20.25 O
ATOM 15655 ND2 ASN B 484 -58.720 -41.622 -21.510 1.00 20.80 N
ATOM 15658 C ASN B 484 -55.723 -41.555 -17.598 1.00 23.83 C
ATOM 15659 O ASN B 484 -56.262 -41.591 -16.484 1.00 23.76 O
ATOM 15661 N LYS B 485 -54.585 -42.190 -17.868 1.00 25.69 N
ATOM 15662 CA LYS B 485 -53.854 -42.937 -16.843 1.00 27.11 C
ATOM 15664 CB LYS B 485 -52.679 -43.712 -17.447 1.00 27.13 C
ATOM 15667 CG LYS B 485 -52.073 -44.755 -16.489 1.00 28.85 C
ATOM 15670 CD LYS B 485 -51.643 -46.082 -17.187 1.00 31.17 C
ATOM 15673 CE LYS B 485 -50.150 -46.132 -17.555 1.00 32.11 C
ATOM 15676 NZ LYS B 485 -49.291 -46.282 -16.344 1.00 33.08 N

ATOM 15680 C LYS B 485 -53.370 -42.035 -15.701 1.00 28.37 C
ATOM 15681 O LYS B 485 -53.288 -42.481 -14.563 1.00 28.59 O
ATOM 15683 N GLU B 486 -53.083 -40.766 -15.980 1.00 29.89 N
ATOM 15684 CA GLU B 486 -52.683 -39.849 -14.910 1.00 31.09 C
ATOM 15686 CB GLU B 486 -52.174 -38.511 -15.470 1.00 31.55 C
ATOM 15689 CG GLU B 486 -51.059 -37.851 -14.643 1.00 32.69 C
ATOM 15692 CD GLU B 486 -49.785 -38.689 -14.605 1.00 34.51 C
ATOM 15693 OE1 GLU B 486 -49.104 -38.682 -13.557 1.00 36.35 O
ATOM 15694 OE2 GLU B 486 -49.476 -39.368 -15.611 1.00 34.55 O
ATOM 15695 C GLU B 486 -53.836 -39.615 -13.939 1.00 31.70 C
ATOM 15696 O GLU B 486 -53.684 -39.868 -12.750 1.00 31.90 O
ATOM 15698 N LYS B 487 -54.983 -39.164 -14.453 1.00 32.71 N
ATOM 15699 CA LYS B 487 -56.177 -38.856 -13.629 1.00 33.57 C
ATOM 15701 CB LYS B 487 -57.343 -38.402 -14.519 1.00 33.54 C
ATOM 15704 CG LYS B 487 -58.703 -38.196 -13.823 1.00 33.45 C
ATOM 15707 CD LYS B 487 -58.686 -37.024 -12.866 1.00 33.71 C
ATOM 15710 CE LYS B 487 -59.906 -36.996 -11.931 1.00 34.48 C
ATOM 15713 NZ LYS B 487 -61.123 -36.378 -12.526 1.00 35.03 N
ATOM 15717 C LYS B 487 -56.626 -40.046 -12.802 1.00 34.60 C
ATOM 15718 O LYS B 487 -57.126 -39.892 -11.681 1.00 34.55 O
ATOM 15720 N LEU B 488 -56.453 -41.233 -13.371 1.00 35.94 N
ATOM 15721 CA LEU B 488 -56.878 -42.451 -12.723 1.00 37.00 C
ATOM 15723 CB LEU B 488 -57.280 -43.489 -13.778 1.00 36.90 C
ATOM 15726 CG LEU B 488 -58.081 -44.714 -13.312 1.00 37.52 C
ATOM 15728 CD1 LEU B 488 -58.758 -44.536 -11.946 1.00 38.76 C
ATOM 15732 CD2 LEU B 488 -59.121 -45.084 -14.346 1.00 38.42 C
ATOM 15736 C LEU B 488 -55.786 -42.980 -11.803 1.00 38.02 C
ATOM 15737 O LEU B 488 -56.063 -43.315 -10.653 1.00 38.19 O
ATOM 15739 N GLY B 489 -54.550 -43.016 -12.298 1.00 39.44 N
ATOM 15740 CA GLY B 489 -53.441 -43.710 -11.621 1.00 40.62 C
ATOM 15743 C GLY B 489 -52.563 -42.837 -10.740 1.00 41.76 C
ATOM 15744 O GLY B 489 -51.357 -42.703 -10.988 1.00 41.83 O
ATOM 15746 N GLY B 490 -53.183 -42.230 -9.726 1.00 43.10 N
ATOM 15747 CA GLY B 490 -52.481 -41.538 -8.636 1.00 43.82 C
ATOM 15750 C GLY B 490 -51.131 -40.924 -8.967 1.00 44.31 C
ATOM 15751 O GLY B 490 -50.084 -41.560 -8.831 1.00 44.25 O
ATOM 15753 N SER B 491 -51.161 -39.672 -9.396 1.00 44.87 N
ATOM 15754 CA SER B 491 -49.939 -38.892 -9.575 1.00 45.22 C
ATOM 15756 CB SER B 491 -50.224 -37.723 -10.537 1.00 45.34 C
ATOM 15759 OG SER B 491 -51.411 -37.032 -10.166 1.00 45.38 O
ATOM 15761 C SER B 491 -49.419 -38.389 -8.203 1.00 45.14 C
ATOM 15762 O SER B 491 -49.896 -38.824 -7.140 1.00 45.11 O
ATOM 15764 N LEU B 492 -48.429 -37.491 -8.227 1.00 44.77 N
ATOM 15765 CA LEU B 492 -48.046 -36.752 -7.018 1.00 44.31 C
ATOM 15767 CB LEU B 492 -46.726 -35.971 -7.188 1.00 44.55 C
ATOM 15770 CG LEU B 492 -45.530 -36.546 -7.972 1.00 45.73 C
ATOM 15772 CD1 LEU B 492 -44.373 -35.556 -7.859 1.00 46.25 C
ATOM 15776 CD2 LEU B 492 -45.084 -37.972 -7.530 1.00 46.14 C
ATOM 15780 C LEU B 492 -49.151 -35.760 -6.703 1.00 43.30 C
ATOM 15781 O LEU B 492 -49.315 -35.370 -5.555 1.00 43.49 O
ATOM 15783 N PHE B 493 -49.903 -35.367 -7.735 1.00 42.05 N
ATOM 15784 CA PHE B 493 -50.822 -34.239 -7.668 1.00 41.03 C
ATOM 15786 CB PHE B 493 -50.913 -33.549 -9.028 1.00 40.81 C
ATOM 15789 CG PHE B 493 -49.696 -32.771 -9.408 1.00 38.96 C
ATOM 15790 CD1 PHE B 493 -49.651 -31.408 -9.233 1.00 37.06 C
ATOM 15792 CE1 PHE B 493 -48.543 -30.697 -9.603 1.00 36.41 C
ATOM 15794 CZ PHE B 493 -47.471 -31.341 -10.158 1.00 35.87 C
ATOM 15796 CE2 PHE B 493 -47.507 -32.690 -10.343 1.00 36.39 C
ATOM 15798 CD2 PHE B 493 -48.612 -33.400 -9.977 1.00 37.36 C
ATOM 15800 C PHE B 493 -52.240 -34.603 -7.268 1.00 40.76 C

ATOM 15801 O PHE B 493 -52.686 -35.733 -7.419 1.00 40.35 O
ATOM 15803 N ALA B 494 -52.943 -33.584 -6.790 1.00 40.72 N
ATOM 15804 CA ALA B 494 -54.355 -33.658 -6.471 1.00 40.68 C
ATOM 15806 CB ALA B 494 -54.786 -32.362 -5.770 1.00 40.70 C
ATOM 15810 C ALA B 494 -55.175 -33.851 -7.744 1.00 40.59 C
ATOM 15811 O ALA B 494 -55.013 -33.099 -8.716 1.00 40.95 O
ATOM 15813 N LYS B 495 -56.071 -34.835 -7.733 1.00 40.12 N
ATOM 15814 CA LYS B 495 -57.000 -35.047 -8.854 1.00 39.67 C
ATOM 15816 CB LYS B 495 -58.008 -36.166 -8.520 1.00 39.98 C
ATOM 15819 CG LYS B 495 -57.388 -37.590 -8.496 1.00 40.57 C
ATOM 15822 CD LYS B 495 -58.468 -38.688 -8.419 1.00 41.18 C
ATOM 15825 CE LYS B 495 -57.878 -40.065 -8.132 1.00 41.28 C
ATOM 15828 NZ LYS B 495 -58.736 -41.159 -8.671 1.00 41.39 N
ATOM 15832 C LYS B 495 -57.717 -33.752 -9.333 1.00 38.82 C
ATOM 15833 O LYS B 495 -57.847 -33.535 -10.537 1.00 38.70 O
ATOM 15835 N PRO B 496 -58.169 -32.890 -8.397 1.00 37.71 N
ATOM 15836 CA PRO B 496 -58.701 -31.551 -8.687 1.00 36.80 C
ATOM 15838 CB PRO B 496 -58.820 -30.937 -7.304 1.00 36.94 C
ATOM 15841 CG PRO B 496 -59.255 -32.073 -6.483 1.00 37.90 C
ATOM 15844 CD PRO B 496 -58.534 -33.294 -7.030 1.00 37.86 C
ATOM 15847 C PRO B 496 -57.845 -30.625 -9.536 1.00 35.57 C
ATOM 15848 O PRO B 496 -58.389 -29.693 -10.139 1.00 35.93 O
ATOM 15849 N PHE B 497 -56.527 -30.836 -9.546 1.00 33.52 N
ATOM 15850 CA PHE B 497 -55.654 -30.083 -10.439 1.00 31.34 C
ATOM 15852 CB PHE B 497 -54.355 -29.710 -9.750 1.00 30.86 C
ATOM 15855 CG PHE B 497 -53.394 -28.989 -10.634 1.00 29.04 C
ATOM 15856 CD1 PHE B 497 -53.639 -27.700 -11.022 1.00 27.89 C
ATOM 15858 CE1 PHE B 497 -52.752 -27.028 -11.834 1.00 27.39 C
ATOM 15860 CZ PHE B 497 -51.599 -27.653 -12.259 1.00 27.40 C
ATOM 15862 CE2 PHE B 497 -51.341 -28.941 -11.877 1.00 27.44 C
ATOM 15864 CD2 PHE B 497 -52.236 -29.604 -11.074 1.00 28.18 C
ATOM 15866 C PHE B 497 -55.390 -30.870 -11.714 1.00 30.24 C
ATOM 15867 O PHE B 497 -55.301 -30.266 -12.786 1.00 30.39 O
ATOM 15869 N VAL B 498 -55.295 -32.200 -11.630 1.00 28.50 N
ATOM 15870 CA VAL B 498 -55.076 -32.983 -12.854 1.00 27.54 C
ATOM 15872 CB VAL B 498 -54.778 -34.472 -12.611 1.00 27.34 C
ATOM 15874 CG1 VAL B 498 -56.027 -35.194 -12.262 1.00 28.14 C
ATOM 15878 CG2 VAL B 498 -53.731 -34.649 -11.530 1.00 27.04 C
ATOM 15882 C VAL B 498 -56.277 -32.857 -13.784 1.00 26.60 C
ATOM 15883 O VAL B 498 -56.129 -32.864 -14.995 1.00 26.33 O
ATOM 15885 N GLU B 499 -57.468 -32.731 -13.214 1.00 25.87 N
ATOM 15886 CA GLU B 499 -58.662 -32.484 -14.022 1.00 25.20 C
ATOM 15888 CB GLU B 499 -59.975 -32.639 -13.206 1.00 25.26 C
ATOM 15891 CG GLU B 499 -61.287 -32.694 -14.028 1.00 25.16 C
ATOM 15894 CD GLU B 499 -61.422 -33.922 -14.973 1.00 26.79 C
ATOM 15895 OE1 GLU B 499 -60.607 -34.880 -14.928 1.00 26.39 O
ATOM 15896 OE2 GLU B 499 -62.379 -33.926 -15.785 1.00 27.83 O
ATOM 15897 C GLU B 499 -58.542 -31.097 -14.641 1.00 24.27 C
ATOM 15898 O GLU B 499 -58.819 -30.948 -15.832 1.00 24.32 O
ATOM 15900 N THR B 500 -58.098 -30.093 -13.882 1.00 22.90 N
ATOM 15901 CA THR B 500 -58.027 -28.764 -14.487 1.00 22.29 C
ATOM 15903 CB THR B 500 -57.908 -27.592 -13.488 1.00 22.43 C
ATOM 15905 OG1 THR B 500 -56.536 -27.259 -13.274 1.00 22.65 O
ATOM 15907 CG2 THR B 500 -58.614 -27.899 -12.183 1.00 22.84 C
ATOM 15911 C THR B 500 -56.940 -28.671 -15.565 1.00 21.20 C
ATOM 15912 O THR B 500 -57.120 -27.939 -16.536 1.00 21.06 O
ATOM 15914 N ALA B 501 -55.845 -29.414 -15.422 1.00 19.88 N
ATOM 15915 CA ALA B 501 -54.906 -29.574 -16.537 1.00 19.24 C
ATOM 15917 CB ALA B 501 -53.704 -30.393 -16.115 1.00 19.22 C
ATOM 15921 C ALA B 501 -55.581 -30.226 -17.757 1.00 18.68 C

ATOM 15922 O ALA B 501 -55.427 -29.768 -18.881 1.00 18.32 O
ATOM 15924 N ILE B 502 -56.324 -31.300 -17.523 1.00 18.11 N
ATOM 15925 CA ILE B 502 -57.023 -31.988 -18.591 1.00 17.68 C
ATOM 15927 CB ILE B 502 -57.750 -33.251 -18.059 1.00 17.63 C
ATOM 15929 CG1 ILE B 502 -56.713 -34.350 -17.769 1.00 18.16 C
ATOM 15932 CD1 ILE B 502 -57.253 -35.645 -17.115 1.00 17.02 C
ATOM 15936 CG2 ILE B 502 -58.756 -33.762 -19.063 1.00 16.93 C
ATOM 15940 C ILE B 502 -57.990 -31.030 -19.289 1.00 17.50 C
ATOM 15941 O ILE B 502 -58.153 -31.071 -20.512 1.00 17.62 O
ATOM 15943 N ASN B 503 -58.604 -30.139 -18.524 1.00 17.23 N
ATOM 15944 CA ASN B 503 -59.545 -29.184 -19.102 1.00 17.07 C
ATOM 15946 CB ASN B 503 -60.184 -28.327 -18.016 1.00 17.21 C
ATOM 15949 CG ASN B 503 -61.155 -29.094 -17.176 1.00 17.29 C
ATOM 15950 OD1 ASN B 503 -61.721 -30.097 -17.609 1.00 16.66 O
ATOM 15951 ND2 ASN B 503 -61.365 -28.621 -15.958 1.00 19.16 N
ATOM 15954 C ASN B 503 -58.920 -28.270 -20.149 1.00 16.59 C
ATOM 15955 O ASN B 503 -59.611 -27.811 -21.071 1.00 16.67 O
ATOM 15957 N LEU B 504 -57.629 -27.992 -20.014 1.00 15.79 N
ATOM 15958 CA LEU B 504 -56.948 -27.204 -21.031 1.00 15.44 C
ATOM 15960 CB LEU B 504 -55.530 -26.865 -20.609 1.00 15.07 C
ATOM 15963 CG LEU B 504 -54.933 -25.837 -21.552 1.00 14.21 C
ATOM 15965 CD1 LEU B 504 -54.246 -24.726 -20.800 1.00 14.21 C
ATOM 15969 CD2 LEU B 504 -54.000 -26.538 -22.462 1.00 14.27 C
ATOM 15973 C LEU B 504 -56.954 -27.933 -22.375 1.00 15.59 C
ATOM 15974 O LEU B 504 -57.177 -27.323 -23.414 1.00 15.30 O
ATOM 15976 N ALA B 505 -56.732 -29.242 -22.341 1.00 15.89 N
ATOM 15977 CA ALA B 505 -56.914 -30.073 -23.514 1.00 16.23 C
ATOM 15979 CB ALA B 505 -56.608 -31.483 -23.188 1.00 16.05 C
ATOM 15983 C ALA B 505 -58.352 -29.955 -24.010 1.00 16.69 C
ATOM 15984 O ALA B 505 -58.598 -29.738 -25.204 1.00 16.88 O
ATOM 15986 N ARG B 506 -59.300 -30.071 -23.090 1.00 16.88 N
ATOM 15987 CA ARG B 506 -60.709 -29.972 -23.457 1.00 17.20 C
ATOM 15989 CB ARG B 506 -61.630 -30.170 -22.248 1.00 17.34 C
ATOM 15992 CG ARG B 506 -61.549 -31.537 -21.614 1.00 17.46 C
ATOM 15995 CD ARG B 506 -62.837 -31.917 -20.962 1.00 17.48 C
ATOM 15998 NE ARG B 506 -62.783 -33.280 -20.435 1.00 18.37 N
ATOM 16000 CZ ARG B 506 -62.404 -33.613 -19.201 1.00 19.03 C
ATOM 16001 NH1 ARG B 506 -62.008 -32.690 -18.324 1.00 18.83 N
ATOM 16004 NH2 ARG B 506 -62.415 -34.892 -18.841 1.00 19.72 N
ATOM 16007 C ARG B 506 -61.038 -28.646 -24.114 1.00 17.32 C
ATOM 16008 O ARG B 506 -61.754 -28.622 -25.111 1.00 17.41 O
ATOM 16010 N GLN B 507 -60.540 -27.543 -23.564 1.00 17.59 N
ATOM 16011 CA GLN B 507 -60.864 -26.233 -24.139 1.00 18.05 C
ATOM 16013 CB GLN B 507 -60.382 -25.090 -23.258 1.00 18.16 C
ATOM 16016 CG GLN B 507 -60.798 -23.709 -23.764 1.00 17.57 C
ATOM 16019 CD GLN B 507 -62.291 -23.508 -23.723 1.00 17.42 C
ATOM 16020 OE1 GLN B 507 -62.953 -23.959 -22.800 1.00 17.55 O
ATOM 16021 NE2 GLN B 507 -62.832 -22.823 -24.722 1.00 17.56 N
ATOM 16024 C GLN B 507 -60.258 -26.060 -25.521 1.00 18.49 C
ATOM 16025 O GLN B 507 -60.855 -25.413 -26.380 1.00 18.73 O
ATOM 16027 N SER B 508 -59.066 -26.619 -25.724 1.00 18.85 N
ATOM 16028 CA SER B 508 -58.427 -26.621 -27.037 1.00 19.07 C
ATOM 16030 CB SER B 508 -57.108 -27.364 -26.969 1.00 19.04 C
ATOM 16033 OG SER B 508 -56.304 -26.772 -25.979 1.00 20.10 O
ATOM 16035 C SER B 508 -59.305 -27.296 -28.065 1.00 19.12 C
ATOM 16036 O SER B 508 -59.438 -26.827 -29.187 1.00 19.00 O
ATOM 16038 N HIS B 509 -59.905 -28.409 -27.674 1.00 19.26 N
ATOM 16039 CA HIS B 509 -60.814 -29.095 -28.559 1.00 19.33 C
ATOM 16041 CB HIS B 509 -61.275 -30.412 -27.959 1.00 19.30 C
ATOM 16044 CG HIS B 509 -60.263 -31.501 -28.067 1.00 18.71 C

ATOM 16045 ND1 HIS B 509 -59.941 -32.089 -29.267 1.00 18.57 N
ATOM 16047 CE1 HIS B 509 -59.020 -33.012 -29.064 1.00 19.07 C
ATOM 16049 NE2 HIS B 509 -58.738 -33.044 -27.774 1.00 18.52 N
ATOM 16051 CD2 HIS B 509 -59.499 -32.105 -27.129 1.00 18.43 C
ATOM 16053 C HIS B 509 -62.017 -28.251 -28.878 1.00 19.60 C
ATOM 16054 O HIS B 509 -62.491 -28.286 -29.969 1.00 19.68 O
ATOM 16056 N CYS B 510 -62.540 -27.502 -27.932 1.00 20.12 N
ATOM 16057 CA CYS B 510 -63.748 -26.738 -28.216 1.00 20.63 C
ATOM 16059 CB CYS B 510 -64.493 -26.492 -26.915 1.00 20.70 C
ATOM 16062 SG CYS B 510 -64.856 -28.020 -26.065 1.00 22.93 S
ATOM 16064 C CYS B 510 -63.465 -25.422 -28.950 1.00 20.55 C
ATOM 16065 O CYS B 510 -64.338 -24.881 -29.622 1.00 20.16 O
ATOM 16067 N THR B 511 -62.236 -24.933 -28.827 1.00 20.89 N
ATOM 16068 CA THR B 511 -61.833 -23.654 -29.378 1.00 21.32 C
ATOM 16070 CB THR B 511 -60.682 -23.107 -28.550 1.00 20.76 C
ATOM 16072 OG1 THR B 511 -61.208 -22.619 -27.324 1.00 19.50 O
ATOM 16074 CG2 THR B 511 -59.961 -21.994 -29.253 1.00 19.79 C
ATOM 16078 C THR B 511 -61.417 -23.735 -30.851 1.00 23.11 C
ATOM 16079 O THR B 511 -61.910 -22.992 -31.694 1.00 22.75 O
ATOM 16081 N TYR B 512 -60.501 -24.646 -31.152 1.00 25.46 N
ATOM 16082 CA TYR B 512 -59.867 -24.704 -32.462 1.00 27.09 C
ATOM 16084 CB TYR B 512 -58.397 -25.107 -32.327 1.00 27.16 C
ATOM 16087 CG TYR B 512 -57.598 -24.056 -31.582 1.00 27.26 C
ATOM 16088 CD1 TYR B 512 -57.300 -22.834 -32.182 1.00 28.18 C
ATOM 16090 CE1 TYR B 512 -56.583 -21.844 -31.511 1.00 27.98 C
ATOM 16092 CZ TYR B 512 -56.164 -22.068 -30.226 1.00 27.72 C
ATOM 16093 OH TYR B 512 -55.462 -21.072 -29.584 1.00 27.09 O
ATOM 16095 CE2 TYR B 512 -56.453 -23.281 -29.602 1.00 27.52 C
ATOM 16097 CD2 TYR B 512 -57.171 -24.262 -30.278 1.00 26.68 C
ATOM 16099 C TYR B 512 -60.633 -25.623 -33.382 1.00 28.79 C
ATOM 16100 O TYR B 512 -61.050 -25.179 -34.444 1.00 28.98 O
ATOM 16102 N HIS B 513 -60.789 -26.893 -32.991 1.00 31.06 N
ATOM 16103 CA HIS B 513 -61.865 -27.800 -33.492 1.00 33.07 C
ATOM 16105 CB HIS B 513 -62.740 -28.208 -32.265 1.00 33.66 C
ATOM 16108 CG HIS B 513 -64.181 -28.602 -32.535 1.00 34.73 C
ATOM 16109 ND1 HIS B 513 -65.035 -27.903 -33.367 1.00 35.70 N
ATOM 16111 CE1 HIS B 513 -66.234 -28.464 -33.343 1.00 35.40 C
ATOM 16113 NE2 HIS B 513 -66.206 -29.469 -32.491 1.00 35.10 N
ATOM 16115 CD2 HIS B 513 -64.943 -29.565 -31.956 1.00 35.07 C
ATOM 16117 C HIS B 513 -62.692 -27.179 -34.623 1.00 34.03 C
ATOM 16118 O HIS B 513 -63.003 -27.848 -35.627 1.00 34.55 O
ATOM 16120 N ASN B 514 -63.047 -25.906 -34.444 1.00 34.65 N
ATOM 16121 CA ASN B 514 -63.713 -25.123 -35.483 1.00 35.15 C
ATOM 16123 CB ASN B 514 -63.845 -23.643 -35.070 1.00 35.01 C
ATOM 16126 CG ASN B 514 -64.704 -23.456 -33.820 1.00 33.48 C
ATOM 16127 OD1 ASN B 514 -64.787 -24.343 -32.968 1.00 30.92 O
ATOM 16128 ND2 ASN B 514 -65.327 -22.295 -33.703 1.00 32.16 N
ATOM 16131 C ASN B 514 -63.192 -25.274 -36.942 1.00 36.08 C
ATOM 16132 O ASN B 514 -62.010 -25.051 -37.254 1.00 35.69 O
ATOM 16134 N GLY B 515 -64.119 -25.765 -37.772 1.00 37.15 N
ATOM 16135 CA GLY B 515 -64.224 -25.493 -39.177 1.00 37.94 C
ATOM 16138 C GLY B 515 -65.269 -24.384 -39.284 1.00 39.01 C
ATOM 16139 O GLY B 515 -64.904 -23.286 -39.702 1.00 39.58 O
ATOM 16141 N ASP B 516 -66.550 -24.585 -38.909 1.00 39.95 N
ATOM 16142 CA ASP B 516 -67.167 -25.810 -38.349 1.00 40.65 C
ATOM 16144 CB ASP B 516 -67.296 -25.652 -36.836 1.00 41.09 C
ATOM 16147 CG ASP B 516 -66.318 -26.511 -36.063 1.00 43.63 C
ATOM 16148 OD1 ASP B 516 -65.697 -27.434 -36.662 1.00 45.83 O
ATOM 16149 OD2 ASP B 516 -66.152 -26.246 -34.843 1.00 47.12 O
ATOM 16150 C ASP B 516 -68.603 -26.067 -38.853 1.00 40.78 C

ATOM 16151 O ASP B 516 -69.134 -25.301 -39.660 1.00 41.28 O
ATOM 16153 N ALA B 517 -69.222 -27.141 -38.349 1.00 40.66 N
ATOM 16154 CA ALA B 517 -70.675 -27.396 -38.468 1.00 40.60 C
ATOM 16156 CB ALA B 517 -71.422 -26.622 -37.359 1.00 40.27 C
ATOM 16160 C ALA B 517 -71.295 -27.106 -39.862 1.00 40.79 C
ATOM 16161 O ALA B 517 -70.654 -27.296 -40.899 1.00 40.67 O
ATOM 16163 N HIS B 518 -72.562 -26.696 -39.874 1.00 41.13 N
ATOM 16164 CA HIS B 518 -73.162 -26.033 -41.039 1.00 41.60 C
ATOM 16166 CB HIS B 518 -74.446 -26.756 -41.480 1.00 42.24 C
ATOM 16169 CG HIS B 518 -74.207 -28.179 -41.910 1.00 45.54 C
ATOM 16170 ND1 HIS B 518 -73.441 -28.509 -43.012 1.00 48.51 N
ATOM 16172 CE1 HIS B 518 -73.392 -29.825 -43.140 1.00 48.79 C
ATOM 16174 NE2 HIS B 518 -74.092 -30.364 -42.156 1.00 49.12 N
ATOM 16176 CD2 HIS B 518 -74.608 -29.357 -41.369 1.00 48.28 C
ATOM 16178 C HIS B 518 -73.377 -24.545 -40.686 1.00 40.84 C
ATOM 16179 O HIS B 518 -74.487 -23.997 -40.769 1.00 40.60 O
ATOM 16181 N THR B 519 -72.261 -23.932 -40.275 1.00 40.10 N
ATOM 16182 CA THR B 519 -72.143 -22.521 -39.878 1.00 39.39 C
ATOM 16184 CB THR B 519 -72.561 -22.263 -38.393 1.00 39.40 C
ATOM 16186 OG1 THR B 519 -71.823 -23.131 -37.517 1.00 39.55 O
ATOM 16188 CG2 THR B 519 -74.074 -22.460 -38.178 1.00 38.98 C
ATOM 16192 C THR B 519 -70.654 -22.164 -40.059 1.00 38.81 C
ATOM 16193 O THR B 519 -69.800 -23.050 -40.067 1.00 38.48 O
ATOM 16195 N SER B 520 -70.338 -20.881 -40.199 1.00 38.19 N
ATOM 16196 CA SER B 520 -68.959 -20.453 -40.521 1.00 37.77 C
ATOM 16198 CB SER B 520 -68.983 -18.976 -40.960 1.00 37.76 C
ATOM 16201 OG SER B 520 -68.760 -18.106 -39.870 1.00 38.49 O
ATOM 16203 C SER B 520 -67.974 -20.724 -39.340 1.00 37.24 C
ATOM 16204 O SER B 520 -68.394 -21.267 -38.320 1.00 36.89 O
ATOM 16206 N PRO B 521 -66.671 -20.350 -39.472 1.00 36.96 N
ATOM 16207 CA PRO B 521 -65.692 -20.638 -38.396 1.00 36.80 C
ATOM 16209 CB PRO B 521 -64.320 -20.354 -39.041 1.00 36.68 C
ATOM 16212 CG PRO B 521 -64.599 -19.593 -40.309 1.00 37.19 C
ATOM 16215 CD PRO B 521 -66.091 -19.469 -40.507 1.00 37.10 C
ATOM 16218 C PRO B 521 -65.915 -19.763 -37.168 1.00 36.68 C
ATOM 16219 O PRO B 521 -66.233 -20.289 -36.105 1.00 36.90 O
ATOM 16220 N ASP B 522 -65.744 -18.445 -37.298 1.00 36.61 N
ATOM 16221 CA ASP B 522 -66.373 -17.528 -36.347 1.00 36.58 C
ATOM 16223 CB ASP B 522 -65.938 -16.070 -36.543 1.00 36.82 C
ATOM 16226 CG ASP B 522 -64.456 -15.846 -36.243 1.00 37.94 C
ATOM 16227 OD1 ASP B 522 -63.848 -16.627 -35.473 1.00 39.62 O
ATOM 16228 OD2 ASP B 522 -63.891 -14.876 -36.790 1.00 39.40 O
ATOM 16229 C ASP B 522 -67.836 -17.718 -36.681 1.00 36.12 C
ATOM 16230 O ASP B 522 -68.150 -18.306 -37.702 1.00 35.98 O
ATOM 16232 N GLU B 523 -68.732 -17.249 -35.830 1.00 35.69 N
ATOM 16233 CA GLU B 523 -70.152 -17.605 -35.927 1.00 35.46 C
ATOM 16235 CB GLU B 523 -70.703 -17.560 -37.379 1.00 35.51 C
ATOM 16238 CG GLU B 523 -70.535 -16.175 -38.061 1.00 36.11 C
ATOM 16241 CD GLU B 523 -70.854 -16.136 -39.572 1.00 36.72 C
ATOM 16242 OE1 GLU B 523 -71.848 -16.767 -40.013 1.00 37.20 O
ATOM 16243 OE2 GLU B 523 -70.101 -15.452 -40.314 1.00 35.53 O
ATOM 16244 C GLU B 523 -70.440 -18.943 -35.216 1.00 34.97 C
ATOM 16245 O GLU B 523 -71.557 -19.148 -34.765 1.00 35.02 O
ATOM 16247 N LEU B 524 -69.462 -19.846 -35.099 1.00 34.59 N
ATOM 16248 CA LEU B 524 -69.503 -20.832 -34.004 1.00 34.45 C
ATOM 16250 CB LEU B 524 -68.735 -22.136 -34.286 1.00 34.21 C
ATOM 16253 CG LEU B 524 -69.530 -23.434 -34.508 1.00 33.92 C
ATOM 16255 CD1 LEU B 524 -68.657 -24.627 -34.227 1.00 32.21 C
ATOM 16259 CD2 LEU B 524 -70.794 -23.520 -33.641 1.00 34.06 C
ATOM 16263 C LEU B 524 -68.901 -20.162 -32.791 1.00 34.38 C

ATOM 16264 O LEU B 524 -69.535 -20.067 -31.741 1.00 34.49 O
ATOM 16266 N THR B 525 -67.670 -19.688 -32.958 1.00 34.30 N
ATOM 16267 CA THR B 525 -66.913 -19.073 -31.874 1.00 34.23 C
ATOM 16269 CB THR B 525 -65.570 -18.524 -32.380 1.00 34.04 C
ATOM 16271 OG1 THR B 525 -64.894 -19.549 -33.112 1.00 33.83 O
ATOM 16273 CG2 THR B 525 -64.689 -18.087 -31.227 1.00 33.37 C
ATOM 16277 C THR B 525 -67.702 -17.960 -31.184 1.00 34.46 C
ATOM 16278 O THR B 525 -67.684 -17.858 -29.955 1.00 34.57 O
ATOM 16280 N ARG B 526 -68.401 -17.144 -31.969 1.00 34.54 N
ATOM 16281 CA ARG B 526 -69.200 -16.056 -31.418 1.00 34.60 C
ATOM 16283 CB ARG B 526 -69.571 -15.059 -32.513 1.00 35.04 C
ATOM 16286 CG ARG B 526 -70.256 -13.800 -32.013 1.00 37.13 C
ATOM 16289 CD ARG B 526 -70.143 -12.656 -33.026 1.00 39.87 C
ATOM 16292 NE ARG B 526 -70.353 -13.075 -34.420 1.00 42.28 N
ATOM 16294 CZ ARG B 526 -71.543 -13.292 -35.000 1.00 44.26 C
ATOM 16295 NH1 ARG B 526 -72.685 -13.159 -34.320 1.00 44.66 N
ATOM 16298 NH2 ARG B 526 -71.593 -13.658 -36.279 1.00 44.49 N
ATOM 16301 C ARG B 526 -70.448 -16.593 -30.735 1.00 33.91 C
ATOM 16302 O ARG B 526 -70.848 -16.074 -29.704 1.00 33.74 O
ATOM 16304 N LYS B 527 -71.048 -17.637 -31.306 1.00 33.39 N
ATOM 16305 CA LYS B 527 -72.240 -18.252 -30.722 1.00 33.15 C
ATOM 16307 CB LYS B 527 -72.837 -19.332 -31.639 1.00 33.42 C
ATOM 16310 CG LYS B 527 -73.898 -18.804 -32.609 1.00 34.55 C
ATOM 16313 CD LYS B 527 -74.643 -19.919 -33.358 1.00 35.43 C
ATOM 16316 CE LYS B 527 -75.230 -19.383 -34.667 1.00 36.11 C
ATOM 16319 NZ LYS B 527 -76.076 -20.372 -35.384 1.00 37.04 N
ATOM 16323 C LYS B 527 -71.925 -18.865 -29.378 1.00 32.36 C
ATOM 16324 O LYS B 527 -72.589 -18.584 -28.387 1.00 32.56 O
ATOM 16326 N ARG B 528 -70.909 -19.713 -29.358 1.00 31.53 N
ATOM 16327 CA ARG B 528 -70.502 -20.401 -28.138 1.00 30.77 C
ATOM 16329 CB ARG B 528 -69.283 -21.286 -28.414 1.00 30.55 C
ATOM 16332 CG ARG B 528 -69.624 -22.519 -29.252 1.00 29.48 C
ATOM 16335 CD ARG B 528 -68.418 -23.417 -29.493 1.00 28.05 C
ATOM 16338 NE ARG B 528 -68.811 -24.774 -29.880 1.00 26.55 N
ATOM 16340 CZ ARG B 528 -67.968 -25.719 -30.288 1.00 25.87 C
ATOM 16341 NH1 ARG B 528 -66.668 -25.472 -30.385 1.00 26.33 N
ATOM 16344 NH2 ARG B 528 -68.424 -26.920 -30.615 1.00 25.49 N
ATOM 16347 C ARG B 528 -70.225 -19.415 -27.004 1.00 30.42 C
ATOM 16348 O ARG B 528 -70.721 -19.582 -25.885 1.00 30.30 O
ATOM 16350 N VAL B 529 -69.455 -18.376 -27.307 1.00 29.96 N
ATOM 16351 CA VAL B 529 -69.194 -17.312 -26.342 1.00 29.47 C
ATOM 16353 CB VAL B 529 -68.261 -16.227 -26.932 1.00 29.40 C
ATOM 16355 CG1 VAL B 529 -68.269 -14.968 -26.081 1.00 29.18 C
ATOM 16359 CG2 VAL B 529 -66.845 -16.782 -27.062 1.00 28.90 C
ATOM 16363 C VAL B 529 -70.516 -16.723 -25.841 1.00 28.98 C
ATOM 16364 O VAL B 529 -70.759 -16.682 -24.641 1.00 28.97 O
ATOM 16366 N LEU B 530 -71.384 -16.308 -26.752 1.00 28.54 N
ATOM 16367 CA LEU B 530 -72.709 -15.824 -26.353 1.00 28.23 C
ATOM 16369 CB LEU B 530 -73.631 -15.604 -27.559 1.00 28.09 C
ATOM 16372 CG LEU B 530 -73.767 -14.150 -28.007 1.00 28.15 C
ATOM 16374 CD1 LEU B 530 -72.412 -13.570 -28.406 1.00 27.99 C
ATOM 16378 CD2 LEU B 530 -74.784 -14.034 -29.150 1.00 28.85 C
ATOM 16382 C LEU B 530 -73.389 -16.767 -25.367 1.00 27.88 C
ATOM 16383 O LEU B 530 -73.932 -16.319 -24.363 1.00 28.11 O
ATOM 16385 N SER B 531 -73.352 -18.066 -25.652 1.00 27.28 N
ATOM 16386 CA SER B 531 -74.081 -19.049 -24.849 1.00 26.68 C
ATOM 16388 CB SER B 531 -74.209 -20.363 -25.612 1.00 26.68 C
ATOM 16391 OG SER B 531 -72.970 -21.033 -25.681 1.00 26.67 O
ATOM 16393 C SER B 531 -73.410 -19.312 -23.514 1.00 26.20 C
ATOM 16394 O SER B 531 -74.076 -19.550 -22.511 1.00 25.86 O

ATOM 16396 N VAL B 532 -72.085 -19.281 -23.512 1.00 25.86 N
ATOM 16397 CA VAL B 532 -71.320 -19.562 -22.306 1.00 25.51 C
ATOM 16399 CB VAL B 532 -69.891 -20.055 -22.651 1.00 25.34 C
ATOM 16401 CG1 VAL B 532 -68.955 -19.932 -21.460 1.00 24.01 C
ATOM 16405 CG2 VAL B 532 -69.950 -21.484 -23.158 1.00 24.95 C
ATOM 16409 C VAL B 532 -71.271 -18.357 -21.373 1.00 25.52 C
ATOM 16410 O VAL B 532 -71.377 -18.523 -20.164 1.00 25.82 O
ATOM 16412 N ILE B 533 -71.137 -17.158 -21.935 1.00 25.39 N
ATOM 16413 CA ILE B 533 -70.875 -15.954 -21.151 1.00 25.48 C
ATOM 16415 CB ILE B 533 -69.666 -15.185 -21.732 1.00 25.30 C
ATOM 16417 CG1 ILE B 533 -68.375 -15.928 -21.451 1.00 24.91 C
ATOM 16420 CD1 ILE B 533 -68.118 -16.120 -19.989 1.00 25.00 C
ATOM 16424 CG2 ILE B 533 -69.553 -13.797 -21.130 1.00 25.81 C
ATOM 16428 C ILE B 533 -72.065 -14.983 -21.030 1.00 25.77 C
ATOM 16429 O ILE B 533 -72.537 -14.707 -19.928 1.00 25.77 O
ATOM 16431 N THR B 534 -72.541 -14.442 -22.142 1.00 25.98 N
ATOM 16432 CA THR B 534 -73.446 -13.295 -22.064 1.00 26.31 C
ATOM 16434 CB THR B 534 -73.094 -12.253 -23.143 1.00 26.21 C
ATOM 16436 OG1 THR B 534 -72.914 -12.909 -24.397 1.00 26.72 O
ATOM 16438 CG2 THR B 534 -71.795 -11.535 -22.781 1.00 25.97 C
ATOM 16442 C THR B 534 -74.961 -13.621 -22.064 1.00 26.50 C
ATOM 16443 O THR B 534 -75.713 -12.974 -21.344 1.00 26.67 O
ATOM 16445 N GLU B 535 -75.410 -14.616 -22.829 1.00 26.55 N
ATOM 16446 CA GLU B 535 -76.851 -14.892 -22.961 1.00 26.50 C
ATOM 16448 CB GLU B 535 -77.197 -15.197 -24.426 1.00 26.68 C
ATOM 16451 CG GLU B 535 -77.226 -13.936 -25.296 1.00 27.68 C
ATOM 16454 CD GLU B 535 -78.193 -14.014 -26.475 1.00 28.75 C
ATOM 16455 OE1 GLU B 535 -79.370 -13.588 -26.330 1.00 27.72 O
ATOM 16456 OE2 GLU B 535 -77.762 -14.492 -27.549 1.00 30.06 O
ATOM 16457 C GLU B 535 -77.355 -16.019 -22.056 1.00 26.19 C
ATOM 16458 O GLU B 535 -77.021 -17.171 -22.279 1.00 26.15 O
ATOM 16460 N PRO B 536 -78.186 -15.697 -21.047 1.00 26.05 N
ATOM 16461 CA PRO B 536 -78.692 -16.763 -20.196 1.00 26.05 C
ATOM 16463 CB PRO B 536 -79.495 -16.018 -19.118 1.00 25.87 C
ATOM 16466 CG PRO B 536 -79.140 -14.621 -19.239 1.00 25.88 C
ATOM 16469 CD PRO B 536 -78.760 -14.402 -20.660 1.00 26.21 C
ATOM 16472 C PRO B 536 -79.608 -17.717 -20.943 1.00 26.14 C
ATOM 16473 O PRO B 536 -80.173 -17.359 -21.973 1.00 25.99 O
ATOM 16474 N ILE B 537 -79.746 -18.924 -20.411 1.00 26.38 N
ATOM 16475 CA ILE B 537 -80.662 -19.905 -20.960 1.00 26.58 C
ATOM 16477 CB ILE B 537 -80.443 -21.292 -20.333 1.00 26.47 C
ATOM 16479 CG1 ILE B 537 -79.023 -21.789 -20.600 1.00 26.38 C
ATOM 16482 CD1 ILE B 537 -78.709 -23.102 -19.907 1.00 26.40 C
ATOM 16486 CG2 ILE B 537 -81.430 -22.300 -20.890 1.00 26.71 C
ATOM 16490 C ILE B 537 -82.072 -19.420 -20.657 1.00 26.93 C
ATOM 16491 O ILE B 537 -82.347 -18.965 -19.545 1.00 26.81 O
ATOM 16493 N LEU B 538 -82.963 -19.491 -21.641 1.00 27.36 N
ATOM 16494 CA LEU B 538 -84.309 -18.984 -21.439 1.00 27.68 C
ATOM 16496 CB LEU B 538 -85.181 -19.094 -22.698 1.00 27.75 C
ATOM 16499 CG LEU B 538 -84.782 -18.291 -23.949 1.00 27.47 C
ATOM 16501 CD1 LEU B 538 -85.992 -18.109 -24.844 1.00 27.11 C
ATOM 16505 CD2 LEU B 538 -84.164 -16.933 -23.621 1.00 26.99 C
ATOM 16509 C LEU B 538 -84.919 -19.752 -20.288 1.00 28.01 C
ATOM 16512 N PRO B 539 -85.645 -19.046 -19.421 1.00 28.69 N
ATOM 16513 CA PRO B 539 -86.028 -19.631 -18.152 1.00 29.05 C
ATOM 16515 CB PRO B 539 -86.640 -18.452 -17.397 1.00 29.08 C
ATOM 16518 CG PRO B 539 -87.144 -17.548 -18.447 1.00 28.86 C
ATOM 16521 CD PRO B 539 -86.298 -17.748 -19.660 1.00 28.62 C
ATOM 16524 C PRO B 539 -87.035 -20.767 -18.259 1.00 29.51 C
ATOM 16525 O PRO B 539 -87.665 -20.970 -19.297 1.00 29.23 O

ATOM 16526 N PHE B 540 -87.164 -21.500 -17.159 1.00 30.25 N
ATOM 16527 CA PHE B 540 -88.089 -22.613 -17.070 1.00 30.56 C
ATOM 16529 CB PHE B 540 -87.971 -23.297 -15.708 1.00 30.73 C
ATOM 16532 CG PHE B 540 -88.848 -24.499 -15.567 1.00 30.49 C
ATOM 16533 CD1 PHE B 540 -89.910 -24.505 -14.683 1.00 30.32 C
ATOM 16535 CE1 PHE B 540 -90.718 -25.614 -14.568 1.00 30.59 C
ATOM 16537 CZ PHE B 540 -90.475 -26.722 -15.346 1.00 30.55 C
ATOM 16539 CE2 PHE B 540 -89.420 -26.720 -16.234 1.00 30.68 C
ATOM 16541 CD2 PHE B 540 -88.619 -25.617 -16.342 1.00 30.43 C
ATOM 16543 C PHE B 540 -89.507 -22.120 -17.257 1.00 30.76 C
ATOM 16544 O PHE B 540 -89.967 -21.257 -16.508 1.00 30.59 O
ATOM 16546 N GLU B 541 -90.184 -22.677 -18.259 1.00 31.13 N
ATOM 16547 CA GLU B 541 -91.553 -22.289 -18.608 1.00 31.45 C
ATOM 16549 CB GLU B 541 -91.525 -21.186 -19.680 1.00 31.60 C
ATOM 16552 CG GLU B 541 -92.860 -20.454 -19.911 1.00 32.56 C
ATOM 16555 CD GLU B 541 -93.773 -21.133 -20.935 1.00 33.64 C
ATOM 16556 OE1 GLU B 541 -93.261 -21.922 -21.771 1.00 35.06 O
ATOM 16557 OE2 GLU B 541 -95.002 -20.868 -20.901 1.00 32.44 O
ATOM 16558 C GLU B 541 -92.326 -23.510 -19.105 1.00 31.31 C
ATOM 16559 O GLU B 541 -92.860 -24.286 -18.310 1.00 31.30 O
ATOM 16562 MG MG C 1 -42.844 11.427 13.309 1.00 46.29 MG
ATOM 16561 MG MG C 2 -46.615 -18.454 -33.231 1.00 48.45 MG
ATOM 16563 O HOH E 1 -50.507 -5.408 -4.491 1.00 17.42 O
ATOM 16566 O HOH E 2 -64.748 -36.007 -11.725 1.00 2.00 O
ATOM 16569 O HOH E 3 -40.643 -2.220 -34.996 1.00 2.00 O
ATOM 16572 O HOH E 4 -36.090 -9.757 -37.074 1.00 17.20 O
ATOM 16575 O HOH E 5 -46.117 -37.662 -22.916 1.00 17.03 O
ATOM 16578 O HOH E 6 -49.541 35.476 6.921 1.00 14.03 O
ATOM 16581 O HOH E 7 -32.288 27.572 16.443 1.00 13.16 O
ATOM 16584 O HOH E 8 -50.706 10.207 -15.061 1.00 18.73 O
ATOM 16587 O HOH E 9 -77.188 36.767 -9.218 1.00 8.05 O
ATOM 16590 O HOH E 10 -90.260 -31.248 -21.071 1.00 2.00 O
ATOM 16593 O HOH E 11 -70.920 -33.414 -3.884 1.00 9.35 O
ATOM 16596 O HOH E 12 -37.761 -21.294 -9.249 1.00 25.78 O
ATOM 16599 O HOH E 13 -76.050 23.855 -18.293 1.00 2.00 O
ATOM 16602 O HOH E 14 -76.876 -19.575 -22.856 1.00 19.25 O
ATOM 16605 O HOH E 15 -40.936 11.629 -24.832 1.00 22.29 O
ATOM 16608 O HOH E 16 -85.551 34.832 3.260 1.00 25.14 O
ATOM 16611 O HOH E 17 -56.825 31.771 -7.464 1.00 17.27 O
ATOM 16614 O HOH E 18 -76.222 39.261 -.613 1.00 25.47 O

[0478] Various modifications and variations of the described method and system of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention, which are obvious to those skilled in the relevant fields, are intended to be within the scope of the following claims.

CLAIMS

We claim:

1. An isolated poplar isoprene synthase variant, wherein said variant comprises a truncation in the N-terminal portion of isoprene synthase.

2. The isolated poplar isoprene synthase variant of claim 1, wherein the isoprene synthase variant has an increased specific activity compared to a full length isoprene synthase.

3. The isolated poplar isoprene synthase variant of claim 1, wherein the isoprene synthase is *P. alba* isoprene synthase of SEQ ID NO:120.

4. The isolated poplar isoprene synthase variant of claim 3, wherein the variant is selected from the group consisting of: an MEA variant (SEQ ID NO:122), an MSV variant (SEQ ID NO:124), an MVS variant (SEQ ID NO:126), an MTE variant (SEQ ID NO:128), an MNV variant (SEQ ID NO:130).

5. The isolated poplar isoprene synthase variant of claim 4, wherein the variant is an MEA variant (SEQ ID NO:122).

6. The isolated poplar isoprene synthase variant of claim 3, wherein the variant is selected from the group consisting of: a TRC (-3) variant (SEQ ID NO:136), a TRC (-4) variant (SEQ ID NO:138), a TRC (-5) variant (SEQ ID NO:140), a TRC (-6) variant (SEQ ID NO:142) and a TRC (-7) variant (SEQ ID NO:144).

7. The isolated poplar isoprene synthase variant of claim 1, wherein the variant is a MET variant of *P. tremuloides* isoprene synthase (SEQ ID NO:146).

8. The isolated poplar isoprene synthase variant of claim 1, wherein the variant is a MET variant of *P. trichocharpa* isoprene synthase (SEQ ID NO:148).

9. An isolated poplar isoprene synthase variant, wherein the variant comprises a substitution of one or more amino acid residues of a wild type isoprene synthase; and wherein the isoprene synthase variant has increased isoprene synthase activity compared to a wild type isoprene synthase.

10. The isolated poplar isoprene synthase variant of claim 9, wherein increased isoprene synthase activity is indicated by a host cell comprising the isoprene variant growing at a faster rate in the presence of dimethylallyl pyrophosphate (DMAPP) compared to a host cell comprising a parent isoprene synthase.

11. The isolated poplar isoprene synthase variant of claim 9, wherein the isoprene synthase is the *P. alba* isoprene synthase of SEQ ID NO:120.

12. The isolated poplar isoprene synthase variant of claim 11, wherein the variant comprises one of more amino acid substitutions selected from the group consisting of V10M, F12S, T15A, E18G, V58I, V58F, L70Q, L70V, L70T, T71P, V79L, E89D, G94A, S119F, F120L, G127R, E175V, T212I, S257A, R262G, A266G, F280L, N297K, F305L, L319M, E323K, A328T, D342E, A359T, K366N, E368D, L374M, S396T, V418S, K438N, H440R, T442I, T442A, I449V, A469S, K500R, K505Q, G507S, S509N, F511Y, and N532K.

13. The isolated poplar isoprene synthase variant of claim 11, wherein at least one amino acid substitution is a L70R substitution.

14. The isolated poplar isoprene synthase variant of claim 11, wherein the variant comprises one of more amino acid substitutions selected from the group consisting of G127R/F511Y, L70Q/G94A/R262G/F305L, F12S/ T15A/E18G/N297K, S396T/T442I, V10M/E323K, F120L/A266G, K438N/K500R, V79L/S509N, E175V/S257A/E368D/A469S, T71P/L374M, F280L/H440R, E89D/H440R, V58F/A328T/N532K, S119F/D342E/I449V, and K366N/G507S.

15. A crystalline form of a polypeptide comprising the amino acid residues of SEQ ID NO:120 (Figure 19).

16. A method of producing isoprene, comprising: (a) providing a host cell comprising an expression vector comprising a polynucleotide sequence encoding an isoprene synthase variant; and (b) culturing the host cell under conditions suitable for producing isoprene.

17. The method of claim 16 further comprising (c) recovering the isoprene.

18. The method of claim 17 further comprising (d) polymerizing the isoprene.

19. A method of detecting isoprene synthase activity, comprising: (a) culturing a host cell comprising the expression vector under conditions suitable for producing an isoprene synthase variant; (b) lysing the host cells with a lysis buffer comprising lysozyme to produce a cell lysate; and (c) detecting isoprene synthase activity in the cell lysate by measuring isoprene production from dimethylallyl diphosphate (DMAPP).

20. The method of claim 19 wherein the host cell is selected from the group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells.

21. The method of claim 19 wherein the host cell is selected from the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).*

22. The method of claim 19 wherein the host cell is cultured in a medium that includes a carbon source selected from the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil.

23. A method of detecting isoprene in a plurality of samples in a high-throughput screening comprising:

(a) providing: i) a plurality of samples each comprising isoprene synthase; ii) a glass plate comprising a plurality of wells; and iii) a seal for the glass plate;

(b) placing the plurality of samples in the plurality of wells of the glass plate;

(c) sealing the glass plate with the seal to produce a sealed glass plate having a headspace associated with the sample in each of the plurality of wells;

(d) incubating the glass plate under conditions in which the isoprene synthase is active; and

(e) detecting isoprene in the headspace.

24. The method of claim 23 wherein the isoprene is detected by gas chromatography-mass spectrometry (GC-MS).

25. The method of claim 23 wherein the plurality of samples comprise host cells comprising an expression vector comprising a polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter.

26. The method of claim 23 wherein the plurality of samples comprise a lysate of the host cells, lysozyme, and dimethylallyl diphosphate (DMAPP).

27. The method of claim 23 wherein the glass plate is a deep-well glass block.

28. The method of claim 23 wherein the plurality of wells comprises at least 24 wells

29. The method of claim 23 wherein the plurality of wells each comprise a volume of 2 ml or less.

30. A host cell comprising a heterologous polynucleotide sequence encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a poplar isoprene synthase.

31. The host cell of claim 30 wherein the isoprene synthase is the *P. alba* isoprene synthase of SEQ ID NO:120.

32. The host cell of claim 31 wherein the variant is selected from the group consisting of: an MEA variant (SEQ ID NO:122), an MSV variant (SEQ ID NO:124), an MVS variant (SEQ ID NO:126), an MTE variant (SEQ ID NO:128), an MNV variant (SEQ ID NO:130).

33. The host cell of claim 31 wherein the variant is selected from the group consisting of: a TRC (-3) variant (SEQ ID NO:136), a TRC (-4) variant (SEQ ID NO:138), a TRC (-5) variant (SEQ ID NO:140), a TRC (-6) variant (SEQ ID NO:142) and a TRC (-7) variant (SEQ ID NO:144).

34. The host cell of claim 30 wherein the variant is a MET variant of *P. tremuloides* isoprene synthase (SEQ ID NO:146).

35. The host cell of claim 30 wherein the variant is a MET variant of *P. trichocharpa* isoprene synthase (SEQ ID NO:148).

36. The host cell of claim 31 wherein the variant comprises one of more amino acid substitutions selected from the group consisting of V10M, F12S, T15A, E18G, V58I, V58F, L70Q, L70V, L70T, T71P, V79L, E89D, G94A, S119F, F120L, G127R, E175V, T212I, S257A, R262G, A266G, F280L, N297K, F305L, L319M, E323K, A328T, D342E, A359T, K366N, E368D, L374M, S396T, V418S, K438N, H440R, T442I, T442A, I449V, A469S, K500R, K505Q, G507S, S509N, F511Y, and N532K.

37. The host cell of claim 36 wherein at least one amino acid substitution is a L70R substitution.

38. The host cell of claim 31 wherein the variant comprises one of more amino acid substitutions selected from the group consisting of G127R/F511Y, L70Q/G94A/R262G/F305L, F12S/ T15A/E18G/N297K, S396T/T442I, V10M/E323K, F120L/A266G, K438N/K500R, V79L/S509N, E175V/S257A/E368D/A469S, T71P/L374M, F280L/H440R, E89D/H440R, V58F/A328T/N532K, S119F/D342E/I449V, and K366N/G507S.

39. The host cell of claim 30 wherein the polynucleotide sequence is contained within a plasmid.

40. The host cell of claim 39 wherein the polynucleotide sequence is integrated into a chromosome of the host cell.

41. The host cell of claim 30 wherein the host is selected from the group consisting of gram-positive bacterial cells, gram-negative bacterial cells, filamentous fungal cells, and yeast cells.

42. The host cell of claim 30 wherein the host is selected from the group consisting of *Escherichia sp. (E. coli), Panteoa sp. (P. citrea), Bacillus sp. (B. subtilis), Yarrowia sp. (Y. lipolytica),* and *Trichoderma (T. reesei).*

43. The host cell of claim 30 wherein the host cell is cultured in a medium comprising a carbon source selected from the group consisting of glucose, glycerol, glycerine, dihydroxyacetone, yeast extract, biomass, molasses, sucrose, and oil.

44. The host cell of claim 30 wherein the host cell further comprises a heterologous or native nucleic acid encoding an IDI polypeptide and/or a heterologous or native nucleic acid encoding a DXS polypeptide, optionally in combination with the native DXP pathway.

45. The host cell of claim 30 wherein the host cell further comprises one or more nucleic acids encoding an IDI polypeptide and a DXS polypeptide.

46. The host cell of claim 30 wherein the host cell comprises one vector encoding the isoprene synthase variant, the IDI polypeptide, and the DXS polypeptide.

47. The host cell of claim 46 wherein the host cell further comprises a heterologous nucleic acid encoding an MVA pathway polypeptide selected from the group consisting of an MVA pathway polypeptide from *Saccharomyces cerevisia* and *Enterococcus faecalis*.

48. The host cell of claim 30 wherein the host cell further comprises one or more nucleic acids encoding an MVA pathway polypeptide and a DXS polypeptide and wherein one vector encodes the isoprene synthase variant, the MVA pathway polypeptide, and the DXS polypeptide.

49. The host cell of claim 48 wherein the host cell further comprises one or more nucleic acids encoding a DXS polypeptide, an IDI polypeptide, or one or more of the rest of the DXP pathway polypeptides, and a MVA pathway polypeptide.

50. A method of producing isoprene, comprising:

(a) culturing the host cells of claim 30 under suitable culture conditions for production of isoprene; and

(b) producing the isoprene.

51. The method of claim 50 further comprising (c) recovering the isoprene.

52. The method of claim 51 further comprising (d) polymerizing isoprene.

53. A method of producing isoprene synthase, comprising:

(a) providing: (i) a host cell; and (ii) a nucleic acid encoding an isoprene synthase variant in operable combination with a promoter, wherein the isoprene synthase variant comprises a substitution at a position corresponding to one or more residues (one, two, three, four, five, six, seven, eight, nine or ten) of a *P. alba* isoprene synthase of SEQ ID NO:120;

(b) contacting the host cell with the nucleic acid to produce a transformed host cell; and

(c) culturing the transformed host cells under suitable culture conditions for production of isoprene synthase.

Figure. 1

Kudzu IspS DNA for *E. coli* (SEQ ID NO:1)

atgtgtgcgacctcttctcaatttactcagattaccgagcataattcccgtcgttccgcaaactatcagccaaacct
gtggaatttcgaattcctgcaatccctggagaacgacctgaaagtggaaaagctggaggagaaagcgaccaaactgg
aggaagaagttcgctgcatgatcaaccgtgtagacacccagccgctgtccctgctggagctgatcgacgatgtgcag
cgcctgggtctgacctacaaatttgaaaaagacatcattaaagccctggaaaacatcgtactgctggacgaaaacaa
aaagaacaaatctgacctgcacgcaaccgctctgtctttccgtctgctgcgtcagcacggtttcgaggtttctcagg
atgtttttgagcgtttcaaggataaagaaggtggtttcagcggtgaactgaaaggtgacgtccaaggcctgctgagc
ctgtatgaagcgtcttacctgggtttcgagggtgagaacctgctggaggaggcgcgtacctttttccatcacccacct
gaagaacaacctgaaagaaggcattaataccaaggttgcagaacaagtgagccacgccctggaactgccatatcacc
agcgtctgcaccgtctggaggcacgttggttcctggataaatacgaaccgaaagaaccgcatcaccagctgctgctg
gagctggcgaagctggattttaacatggtacagaccctgcaccagaaagagctgcaagatctgtcccgctggtggac
cgagatgggcctggctagcaaactggattttgtacgcgaccgcctgatggaagtttatttctgggcactgggtatgg
cgccagacccgcagtttggtgaatgtcgcaaagctgttactaaaatgtttggtctggtgacgatcatcgatgacgtg
tatgacgtttatggcactctggacgaactgcaactgttcaccgatgctgtagagcgctgggacgttaacgctattaa
caccctgccggactatatgaaactgtgtttcctggcactgtacaacaccgttaacgacacgtcctattctattctga
aagagaaaggtcataacaacctgtcctatctgacgaaaagctggcgtgaactgtgcaaagcctttctgcaagaggcg
aaatggtccaacaacaaaattatcccggctttctccaagtacctggaaaacgccagcgtttcctcctccggtgtagc
gctgctggcgccgtcttacttttccgtatgccagcagcaggaagacatctccgaccacgcgctgcgttccctgaccg
acttccatggtctggtgcgttctagctgcgttatcttccgcctgtgcaacgatctggccacctctgcggcggagctg
gaacgtggcgagactaccaattctatcattagctacatgcacgaaaacgatggtaccagcgaggaacaggcccgcga
agaactgcgtaaactgatcgacgccgaatggaaaaagatgaatcgtgaacgcgttagcgactccaccctgctgccta
aagcgttcatggaaatcgcagttaacatggcacgtgtttcccactgcacctaccagtatggcgatggtctgggtcgc
ccagactacgcgactgaaaaccgcatcaaactgctgctgattgacccttcccgattaaccagctgatgtatgtc**ta**
a

Figure 2

Kudzu IspS protein (SEQ ID NO:2)

MCATSSQFTQITEHNSRRSANYQPNLWNFEFLQSLENDLKVEKLEEKATKLEEEVRCMINRVDTQPLSLLELIDDVQ
RLGLTYKFEKDIIKALENIVLLDENKKNKSDLHATALSFRLLRQHGFEVSQDVFERFKDKEGGFSGELKGDVQGLLS
LYEASYLGFEGENLLEEARTFSITHLKNNLKEGINTKVAEQVSHALELPYHQRLHRLEARWFLDKYEPKEPHHQLLL
ELAKLDFNMVQTLHQKELQDLSRWWTEMGLASKLDFVRDRLMEVYFWALGMAPDPQFGECRKAVTKMFGLVTIIDDV
YDVYGTLDELQLFTDAVERWDVNAINTLPDYMKLCFLALYNTVNDTSYSILKEKGHNNLSYLTKSWRELCKAFLQEA
KWSNNKIIPAFSKYLENASVSSSGVALLAPSYFSVCQQQEDISDHALRSLTDFHGLVRSSCVIFRLCNDLATSAAEL
ERGETTNSIISYMHENDGTSEEQAREELRKLIDAEWKKMNRERVSDSTLLPKAFMEIAVNMARVSHCTYQYGDGLGR
PDYATENRIKLLLIDPFPINQLMYV

Figure 3

Poplar IspS DNA for *E. coli* (SEQ ID NO:6)

atgtgctctgtttctaccgagaacgtttccttcactgagacggaaaccgaggcacgtcgtagcgcgaactacgagcc
gaatagctgggactacgatttcctgctgtcttccgatactgacgaatctattgaggtgtacaaagacaaagcaaaga
aactggaggctgaagtgcgccgcgaaattaacaacgagaaagctgaattcctgactctgctggagctgatcgataac
gtacagcgcctgggtctgggttaccgcttcgaatctgatatccgtcgcgcactggatcgtttcgtaagcagcggcgg
tttcgatggcgtgaccaaaacgagcctgcacgctaccgcgctgtccttccgtctgctgcgtcagcacggcttcgaag
tttctcaggaagcattctccggtttcaaagatcaaaacggtaacttcctggaaaacctgaaagaagacactaaggcg
atcctgagcctgtatgaggcaagctttctggccctggagggtgagaacatcctggatgaggcgcgcgtattcgccat
ctcccatctgaaagagctgtctgaagagaaaatcggtaaggaactggcagagcaggttaatcacgcactggaactgc
cgctgcatcgtcgtacccagcgtctggaggcggtttggtccatcgaagcgtaccgcaaaaaggaggatgctaaccag
gttctgctggaactggccatcctggactacaacatgatccagtccgtttaccagcgtgatctgcgtgaaacctcccg
ttggtggcgccgtgtgggcctggcgaccaaactgcacttcgctaaggaccgcctgattgagtctttttactgggcag
tcggcgttgcgttcgaacctcagtattctgactgccgtaacagcgttgcgaaaatgttcagcttcgttactattatc
gacgacatctacgacgtttacggtactctggacgagctggaactgtttaccgacgctgtcgaacgttgggatgttaa
cgccatcaacgatctgcctgactacatgaaactgtgcttcctggcactgtataacacgatcaacgaaattgcatacg
acaacctgaaagacaaaggtgaaaacatcctgccgtacctgactaaagcgtgggcggatctgtgtaacgcttttctg
caagaagcgaaatggctgtataacaaatccactccgacctttgacgattatttcggcaatgcctggaaatccagctc
tggcccgctgcaactgatcttcgcttattttgcggttgtccaaaacatcaaaaaggaggaaattgaaaacctgcaaa
aataccacgatatcattagccgtccttctcatatctttcgcctgtgcaacgacctggcaagcgcgtccgcagagatc
gcacgtggcgaaaccgctaactctgtttcctgctacatgcgcaccaagggcatttccgaagagctggcaaccgagag
cgtaatgaatctgatcgacgaaacctgtaagaaaatgaacaaagaaaaactgggtggctccctgttcgctaaaccgt
tcgtagagactgctattaacctggcacgtcagagccactgcacctaccacaatggtgacgcacatactagcccggat
gaactgactcgtaaacgtgtactgtctgttatcaccgaaccgattctgccgttcgaacgt**taa**

Figure 4

Poplar IspS protein (SEQ ID NO:7)

MCSVSTENVSFTETETEARRSANYEPNSWDYDFLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDN
VQRLGLGYRFESDIRRALDRFVSSGGFDGVTKTSLHATALSFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDTKA
ILSLYEASFLALEGENILDEARVFAISHLKELSEEKIGKELAEQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQ
VLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFAKDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTII
DDIYDVYGTLDELELFTDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFL
QEAKWLYNKSTPTFDDYFGNAWKSSSGPLQLIFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCNDLASASAEI
ARGETANSVSCYMRTKGISEELATESVMNLIDETCKKMNKEKLGGSLFAKPFVETAINLARQSHCTYHNGDAHTSPD
ELTRKRVLSVITEPILPFER

Figure 5



Figure 6

Poplar Isoprene Synthase

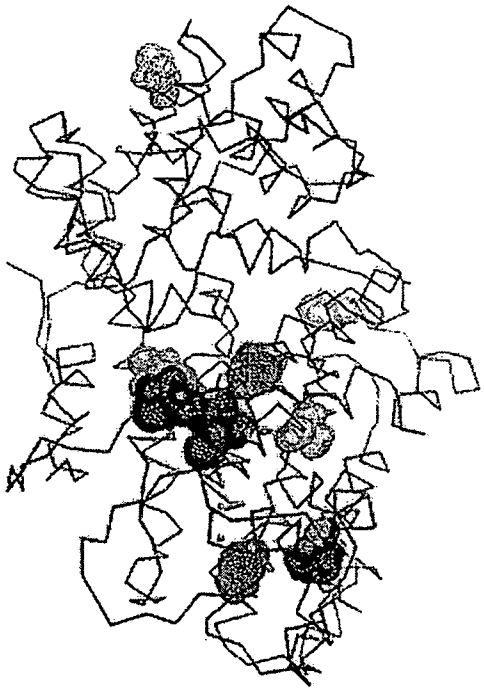


Figure 7

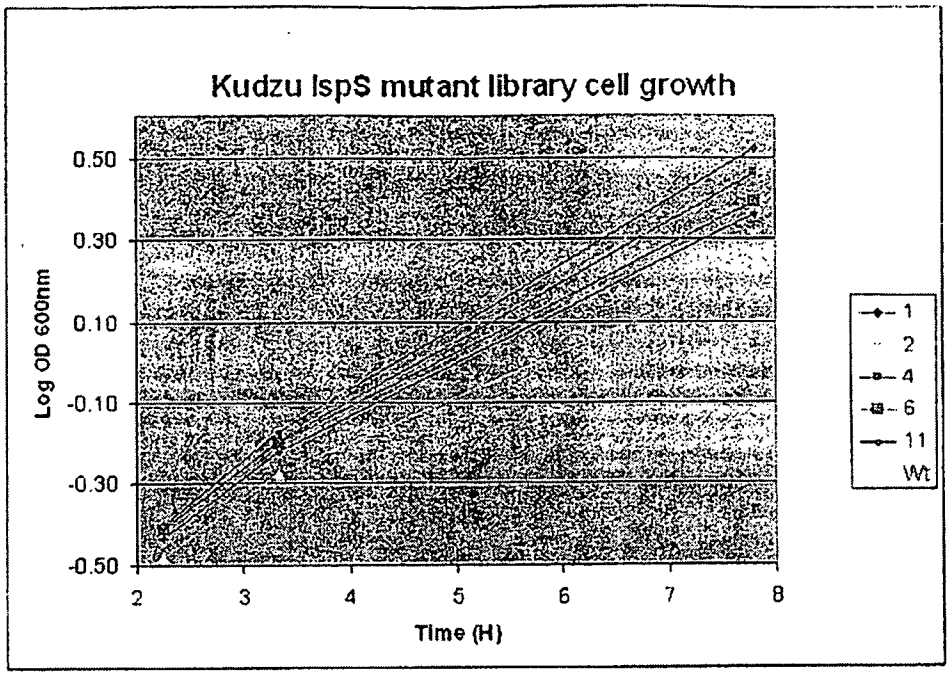

Kudzu IspS mutant library cell growth
Log OD 600nm
0.50
0.30
0.10
-0.10
-0.30
-0.50
2
3
4
5
6
7
8
Time (H)
1
2
4
6
11
Wt

Figure 8

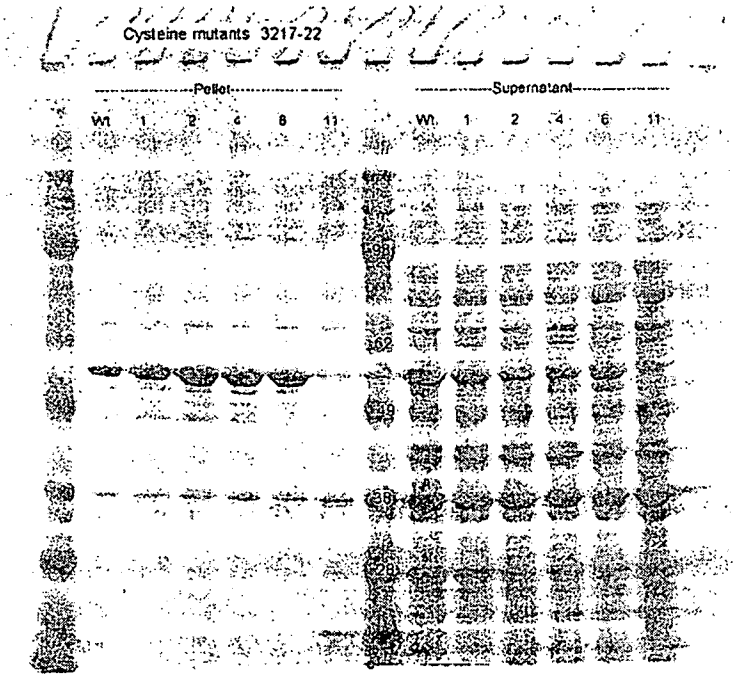

Cysteine mutants 3217-22
Pellet
Supernatant
Wt
1
2
4
6
11
Wt
1
2
4
6
11
199
62
49
38
28
17

Figure 9

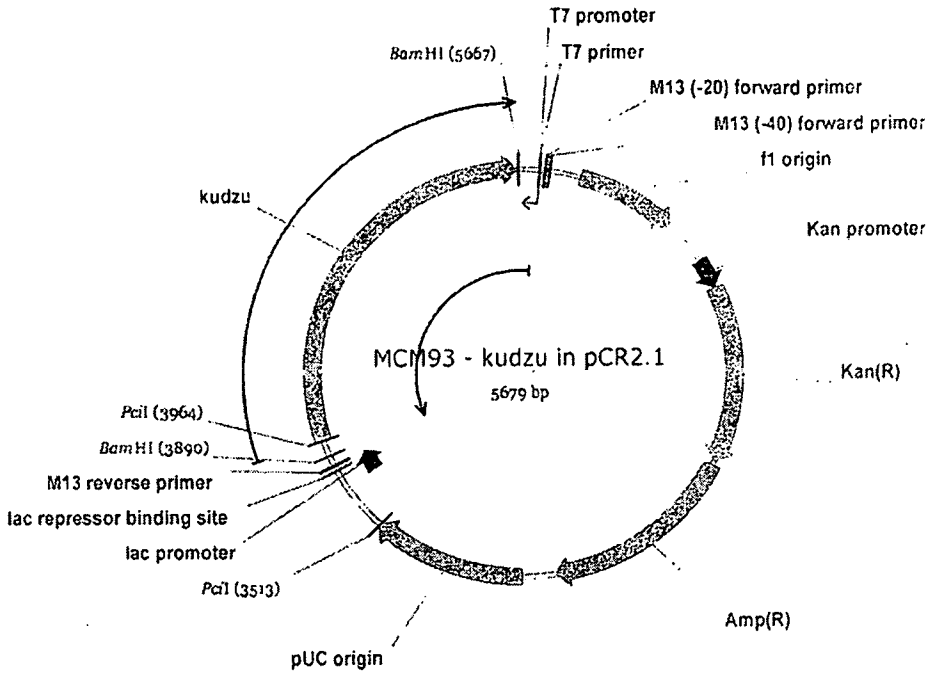

T7 promoter
BamHI (5667)
T7 primer
M13 (-20) forward primer
M13 (-40) forward primer
f1 origin
kudzu
Kan promoter
MCM93 - kudzu in pCR2.1
5679 bp
Kan(R)
PciI (3964)
BamHI (3890)
M13 reverse primer
lac repressor binding site
lac promoter
PciI (3513)
Amp(R)
pUC origin

Figure 10A

plasmid MCM93 = pCR2.1-Kudzu (SEQ ID NO:22)

aagggcgaattctgcagatatccatcacactggcggccgctcgagcatgcatctagagggcccaattcgccctatag
tgagtcgtattacaattcactggccgtcgttttacaacgtcgtgactgggaaaaccctggcgttacccaacttaatc
gccttgcagcacatccccctttcgccagctggcgtaatagcgaagaggcccgcaccgatcgcccttcccaacagttg
cgcagcctgaatggcgaatggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagcgtg
accgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcgccacgttcgccggctt
tccccgtcaagctctaaatcgggggctccctttagggttccgatttagtgctttacggcacctcgaccccaaaaaac
ttgattagggtgatggttcacgtagtgggccatcgccctgatagacggtttttcgccctttgacgttggagtccacg
ttctttaatagtggactcttgttccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagg
gattttgccgatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaaattc
agggcgcaagggctgctaaaggaagcggaacacgtagaaagccagtccgcagaaacggtgctgaccccggatgaatg
tcagctactgggctatctggacaagggaaaacgcaagcgcaaagagaaagcaggtagcttgcagtgggcttacatgg
cgatagctagactgggcggttttatggacagcaagcgaaccggaattgccagctggggcgccctctggtaaggttgg
gaagccctgcaaagtaaactggatggctttcttgccgccaaggatctgatggcgcaggggatcaagatctgatcaag
agacaggatgaggatcgtttcgcatgattgaacaagatggattgcacgcaggttctccggccgcttgggtggagagg
ctattcggctatgactgggcacaacagacaatcggctgctctgatgccgccgtgttccggctgtcagcgcaggggcg
cccggttctttttgtcaagaccgacctgtccggtgccctgaatgaactgcaggacgaggcagcgcggctatcgtggc
tggccacgacgggcgttccttgcgcagctgtgctcgacgttgtcactgaagcgggaagggactggctgctattgggc
gaagtgccggggcaggatctcctgtcatcccaccttgctcctgccgagaaagtatccatcatggctgatgcaatgcg
gcggctgcatacgcttgatccggctacctgcccattcgaccaccaagcgaaacatcgcatcgagcgagcacgtactc
ggatggaagccggtcttgtcgatcaggatgatctggacgaagagcatcaggggctcgcgccagccgaactgttcgcc
aggctcaaggcgcgcatgcccgacggcgaggatctcgtcgtgacccatggcgatgcctgcttgccgaatatcatggt
ggaaaatggccgcttttctggattcatcgactgtggccggctgggtgtggcggaccgctatcaggacatagcgttgg
ctacccgtgatattgctgaagagcttggcggcgaatgggctgaccgcttcctcgtgctttacggtatcgccgctccc
gattcgcagcgcatcgccttctatcgccttcttgacgagttcttctgaattgaaaaaggaagagtatgagtattcaa
catttccgtgtcgcccttattccctttttttgcggcattttgccttcctgtttttgctcacccagaaacgctggtgaa
agtaaaaagatgctgaagatcagttgggtgcacgagtgggttacatcgaactggatctcaacagcggtaagatccttg
agagttttcgccccgaagaacgttttccaatgatgagcacttttaaagttctgctatgtggcgcggtattatcccgt
attgacgccgggcaagagcaactcggtcgccgcatacactattctcagaatgacttggttgagtactcaccagtcac
agaaaagcatcttacggatggcatgacagtaagagaattatgcagtgctgccataaccatgagtgataacactgcgg
ccaacttacttctgacaacgatcggaggaccgaaggagctaaccgcttttttgcacaacatgggggatcatgtaact
cgccttgatcgttgggaaccggagctgaatgaagccataccaaacgacgagcgtgacaccacgatgcctgtagcaat
ggcaacaacgttgcgcaaactattaactggcgaactacttactctagcttcccggcaacaattaatagactggatgg
aggcggataaagttgcaggaccacttctgcgctcggcccttccggctggctggtttattgctgataaatctggagcc
ggtgagcgtgggtctcgcggtatcattgcagcactggggccagatggtaagccctcccgtatcgtagttatctacac
gacggggagtcaggcaactatggatgaacgaaatagacagatcgctgagataggtgcctcactgattaagcattggt
aactgtcagaccaagtttactcatatatactttagattgatttaaaacttcatttttaatttaaaaggatctaggtg
aagatccttttgataatctcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccccgtaga
aaagatcaaaggatcttcttgagatcctttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctac
cagcggtggtttgtttgccggatcaagagctaccaactctttttccgaaggtaactggcttcagcagagcgcagata
ccaaatactgttcttctagtgtagccgtagttaggccaccacttcaagaactctgtagcaccgcctacatacctcgc
tctgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagt
taccggataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgacctacacc
gaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggt
aagcggcagggtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatctttatagtcctgtcg
ggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagc
aacgcggccttttacggttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattc
tgtggataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcagcgagtcag
tgagcgaggaagcggaagagcgcccaatacgcaaaccgcctctccccgcgcgttggccgattcattaatgcagctgg
cacgacaggtttcccgactggaaagcgggcagtgagcgcaacgcaattaatgtgagttagctcactcattaggcacc
ccaggctttacactttatgcttccggctcgtatgttgtgtggaattgtgagcggataacaatttcacacaggaaaca
gctatgaccatgattacgccaagcttggtaccgagctcggatccnctagtaacggccgccagtgtgctggaattcgc
ccttgatcatgcattcgcccttaggaggtaaaaaaacatgtgtgcgacctcttctcaatttactcagattaccgagc
ataattcccgtcgttccgcaaactatcagccaaacctgtggaatttcgaattcctgcaatccctggagaacgacctg

Figure 10B

aaagtggaaaagctggaggagaaagcgaccaaactggaggaagaagttcgctgcatgatcaaccgtgtagacaccca
gccgctgtccctgctggagctgatcgacgatgtgcagcgcctgggtctgacctacaaatttgaaaaagacatcatta
aagccctggaaaacatcgtactgctggacgaaaacaaaaagaacaaatctgacctgcacgcaaccgctctgtctttc
cgtctgctgcgtcagcacggtttcgaggtttctcaggatgtttttgagcgtttcaaggataaagaaggtggtttcag
cggtgaactgaaaggtgacgtccaaggcctgctgagcctgtatgaagcgtcttacctgggtttcgagggtgagaacc
tgctggaggaggcgcgtacctttccatcacccacctgaagaacaacctgaaagaaggcattaataccaaggttgca
gaacaagtgagccacgccctggaactgccatatcaccagcgtctgcaccgtctggaggcacgttggttcctggataa
atacgaaccgaaagaaccgcatcaccagctgctgctggagctggcgaagctggattttaacatggtacagaccctgc
accagaaagagctgcaagatctgtcccgctggtggaccgagatgggcctggctagcaaactggattttgtacgcgac
cgcctgatggaagtttatttctgggcactgggtatggcgccagacccgcagtttggtgaatgtcgcaaagctgttac
taaaatgtttggtctggtgacgatcatcgatgacgtgtatgacgtttatggcactctggacgaactgcaactgttca
ccgatgctgtagagcgctgggacgttaacgctattaacaccctgccggactatatgaaactgtgtttcctggcactg
tacaacaccgttaacgacacgtcctattctattctgaaagagaaaggtcataacaacctgtcctatctgacgaaaag
ctggcgtgaactgtgcaaagcctttctgcaagaggcgaaatggtccaacaacaaaattatcccggctttctccaagt
acctggaaaacgccagcgtttcctcctccggtgtagcgctgctggcgccgtcttacttttccgtatgccagcagcag
gaagacatctccgaccacgcgctgcgttccctgaccgacttccatggtctggtgcgttctagctgcgttatcttccg
cctgtgcaacgatctggccacctctgcggcggagctggaacgtggcgagactaccaattctatcattagctacatgc
acgaaaacgatggtaccagcgaggaacaggcccgcgaagaactgcgtaaactgatcgacgccgaatggaaaaagatg
aatcgtgaacgcgttagcgactccaccctgctgcctaaagcgttcatggaaatcgcagttaacatggcacgtgtttc
ccactgcacctaccagtatggcgatggtctgggtcgcccagactacgcgactgaaaaccgcatcaaactgctgctga
ttgacccctttcccgattaaccagctgatgtatgtctaactgcagggatccgtcgaccg

Figure 11

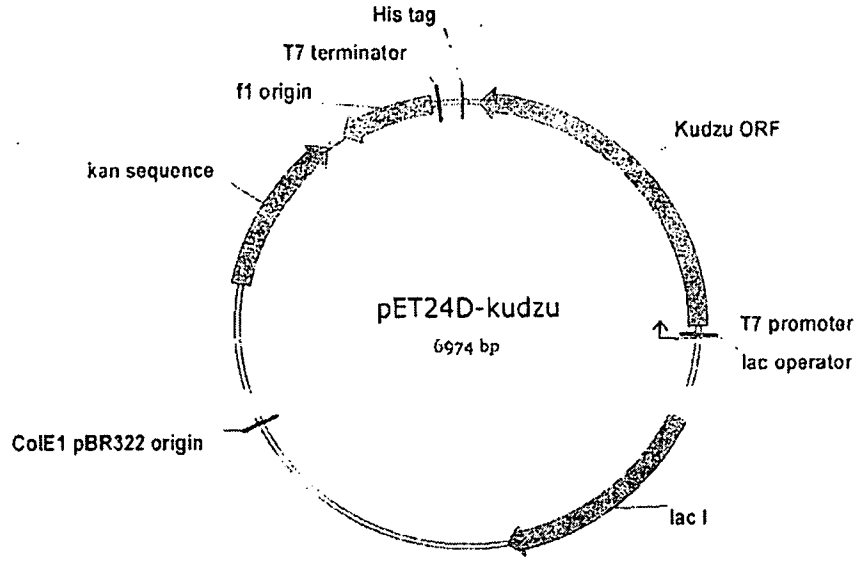

His tag
T7 terminator
f1 origin
Kudzu ORF
kan sequence
pET24D-kudzu
6974 bp
T7 promoter
lac operator
ColE1 pBR322 origin
lac I

Figure 12A

pET24D-Kudzu (SEQ ID NO:23) Kudzu IspS ORF 48-1742 (complementary)

gtgcggccgcaagcttgtcgacggagctcgaattcggatccctgcagttagacatacatcagctggttaatcgggaa
agggtcaatcagcagcagtttgatgcggttttcagtcgcgtagtctgggcgacccagaccatcgccatactggtagg
tgcagtgggaaacacgtgccatgttaactgcgatttccatgaacgctttaggcagcagggtggagtcgctaacgcgt
tcacgattcatctttttccattcggcgtcgatcagtttacgcagttcttcgcgggcctgttcctcgctggtaccatc
gttttcgtgcatgtagctaatgatagaattggtagtctcgccacgttccagctccgccgcagaggtggccagatcgt
tgcacaggcggaagataacgcagctagaacgcaccagaccatggaagtcggtcagggaacgcagcgcgtggtcggag
atgtcttcctgctgctggcatacggaaaagtaagacggcgccagcagcgctacaccggaggaggaaacgctggcgtt
ttccaggtacttggagaaagccgggataattttgttgttggaccatttcgcctcttgcagaaaggctttgcacagtt
cacgccagcttttcgtcagataggacaggttgttatgacctttctctttcagaatagaataggacgtgtcgttaacg
gtgttgtacagtgccaggaaacacagtttcatatagtccggcagggtgttaatagcgttaacgtcccagcgctctac
agcatcggtgaacagttgcagttcgtccagagtgccataaacgtcatacacgtcatcgatgatcgtcaccagaccaa
acattttagtaacagctttgcgacattcaccaaactgcgggtctggcgccatacccagtgcccagaaataaacttcc
atcaggcggtcgcgtacaaaatccagtttgctagccaggcccatctcggtccaccagcgggacagatcttgcagctc
tttctggtgcagggtctgtaccatgttaaaatccagcttcgccagctccagcagcagctggtgatgcggttctttcg
gttcgtatttatccaggaaccaacgtgcctccagacggtgcagacgctggtgatatggcagttccagggcgtggctc
acttgttctgcaaccttggtattaatgccttctttcaggttgttcttcaggtgggtgatggaaaaggtacgcgcctc
ctccagcaggttctcaccctcgaaacccaggtaagacgcttcatacaggctcagcaggccttggacgtcacctttca
gttcaccgctgaaaccaccttctttatccttgaaacgctcaaaaacatcctgagaaacctcgaaaccgtgctgacgc
agcagacggaaagacagagcggttgcgtgcaggtcagatttgttctttttgttttcgtccagcagtacgatgttttc
cagggctttaatgatgtctttttcaaatttgtaggtcagacccaggcgctgcacatcgtcgatcagctccagcaggg
acagcggctgggtgtctacacggttgatcatgcagcgaacttcttcctccagtttggtcgctttctcctccagcttt
tccactttcaggtcgttctccagggattgcaggaattcgaaattccacaggtttggctgatagtttgcggaacgacg
ggaattatgctcggtaatctgagtaaattgagaagaggtcgcacacatggtatatctccttcttaaagttaaacaaa
attatttctagaggggaattgttatccgctcacaattcccctatagtgagtcgtattaatttcgcgggatcgagatc
tcgatcctctacgccggacgcatcgtggccggcatcaccggcgccacaggtgcggttgctggcgcctatatcgccga
catcaccgatggggaagatcgggctcgccacttcgggctcatgagcgcttgtttcggcgtgggtatggtggcaggcc
ccgtggccgggggactgttgggcgccatctccttgcatgcaccattccttgcggcggcggtgctcaacggcctcaac
ctactactgggctgcttcctaatgcaggagtcgcataagggagagcgtcgagatcccggacaccatcgaatggcgca
aaacctttcgcggtatggcatgatagcgcccggaagagagtcaattcagggtggtgaatgtgaaaccagtaacgtta
tacgatgtcgcagagtatgccggtgtctcttatcagaccgtttcccgcgtggtgaaccaggccagccacgtttctgc
gaaaacgcgggaaaaagtggaagcggcgatggcggagctgaattacattcccaaccgcgtggcacaacaactggcgg
gcaaacagtcgttgctgattggcgttgccacctccagtctggccctgcacgcgccgtcgcaaattgtcgcggcgatt
aaatctcgcgccgatcaactgggtgccagcgtggtggtgtcgatggtagaacgaagcggcgtcgaagcctgtaaagc
ggcggtgcacaatcttctcgcgcaacgcgtcagtgggctgatcattaactatccgctggatgaccaggatgccattg
ctgtggaagctgcctgcactaatgttccggcgttatttcttgatgtctctgaccagacacccatcaacagtattatt
ttctcccatgaagacggtacgcgactgggcgtggagcatctggtcgcattgggtcaccagcaaatcgcgctgttagc
gggcccattaagttctgtctcggcgcgtctgcgtctggctggctggcataaatatctcactcgcaatcaaattcagc
cgatagcggaacgggaaggcgactggagtgccatgtccggttttcaacaaaccatgcaaatgctgaatgagggcatc
gttcccactgcgatgctggttgccaacgatcagatggcgctgggcgcaatgcgcgccattaccgagtccgggctgcg
cgttggtgcggatatctcggtagtgggatacgacgataccgaagacagctcatgttatatcccgccgttaaccacca
tcaaacaggattttcgcctgctggggcaaaccagcgtggaccgcttgctgcaactctctcagggccaggcggtgaag
ggcaatcagctgttgcccgtctcactggtgaaaagaaaaaccaccctggcgcccaatacgcaaaccgcctctccccg
cgcgttggccgattcattaatgcagctggcacgacaggtttcccgactggaaagcgggcagtgagcgcaacgcaatt
aatgtaagttagctcactcattaggcaccgggatctcgaccgatgcccttgagagccttcaacccagtcagctcctt
ccggtgggcgcggggcatgactatcgtcgccgcacttatgactgtcttctttatcatgcaactcgtaggacaggtgc
cggcagcgctctgggtcattttcggcgaggaccgctttcgctggagcgcgacgatgatcggcctgtcgcttgcggta
ttcggaatcttgcacgccctcgctcaagccttcgtcactggtcccgccaccaaacgtttcggcgagaagcaggccat
tatcgccggcatggcggccccacgggtgcgcatgatcgtgctcctgtcgttgaggacccggctaggctggcggggtt
gccttactggttagcagaatgaatcaccgatacgcgagcgaacgtgaagcgactgctgctgcaaaacgtctgcgacc
tgagcaacaacatgaatggtcttcggtttccgtgtttcgtaaagtctggaaacgcggaagtcagcgccctgcaccat
tatgttccggatctgcatcgcaggatgctgctggctaccctgtggaacacctacatctgtattaacgaagcgctggc
attgaccctgagtgatttttctctggtcccgccgcatccataccgccagttgtttaccctcacaacgttccagtaac
cgggcatgttcatcatcagtaacccgtatcgtgagcatcctctctcgtttcatcggtatcattacccccatgaacag

Figure 12B

aaatccccttacacggaggcatcagtgaccaaacaggaaaaaaccgcccttaacatggcccgctttatcagaagcc
agacattaacgcttctggagaaactcaacgagctggacgcggatgaacaggcagacatctgtgaatcgcttcacgac
cacgctgatgagctttaccgcagctgcctcgcgcgtttcggtgatgacggtgaaaacctctgacacatgcagctccc
ggagacggtcacagcttgtctgtaagcggatgccgggagcagacaagcccgtcagggcgcgtcagcgggtgttggcg
ggtgtcggggcgcagccatgacccagtcacgtagcgatagcggagtgtatactggcttaactatgcggcatcagagc
agattgtactgagagtgcaccatatatgcggtgtgaaataccgcacagatgcgtaaggagaaaataccgcatcaggc
gctcttccgcttcctcgctcactgactcgctgcgctcggtcgttcggctgcggcgagcggtatcagctcactcaaag
gcggtaatacggttatccacagaatcaggggataacgcaggaaagaacatgtgagcaaaaggccagcaaaaggccag
gaaccgtaaaaaggccgcgttgctggcgtttttccataggctccgccccctgacgagcatcacaaaaatcgacgct
caagtcagaggtggcgaaacccgacaggactataaagataccaggcgtttccccctggaagctccctcgtgcgctct
cctgttccgaccctgccgcttaccggatacctgtccgcctttctcccttcgggaagcgtggcgctttctcatagctc
acgctgtaggtatctcagttcggtgtaggtcgttcgctccaagctgggctgtgtgcacgaacccccgttcagcccg
accgctgcgccttatccggtaactatcgtcttgagtccaacccggtaagacacgacttatcgccactggcagcagcc
actggtaacaggattagcagagcgaggtatgtaggcggtgctacagagttcttgaagtggtggcctaactacggcta
cactagaaggacagtatttggtatctgcgctctgctgaagccagttaccttcggaaaaagagttggtagctcttgat
ccggcaaacaaaccaccgctggtagcggtggtttttttgtttgcaagcagcagattacgcgcagaaaaaaaggatct
caagaagatcctttgatcttttctacggggtctgacgctcagtggaacgaaaactcacgttaagggattttggtcat
gaacaataaaactgtctgcttacataaacagtaatacaaggggtgttatgagccatattcaacgggaaacgtcttgc
tctaggccgcgattaaattccaacatggatgctgatttatatgggtataaatgggctcgcgataatgtcgggcaatc
aggtgcgacaatctatcgattgtatgggaagcccgatgcgccagagttgtttctgaaacatggcaaaggtagcgttg
ccaatgatgttacagatgagatggtcagactaaactggctgacggaatttatgcctcttccgaccatcaagcatttt
atccgtactcctgatgatgcatggttactcaccactgcgatccccgggaaaacagcattccaggtattagaagaata
tcctgattcaggtgaaaatattgttgatgcgctggcagtgttcctgcgccggttgcattcgattcctgtttgtaatt
gtccttttaacagcgatcgcgtatttcgtctcgctcaggcgcaatcacgaatgaataacggtttggttgatgcgagt
gattttgatgacgagcgtaatggctggcctgttgaacaagtctggaaagaaatgcataaacttttgccattctcacc
ggattcagtcgtcactcatggtgatttctcacttgataaccttatttttgacgaggggaaattaataggttgtattg
atgttggacgagtcggaatcgcagaccgataccaggatcttgccatcctatggaactgcctcggtgagttttctcct
tcattacagaaacggctttttcaaaaatatggtattgataatcctgatatgaataaattgcagtttcatttgatgct
cgatgagtttttctaagaattaattcatgagcggatacatatttgaatgtatttagaaaaataaacaaatagggttt
ccgcgcacatttccccgaaaagtgccacctgaaattgtaaacgttaatattttgttaaaattcgcgttaaatttttg
ttaaatcagctcatttttaaccaataggccgaaatcggcaaaatcccttataaatcaaaagaatagaccgagatag
ggttgagtgttgttccagtttggaacaagagtccactattaaagaacgtggactccaacgtcaaagggcgaaaaacc
gtctatcagggcgatggcccactacgtgaaccatcaccctaatcaagtttttggggtcgaggtgccgtaaagcact
aaatcggaaccctaaagggagcccccgatttagagcttgacggggaaagccggcgaacgtggcgagaaaggaaggga
agaaagcgaaaggagcgggcgctagggcgctggcaagtgtagcggtcacgctgcgcgtaaccaccacacccgccgcg
cttaatgcgccgctacagggcgcgtcccattcgccaatccggatatagttcctcctttcagcaaaaaaccctcaag
acccgtttagaggccccaaggggttatgctagttattgctcagcggtggcagcagccaactcagcttcctttcgggc
tttgttagcagccggatctcagtggtggtggtggtggtgctcga

Figure 13

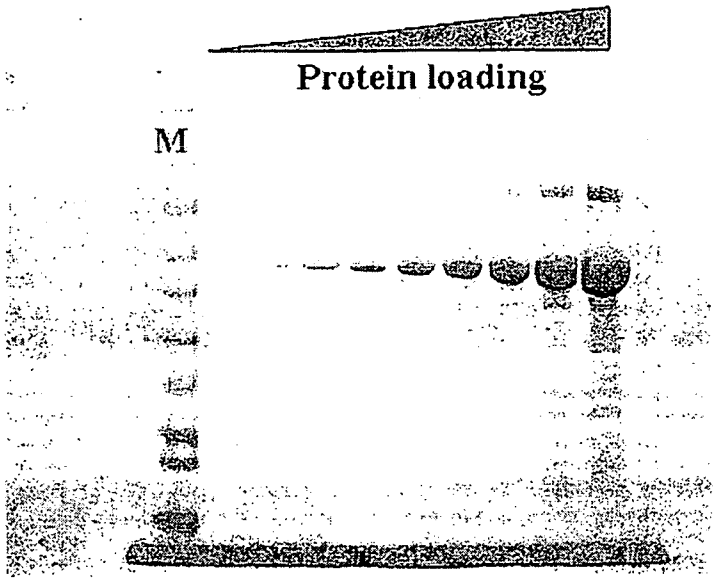


Figure 14

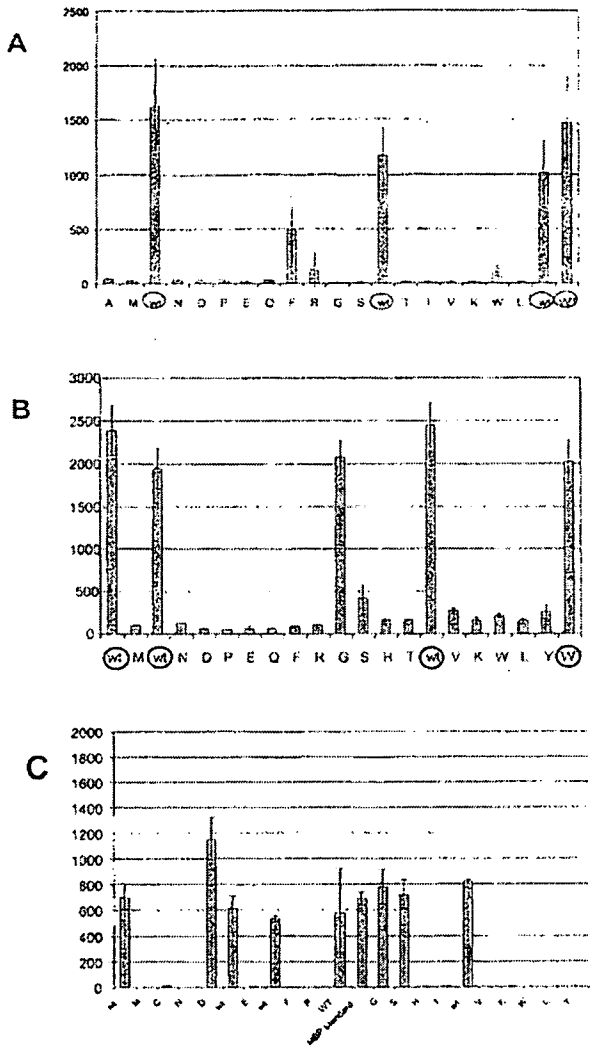

A
2500
2000
1500
1000
500
0
B
3000
2500
2000
1500
1000
500
0
C
2000
1800
1600
1400
1200
1000
800
600
400
200
0

Figure 15

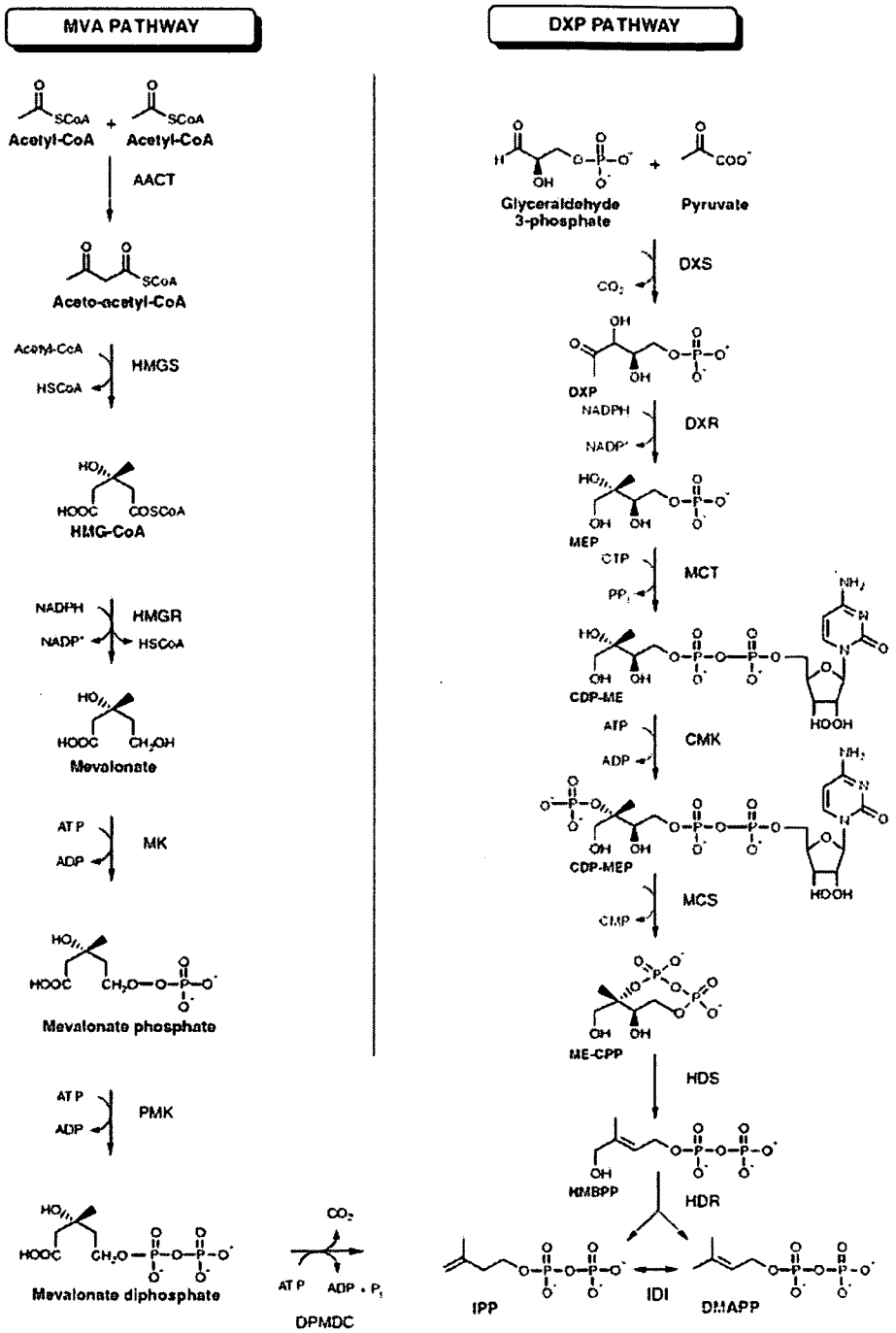

MVA PATHWAY
DXP PATHWAY
Acetyl-CoA
Acetyl-CoA
AACT
Aceto-acetyl-CoA
HMGS
HMG-CoA
HMGR
Mevalonate
MK
Mevalonate phosphate
PMK
Mevalonate diphosphate
DPMDC
Glyceraldehyde 3-phosphate
Pyruvate
DXS
DXP
DXR
MEP
MCT
CDP-ME
CMK
CDP-MEP
MCS
ME-CPP
HDS
HMBPP
HDR
IPP
IDI
DMAPP

Figure 16

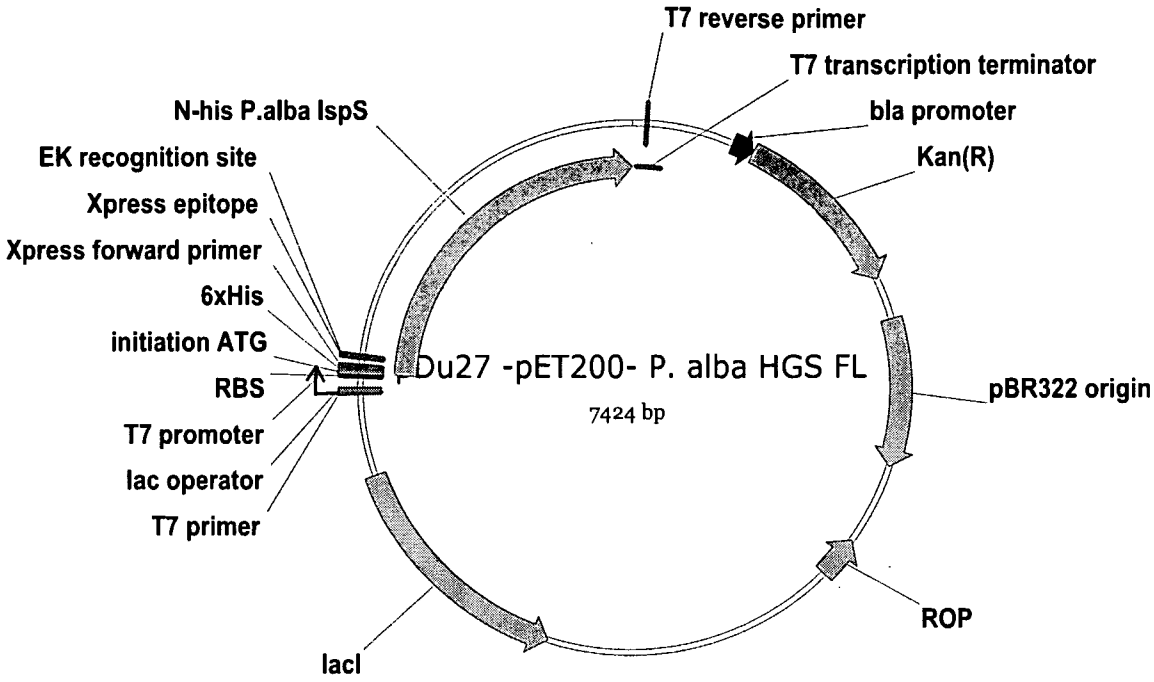

T7 reverse primer
T7 transcription terminator
N-his P.alba IspS
bla promoter
EK recognition site
Kan(R)
Xpress epitope
Xpress forward primer
6xHis
initiation ATG
RBS
T7 promoter
lac operator
T7 primer
pBR322 origin
ROP
lacI
Du27 -pET200- P. alba HGS FL
7424 bp

Figure 17

Amino acid sequence of 6XHis N-terminally tagged *P. alba* IspS (SEQ ID NO:118)

MRGSHHHHHHGMASMTGGQQMGRDLYDDDDKDHPFTMRCSVSTENVSFTETETEARRSANYEPN
SWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQRLGLGYRFESDI
RGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAI
LSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALELPLHRRTQRLEAVWS
IEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLIESFYWAV
GVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNAINDLPDYMKLCF
LALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTFDDYFGNAWKSSS
GPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASAEIARGETANSVSCYM
RTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHCTYHNGDAHTSPD
ELTRKRVLSVITEPILPFER

Figure 18A

Nucleotide sequence of pDu27 (SEQ ID NO:119)

aagggcgagctcaacgatccggctgctaacaaagcccgaaaggaagctgagttggctgctgcca
ccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgaggagttttttgct
gaaaggaggaactatatccggatatcccgcaagaggcccggcagtaccggcataaccaagccta
tgcctacagcatccagggtgacggtgccgaggatgacgatgagcgcattgttagatttcataca
cggtgcctgactgcgttagcaatttaactgtgataaactaccgcattaaagcttatcgatgata
agctgtcaaacatgagaattaattcttgaagacgaaagggcctcgtgatacgcctatttttata
ggttaatgtcatgataataatggtttcttagacgtcaggtggcacttttcggggaaatgtgcgc
ggaacccctatttgtttatttttctaaatacattcaaatatgtatccgctcatgagacaataac
cctgataaatgcttcaataatattgaaaaaggaagagtatgattgaacaagatggattgcacgc
aggttctccggccgcttgggtggagaggctattcggctatgactgggcacaactgacaatcggc
tgctctgatgccgccgtgttccggctgtcagcgcaggggcgcccggttctttttgtcaagaccg
acctgtccggtgccctgaatgaactgcaggacgaggcagcgcggctatcgtggctggccacgac
gggcgttccttgcgcagctgtgctcgacgttgtcactgaagcgggaagggactggctgctattg
ggcgaagtgccggggcaggatctcctgtcatctcaccttgctcctgccgagaaagtatccatca
tggctgatgcaatgcggcggctgcatacgcttgatccggctacctgcccattcgaccaccaagc
gaaacatcgcatcgagcgggcacgtactcggatggaagccggtcttgtcgatcaggatgatctg
gacgaagagcatcaggggctcgcgccagccgaactgttcgccaggctcaaggcgcgcatgcccg
acggcgaggatctcgtcgtgacacatggcgatgcctgcttgccgaatatcatggtggaaaatgg
ccgcttttctggattcatcgactgtggccggctgggtgtggcggaccgctatcaggacatagcg
ttggctacccgtgatattgctgaagagcttggcggcgaatgggctgaccgcttcctcgtgcttt
acggtatcgccgctcccgattcgcagcgcatcgccttctatcgccttcttgacgagttcttctg
agcgggactctggggttcgaaatgaccgaccaagcgacgcctaactgtcagaccaagtttactc
atatatactttagattgatttaaaacttcatttttaatttaaaaggatctaggtgaagatcctt
tttgataatctcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccccg
tagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaaac
aaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttccg
aaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagttag
gccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttaccagt
ggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccggat
aaggcgcagcggtcgggctgaacgggggggttcgtgcacacagcccagcttggagcgaacgacct
acaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggagaaa
ggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccaggg
ggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatttt
tgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacggtt
cctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtggat
aaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcagcg
agtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgcgg
tatttcacaccgcaatggtgcactctcagtacaatctgctctgatgccgcatagttaagccagt
atacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacacccgct
gacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgtctccg
ggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcggtaaag
ctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagctcgttg
agtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggttttt

Figure 18B

Nucleotide sequence of pDu27

cctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgataccgat
gaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactggaacgt
tgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcagggtcaat
gccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcgatgca
gatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacacggaaa
ccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttcacgttc
gctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgggtcct
caacgacaggagcacgatcatgcgcacccgtggccaggacccaacgctgcccgagatgcgccgc
gtgcggctgctggagatggcggacgcgatggatatgttctgccaagggttggtttgcgcattca
cagttctccgcaagaattgattggctccaattcttggagtggtgaatccgttagcgaggtgccg
ccggcttccattcaggtcgaggtggcccggctccatgcaccgcgacgcaacgcggggaggcaga
caaggtatagggcggcgcctacaatccatgccaacccgttccatgtgctcgccgaggcggcata
aatcgccgtgacgatcagcggtccaatgatcgaagttaggctggtaagagccgcgagcgatcct
tgaagctgtccctgatggtcgtcatctacctgcctggacagcatggcctgcaacgcgggcatcc
cgatgccgccggaagcgagaagaatcataatggggaaggccatccagcctcgcgtcgcgaacgc
cagcaagacgtagcccagcgcgtcggccgccatgccggcgataatggcctgcttctcgccgaaa
cgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagattccgaataccgcaa
gcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaaatgacccagagcgc
tgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtgcggcgacgatagtc
atgccccgcgcccaccggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatc
ccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactgcccgctttccagtc
gggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcggggagaggcggtttgcgt
attgggcgccagggtggtttttcttttcaccagtgagacgggcaacagctgattgcccttcacc
gcctggccctgagagagttgcagcaagcggtccacgctggtttgccccagcaggcgaaaatcct
gtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcgtcgtatcccactac
cgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattgcgcccagcgccatc
tgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcatttgcatggtttgtt
gaaaaccggacatggcactccagtcgccttcccgttccgctatcggctgaatttgattgcgagt
gagatatttatgccagccagccagacgcagacgcgccgagacagaacttaatgggcccgctaac
agcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcgcgtaccgtcttcat
gggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaataacgccggaacatt
agtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagttaatgatcagccca
ctgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttcta
ccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatcgccgcgacaatttg
cgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacgactgtttgcccgcc
agttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgcttccacttttccc
gcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtctgataagagacacc
ggcatactctgcgacatcgtataacgttactggtttcacattcaccaccctgaattgactctct
tccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggtgtccgggatctcga
cgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggttgaggccgttgagca
ccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtcccccggccacggggcc
tgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgagcccgatcttcccca

Figure 18C

Nucleotide sequence of pDu27

tcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggtgatgccggccacga
tgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgactcactataggggaa
ttgtgagcggataacaattcccctctagaaataattttgtttaactttaagaaggagatataca
tatgcggggttctcatcatcatcatcatcatggtatggctagcatgactggtggacagcaaatg
ggtcgggatctgtacgacgatgacgataaggatcatccttcaccatgcgttgtagcgtgtcca
ccgaaaatgtgtctttcaccgaaactgaaaccgaagctcgtcgttctgcgaactacgaacctaa
cagctgggactatgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagac
aaagcgaaaaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctga
ccctgctggaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatat
ccgtggtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctg
cacggtacggcactgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgt
tcagcggcttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctat
cctgagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaag
gttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaac
aggtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtc
tatcgaggcctaccgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggat
tacaacatgatccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtg
tgggtctggcgaccaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgt
gggtgtagcattcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttc
gtaaccattatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactg
atgcagttgagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctt
tctggctctgtataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaac
atcctgccgtatctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagt
ggctgtacaacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttc
tggcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatc
gaaaacctgcaaaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatg
acctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacat
gcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacc
tggaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccg
cgatcaacctggcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccgga
tgagctgacccgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaa

Figure 19

Amino acid sequence of full length *P. alba* IspS in P. alba (SEQ ID NO:120)

MRCSVSTENVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINN
EKAEFLTLLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGF
EVSQEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKI
GKELAEQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRET
SRWWRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLD
ELELFTDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNA
FLQEAKWLYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSH
IFRLCNDLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFA
KPFVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 20A

Nucleotide sequence of P. alba pET24a (SEQ ID NO:121)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctccctttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 20B

Nucleotide sequence of P. alba pET24a

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaacttta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgcgttgtagcgtgtccaccgaaaatgtgtctttcaccgaaactgaaa
ccgaagctcgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctc
cgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttcgt
cgcgagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaacgtccagc
gcctgggcctgggttaccgtttcgagtctgatatccgtggtgcgctggatcgcttcgtttcctc
cggcggcttcgatgcggtaaccaagacttccctgcacggtacggcactgtctttccgtctgctg
cgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaagaccaaaacggcaact

Figure 20C

Nucleotide sequence of P. alba pET24a

tcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggc
tctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactg
tctgaagaaaagatcggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgc
atcgccgtactcagcgtctggaagcagtatggtctatcgaggcctaccgtaaaaaggaggacgc
gaatcaggttctgctggagctggcaattctggattacaacatgatccagtctgtataccagcgt
gatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctc
gtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccga
ctgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgta
tacggcaccctggacgaactggagctgtttactgatgcagttgagcgttgggacgtaaacgcca
tcaacgacctgccggattacatgaaactgtgctttctggctctgtataacactattaacgaaat
cgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatctgaccaaagcctgggct
gacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaatctactccgacctttg
acgactacttcggcaacgcatggaaatcctcttctggcccgctgcaactggtgttcgcttactt
cgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatc
tctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgc
gtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggtatctccgaagaactggc
taccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggt
ggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgca
cttatcataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgt
aatcactgaaccgattctgccgtttgaacgctaaggatccgaattcgagctccgtcgacaagct
tgcggccgcactcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaag
gaagctgagttggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaac
gggtcttgaggggtttttgctgaaaggaggaactatatccggat

Figure 21

10% NUPAGE Bis-Tris Gel, Reduced

Lane	Gel No. 1 Volume	Description
1	10	MW Marker
2	1.5	Purif IsoS 0.5 ug
3	3.1	Purif IsoS 1 ug
4	6.3	Purif IsoS 2 ug
5	15	P alba Uninduced
6	15	P alba Induced
7	15	P alba Lysate
8	15	P alba Supernatant
9	10	P alba Pellet
10	0	Blank
Function	Coomassie Stain	

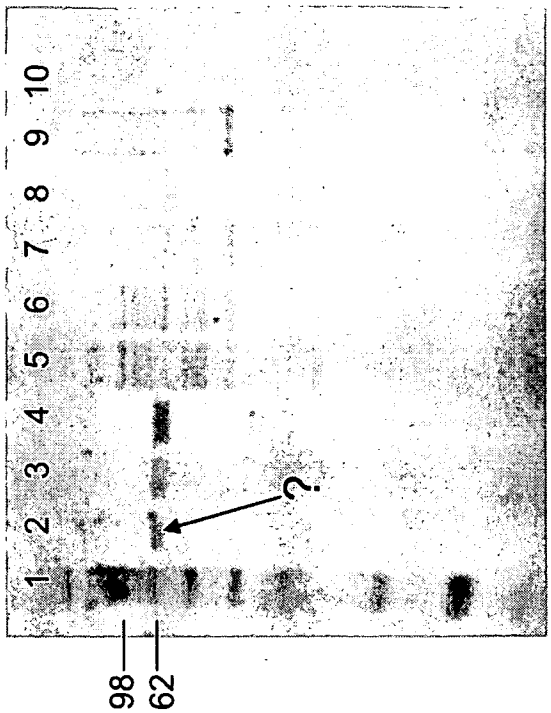


Figure 22

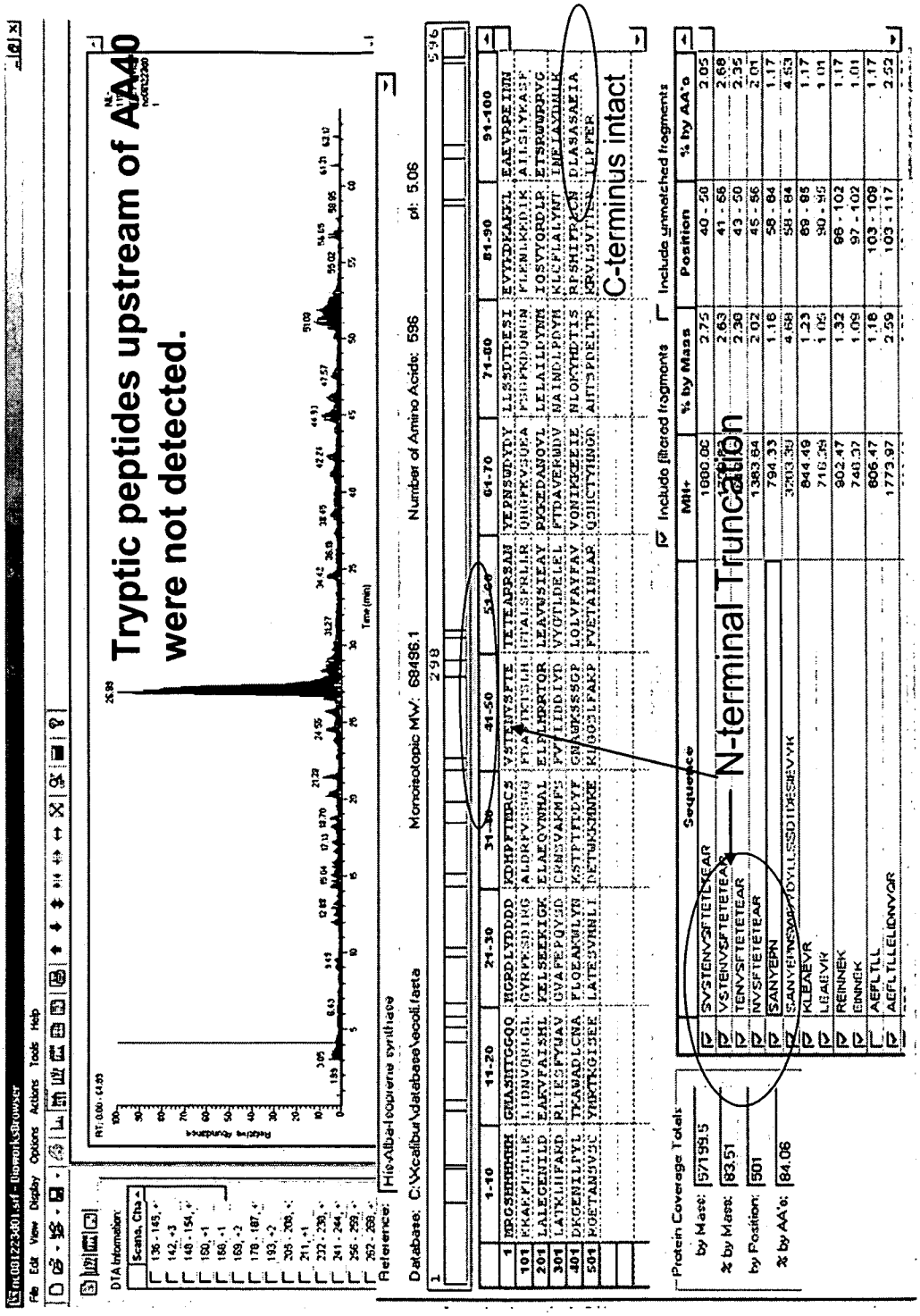

Tryptic peptides upstream of A40 were not detected.
N-terminal Truncation
C-terminus intact

Figure 23

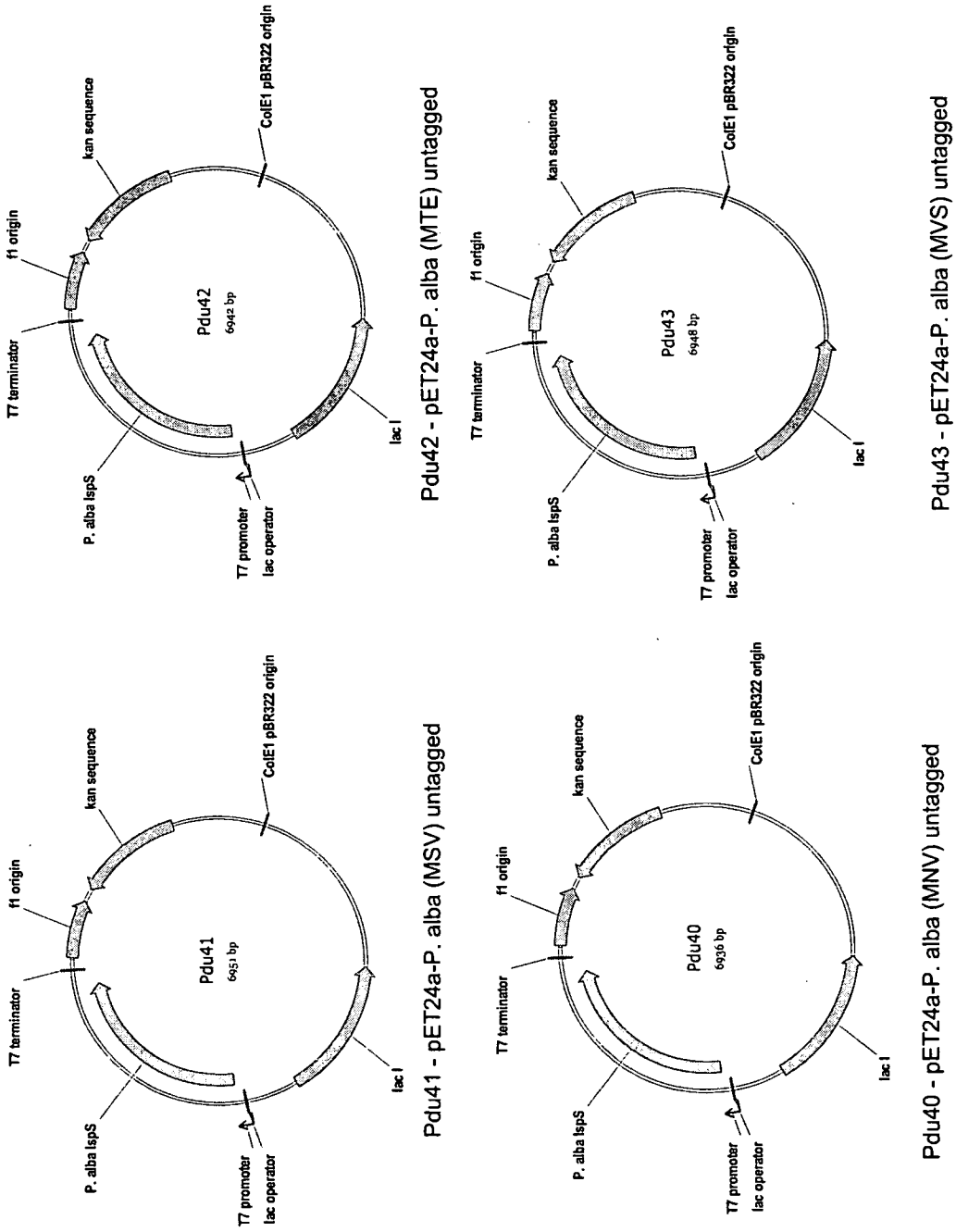

Pdu42
6942 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
lac I
P. alba IspS
T7 promoter
lac operator
Pdu42 - pET24a-P. alba (MTE) untagged
Pdu43
6948 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
lac I
P. alba IspS
T7 promoter
lac operator
Pdu43 - pET24a-P. alba (MVS) untagged
Pdu41
6951 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
lac I
P. alba IspS
T7 promoter
lac operator
Pdu41 - pET24a-P. alba (MSV) untagged
Pdu40
6936 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
lac I
P. alba IspS
T7 promoter
lac operator
Pdu40 - pET24a-P. alba (MNV) untagged

Figure 24

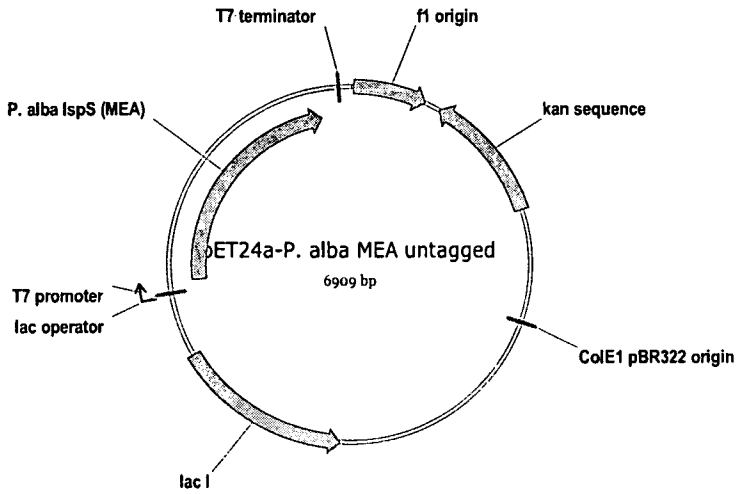

T7 terminator
f1 origin
P. alba IspS (MEA)
kan sequence
pET24a-P. alba MEA untagged
6909 bp
T7 promoter
lac operator
ColE1 pBR322 origin
lac I

Figure 25

Amino acid sequence of "MEA" variant of *P. alba* IspS (SEQ ID NO:122)

MEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQ
RLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGN
FLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALELPL
HRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFA
RDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNA
INDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTF
DDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASAEIA
RGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHC
TYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 26A

Nucleotide sequence of pDu39 (SEQ ID NO:123)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactcttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 26B

Nucleotide sequence of pDu39

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaagctcgtcgttctgcgaactacgaacctaacagctgggactatg
attacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaagct
ggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactg
attgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtggtgcgctgg
atcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacggtacggcact
gtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaa
gaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacg

Figure 26C

Nucleotide sequence of pDu39

aggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctc
tcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtgaaccatgca
ctggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcgaggcctacc
gtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggattacaacatgatcca
gtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgacc
aaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcg
aaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcga
cgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgcagttgagcgt
tgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctggctctgtata
acactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatct
gaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaa
tctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccgctgcaac
tggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaa
ataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcg
tctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggta
tctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaa
caaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggca
cgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgacccgca
aacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatccgaattcga
gctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgagatccggctgc
taacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcataaccc
cttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatatccggat

Figure 27

Amino acid sequence of truncated "MSV" variant of *P. alba* IspS (SEQ ID NO:124)

MSVSTENVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEK
AEFLTLLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEV
SQEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGK
ELAEQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSR
WWRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDEL
ELFTDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFL
QEAKWLYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIF
RLCNDLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKP
FVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 28A

Nucleotide sequence of pDu41 (pET24a-P.alba (MSV) Untagged) (SEQ ID NO:125)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatattttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt

Figure 28B

Nucleotide sequence of pDu41 (pET24a-P.alba (MSV) Untagged)

ttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata
ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgagcgtgtccaccgaaaatgtgtctttcaccgaaactgaaaccgaag
ctcgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccgacac
ggacgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttcgtcgcgag
attaataacgaaaaagcagaatttctgaccctgctggaactgattgacaacgtccagcgcctgg
gcctgggttaccgtttcgagtctgatatccgtggtgcgctggatcgcttcgtttcctccggcgg
cttcgatgcggtaaccaagacttccctgcacggtacggcactgtctttccgtctgctgcgtcaa

Figure 28C

Nucleotide sequence of pDu41 (pET24a-P.alba (MSV) Untagged)

cacggttttgaggtttctcaggaagcgttcagcggcttcaaagaccaaaacggcaacttcctgg
agaacctgaaggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggctctgga
aggcgaaaacatcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactgtctgaa
gaaaagatcggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgcatcgcc
gtactcagcgtctggaagcagtatggtctatcgaggcctaccgtaaaaaggaggacgcgaatca
ggttctgctggagctggcaattctggattacaacatgatccagtctgtataccagcgtgatctg
cgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgacc
gcctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgactgccg
taactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgtatacggc
accctggacgaactggagctgtttactgatgcagttgagcgttgggacgtaaacgccatcaacg
acctgccggattacatgaaactgtgctttctggctctgtataacactattaacgaaatcgccta
cgacaacctgaaagataaaggtgagaacatcctgccgtatctgaccaaagcctgggctgacctg
tgcaacgctttcctgcaagaagccaagtggctgtacaacaaatctactccgacctttgacgact
acttcggcaacgcatggaaatcctcttctggcccgctgcaactggtgttcgcttacttcgctgt
cgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatctctcgt
ccttcccatatcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtg
aaaccgcaaatagcgtttcttgttacatgcgcactaaaggtatctccgaagaactggctaccga
aagcgtgatgaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagc
ctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatc
ataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgtaatcac
tgaaccgattctgccgtttgaacgctaaggatccgaattcgagctccgtcgacaagcttgcggc
cgcactcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagct
gagttggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtct
tgaggggtttttgctgaaaggaggaactatatccggat

Figure 29

Amino acid sequence of truncated "MVS" Variant of *P. alba* IspS (SEQ ID NO:126)

MVSTENVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKA
EFLTLLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVS
QEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKE
LAEQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRW
WRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELE
LFTDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQ
EAKWLYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFR
LCNDLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPF
VETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 30A

Nucleotide sequence of pDu43 (pET24a-P.alba (MVS) Untagged) (SEQ ID NO:127)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata

Figure 30B

Nucleotide sequence of pDu43 (pET24a-P.alba (MVS) Untagged)

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggtgtccaccgaaaatgtgtctttcaccgaaactgaaaccgaagctc
gtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccgacacgga
cgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttcgtcgcgagatt
aataacgaaaaagcagaatttctgaccctgctggaactgattgacaacgtccagcgcctgggcc
tgggttaccgtttcgagtctgatatccgtggtgcgctggatcgcttcgtttcctccggcggctt
cgatgcggtaaccaagacttccctgcacggtacggcactgtctttccgtctgctgcgtcaacac
ggttttgaggtttctcaggaagcgttcagcggcttcaaagaccaaaacggcaacttcctggaga

Figure 30C

Nucleotide sequence of pDu43 (pET24a-P.alba (MVS) Untagged)

acctgaaggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggctctggaagg
cgaaaacatcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactgtctgaagaa
aagatcggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgcatcgccgta
ctcagcgtctggaagcagtatggtctatcgaggcctaccgtaaaaaggaggacgcgaatcaggt
tctgctggagctggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgt
gaaacgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccgcc
tgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgactgccgtaa
ctccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgtatacggcacc
ctggacgaactggagctgtttactgatgcagttgagcgttgggacgtaaacgccatcaacgacc
tgccggattacatgaaactgtgctttctggctctgtataacactattaacgaaatcgcctacga
caacctgaaagataaaggtgagaacatcctgccgtatctgaccaaagcctgggctgacctgtgc
aacgctttcctgcaagaagccaagtggctgtacaacaaatctactccgacctttgacgactact
tcggcaacgcatggaaatcctcttctggcccgctgcaactggtgttcgcttacttcgctgtcgt
gcagaacattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatctctcgtcct
tcccatatcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaa
ccgcaaatagcgtttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaag
cgtgatgaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctg
ttcgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatcata
acggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgtaatcactga
accgattctgccgtttgaacgctaaggatccgaattcgagctccgtcgacaagcttgcggccgc
actcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgag
ttggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtcttga
ggggttttttgctgaaaggaggaactatatccggat

Figure 31

Amino acid sequence of truncated "MTE" variant of *P. alba* IspS (SEQ ID NO:128)

MTENVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEF
LTLLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQE
AFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELA
EQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWR
RVGLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELF
TDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEA
KWLYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLC
NDLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVE
TAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 32A

Nucleotide sequence of pDu42 (pET24a-P.alba (MTE) Untagged) (SEQ ID NO:129)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 32B

Nucleotide sequence of pDu42 (pET24a-P.alba (MTE) Untagged)

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgaccgaaaatgtgtctttcaccgaaactgaaaccgaagctcgtcgtt
ctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccgacacggacgagtc
catcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttcgtcgcgagattaataac
gaaaaagcagaatttctgaccctgctggaactgattgacaacgtccagcgcctgggcctgggtt
accgtttcgagtctgatatccgtggtgcgctggatcgcttcgtttcctccggcggcttcgatgc
ggtaaccaagacttccctgcacggtacggcactgtctttccgtctgctgcgtcaacacggtttt
gaggtttctcaggaagcgttcagcggcttcaaagaccaaaacggcaacttcctggagaacctga

Figure 32C

Nucleotide sequence of pDu42 (pET24a-P.alba (MTE) Untagged)

aggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggctctggaaggcgaaaa
catcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatc
ggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgcatcgccgtactcagc
gtctggaagcagtatggtctatcgaggcctaccgtaaaaaggaggacgcgaatcaggttctgct
ggagctggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtgaaacg
tcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccgcctgattg
agagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgactgccgtaactccgt
cgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgtatacggcaccctggac
gaactggagctgtttactgatgcagttgagcgttgggacgtaaacgccatcaacgacctgccgg
attacatgaaactgtgctttctggctctgtataacactattaacgaaatcgcctacgacaacct
gaaagataaaggtgagaacatcctgccgtatctgaccaaagcctgggctgacctgtgcaacgct
ttcctgcaagaagccaagtggctgtacaacaaatctactccgacctttgacgactacttcggca
acgcatggaaatcctcttctggcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaa
cattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatctctcgtccttcccat
atcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaa
atagcgtttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgat
gaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcg
aaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatcataacggcg
acgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgtaatcactgaaccgat
tctgccgtttgaacgctaaggatccgaattcgagctccgtcgacaagcttgcggccgcactcga
gcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgagttggct
gctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgaggggtt
ttttgctgaaaggaggaactatatccggat

Figure 33

Amino acid Sequence of truncated "MNV" variant of *P. alba* IspS (SEQ ID NO:130)

MNVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLT
LLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAF
SGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQ
VNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRV
GLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTD
AVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKW
LYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCND
LASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETA
INLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 34A

Nucleotide sequence of pDu40 (pET24a-P.alba (MNV) Untagged) (SEQ ID NO:131)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 34B

Nucleotide sequence of pDu40 (pET24a-P.alba (MNV) Untagged)

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgaatgtgtctttcaccgaaactgaaaccgaagctcgtcgttctgcga
actacgaacctaacagctgggactatgattacctgctgtcctccgacacggacgagtccatcga
agtatacaaagacaaagcgaaaaagctggaagccgaagttcgtcgcgagattaataacgaaaaa
gcagaatttctgaccctgctggaactgattgacaacgtccagcgcctgggcctgggttaccgtt
tcgagtctgatatccgtggtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaac
caagacttccctgcacggtacggcactgtctttccgtctgctgcgtcaacacggttttgaggtt
tctcaggaagcgttcagcggcttcaaagaccaaaacggcaacttcctggagaacctgaaggaag

Figure 34C

Nucleotide sequence of pDu40 (pET24a-P.alba (MNV) Untagged)

atatcaaagctatcctgagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcct
ggacgaggcgaaggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaa
gagctggcagaacaggtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctgg
aagcagtatggtctatcgaggcctaccgtaaaaaggaggacgcgaatcaggttctgctggagct
ggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtgaaacgtcccgt
tggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccgcctgattgagagct
tctactgggccgtgggtgtagcattcgaaccgcaatactccgactgccgtaactccgtcgcaaa
aatgttttctttcgtaaccattatcgacgatatctacgatgtatacggcaccctggacgaactg
gagctgtttactgatgcagttgagcgttgggacgtaaacgccatcaacgacctgccggattaca
tgaaactgtgctttctggctctgtataacactattaacgaaatcgcctacgacaacctgaaaga
taaaggtgagaacatcctgccgtatctgaccaaagcctgggctgacctgtgcaacgctttcctg
caagaagccaagtggctgtacaacaaatctactccgacctttgacgactacttcggcaacgcat
ggaaatcctcttctggcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaa
aaaggaagagatcgaaaacctgcaaaaataccatgacaccatctctcgtccttcccatatcttc
cgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcg
tttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatgaatct
gatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccg
ttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatcataacggcgacgcgc
atacctctccggatgagctgacccgcaaacgcgttctgtctgtaatcactgaaccgattctgcc
gtttgaacgctaaggatccgaattcgagctccgtcgacaagcttgcggccgcactcgagcacca
ccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgagttggctgctgcc
accgctgagcaataactagcataaccccttggggcctctaaacgggtcttgaggggttttttgc
tgaaaggaggaactatatccggat

Figure 35

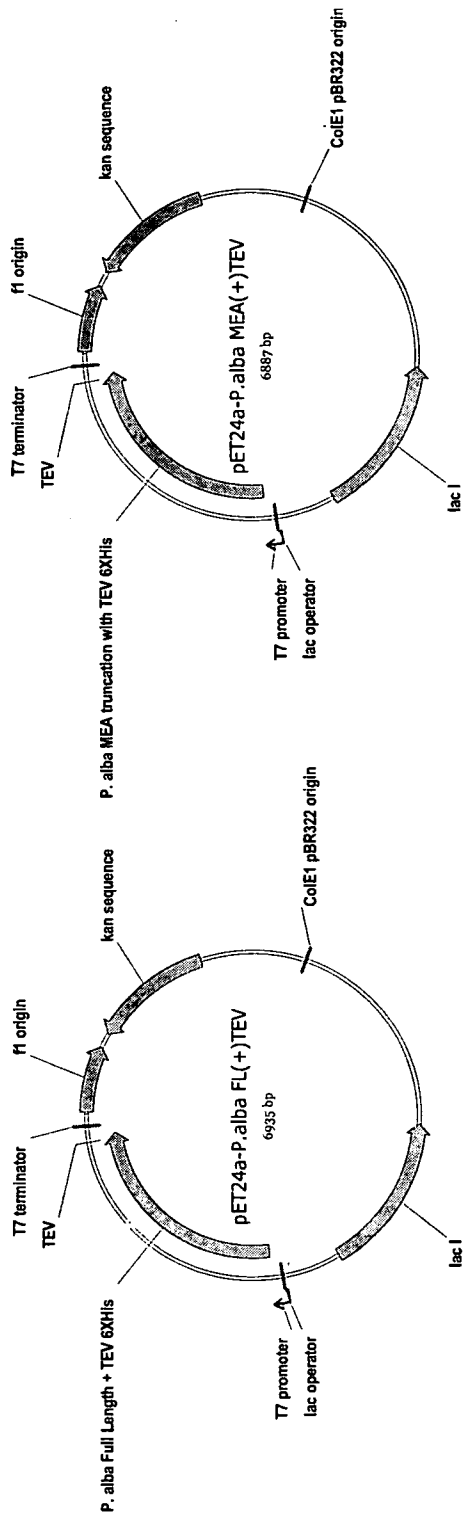

pET24a-P.alba MEA(+)TEV
6887 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
TEV
P. alba MEA truncation with TEV 6XHis
T7 promoter
lac operator
lac I
MD09-163
pET24a-P.alba FL(+)TEV
6935 bp
kan sequence
ColE1 pBR322 origin
f1 origin
T7 terminator
TEV
P. alba Full Length + TEV 6XHis
T7 promoter
lac operator
lac I
MD09-161

Figure 36

Amino acid sequence of *P. alba* MEA(+)TEV (SEQ ID NO:132)

MEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQ
RLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGN
FLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALELPL
HRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFA
RDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNA
INDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTF
DDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASAEIA
RGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHC
TYHNGDAHTSPDELTRKRVLSVITEPILPFERENLYFQGLEHHHHHH

Figure 37A

Nucleotide sequence of MD09-163 (pET24a-P. alba MEA(+)TEV) (SEQ ID NO:133)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt

Figure 37B

Nucleotide sequence of MD09-163 (pET24a-P. alba MEA(+)TEV)

ttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata
ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaagctcgtcgttctgcgaactacgaacctaacagctgggactatg
attacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaagct
ggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactg
attgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtggtgcgctgg
atcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacggtacggcact
gtcttttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaa

Figure 37C

Nucleotide sequence of MD09-163 (pET24a-P. alba MEA(+)TEV)

gaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacg
aggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctc
tcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtgaaccatgca
ctggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcgaggcctacc
gtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggattacaacatgatcca
gtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgacc
aaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcg
aaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcga
cgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgcagttgagcgt
tgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctggctctgtata
acactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatct
gaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaa
tctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccgctgcaac
tggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaa
ataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcg
tctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggta
tctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaa
caaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggca
cgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgacccgca
aacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgc**gaaaacctgtattttca**
gggcctcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagct
gagttggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtct
tgaggggttttttgctgaaaggaggaactatatccggat

Figure 38

Amino acid sequence of *P. alba* FL (+) TEV (SEQ ID NO:134)

MRCSVSTENVSFTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINN
EKAEFLTLLELIDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGF
EVSQEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKI
GKELAEQVNHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRET
SRWWRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLD
ELELFTDAVERWDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNA
FLQEAKWLYNKSTPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSH
IFRLCNDLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFA
KPFVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFERENLYFQGLEHHHHHH

Figure 39A

Nucleotide sequence of MD09-161 (pET24a-P. alba FL(+)TEV) (SEQ ID NO:135)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactcttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt

Figure 39B

Nucleotide sequence of MD09-161 (pET24a-P. alba FL(+)TEV)

ttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata
ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgcgttgtagcgtgtccaccgaaaatgtgtctttcaccgaaactgaaa
ccgaagctcgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctc
cgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttcgt
cgcgagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaacgtccagc
gcctgggcctgggttaccgtttcgagtctgatatccgtggtgcgctggatcgcttcgtttcctc
cggcggcttcgatgcggtaaccaagacttccctgcacggtacggcactgtctttccgtctgctg

Figure 39C

Nucleotide sequence of MD09-161 (pET24a-P. alba FL(+)TEV)

cgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaagaccaaaacggcaact
tcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggc
tctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactg
tctgaagaaaagatcggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgc
atcgccgtactcagcgtctggaagcagtatggtctatcgaggcctaccgtaaaaaggaggacgc
gaatcaggttctgctggagctggcaattctggattacaacatgatccagtctgtataccagcgt
gatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctc
gtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccga
ctgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgta
tacggcaccctggacgaactggagctgtttactgatgcagttgagcgttgggacgtaaacgcca
tcaacgacctgccggattacatgaaactgtgctttctggctctgtataacactattaacgaaat
cgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatctgaccaaagcctgggct
gacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaatctactccgacctttg
acgactacttcggcaacgcatggaaatcctcttctggcccgctgcaactggtgttcgcttactt
cgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatc
tctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgc
gtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggtatctccgaagaactggc
taccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggt
ggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgca
cttatcataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgt
aatcactgaaccgattctgccgtttgaacgc**gaaaacctgtattttcagggc**ctcgagcaccac
caccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgagttggctgctgcca
ccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgaggggttttttgct
gaaaggaggaactatatccggat

Figure 40

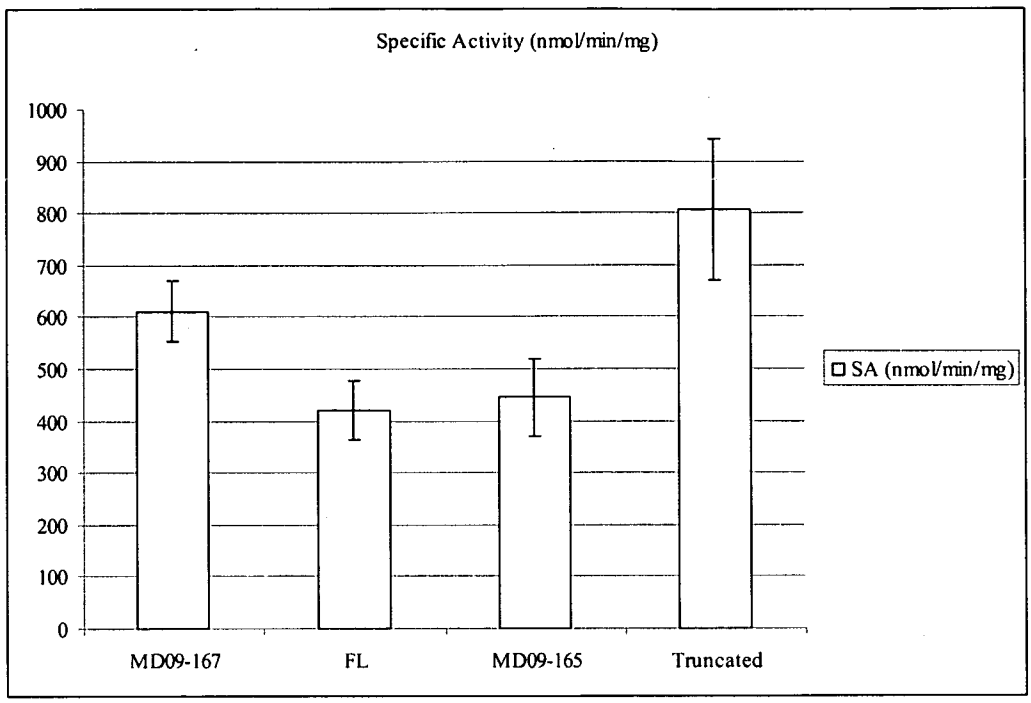

Specific Activity (nmol/min/mg)
1000
900
800
700
600
500
400
300
200
100
0
MD09-167
FL
MD09-165
Truncated
SA (nmol/min/mg)

Figure 41

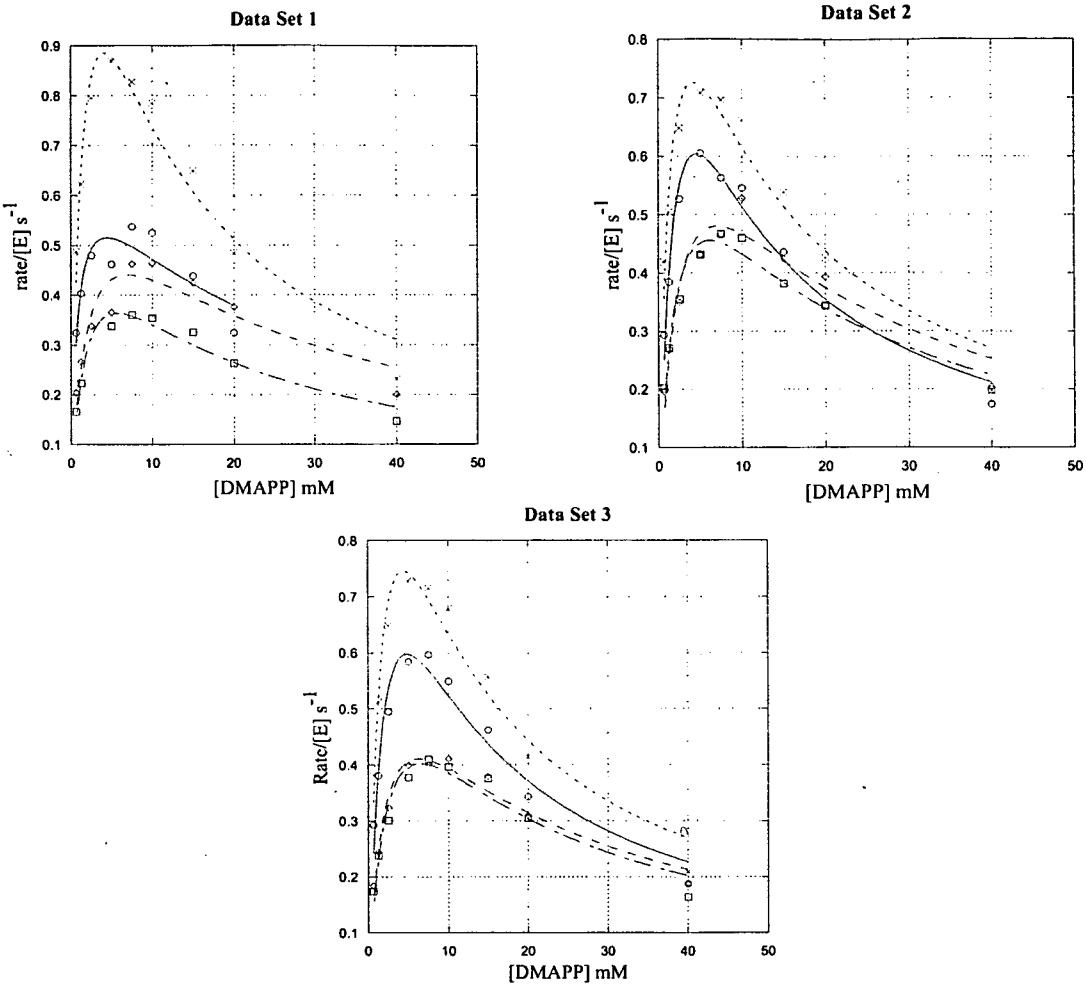

Data Set 1
rate/[E] s-1
[DMAPP] mM
Data Set 2
rate/[E] s-1
[DMAPP] mM
Data Set 3
Rate/[E] s-1
[DMAPP] mM

Figure 42

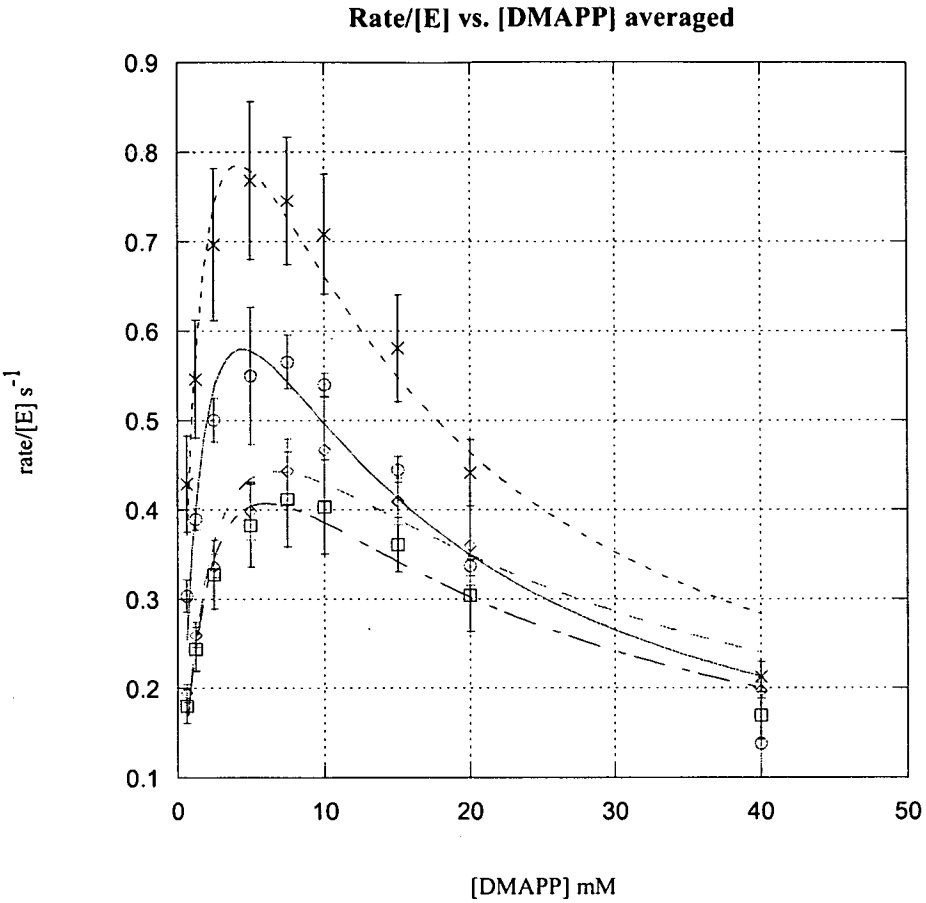
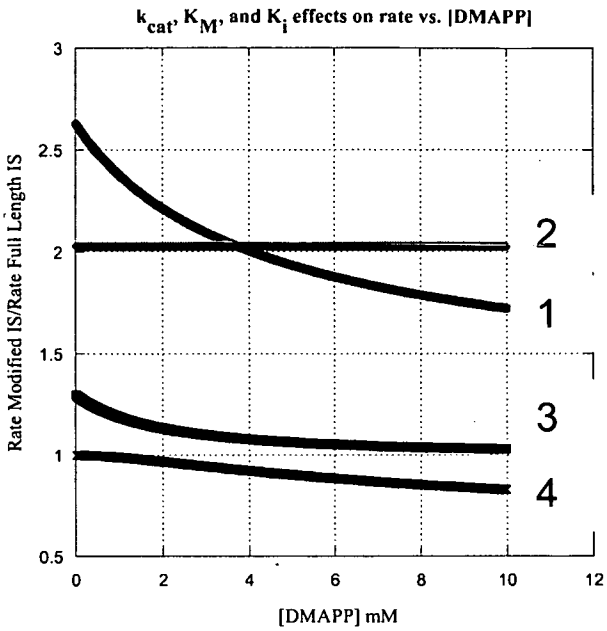

Rate/[E] vs. [DMAPP] averaged
rate/[E] s-1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
10
20
30
40
50
[DMAPP] mM

Figure 43

A.


k_{cat}, K_M, and K_i effects on rate vs. [DMAPP]
Rate Modified IS/Rate Full Length IS
[DMAPP] mM
1
2
3
4

B.

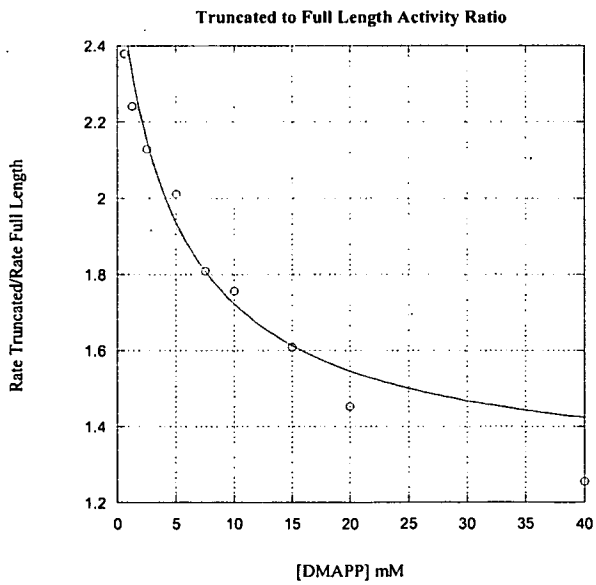
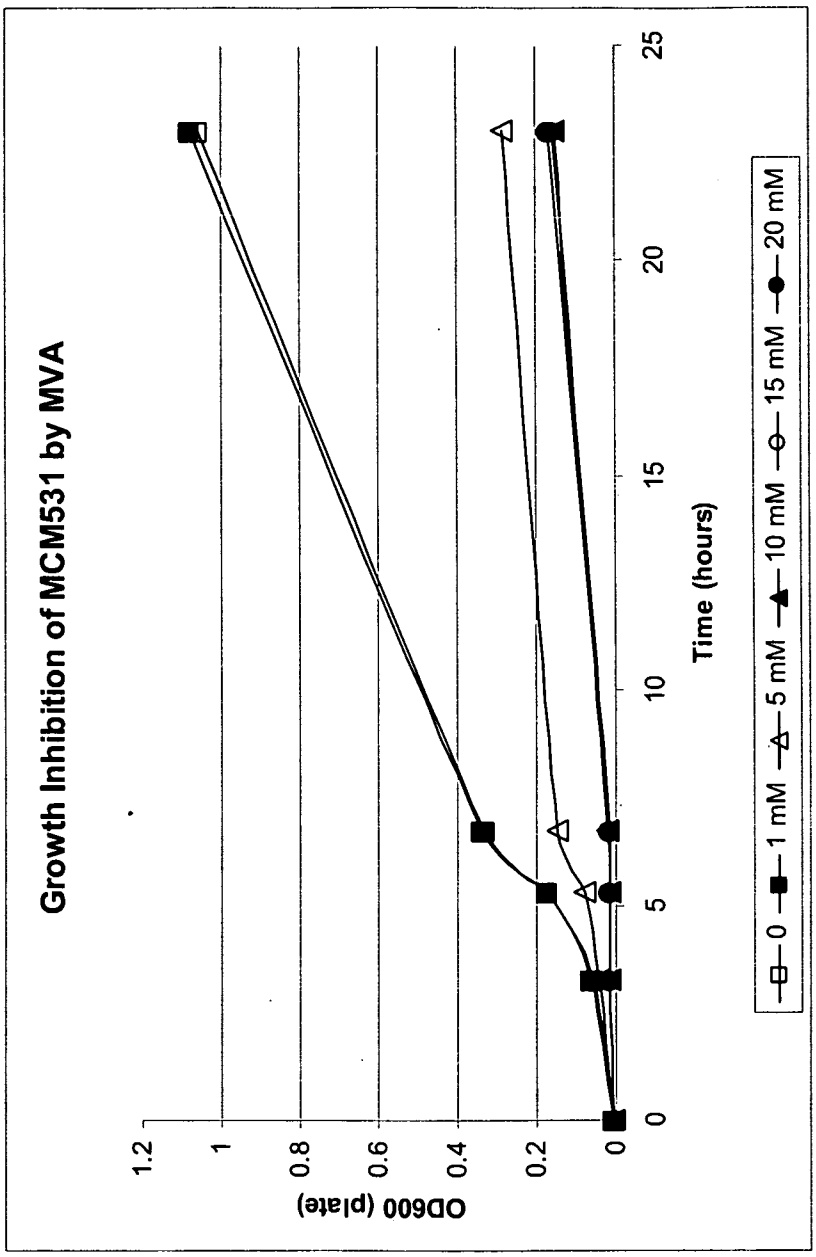
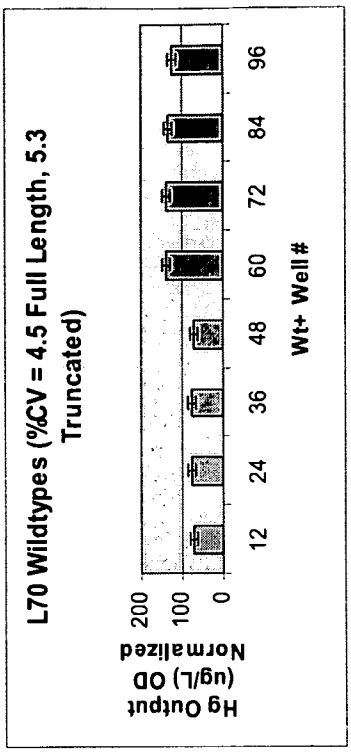

Truncated to Full Length Activity Ratio
Rate Truncated/Rate Full Length
[DMAPP] mM

Figure 44


Growth Inhibition of MCM531 by MVA
OD600 (plate)
1.2
1
0.8
0.6
0.4
0.2
0
0
5
10
15
20
25
Time (hours)
0
1 mM
5 mM
10 mM
15 mM
20 mM


L70 Wildtypes (%CV = 4.5 Full Length, 5.3 Truncated)
Hg Output (ug/L) OD Normalized
200
100
0
12
24
36
48
60
72
84
96
Wt+ Well#

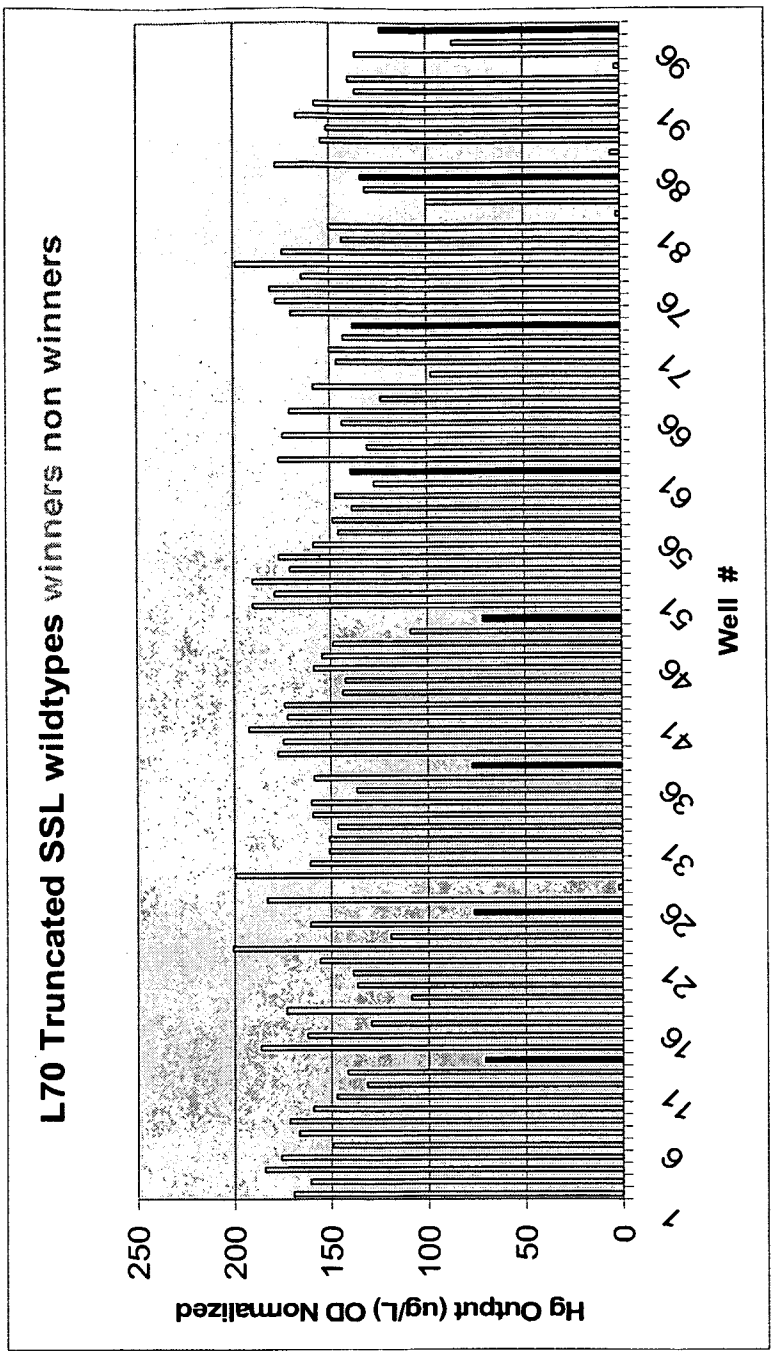

L70 Truncated SSL wildtypes winners non winners
Hg Output (ug/L) OD Normalized
250
200
150
100
50
0
Well #

Figure 45

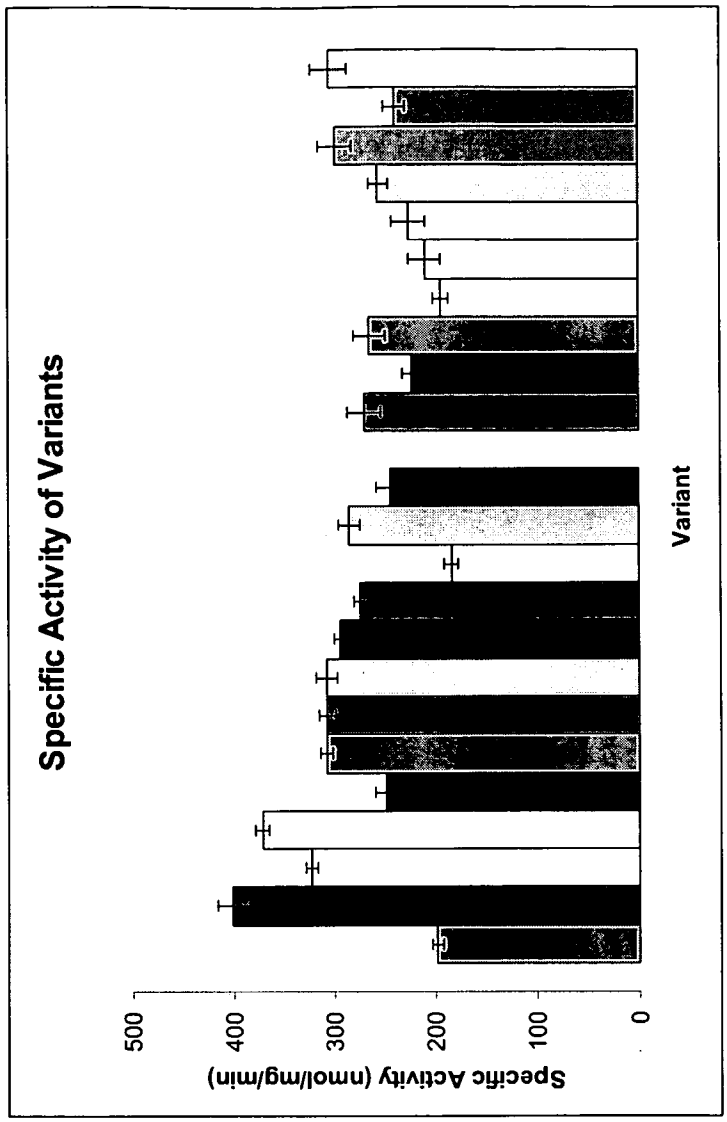

Specific Activity of Variants
Specific Activity (nmol/mg/min)
0
100
200
300
400
500
Variant

Figure 46

Figure 47

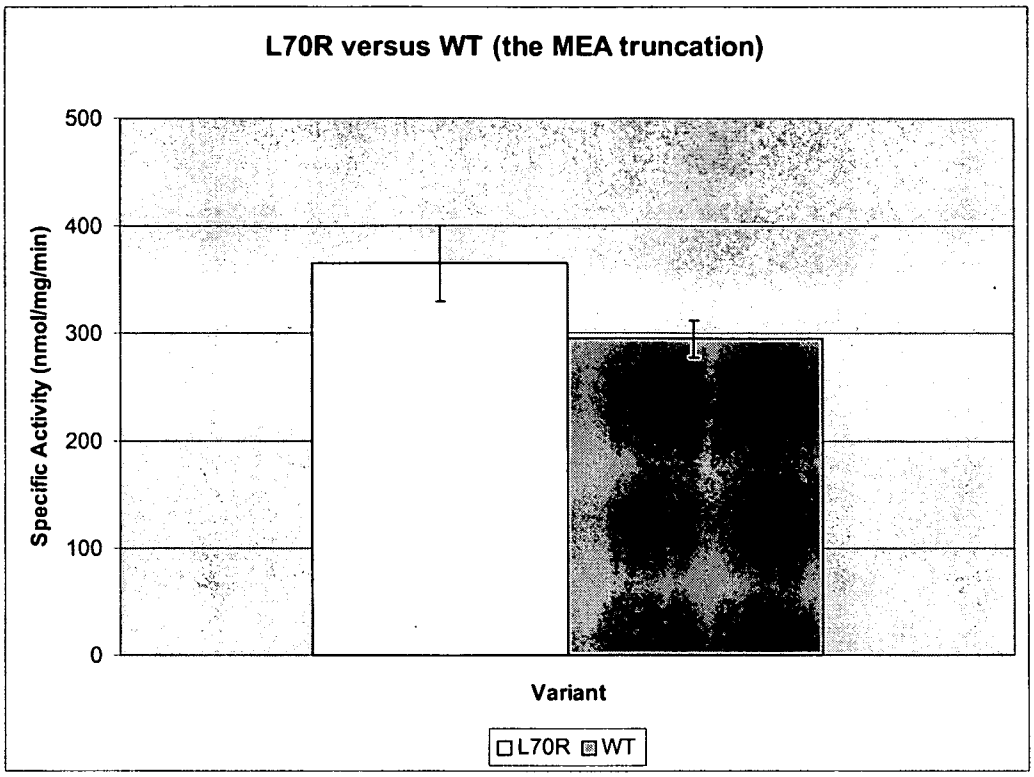
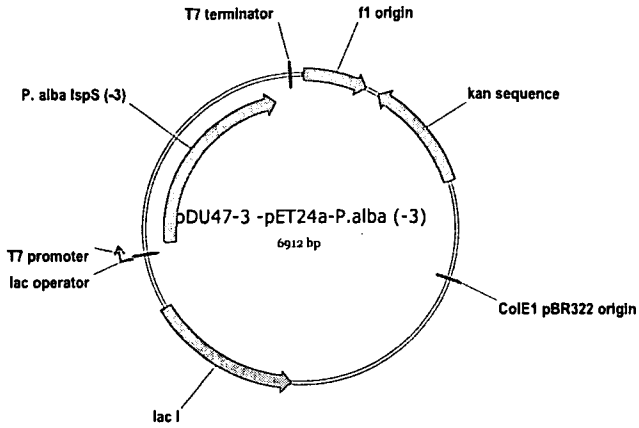
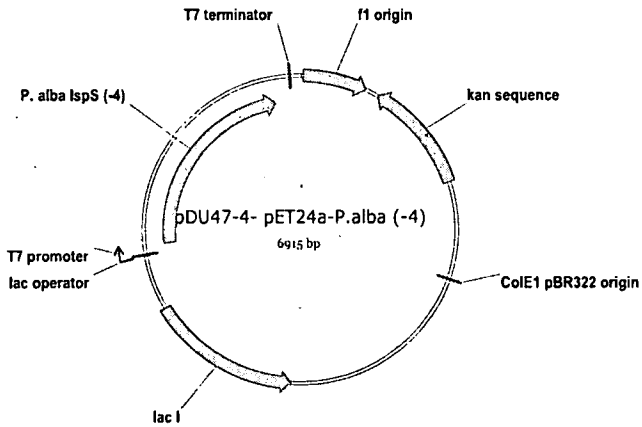

L70R versus WT (the MEA truncation)
Specific Activity (nmol/mg/min)
500
400
300
200
100
0
Variant
L70R
WT

Figure 48

A.



B.



C.

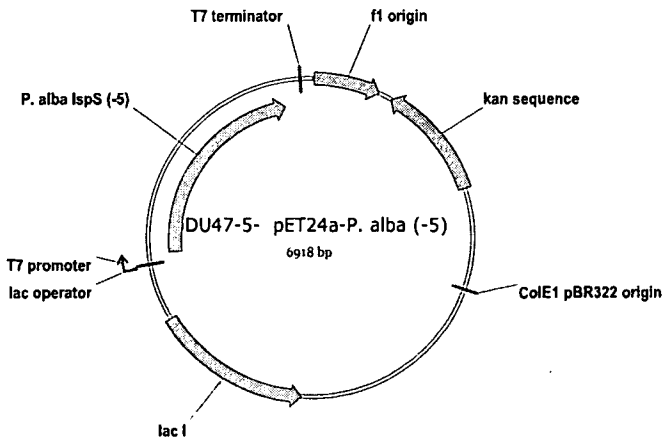
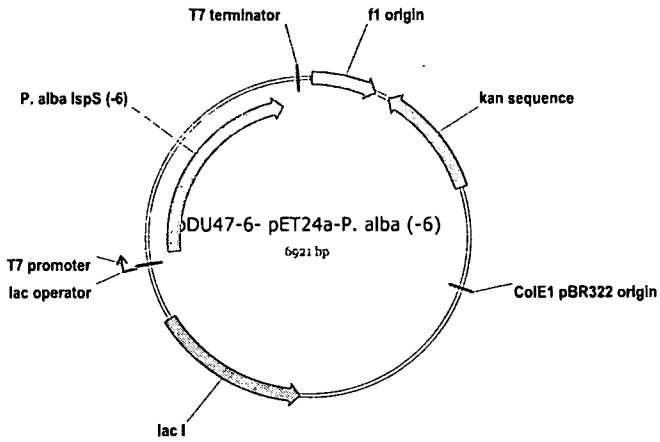
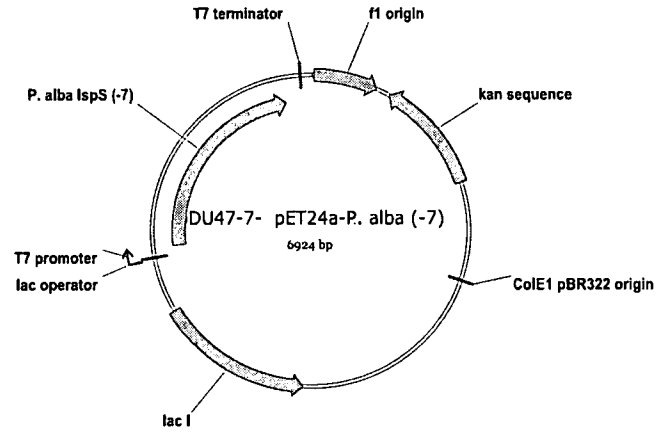


Figure 49

A.



B.



C.

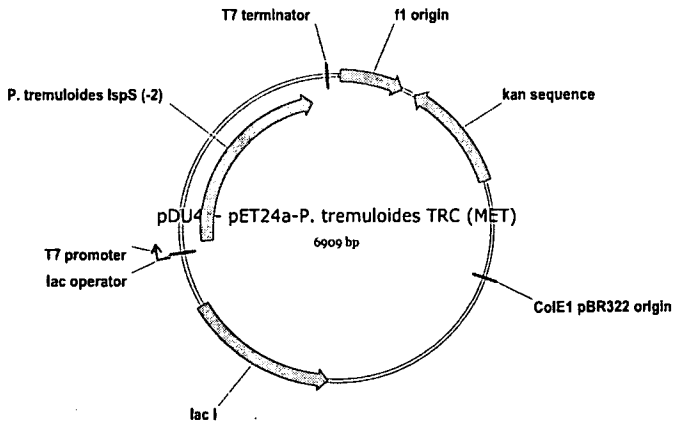
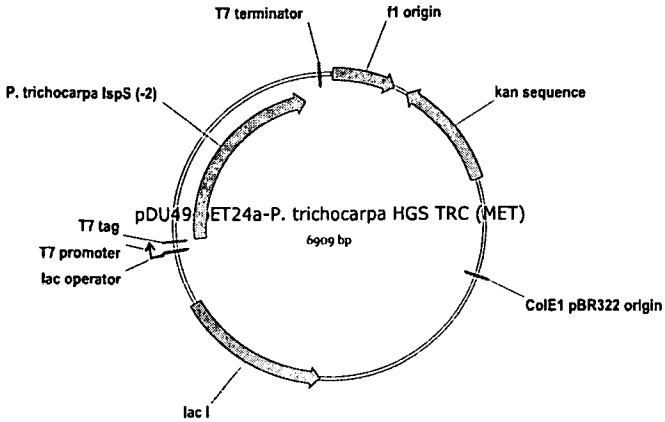
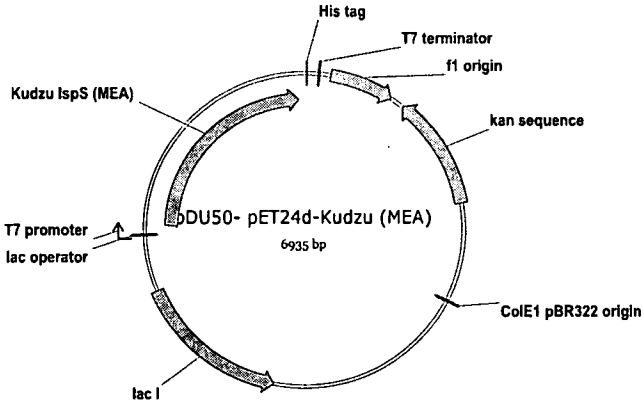


Figure 50

A.



B.



C.

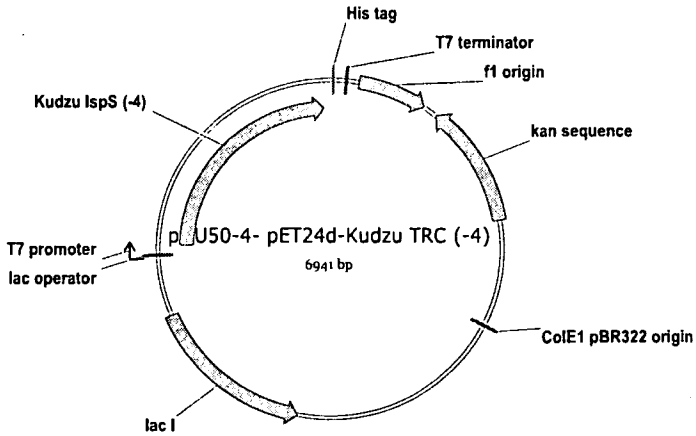


Figure 51

Amino acid sequence of *P.alba* TRC (-3) (SEQ ID NO:136)

MTEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNV
QRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNG
NFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALELP
LHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHF
ARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVN
AINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPT
FDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASAEI
ARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSH
CTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 52A

Nucleotide sequence of pDu47-3 (SEQ ID NO:137)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 52B

Nucleotide sequence of pDu47-3

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactataggggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgaccgaagctcgtcgttctgcgaactacgaacctaacagctgggact
atgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaa
gctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaa
ctgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtggtgcgc
tggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacggtacggc
actgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttc
aaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcctgt

Figure 52C

Nucleotide sequence of pDu47-3

acgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaat
ctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtgaaccat
gcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcgaggcct
accgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggattacaacatgat
ccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcg
accaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcat
tcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccattat
cgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgcagttgag
cgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctggctctgt
ataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgta
tctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaac
aaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccgctgc
aactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgca
aaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgacctggctagc
gcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaag
gtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagat
gaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctg
gcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgaccc
gcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatccgaatt
cgagctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgagatccggc
tgctaacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcataa
ccccttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatatccggat

Figure 53

Amino acid sequence of *P.alba* TRC (-4) (SEQ ID NO:138)

METEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDN
VQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQN
GNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALEL
PLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLH
FARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDV
NAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTP
TFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASAE
IARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQS
HCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 54A

Nucleotide sequence of pDu47-4 (SEQ ID NO:139)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 54B

Nucleotide sequence of pDu47-4

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactataggggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaaaccgaagctcgtcgttctgcgaactacgaacctaacagctggg
actatgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcgaa
aaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctg
gaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtggtg
cgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacggtac
ggcactgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggc
ttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcc

Figure 54C

Nucleotide sequence of pDu47-4

tgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgc
aatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtgaac
catgcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcgagg
cctaccgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggattacaacat
gatccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctg
gcgaccaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtag
cattcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccat
tatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgcagtt
gagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctggctc
tgtataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgcc
gtatctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtac
aacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccgc
tgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacct
gcaaaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgacctggct
agcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcacta
aaggtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaa
gatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaac
ctggcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctga
cccgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatccga
attcgagctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgagatcc
ggctgctaacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagca
taacccttggggcctctaaacgggtcttgaggggttttttgctgaaaggaggaactatatccg
gat

Figure 55

Amino acid sequence of *P.alba* TRC (-5) (SEQ ID NO:140)

MTETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELID
NVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQ
NGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALE
LPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKL
HFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWD
VNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKST
PTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASASA
EIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQ
SHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 56A

Nucleotide sequence of pDu47-5 (SEQ ID NO:141)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctccctttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactcttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggcctttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 56B

Nucleotide sequence of pDu47-5

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgactgaaaccgaagctcgtcgttctgcgaactacgaacctaacagct
gggactatgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagc
gaaaaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctg
ctggaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtg
gtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacgg
tacggcactgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagc
ggcttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctga

Figure 56C

Nucleotide sequence of pDu47-5

gcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggtttt
cgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtg
aaccatgcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcg
aggcctaccgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggattacaa
catgatccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggt
ctggcgaccaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtg
tagcattcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaac
cattatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgca
gttgagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctgg
ctctgtataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcct
gccgtatctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctg
tacaacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcc
cgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaa
cctgcaaaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgacctg
gctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgca
ctaaaggtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaa
aaagatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatc
aacctggcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagc
tgácccgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatc
cgaattcgagctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgaga
tccggctgctaacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataacta
gcataaccccttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatat
ccggat

Figure 57

Amino acid sequence of *P.alba* TRC (-6) (SEQ ID NO:142)

METETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELI
DNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKD
QNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHAL
ELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATK
LHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERW
DVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKS
TPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASAS
AEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLAR
QSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 58A

Nucleotide sequence of pDu47-6 (SEQ ID NO:143)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 58B

Nucleotide sequence of pDu47-6

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactataggggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaaactgaaaccgaagctcgtcgttctgcgaactacgaacctaaca
gctgggactatgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaa
agcgaaaaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgacc
ctgctggaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatcc
gtggtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgca
cggtacggcactgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttc
agcggcttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcc

Figure 58C

Nucleotide sequence of pDu47-6

tgagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggt
tttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacag
gtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtcta
tcgaggcctaccgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctggatta
caacatgatccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtg
ggtctggcgaccaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgg
gtgtagcattcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgt
aaccattatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactgat
gcagttgagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttc
tggctctgtataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacat
cctgccgtatctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtgg
ctgtacaacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctg
gcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcga
aaacctgcaaaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaatgac
ctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgc
gcactaaaggtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctg
gaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcg
atcaacctggcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatg
agctgacccgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaagg
atccgaattcgagctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactg
agatccggctgctaacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataa
ctagcataaccccttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaacta
tatccggat

Figure 59

Amino acid sequence of *P.alba* TRC (-7) (SEQ ID NO:144)

MTETETEARRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLEL
IDNVQRLGLGYRFESDIRGALDRFVSSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFK
DQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHA
LELPLHRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLAT
KLHFARDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVER
WDVNAINDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNK
STPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCNDLASA
SAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLA
RQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 60A

Nucleotide sequence of pDu47-7 (SEQ ID NO:145)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata

Figure 60B

Nucleotide sequence of pDu47-7

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactatagggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatgaccgaaactgaaaccgaagctcgtcgttctgcgaactacgaaccta
acagctgggactatgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaaga
caaagcgaaaaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctg
accctgctggaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgata
tccgtggtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccct
gcacggtacggcactgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcg
ttcagcggcttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagcta

Figure 60C

Nucleotide sequence of pDu47-7

tcctgagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaa
ggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaa
caggtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctggaagcagtatggt
ctatcgaggcctaccgtaaaaaggaggacgcgaatcaggttctgctggagctggcaattctgga
ttacaacatgatccagtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgt
gtgggtctggcgaccaaactgcactttgctcgtgaccgcctgattgagagcttctactgggccg
tgggtgtagcattcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttcttt
cgtaaccattatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttact
gatgcagttgagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgct
ttctggctctgtataacactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaa
catcctgccgtatctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaag
tggctgtacaacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctctt
ctggcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagat
cgaaaacctgcaaaaataccatgacaccatctctcgtccttcccatatcttccgtctgtgcaat
gacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttaca
tgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaac
ctggaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaacc
gcgatcaacctggcacgtcaatctcactgcacttatcataacggcgacgcgcatacctctccgg
atgagctgacccgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgcta
aggatccgaattcgagctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccacca
ctgagatccggctgctaacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaa
taactagcataaccccttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaa
ctatatccggat

Figure 61

Amino acid sequence of *P. tremu* TRC (MET) (SEQ ID NO:146)

METRRSANYEPNSWDYDYLLSSDTDESIEVHKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQ
RLGLGYRFESDIRRALDRFVSSGGFDGVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGN
FLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVSHALELPL
HRRTQRLEAVWSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFA
RDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNA
INDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTF
DDYFGNAWKSSSGPLQLIFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCNDLASASAEIA
RGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHC
TYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 62A

Nucleotide sequence of pDu48 (SEQ ID NO:147)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaatgata

Figure 62B

Nucleotide sequence of pDu48

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactataggggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaaacgcgtcgttctgcgaactacgaacctaacagctgggactatg
attacctgctgtcctccgacacggacgagtccatcgaagtacacaaagacaaagcgaaaaagct
ggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactg
attgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctgg
atcgcttcgtttcctccggcggcttcgatggcgtaaccaagacttccctgcacggtacggcact
gtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaa
gaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacg

Figure 62C

Nucleotide sequence of pDu48

aggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctc
tcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcagaacaggtgtcccatgca
ctggaactgccactgcatcgccgtactcagcgtctggaagcagtatggtctatcgaggcctacc
gtaaaaaggaggacgcgaaccaggttctgctggagctggcaattctggattacaacatgatcca
gtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgacc
aaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcg
aaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcga
cgatatctacgatgtatacggcaccctggacgaactggagctgtttactgatgcagttgagcgt
tgggacgtaaacgccatcaacgacctgccggattacatgaaactgtgctttctggctctgtata
acactattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatct
gaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaa
tctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccgctgcaac
tgatcttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaa
ataccatgacatcatctctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcg
tctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggta
tctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaa
caaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggca
cgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgacccgca
aacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatccgaattcga
gctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgagatccggctgc
taacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcataaccc
cttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatatccggat

Figure 63

Amino acid sequence of *P. tricho* (TRC) (SEQ ID NO:148)

METRRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQ
RLGLGYRFESDIRRALDRFVSSGGFDAVTKTSLHATALSFRLLRQHGFEVSQEAFSGFKDQNGN
FLENLKEDIKAILSLYEASFLALEGENILDEAKVFAISHLKELSEEKIGKDLAEQVNHALELPL
HRRTQRLEAVLSIEAYRKKEDADQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFA
RDRLIESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTNAVERWDVNA
IDDLPDYMKLCFLALYNTINEIAYDNLKEKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTF
DEYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCNDLASASAEIA
RGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHC
TYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 64A

Nucleotide sequence of pDu49 (SEQ ID NO:149)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgcgcagc
gtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttcccttcctttctcg
ccacgttcgccggctttccccgtcaagctctaaatcgggggctccctttagggttccgatttag
tgctttacggcacctcgaccccaaaaaacttgattagggtgatggttcacgtagtgggccatcg
ccctgatagacggtttttcgccctttgacgttggagtccacgttctttaatagtggactcttgt
tccaaactggaacaacactcaaccctatctcggtctattcttttgatttataagggattttgcc
gatttcggcctattggttaaaaaatgagctgatttaacaaaaatttaacgcgaattttaacaaa
atattaacgtttacaatttcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtt
tatttttctaaatacattcaaatatgtatccgctcatgaattaattcttagaaaaactcatcga
gcatcaaatgaaactgcaatttattcatatcaggattatcaataccatatttttgaaaaagccg
tttctgtaatgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcgg
tctgcgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataaggt
tatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagtttatgcat
ttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcactcgcatcaacc
aaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcgatcgctgttaaaaggac
aattacaaacaggaatcgaatgcaaccggcgcaggaacactgccagcgcatcaacaatattttc
acctgaatcaggatattcttctaatacctggaatgctgttttcccggggatcgcagtggtgagt
aaccatgcatcatcaggagtacggataaaatgcttgatggtcggaagaggcataaattccgtca
gccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccatgtttcag
aaacaactctggcgcatcgggcttcccatacaatcgatagattgtcgcacctgattgcccgaca
ttatcgcgagcccatttatacccatataaatcagcatccatgttggaatttaatcgcggcctag
agcaagacgtttcccgttgaatatggctcataacacccttgtattactgtttatgtaagcaga
cagttttattgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatccttttttctgcgcgtaatctgctgcttgcaa
acaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaactctttttc
cgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagtt
aggccaccacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgac
ctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggaga
aaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttccag
ggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatt
tttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgcggccttttacgg
ttcctggccttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtgg
ataaccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcag
cgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctgtgc
ggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgcatagttaag
ccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacac
ccgctgacgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgt
ctccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcgg
taaagctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccagct
cgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggt
tttttcctgtttggtcactgatgcctccgtgtaaggggatttctgttcatgggggtaatgata

Figure 64B

Nucleotide sequence of pDu49

ccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgcccggttactgg
aacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagagaaaaatcactcaggg
tcaatgccagcgcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcg
atgcagatccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacac
ggaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgcttca
cgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccagcctagccgg
gtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgccggcgataatggcct
gcttctcgccgaaacgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagat
tccgaataccgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaa
atgacccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagtg
cggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctctcaaggg
catcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgttgcgctcactg
cccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcgggga
gaggcggtttgcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagct
gattgcccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcgcattg
cgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccctcattcagcat
ttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgttccgctatcggctga
atttgattgcgagtgagatatttatgccagccagccagacgcagacgcgccgagacagaactta
atgggcccgctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcg
cgtaccgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaaat
aacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagcggatagt
taatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgac
gccgcttcgttctaccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatc
gccgcgacaatttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacg
actgtttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgc
ttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggtc
tgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattcaccaccc
tgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgccattcgatggt
gtccgggatctcgacgctctcccttatgcgactcctgcattaggaagcagcccagtagtaggtt
gaggccgttgagcaccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtccc
ccggccacggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgag
cccgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgccggt
gatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaattaatacgac
tcactataggggaattgtgagcggataacaattcccctctagaaataattttgtttaactttaa
gaaggagatatacatatggaaacgcgtcgttctgcgaactacgaacctaacagctgggactatg
attacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcgaaaaagct
ggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactg
attgacaacgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctgg
atcgcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacgcgacggcact
gtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaaa
gaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcctgtacg

Figure 64C

Nucleotide sequence of pDu49

aggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggttttcgcaatctc
tcatctgaaagaactgtctgaagaaaagatcggtaaagatctggcagaacaggtgaaccatgca
ctggaactgccactgcatcgccgtactcagcgtctggaagcagtactgtctatcgaggcctacc
gtaaaaaggaggacgcggatcaggttctgctggagctggcaattctggattacaacatgatcca
gtctgtataccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgacc
aaactgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcattcg
aaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcga
cgatatctacgatgtatacggcaccctggacgaactggagctgtttactaacgcagttgagcgt
tgggacgtaaacgccatcgacgatctgccggattacatgaaactgtgctttctggctctgtata
acactattaacgaaatcgcctacgacaacctgaaagaaaaaggtgagaacatcctgccgtatct
gaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaacaaa
tctactccgacctttgacgaatacttcggcaacgcatggaaatcctcttctggcccgctgcaac
tggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcgaaaacctgcaaaa
ataccatgacatcatctctcgtccttcccatatcttccgtctgtgcaatgacctggctagcgcg
tctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggta
tctccgaagaactggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaa
caaggaaaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggca
cgtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgacccgca
aacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaaggatccgaattcga
gctccgtcgacaagcttgcggccgcactcgagcaccaccaccaccaccactgagatccggctgc
taacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcataaccc
cttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatatccggat

Figure 65

Amino acid sequence of kudzu TRC (MEA) (SEQ ID NO:150)

MEARRSANYQPNLWNFEFLQSLENDLKVEKLEEKATKLEEEVRCMINRVDTQPLSLLELIDDVQ
RLGLTYKFEKDIIKALENIVLLDENKKNKSDLHATALSFRLLRQHGFEVSQDVFERFKDKEGGF
SGELKGDVQGLLSLYEASYLGFEGENLLEEARTFSITHLKNNLKEGINTKVAEQVSHALELPYH
QRLHRLEARWFLDKYEPKEPHHQLLLELAKLDFNMVQTLHQKELQDLSRWWTEMGLASKLDFVR
DRLMEVYFWALGMAPDPQFGECRKAVTKMFGLVTIIDDVYDVYGTLDELQLFTDAVERWDVNAI
NTLPDYMKLCFLALYNTVNDTSYSILKEKGHNNLSYLTKSWRELCKAFLQEAKWSNNKIIPAFS
KYLENASVSSSGVALLAPSYFSVCQQQEDISDHALRSLTDFHGLVRSSCVIFRLCNDLATSAAE
LERGETTNSIISYMHENDGTSEEQAREELRKLIDAEWKKMNRERVSDSTLLPKAFMEIAVNMAR
VSHCTYQYGDGLGRPDYATENRIKLLLIDPFPINQLMYV

Figure 66A

Nucleotide sequence of pDu50 (SEQ ID NO:151)

tcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgagtt
ggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgagg
ggttttttgctgaaaggaggaactatatccggattggcgaatgggacgcgccctgtagcggcgc
attaagcgcggcgggtgtggtggttacgcgcagcgtgaccgctacacttgccagcgccctagcg
cccgctcctttcgctttcttcccttcctttctcgccacgttcgccggctttccccgtcaagctc
taaatcgggggctccctttagggttccgatttagtgctttacggcacctcgaccccaaaaaact
tgattagggtgatggttcacgtagtgggccatcgccctgatagacggtttttcgccctttgacg
ttggagtccacgttctttaatagtggactcttgttccaaactggaacaacactcaaccctatct
cggtctattcttttgatttataagggattttgccgatttcggcctattggttaaaaaatgagct
gatttaacaaaaatttaacgcgaattttaacaaaatattaacgtttacaatttcaggtggcact
tttcggggaaatgtgcgcggaacccctatttgtttatttttctaaatacattcaaatatgtatc
cgctcatgaattaattcttagaaaaactcatcgagcatcaaatgaaactgcaatttattcatat
caggattatcaataccatatttttgaaaaagccgtttctgtaatgaaggagaaaactcaccgag
gcagttccataggatggcaagatcctggtatcggtctgcgattccgactcgtccaacatcaata
caacctattaatttcccctcgtcaaaaataaggttatcaagtgagaaatcaccatgagtgacga
ctgaatccggtgagaatggcaaaagtttatgcatttctttccagacttgttcaacaggccagcc
attacgctcgtcatcaaaatcactcgcatcaaccaaaccgttattcattcgtgattgcgcctga
gcgagacgaaatacgcgatcgctgttaaaaggacaattacaaacaggaatcgaatgcaaccggc
gcaggaacactgccagcgcatcaacaatattttcacctgaatcaggatattcttctaatacctg
gaatgctgttttcccggggatcgcagtggtgagtaaccatgcatcatcaggagtacggataaaa
tgcttgatggtcggaagaggcataaattccgtcagccagtttagtctgaccatctcatctgtaa
catcattggcaacgctacctttgccatgtttcagaaacaactctggcgcatcgggcttcccata
caatcgatagattgtcgcacctgattgcccgacattatcgcgagcccatttatacccatataaa
tcagcatccatgttggaatttaatcgcggcctagagcaagacgtttcccgttgaatatggctca
taacacccttgtattactgtttatgtaagcagacagttttattgttcatgaccaaaatccctt
aacgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttcttgaga
tccttttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctaccagcggtggtt
tgtttgccggatcaagagctaccaactctttttccgaaggtaactggcttcagcagagcgcaga
taccaaatactgtccttctagtgtagccgtagttaggccaccacttcaagaactctgtagcacc
gcctacatacctcgctctgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgt
cttaccgggttggactcaagacgatagttaccggataaggcgcagcggtcgggctgaacggggg
gttcgtgcacacagcccagcttggagcgaacgacctacaccgaactgagatacctacagcgtga
gctatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggtaagcggcagg
gtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatctttatagtcctg
tcgggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcct
atggaaaaacgccagcaacgcggcctttttacggttcctggccttttgctggccttttgctcac
atgttctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagtgagctg
ataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcggaagagcg
cctgatgcggtattttctccttacgcatctgtgcggtatttcacaccgcatatatggtgcactc
tcagtacaatctgctctgatgccgcatagttaagccagtatacactccgctatcgctacgtgac
tgggtcatggctgcgccccgacacccgccaacacccgctgacgcgccctgacgggcttgtctgc
tcccggcatccgcttacagacaagctgtgaccgtctccgggagctgcatgtgtcagaggttttc
accgtcatcaccgaaacgcgcgaggcagctgcggtaaagctcatcagcgtggtcgtgaagcgat

Figure 66B

Nucleotide sequence of pDu50

tcacagatgtctgcctgttcatccgcgtccagctcgttgagtttctccagaagcgttaatgtct
ggcttctgataaagcgggccatgttaagggcggttttttcctgtttggtcactgatgcctccgt
gtaaggggatttctgttcatgggggtaatgataccgatgaaacgagagaggatgctcacgata
cgggttactgatgatgaacatgcccggttactggaacgttgtgagggtaaacaactggcggtat
ggatgcggcgggaccagagaaaaatcactcagggtcaatgccagcgcttcgttaatacagatgt
aggtgttccacagggtagccagcagcatcctgcgatgcagatccggaacataatggtgcagggc
gctgacttccgcgtttccagactttacgaaacacggaaaccgaagaccattcatgttgttgctc
aggtcgcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcggtgattcattctg
ctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgacaggagcacgatcatgcgc
acccgtggggccgccatgccggcgataatggcctgcttctcgccgaaacgtttggtggcgggac
cagtgacgaaggcttgagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcat
cgtcgcgctccagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcct
acgagttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgcccacc
ggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtgcctaatgagt
gagctaacttacattaattgcgttgcgctcactgcccgctttccagtcgggaaacctgtcgtgc
cagctgcattaatgaatcggccaacgcgcggggagaggcggtttgcgtattgggcgccagggtg
gtttttcttttcaccagtgagacgggcaacagctgattgcccttcaccgcctggccctgagaga
gttgcagcaagcggtccacgctggtttgccccagcaggcgaaaatcctgtttgatggtggttaa
cggcgggatataacatgagctgtcttcggtatcgtcgtatcccactaccgagatatccgcacca
acgcgcagcccggactcggtaatggcgcgcattgcgcccagcgccatctgatcgttggcaacca
gcatcgcagtgggaacgatgccctcattcagcatttgcatggtttgttgaaaaccggacatggc
actccagtcgccttcccgttccgctatcggctgaatttgattgcgagtgagatatttatgccag
ccagccagacgcagacgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggt
gacccaatgcgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatact
gttgatgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggcagcttcc
acagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgacgcgttgcgcga
gaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttctaccatcgacaccaccac
gctggcacccagttgatcggcgcgagatttaatcgccgcgacaatttgcgacggcgcgtgcagg
gccagactggaggtggcaacgccaatcagcaacgactgtttgcccgccagttgttgtgccacgc
ggttgggaatgtaattcagctccgccatcgccgcttccacttttcccgcgttttcgcagaaac
gtggctggcctggttcaccacgcgggaaacggtctgataagagacaccggcatactctgcgaca
tcgtataacgttactggtttcacattcaccaccctgaattgactctcttccgggcgctatcatg
ccataccgcgaaaggttttgcgccattcgatggtgtccgggatctcgacgctctcccttatgcg
actcctgcattaggaagcagcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaa
tggtgcatgcaaggagatggcgcccaacagtcccccggccacggggcctgccaccatacccacg
ccgaaacaagcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggcga
tataggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccggcgtagag
gatcgagatctcgatcccgcgaaattaatacgactcactatagggaattgtgagcggataaca
attcccctctagaaataattttgtttaactttaagaaggagatataccatggaagctcgtcgtt
ccgcaaactatcagccaaacctgtggaatttcgaattcctgcaatccctggagaacgacctgaa
agtggaaaagctggaggagaaagcgaccaaactggaggaagaagttcgctgcatgatcaaccgt
gtagacacccagccgctgtccctgctggagctgatcgacgatgtgcagcgcctgggtctgacct
acaaatttgaaaaagacatcattaaagccctggaaaacatcgtactgctggacgaaaacaaaaa

Figure 66C

Nucleotide sequence of pDu50

gaacaaatctgacctgcacgcaaccgctctgtctttccgtctgctgcgtcagcacggtttcgag
gtttctcaggatgtttttgagcgtttcaaggataaagaaggtggtttcagcggtgaactgaaag
gtgacgtccaaggcctgctgagcctgtatgaagcgtcttacctgggtttcgagggtgagaacct
gctggaggaggcgcgtacctttccatcacccacctgaagaacaacctgaaagaaggcattaat
accaaggttgcagaacaagtgagccacgccctggaactgccatatcaccagcgtctgcaccgtc
tggaggcacgttggttcctggataaatacgaaccgaaagaaccgcatcaccagctgctgctgga
gctggcgaagctggattttaacatggtacagaccctgcaccagaaagagctgcaagatctgtcc
cgctggtggaccgagatgggcctggctagcaaactggattttgtacgcgaccgcctgatggaag
tttatttctgggcactgggtatggcgccagacccgcagtttggtgaatgtcgcaaagctgttac
taaaatgtttggtctggtgacgatcatcgatgacgtgtatgacgtttatggcactctggacgaa
ctgcaactgttcaccgatgctgtagagcgctgggacgttaacgctattaacaccctgccggact
atatgaaactgtgtttcctggcactgtacaacaccgttaacgacacgtcctattctattctgaa
agagaaaggtcataacaacctgtcctatctgacgaaaagctggcgtgaactgtgcaaagccttt
ctgcaagaggcgaaatggtccaacaacaaaattatcccggctttctccaagtacctggaaaacg
ccagcgtttcctcctccggtgtagcgctgctggcgccgtcttacttttccgtatgccagcagca
ggaagacatctccgaccacgcgctgcgttccctgaccgacttccatggtctggtgcgttctagc
tgcgttatcttccgcctgtgcaacgatctggccacctctgcggcggagctggaacgtggcgaga
ctaccaattctatcattagctacatgcacgaaaacgatggtaccagcgaggaacaggcccgcga
agaactgcgtaaactgatcgacgccgaatggaaaaagatgaatcgtgaacgcgttagcgactcc
accctgctgcctaaagcgttcatggaaatcgcagttaacatggcacgtgtttcccactgcacct
accagtatggcgatggtctgggtcgcccagactacgcgactgaaaaccgcatcaaactgctgct
gattgacccttttcccgattaaccagctgatgtatgtctaactgcagggatccgaattcgagctc
cgtcgacaagcttgcggccgcac

Figure 67

Amino acid sequence of kudzu TRC (-4) (SEQ ID NO:152)

MEHNSRRSANYQPNLWNFEFLQSLENDLKVEKLEEKATKLEEEVRCMINRVDTQPLSLLELIDD
VQRLGLTYKFEKDIIKALENIVLLDENKKNKSDLHATALSFRLLRQHGFEVSQDVFERFKDKEG
GFSGELKGDVQGLLSLYEASYLGFEGENLLEEARTFSITHLKNNLKEGINTKVAEQVSHALELP
YHQRLHRLEARWFLDKYEPKEPHHQLLLELAKLDFNMVQTLHQKELQDLSRWWTEMGLASKLDF
VRDRLMEVYFWALGMAPDPQFGECRKAVTKMFGLVTIIDDVYDVYGTLDELQLFTDAVERWDVN
AINTLPDYMKLCFLALYNTVNDTSYSILKEKGHNNLSYLTKSWRELCKAFLQEAKWSNNKIIPA
FSKYLENASVSSSGVALLAPSYFSVCQQQEDISDHALRSLTDFHGLVRSSCVIFRLCNDLATSA
AELERGETTNSIISYMHENDGTSEEQAREELRKLIDAEWKKMNRERVSDSTLLPKAFMEIAVNM
ARVSHCTYQYGDGLGRPDYATENRIKLLLIDPFPINQLMYV

Figure 68A

Nucleotide sequence of pDu50-4 (SEQ ID NO:153)

tcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccgaaaggaagctgagtt
ggctgctgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgagg
ggtttttgctgaaaggaggaactatatccggattggcgaatgggacgcgccctgtagcggcgc
attaagcgcggcgggtgtggtggttacgcgcagcgtgaccgctacacttgccagcgccctagcg
cccgctcctttcgctttcttcccttcctttctcgccacgttcgccggctttccccgtcaagctc
taaatcgggggctcccttagggttccgatttagtgctttacggcacctcgaccccaaaaaact
tgattagggtgatggttcacgtagtgggccatcgccctgatagacggtttttcgccctttgacg
ttggagtccacgttctttaatagtggactcttgttccaaactggaacaacactcaaccctatct
cggtctattcttttgatttataagggattttgccgatttcggcctattggttaaaaaatgagct
gatttaacaaaaatttaacgcgaattttaacaaaatattaacgtttacaatttcaggtggcact
tttcggggaaatgtgcgcggaacccctatttgtttatttttctaaatacattcaaatatgtatc
cgctcatgaattaattcttagaaaaactcatcgagcatcaaatgaaactgcaatttattcatat
caggattatcaataccatatttttgaaaaagccgtttctgtaatgaaggagaaaactcaccgag
gcagttccataggatggcaagatcctggtatcggtctgcgattccgactcgtccaacatcaata
caacctattaatttcccctcgtcaaaaataaggttatcaagtgagaaatcaccatgagtgacga
ctgaatccggtgagaatggcaaaagtttatgcatttctttccagacttgttcaacaggccagcc
attacgctcgtcatcaaaatcactcgcatcaaccaaaccgttattcattcgtgattgcgcctga
gcgagacgaaatacgcgatcgctgttaaaaggacaattacaaacaggaatcgaatgcaaccggc
gcaggaacactgccagcgcatcaacaatattttcacctgaatcaggatattcttctaatacctg
gaatgctgttttcccggggatcgcagtggtgagtaaccatgcatcatcaggagtacggataaaa
tgcttgatggtcggaagaggcataaattccgtcagccagtttagtctgaccatctcatctgtaa
catcattggcaacgctacctttgccatgtttcagaaacaactctggcgcatcgggcttcccata
caatcgatagattgtcgcacctgattgcccgacattatcgcgagcccatttatacccatataaa
tcagcatccatgttggaatttaatcgcggcctagagcaagacgtttcccgttgaatatggctca
taacacccttgtattactgtttatgtaagcagacagttttattgttcatgaccaaaatccctt
aacgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttcttgaga
tccttttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctaccagcggtggtt
tgtttgccggatcaagagctaccaactctttttccgaaggtaactggcttcagcagagcgcaga
taccaaatactgtccttctagtgtagccgtagttaggccaccacttcaagaactctgtagcacc
gcctacatacctcgctctgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgt
cttaccgggttggactcaagacgatagttaccggataaggcgcagcggtcgggctgaacggggg
gttcgtgcacacagcccagcttggagcgaacgacctacaccgaactgagatacctacagcgtga
gctatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggtaagcggcagg
gtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatctttatagtcctg
tcgggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcct
atggaaaaacgccagcaacgcggccttttacggttcctggccttttgctggccttttgctcac
atgttctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagtgagctg
ataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcggaagagcg
cctgatgcggtattttctccttacgcatctgtgcggtatttcacaccgcatatatggtgcactc
tcagtacaatctgctctgatgccgcatagttaagccagtatacactccgctatcgctacgtgac
tgggtcatggctgcgccccgacacccgccaacacccgctgacgcgccctgacgggcttgtctgc
tcccggcatccgcttacagacaagctgtgaccgtctccgggagctgcatgtgtcagaggttttc
accgtcatcaccgaaacgcgcgaggcagctgcggtaaagctcatcagcgtggtcgtgaagcgat

Figure 68B

Nucleotide sequence of pDu50-4

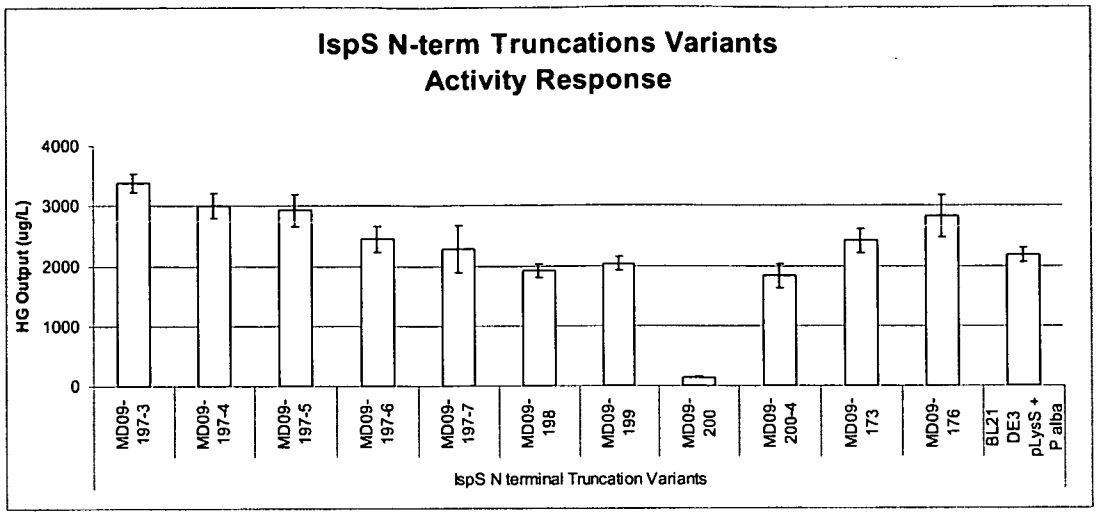
tcacagatgtctgcctgttcatccgcgtccagctcgttgagtttctccagaagcgttaatgtct
ggcttctgataaagcgggccatgttaagggcggttttttcctgtttggtcactgatgcctccgt
gtaaggggatttctgttcatgggggtaatgataccgatgaaacgagagaggatgctcacgata
cgggttactgatgatgaacatgcccggttactggaacgttgtgagggtaaacaactggcggtat
ggatgcggcgggaccagagaaaaatcactcagggtcaatgccagcgcttcgttaatacagatgt
aggtgttccacagggtagccagcagcatcctgcgatgcagatccggaacataatggtgcagggc
gctgacttccgcgtttccagactttacgaaacacggaaaccgaagaccattcatgttgttgctc
aggtcgcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcggtgattcattctg
ctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgacaggagcacgatcatgcgc
acccgtggggccgccatgccggcgataatggcctgcttctcgccgaaacgtttggtggcgggac
cagtgacgaaggcttgagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcat
cgtcgcgctccagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcct
acgagttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgcccacc
ggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtgcctaatgagt
gagctaacttacattaattgcgttgcgctcactgcccgctttccagtcgggaaacctgtcgtgc
cagctgcattaatgaatcggccaacgcgcggggagaggcggtttgcgtattgggcgccagggtg
gtttttcttttcaccagtgagacgggcaacagctgattgcccttcaccgcctggccctgagaga
gttgcagcaagcggtccacgctggtttgccccagcaggcgaaaatcctgtttgatggtggttaa
cggcgggatataacatgagctgtcttcggtatcgtcgtatcccactaccgagatatccgcacca
acgcgcagcccggactcggtaatggcgcgcattgcgcccagcgccatctgatcgttggcaacca
gcatcgcagtgggaacgatgccctcattcagcatttgcatggtttgttgaaaaccggacatggc
actccagtcgccttcccgttccgctatcggctgaatttgattgcgagtgagatatttatgccag
ccagccagacgcagacgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggt
gacccaatgcgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatact
gttgatgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggcagcttcc
acagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgacgcgttgcgcga
gaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttctaccatcgacaccaccac
gctggcacccagttgatcggcgcgagatttaatcgccgcgacaatttgcgacggcgcgtgcagg
gccagactggaggtggcaacgccaatcagcaacgactgtttgcccgccagttgttgtgccacgc
ggttgggaatgtaattcagctccgccatcgccgcttccacttttcccgcgttttcgcagaaac
gtggctggcctggttcaccacgcgggaaacggtctgataagagacaccggcatactctgcgaca
tcgtataacgttactggtttcacattcaccaccctgaattgactctcttccgggcgctatcatg
ccataccgcgaaaggttttgcgccattcgatggtgtccgggatctcgacgctctcccttatgcg
actcctgcattaggaagcagcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaa
tggtgcatgcaaggagatggcgcccaacagtcccccggccacggggcctgccaccatacccacg
ccgaaacaagcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggcga
tataggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccggcgtagag
gatcgagatctcgatcccgcgaaattaatacgactcactatagggaattgtgagcggataaca
attcccctctagaaataattttgtttaactttaagaaggagatataccatggagcataattccc
gtcgttccgcaaactatcagccaaacctgtggaatttcgaattcctgcaatccctggagaacga
cctgaaagtggaaaagctggaggagaaagcgaccaaactggaggaagaagttcgctgcatgatc
aaccgtgtagacacccagccgctgtccctgctggagctgatcgacgatgtgcagcgcctgggtc
tgacctacaaatttgaaaaagacatcattaaagccctggaaaacatcgtactgctggacgaaaa

Figure 68C

Nucleotide sequence of pDu50-4

caaaaagaacaaatctgacctgcacgcaaccgctctgtctttccgtctgctgcgtcagcacggt
ttcgaggtttctcaggatgtttttgagcgtttcaaggataaagaaggtggtttcagcggtgaac
tgaaaggtgacgtccaaggcctgctgagcctgtatgaagcgtcttacctgggtttcgagggtga
gaacctgctggaggaggcgcgtacctttccatcacccacctgaagaacaacctgaaagaaggc
attaataccaaggttgcagaacaagtgagccacgccctggaactgccatatcaccagcgtctgc
accgtctggaggcacgttggttcctggataaatacgaaccgaaagaaccgcatcaccagctgct
gctggagctggcgaagctggattttaacatggtacagaccctgcaccagaaagagctgcaagat
ctgtcccgctggtggaccgagatgggcctggctagcaaactggattttgtacgcgaccgcctga
tggaagtttatttctgggcactgggtatggcgccagacccgcagtttggtgaatgtcgcaaagc
tgttactaaaatgtttggtctggtgacgatcatcgatgacgtgtatgacgtttatggcactctg
gacgaactgcaactgttcaccgatgctgtagagcgctgggacgttaacgctattaacaccctgc
cggactatatgaaactgtgtttcctggcactgtacaacaccgttaacgacacgtcctattctat
tctgaaagagaaaggtcataacaacctgtcctatctgacgaaaagctggcgtgaactgtgcaaa
gcctttctgcaagaggcgaaatggtccaacaacaaaattatcccggctttctccaagtacctgg
aaaacgccagcgtttcctcctccggtgtagcgctgctggcgccgtcttacttttccgtatgcca
gcagcaggaagacatctccgaccacgcgctgcgttccctgaccgacttccatggtctggtgcgt
tctagctgcgttatcttccgcctgtgcaacgatctggccacctctgcggcggagctggaacgtg
gcgagactaccaattctatcattagctacatgcacgaaaacgatggtaccagcgaggaacaggc
ccgcgaagaactgcgtaaactgatcgacgccgaatggaaaaagatgaatcgtgaacgcgttagc
gactccaccctgctgcctaaagcgttcatggaaatcgcagttaacatggcacgtgtttcccact
gcacctaccagtatggcgatggtctgggtcgcccagactacgcgactgaaaaccgcatcaaact
gctgctgattgacccttcccgattaaccagctgatgtatgtctaactgcagggatccgaattc
gagctccgtcgacaagcttgcggccgcac

Figure 69


IspS N-term Truncations Variants
Activity Response
HG Output (ug/L)
4000
3000
2000
1000
0
MD09-197-3
MD09-197-4
MD09-197-5
MD09-197-6
MD09-197-7
MD09-198
MD09-199
MD09-200
MD09-200-4
MD09-173
MD09-176
BL21 DE3 pLysS + P alba
IspS N terminal Truncation Variants

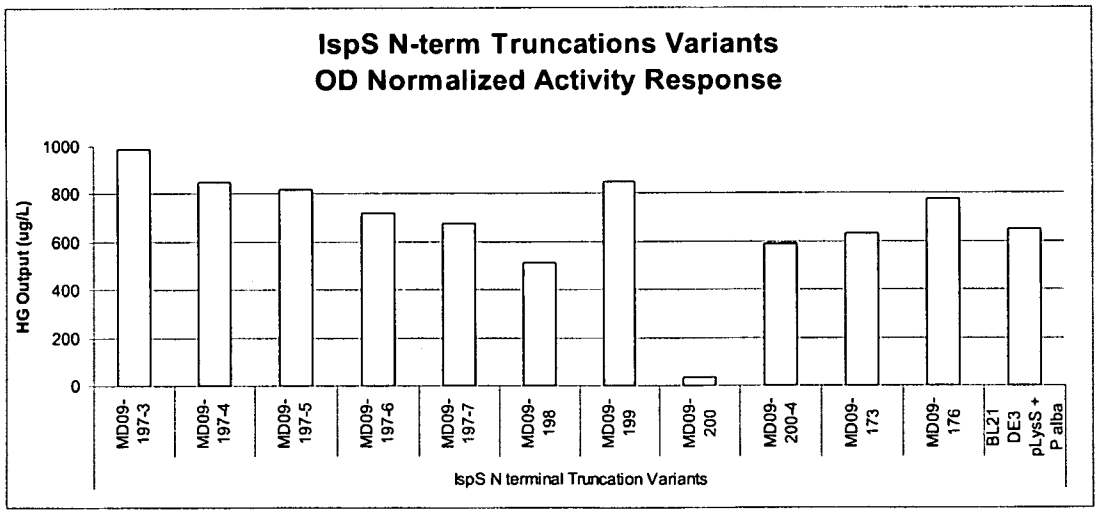

IspS N-term Truncations Variants
OD Normalized Activity Response
HG Output (ug/L)
1000
800
600
400
200
0
MD09-197-3
MD09-197-4
MD09-197-5
MD09-197-6
MD09-197-7
MD09-198
MD09-199
MD09-200
MD09-200-4
MD09-173
MD09-176
BL21 DE3 pLysS + P alba
IspS N terminal Truncation Variants

Figure 70

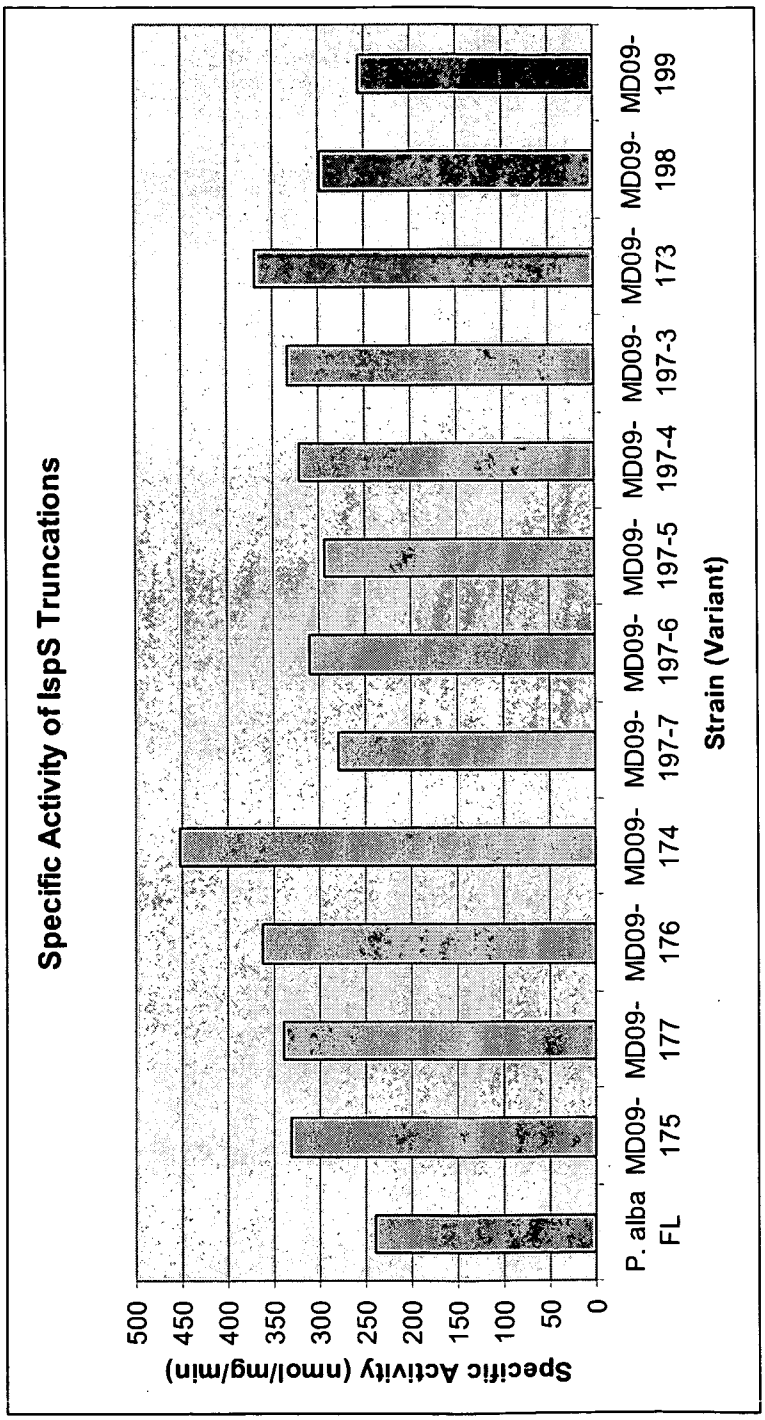

Specific Activity of IspS Truncations
Specific Activity (nmol/mg/min)
500
450
400
350
300
250
200
150
100
50
0
P. alba FL
MD09-175
MD09-177
MD09-176
MD09-174
MD09-197-7
MD09-197-6
MD09-197-5
MD09-197-4
MD09-197-3
MD09-173
MD09-198
MD09-199
Strain (Variant)

Figure 71


ApaLI (3894)
AvaI (3343)
p9795
4352 bp
XmaI (1152)
AvaI (1152)
SmaI (1154)
PstI (1194)
Stop codon
ATG
EcoRI (2798)
NcoI (1572)
ClaI (1974)
IS kud ordered

Figure 72A

Nucleotide sequence of p9795 (SEQ ID NO:154)

tagaaaaactcatcgagcatcaaatgaaactgcaatttattcatatcaggattatcaat
accatatttttgaaaaagccgtttctgtaatgaaggagaaaactcaccgaggcagttcc
ataggatggcaagatcctggtatcggtctgcgattccgactcgtccaacatcaatacaa
cctattaatttcccctcgtcaaaaataaggttatcaagtgagaaatcaccatgagtgac
gactgaatccggtgagaatggcaaaagtttatgcatttctttccagacttgttcaacag
gccagccattacgctcgtcatcaaaatcactcgcatcaaccaaaccgttattcattcgt
gattgcgcctgagcgaggcgaaatacgcgatcgctgttaaaaggacaattacaaacagg
aatcgagtgcaaccggcgcaggaacactgccagcgcatcaacaatattttcacctgaat
caggatattcttctaatacctggaacgctgtttttccggggatcgcagtggtgagtaac
catgcatcatcaggagtacggataaaatgcttgatggtcggaagtggcataaattccgt
cagccagtttagtctgaccatctcatctgtaacatcattggcaacgctacctttgccat
gtttcagaaacaactctggcgcatcgggcttcccatacaagcgatagattgtcgcacct
gattgcccgacattatcgcgagcccatttatacccatataaatcagcatccatgttgga
atttaatcgcggcctcgacgtttcccgttgaatatggctcatattcttcctttttcaat
attattgaagcatttatcagggttattgtctcatgagcggatacatatttgaatgtatt
tagaaaaataaacaaataggggtcagtgttacaaccaattaaccaattctgaacattat
cgcgagcccatttatacctgaatatggctcataacacccttgtttgcctggcggcagt
agcgcggtggtcccacctgaccccatgccgaactcagaagtgaaacgccgtagcgccga
tggtagtgtggggactccccatgcgagagtagggaactgccaggcatcaaataaaacga
aaggctcagtcgaaagactgggcctttcgcccgggctaattagggggtgtcgcccttc
gattgacgctgcagttagacatacatcagctggttaatcgggaaagggtcaatcagcag
cagtttgatgcggttttcagtcgcgtagtctgggcgacccagaccatcgccatactggt
aggtgcagtgggaaacacgtgccatgttaactgcgatttccatgaacgctttaggcagc
agggtggagtcgctaacgcgttcacgattcatcttttccattcggcgtcgatcagttt
acgcagttcttcgcgggcctgttcctcgctggtaccatcgttttcgtgcatgtagctaa
tgatagaattggtagtctcgccacgttccagctccgccgcagaggtggccagatcgttg
cacaggcggaagataacgcagctagaacgcaccagaccatggaagtcggtcagggaacg
cagcgcgtggtcggagatgtcttcctgctgctggcatacggaaaagtaagacggcgcca
gcagcgctacaccggaggaggaaacgctggcgttttccaggtacttggagaaagccggg
ataattttgttgttggaccatttcgcctcttgcagaaaggctttgcacagttcacgcca
gcttttcgtcagataggacaggttgttatgacctttctctttcagaatagaataggacg
tgtcgttaacggtgttgtacagtgccaggaaacacagtttcatatagtccggcagggtg
ttaatagcgttaacgtcccagcgctctacagcatcggtgaacagttgcagttcgtccag
agtgccataaacgtcatacacgtcatcgatgatcgtcaccagaccaaacattttagtaa
cagctttgcgacattcaccaaactgcgggtctggcgccatacccagtgcccagaaataa
acttccatcaggcggtcgcgtacaaaatccagtttgctagccaggcccatctcggtcca
ccagcgggacagatcttgcagctctttctggtgcagggtctgtaccatgttaaaatcca
gcttcgccagctccagcagcagctggtgatgcggttctttcggttcgtatttatccagg
aaccaacgtgcctccagacggtgcagacgctggtgatatggcagttccagggcgtggct
cacttgttctgcaaccttggtattaatgccttctttcaggttgttcttcaggtgggtga
tggaaaaggtacgcgcctcctccagcaggttctcaccctcgaaacccaggtaagacgct
tcatacaggctcagcaggccttggacgtcacctttcagttcaccgctgaaaccaccttc
tttatccttgaaacgctcaaaaacatcctgagaaacctcgaaaccgtgctgacgcagca

Figure 72B

Nucleotide sequence of p9795

gacggaaagacagagcggttgcgtgcaggtcagatttgttctttttgttttcgtccagc
agtacgatgttttccagggctttaatgatgtctttttcaaatttgtaggtcagacccag
gcgctgcacatcgtcgatcagctccagcagggacagcggctgggtgtctacacggttga
tcatgcagcgaacttcttcctccagtttggtcgctttctcctccagcttttccactttc
aggtcgttctccagggattgcaggaattcgaaattccacaggtttggctgatagtttgc
ggaacgacgggaattatgctcggtaatctgagtaaattgagaagaggtcgcacacatgt
tcagcgacaagggcgacacaaaatttattctaaatgcataataaatactgataacatct
tatagtttgtattatattttgtattatcgttgacatgtataattttgatatcaaaaact
gattttccctttattattttcgagatttattttcttaattctctttaacaaactagaaa
tattgtatatacaaaaaatcataaataatagatgaatagtttaattataggtgttcatc
aatcgaaaaagcaacgtatcttatttaaagtgcgttgctttttctcatttataaggtt
aaataattctcatatatcaagcaaagtgaçaggcgcccttaaatattctgacaaatgct
ctttccctaaactcccccataaaaaaacccgccgaagcgggtttttacgttatttgcg
gattaacgattactcgttatcagaaccgcccaggggcccgagcttaagactggccgtc
gttttacaacacagaaagagtttgtagaaacgcaaaaaggccatccgtcaggggccttc
tgcttagtttgatgcctggcagttccctactctcgccttccgcttcctcgctcactgac
tcgctgcgctcggtcgttcggctgcggcgagcggtatcagctcactcaaaggcggtaat
acggttatccacagaatcaggggataacgcaggaaagaacatgtgagcaaaaggccagc
aaaaggccaggaaccgtaaaaaggccgcgttgctggcgtttttccataggctccgcccc
cctgacgagcatcacaaaaatcgacgctcaagtcagaggtggcgaaacccgacaggact
ataaagataccaggcgtttcccccctggaagctccctcgtgcgctctcctgttccgaccc
tgccgcttaccggatacctgtccgcctttctcccttcgggaagcgtggcgctttctcat
agctcacgctgtaggtatctcagttcggtgtaggtcgttcgctccaagctgggctgtgt
gcacgaaccccccgttcagcccgaccgctgcgccttatccggtaactatcgtcttgagt
ccaacccggtaagacacgacttatcgccactggcagcagccactggtaacaggattagc
agagcgaggtatgtaggcggtgctacagagttcttgaagtggtgggctaactacggcta
cactagaagaacagtatttggtatctgcgctctgctgaagccagttaccttcggaaaaa
gagttggtagctcttgatccggcaaacaaaccaccgctggtagcggtggtttttttgtt
tgcaagcagcagattacgcgcagaaaaaaaggatctcaagaagatcctttgatcttttc
tacggggtctgacgctcagtggaacgacgcgcgcgtaactcacgttaagggattttggt
catgagcttgcgccgtcccgtcaagtcagcgtaatgctctgcttt

Figure 73

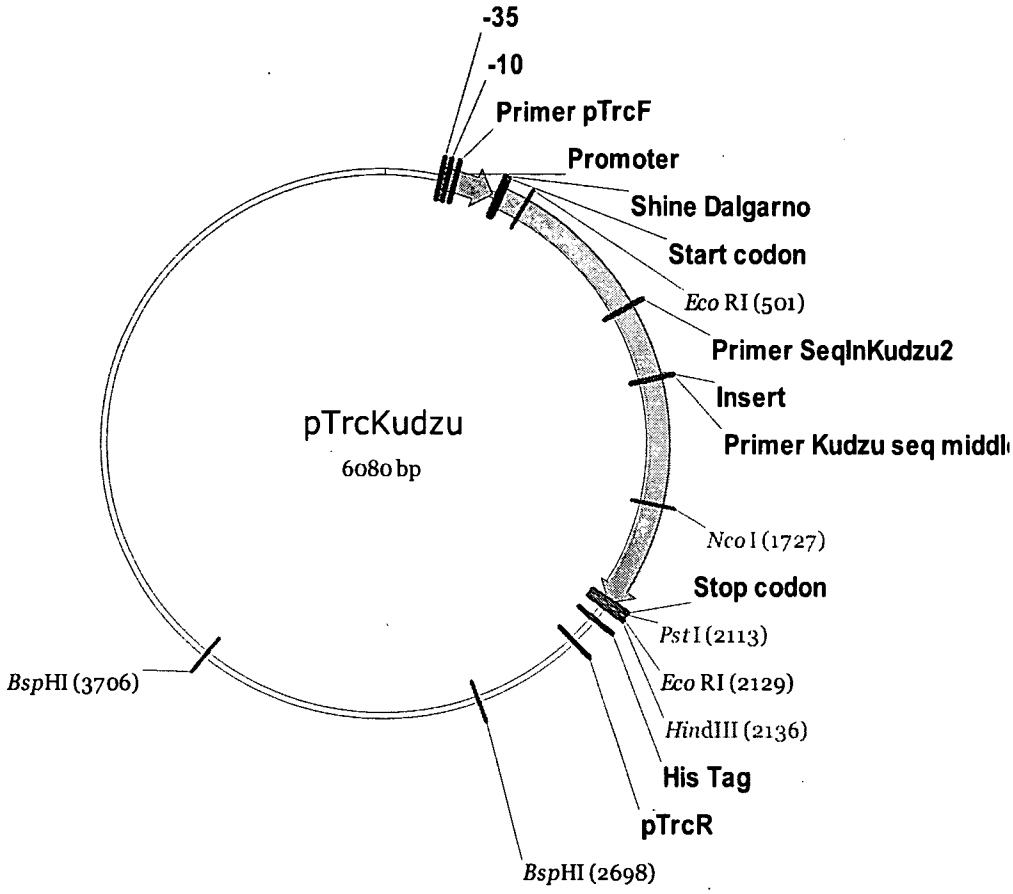

-35
-10
Primer pTrcF
Promoter
Shine Dalgarno
Start codon
Eco RI (501)
Primer SeqInKudzu2
Insert
Primer Kudzu seq middl
pTrcKudzu
6080 bp
Nco I (1727)
Stop codon
Pst I (2113)
Eco RI (2129)
HindIII (2136)
His Tag
pTrcR
BspHI (2698)
BspHI (3706)

Figure 74A

Nucleotide sequence of pTrcKudzu (SEQ ID NO:155)

gtttgacagcttatcatcgactgcacggtgcaccaatgcttctggcgtcaggcagccat
cggaagctgtggtatggctgtgcaggtcgtaaatcactgcataattcgtgtcgctcaag
gcgcactcccgttctggataatgtttttgcgccgacatcataacggttctggcaaata
ttctgaaatgagctgttgacaattaatcatccggctcgtataatgtgtggaattgtgag
cggataacaatttcacacaggaaacagcgccgctgagaaaaagcgaagcggcactgctc
tttaacaatttatcagacaatctgtgtgggcactcgaccggaattatcgattaacttta
ttattaaaaattaaagaggtatatattaatgtatcgattaaataaggaggaataaacca
tgtgtgcgacctcttctcaatttactcagattaccgagcataattcccgtcgttccgca
aactatcagccaaacctgtggaatttcgaattcctgcaatccctggagaacgacctgaa
agtggaaaagctggaggagaaagcgaccaaactggaggaagaagttcgctgcatgatca
accgtgtagacacccagccgctgtccctgctggagctgatcgacgatgtgcagcgcctg
ggtctgacctacaaatttgaaaaagacatcattaaagccctggaaaacatcgtactgct
ggacgaaaacaaaaagaacaaatctgacctgcacgcaaccgctctgtctttccgtctgc
tgcgtcagcacggtttcgaggtttctcaggatgttttgagcgtttcaaggataaagaa
ggtggtttcagcggtgaactgaaaggtgacgtccaaggcctgctgagcctgtatgaagc
gtcttacctgggtttcgagggtgagaacctgctggaggaggcgcgtacctttccatca
cccacctgaagaacaacctgaaagaaggcattaataccaaggttgcagaacaagtgagc
cacgccctggaactgccatatcaccagcgtctgcaccgtctggaggcacgttggttcct
ggataaatacgaaccgaaagaaccgcatcaccagctgctgctggagctggcgaagctgg
attttaacatggtacagaccctgcaccagaaagagctgcaagatctgtcccgctggtgg
accgagatgggcctggctagcaaactggattttgtacgcgaccgcctgatggaagttta
tttctgggcactgggtatggcgccagacccgcagtttggtgaatgtcgcaaagctgtta
ctaaaatgtttggtctggtgacgatcatcgatgacgtgtatgacgtttatggcactctg
gacgaactgcaactgttcaccgatgctgtagagcgctgggacgttaacgctattaacac
cctgccggactatatgaaactgtgtttcctggcactgtacaacaccgttaacgacacgt
cctattctattctgaaagagaaaggtcataacaacctgtcctatctgacgaaaagctgg
cgtgaactgtgcaaagcctttctgcaagaggcgaaatggtccaacaacaaaattatccc
ggctttctccaagtacctggaaaacgccagcgtttcctcctccggtgtagcgctgctgg
cgccgtcttacttttccgtatgccagcagcaggaagacatctccgaccacgcgctgcgt
tccctgaccgacttccatggtctggtgcgttctagctgcgttatcttccgcctgtgcaa
cgatctggccacctctgcggcggagctggaacgtggcgagactaccaattctatcatta
gctacatgcacgaaaacgatggtaccagcgaggaacaggcccgcgaagaactgcgtaaa
ctgatcgacgccgaatggaaaaagatgaatcgtgaacgcgttagcgactccaccctgct
gcctaaagcgttcatggaaatcgcagttaacatggcacgtgtttcccactgcacctacc
agtatggcgatggtctgggtcgcccagactacgcgactgaaaaccgcatcaaactgctg
ctgattgacccttttcccgattaaccagctgatgtatgtctaactgcagctggtaccata
tgggaattcgaagctttctagaacaaaaactcatctcagaagaggatctgaatagcgcc
gtcgaccatcatcatcatcatcattgagtttaaacggtctccagcttggctgttttggc
ggatgagagaagattttcagcctgatacagattaaatcagaacgcagaagcggtctgat
aaaacagaatttgcctggcggcagtagcgcggtggtcccacctgaccccatgccgaact
cagaagtgaaacgccgtagcgccgatggtagtgtggggtctccccatgcgagagtaggg
aactgccaggcatcaaataaaacgaaaggctcagtcgaaagactgggcctttcgtttta
tctgttgtttgtcggtgaacgctctcctgagtaggacaaatccgccgggagcggatttg

Figure 74B

Nucleotide sequence of pTrcKudzu

aacgttgcgaagcaacggcccggagggtggcgggcaggacgcccgccataaactgccag
gcatcaaattaagcagaaggccatcctgacggatggccttttgcgtttctacaaactc
tttttgtttatttttctaaatacattcaaatatgtatccgctcatgagacaataaccct
gataaatgcttcaataatattgaaaaaggaagagtatgagtattcaacatttccgtgtc
gcccttattccctttttgcggcattttgccttcctgtttttgctcacccagaaacgct
ggtgaaagtaaaagatgctgaagatcagttgggtgcacgagtgggttacatcgaactgg
atctcaacagcggtaagatccttgagagttttcgccccgaagaacgttttccaatgatg
agcacttttaaagttctgctatgtggcgcggtattatcccgtgttgacgccgggcaaga
gcaactcggtcgccgcatacactattctcagaatgacttggttgagtactcaccagtca
cagaaaagcatcttacggatggcatgacagtaagagaattatgcagtgctgccataacc
atgagtgataacactgcggccaacttacttctgacaacgatcggaggaccgaaggagct
aaccgcttttttgcacaacatgggggatcatgtaactcgccttgatcgttgggaaccgg
agctgaatgaagccataccaaacgacgagcgtgacaccacgatgcctgtagcaatggca
acaacgttgcgcaaactattaactggcgaactacttactctagcttcccggcaacaatt
aatagactggatggaggcggataaagttgcaggaccacttctgcgctcggcccttccgg
ctggctggtttattgctgataaatctggagccggtgagcgtgggtctcgcggtatcatt
gcagcactggggccagatggtaagccctcccgtatcgtagttatctacacgacggggag
tcaggcaactatggatgaacgaaatagacagatcgctgagataggtgcctcactgatta
agcattggtaactgtcagaccaagtttactcatatatactttagattgatttaaaactt
cattttaatttaaaaggatctaggtgaagatccttttgataatctcatgaccaaaat
cccttaacgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggat
cttcttgagatccttttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccg
ctaccagcggtggtttgtttgccggatcaagagctaccaactctttttccgaaggtaac
tggcttcagcagagcgcagataccaaatactgtccttctagtgtagccgtagttaggcc
accacttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttacca
gtggctgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagtt
accggataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttgg
agcgaacgacctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacg
cttcccgaagggagaaaggcggacaggtatccggtaagcggcagggtcggaacaggaga
gcgcacgagggagcttccagggggaaacgcctggtatctttatagtcctgtcgggtttc
gccacctctgacttgagcgtcgattttgtgatgctcgtcaggggggcggagcctatgg
aaaaacgccagcaacgcggccttttacggttcctggccttttgctggccttttgctca
catgttctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagt
gagctgataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaa
gcggaagagcgcctgatgcggtattttctccttacgcatctgtgcggtatttcacaccg
catatggtgcactctcagtacaatctgctctgatgccgcatagttaagccagtatacac
tccgctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacacccgctg
acgcgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgtc
tccgggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagca
gatcaattcgcgcgcgaaggcgaagcggcatgcatttacgttgacaccatcgaatggtg
caaaaccttcgcggtatggcatgatagcgcccggaagagagtcaattcagggtggtga
atgtgaaaccagtaacgttatacgatgtcgcagagtatgccggtgtctcttatcagacc
gtttcccgcgtggtgaaccaggccagccacgtttctgcgaaaacgcgggaaaaagtgga

Figure 74C

Nucleotide sequence of pTrcKudzu

agcggcgatggcggagctgaattacattcccaaccgcgtggcacaacaactggcgggca
aacagtcgttgctgattggcgttgccacctccagtctggccctgcacgcgccgtcgcaa
attgtcgcggcgattaaatctcgcgccgatcaactgggtgccagcgtggtggtgtcgat
ggtagaacgaagcggcgtcgaagcctgtaaagcggcggtgcacaatcttctcgcgcaac
gcgtcagtgggctgatcattaactatccgctggatgaccaggatgccattgctgtggaa
gctgcctgcactaatgttccggcgttatttcttgatgtctctgaccagacacccatcaa
cagtattattttctcccatgaagacggtacgcgactgggcgtggagcatctggtcgcat
tgggtcaccagcaaatcgcgctgttagcgggcccattaagttctgtctcggcgcgtctg
cgtctggctggctggcataaatatctcactcgcaatcaaattcagccgatagcggaacg
ggaaggcgactggagtgccatgtccggttttcaacaaaccatgcaaatgctgaatgagg
gcatcgttcccactgcgatgctggttgccaacgatcagatggcgctgggcgcaatgcgc
gccattaccgagtccgggctgcgcgttggtgcggatatctcggtagtgggatacgacga
taccgaagacagctcatgttatatcccgccgtcaaccaccatcaaacaggattttcgcc
tgctggggcaaaccagcgtggaccgcttgctgcaactctctcagggccaggcggtgaag
ggcaatcagctgttgcccgtctcactggtgaaaagaaaaaccaccctggcgcccaatac
gcaaaccgcctctccccgcgcgttggccgattcattaatgcagctggcacgacaggttt
cccgactggaaagcgggcagtgagcgcaacgcaattaatgtgagttagcgcgaattgat
ctg

Figure 75

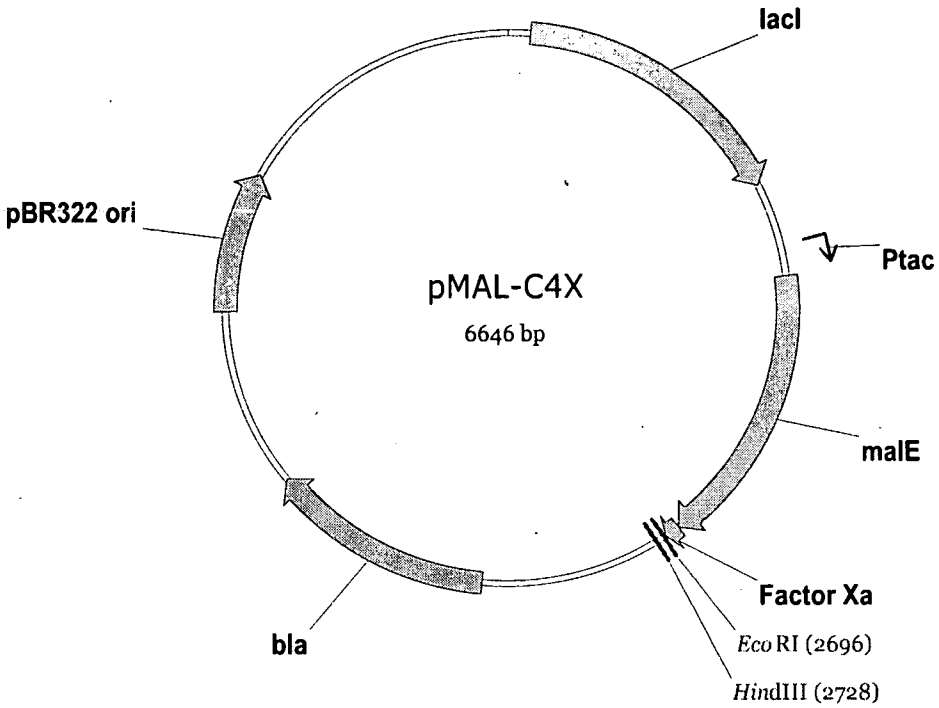

lacI
pBR322 ori
Ptac
pMAL-C4X
6646 bp
malE
Factor Xa
bla
EcoRI (2696)
HindIII (2728)

Figure 76A

Nucleotide sequence of pMAL-C4X (SEQ ID NO:156)

ccgacaccatcgaatggtgcaaaacctttcgcggtatggcatgatagcgcccggaagag
agtcaattcagggtggtgaatgtgaaaccagtaacgttatacgatgtcgcagagtatgc
cggtgtctcttatcagaccgtttcccgcgtggtgaaccaggccagccacgtttctgcga
aaacgcgggaaaaagtggaagcggcgatggcggagctgaattacattcccaaccgcgtg
gcacaacaactggcgggcaaacagtcgttgctgattggcgttgccacctccagtctggc
cctgcacgcgccgtcgcaaattgtcgcggcgattaaatctcgcgccgatcaactgggtg
ccagcgtggtggtgtcgatggtagaacgaagcggcgtcgaagcctgtaaagcggcggtg
cacaatcttctcgcgcaacgcgtcagtgggctgatcattaactatccgctggatgacca
ggatgccattgctgtggaagctgcctgcactaatgttccggcgttatttcttgatgtct
ctgaccagacacccatcaacagtattattttctcccatgaagacggtacgcgactgggc
gtggagcatctggtcgcattgggtcaccagcaaatcgcgctgttagcgggcccattaag
ttctgtctcggcgcgtctgcgtctggctggctggcataaatatctcactcgcaatcaaa
ttcagccgatagcggaacgggaaggcgactggagtgccatgtccggttttcaacaaacc
atgcaaatgctgaatgagggcatcgttcccactgcgatgctggttgccaacgatcagat
ggcgctgggcgcaatgcgcgccattaccgagtccgggctgcgcgttggtgcggatatct
cggtagtgggatacgacgataccgaagacagctcatgttatatcccgccgttaaccacc
atcaaacaggattttcgcctgctggggcaaaccagcgtggaccgcttgctgcaactctc
tcagggccaggcggtgaagggcaatcagctgttgcccgtctcactggtgaaaagaaaaa
ccaccctggcgcccaatacgcaaaccgcctctccccgcgcgttggccgattcattaatg
cagctggcacgacaggtttcccgactggaaagcgggcagtgagcgcaacgcaattaatg
taagttagctcactcattaggcacaattctcatgtttgacagcttatcatcgactgcac
ggtgcaccaatgcttctggcgtcaggcagccatcggaagctgtggtatggctgtgcagg
tcgtaaatcactgcataattcgtgtcgctcaaggcgcactcccgttctggataatgttt
tttgcgccgacatcataacggttctggcaaatattctgaaatgagctgttgacaattaa
tcatcggctcgtataatgtgtggaattgtgagcggataacaatttcacacaggaaacag
ccagtccgtttaggtgttttcacgagcacttcaccaacaaggaccatagcatatgaaaa
tcgaagaaggtaaactggtaatctggattaacggcgataaaggctataacggtctcgct
gaagtcggtaagaaattcgagaaagataccggaattaaagtcaccgttgagcatccgga
taaactggaagagaaattcccacaggttgcggcaactggcgatggccctgacattatct
tctgggcacacgaccgctttggtggctacgctcaatctggcctgttggctgaaatcacc
ccggacaaagcgttccaggacaagctgtatccgtttacctgggatgccgtacgttacaa
cggcaagctgattgcttacccgatcgctgttgaagcgttatcgctgatttataacaaag
atctgctgccgaacccgccaaaaacctgggaagagatcccggcgctggataaagaactg
aaagcgaaaggtaagagcgcgctgatgttcaacctgcaagaaccgtacttcacctggcc
gctgattgctgctgacgggggttatgcgttcaagtatgaaaacggcaagtacgacatta
aagacgtgggcgtggataacgctggcgcgaaagcgggtctgaccttcctggttgacctg
attaaaaacaaacacatgaatgcagacaccgattactccatcgcagaagctgcctttaa
taaaggcgaaacagcgatgaccatcaacggcccgtgggcatggtccaacatcgacacca
gcaaagtgaattatggtgtaacggtactgccgaccttcaagggtcaaccatccaaaccg
ttcgttggcgtgctgagcgcaggtattaacgccgccagtccgaacaaagagctggcaaa
agagttcctcgaaaactatctgctgactgatgaaggtctggaagcggttaataaagaca
aaccgctgggtgccgtagcgctgaagtcttacgaggaagagttggtgaaagatccgcgg
attgccgccactatggaaaacgcccagaaaggtgaaatcatgccgaacatcccgcagat

Figure 76B

Nucleotide sequence of pMAL-C4X

gtccgctttctggtatgccgtgcgtactgcggtgatcaacgccgccagcggtcgtcaga
ctgtcgatgaagccctgaaagacgcgcagactaattcgagctcgaacaacaacaacaat
aacaataacaacaacctcgggatcgagggaaggatttcagaattcggatcctctagagt
cgacctgcaggcaagcttggcactggccgtcgttttacaacgtcgtgactgggaaaacc
ctggcgttacccaacttaatcgccttgcagcacatccccctttcgccagctggcgtaat
agcgaagaggcccgcaccgatcgcccttcccaacagttgcgcagcctgaatggcgaatg
gcagcttggctgttttggcggatgagataagattttcagcctgatacagattaaatcag
aacgcagaagcggtctgataaaacagaatttgcctggcggcagtagcgcggtggtccca
cctgaccccatgccgaactcagaagtgaaacgccgtagcgccgatggtagtgtggggtc
tccccatgcgagagtagggaactgccaggcatcaaataaaacgaaaggctcagtcgaaa
gactgggcctttcgttttatctgttgtttgtcggtgaacgctctcctgagtaggacaaa
tccgccgggagcggatttgaacgttgcgaagcaacggcccggagggtggcgggcaggac
gcccgccataaactgccaggcatcaaattaagcagaaggccatcctgacggatggcctt
tttgcgtttctacaaactctttttgtttatttttctaaatacattcaaatatgtatccg
ctcatgagacaataaccctgataaatgcttcaataatattgaaaaaggaagagtatgag
tattcaacatttccgtgtcgcccttattccctttttgcggcattttgccttcctgttt
ttgctcacccagaaacgctggtgaaagtaaaagatgctgaagatcagttgggtgcacga
gtgggttacatcgaactggatctcaacagcggtaagatccttgagagttttcgccccga
agaacgttctccaatgatgagcacttttaaagttctgctatgtggcgcggtattatccc
gtgttgacgccgggcaagagcaactcggtcgccgcatacactattctcagaatgacttg
gttgagtactcaccagtcacagaaaagcatcttacggatggcatgacagtaagagaatt
atgcagtgctgccataaccatgagtgataacactgcggccaacttacttctgacaacga
tcggaggaccgaaggagctaaccgcttttttgcacaacatgggggatcatgtaactcgc
cttgatcgttgggaaccggagctgaatgaagccataccaaacgacgagcgtgacaccac
gatgcctgtagcaatggcaacaacgttgcgcaaactattaactggcgaactacttactc
tagcttcccggcaacaattaatagactggatggaggcggataaagttgcaggaccactt
ctgcgctcggcccttccggctggctggtttattgctgataaatctggagccggtgagcg
tgggtctcgcggtatcattgcagcactggggccagatggtaagccctcccgtatcgtag
ttatctacacgacggggagtcaggcaactatggatgaacgaaatagacagatcgctgag
ataggtgcctcactgattaagcattggtaactgtcagaccaagtttactcatatatact
ttagattgatttaccccggttgataatcagaaaagccccaaaaacaggaagattgtata
agcaaatatttaaattgtaaacgttaatattttgttaaaattcgcgttaaatttttgtt
aaatcagctcatttttaaccaataggccgaaatcggcaaaatcccttataaatcaaaa
gaatagaccgagatagggttgagtgttgttccagtttggaacaagagtccactattaaa
gaacgtggactccaacgtcaaagggcgaaaaaccgtctatcagggcgatggcccactac
gtgaaccatcacccaaatcaagtttttggggtcgaggtgccgtaaagcactaaatcgg
aaccctaaagggagcccccgatttagagcttgacggggaaagccggcgaacgtggcgag
aaaggaagggaagaaagcgaaaggagcgggcgctagggcgctggcaagtgtagcggtca
cgctgcgcgtaaccaccacacccgccgcgcttaatgcgccgctacagggcgcgtaaaag
gatctaggtgaagatccttttgataatctcatgaccaaaatcccttaacgtgagtttt
cgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttcttgagatccttt
tttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctaccagcggtggtttg
tttgccggatcaagagctaccaactctttttccgaaggtaactggcttcagcagagcgc

Figure 76C

Nucleotide sequence of pMAL-C4X

agataccaaatactgtccttctagtgtagccgtagttaggccaccacttcaagaactct
gtagcaccgcctacatacctcgctctgctaatcctgttaccagtggctgctgccagtgg
cgataagtcgtgtcttaccgggttggactcaagacgatagttaccggataaggcgcagc
ggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaacgacctacacc
gaactgagatacctacagcgtgagctatgagaaagcgccacgcttcccgaagggagaaa
ggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcacgagggagcttc
cagggggaaacgcctggtatctttatagtcctgtcgggtttcgccacctctgacttgag
cgtcgatttttgtgatgctcgtcaggggggcggagcctatggaaaaacgccagcaacgc
ggccttttacggttcctggccttttgctggccttttgctcacatgttctttcctgcgt
tatcccctgattctgtggataaccgtattaccgcctttgagtgagctgataccgctcgc
cgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcggaagagcgcctgat
gcggtattttctccttacgcatctgtgcggtatttcacaccgcatatatggtgcactct
cagtacaatctgctctgatgccgcatagttaagccagtatacactccgctatcgctacg
tgactgggtcatggctgcgccccgacacccgccaacacccgctgacgcgccctgacggg
cttgtctgctcccggcatccgcttacagacaagctgtgaccgtctccgggagctgcatg
tgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcggtaaagctcatc
agcgtggtcgtgcagcgattcacagatgtctgcctgttcatccgcgtccagctcgttga
gtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaagggcggtt
ttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatgggggtaat
gataccgatgaaacgagagaggatgctcacgatacgggttactgatgatgaacatgccc
ggttactggaacgttgtgagggtaaacaactggcggtatggatgcggcgggaccagaga
aaaatcactcagggtcaatgccagcgcttcgttaatacagatgtaggtgttccacaggg
tagccagcagcatcctgcgatgcagatccggaacataatggtgcagggcgctgacttcc
gcgtttccagactttacgaaacacggaaaccgaagaccattcatgttgttgctcaggtc
gcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcggtgattcattctg
ctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgacaggagcacgatca
tgcgcacccgtggccaggacccaacgctgcccgaaatt

Figure 77

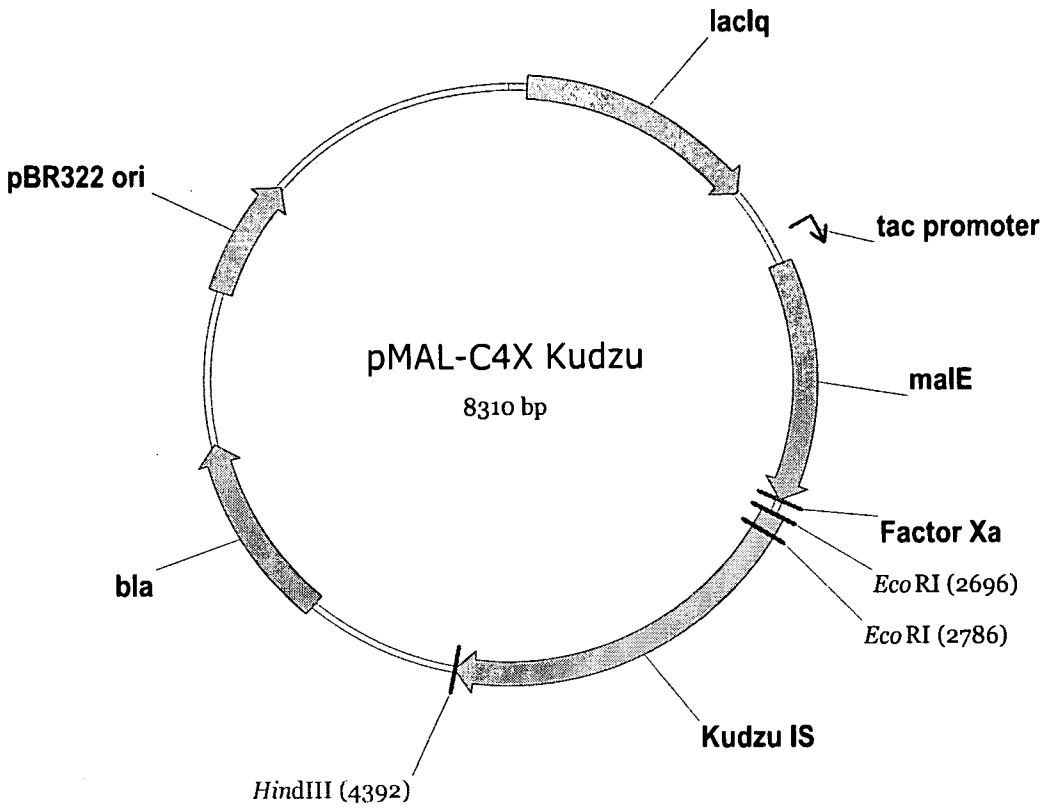

lacIq
pBR322 ori
tac promoter
pMAL-C4X Kudzu
8310 bp
malE
Factor Xa
EcoRI (2696)
EcoRI (2786)
bla
Kudzu IS
HindIII (4392)

Figure 78A

Nucleotide sequence of pMAL-C4X Kudzu (SEQ ID NO:157)

ccgacaccatcgaatggtgcaaaacctttcgcggtatggcatgatagcgcccggaagag
agtcaattcagggtggtgaatgtgaaaccagtaacgttatacgatgtcgcagagtatgc
cggtgtctcttatcagaccgtttcccgcgtggtgaaccaggccagccacgtttctgcga
aaacgcgggaaaaagtggaagcggcgatggcggagctgaattacattcccaaccgcgtg
gcacaacaactggcgggcaaacagtcgttgctgattggcgttgccacctccagtctggc
cctgcacgcgccgtcgcaaattgtcgcggcgattaaatctcgcgccgatcaactgggtg
ccagcgtggtggtgtcgatggtagaacgaagcggcgtcgaagcctgtaaagcggcggtg
cacaatcttctcgcgcaacgcgtcagtgggctgatcattaactatccgctggatgacca
ggatgccattgctgtggaagctgcctgcactaatgttccggcgttatttcttgatgtct
ctgaccagacacccatcaacagtattattttctcccatgaagacggtacgcgactgggc
gtggagcatctggtcgcattgggtcaccagcaaatcgcgctgttagcgggcccattaag
ttctgtctcggcgcgtctgcgtctggctggctggcataaatatctcactcgcaatcaaa
ttcagccgatagcggaacgggaaggcgactggagtgccatgtccggttttcaacaaacc
atgcaaatgctgaatgagggcatcgttcccactgcgatgctggttgccaacgatcagat
ggcgctgggcgcaatgcgcgccattaccgagtccgggctgcgcgttggtgcggatatct
cggtagtgggatacgacgataccgaagacagctcatgttatatcccgccgttaaccacc
atcaaacaggattttcgcctgctggggcaaaccagcgtggaccgcttgctgcaactctc
tcagggccaggcggtgaagggcaatcagctgttgcccgtctcactggtgaaaagaaaaa
ccaccctggcgcccaatacgcaaaccgcctctccccgcgcgttggccgattcattaatg
cagctggcacgacaggtttcccgactggaaagcgggcagtgagcgcaacgcaattaatg
taagttagctcactcattaggcacaattctcatgtttgacagcttatcatcgactgcac
ggtgcaccaatgcttctggcgtcaggcagccatcggaagctgtggtatggctgtgcagg
tcgtaaatcactgcataattcgtgtcgctcaaggcgcactcccgttctggataatgttt
tttgcgccgacatcataacggttctggcaaatattctgaaatgagctgttgacaattaa
tcatcggctcgtataatgtgtggaattgtgagcggataacaatttcacacaggaaacag
ccagtccgtttaggtgttttcacgagcacttcaccaacaaggaccatagcatatgaaaa
tcgaagaaggtaaactggtaatctggattaacggcgataaaggctataacggtctcgct
gaagtcggtaagaaattcgagaaagataccggaattaaagtcaccgttgagcatccgga
taaactggaagagaaattcccacaggttgcggcaactggcgatggccctgacattatct
tctgggcacacgaccgctttggtggctacgctcaatctggcctgttggctgaaatcacc
ccggacaaagcgttccaggacaagctgtatccgtttacctgggatgccgtacgttacaa
cggcaagctgattgcttacccgatcgctgttgaagcgttatcgctgatttataacaaag
atctgctgccgaacccgccaaaaacctgggaagagatcccggcgctggataaagaactg
aaagcgaaaggtaagagcgcgctgatgttcaacctgcaagaaccgtacttcacctggcc
gctgattgctgctgacgggggttatgcgttcaagtatgaaaacggcaagtacgacatta
aagacgtgggcgtggataacgctggcgcgaaagcgggtctgaccttcctggttgacctg
attaaaaacaaacacatgaatgcagacaccgattactccatcgcagaagctgcctttaa
taaaggcgaaacagcgatgaccatcaacggcccgtgggcatggtccaacatcgacacca
gcaaagtgaattatggtgtaacggtactgccgaccttcaagggtcaaccatccaaaccg
ttcgttggcgtgctgagcgcaggtattaacgccgccagtccgaacaaagagctggcaaa
agagttcctcgaaaactatctgctgactgatgaaggtctggaagcggttaataaagaca
aaccgctgggtgccgtagcgctgaagtcttacgaggaagagttggtgaaagatccgcgg
attgccgccactatggaaaacgcccagaaaggtgaaatcatgccgaacatcccgcagat

Figure 78B

Nucleotide sequence of pMAL-C4X Kudzu

gtccgctttctggtatgccgtgcgtactgcggtgatcaacgccgccagcggtcgtcaga
ctgtcgatgaagccctgaaagacgcgcagactaattcgagctcgaacaacaacaacaat
aacaataacaacaacctcgggatcgagggaaggatttcagaattctgtgcgacctcttc
tcaatttactcagattaccgagcataattcccgtcgttccgcaaactatcagccaaacc
tgtggaatttcgaattcctgcaatccctggagaacgacctgaaagtggaaaagctggag
gagaaagcgaccaaactggaggaagaagttcgctgcatgatcaaccgtgtagacaccca
gccgctgtccctgctggagctgatcgacgatgtgcagcgcctgggtctgacctacaaat
ttgaaaaagacatcattaaagccctggaaaacatcgtactgctggacgaaaacaaaaag
aacaaatctgacctgcacgcaaccgctctgtctttccgtctgctgcgtcagcacggttt
cgaggtttctcaggatgtttttgagcgtttcaaggataaagaaggtggtttcagcggtg
aactgaaaggtgacgtccaaggcctgctgagcctgtatgaagcgtcttacctgggtttc
gagggtgagaacctgctggaggaggcgcgtacctttccatcacccacctgaagaacaa
cctgaaagaaggcattaataccaaggttgcagaacaagtgagccacgccctggaactgc
catatcaccagcgtctgcaccgtctggaggcacgttggttcctggataaatacgaaccg
aaagaaccgcatcaccagctgctgctggagctggcgaagctggattttaacatggtaca
gaccctgcaccagaaagagctgcaagatctgtcccgctggtggaccgagatgggcctgg
ctagcaaactggattttgtacgcgaccgcctgatggaagtttatttctgggcactgggt
atggcgccagacccgcagtttggtgaatgtcgcaaagctgttactaaaatgtttggtct
ggtgacgatcatcgatgacgtgtatgacgtttatggcactctggacgaactgcaactgt
tcaccgatgctgtagagcgctgggacgttaacgctattaacaccctgccggactatatg
aaactgtgtttcctggcactgtacaacaccgttaacgacacgtcctattctattctgaa
agagaaaggtcataacaacctgtcctatctgacgaaaagctggcgtgaactgtgcaaag
cctttctgcaagaggcgaaatggtccaacaacaaaattatcccggctttctccaagtac
ctggaaaacgccagcgtttcctcctccggtgtagcgctgctggcgccgtcttacttttc
cgtatgccagcagcaggaagacatctccgaccacgcgctgcgttccctgaccgacttcc
atggtctggtgcgttctagctgcgttatcttccgcctgtgcaacgatctggccacctct
gcggcggagctggaacgtggcgagactaccaattctatcattagctacatgcacgaaaa
cgatggtaccagcgaggaacaggcccgcgaagaactgcgtaaactgatcgacgccgaat
ggaaaaagatgaatcgtgaacgcgttagcgactccaccctgctgcctaaagcgttcatg
gaaatcgcagttaacatggcacgtgtttcccactgcacctaccagtatggcgatggtct
gggtcgcccagactacgcgactgaaaaccgcatcaaactgctgctgattgacccttttcc
cgattaaccagctgatgtatgtctaagcttggcactggccgtcgttttacaacgtcgtg
actgggaaaaccctggcgttacccaacttaatcgccttgcagcacatccccctttcgcc
agctggcgtaatagcgaagaggcccgcaccgatcgcccttcccaacagttgcgcagcct
gaatggcgaatggcagcttggctgttttggcggatgagataagattttcagcctgatac
agattaaatcagaacgcagaagcggtctgataaaacagaatttgcctggcggcagtagc
gcggtggtcccacctgaccccatgccgaactcagaagtgaaacgccgtagcgccgatgg
tagtgtggggtctccccatgcgagagtagggaactgccaggcatcaaataaaacgaaag
gctcagtcgaaagactgggcctttcgttttatctgttgtttgtcggtgaacgctctcct
gagtaggacaaatccgccgggagcggatttgaacgttgcgaagcaacggcccggagggt
ggcgggcaggacgcccgccataaactgccaggcatcaaattaagcagaaggccatcctg
acggatggccttttgcgtttctacaaactcttttttgtttatttttctaaatacattca
aatatgtatccgctcatgagacaataaccctgataaatgcttcaataatattgaaaaag

Figure 78C

Nucleotide sequence of pMAL-C4X Kudzu

gaagagtatgagtattcaacatttccgtgtcgcccttattccctttttttgcggcatttt
gccttcctgtttttgctcacccagaaacgctggtgaaagtaaaagatgctgaagatcag
ttgggtgcacgagtgggttacatcgaactggatctcaacagcggtaagatccttgagag
ttttcgccccgaagaacgttctccaatgatgagcacttttaaagttctgctatgtggcg
cggtattatcccgtgttgacgccgggcaagagcaactcggtcgccgcatacactattct
cagaatgacttggttgagtactcaccagtcacagaaaagcatcttacggatggcatgac
agtaagagaattatgcagtgctgccataaccatgagtgataacactgcggccaacttac
ttctgacaacgatcggaggaccgaaggagctaaccgcttttttgcacaacatgggggat
catgtaactcgccttgatcgttgggaaccggagctgaatgaagccataccaaacgacga
gcgtgacaccacgatgcctgtagcaatggcaacaacgttgcgcaaactattaactggcg
aactacttactctagcttcccggcaacaattaatagactggatggaggcggataaagtt
gcaggaccacttctgcgctcggcccttccggctggctggtttattgctgataaatctgg
agccggtgagcgtgggtctcgcggtatcattgcagcactggggccagatggtaagccct
cccgtatcgtagttatctacacgacggggagtcaggcaactatggatgaacgaaataga
cagatcgctgagataggtgcctcactgattaagcattggtaactgtcagaccaagttta
ctcatatatactttagattgatttaccccggttgataatcagaaaagccccaaaaacag
gaagattgtataagcaaatatttaaattgtaaacgttaatattttgttaaaattcgcgt
taaatttttgttaaatcagctcatttttaaccaataggccgaaatcggcaaaatccct
tataaatcaaaagaatagaccgagatagggttgagtgttgttccagtttggaacaagag
tccactattaaagaacgtggactccaacgtcaaagggcgaaaaaccgtctatcagggcg
atggcccactacgtgaaccatcacccaaatcaagtttttggggtcgaggtgccgtaaa
gcactaaatcggaaccctaaagggagcccccgatttagagcttgacggggaaagccggc
gaacgtggcgagaaaggaagggaagaaagcgaaaggagcgggcgctagggcgctggcaa
gtgtagcggtcacgctgcgcgtaaccaccacacccgccgcgcttaatgcgccgctacag
ggcgcgtaaaaggatctaggtgaagatccttttgataatctcatgaccaaaatccctt
aacgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttct
tgagatccttttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctacc
agcggtggtttgtttgccggatcaagagctaccaactcttttccgaaggtaactggct
tcagcagagcgcagataccaaatactgtccttctagtgtagccgtagttaggccaccac
ttcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttaccagtggc
tgctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgg
ataaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcga
acgacctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttcc
cgaagggagaaaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgca
cgagggagcttccagggggaaacgcctggtatctttatagtcctgtcgggtttcgccac
ctctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcctatggaaaaa
cgccagcaacgcggccttttacggttcctggccttttgctggccttttgctcacatgt
tctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagtgagct
gataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcgga
agagcgcctgatgcggtattttctccttacgcatctgtgcggtatttcacaccgcatat
atggtgcactctcagtacaatctgctctgatgccgcatagttaagccagtatacactcc
gctatcgctacgtgactgggtcatggctgcgccccgacacccgccaacacccgctgacg
cgccctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgtctcc

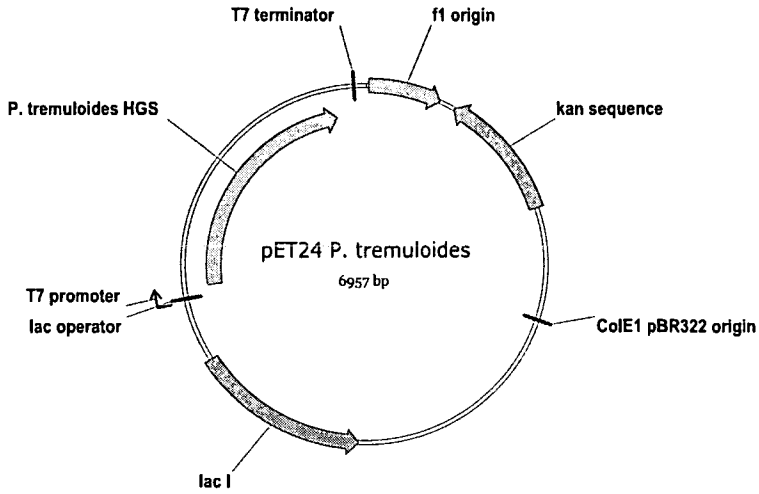
Figure 78D

Nucleotide sequence of pMAL-C4X Kudzu

gggagctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcg
gtaaagctcatcagcgtggtcgtgcagcgattcacagatgtctgcctgttcatccgcgt
ccagctcgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatg
ttaagggcggttttttcctgtttggtcactgatgcctccgtgtaagggggatttctgtt
catgggggtaatgataccgatgaaacgagagaggatgctcacgatacgggttactgatg
atgaacatgcccggttactggaacgttgtgagggtaaacaactggcggtatggatgcgg
cgggaccagagaaaaatcactcagggtcaatgccagcgcttcgttaatacagatgtagg
tgttccacagggtagccagcagcatcctgcgatgcagatccggaacataatggtgcagg
gcgctgacttccgcgtttccagactttacgaaacacggaaaccgaagaccattcatgtt
gttgctcaggtcgcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcgg
tgattcattctgctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgaca
ggagcacgatcatgcgcacccgtggccaggacccaacgctgcccgaaatt

Figure 79

A.


T7 terminator
f1 origin
P. tremuloides HGS
kan sequence
pET24 P. tremuloides
6957 bp
T7 promoter
lac operator
ColE1 pBR322 origin
lac I

B.

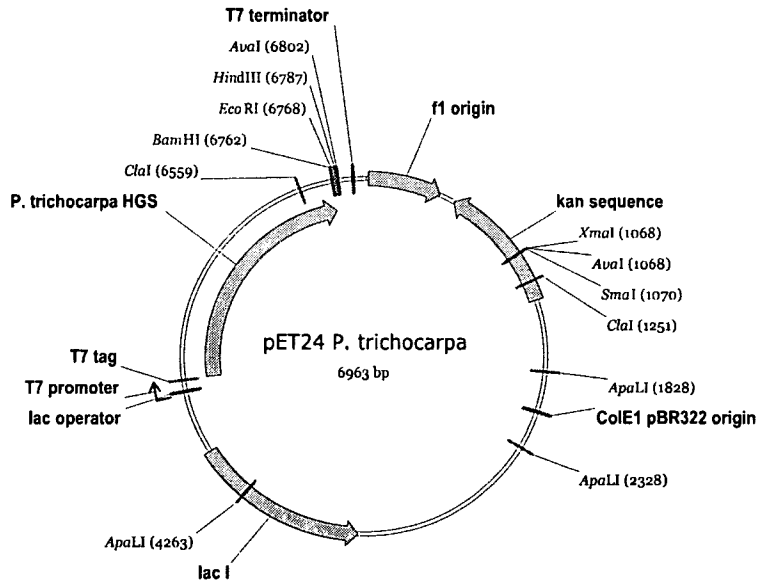

T7 terminator
AvaI (6802)
HindIII (6787)
EcoRI (6768)
BamHI (6762)
ClaI (6559)
f1 origin
P. trichocarpa HGS
kan sequence
XmaI (1068)
AvaI (1068)
SmaI (1070)
ClaI (1251)
pET24 P. trichocarpa
6963 bp
T7 tag
T7 promoter
lac operator
ApaLI (1828)
ColE1 pBR322 origin
ApaLI (2328)
ApaLI (4263)
lac I

Figure 80

Amino acid sequence of *P. tremuloides* IspS (SEQ ID NO:158)

MRCSVSTENVSFSETETETRRSANYEPNSWDYDYLLSSDTDESIEVHKDKAKKLEAEVR
REINNEKAEFLTLLELIDNVQRLGLGYRFESDIRRALDRFVSSGGFDGVTKTSLHGTAL
SFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAK
VFAISHLKELSEEKIGKELAEQVSHALELPLHRRTQRLEAVWSIEAYRKKEDANQVLLE
LAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDC
RNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNAINDLPDYMKLCFLALYNT
INEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTFDDYFGNAWKSSSG
PLQLIFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCNDLASASAEIARGETANSV
SCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHCTYH
NGDAHTSPDELTRKRVLSVITEPILPFER

Figure 81A

Nucleotide sequence of P. tremuloides pET24a (SEQ ID NO:159)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgc
gcagcgtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttccct
tcctttctcgccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttt
agggttccgatttagtgctttacggcacctcgaccccaaaaaacttgattagggtgatg
gttcacgtagtgggccatcgccctgatagacggtttttcgccctttgacgttggagtcc
acgttctttaatagtggactcttgttccaaactggaacaacactcaaccctatctcggt
ctattcttttgatttataagggattttgccgatttcggcctattggttaaaaaatgagc
tgatttaacaaaaatttaacgcgaattttaacaaaatattaacgtttacaatttcaggt
ggcacttttcggggaaatgtgcgcggaacccctatttgtttatttttctaaatacattc
aaatatgtatccgctcatgaattaattcttagaaaaactcatcgagcatcaaatgaaac
tgcaatttattcatatcaggattatcaataccatatttttgaaaaagccgtttctgtaa
tgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcggtctg
cgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataagg
ttatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagttt
atgcatttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcac
tcgcatcaaccaaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcga
tcgctgttaaaaggacaattacaaacaggaatcgaatgcaaccggcgcaggaacactgc
cagcgcatcaacaatattttcacctgaatcaggatattcttctaatacctggaatgctg
ttttcccggggatcgcagtggtgagtaaccatgcatcatcaggagtacggataaaatgc
ttgatggtcggaagaggcataaattccgtcagccagtttagtctgaccatctcatctgt
aacatcattggcaacgctacctttgccatgtttcagaaacaactctggcgcatcgggct
tcccatacaatcgatagattgtcgcacctgattgcccgacattatcgcgagcccattta
tacccatataaatcagcatccatgttggaatttaatcgcggcctagagcaagacgtttc
ccgttgaatatggctcataacacccttgtattactgtttatgtaagcagacagtttta
ttgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccccgt
agaaaagatcaaaggatcttcttgagatcctttttttctgcgcgtaatctgctgcttgc
aaacaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaact
ctttttccgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagt
gtagccgtagttaggccaccacttcaagaactctgtagcaccgcctacatacctcgctc
tgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgtcttaccgggttg
gactcaagacgatagttaccggataaggcgcagcggtcgggctgaacgggggttcgtg
cacacagcccagcttggagcgaacgacctacaccgaactgagatacctacagcgtgagc
tatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggtaagcggc
agggtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatcttta
tagtcctgtcgggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgtcag
gggggcggagcctatggaaaaacgccagcaacgcggccttttacggttcctggccttt
tgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtggataaccg
tattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcagcg
agtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctg
tgcggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgca
tagttaagccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccga
cacccgccaacacccgctgacgcgccctgacgggcttgtctgctcccggcatccgctta
cagacaagctgtgaccgtctccgggagctgcatgtgtcagaggttttcaccgtcatcac

Figure 81B

Nucleotide sequence of P. tremuloides pET24a

cgaaacgcgcgaggcagctgcggtaaagctcatcagcgtggtcgtgaagcgattcacag
atgtctgcctgttcatccgcgtccagctcgttgagtttctccagaagcgttaatgtctg
gcttctgataaagcgggccatgttaagggcggttttttcctgtttggtcactgatgcct
ccgtgtaaggggatttctgttcatgggggtaatgataccgatgaaacgagagaggatg
ctcacgatacgggttactgatgatgaacatgcccggttactggaacgttgtgagggtaa
acaactggcggtatggatgcggcgggaccagagaaaaatcactcagggtcaatgccagc
gcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcgatgcag
atccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacacg
gaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgc
ttcacgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccag
cctagccgggtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgcc
ggcgataatggcctgcttctcgccgaaacgtttggtggcgggaccagtgacgaaggctt
gagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcatcgtcgcgctc
cagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcctacgag
ttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgcccacc
ggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtgcctaa
tgagtgagctaacttacattaattgcgttgcgctcactgcccgctttccagtcgggaaa
cctgtcgtgccagctgcattaatgaatcggccaacgcgcggggagaggcggtttgcgta
ttgggcgccagggtggtttttcttttcaccagtgagacgggcaacagctgattgcccct
caccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccagcaggc
gaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcg
cattgcgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccct
cattcagcatttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgt
tccgctatcggctgaatttgattgcgagtgagatatttatgccagccagccagacgcag
acgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggtgacccaatg
cgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatactgttg
atgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggcagcttc
cacagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgacgcgtt
gcgcgagaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttctaccatc
gacaccaccacgctggcacccagttgatcggcgcgagatttaatcgccgcgacaatttg
cgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacgactgtttgc
ccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgcttcc
actttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggt
ctgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattca
ccaccctgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgc
cattcgatggtgtccgggatctcgacgctctcccttatgcgactcctgcattaggaagc
agcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaatggtgcatgcaag
gagatggcgcccaacagtcccccggccacggggcctgccaccatacccacgccgaaaca
agcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggcgatat
aggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccggcgtag
aggatcgagatctcgatcccgcgaaattaatacgactcactatagggaattgtgagcg
gataacaattcccctctagaaataattttgtttaactttaagaaggagatatacatatg

Figure 81C

Nucleotide sequence of P. tremuloides pET24a

cgttgtagcgtgtccaccgaaaatgtgtctttctctgaaactgaaaccgaaacgcgtcg
ttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccgacacgg
acgagtccatcgaagtacacaaagacaaagcgaaaaagctggaagccgaagttcgtcgc
gagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaacgtcca
gcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctggatcgcttcg
tttcctccggcggcttcgatggcgtaaccaagacttccctgcacggtacggcactgtct
ttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggcttcaa
agaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcctgagcc
tgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcgaaggtt
ttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctggcaga
acaggtgtcccatgcactggaactgccactgcatcgccgtactcagcgtctggaagcag
tatggtctatcgaggcctaccgtaaaaaggaggacgcgaaccaggttctgctggagctg
gcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtgaaacgtc
ccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccgcctga
ttgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgactgccgt
aactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgatgtata
cggcaccctggacgaactggagctgtttactgatgcagttgagcgttgggacgtaaacg
ccatcaacgacctgccggattacatgaaactgtgctttctggctctgtataacactatt
aacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgtatctgac
caaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgtacaaca
aatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctggcccg
ctgcaactgatcttcgcttacttcgctgtcgtgcagaacattaaaaaggaagagatcga
aaacctgcaaaaataccatgacatcatctctcgtccttcccatatcttccgtctgtgca
atgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcgtttct
tgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatgaatct
gatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgttcgcga
aaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatcataac
ggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgtaatcac
tgaaccgattctgccgtttgaacgctaaggatccgaattcgagctccgtcgacaagctt
gcggccgcactcgagcaccaccaccaccaccactgagatccggctgctaacaaagcccg
aaaggaagctgagttggctgctgccaccgctgagcaataactagcataacccccttgggg
cctctaaacgggtcttgaggggttttttgctgaaaggaggaactatatccggat

Figure 82

Amino acid sequence of *P. trichocharpa* IspS (SEQ ID NO:160)

MRCSVSTENVSFTETETETRRSANYEPNSWDYDYLLSSDTDESIEVYKDKAKKLEAEVR
REINNEKAEFLTLLELIDNVQRLGLGYRFESDIRRALDRFVSSGGFDAVTKTSLHATAL
SFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAILSLYEASFLALEGENILDEAK
VFAISHLKELSEEKIGKDLAEQVNHALELPLHRRTQRLEAVLSIEAYRKKEDADQVLLE
LAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLIESFYWAVGVAFEPQYSDC
RNSVAKMFSFVTIIDDIYDVYGTLDELELFTNAVERWDVNAIDDLPDYMKLCFLALYNT
INEIAYDNLKEKGENILPYLTKAWADLCNAFLQEAKWLYNKSTPTFDEYFGNAWKSSSG
PLQLVFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCNDLASASAEIARGETANSV
SCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAKPFVETAINLARQSHCTYH
NGDAHTSPDELTRKRVLSVITEPILPFER

Figure 83A

Nucleotide sequence of P. trichocharpa pET24a (SEQ ID NO:161)

tggcgaatgggacgcgccctgtagcggcgcattaagcgcggcgggtgtggtggttacgc
gcagcgtgaccgctacacttgccagcgccctagcgcccgctcctttcgctttcttccct
tcctttctcgccacgttcgccggctttccccgtcaagctctaaatcgggggctcccttt
agggttccgatttagtgctttacggcacctcgaccccaaaaaacttgattagggtgatg
gttcacgtagtgggccatcgccctgatagacggtttttcgccctttgacgttggagtcc
acgttctttaatagtggactcttgttccaaactggaacaacactcaaccctatctcggt
ctattcttttgatttataagggattttgccgatttcggcctattggttaaaaaatgagc
tgatttaacaaaaatttaacgcgaattttaacaaaatattaacgtttacaatttcaggt
ggcacttttcggggaaatgtgcgcggaacccctatttgtttatttttctaaatacattc
aaatatgtatccgctcatgaattaattcttagaaaaactcatcgagcatcaaatgaaac
tgcaatttattcatatcaggattatcaataccatatttttgaaaaagccgtttctgtaa
tgaaggagaaaactcaccgaggcagttccataggatggcaagatcctggtatcggtctg
cgattccgactcgtccaacatcaatacaacctattaatttcccctcgtcaaaaataagg
ttatcaagtgagaaatcaccatgagtgacgactgaatccggtgagaatggcaaaagttt
atgcatttctttccagacttgttcaacaggccagccattacgctcgtcatcaaaatcac
tcgcatcaaccaaaccgttattcattcgtgattgcgcctgagcgagacgaaatacgcga
tcgctgttaaaaggacaattacaaacaggaatcgaatgcaaccggcgcaggaacactgc
cagcgcatcaacaatattttcacctgaatcaggatattcttctaatacctggaatgctg
ttttcccggggatcgcagtggtgagtaaccatgcatcatcaggagtacggataaaatgc
ttgatggtcggaagaggcataaattccgtcagccagtttagtctgaccatctcatctgt
aacatcattggcaacgctacctttgccatgtttcagaaacaactctggcgcatcgggct
tcccatacaatcgatagattgtcgcacctgattgcccgacattatcgcgagcccattta
tacccatataaatcagcatccatgttggaatttaatcgcggcctagagcaagacgtttc
ccgttgaatatggctcataacacccttgtattactgtttatgtaagcagacagtttta
ttgttcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccccgt
agaaaagatcaaaggatcttcttgagatccttttttttctgcgcgtaatctgctgcttgc
aaacaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctaccaact
ctttttccgaaggtaactggcttcagcagagcgcagataccaaatactgtccttctagt
gtagccgtagttaggccaccacttcaagaactctgtagcaccgcctacatacctcgctc
tgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgtcttaccgggttg
gactcaagacgatagttaccggataaggcgcagcggtcgggctgaacgggggttcgtg
cacacagcccagcttggagcgaacgacctacaccgaactgagatacctacagcgtgagc
tatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggtaagcggc
agggtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatcttta
tagtcctgtcgggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgtcag
gggggcggagcctatggaaaaacgccagcaacgcggccttttacggttcctggccttt
tgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtggataaccg
tattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgcagcg
agtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcatctg
tgcggtatttcacaccgcatatatggtgcactctcagtacaatctgctctgatgccgca
tagttaagccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccga
cacccgccaacacccgctgacgcgccctgacgggcttgtctgctcccggcatccgctta
cagacaagctgtgaccgtctccgggagctgcatgtgtcagaggttttcaccgtcatcac

Figure 83B

Nucleotide sequence of P. trichocharpa pET24a

cgaaacgcgcgaggcagctgcggtaaagctcatcagcgtggtcgtgaagcgattcacag
atgtctgcctgttcatccgcgtccagctcgttgagtttctccagaagcgttaatgtctg
gcttctgataaagcgggccatgttaagggcggttttttcctgtttggtcactgatgcct
ccgtgtaagggggatttctgttcatgggggtaatgataccgatgaaacgagagaggatg
ctcacgatacgggttactgatgatgaacatgcccggttactggaacgttgtgagggtaa
acaactggcggtatggatgcggcgggaccagagaaaaatcactcagggtcaatgccagc
gcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcgatgcag
atccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacacg
gaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgc
ttcacgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccag
cctagccgggtcctcaacgacaggagcacgatcatgcgcacccgtggggccgccatgcc
ggcgataatggcctgcttctcgccgaaacgtttggtggcgggaccagtgacgaaggctt
gagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcatcgtcgcgctc
cagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcctacgag
ttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgcccacc
ggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtgcctaa
tgagtgagctaacttacattaattgcgttgcgctcactgcccgctttccagtcgggaaa
cctgtcgtgccagctgcattaatgaatcggccaacgcgcggggagaggcggtttgcgta
ttgggcgccagggtggtttttcttttcaccagtgagacgggcaacagctgattgcccct
caccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccagcaggc
gaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcggtatcg
tcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatggcgcg
cattgcgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgatgccct
cattcagcatttgcatggtttgttgaaaaccggacatggcactccagtcgccttcccgt
tccgctatcggctgaatttgattgcgagtgagatatttatgccagccagccagacgcag
acgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggtgacccaatg
cgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatactgttg
atgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggcagcttc
cacagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgacgcgtt
gcgcgagaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttctaccatc
gacaccaccacgctggcacccagttgatcggcgcgagatttaatcgccgcgacaatttg
cgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacgactgtttgc
ccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccgcttcc
actttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaaacggt
ctgataagagacaccggcatactctgcgacatcgtataacgttactggtttcacattca
ccaccctgaattgactctcttccgggcgctatcatgccataccgcgaaaggttttgcgc
cattcgatggtgtccgggatctcgacgctctcccttatgcgactcctgcattaggaagc
agcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaatggtgcatgcaag
gagatggcgcccaacagtcccccggccacggggcctgccaccatacccacgccgaaaca
agcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggcgatat
aggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccggcgtag
aggatcgagatctcgatcccgcgaaattaatacgactcactatagggaattgtgagcg
gataacaattcccctctagaaataattttgtttaactttaagaaggagatatacatatg

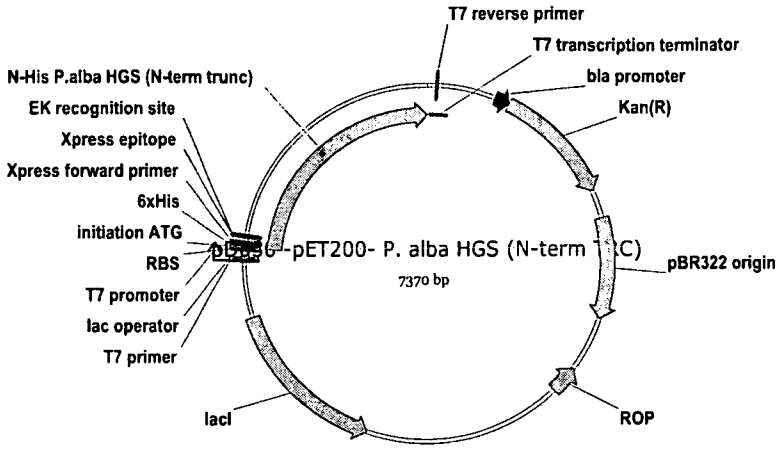
Figure 83C

Nucleotide sequence of P. trichocharpa pET24a

catatgcgttgtagcgtgtccaccgaaaatgtgtctttcaccgaaactgaaaccgaaac
gcgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccg
acacggacgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagtt
cgtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaa
cgtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctggatc
gcttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacgcgacggca
ctgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcgg
cttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcc
tgagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcg
aaggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagatct
ggcagaacaggtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctgg
aagcagtactgtctatcgaggcctaccgtaaaaaggaggacgcggatcaggttctgctg
gagctggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtga
aacgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgacc
gcctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgac
tgccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacga
tgtatacggcaccctggacgaactggagctgtttactaacgcagttgagcgttgggacg
taaacgccatcgacgatctgccggattacatgaaactgtgctttctggctctgtataac
actattaacgaaatcgcctacgacaacctgaaagaaaaaggtgagaacatcctgccgta
tctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgt
acaacaaatctactccgacctttgacgaatacttcggcaacgcatggaaatcctcttct
ggcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaaga
gatcgaaaacctgcaaaaataccatgacatcatctctcgtccttcccatatcttccgtc
tgtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagc
gtttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgat
gaatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgt
tcgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttat
cataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgt
aatcactgaaccgattctgccgtttgaacgctaaggatccgaattcgagctccgtcgac
aagcttgcggccgcactcgagcaccaccaccaccaccactgagatccggctgctaacaa
agcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcataacccc
ttggggcctctaaacgggtcttgaggggtttttgctgaaaggaggaactatatccgga
t

Figure 84

A.


T7 reverse primer
T7 transcription terminator
bla promoter
Kan(R)
N-His P.alba HGS (N-term trunc)
EK recognition site
Xpress epitope
Xpress forward primer
6xHis
initiation ATG
RBS
T7 promoter
lac operator
T7 primer
pD[illegible]-pET200- P. alba HGS (N-term [illegible]C)
7370 bp
pBR322 origin
lacI
ROP

B.

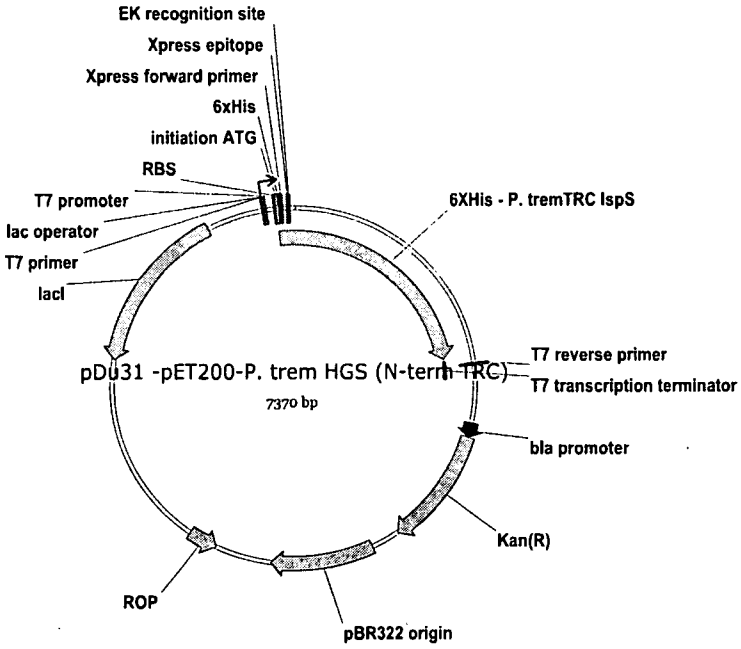

EK recognition site
Xpress epitope
Xpress forward primer
6xHis
initiation ATG
RBS
T7 promoter
lac operator
T7 primer
lacI
6XHis - P. tremTRC IspS
pDU31 -pET200-P. trem HGS (N-term TRC)
7370 bp
T7 reverse primer
T7 transcription terminator
bla promoter
Kan(R)
ROP
pBR322 origin

Figure 84C

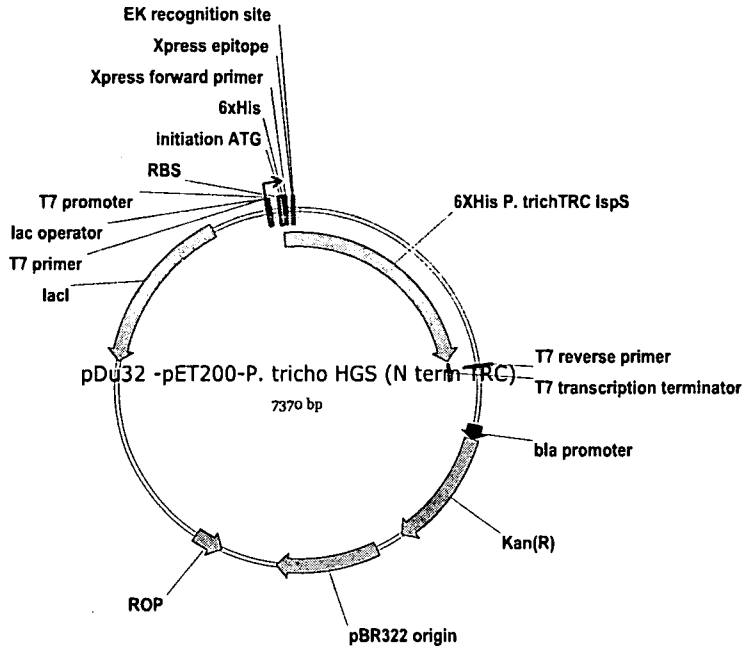

EK recognition site
Xpress epitope
Xpress forward primer
6xHis
Initiation ATG
RBS
T7 promoter
lac operator
T7 primer
lacI
6XHis P. trichTRC IspS
T7 reverse primer
T7 transcription terminator
pDu32 -pET200-P. tricho HGS (N term TRC)
7370 bp
bla promoter
Kan(R)
ROP
pBR322 origin

Figure 85

Amino acid sequence of IspS variant P. albaTRC-pET200 (SEQ ID NO:162)

MRGSHHHHHHGMASMTGGQQMGRDLYDDDDKDHPFTMRRSANYEPNSWDYDYLLSSDTD
ESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQRLGLGYRFESDIRGALDRFV
SSGGFDAVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAILSL
YEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVNHALELPLHRRTQRLEAV
WSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLI
ESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNA
INDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNK
STPTFDDYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDTISRPSHIFRLCN
DLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAK
PFVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 86A

Nucleotide Sequence of pDu30 (SEQ ID NO:163)

aagggcgagctcaacgatccggctgctaacaaagcccgaaaggaagctgagttggctgc
tgccaccgctgagcaataactagcataaccccttggggcctctaaacgggtcttgagga
gtttttgctgaaaggaggaactatatccggatatcccgcaagaggcccggcagtaccg
gcataaccaagcctatgcctacagcatccagggtgacggtgccgaggatgacgatgagc
gcattgttagatttcatacacggtgcctgactgcgttagcaatttaactgtgataaact
accgcattaaagcttatcgatgataagctgtcaaacatgagaattaattcttgaagacg
aaagggcctcgtgatacgcctatttttataggttaatgtcatgataataatggtttctt
agacgtcaggtggcacttttcggggaaatgtgcgcggaacccctatttgtttatttttc
taaatacattcaaatatgtatccgctcatgagacaataaccctgataaatgcttcaata
atattgaaaaaggaagagtatgattgaacaagatggattgcacgcaggttctccggccg
cttgggtggagaggctattcggctatgactgggcacaactgacaatcggctgctctgat
gccgccgtgttccggctgtcagcgcaggggcgcccggttctttttgtcaagaccgacct
gtccggtgccctgaatgaactgcaggacgaggcagcgcggctatcgtggctggccacga
cgggcgttccttgcgcagctgtgctcgacgttgtcactgaagcgggaagggactggctg
ctattgggcgaagtgccggggcaggatctcctgtcatctcaccttgctcctgccgagaa
agtatccatcatggctgatgcaatgcggcggctgcatacgcttgatccggctacctgcc
cattcgaccaccaagcgaaacatcgcatcgagcgggcacgtactcggatggaagccggt
cttgtcgatcaggatgatctggacgaagagcatcaggggctcgcgccagccgaactgtt
cgccaggctcaaggcgcgcatgcccgacggcgaggatctcgtcgtgacacatggcgatg
cctgcttgccgaatatcatggtggaaaatggccgcttttctggattcatcgactgtggc
cggctgggtgtggcggaccgctatcaggacatagcgttggctacccgtgatattgctga
agagcttggcggcgaatgggctgaccgcttcctcgtgctttacggtatcgccgctcccg
attcgcagcgcatcgccttctatcgccttcttgacgagttcttctgagcgggactctgg
ggttcgaaatgaccgaccaagcgacgcctaactgtcagaccaagtttactcatatatac
tttagattgatttaaaacttcatttttaatttaaaaggatctaggtgaagatccttttt
gataatctcatgaccaaaatcccttaacgtgagttttcgttccactgagcgtcagaccc
cgtagaaaagatcaaaggatcttcttgagatcctttttttctgcgcgtaatctgctgct
tgcaaacaaaaaaaccaccgctaccagcggtggtttgtttgccggatcaagagctacca
actcttttccgaaggtaactggcttcagcagagcgcagataccaaatactgtccttct
agtgtagccgtagttaggccaccacttcaagaactctgtagcaccgcctacatacctcg
ctctgctaatcctgttaccagtggctgctgccagtggcgataagtcgtgtcttaccggg
ttggactcaagacgatagttaccggataaggcgcagcggtcgggctgaacgggggttc
gtgcacacagcccagcttggagcgaacgacctacaccgaactgagatacctacagcgtg
agctatgagaaagcgccacgcttcccgaagggagaaaggcggacaggtatccggtaagc
ggcagggtcggaacaggagagcgcacgagggagcttccagggggaaacgcctggtatct
ttatagtcctgtcgggtttcgccacctctgacttgagcgtcgatttttgtgatgctcgt
caggggggcggagcctatggaaaaacgccagcaacgcggccttttacggttcctggcc
ttttgctggccttttgctcacatgttctttcctgcgttatcccctgattctgtggataa
ccgtattaccgcctttgagtgagctgataccgctcgccgcagccgaacgaccgagcgca
gcgagtcagtgagcgaggaagcggaagagcgcctgatgcggtattttctccttacgcat
ctgtgcggtatttcacaccgcaatggtgcactctcagtacaatctgctctgatgccgca
tagttaagccagtatacactccgctatcgctacgtgactgggtcatggctgcgccccga
cacccgccaacacccgctgacgcgccctgacgggcttgtctgctcccggcatccgctta

Figure 86B

Nucleotide Sequence of pDu30

cagacaagctgtgaccgtctccgggagctgcatgtgtcagaggttttcaccgtcatcac
cgaaacgcgcgaggcagctgcggtaaagctcatcagcgtggtcgtgaagcgattcacag
atgtctgcctgttcatccgcgtccagctcgttgagtttctccagaagcgttaatgtctg
gcttctgataaagcgggccatgttaagggcggttttttcctgtttggtcactgatgcct
ccgtgtaagggggatttctgttcatgggggtaatgataccgatgaaacgagagaggatg
ctcacgatacgggttactgatgatgaacatgcccggttactggaacgttgtgagggtaa
acaactggcggtatggatgcggcgggaccagagaaaaatcactcagggtcaatgccagc
gcttcgttaatacagatgtaggtgttccacagggtagccagcagcatcctgcgatgcag
atccggaacataatggtgcagggcgctgacttccgcgtttccagactttacgaaacacg
gaaaccgaagaccattcatgttgttgctcaggtcgcagacgttttgcagcagcagtcgc
ttcacgttcgctcgcgtatcggtgattcattctgctaaccagtaaggcaaccccgccag
cctagccgggtcctcaacgacaggagcacgatcatgcgcacccgtggccaggacccaac
gctgcccgagatgcgccgcgtgcggctgctggagatggcggacgcgatggatatgttct
gccaagggttggtttgcgcattcacagttctccgcaagaattgattggctccaattctt
ggagtggtgaatccgttagcgaggtgccgccggcttccattcaggtcgaggtggcccgg
ctccatgcaccgcgacgcaacgcggggaggcagacaaggtatagggcggcgcctacaat
ccatgccaacccgttccatgtgctcgccgaggcggcataaatcgccgtgacgatcagcg
gtccaàtgatcgaagttaggctggtaagagccgcgagcgatccttgaagctgtccctga
tggtcgtcatctacctgcctggacagcatggcctgcaacgcgggcatcccgatgccgcc
ggaagcgagaagaatcataatggggaaggccatccagcctcgcgtcgcgaacgccagca
agacgtagcccagcgcgtcggccgccatgccggcgataatggcctgcttctcgccgaaa
cgtttggtggcgggaccagtgacgaaggcttgagcgagggcgtgcaagattccgaatac
cgcaagcgacaggccgatcatcgtcgcgctccagcgaaagcggtcctcgccgaaaatga
cccagagcgctgccggcacctgtcctacgagttgcatgataaagaagacagtcataagt
gcggcgacgatagtcatgccccgcgcccaccggaaggagctgactgggttgaaggctct
caagggcatcggtcgagatcccggtgcctaatgagtgagctaacttacattaattgcgt
tgcgctcactgcccgctttccagtcgggaaacctgtcgtgccagctgcattaatgaatc
ggccaacgcgcggggagaggcggtttgcgtattgggcgccagggtggtttttcttttca
ccagtgagacgggcaacagctgattgcccttcaccgcctggccctgagagagttgcagc
aagcggtccacgctggtttgccccagcaggcgaaaatcctgtttgatggtggttaacgg
cgggatataacatgagctgtcttcggtatcgtcgtatcccactaccgagatatccgcac
caacgcgcagcccggactcggtaatggcgcgcattgcgcccagcgccatctgatcgttg
gcaaccagcatcgcagtgggaacgatgccctcattcagcatttgcatggtttgttgaaa
accggacatggcactccagtcgccttcccgttccgctatcggctgaatttgattgcgag
tgagatatttatgccagccagccagacgcagacgcgccgagacagaacttaatgggccc
gctaacagcgcgatttgctggtgacccaatgcgaccagatgctccacgcccagtcgcgt
accgtcttcatgggagaaaataatactgttgatgggtgtctggtcagagacatcaagaa
ataacgccggaacattagtgcaggcagcttccacagcaatggcatcctggtcatccagc
ggatagttaatgatcagcccactgacgcgttgcgcgagaagattgtgcaccgccgcttt
acaggcttcgacgccgcttcgttctaccatcgacaccaccacgctggcacccagttgat
cggcgcgagatttaatcgccgcgacaatttgcgacggcgcgtgcagggccagactggag
gtggcaacgccaatcagcaacgactgtttgcccgccagttgttgtgccacgcggttggg
aatgtaattcagctccgccatcgccgcttccacttttcccgcgttttcgcagaaacgt

Figure 86C

Nucleotide Sequence of pDu30

ggctggcctggttcaccacgcgggaaacggtctgataagagacaccggcatactctgcg
acatcgtataacgttactggtttcacattcaccaccctgaattgactctcttccgggcg
ctatcatgccataccgcgaaaggttttgcgccattcgatggtgtccgggatctcgacgc
tctcccttatgcgactcctgcattaggaagcagcccagtagtaggttgaggccgttgag
caccgccgccgcaaggaatggtgcatgcaaggagatggcgcccaacagtcccccggcca
cggggcctgccaccatacccacgccgaaacaagcgctcatgagcccgaagtggcgagcc
cgatcttccccatcggtgatgtcggcgatataggcgccagcaaccgcacctgtggcgcc
ggtgatgccggccacgatgcgtccggcgtagaggatcgagatctcgatcccgcgaaatt
aatacgactcactataggggaattgtgagcggataacaattcccctctagaaataatttt
tgtttaactttaagaaggagatatacatatgcggggttctcatcatcatcatcatcatg
gtatggctagcatgactggtggacagcaaatgggtcgggatctgtacgacgatgacgat
aaggatcatcccttcaccatgcgtcgttctgcgaactacgaacctaacagctgggacta
tgattacctgctgtcctccgacacggacgagtccatcgaagtatacaaagacaaagcga
aaaagctggaagccgaagttcgtcgcgagattaataacgaaaaagcagaatttctgacc
ctgctggaactgattgacaacgtccagcgcctgggcctgggttaccgtttcgagtctga
tatccgtggtgcgctggatcgcttcgtttcctccggcggcttcgatgcggtaaccaaga
cttccctgcacggtacggcactgtctttccgtctgctgcgtcaacacggttttgaggtt
tctcaggaagcgttcagcggcttcaaagaccaaaacggcaacttcctggagaacctgaa
ggaagatatcaaagctatcctgagcctgtacgaggccagcttcctggctctggaaggcg
aaaacatcctggacgaggcgaaggttttcgcaatctctcatctgaaagaactgtctgaa
gaaaagatcggtaaagagctggcagaacaggtgaaccatgcactggaactgccactgca
tcgccgtactcagcgtctggaagcagtatggtctatcgaggcctaccgtaaaaaggagg
acgcgaatcaggttctgctggagctggcaattctggattacaacatgatccagtctgta
taccagcgtgatctgcgtgaaacgtcccgttggtggcgtcgtgtgggtctggcgaccaa
actgcactttgctcgtgaccgcctgattgagagcttctactgggccgtgggtgtagcat
tcgaaccgcaatactccgactgccgtaactccgtcgcaaaaatgttttctttcgtaacc
attatcgacgatatctacgatgtatacggcaccctggacgaactggagctgtttactga
tgcagttgagcgttgggacgtaaacgccatcaacgacctgccggattacatgaaactgt
gctttctggctctgtataacactattaacgaaatcgcctacgacaacctgaaagataaa
ggtgagaacatcctgccgtatctgaccaaagcctgggctgacctgtgcaacgctttcct
gcaagaagccaagtggctgtacaacaaatctactccgacctttgacgactacttcggca
acgcatggaaatcctcttctggcccgctgcaactggtgttcgcttacttcgctgtcgtg
cagaacattaaaaaggaagagatcgaaaacctgcaaaaataccatgacaccatctctcg
tccttcccatatcttccgtctgtgcaatgacctggctagcgcgtctgcggaaattgcgc
gtggtgaaaccgcaaatagcgtttcttgttacatgcgcactaaaggtatctccgaagaa
ctggctaccgaaagcgtgatgaatctgatcgatgaaacctggaaaaagatgaacaagga
aaaactgggtggtagcctgttcgcgaaaccgttcgtggaaaccgcgatcaacctggcac
gtcaatctcactgcacttatcataacggcgacgcgcatacctctccggatgagctgacc
cgcaaacgcgttctgtctgtaatcactgaaccgattctgccgtttgaacgctaa

Figure 87

Amino acid sequence of IspS variant *P.trem*TRC-pET200 (SEQ ID NO:164)

MRGSHHHHHHGMASMTGGQQMGRDLYDDDDKDHPFTMRRSANYEPNSWDYDYLLSSDTD
ESIEVHKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQRLGLGYRFESDIRRALDRFV
SSGGFDGVTKTSLHGTALSFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAILSL
YEASFLALEGENILDEAKVFAISHLKELSEEKIGKELAEQVSHALELPLHRRTQRLEAV
WSIEAYRKKEDANQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLI
ESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTDAVERWDVNA
INDLPDYMKLCFLALYNTINEIAYDNLKDKGENILPYLTKAWADLCNAFLQEAKWLYNK
STPTFDDYFGNAWKSSSGPLQLIFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCN
DLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAK
PFVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 88A

Nucleotide sequence of pDu31 (SEQ ID NO:165)

cgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccga
cacggacgagtccatcgaagtacacaaagacaaagcgaaaaagctggaagccgaagttc
gtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaac
gtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctggatcg
cttcgtttcctccggcggcttcgatggcgtaaccaagacttccctgcacggtacggcac
tgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggc
ttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcct
gagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcga
aggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagagctg
gcagaacaggtgtcccatgcactggaactgccactgcatcgccgtactcagcgtctgga
agcagtatggtctatcgaggcctaccgtaaaaaggaggacgcgaaccaggttctgctgg
agctggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtgaa
acgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccg
cctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgact
gccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgat
gtatacggcaccctggacgaactggagctgtttactgatgcagttgagcgttgggacgt
aaacgccatcaacgacctgccggattacatgaaactgtgctttctggctctgtataaca
ctattaacgaaatcgcctacgacaacctgaaagataaaggtgagaacatcctgccgtat
ctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgta
caacaaatctactccgacctttgacgactacttcggcaacgcatggaaatcctcttctg
gcccgctgcaactgatcttcgcttacttcgctgtcgtgcagaacattaaaaaggaagag
atcgaaaacctgcaaaaataccatgacatcatctctcgtccttcccatatcttccgtct
gtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcg
tttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatg
aatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgtt
cgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatc
ataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgta
atcactgaaccgattctgccgtttgaacgctaaaagggcgagctcaacgatccggctgc
taacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcat
aacccttggggcctctaaacgggtcttgaggagttttttgctgaaaggaggaactata
tccggatatcccgcaagaggcccggcagtaccggcataaccaagcctatgcctacagca
tccagggtgacggtgccgaggatgacgatgagcgcattgttagatttcatacacggtgc
ctgactgcgttagcaatttaactgtgataaactaccgcattaaagcttatcgatgataa
gctgtcaaacatgagaattaattcttgaagacgaaagggcctcgtgatacgcctatttt
tataggttaatgtcatgataataatggtttcttagacgtcaggtggcacttttcggggga
aatgtgcgcggaacccctatttgtttatttttctaaatacattcaaatatgtatccgct
catgagacaataaccctgataaatgcttcaataatattgaaaaaggaagagtatgattg
aacaagatggattgcacgcaggttctccggccgcttgggtggagaggctattcggctat
gactgggcacaactgacaatcggctgctctgatgccgccgtgttccggctgtcagcgca
ggggcgcccggttctttttgtcaagaccgacctgtccggtgccctgaatgaactgcagg
acgaggcagcgcggctatcgtggctggccacgacgggcgttccttgcgcagctgtgctc
gacgttgtcactgaagcgggaagggactggctgctattgggcgaagtgccggggcagga
tctcctgtcatctcaccttgctcctgccgagaaagtatccatcatggctgatgcaatgc

Figure 88B

Nucleotide sequence of pDu31

ggcggctgcatacgcttgatccggctacctgcccattcgaccaccaagcgaaacatcgc
atcgagcgggcacgtactcggatggaagccggtcttgtcgatcaggatgatctggacga
agagcatcaggggctcgcgccagccgaactgttcgccaggctcaaggcgcgcatgcccg
acggcgaggatctcgtcgtgacacatggcgatgcctgcttgccgaatatcatggtggaa
aatggccgcttttctggattcatcgactgtggccggctgggtgtggcggaccgctatca
ggacatagcgttggctacccgtgatattgctgaagagcttggcggcgaatgggctgacc
gcttcctcgtgctttacggtatcgccgctcccgattcgcagcgcatcgccttctatcgc
cttcttgacgagttcttctgagcgggactctggggttcgaaatgaccgaccaagcgacg
cctaactgtcagaccaagtttactcatatatactttagattgatttaaaacttcatttt
taatttaaaaggatctaggtgaagatccttttgataatctcatgaccaaaatccctta
acgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttctt
gagatccttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctacca
gcggtggtttgtttgccggatcaagagctaccaactctttttccgaaggtaactggctt
cagcagagcgcagataccaaatactgtccttctagtgtagccgtagttaggccaccact
tcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttaccagtggct
gctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgga
taaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaa
cgacctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttccc
gaagggagaaaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcac
gagggagcttccagggggaaacgcctggtatctttatagtcctgtcgggtttcgccacc
tctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcctatggaaaaac
gccagcaacgcggcctttttacggttcctggccttttgctggccttttgctcacatgtt
ctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagtgagctg
ataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcggaa
gagcgcctgatgcggtattttctccttacgcatctgtgcggtatttcacaccgcaatgg
tgcactctcagtacaatctgctctgatgccgcatagttaagccagtatacactccgcta
tcgctacgtgactgggtcatggctgcgccccgacacccgccaacacccgctgacgcgcc
ctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgtctccggga
gctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcggtaa
agctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccag
ctcgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaa
gggcggtttttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatg
ggggtaatgataccgatgaaacgagagaggatgctcacgatacgggttactgatgatga
acatgcccggttactggaacgttgtgagggtaaacaactggcggtatggatgcggcggg
accagagaaaaatcactcagggtcaatgccagcgcttcgttaatacagatgtaggtgtt
ccacagggtagccagcagcatcctgcgatgcagatccggaacataatggtgcagggcgc
tgacttccgcgtttccagactttacgaaacacggaaaccgaagaccattcatgttgttg
ctcaggtcgcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcggtgat
tcattctgctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgacaggag
cacgatcatgcgcacccgtggccaggacccaacgctgcccgagatgcgccgcgtgcggc
tgctggagatggcggacgcgatggatatgttctgccaagggttggtttgcgcattcaca
gttctccgcaagaattgattggctccaattcttggagtggtgaatccgttagcgaggtg
ccgccggcttccattcaggtcgaggtggcccggctccatgcaccgcgacgcaacgcggg

Figure 88C

Nucleotide sequence of pDu31

gaggcagacaaggtatagggcggcgcctacaatccatgccaacccgttccatgtgctcg
ccgaggcggcataaatcgccgtgacgatcagcggtccaatgatcgaagttaggctggta
agagccgcgagcgatccttgaagctgtccctgatggtcgtcatctacctgcctggacag
catggcctgcaacgcgggcatcccgatgccgccggaagcgagaagaatcataatgggga
aggccatccagcctcgcgtcgcgaacgccagcaagacgtagcccagcgcgtcggccgcc
atgccggcgataatggcctgcttctcgccgaaacgtttggtggcgggaccagtgacgaa
ggcttgagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcatcgtcg
cgctccagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcct
acgagttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgc
ccaccggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtg
cctaatgagtgagctaacttacattaattgcgttgcgctcactgcccgctttccagtcg
ggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcggggagaggcggttt
gcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagctgattg
cccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcgg
tatcgtcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatg
gcgcgcattgcgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgat
gccctcattcagcatttgcatggtttgttgaaaaccggacatggcactccagtcgcctt
cccgttccgctatcggctgaatttgattgcgagtgagatatttatgccagccagccaga
cgcagacgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggtgacc
caatgcgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatac
tgttgatgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggca
gcttccacagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgac
gcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttcta
ccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatcgccgcgaca
atttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacgactg
tttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccg
cttccactttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaa
acggtctgataagagacaccggcatactctgcgacatcgtataacgttactggtttcac
attcaccaccctgaattgactctcttccgggcgctatcatgccataccgcgaaaggttt
tgcgccattcgatggtgtccgggatctcgacgctctcccttatgcgactcctgcattag
gaagcagcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaatggtgcat
gcaaggagatggcgcccaacagtcccccggccacggggcctgccaccatacccacgccg
aaacaagcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggc
gatataggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccgg
cgtagaggatcgagatctcgatcccgcgaaattaatacgactcactatagggaattgt
gagcggataacaattcccctctagaaataattttgtttaactttaagaaggagatatac
atatgcggggttctcatcatcatcatcatcatggtatggctagcatgactggtggacag
caaatgggtcgggatctgtacgacgatgacgataaggatcatcccttcaccatg

Figure 89

Amino acid sequence of IspS variant P.trichTRC-pET200 (SEQ ID NO:166)

MRGSHHHHHHGMASMTGGQQMGRDLYDDDDKDHPFTMRRSANYEPNSWDYDYLLSSDTD
ESIEVYKDKAKKLEAEVRREINNEKAEFLTLLELIDNVQRLGLGYRFESDIRRALDRFV
SSGGFDAVTKTSLHATALSFRLLRQHGFEVSQEAFSGFKDQNGNFLENLKEDIKAILSL
YEASFLALEGENILDEAKVFAISHLKELSEEKIGKDLAEQVNHALELPLHRRTQRLEAV
LSIEAYRKKEDADQVLLELAILDYNMIQSVYQRDLRETSRWWRRVGLATKLHFARDRLI
ESFYWAVGVAFEPQYSDCRNSVAKMFSFVTIIDDIYDVYGTLDELELFTNAVERWDVNA
IDDLPDYMKLCFLALYNTINEIAYDNLKEKGENILPYLTKAWADLCNAFLQEAKWLYNK
STPTFDEYFGNAWKSSSGPLQLVFAYFAVVQNIKKEEIENLQKYHDIISRPSHIFRLCN
DLASASAEIARGETANSVSCYMRTKGISEELATESVMNLIDETWKKMNKEKLGGSLFAK
PFVETAINLARQSHCTYHNGDAHTSPDELTRKRVLSVITEPILPFER

Figure 90A

Nucleotide Sequence of pDu32 (SEQ ID NO:167)

cgtcgttctgcgaactacgaacctaacagctgggactatgattacctgctgtcctccga
cacggacgagtccatcgaagtatacaaagacaaagcgaaaaagctggaagccgaagttc
gtcgcgagattaataacgaaaaagcagaatttctgaccctgctggaactgattgacaac
gtccagcgcctgggcctgggttaccgtttcgagtctgatatccgtcgtgcgctggatcg
cttcgtttcctccggcggcttcgatgcggtaaccaagacttccctgcacgcgacggcac
tgtctttccgtctgctgcgtcaacacggttttgaggtttctcaggaagcgttcagcggc
ttcaaagaccaaaacggcaacttcctggagaacctgaaggaagatatcaaagctatcct
gagcctgtacgaggccagcttcctggctctggaaggcgaaaacatcctggacgaggcga
aggttttcgcaatctctcatctgaaagaactgtctgaagaaaagatcggtaaagatctg
gcagaacaggtgaaccatgcactggaactgccactgcatcgccgtactcagcgtctgga
agcagtactgtctatcgaggcctaccgtaaaaaggaggacgcggatcaggttctgctgg
agctggcaattctggattacaacatgatccagtctgtataccagcgtgatctgcgtgaa
acgtcccgttggtggcgtcgtgtgggtctggcgaccaaactgcactttgctcgtgaccg
cctgattgagagcttctactgggccgtgggtgtagcattcgaaccgcaatactccgact
gccgtaactccgtcgcaaaaatgttttctttcgtaaccattatcgacgatatctacgat
gtatacggcaccctggacgaactggagctgtttactaacgcagttgagcgttgggacgt
aaacgccatcgacgatctgccggattacatgaaactgtgctttctggctctgtataaca
ctattaacgaaatcgcctacgacaacctgaaagaaaaaggtgagaacatcctgccgtat
ctgaccaaagcctgggctgacctgtgcaacgctttcctgcaagaagccaagtggctgta
caacaaatctactccgacctttgacgaatacttcggcaacgcatggaaatcctcttctg
gcccgctgcaactggtgttcgcttacttcgctgtcgtgcagaacattaaaaaggaagag
atcgaaaacctgcaaaaataccatgacatcatctctcgtccttcccatatcttccgtct
gtgcaatgacctggctagcgcgtctgcggaaattgcgcgtggtgaaaccgcaaatagcg
tttcttgttacatgcgcactaaaggtatctccgaagaactggctaccgaaagcgtgatg
aatctgatcgatgaaacctggaaaaagatgaacaaggaaaaactgggtggtagcctgtt
cgcgaaaccgttcgtggaaaccgcgatcaacctggcacgtcaatctcactgcacttatc
ataacggcgacgcgcatacctctccggatgagctgacccgcaaacgcgttctgtctgta
atcactgaaccgattctgccgtttgaacgctaaaagggcgagctcaacgatccggctgc
taacaaagcccgaaaggaagctgagttggctgctgccaccgctgagcaataactagcat
aacccccttggggcctctaaacgggtcttgaggagtttttgctgaaaggaggaactata
tccggatatcccgcaagaggcccggcagtaccggcataaccaagcctatgcctacagca
tccagggtgacggtgccgaggatgacgatgagcgcattgttagatttcatacacggtgc
ctgactgcgttagcaatttaactgtgataaactaccgcattaaagcttatcgatgataa
gctgtcaaacatgagaattaattcttgaagacgaaagggcctcgtgatacgcctatttt
tataggttaatgtcatgataataatggtttcttagacgtcaggtggcacttttcgggga
aatgtgcgcggaacccctatttgtttatttttctaaatacattcaaatatgtatccgct
catgagacaataaccctgataaatgcttcaataatattgaaaaaggaagagtatgattg
aacaagatggattgcacgcaggttctccggccgcttgggtggagaggctattcggctat
gactgggcacaactgacaatcggctgctctgatgccgccgtgttccggctgtcagcgca
ggggcgcccggttctttttgtcaagaccgacctgtccggtgccctgaatgaactgcagg
acgaggcagcgcggctatcgtggctggccacgacgggcgttccttgcgcagctgtgctc
gacgttgtcactgaagcgggaagggactggctgctattgggcgaagtgccggggcagga
tctcctgtcatctcaccttgctcctgccgagaaagtatccatcatggctgatgcaatgc

Figure 90B

Nucleotide Sequence of pDu32

ggcggctgcatacgcttgatccggctacctgcccattcgaccaccaagcgaaacatcgc
atcgagcgggcacgtactcggatggaagccggtcttgtcgatcaggatgatctggacga
agagcatcaggggctcgcgccagccgaactgttcgccaggctcaaggcgcgcatgcccg
acggcgaggatctcgtcgtgacacatggcgatgcctgcttgccgaatatcatggtggaa
aatggccgcttttctggattcatcgactgtggccggctgggtgtggcggaccgctatca
ggacatagcgttggctacccgtgatattgctgaagagcttggcggcgaatgggctgacc
gcttcctcgtgctttacggtatcgccgctcccgattcgcagcgcatcgccttctatcgc
cttcttgacgagttcttctgagcgggactctggggttcgaaatgaccgaccaagcgacg
cctaactgtcagaccaagtttactcatatatactttagattgatttaaaacttcatttt
taatttaaaaggatctaggtgaagatccttttgataatctcatgaccaaaatccctta
acgtgagttttcgttccactgagcgtcagaccccgtagaaaagatcaaaggatcttctt
gagatccttttttctgcgcgtaatctgctgcttgcaaacaaaaaaaccaccgctacca
gcggtggtttgtttgccggatcaagagctaccaactctttttccgaaggtaactggctt
cagcagagcgcagataccaaatactgtccttctagtgtagccgtagttaggccaccact
tcaagaactctgtagcaccgcctacatacctcgctctgctaatcctgttaccagtggct
gctgccagtggcgataagtcgtgtcttaccgggttggactcaagacgatagttaccgga
taaggcgcagcggtcgggctgaacgggggttcgtgcacacagcccagcttggagcgaa
cgacctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttccc
gaagggagaaaggcggacaggtatccggtaagcggcagggtcggaacaggagagcgcac
gagggagcttccagggggaaacgcctggtatctttatagtcctgtcgggtttcgccacc
tctgacttgagcgtcgatttttgtgatgctcgtcaggggggcggagcctatggaaaaac
gccagcaacgcggcctttttacggttcctggccttttgctggccttttgctcacatgtt
ctttcctgcgttatcccctgattctgtggataaccgtattaccgcctttgagtgagctg
ataccgctcgccgcagccgaacgaccgagcgcagcgagtcagtgagcgaggaagcggaa
gagcgcctgatgcggtattttctccttacgcatctgtgcggtatttcacaccgcaatgg
tgcactctcagtacaatctgctctgatgccgcatagttaagccagtatacactccgcta
tcgctacgtgactgggtcatggctgcgccccgacacccgccaacacccgctgacgcgcc
ctgacgggcttgtctgctcccggcatccgcttacagacaagctgtgaccgtctccggga
gctgcatgtgtcagaggttttcaccgtcatcaccgaaacgcgcgaggcagctgcggtaa
agctcatcagcgtggtcgtgaagcgattcacagatgtctgcctgttcatccgcgtccag
ctcgttgagtttctccagaagcgttaatgtctggcttctgataaagcgggccatgttaa
gggcggtttttttcctgtttggtcactgatgcctccgtgtaagggggatttctgttcatg
ggggtaatgataccgatgaaacgagagaggatgctcacgatacgggttactgatgatga
acatgcccggttactggaacgttgtgagggtaaacaactggcggtatggatgcggcggg
accagagaaaaatcactcagggtcaatgccagcgcttcgttaatacagatgtaggtgtt
ccacagggtagccagcagcatcctgcgatgcagatccggaacataatggtgcagggcgc
tgacttccgcgtttccagactttacgaaacacggaaaccgaagaccattcatgttgttg
ctcaggtcgcagacgttttgcagcagcagtcgcttcacgttcgctcgcgtatcggtgat
tcattctgctaaccagtaaggcaaccccgccagcctagccgggtcctcaacgacaggag
cacgatcatgcgcacccgtggccaggacccaacgctgcccgagatgcgccgcgtgcggc
tgctggagatggcggacgcgatggatatgttctgccaagggttggtttgcgcattcaca
gttctccgcaagaattgattggctccaattcttggagtggtgaatccgttagcgaggtg
ccgccggcttccattcaggtcgaggtggcccggctccatgcaccgcgacgcaacgcggg

Figure 90C

Nucleotide Sequence of pDu32

gaggcagacaaggtatagggcggcgcctacaatccatgccaacccgttccatgtgctcg
ccgaggcggcataaatcgccgtgacgatcagcggtccaatgatcgaagttaggctggta
agagccgcgagcgatccttgaagctgtccctgatggtcgtcatctacctgcctggacag
catggcctgcaacgcgggcatcccgatgccgccggaagcgagaagaatcataatgggga
aggccatccagcctcgcgtcgcgaacgccagcaagacgtagcccagcgcgtcggccgcc
atgccggcgataatggcctgcttctcgccgaaacgtttggtggcgggaccagtgacgaa
ggcttgagcgagggcgtgcaagattccgaataccgcaagcgacaggccgatcatcgtcg
cgctccagcgaaagcggtcctcgccgaaaatgacccagagcgctgccggcacctgtcct
acgagttgcatgataaagaagacagtcataagtgcggcgacgatagtcatgccccgcgc
ccaccggaaggagctgactgggttgaaggctctcaagggcatcggtcgagatcccggtg
cctaatgagtgagctaacttacattaattgcgttgcgctcactgcccgctttccagtcg
ggaaacctgtcgtgccagctgcattaatgaatcggccaacgcgcggggagaggcggttt
gcgtattgggcgccagggtggtttttcttttcaccagtgagacgggcaacagctgattg
cccttcaccgcctggccctgagagagttgcagcaagcggtccacgctggtttgccccag
caggcgaaaatcctgtttgatggtggttaacggcgggatataacatgagctgtcttcgg
tatcgtcgtatcccactaccgagatatccgcaccaacgcgcagcccggactcggtaatg
gcgcgcattgcgcccagcgccatctgatcgttggcaaccagcatcgcagtgggaacgat
gccctcattcagcatttgcatggtttgttgaaaaccggacatggcactccagtcgcctt
cccgttccgctatcggctgaatttgattgcgagtgagatatttatgccagccagccaga
cgcagacgcgccgagacagaacttaatgggcccgctaacagcgcgatttgctggtgacc
caatgcgaccagatgctccacgcccagtcgcgtaccgtcttcatgggagaaaataatac
tgttgatgggtgtctggtcagagacatcaagaaataacgccggaacattagtgcaggca
gcttccacagcaatggcatcctggtcatccagcggatagttaatgatcagcccactgac
gcgttgcgcgagaagattgtgcaccgccgctttacaggcttcgacgccgcttcgttcta
ccatcgacaccaccacgctggcacccagttgatcggcgcgagatttaatcgccgcgaca
atttgcgacggcgcgtgcagggccagactggaggtggcaacgccaatcagcaacgactg
tttgcccgccagttgttgtgccacgcggttgggaatgtaattcagctccgccatcgccg
cttccacttttcccgcgttttcgcagaaacgtggctggcctggttcaccacgcgggaa
acggtctgataagagacaccggcatactctgcgacatcgtataacgttactggtttcac
attcaccaccctgaattgactctcttccgggcgctatcatgccataccgcgaaaggttt
tgcgccattcgatggtgtccgggatctcgacgctctcccttatgcgactcctgcattag
gaagcagcccagtagtaggttgaggccgttgagcaccgccgccgcaaggaatggtgcat
gcaaggagatggcgcccaacagtcccccggccacggggcctgccaccatacccacgccg
aaacaagcgctcatgagcccgaagtggcgagcccgatcttccccatcggtgatgtcggc
gatataggcgccagcaaccgcacctgtggcgccggtgatgccggccacgatgcgtccgg
cgtagaggatcgagatctcgatcccgcgaaattaatacgactcactataggggaattgt
gagcggataacaattcccctctagaaataattttgtttaactttaagaaggagatatac
atatgcggggttctcatcatcatcatcatcatggtatggctagcatgactggtggacag
caaatgggtcgggatctgtacgacgatgacgataaggatcatcccttcaccatg

Figure 91

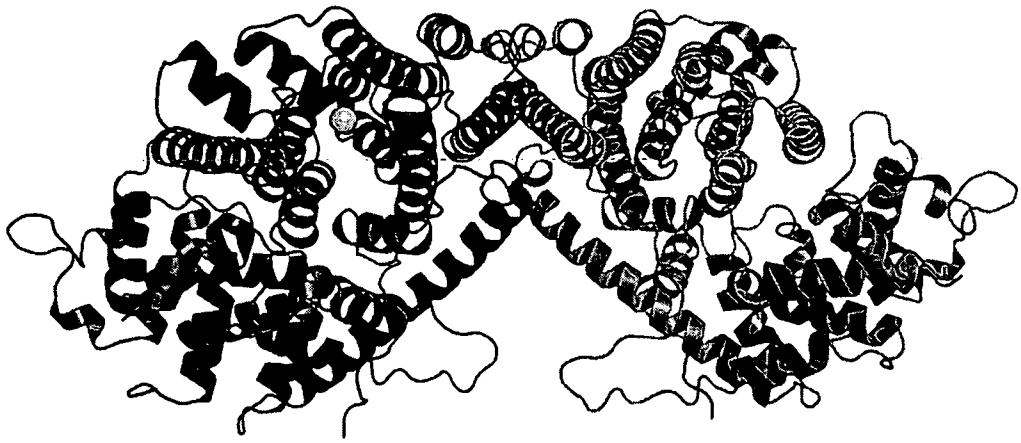


Figure 92

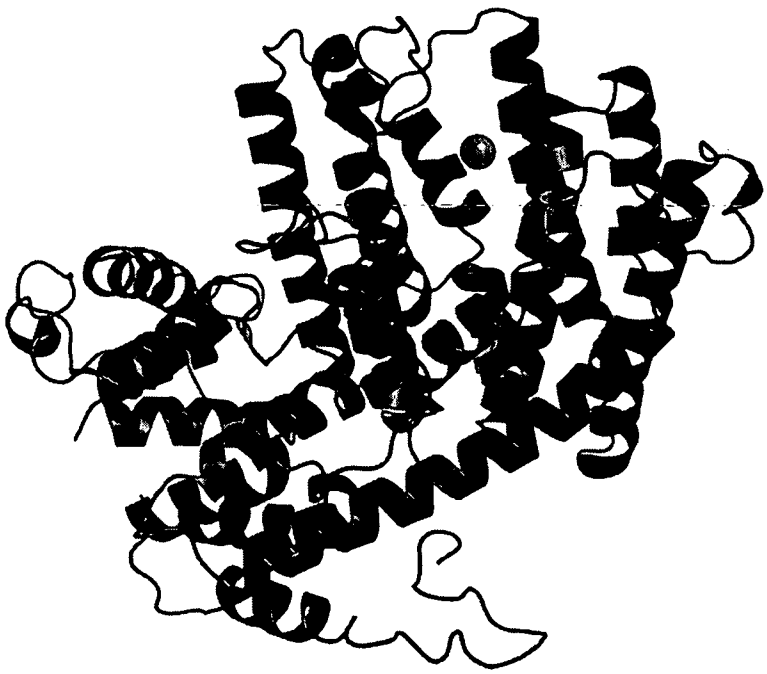


Figure 93

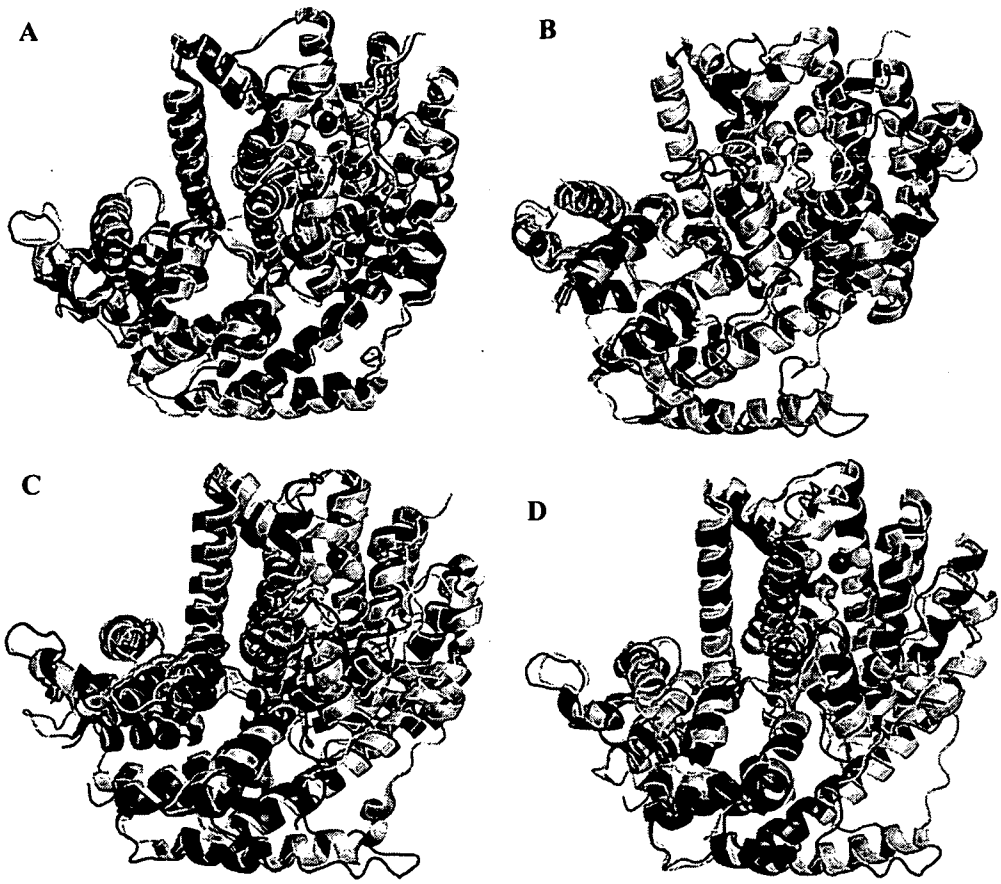


Figure 94

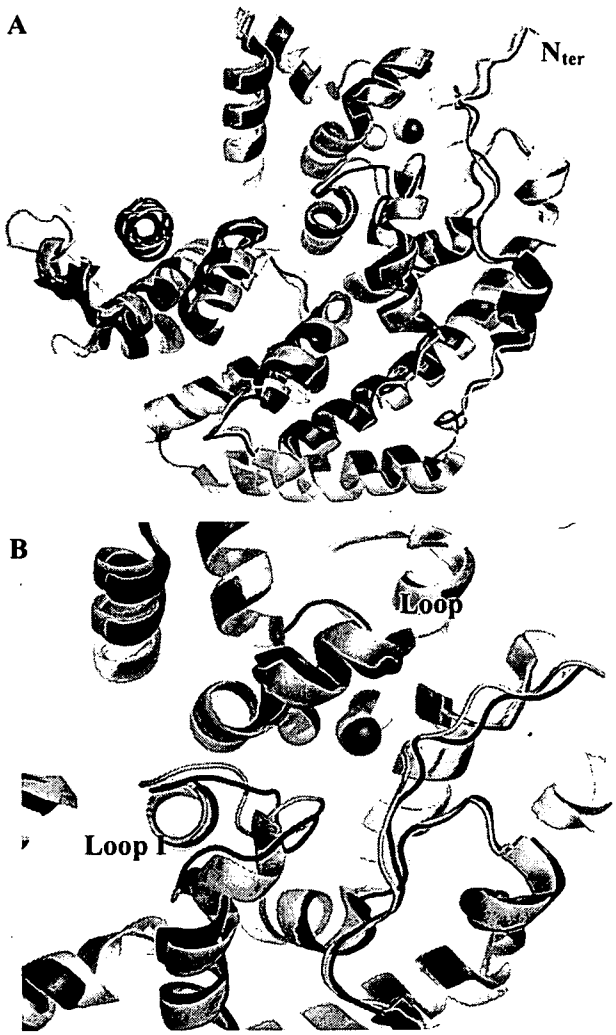


Figure 95

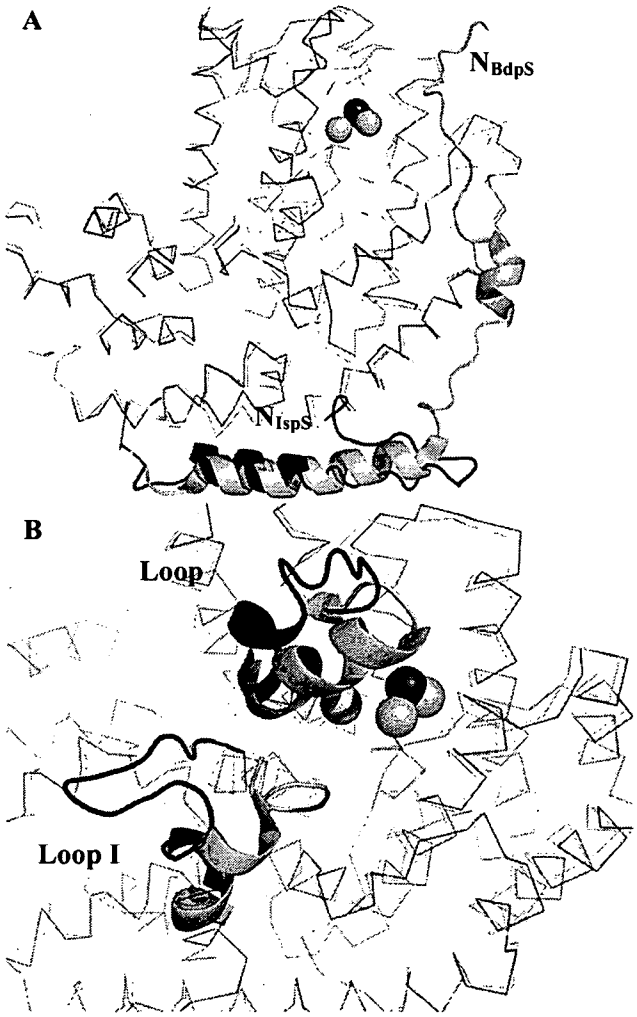


Figure 96

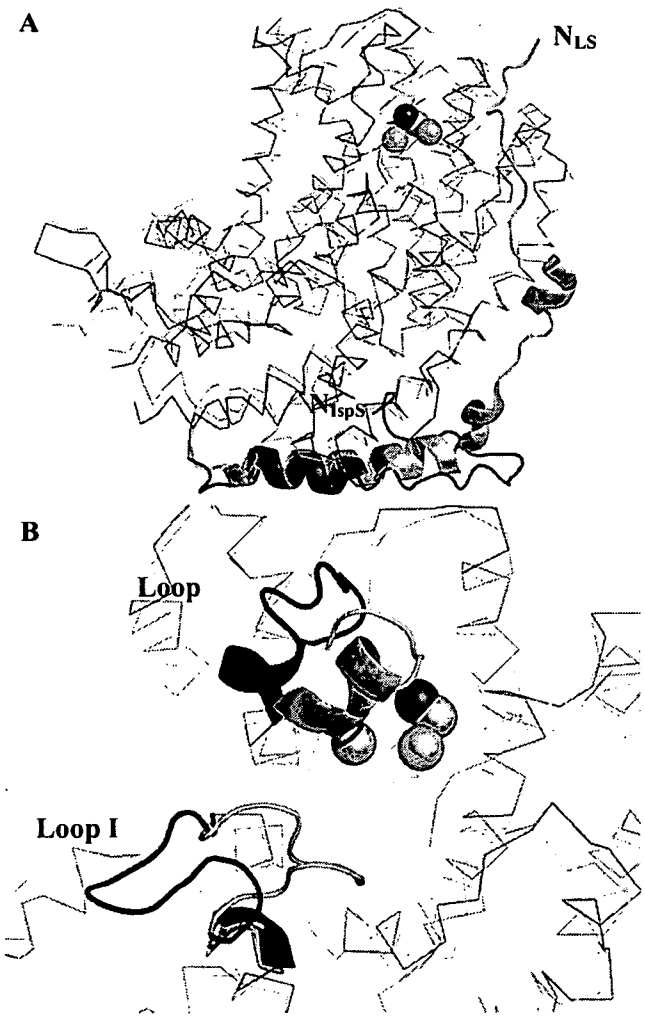


Figure 97

