



Office de la Propriété
Intellectuelle
du Canada

Un organisme
d'Industrie Canada

Canadian
Intellectual Property
Office

An agency of
Industry Canada

CA 2472846 A1 2005/01/01

(21) **2 472 846**

(12) **DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION**

(13) **A1**

(22) Date de dépôt/Filing Date: 2004/07/02

(41) Mise à la disp. pub./Open to Public Insp.: 2005/01/01

(30) Priorité/Priority: 2003/07/01 (10/611,446) US

(51) Cl.Int.⁷/Int.Cl.⁷ C12Q 1/68, A61K 31/47, A61P 35/00,
C12Q 1/02, G01N 33/574

(71) Demandeur/Applicant:
VERIDEX, LLC, US

(72) Inventeur/Inventor:
RAPONI, MITCH, US

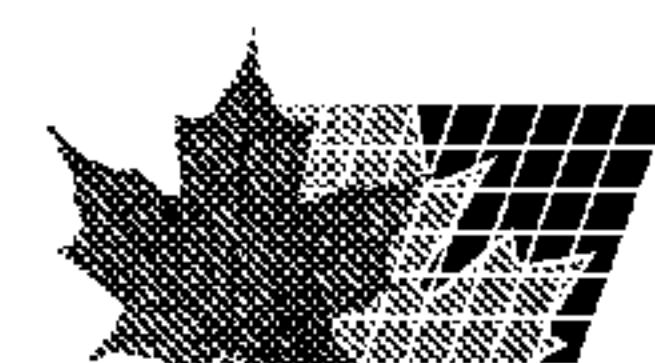
(74) Agent: OGILVY RENAULT

(54) Titre : METHODES D'EVALUATION ET DE TRAITEMENT DE LA LEUCEMIE

(54) Title: METHODS FOR ASSESSING AND TREATING LEUKEMIA

(57) **Abrégé/Abstract:**

Methods for treating cancer, and preferably hematological malignancy, patients include analyzing gene expression profiles and/or molecular markers of a patient to determine whether the patient is likely to respond to treatment with farnesyl transferase inhibitor (FTI) and, optionally, other therapeutics. The methods are also useful for monitoring patient therapy and for selecting a course of therapy. Genes modulated in response to FTI treatment are provided and are used in formulating the profiles.



Abstract of the Invention

METHODS FOR ASSESSING AND TREATING CANCER

5

Methods for treating cancer, and preferably hematological malignancy, patients include analyzing gene expression profiles and/or molecular markers of a patient to determine whether the patient is likely to respond to treatment with farnesyl transferase inhibitor (FTI) and, optionally, other therapeutics. The methods are also useful for
10 monitoring patient therapy and for selecting a course of therapy. Genes modulated in response to FTI treatment are provided and are used in formulating the profiles.

METHODS FOR ASSESSING AND TREATING CANCER

BACKGROUND

This invention relates to diagnostics, prognostics, and treatments for cancer
5 based on the detection of molecular markers and/or gene expression analysis.

Some molecules, such as Ras, that are implicated in cancers must be
farnesylated by the farnesyl transferase enzyme in order to interact with the inner leaflet
of the plasma membrane of the cell and become involved in various signaling pathways.
However, Ras is not the only protein implicated in cancer that has a CAAX box that is
10 prenylated. Farnesyl transferase inhibitors (FTIs) are therapeutic agents that inhibit the
covalent attachment of the carbon farnesyl moieties to the C-terminal CAAX motif of
various proteins. They have utility in the treatment of cancers and proliferative
disorders such as hematological malignancies. Hematological malignancies such as
leukemias, lymphomas, and myelomas (e.g, acute myeloid leukemia; AML) are among
15 the diseases that can most beneficially be addressed with FTIs. Solid tumors such as
breast cancer and glioblastomas may also be treated with FTIs.

As is true in the case of many treatment regimens, some patients respond to
treatment with FTIs and others do not. Prescribing the treatment to a patient who is
unlikely to respond to it is not desirable. Thus, it would be useful to know how a
20 patient could be expected to respond to such treatment before a drug is administered so
that non-responders would not be unnecessarily treated and so that those with the best
chance of benefiting from the drug are properly treated and monitored. Further, of
those who respond to treatment there may be varying degrees of response. Treatment
with therapeutics other than FTIs or treatment with therapeutics in addition to FTIs may
25 be beneficial for those patients who would not respond to FTIs or in whom response to
FTIs alone is less than desired.

SUMMARY OF THE INVENTION

The invention is a method of treating a cancer patient with an FTI. In one such method, the presence or absence of a molecular marker is determinative of whether the patient is likely to respond to the FTI. The patient is treated with an FTI if they are likely to respond. If the patient is not likely to respond to treatment with an FTI, then it may be withheld. In one aspect of the invention, gene expression profiles are obtained for a set of genes that are predictive of FTI response. In another aspect of the invention, the presence of a molecular marker and gene expression profiles are used in combination to determine likelihood of response to FTI treatment. In yet another aspect of the invention, expression profiles are used in combination with leukemic blast counts and/or leukemic cell antigen expression to determine likelihood of response to FTI treatment. In yet another aspect of the invention, the samples used in the assays are obtained from bone marrow.

In another aspect of the invention, a cancer patient is monitored for treatment with an FTI in which the patient's gene expression profile and/or the presence of a molecular marker is analyzed to determine whether the patient is responding to the FTI and treating a patient with the FTI if they are likely to respond in a desirable fashion.

In yet another aspect of the invention, a patient is treated if the gene expression profile shows modulation of one or more particular genes indicative of FTI responders.

In yet another aspect of the invention, a patient is treated if the gene expression profile shows modulation of one or more particular genes indicative of FTI responders and either a bone marrow blast cell count of 0 – 60%, or the presence of less than 60% of cells having positive expression of the CD33 cell surface antigen and/or the presence of less than 10% of cells having positive expression of the CD34 cell surface antigen.

In yet another aspect of the invention, the molecular marker is one or more of the following: the lbc oncogene, AHR, DKFZp667G2110, IDS, , GPR105, TEM6,

TNFSF13, SVIL, KIAA0680, FRAG1, DKFZp566B213, KIAA1036, BTG3, MAPK8IP3, ARHH, NPTX2. The marker can also be OPN3 and/or IL3RA in combination with one or more of the above.

5 In yet another aspect of the invention, the FTI is a quinilone or quinoline derivative.

In yet another aspect of the invention, the FTI is (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone).

10 Articles used in practicing the methods are also an aspect of the invention. Such articles include gene expression profiles or representations of them. The representations can be fixed in computer readable media. Other articles according to the invention include nucleic acid arrays used to determine the gene expression profiles of the invention and devices and components for practicing other nucleic acid detection technologies.

15 Kits are also an aspect of the invention. Such kits include reagents for detecting the expression of genes and/or the presence of a molecular marker that distinguish responders from non-responders to FTI treatment. The kits can include instructions.

In another aspect of the invention, a method of treating a cancer patient comprises administering an FTI and a therapeutic composition that modulates the 20 MAPK/ERK signaling pathways, TGF β , WNT, Rho, or apoptotic pathways.

In another aspect of the invention, the patient is treated with an FTI and a therapeutic composition selected from the group consisting of tyrosine kinase inhibitors, MEK kinase inhibitors, PI3K kinase inhibitors, MAP kinase inhibitors, apoptosis modulators and combinations thereof.

25 In yet another aspect of this invention, the gene expression profile and/or the presence or absence of a molecular marker of a patient is analyzed to determine whether the patient would likely benefit from the combination of an FTI and another drug. The

patient is then treated with such combination or, if the patient is unlikely to respond to an FTI, the patient is treated with another drug such as one selected from the group consisting of tyrosine kinase inhibitors, MEK kinase inhibitors, PI3K kinase inhibitors, MAP kinase inhibitors, apoptosis modulators and combinations thereof.

- 5 In yet another aspect of this invention, the gene expression profile and/or the presence of a molecular marker of a patient is analyzed to determine whether the patient would likely benefit from the combination of an FTI and another form of therapy. The patient is then treated with such combination or, if the patient is unlikely to respond to an FTI, the patient is treated with another therapy without the inclusion of an FTI.

10

BRIEF DESCRIPTION OF DRAWINGS

Fig 1 is a graphical presentation of a Kaplan-Meier analysis of patients with high and low CD33 antigen expression.

- 15 Fig 2 is a graphical presentation of a Kaplan-Meier analysis of patients with high and low blast counts.

Fig 3A is a graphical presentation of a Kaplan-Meier survival analysis of patients using clinical response classifiers.

20

Fig 3B is a graphical presentation of a Kaplan-Meier survival analysis of patients using oncoLBC gene expression to classify patients.

- 25 Fig 3C is a graphical presentation of a Kaplan-Meier survival analysis of patients using oncoLBC and AHR gene expressions to classify patients.

DETAILED DESCRIPTION

- 30 The therapeutic agents referred to in this specification are FTIs. They take on a multitude of forms but share the essential inhibitory function of interfering with or lessening the farnesylation of proteins implicated in cancer and proliferative diseases. Preferably, the FTIs are those indicated for the treatment of solid tumors such as glioblastoma and breast cancer. More preferably, the FTIs are indicated for the

treatment of hematological malignancies such as leukemias, lymphomas, and myelomas. Most preferably, the FTIs are contemplated for use in AML, myelodysplastic syndrome (MDS), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), and multiple myeloma (MM). In the case of

5 hematological malignancies, a patient who responds to an FTI is one in whom a reduction of more than 50% of blast cells is seen in bone marrow following treatment with the FTI. In solid tumors, a patient who responds to an FTI is one in whom their tumor ceases to grow. Response in patients with solid tumor can alternatively be measured according to RECIST (Response Evaluation Criteria in Solid Tumors) criteria

10 as such term is commonly used in oncology.

Numerous FTIs are within the scope of the invention and include those described in U.S. Patents: 5,976,851 to Brown et al.; 5,972,984 to Anthony et al.; 5,972,966 to deSolms; 5,968,965 to Dinsmore et al.; 5,968,952 to Venet et al.; 6,187,786 to Venet et al.; 6,169,096 to Venet et al.; 6,037,350 to Venet et al.;

15 6,177,432 to Angibaud et al.; 5,965,578 to Graham et al.; 5,965,539 to Sebti et al.; 5,958,939 to Afonso et al.; 5,939,557 to Anthony et al.; 5,936,097 to Commercon et al.; 5,891,889 to Anthony et al.; 5,889,053 to Baudin et al.; 5,880,140 to Anthony; 5,872,135 to deSolms; 5,869,682 to deSolms; 5,861,529 to Baudoin; 5,859,015 to Graham et al.; 5,856,439 to Clerc; 5,856,326 to Anthony et al.; 5,852,010 to Graham et

20 al.; 5,843,941 to Marsters et al.; 5,807,852 to Doll; 5,780,492 to Dinsmore et al.; 5,773,455 to Dong et al.; 5,767,274 to Kim et al.; 5,756,528 to Anthony et al.; 5,750,567 to Baudoin et al.; 5,721,236 to Bishop et al.; 5,700,806 to Doll et al.; 5,661,161 to Anthony et al.; 5,602,098 to Sebti et al.; 5,585,359 to Breslin et al.; 5,578,629 to Ciccarone et al.; 5,534,537 to Ciccarone et al.; 5,532,359 to Marsters et al.;

25 5,523,430 to Patel et al.; 5,504,212 to de Solms et al.; 5,491,164 to deSolms et al.; 5,420,245 to Brown et al.; and 5,238,922 to Graham et al. each of which is incorporated herein by reference. Non-peptidal, so-called "small molecule"

therapeutics are preferred. More preferred FTIs are quinolines or quinoline derivatives such as:

5 7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-2,3-dihydro-1H,5H-benzo[*ij*]quinolizin-5-one,

7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-1,2-dihydro-4H-pyrrolo[3,2,*i*]-quinoline-4-one,

10 8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-6-(3-chlorophenyl)-1,2-dihydro-4H-pyrrolo[3,2,*i*]quinolin-4-one, and

8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-6-(3-chlorophenyl)-2,3-dihydro-1H,5H-benzo[*ij*]quinolizin-5-one.

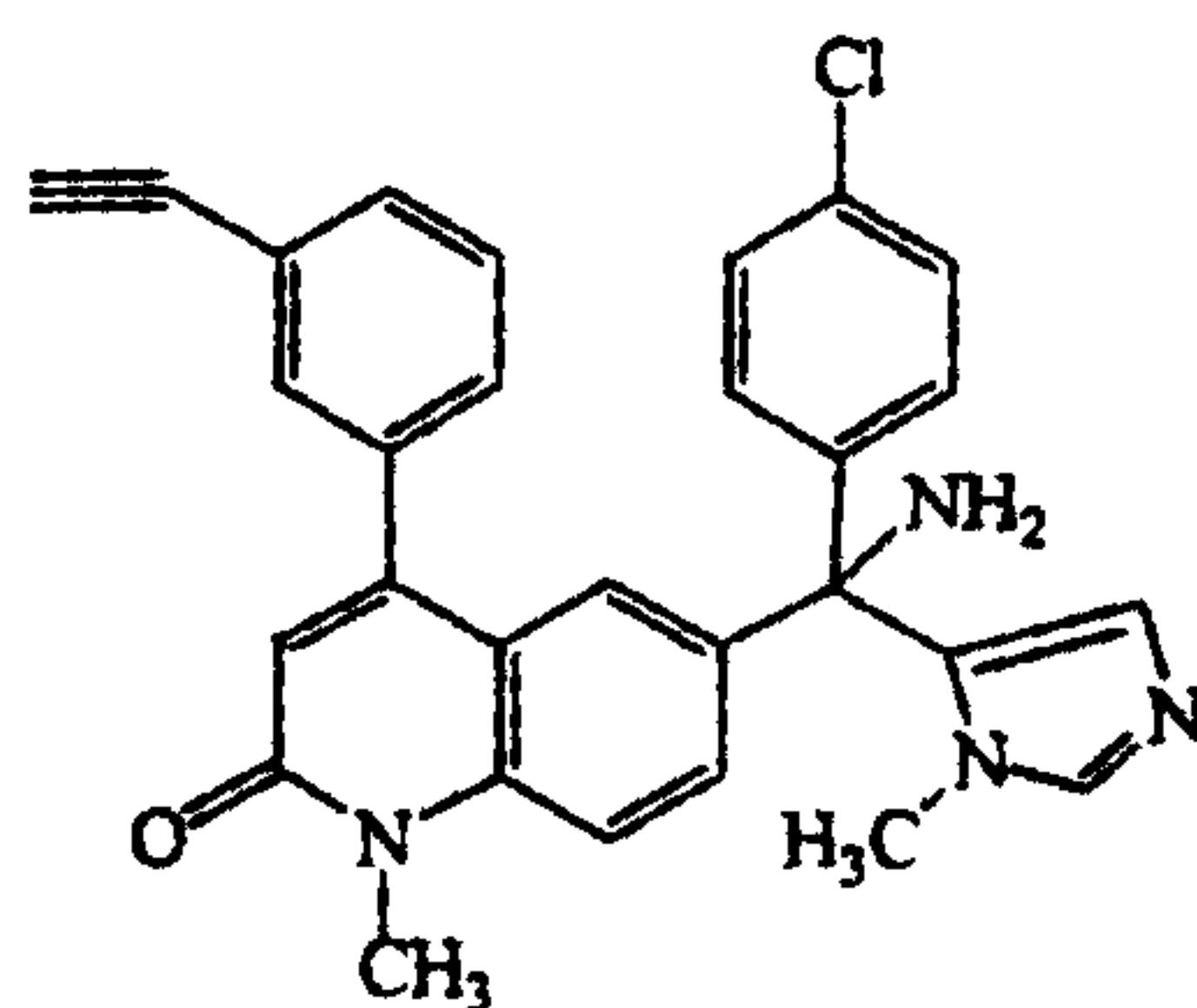
15

The most preferred FTI is (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone), described in U.S. Patent 6,420,387 to Venet et al as the (+) enantiomer.

20 Another preferred FTI is (-)-5-(3-chlorophenyl)- α -(4-chlorophenyl)- α -(1-methyl-1H-imidazol-5-yl)tetrazolo[1,5-*a*]quinazoline-7-methanamine and its pharmaceutically acceptable acid addition salts, described in WO 01/98302.

25 Other useful FTIs include Argabin (i.e. 1(R)-10-epoxy-5(S),7(S)-guaia-3(4),11(13)-dien-6,12-olide described in WO-98/28303; perrilyl alcohol described in WO-99/45912; SCH-66336, i.e. (+)-(R)-4-[2-[4-(3,10-dibromo-8-chloro-5,6-dihydro-1H-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-yl)piperidin-1-yl]-2-oxoethyl]piperidine-1-

carboxamide, described in U.S. Patent No. 5874442 ; L778123, i.e. 1-(3-chlorophenyl)-
 4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone, described in WO-00/01691;
 compound 2(S)-[2(S)-[2(R)-amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-
 phenylpropionyl-methionine sulfone described in WO-94/10138; and BMS 214662, i.e.
 5 (R)-2,3,4,5-tetrahydro-1-(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-
 thienylsulphonyl)-1H-1,4-benzodiazapine-7-carbonitrile, described in WO 97/30992;
 CP 609754, i.e. N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine,
 described in US Patent 5,747,498; and 6-[amino-(4-chloro-phenyl)-(3-methyl-3H-
 imidazol-4-yl)-methyl]-4-(3-ethynyl-phenyl)-1-methyl-1H-quinolin-2-one described in
 10 WO-00/12499:



The mere presence of nucleic acid sequences having the potential to express
 15 proteins or peptides ("genes") within the genome is not determinative of whether a
 protein or peptide is expressed in a given cell. Whether or not a given gene capable of
 expressing proteins or peptides or transcribing RNA does so and to what extent such
 expression or transcription occurs, if at all, is determined by a variety of complex
 factors. Nevertheless, assaying gene expression can provide useful information about
 20 the cellular response to a given stimulus such as the introduction of a drug or other
 therapeutic agent. Relative indications of the degree to which genes are active or
 inactive can be found in such gene expression profiles. In some instances, the presence
 of a molecular marker can, by itself or with the use of gene expression information,

provide useful information about treatment efficacy too. The gene expression profiles and molecular markers of this invention are used to identify and treat patients who will likely benefit from FTI therapy or exclude patients from FTI therapy where the patient likely would experience little or no beneficial response to the drug or therapy.

5 Cancers, including hematological malignancies, typically arise from mutations in a variety of genes. The same type of cancer may arise as a result of, or coincident with, one or more mutations that differ from those of another patient having the same type of cancer. The fact that there are often multiple molecular bases underlying the same cancers is consistent with the observation that some therapies that affect one
10 patient do not necessarily equally affect another patient with the same type of cancer. Further, from a diagnostic point of view, the presence of particular mutations such as translocations, deletions, or SNPs can have powerful implications. In some instances, such molecular markers are themselves useful indicators for diagnosis, prognosis, or treatment response determinations. This is particularly true where the molecular
15 mutations can be associated with response to particular treatments. In the instant invention, cancers coincident with the absence of the lbc oncogene (the lymphoid blast crisis oncogene) respond to FTI treatment. Therefore, the expression of this gene, the lack of expression of the gene and its presence or absence are useful in predicting resistance to FTI treatment prior to actually prescribing such treatment.

20 The lbc oncogene (Seq. ID No. 2) is a chimera derived from the fusion of an lbc proto-oncogene (Seq. ID No. 23-27) on chromosome 15q with an unrelated sequence originating in chromosome 7q. The truncation of the proto-oncogene at the C-terminus of the sequence results in the gene gaining transforming ability. This truncation could also arise from other mechanisms other than a translocation. For example, aberrant
25 splicing could result in RNA transcripts with C-terminus truncations. The gene has a number of expression products including mRNA and a protein (Seq. ID No. 29, Human LBC protein, Genbank Accession number GI: 29791897). While the precise manner in

which the lbc oncogene functions is not completely understood, it is clear that it can be present in a range of tissues including skeletal muscle, heart, lung, prostate, ovary, small intestine, and hematopoietic cells. Treatment of cancers originating in tissues where the oncogene could be manifested (but is not) is within the scope of this invention.

5 There is great flexibility available in formatting the assays of this invention because the gene is the product of a truncation and because it produces recognizable expression products. Not only can the absence of the gene or its products be used, but so too can detection of the modulated expression of this gene. Thus, a gene expression profile can include this gene. Preferably, the absence or modulation of the gene is used
10 as an indicator of FTI treatment response in hematological malignancies, more preferably in leukemias, and most preferably in AML

Where identification of the lbc oncogene as a molecular marker is undertaken, any suitable method of detection may be used. The presence of the molecular marker is indicative of a poor prognosis for treatment with an FTI and its absence is indicative of
15 an greater likelihood of response to such treatment. Methods useful for detecting the presence of the lbc oncogene include any method for detecting known mutant genes or sequences including, without limitation, the single strand conformation polymorphism technique, chemical and thermal denaturing gradient analysis, chemical and enzymatic cleavage methods, mass spectrometry, RFLP and allele specific amplification,
20 ratiometric PCR, bead-based and microarray-based systems as well as in situ hybridization, heteroduplex analysis, and microarray analysis, ELISA, western, FACS, antibody-based techniques, methylation-based PCR, and SNP detection.

The most preferred method for detecting the presence or absence of the lbc oncogene is via PCR. In this method, cells are first obtained from the patient according
25 to routine sample preparation methods. Where the malignancy is hematological, a simple peripheral blood sample or a bone marrow sample is preferable. RNA is then extracted according to well-accepted procedures and amplified as follows. Target

sequences are amplified using, e.g., 250 nM of primers and 250 nM of Taqman probe in ABI Taqman buffer. Thermal cycling is conducted at 50 °C for 2 minutes, 95 °C for 10 minutes, followed by 50 cycles of 95 °C for 15 minutes and 62 °C for 1 minute. Examples of the primers and probe are shown in Table 1.

- 5 This technique measures the amount of LBC transcript present in the sample. Measured quantities can be normalized by running similar RT-PCR experiments in which the same samples are used to amplify endogenous control genes such as HPRT.

Table 1

Name	Sequence (5'-3')
LBC forward	GGTCAGATGTTTGCCAAGGAA
LBC reverse	TCTTCAGAAACACACTCCCATCAC
LBC TaqMan probe	TGAAACGGAAGAAGCTTGTA

10

- Another method for determining the presence or absence of the lbc oncogene is to assay the length of the RNA transcript. Since the LBC oncogene has a 3' translocation the transcript length will be shorter than the LBC proto-oncogene transcript. This end point is favored as a diagnostic. To diagnose the transcript size a forward primer homologous to both the proto- and onco LBC transcripts is used (eg LBC forward primer from above Table 1) in conjunction with a reverse primer homologous to the universal poly A tail of RNA transcripts. Preferably initial cDNA synthesis will incorporate an additional unique sequence tag 3' of the polyA sequence to confer additional specificity for the PCR reaction.
- 15
- 20

If the genomic translocation is being measured then genomic DNA will be isolated using standard techniques and PCR primers used that are specific for the lbc oncogene. For example, the forward primer homologous for both the onco- and proto-LBC genes could be used in conjunction with the polyA sequence as described above.

Alternatively, the reverse primer could be homologous to the 3' translocated sequence. The readout would be the size of the amplicon where presence of the oncogene is consistent with a shorter product than the protooncogene, or presence or absence of an oncoLBC-specific amplicon.

5 Assays for the lbc oncogene status of the cell also can determine normal/abnormal tissue distribution for diagnostic purposes using techniques such as Immunohistochemical analysis (IHC). For example, the antibodies to lbc protein may be used in conjunction with both fresh-frozen and formalin-fixed, paraffin-embedded tissue blocks prepared for study by immunohistochemistry (IHC). Each tissue block
10 may consist of 50 mg of residual "pulverized" tumor.

Briefly, frozen-sections may be prepared by rehydrating 50 ng of frozen pulverized tumor at room temperature in PBS in small plastic capsules; pelleting the particles by centrifugation; resuspending them in a viscous embedding medium (OCT); inverting the capsule and pelleting again by centrifugation; snap-freezing in -70C.
15 isopentane; cutting the plastic capsule and removing the frozen cylinder of tissue; securing the tissue cylinder on a cryostat microtome chuck; and cutting 25-50 serial sections containing intact tumor cells.

Permanent-sections may be prepared by a similar method involving rehydration of the 50 mg sample in a plastic microfuge tube; pelleting; resuspending in
20 10% formalin for 4 hours fixation; washing/pelleting; resuspending in warm 2.5% agar; pelleting; cooling in ice water to harden the agar; removing the tissue/agar block from the tube; infiltrating and embedding the block in paraffin; and cutting up to 50 serial permanent sections.

For the immunohistochemical assay, the sections are overlaid with a blocking
25 solution containing: 3% bovine serum albumin (BSA) in PBS or other blocking reagents. The blocking reagents include non-specific serum or dry milk. The blocking treatment is allowed to proceed for 1 hr. at room temperature. Anti-lbc protein antibody

is diluted with PBS buffer containing 3% BSA, 0.1% TRITON X.TM.-100, t-octylphenoxypolyethoxyethanol, at a ratio of 1:100. The sample sections are generally overlaid with the antibody solution for 16 hrs. at 4C. The duration and temperature conditions may be varied according to the antibody selected and the material tested. The
5 optimal conditions should be determined empirically. The antibody treated sections are then washed three times in PBS for 15 min. each to remove unbound antibody and then overlaid with PBS containing 3% BSA and a secondary antibody at a dilution of 1:2000. The secondary antibodies may be coupled to a chromogenic enzyme such as: horseradish peroxidase, alkaline phosphatase, fluorescein iso-thiocyanate, or other
10 suitable enzymes. Alternatively, the secondary antibody may be conjugated to biotin and used in conjunction with chromophore-labeled avidin.

Another exemplary method for detecting the presence of the lbc oncogene is via in situ hybridization. Generally, in situ hybridization comprises the following major steps: (1) fixation of tissue or biological structure to be analyzed; (2) prehybridization
15 treatment of the biological structure to increase accessibility of target DNA, and to reduce nonspecific binding; (3) hybridization of the mixture of nucleic acids to the nucleic acid in the biological structure or tissue; (4) post-hybridization washes to remove nucleic acid fragments not bound in the hybridization and (5) detection of the hybridized nucleic acid fragments. The reagent used in each of these steps and the
20 conditions for use vary depending on the particular application.

In this case, a hybridization solution comprising at least one detectable nucleic acid probe capable of hybridizing to the lbc oncogene (at its chromosomal locus) is contacted with the cell under hybridization conditions. Any hybridization is then detected and compared to a predetermined hybridization pattern from normal or control
25 cells. Preferably, the probes are alpha-centromeric probes. Such probes can be made commercially available from a number of sources (e.g., from Visys Inc., Downers Grove, IL). In a preferred embodiment, the hybridization solution contains a

multiplicity of probes, specific for an area on the chromosome that corresponds to the translocation of the sequences that make up the chimera (e.g., 15q24-25).

Hybridization protocols suitable for use with the methods of the invention are described, e.g., in Albertson (1984) EMBO J. 3: 1227-1234; Pinkel (1988) Proc. Natl. Acad. Sci. USA 85: 9138-9142; EPO Pub. No. 430,402; Methods in Molecular Biology, Vol. 33: In Situ Hybridization Protocols, Choo, ed., Humana Press, Totowa, N.J. (1994), etc. In one particularly preferred embodiment, the hybridization protocol of Pinkel et al. (1998) Nature Genetics 20:207-211 or of Kallioniemi (1992) Proc. Natl Acad Sci USA 89:5321-5325 (1992) is used. Methods of optimizing hybridization conditions are well known (see, e.g., Tijssen (1993) Laboratory Techniques in Biochemistry and Molecular Biology, Vol. 24: Hybridization With Nucleic Acid Probes, Elsevier, N.Y.).

In a preferred embodiment, background signal is reduced by the use of a detergent (e.g., C-TAB) or a blocking reagent (e.g., sperm DNA, cot-1 DNA, etc.) during the hybridization to reduce non-specific binding. In a particularly preferred embodiment, the hybridization is performed in the presence of about 0.1 to about 0.5 mg/ml DNA (e.g., cot-1 DNA).

The probes may be prepared by any method known in the art, including synthetically or grown in a biological host. Synthetic methods include oligonucleotide synthesis, riboprobes, and PCR.

The probe may be labeled with a detectable marker by any method known in the art. Methods for labeling probes include random priming, end labeling, PCR and nick translation. Enzymatic labeling is conducted in the presence of nucleic acid polymerase, three unlabeled nucleotides, and a fourth nucleotide which is either directly labeled, contains a linker arm for attaching a label, or is attached to a hapten or other molecule to which a labeled binding molecule may bind. Suitable direct labels include radioactive labels such as ^{32}P , ^3H , and ^{35}S and non-radioactive labels such as fluorescent markers,

such as fluorescein, Texas Red, AMCA blue, lucifer yellow, rhodamine, and the like; cyanin dyes which are detectable with visible light; enzymes and the like. Labels may also be incorporated chemically into DNA probes by bisulfite-mediated transamination or directly during oligonucleotide synthesis.

5 Fluorescent markers can readily be attached to nucleotides with activated linker arms which have been incorporated into the probe. Probes may be indirectly labeled by the methods disclosed above, by incorporating a nucleotide covalently linked to a hapten or other molecule such as biotin or digoxigenin, and performing a sandwich hybridization with a labeled antibody directed to that hapten or other molecule, or in the
10 case of biotin, with avidin conjugated to a detectable label. Antibodies and avidin may be conjugated with a fluorescent marker, or with an enzymatic marker such as alkaline phosphatase or horseradish peroxidase to render them detectable. Conjugated avidin and antibodies are commercially available from companies such as Vector Laboratories (Burlingame, Calif.) and Boehringer Mannheim (Indianapolis, Ind.).

15 The enzyme can be detected through a colorimetric reaction by providing a substrate for the enzyme. In the presence of various substrates, different colors are produced by the reaction, and these colors can be visualized to separately detect multiple probes. Any substrate known in the art may be used. Preferred substrates for alkaline phosphatase include 5-bromo-4-chloro-3-indolylphosphate (BCIP) and nitro
20 blue tetrazolium (NBT). The preferred substrate for horseradish peroxidase is diaminobenzoate (DAB).

Fluorescently labelled probes suitable for use in the in situ hybridization methods of the invention are preferably in the range of 150-500 nucleotides long. Probes may be DNA or RNA, preferably DNA.

25 Hybridization of the detectable probes to the cells is conducted with a probe concentration of 0.1-500 ng/. μ l, preferably 5-250 ng/. μ l. The hybridization mixture will preferably contain a denaturing agent such as formamide. In general, hybridization

is carried out at 25C.-45C., more preferably at 32C.-40 C., and most preferably at 37C.-38C. The time required for hybridization is about 0.25-96 hours, more preferably 1-72 hours, and most preferably for 4-24 hours. Hybridization time will be varied based on probe concentration and hybridization solution content which may contain accelerators
5 such as hnRNP binding protein, trialkyl ammonium salts, lactams, and the like. Slides are then washed with solutions containing a denaturing agent, such as formamide, and decreasing concentrations of sodium chloride or in any solution that removes unbound and mismatched probe.

The temperature and concentration of salt will vary depending on the stringency
10 of hybridization desired. For example, high stringency washes may be carried out at 42C.-68C., while intermediate stringency may be in the range of 37C.-55C., and low stringency may be in the range of 30C.-37C. Salt concentration for a high stringency wash may be 0.5-1 times SSC (0.15M NaCl, 0.015M Na citrate), while medium stringency may be 1.-4times., and low stringency may be 2-6 times SSC.

The detection incubation steps, if required, should preferably be carried out in a
15 moist chamber at 23C.-42C., more preferably at 25C.-38C. and most preferably at 37-38C. Labeled reagents should preferably be diluted in a solution containing a blocking reagent, such as bovine serum albumin, non-fat dry milk, or the like. Dilutions may range from 1:10-1:10,000, more preferably 1:50-1:5,000, and most preferably at 1:100-
20 1:1,000. The slides or other solid support should be washed between each incubation step to remove excess reagent.

Slides may then be mounted and analyzed by microscopy in the case of a visible detectable marker, or by exposure to autoradiographic film in the case of a radioactive marker. In the case of a fluorescent marker, slides are preferably mounted in a solution
25 that contains an antifade reagent, and analyzed using a fluorescence microscope. Multiple nuclei may be examined for increased accuracy of detection.

Additionally, assays for the expression product of the lbc oncogene can also be used to determine whether the lbc oncogene mutation has occurred. Most preferably, such assays are immunoassays. Immunoassays, in their most simple and direct sense, are binding assays. Certain preferred immunoassays are the various types of enzyme
5 linked immunosorbent assays (ELISAs) and radioimmunoassays (RIA) known in the art. Immunohistochemical detection using tissue sections is also particularly useful.

In one exemplary ELISA, anti-oncolbc protein -specific antibodies are immobilized onto a selected surface exhibiting protein affinity, such as a well in a polystyrene microtiter plate. Then, a test composition containing the desired antigen,
10 such as a clinical sample, is added to the wells. After binding and washing to remove non-specifically bound immune complexes, the bound antigen may be detected. Detection is generally achieved by the addition of another antibody, specific for the desired antigen, that is linked to a detectable label. This type of ELISA is a simple "sandwich ELISA". Detection may also be achieved by the addition of a second
15 antibody specific for the desired antigen, followed by the addition of a third antibody that has binding affinity for the second antibody, with the third antibody being linked to a detectable label.

Variations of ELISA techniques are well known. In one such variation, the samples containing the desired antigen are immobilized onto the well surface and then
20 contacted with the antibodies of the invention. After binding and appropriate washing, the bound immune complexes are detected. Where the initial antigen specific antibodies are linked to a detectable label, the immune complexes may be detected directly. Again, the immune complexes may be detected using a second antibody that has binding affinity for the first antigen specific antibody, with the second antibody being linked to
25 a detectable label.

Competitive ELISAs are also possible in which test samples compete for binding with known amounts of labeled antigens or antibodies. The amount of reactive

species in the unknown sample is determined by mixing the sample with the known labeled species before or during incubation with coated wells. The presence of reactive species in the sample acts to reduce the amount of labeled species available for binding to the well and thus reduces the ultimate signal.

5 Antigen or antibodies may also be linked to a solid support, such as in the form of plate, beads, dipstick, membrane or column matrix, and the sample to be analyzed applied to the immobilized antigen or antibody. In coating a plate with either antigen or antibody, one will generally incubate the wells of the plate with a solution of the antigen or antibody, either overnight or for a specified period. The wells of the plate
10 will then be washed to remove incompletely adsorbed material. Any remaining available surfaces of the wells are then "coated" with a nonspecific protein that is antigenically neutral with regard to the test antisera. These include bovine serum albumin (BSA), casein and solutions of milk powder. The coating allows for blocking of nonspecific adsorption sites on the immobilizing surface and thus reduces the
15 background caused by nonspecific binding of antisera onto the surface.

 In ELISAs, it is customary to use a secondary or tertiary detection means rather than a direct procedure. Thus, after binding of the antigen or antibody to the well, coating with a non-reactive material to reduce background, and washing to remove unbound material, the immobilizing surface is contacted with the clinical or biological
20 sample to be tested under conditions effective to allow immune complex (antigen/antibody). This can include diluting the antigens and antibodies with solutions such as BSA, bovine gamma globulin (BGG) and phosphate buffered saline (PBS)/Tween. These added agents also tend to assist in the reduction of nonspecific background. Detection of the immune complex then requires a labeled secondary
25 binding ligand or antibody, or a secondary binding ligand or antibody in conjunction with a labeled tertiary antibody or third binding ligand.

Following all incubation steps in an ELISA, the contacted surface is washed so as to remove non-complexed material. Washing often includes washing with a solution of PBS/Tween, or borate buffer. Following the formation of specific immune complexes between the test sample and the originally bound material, and subsequent
5 washing, the occurrence of even minute amounts of immune complexes may be determined.

To provide a detecting means, the second or third antibody will have an associated label to allow detection. Preferably, this will be an enzyme that will generate color development upon incubating with an appropriate chromogenic substrate. Thus,
10 for example, one will desire to contact and incubate the first or second immune complex with a urease, glucose oxidase, alkaline phosphatase or hydrogen peroxidase-conjugated antibody for a period of time and under conditions that favor the development of further immune complex formation, e.g., incubation for 2 hours at room temperature in a PBS-containing solution such as PBS-Tween.

15 After incubation with the labeled antibody, and subsequent to washing to remove unbound material, the amount of label is quantified, e.g., by incubation with a chromogenic substrate such as urea and bromocresol purple and H_2O_2 , in the case of peroxidase as the enzyme label. Quantification is then achieved by measuring the degree of color generation, e.g., using a visible spectra spectrophotometer.

20 Alternatively, the label may be a chemiluminescent one. The use of such labels is described in U.S. Pat. Nos. 5,310,687, 5,238,808 and 5,221,605.

In embodiments of the invention in which gene expression is detected for determining response to FTIs, the use of gene expression portfolios is most preferred. A portfolio of genes is a set of genes grouped so that expression information obtained
25 about them provides the basis for making a clinically relevant judgment such as a diagnosis, prognosis, or treatment choice. In this case, gene expression portfolios can

be fashioned to help make therapeutic decisions regarding the use of FTIs in cancer patients.

It is most preferred to detect the expression of the lbc oncogene as part of a gene expression profile with one or more other genes whose differential expression is indicative of likelihood of response to FTI treatment. In this aspect of the invention, the gene expression profiles are made up the lbc oncogene (also referred to as AKAP13). One or more of the following genes can also be used, most preferably, in combination with the lbc oncogene: AHR, DKFZp667G2110, IDS, OPN3, GPR105, TEM6, TNFSF13, SVIL, IL3RA, KIAA0680, FRAG1, DKFZp566B213, KIAA1036, BTG3, MAPK8IP3, ARHH, NPTX2 (Seq ID No. 1, 3-18). OPN3 and IL3RA are used in combination with one or more other genes and preferably, the profile includes two or more of any of the genes. The most preferred gene expression profile detects the differential expression of lbc oncogene and AHR. Variants, such as splice variants, of the aforementioned genes are also useful in this application.

Preferred methods for establishing gene expression profiles (including those used to arrive at the explication of the relevant biological pathways) include determining the amount of RNA that is produced by a gene that can code for a protein or peptide or transcribe RNA. This is best accomplished by reverse transcription PCR (RT-PCR), competitive RT-PCR, real time RT-PCR, differential display RT-PCR, Northern Blot analysis and other related tests. While it is possible to conduct these techniques using individual PCR reactions, it is often desirable to amplify copy DNA (cDNA) or copy RNA (cRNA) produced from mRNA and analyze it via microarray. A number of different array configurations and methods for their production are known to those of skill in the art and are described in U.S. Patents such as: 5,445,934; 5,532,128; 5,556,752; 5,242,974; 5,384,261; 5,405,783; 5,412,087; 5,424,186; 5,429,807; 5,436,327; 5,472,672; 5,527,681; 5,529,756; 5,545,531; 5,554,501; 5,561,071;

5,571,639; 5,593,839; 5,599,695; 5,624,711; 5,658,734; and 5,700,637; the disclosures of which are herein incorporated by reference.

Microarray technology allows for the measurement of the steady-state mRNA level of thousands of genes simultaneously thereby presenting a powerful tool for
5 identifying the effect of FTIs on cell biology and the likely effect of treatment based on analysis of such effects. Two microarray technologies are currently in wide use. The first are cDNA arrays and the second are oligonucleotide arrays. Although differences exist in the construction of these chips, essentially all downstream data analysis and output are the same. The product of these analyses are typically measurements of the
10 intensity of the signal received from a labeled probe used to detect a cDNA sequence from the sample that hybridizes to a nucleic acid sequence at a known location on the microarray. Typically, the intensity of the signal is proportional to the quantity of cDNA, and thus mRNA, expressed in the sample cells. A large number of such techniques are available and useful. Preferred methods for determining gene expression
15 can be found in US Patents 6,271,002 to Linsley, et al.; 6,218,122 to Friend, et al.; 6,218,114 to Peck, et al.; and 6,004,755 to Wang, et al., the disclosure of each of which is incorporated herein by reference.

Analysis of the expression levels is conducted by comparing such intensities. This is best done by generating a ratio matrix of the expression intensities of genes in a
20 test sample versus those in a control sample. For instance, the gene expression intensities from a tissue that has been treated with a drug can be compared with the expression intensities generated from the same tissue that has not been treated with the drug. A ratio of these expression intensities indicates the fold-change in gene expression between the test and control samples.

25 Gene expression profiles can also be displayed in a number of ways. A common method is to arrange a ratio matrix into a graphical dendogram where columns indicate test samples and rows indicate genes. The data is arranged so genes that have similar

expression profiles are proximal to each other. The expression ratio for each gene is visualized as a color. For example, a ratio less than one (indicating down-regulation) may appear in the blue portion of the spectrum while a ratio greater than one (indicating up-regulation) may appear as a color in the red portion of the spectrum. Commercially
5 available computer software programs are available to display such data including "GENESPRINT" from Silicon Genetics, Inc. and "DISCOVERY" and "INFER" software from Partek, Inc.

The genes that are differentially expressed are either up regulated or down regulated in diseased cells following treatment with an FTL, or in responders versus
10 non-responders prior to treatment, as deduced by an assessment of gene expression as described above. Up regulation and down regulation are relative terms meaning that a detectable difference (beyond the contribution of noise in the system used to measure it) is found in the amount of expression of the genes relative to some baseline. In this case, the baseline is the measured gene expression of the untreated diseased cell. The genes
15 of interest in the treated diseased cells are then either up regulated or down regulated relative to the baseline level using the same measurement method. Preferably, levels of up and down regulation are distinguished based on fold changes of the intensity measurements of hybridized microarray probes. A 1.5 fold difference is preferred for making such distinctions. That is, before a gene is said to be differentially expressed in
20 treated versus untreated diseased cells, the treated cell is found to yield at least 1.5 times more, or 1.5 times less intensity than the untreated cells. A 1.7 fold difference is more preferred and a 2 or more fold difference in gene expression measurement is most preferred.

One method of the invention involves comparing gene expression profiles for
25 various genes to determine whether a person is likely to respond to the use of a therapeutic agent. Having established the gene expression profiles that distinguish responder from nonresponder, the gene expression profiles of each are fixed in a

medium such as a computer readable medium as described below. A patient sample is obtained that contains diseased cells (such as hematopoietic blast cells in the case of AML) is then obtained. Most preferably, the samples are of bone marrow and are extracted from the patient's sternum or iliac crest according to routine methods before the patient has been treated with drug. Preferably the bone marrow aspirate is processed to enrich for leukemic blast cells using routine methods. Sample RNA is then obtained and amplified from the diseased patient cell and a gene expression profile is obtained, preferably (in the case of a large gene portfolio) via micro-array, for genes in the appropriate portfolios. The expression profiles of the samples are then compared to those previously determined as responder and non-responder. If the sample expression patterns are consistent with an FTI responder expression pattern then treatment with an FTI could be indicated (in the absence of countervailing medical considerations). If the sample expression patterns are consistent with an FTI non-responder expression pattern then treatment with an FTI would not be indicated. When a small number of genes are used in the portfolio such as when the single gene, lymphoid blast crisis oncogene (oncoLBC, Seq. ID No. 2), is used, a simple nucleic acid amplification and detection scheme are most preferred methods of measuring the modulation of the gene. In such a case, PCR, NASBA, rolling circle, LCR, and other amplification schemes known to skilled artisans can be used with PCR being most preferred. Where the portfolios include a large number of genes or it is desirable to measure the expression of numerous other genes then it is preferred to assess the expression patterns based on intensity measurements of micro-arrays as described above.

In similar fashion, gene expression profile analysis can be conducted to monitor treatment response. In one aspect of this method, gene expression analysis as described above is conducted on a patient treated with an FTI at various periods throughout the course of treatment. If the gene expression patterns are consistent with a responder then the patient's therapy is continued. If it is not, then the patient's therapy is altered as

with additional therapeutics such as tyrosine kinase inhibitor, changes to the dosage, or elimination of FTI treatment. Such analysis permits intervention and therapy adjustment prior to detectable clinical indicia or in the face of otherwise ambiguous clinical indicia.

5 With respect to the molecular markers of the invention, a number of other formats and approaches are available for diagnostic use. Methylation of genomic regions can affect gene expression levels. For example, hypermethylation of gene promoter regions can constitutively down-regulate gene expression whereas hypomethylation can lead to an increase in steady-state mRNA levels. As such,
10 detection of methylated regions associated to genes predictive of drug response can be used as an alternative method for diagnosing gene expression levels. Such methods are known to those skilled in the art. Alternatively, single nucleotide polymorphisms (SNPs) that are present in promoter regions can also affect transcriptional activity of a gene. Therefore, detection of these SNPs by methods known to those skilled in the art
15 can also be used as a diagnostic for detecting genes that are differentially expressed between responders and non-responders.

 The distinction between responder and non-responder can also be advantageously made with the additional assay of the proportion of bone marrow leukemic blasts present prior to treatment and/or the presence of cell surface antigens
20 such as CD33 and/or CD34. Low expression of CD33 and CD34 surface antigens indicates an increased likelihood of response to FTI treatment. This is most conveniently measured as the percent of cells in a sample that express such antigens with responders having about 60% or less of such cells expressing CD33 and about 15% or less expressing CD34. A percentage of such cells exceeding 60% expressing CD33
25 or 15% CD34 antigens indicates that the patient is likely a non-responder to FTI treatment. Further, a sample taken as described above in which the percentage of cells that are blast cells is less than about 60% is likely to respond to FTI treatment while

those with blast cell counts that exceed this percentage is not. Determinations of percent of CD33+, CD34+, and blast cell count are conducted according to any of the well known methods and are most efficiently conducted using standard pathological tests and preparations conducted in most clinical laboratories.

5 Articles of this invention are representations of the gene expression profiles useful for treating, diagnosing, prognosticating, staging, and otherwise assessing diseases. Preferably they are reduced to a medium that can be automatically read such as computer readable media (magnetic, optical, and the like). The articles can also include instructions for assessing the gene expression profiles in such media. For
10 example, the articles may comprise a CD ROM having computer instructions for comparing gene expression profiles of the portfolios of genes described above. The articles may also have gene expression profiles digitally recorded therein so that they may be compared with gene expression data from patient samples. Alternatively, the profiles can be recorded in different representational format. Clustering algorithms
15 such as those incorporated in "DISCOVERY" and "INFER" software from Partek, Inc. mentioned above can best assist in the visualization of such data.

 Additional articles according to the invention are kits for conducting the assays described above. Each such kit would preferably include instructions in human or machine readable form as well as the reagents typical for the type of assay described.
20 These can include, for example, nucleic acid arrays (e.g. cDNA or oligonucleotide arrays), as described above, configured to discern the gene expression profiles of the invention. They can also contain reagents used to conduct nucleic acid amplification and detection including, for example, reverse transcriptase, reverse transcriptase primer, a corresponding PCR primer set, a thermostable DNA polymerase, such as Taq
25 polymerase, and a suitable detection reagent(s), such as, without limitation, a scorpion probe, a probe for a fluorescent 5'nuclease assay, a molecular beacon probe, a single dye primer or a fluorescent dye specific to double-stranded DNA, such as ethidium

bromide. Kits for detecting surface antigens contain staining materials or are antibody based cased including components such as buffer, anti-antigenic antibody, detection enzyme and substrate such as Horse Radish Peroxidase or biotin-avidin based reagents. Kit components for detecting blast cells generally include reagents for conducting flow
5 cytometry, blast cell adhesion assays, and other commonly practiced blast cell assays.

As described in the pending application of the inventor entitled, METHODS FOR ASSESSING AND TREATING LEUKEMIA, and filed October 30, 2002 (Serial Number 10/283975), in addition to the FTIs that are preferred, the preferred drugs of this invention are those that modulate the MAPK/ERK signaling pathways, TGF β ,
10 WNT or apoptotic pathways. These include, without limitation, tyrosine kinase inhibitors, MEK kinase inhibitors, P13K kinase inhibitors, MAP kinase inhibitors, apoptosis modulators and combinations thereof. Exemplary drugs that are most preferred among these are the "GLEEVEC" tyrosine kinase inhibitor of Novartis, U-0126 MAP kinase inhibitor, PD-098059 MAP kinase inhibitor, SB-203580 MAP kinase
15 inhibitor, and antisense, ribozyme, and DNAzyme, Bcl-XL, and anti-apoptotics. Examples of other useful drugs include, without limitation, the calanolides of US Patent 6,306,897; the substituted bicyclics of US Patent 6,284,764; the indolines of US Patent 6,133,305; and the antisense oligonucleotides of US Patent 6,271,210.

The FTI may also be used in combination with other conventional anti-cancer
20 agents for example selected from platinum coordination compounds for example cisplatin or carboplatin, taxane compounds for example paclitaxel or docetaxel, camptothecin compounds for example irinotecan or topotecan, anti-tumor vinca alkaloids for example vinblastine, vincristine or vinorelbine, anti-tumor nucleoside derivatives for example 5-fluorouracil, gemcitabine or capecitabine, nitrogen mustard or
25 nitrosourea alkylating agents for example cyclophosphamide, chlorambucil, carmustine or lomustine, anti-tumor anthracycline derivatives for example daunorubicin, doxorubicin or idarubicin; HER2 antibodies for example trastuzumab; and anti-tumor

podophyllotoxin derivatives for example etoposide or teniposide; and antiestrogen agents including estrogen receptor antagonists or selective estrogen receptor modulators preferably tamoxifen, or alternatively toremifene, droloxifene, faslodex and raloxifene, or aromatase inhibitors such as exemestane, anastrozole, letrozole and vorozole.

5 The FTI can administered to a patient as described above in conjunction with irradiation; such treatment is may be especially beneficial as farnesyl transferase inhibitors can act as radiosensitisers for example as described in International Patent Specification WO 00/01411, enhancing the therapeutic effect of such irradiation. Irradiation means ionizing radiation and in particular gamma radiation, especially that
10 emitted by linear accelerators or by radionuclides that are in common use today. The irradiation of the tumor by radionuclides can be external or internal.

 Preferably, the administration of the farnesyl transferase inhibitor commences up to one month, in particular up to 10 days or a week, before the irradiation of the tumor. Additionally, it is advantageous to fractionate the irradiation of the tumor and maintain
15 the administration of the farnesyl transferase inhibitor in the interval between the first and the last irradiation session. The amount of farnesyl protein transferase inhibitor, the dose of irradiation and the intermittence of the irradiation doses will depend on a series of parameters such as the type of tumor, its location, the patients' reaction to chemo- or radiotherapy and ultimately is for the physician and radiologists to determine in each
20 individual case. Thus, cancer therapy according to the inventive method also includes, for a host harboring a tumor, administering a radiation-sensitizing effective amount of a farnesyl protein transferase inhibitor according to the invention before, during or after administering radiation to said host in the proximity to the tumor.

 As noted, the drugs of the instant invention can be therapeutics directed to gene
25 therapy or antisense therapy or RNA interference. Oligonucleotides with sequences complementary to a mRNA sequence can be introduced into cells to block the translation of the mRNA, thus blocking the function of the gene encoding the mRNA.

The use of oligonucleotides to block gene expression is described, for example, in, Strachan and Read, Human Molecular Genetics, 1996, incorporated herein by reference.

These antisense molecules may be DNA, stable derivatives of DNA such as phosphorothioates or methylphosphonates, RNA, stable derivatives of RNA such as 2'-
 5 O-alkylRNA, or other antisense oligonucleotide mimetics. Antisense molecules may be introduced into cells by microinjection, liposome encapsulation or by expression from vectors harboring the antisense sequence.

In the case of gene therapy, the gene of interest can be ligated into viral vectors that mediate transfer of the therapeutic DNA by infection of recipient host
 10 cells. Suitable viral vectors include retrovirus, adenovirus, adeno-associated virus, herpes virus, vaccinia virus, polio virus and the like. Alternatively, therapeutic DNA can be transferred into cells for gene therapy by non-viral techniques including receptor-mediated targeted DNA transfer using ligand-DNA conjugates or adenovirus-ligand-DNA conjugates, lipofection membrane fusion or direct
 15 microinjection. These procedures and variations thereof are suitable for *ex vivo* as well as *in vivo* gene therapy. Protocols for molecular methodology of gene therapy suitable for use with the gene is described in Gene Therapy Protocols, edited by Paul D. Robbins, Human press, Totawa NJ, 1996.

The FTI may be used to treat various types of cancer including lung cancer (e.g.
 20 adenocarcinoma and including non-small cell lung cancer), pancreatic cancers (e.g. pancreatic carcinoma such as, for example exocrine pancreatic carcinoma), colon cancers (e.g. colorectal carcinomas, such as, for example, colon adenocarcinoma and colon adenoma), prostate cancer including the advanced disease, hematopoietic tumors of lymphoid lineage (e.g. acute lymphocytic leukemia, B-cell lymphoma, Burkitt's
 25 lymphoma), myeloid leukemias (for example, acute myelogenous leukemia (AML)), thyroid follicular cancer, myelodysplastic syndrome (MDS), tumors of mesenchymal origin (e.g. fibrosarcomas and rhabdomyosarcomas), melanomas, teratocarcinomas,

neuroblastomas, gliomas, benign tumor of the skin (e.g. keratoacanthomas), breast carcinoma (e.g. advanced breast cancer), kidney carcinoma, ovary carcinoma, bladder carcinoma and epidermal carcinoma.

Pharmaceutically useful compositions comprising the drugs of this invention
5 may be formulated according to known methods such as by the admixture of a pharmaceutically acceptable carrier. Examples of such carriers and methods of formulation may be found in Remington's Pharmaceutical Sciences. To form a pharmaceutically acceptable composition suitable for effective administration, such compositions will contain an effective amount of the drug. The effective amount of
10 the drug may vary according to a variety of factors such as the individual's condition, weight, sex and age. Other factors include the mode of administration. The pharmaceutical compositions may be provided to the individual by a variety of routes such as subcutaneous, topical, oral and intramuscular.

The drugs of this invention include chemical derivatives of the base
15 molecules of the drug. That is, they may contain additional chemical moieties that are not normally a part of the base molecule. Such moieties may improve the solubility, half-life, absorption, etc. of the base molecule. Alternatively the moieties may attenuate undesirable side effects of the base molecule or decrease the toxicity of the base molecule. Examples of such moieties are described in a variety of texts,
20 such as Remington's Pharmaceutical Sciences.

Compounds identified according to the methods disclosed herein may be used alone at appropriate dosages defined by routine testing in order to obtain optimal inhibition or activity while minimizing any potential toxicity. In addition, co-administration or sequential administration of other agents may be desirable.

25 The drugs of this invention can be administered in a wide variety of therapeutic dosage forms in conventional vehicles for administration. For example, the drugs can be administered in such oral dosage forms as tablets, capsules (each

including timed release and sustained release formulations), pills, powders, granules, elixirs, tinctures, solutions, suspensions, syrups and emulsions, or by injection. Likewise, they may also be administered in intravenous (both bolus and infusion), intraperitoneal, subcutaneous, topical with or without occlusion, or
5 intramuscular form, all using forms well known to those of ordinary skill in the pharmaceutical arts. An effective but non-toxic amount of the compound desired can be employed as a modulating agent.

The daily dosage of the products may be varied over a wide range from 0.01 to 1,000 mg per patient, per day. For oral administration, the compositions are
10 preferably provided in the form of scored or unscored tablets containing 0.01, 0.05, 0.1, 0.5, 1.0, 2.5, 5.0, 10.0, 15.0, 25.0, and 50.0 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. An effective amount of the drug is ordinarily supplied at a dosage level of from about 0.0001 mg/kg to about 100 mg/kg of body weight per day. The range is more
15 particularly from about 0.001 mg/kg to 10 mg/kg of body weight per day. The dosages are adjusted when combined to achieve desired effects. On the other hand, dosages of these various agents may be independently optimized and combined to achieve a synergistic result wherein the pathology is reduced more than it would be if either agent were used alone.

20 Advantageously, compounds or modulators used in the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three or four times daily. Furthermore, compounds or modulators for the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal
25 routes, using those forms of transdermal skin patches well known to those of ordinary skill in that art. To be administered in the form of a transdermal delivery

system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

For combination treatment with more than one active agent, where the active agents are in separate dosage formulations, the active agents can be administered
5 concurrently, or they each can be administered at separately staggered times.

The dosage regimen utilizing the compounds or modulators in the present invention is selected in accordance with a variety of factors including type, species, age, weight, sex and medical condition of the patient; the severity of the condition to be treated; the route of administration; the renal and hepatic function of the patient;
10 and the particular drug employed. A physician or veterinarian of ordinary skill can readily determine and prescribe the effective amount of the drug required to prevent, counter or arrest the progress of the condition. Optimal precision in achieving concentrations of drug within the range that yields efficacy without toxicity requires a regimen based on the kinetics of the drug's availability to target sites. This
15 involves a consideration of the distribution, equilibrium, and elimination of a drug.

The drugs of this invention can form the active ingredient, and are typically administered in admixture with suitable pharmaceutical diluents, excipients or carriers (collectively referred to herein as "carrier" materials) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs,
20 syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic pharmaceutically acceptable inert carrier such as ethanol, glycerol, water and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents and
25 coloring agents can also be incorporated into the mixture. Suitable binders include, without limitation, starch, gelatin, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth or sodium

alginate, carboxymethylcellulose, polyethylene glycol, waxes and the like.

Lubricants used in these dosage forms include, without limitation, sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride and the like. Disintegrators include, without limitation, starch, methyl
5 cellulose, agar, bentonite, xanthan gum and the like.

For liquid forms the active drug component can be combined in suitably flavored suspending or dispersing agents such as the synthetic and natural gums, for example, tragacanth, acacia, methyl-cellulose and the like. Other dispersing agents that may be employed include glycerin and the like. For parenteral administration, sterile
10 suspensions and solutions are desired. Isotonic preparations, which generally contain suitable preservatives, are employed when intravenous administration is desired.

The drugs in the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids,
15 such as cholesterol, stearylamine or phosphatidylcholines.

Drugs in the present invention may also be delivered by the use of monoclonal antibodies as individual carriers to which the compound molecules are coupled. The drugs in the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinyl-
20 pyrrolidone, pyran copolymer, polyhydroxypropylmethacryl-amidephenol, polyhydroxy-ethylaspartamidephenol, or polyethyl-eneoxidepolylysine substituted with palmitoyl residues. Furthermore, the drugs in the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyepsilon caprolactone, polyhydroxy
25 butyric acid, polyorthoesters, polyacetals, polydihydro-pyrans, polycyanoacrylates and cross-linked or amphipathic block copolymers of hydrogels.

For oral administration, the drugs may be administered in capsule, tablet, or bolus form or alternatively they can be mixed with feed. The capsules, tablets, and boluses are comprised of the active ingredient in combination with an appropriate carrier vehicle such as starch, talc, magnesium stearate, or di-
5 calcium phosphate. These unit dosage forms are prepared by intimately mixing the active ingredient with suitable finely-powdered inert ingredients including diluents, fillers, disintegrating agents, and/or binders such that a uniform mixture is obtained. An inert ingredient is one that will not react with the drugs and which is non-toxic to the animal being treated. Suitable inert ingredients
10 include starch, lactose, talc, magnesium stearate, vegetable gums and oils, and the like. These formulations may contain a widely variable amount of the active and inactive ingredients depending on numerous factors such as the size and type of the animal species to be treated and the type and severity of the infection. The active ingredient may also be administered by simply mixing the
15 compound with the feedstuff or by applying the compound to the surface of the foodstuff.

The compounds or modulators may alternatively be administered parenterally via injection of a formulation consisting of the active ingredient dissolved in an inert liquid carrier. Injection may be either intramuscular,
20 intraruminal, intratracheal, or subcutaneous. The injectable formulation consists of the active ingredient mixed with an appropriate inert liquid carrier. Acceptable liquid carriers include the vegetable oils such as peanut oil, cotton seed oil, sesame oil and the like as well as organic solvents such as solketal, glycerol formal and the like. As an alternative, aqueous parenteral formulations
25 may also be used. The vegetable oils are the preferred liquid carriers. The formulations are prepared by dissolving or suspending the active ingredient in

the liquid carrier such that the final formulation contains from 0.005 to 10% by weight of the active ingredient.

The invention is further illustrated by the following nonlimiting examples.

5 **Examples**

In the nonprophetic examples, AML patients were administered 600 mg of (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone) (referred to as Zarnestra) at a starting oral dose of 600 mg b.i.d. for the first 21 days of each 28 day cycle in AML. Subjects were enrolled into two
10 cohorts, those with relapsed AML and those with refractory AML. A total of 257 patients (135 relapsed and 117 refractory) were treated.

Response to Zarnestra treatment was defined as patients who had an objective response (CR, CRp, or PR) as shown in Table 2, or patients who demonstrated stable disease and anti-leukemic activity (decrease of >50% of leukemic blast cells) as
15 determined by either central review or the clinical site. Anti-leukemic activity is defined as any bone marrow blast count less than 5% or a reduction in bone marrow blasts by at least half.

20

25

Table 2

Response	Criteria
Complete Response (CR)	Neutrophil count > 1,000/ μ L AND < 5% blasts in bone marrow aspirate AND platelet count > 100,000/ μ L and no extramedullary disease.
Complete Response-incomplete platelet recovery (CRp)	Meets all the criteria for CR except recovery up to 100,000/ μ L platelets, but have sufficient bone marrow recovery to be platelet transfusion independent.
Partial Response (PR)	At least a 50% decrease in bone marrow blasts AND partial recovery of neutrophil count (> 500/ μ L) AND platelet count > 50,000/ μ L.
Stable Disease (SD)	Any response not meeting CR, CRp, PR or PD Criteria AND absence of clinical deterioration.
Progressive Disease (PD)	> 50% increase in bone marrow blasts OR circulating blasts OR interval development of circulating blasts that persists on at least two consecutive occasions OR interval development of extramedullary disease.

Example 1. Microarray Analysis

Bone marrow samples were collected from consenting patients both before and after
5 treatment with Zarnestra FTI (active ingredient, (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone),
diluted with PBS and centrifuged with Ficoll-diatrizoate (1.077g/ml). White blood cells
were washed twice with PBS, resuspended in FBS with 10% DMSO and immediately
frozen at -80°C. Samples were thawed at 37°C and 10X volume of RPMI with 20% FBS
10 was added drop-wise over a period of 5 min. Cells were centrifuged at 500g for 10 min
and resuspended in 10 ml PBS with 2 mM EDTA and 0.5% BSA. Samples were then
passed through a 70 μ M filter (Becton Dickinson Labware, Franklin lakes, NJ) to

remove any cell clumps. Cell viability was determined by trypan blue dye exclusion assay. The mean viability of the bone marrow samples upon thawing was 35% (range 0-96%). Due to the relatively low number of viable cells present the samples were not further enriched for myeloid cells. Approximately 2×10^5 cells were double labeled with
5 CD33-FITC and CD34-PE antibodies (Becton Dickinson Biosciences Pharmingen, San Diego, CA) and FACS analysis was performed.

Total RNA was extracted from cell samples using the RNeasy Kit (Qiagen, Santa Clarita, CA). Synthesis of cDNA and cRNA were performed according to Affymetrix
10 (Santa Clara, CA) protocols. Two rounds of linear amplification was performed since the RNA yield for several samples was less than 1 μ g. For hybridization, 11 μ g of cRNA were fragmented randomly by incubation at 94°C for 35 min in 40 mM Tris-acetate, pH 8.1, 100 mM potassium acetate, and 30 mM magnesium acetate. Fragmented cRNA was hybridized to U133A arrays at 45°C for 16 h in a rotisserie oven
15 set at 60 rpm. Following hybridization, arrays were washed (with 6x SSPE and 0.5x SSPE containing Triton X-100 (0.005%)), and stained with streptavidin-phycoerythrin (SAPE; Molecular Probes, Eugene, OR). Quantification of bound labeled probe was conducted using the Agilent G2500A GeneArray scanner (Agilent Technologies, Palo Alto, CA).

20

The total fluorescence intensity for each array was scaled to the uniform value of 600. Chip performance was quantitated by calculating a signal to noise ratio (raw average signal/noise). Chips were removed from further analysis if their signal-to-noise ratio was less than 5. Genes were only included in further analysis if they were called
25 “present” in at least 10% of the chips. Approximately 12,000 Affymetrix probe sets remained following this cut-off. The quality of the gene expression data was further

controlled by identifying outliers based on principal components analysis and by analyzing the normal distributions of the gene intensities.

Chi-squared tests and Student's t-test were used to identify correlations between patient
5 response and patient co-variables, mutational status, CD33 and CD34 antigen expression, leukemic blast counts, and gene expression. To identify genes that could predict response with high sensitivity, a percentile analysis was employed. For example, genes that were up- or down-regulated in all responders compared to at least 40% of non-responders were identified. Genes that did not reveal significant p-values ($P < 0.05$)
10 based on a two-tailed Student's t-test (unequal variance) were removed. The predictive value of the top gene(s) was analyzed by a leave-one-out cross validation method. Here, one sample was removed from the data set and the marker was reselected from the 12,000 genes. The predictive value of this gene was then tested on the left-out sample using a linear discriminant analysis. Sensitivity was calculated as the number of true
15 positives divided by the sum of true positives plus false negatives. Specificity was calculated as the number of true negatives divided by the sum of true negatives and false positives. Positive predictive value was calculated as the number of true positives divided by the sum of true positives and false positives. Negative predictive value was calculated as the number of true negatives divided by the sum of false negatives and
20 true negatives.

Univariate cox proportional hazard models were used to assess the association of each parameter (genes or blast counts) with patient survival outcome. The coefficient estimate of each parameter from the cox model measures the strength of such
25 association. When more than one gene was used a multivariate hazard model was employed. The classifier that distinguishes responders from non-responders was defined as:

$$b1*x1 + b2*x2 + b3*x3 + \dots$$

where $b1$, $b2$, $b3$ are coefficient estimates from the cox model, and $x1$, $x2$, $x3$ are standardized parameter values (blast counts or $\log_{10}$ of gene expression values).

- 5 Receiver operator curves (ROC) were used to choose appropriate thresholds for each classifier, requiring a sensitivity of at least 90%. The ROC diagnostic calculates the sensitivity and specificity for each parameter. In addition, gene markers were first ranked for their ability to stratify good outcome from poor outcome using a training set of 29 randomly chosen samples. The predictive value of each gene was then tested on
10 the remaining 29 samples. This allowed for the identification of genes with the most robust predictive values.

Example 2: Leukemic Cell Antigen Expression

- Leukemic blast cells are known to express the surface antigens CD33 and CD34. 95%
15 and 55% of patient bone marrow leukemic cells were positive for CD33 and CD34, respectively. The mean percentage of cells expressing the antigens in each sample was 13% for CD34 and 43% for CD33. Chi-squared analysis was performed to investigate the correlation between the level of antigen expression and patient outcome. Cutoffs of 15% and 60% were chosen for CD34 and CD33 levels, respectively. Low expression
20 (positive in less than about 15% of the cell population for CD34 and positive in less than about 60% of the cell population for CD33) of CD33 and CD34 correlated with patient response to Zarnestra™ ($p=0.137$, $p=0.052$, respectively). High expression of both antigens (positive in more than about 15% of the cell population for CD34 and positive in less than about 60% of the cell population for CD33) was also positively
25 correlated with high blast counts. A Kaplan Meier analysis also indicated that high CD33 expression correlated with poor overall survival (Fig. 1).

Example 3: Leukemic Blast Count Analysis

The analysis of CD33 and CD34 antigen expression suggested that the level of leukemic blast cells correlated with patient response. The average value of the site and
5 DCL blast count measurements were calculated and a Student's t-test was performed to investigate if blast counts correlated with patient response in the AML patients. From a total of 199 evaluable patients, 24 of which had a CR, CRp, PR, or SD, the percentage of blasts correlated significantly with patient outcome ($p = 0.0006$). Responders had a lower number of blasts (mean 34%) than those with progressive disease (mean 51%).
10 Only one of the 24 total responders (defined as having SD) had a blast count higher than 60%. Chi-squared analysis for all evaluable patients also found a significant correlation between high blast counts and resistance to treatment ($\chi^2 = 9.53$).

A Kaplan-Meier analysis found that those patients with a low level of blast counts
15 (<60%) had a significantly better overall survival than those with high blast counts (Fig. 2). These analyses indicate that patients with blast counts higher than approximately 60% will be unlikely to respond to Zarnestra™.

Example 4: Identification of genes that are differentially expressed between responders and non-responders

Bone marrow samples were obtained for gene expression analysis from 80 patients prior to drug treatment. Of the 80 base-line samples, 14 were removed from the analysis since
5 they came from non-evaluable patients. Samples were enriched for myeloid cells, processed for messenger RNA (the molecules that encode for gene-specific proteins), and hybridized to the Affymetrix U133A gene chip. 58 of the 66 samples passed additional quality control measures following hybridization to the U133A chip. The gene expression data was integrated with the clinical information and retrospective
10 analyses were performed to identify genes that could stratify responders from non-responders with a high level of sensitivity. Several gene markers were identified that are useful in predicting response to Zarnestra™ (Table 3). In the case of the lymphoid blast crisis oncogene (oncoLBC) the predictive value of this gene was calculated for the dataset using a leave-one-out cross validation (Table 3). The oncoLBC gene expression
15 levels were able to capture all of the clinically identified responders while removing over half of the non-responders.

Table 3: Genes Differentially Expressed in Responders versus Non-Responders

Title	Gene Symbol	ttest	Ratio*	RefSeq	Seq. ID No.
aryl hydrocarbon receptor	AHR	2.55E-06	0.39	NM_001621	1
A kinase (PRKA) anchor protein 13 (oncoLBC)	AKAP13	6.13E-05	0.51	NM_006738	2
hypothetical protein DKFZp667G2110	DKFZp667G2110	6.93E-05	0.71	NM_153605	3
iduronate 2-sulfatase (Hunter syndrome)	IDS	0.00024	0.36	NM_000202	4
opsin 3 (encephalopsin, panopsin)	OPN3	0.000643	0.54	NM_014322	5
G protein-coupled receptor 105	GPR105	0.000876	0.34	NM_014879	6
tumor endothelial marker 6	TEM6	0.001031	0.62	NM_022748	7
tumor necrosis factor (ligand) superfamily, member 13	TNFSF13	0.001042	0.59	NM_003808	8
Supervillin	SVIL	0.001457	0.62	NM_003174	9
interleukin 3 receptor, alpha (low affinity)	IL3RA	0.001984	0.40	NM_002183	10
KIAA0680 gene product	KIAA0680	0.002616	0.57	NM_014721	11
FGF receptor activating protein 1	FRAG1	0.00299	1.24	NM_014489	12
cDNA DKFZp566B213	DKFZp566B213	0.012011	1.50		13
KIAA1036 protein	KIAA1036	0.012621	0.72	NM_014909	14
BTG family, member 3	BTG3	0.016594	1.48	NM_006806	15
mitogen-activated protein kinase 8 interacting protein 3	MAPK8IP3	0.018174	1.39	NM_015133	16
ras homolog gene family, member H	ARHH	0.027219	1.64	NM_004310	17
neuronal pentraxin II	NPTX2	0.033468	0.14	NM_002523	18

5 *Ratios indicate fold-change in responders compared to non-responders

Table 4: Leave-one-out cross validation using oncoLBC as a marker of response.

		Gold Std	
		Resp .	Non -resp .
Test	Predict response	14	20
	Predict non-resp.	0	24
Total		14	44
Sensitivity		= 100%	
Specificity		= 55%	
Positive predictive value		= 41%	
Negative predictive value		= 100%	

5

A survival analysis showed that patients who were classified as responders based on oncoLBC expression (Fig 3A, $p = 0.00841$) significantly outperformed patient classification using the clinical data (Fig 3B, $p = 0.0827$). This was due to the oncoLBC marker identifying a subset of non-responders with an increased overall survival. Based on the Cox hazard model, combining the oncoLBC and a second gene marker, the aryl hydrocarbon receptor (AHR), increased the specificity and positive predictive value to 75% and 56%, respectively (Fig. 3C). These results indicated that using either the oncoLBC alone, or in combination with the AHR gene presents an effective array for predicting response to Zarnestra™ treatment.

15

A leave-one-out cross validation using the oncoLBC and aryl hydrocarbon receptor (AHR) as markers was also performed. When using the cut-off to identify the highest sensitivity and best specificity the PPV and sensitivity remained the same. Results of leave-one out cross validation of other gene combinations are shown in Table 5. This

illustrates that combinations of markers can improve the predictive value of this method.

Table 5

Markers	sensitivity	specificity	PPV	NPV	prior probability*
LBC, AHR, katanin, IDS, DKFZp667G2110	100	73	54	100	0.32
LBC, katanin, DKFZp667G2110	100	70	52	100	0.47
LBC, AHR, DKFZp667G2110	100	66	48	100	0.23
LBC, AHR, IDS, DKFZp667G2110	100	66	48	100	0.28
LBC, AHR, IDS	100	61	45	100	0.2
LBC, katanin	100	61	45	100	0.41
LBC, DKFZp667G2110	100	57	42	100	0.2
Katanin	100	56	42	100	0.49
LBC	100	55	41	100	0.4
LBC, AHR	100	55	41	100	0.19
LBC, IDS, katanin	100	55	41	100	0.38
LBC, AHR, katanin	100	52	40	100	0.18
LBC, IDS	100	50	39	100	0.38
IDS	100	50	39	100	0.42
DKFZp667G2110	100	45	37	100	0.39
AHR	100	45	37	100	0.17
AHR, katanin	100	43	36	100	0.17

5

Furthermore, stratification of patients using the LBC and AHR classifier showed a similar difference in median survival time between the two patient populations compared with using the oncoLBC gene or the clinical response definitions (Fig. 4C).

- 10 These results indicated that using either the oncoLBC alone, or in combination with the AHR gene could be used as effective biomarkers for predicting response to ZARNESTRA in the current dataset.

A Cox hazard model was used to analyze other combinations of markers in stratifying poor survivors from good survivors (Table 6). Here, data from 51 patients was used since only this number of patient samples had CD33 and CD34 antigen levels measured. A sensitivity of greater than 90% was used in determining the appropriate cut-offs for the markers. The use of multiple markers can improve the difference in median survival times of the 2 survival groups.

Table. 6

Markers*	P-value	Median survival poor (days)	Median survival good (days)	Delta (days)	Sens (%)	Spec (%)
LBC	0.0098	64	177	113	91	65
CD33	0.0029	40	105	65	91	23
CD34	0.643	64	103	39	91	35
AHR	0.12	59	106	47	91	53
% blasts*	0.1241	60	103	43	91	38
LBC + % Blasts	0.00223	59	154	95	93	61
LBC + AHR	0.0111	71	171	100	91	73
LBC + CD33	0.00266	71	182	111	91	73
LBC + CD34	0.00038	64	192	128	91	80
LBC + AHR + CD34	0.003	71	213	142	91	83
LBC + AHR + CD33	0.00062	64	192	128	91	80

10

Example 5: Antibodies (Prophetic)

An lbc oncogene-derived peptide is synthesized, coupled to keyhole limpet hemocyanin, and used to immunize rabbits for production of polyclonal antibodies. The sera are tested for reactivity against the corresponding peptide with ELISA, and the positive batches are affinity-purified. The purified antibody specifically detects the peptide that has the epitope in tissue sections. This is verified by complete abolishment

15

of the signal if the corresponding peptide is added simultaneously with the antibody. In addition to this polyclonal antibody, which works well in immunohistochemistry, monoclonal antibodies able to detect the protein in its natural fold are produced. To produce monoclonal antibodies, a purified antigen, produced in mammalian cells to ensure natural fold and posttranslational modifications, is generated. The antigen, lbc onco protein-IgG constant part fusion protein, is expressed in mouse myeloma cells, and the protein is purified using the Fc part as bait. This purified antigen is recognized in Western blot by the C-terminal polyclonal antibody. The antigen is used to generate mouse monoclonal antibodies against lbc peptides by selecting out of the positive clones those that produce antibodies that react against lbc peptide instead of the IgG constant part.

Kits for the clinical identification of lbc oncogene can be readily fashioned employing these and similar antibodies. Such kits would include antibodies directed to lbc peptide identification (and hence, lbc oncogene), appropriate indicator reagents (e.g., enzymes, labels, and the like), and (optionally) other reagents useful in the clinical application of such a kit such as dilution buffers, stabilizers, and other materials typically used in such assays.

Example 6: In situ hybridization (Prophetic)

Formalin fixed paraffin embedded tissue samples are cut into 5-7 μm thick sections, mounted on silane coated glass slides, and incubated at 37°C over night and at 65°C for 30 min before deparaffinating twice for 10 min in xylene. Thereafter the samples are rehydrated through a graded series of ethanol solutions (100 to 70%), and rinsed twice for 5 min in phosphate buffered saline (PBS pH 7.0), treated twice for 5 min with 0.1 mol/L glycine in PBS, permeabilized for 15 min with 0.3% Triton X-100 in PBS. The sections are treated with proteinase K (Finnzymes, Helsinki, Finland) treatment ($\mu\text{g/ml}$, in TE buffer; 100 mmol/L Tris-HCl, 50 mmol/L EDTA, pH 8.0) at

37°C for 30 min, postfixed in 3% paraformaldehyde in PBS at 4°C for 5 min and rinsed twice in PBS. Positive charges are blocked by soaking the slides in 0.25% (v/v) acetic anhydride, 100 mmol/L triethanolamine, pH 8.0, twice for 5 min. The slides are equilibrated in 4xSSC, 50% (v/v) deionized formamide at 37°C for 10 min.

5 Probes are prepared by ligating a PCR-amplified 0.4 kb lbc oncogene cDNA insert into the pCR-II vector using a TA cloning kit (Invitrogen, San Diego CA, USA). The templates for lbc oncogene antisense or sense RNA probes are generated by linearizing the appropriate vector construct (in 3' to 5' direction or 5' to 3' direction, respectively). An RNA Labeling Kit (Boehringer-Mannheim) is used to generate
10 digoxigenin labeled RNA probes by in vitro transcription. The hybridization is performed overnight at 45°C using a hybridization mixture containing 1xDenhart's solution (0.2g/L Ficoll Type 400, Pharmacia), 0.2g/L polyvinylpyrrolidone, 0.2g/L bovine serum albumin (fraction V; Sigma), 40% formamide, 10% dextran sulfate, 4xSSC, 10 mmol/L dithiothreitol, 1mg/mL yeast tRNA, 1 mg/mL herring sperm DNA
15 and 300 ng/mL digoxigenin-labeled RNA probe. After hybridization, the tissue sections are washed at 37°C twice for 5 min in 2xSSC and once for 15 min in 60% formamide, 0.2xSSC, followed by two 5 minute rinses in 2xSSC at room temperature and two 10 minute washes in 100 mmol/L Tris-HCl, pH 8.0, 150 mmol/L NaCl. The signal detection is carried out using 1:250 alkaline phosphatase-conjugated sheep
20 antidigoxigenin fab fragments (Boehringer Mannheim). The signal is visualized by incubating the sections with NBT/BCIP Stock Solution (Boehringer Mannheim) for 1.5 hours.

Lbc oncogene-positive cells seen in the tumorigenic cells of cancer patients indicates that response to an FTI is unlikely.

25

Example 7: Immunohistochemistry (Prophetic)

An affinity-purified polyclonal antibody against the C-terminal peptide of lbc oncogene is used for the immunohistochemical detection and localization of lbc oncogene. Four μm sections from formalin-fixed and paraffin embedded normal and tumor tissue is mounted on 3-aminopropyl-triethoxy-silane (APES, Sigma, St. Louis, MO, U.S.A) coated slides. The sections are deparaffinized and rehydrated in graded concentrations of ethanol and treated with methanolic peroxide (0.5% hydrogen peroxide in absolute methanol) for 30 minutes at room temperature to block the endogenous peroxidase activity. Antigen retrieval is done in a microwave oven twice for 5 minutes (650W). An Elite ABC Kit (Vectastain, Vector Laboratories, Burlingame, CA, U.S.A) is used for immunoperoxidase staining. The lbc peptide antibody is used at an optimal dilution of 1:2000. Both the biotinylated second antibody and the peroxidase-labeled avidin-biotin complex are incubated on the sections for 30 minutes. The dilutions are made in PBS (pH 7.2), and all incubations are carried out in a moist chamber at room temperature. Between the different staining steps the slides are rinsed three times with PBS. The peroxidase staining is visualized with a 3-amino-9-ethylcarbazole (Sigma) solution (0.2 mg/ml in 0.05 M acetate buffer containing 0.03% hydrogen peroxide, pH 5.0) at room temperature for 15 minutes. Finally, the sections are lightly counterstained with Mayer's haematoxylin and mounted with aqueous mounting media (Aquamount, BDH). In control experiments the primary antibodies are replaced with the IgG fraction of normal rabbit serum or the primary antibody was preabsorbed with the lbc peptide. These stainings indicate the presence of the lbc oncogene in a subset of cells.

Example 8: Enzyme Immunoassay (Prophetic)

Immunoassays are prepared for the lbc protein or characteristic peptides related to the lbc oncogene. Antigen standards comprising a digest of colon tumor specimens (shown to contain the antigen by immunoperoxidase staining) are used. Human white

blood cells from AML patients. The specimens are pooled and homogenized in 10 volumes of 10 mM Tris buffer, pH 7.4, containing 0.2% (w/v) sodium deoxycholate at 4C. The homogenate is quickly brought to 37 C and the following reagents (final concentration) are added while stirring: 1 mM cysteine (Sigma), 1 mM EDTA (Sigma),
5 and papain (0.8 unit/ml) (Boehringer-Mannheim, Indianapolis, Ind.). After 5 minutes, digestion is stopped by the addition of 5 mM iodoacetamide (Sigma). The homogenate is centrifuged at 100,000Xg for 1 hour at 4C, then extensively dialyzed against 10 mM Tris/0.9% NaCl solution buffer, pH 7.4, containing phenylmethsulfonyl fluoride and aminocaproic acid, each at 10 mM. The homogenate is frozen in small aliquots at a
10 concentration of 0.5 mg of protein/ml.

The dose response curve that will be generated for the immunoassay procedure measuring lbc protein or peptides demonstrates linearity between antigen input of 100ng to 100µg/ml. For serum analysis, the range is 1ng to 1000ng/ml, since these samples are diluted 10-fold prior to assay.

15 Solid-phase preparations of the antibodies described the examples above are prepared using CNBr-activated Sepharose (Pharmacia). Microtiter plates (Nunc I Immunoplates; Grand Island Biological Co., Grand Island, N.Y.) are coated with the antibodies (200 µl /well) in 50 mM carbonate-bicarbonate buffer, pH 9.6, for 18 hours at 4C. After removal of the antibody solution, residual protein binding sites on the
20 plastic are blocked by the addition of 200 µl of assay buffer [PBS containing 1% (v/v) rabbit *serum* and 1% (w/v) bovine albumin]. After 1 hour of incubation at room temperature, the coated plates are used immediately for the assay procedure.

To perform the assay, 200 µl samples, diluted in assay buffer, are applied for 1-5 hours at 37C. After 3 washes using assay buffer, 200 µl of the antibody covalently
25 conjugated to horseradish peroxidase (Sigma, Type VI) is applied to each well for 1.5 hours at 37C. The conjugate is diluted to a concentration of 0.5 µg of immunoglobulin per ml of PBS containing 10% (v/v) murine serum. Following a wash procedure as

above, 200 µl of substrate per well are applied for 0.5 hours at room temperature. Substrate solution contains 0.4 mg of o-phenylenediamine per ml of pH 5.0 citrate buffer and 0.003% hydrogen peroxide. The reaction is stopped by addition of 50 µl of 2N sulfuric acid, and absorbance is monitored at 488 nM using an enzyme assay plate reader (Fisher Scientific Co., Pittsburgh, Pa.).

The percentage of bound enzyme conjugate is calculated by the formula:

$$(B-B_0)/(B_t-B_0)(100)$$

where B=absorbance of the sample, B_t =maximal absorbance, and B_0 =absorbance of the blank. Each assay is performed in triplicate using a standard digest and 26-fold diluted serum samples diluted in assay buffer. Specificity of the immunoassay is examined by substituting various antibody reagents at the solid phase, including an antibody to an unrelated protein and nonimmune rabbit serum. Of the solid phase antibodies only antibody prepared according to the examples above bind antigen at high dilutions.

Levels of serum lbc protein are detected for normal control subjects, patients with benign and malignant hematological disorders.

Sera obtained from apparently healthy individuals exhibits no lbc protein. Only 5% of the samples express serum antigen at the limit of detection or above, and this value is chosen as the cutoff for elevated serum levels. Cancer patients below the cutoff are likely to respond to treatment with an FTI.

ADS5001.ST25.txt
SEQUENCE LISTING

<110> Ortho-Clinical Diagnostics
RAPONI, MITCH

<120> METHODS FOR ASSESSING AND TREATING CANCER

<130> 1011-4483CA

<160> 28

<170> PatentIn version 3.1

<210> 1

<211> 5496

<212> DNA

<213> Human

<400> 1

```

attcagccgg tgcgcgcggc ggcgggaggg agtggctggg gagtcccgtc gacgctctgt      60
tccgagagcg tgccccggac cgccagctca gaacaggggc agccgtgtag ccgaacggaa      120
gctgggagca gccgggactg gtggcccgcg cccgagctcc gcaggcggga agcaccctgg      180
at ttgggaag tcccgggagc agcgcgggcg cacctccctc acccaagggg ccgcggcgac      240
ggtcacgggg cgcggcgcca ccgtgagcga cccaggccag gattctaaat agacggccca      300
ggctcctcct ccgcccgggc cgctcacct gcgggcattg ccgcgccgcc tccgccggtg      360
tagacggcac ctgcgccgcc ttgctcgcg gtctccgccc ctgcgccacc ctactgcg      420
caggcccagg cagctcacct gtactggcg gggctgcgga agcctgcgtg agccgaggcg      480
ttgaggcgcg gcgcccacgc cactgtccc agaggacgca ggtggagcgg gcgcggcttc      540
gcggaacccg gcgcgggccg ccgcagtggg cccagcctac accgggttcc ggggacccgg      600
ccgccagtgc ccggggagta gccgccgcgc tcggctgggc accatgaaca gcagcagcgc      660
caacatcacc tacgccagtc gcaagcggcg gaagccggtg cagaaaacag taaagccaat      720
cccagctgaa ggaatcaagt caaatccttc caagcggcat agagaccgac ttaatacaga      780
gttggaccgt ttggctagcc tgctgccttt cccacaagat gttattaata agttggacaa      840
actttcagtt cttaggctca gcgtcagtta cctgagagcc aagagcttct ttgatgttgc      900
attaataatc tcccctactg aaagaaacgg aggccaggat aactgtagag cagcaaattt      960
cagagaaggc ctgaacttac aagaaggaga attcttatta caggctctga atggctttgt     1020
attagttgtc actacagatg ctttggctct ttatgcttct tctactatac aagattatct     1080
agggtttcag cagtctgatg tcatacatca gagtgtatat gaacttatcc ataccgaaga     1140
ccgagctgaa tttcagcgtc agctacactg ggcattaaat ctttctcagt gtacagagtc     1200
tggaacaagga attgaagaag ccactgggtc cccccagaca gtagtctggt ataaccaga     1260
ccagattcct ccagaaaact ctctttaa gtagaggtgc ttcatatgtc gtctaagggt     1320
tctgctggat aattcatctg gttttctggc aatgaatttc caagggaagt taaagtatct     1380

```

ADS5001.ST25.txt

tcatggacag	aaaaagaaag	ggaaagatgg	atcaatactt	ccacctcagt	tggctttgtt	1440
tgcgatagct	actccacttc	agccaccatc	catacttgaa	atccggacca	aaaattttat	1500
ctttagaacc	aaacacaaac	tagacttcac	acctattggt	tgtgatgcca	aaggaagaat	1560
tgttttagga	tatactgaag	cagagctgtg	cacgagaggc	tcaggttatc	agtttattca	1620
tgcagctgat	atgctttatt	gtgccgagtc	ccatatccga	atgattaaga	ctggagaaag	1680
tggcatgata	gttttccggc	ttcttacaaa	aaacaaccga	tggacttggg	tccagtctaa	1740
tgcacgcctg	ctttataaaa	atggaagacc	agattatata	attgtaactc	agagaccact	1800
aacagatgag	gaaggaacag	agcatttacg	aaaacgaaat	acgaagtgc	cttttatgtt	1860
taccactgga	gaagctgtgt	tgtatgaggc	aaccaaccct	tttcctgcca	taatggatcc	1920
cttaccacta	aggactaaaa	atggcactag	tggaaaagac	tctgctacca	catccactct	1980
aagcaaggac	tctctcaatc	ctagttccct	cctggctgcc	atgatgcaac	aagatgagtc	2040
tatttatctc	tatcctgctt	caagtacttc	aagtactgca	ccttttgaaa	acaacttttt	2100
caacgaatct	atgaatgaat	gcagaaattg	gcaagataat	actgcaccga	tgggaaatga	2160
tactatcctg	aaacatgagc	aaattgacca	gcctcaggat	gtgaactcat	ttgctggagg	2220
tcacccaggg	ctctttcaag	atagtaaaaa	cagtgacttg	tacagcataa	tgaaaaacct	2280
aggcattgat	tttgaagaca	tcagacacat	gcagaatgaa	aaatttttca	gaaatgattt	2340
ttctggtgag	gttgacttca	gagacattga	cttaacggat	gaaatcctga	cgtatgtcca	2400
agattcttta	agtaagtctc	ccttcatacc	ttcagattat	caacagcaac	agtccttggc	2460
tctgaactca	agctgtatgg	tacaggaaca	cctacatcta	gaacagcaac	agcaacatca	2520
ccaaaagcaa	gtagtagtgg	agccacagca	acagctgtgt	cagaagatga	agcacatgca	2580
agttaatggc	atgtttgaaa	attggaactc	taaccaattc	gtgcctttca	attgtccaca	2640
gcaagaccca	caacaatata	atgtctttac	agacttacat	gggatcagtc	aagagttccc	2700
ctacaaatct	gaaatggatt	ctatgcctta	tacacagaac	tttatttcct	gtaatcagcc	2760
tgtattacca	caacattcca	aatgtacaga	gctggactac	cctatgggga	gttttgaacc	2820
atccccatac	cccactactt	ctagttttaga	agattttgtc	acttgtttac	aacttcctga	2880
aaaccaaaaag	catggattaa	atccacagtc	agccataata	actcctcaga	catgttatgc	2940
tggggccgtg	tcgatgtatc	agtgccagcc	agaacctcag	cacaccacg	tgggtcagat	3000
gcagtacaat	ccagtactgc	caggccaaca	ggcattttta	aacaagtttc	agaatggagt	3060
tttaaatagaa	acatatccag	ctgaattaaa	taacataaat	aacactcaga	ctaccacaca	3120
tcttcagcca	cttcatcatc	cgtcagaagc	cagacctttt	cctgatttga	catccagtgg	3180
attcctgtaa	ttccaagccc	aattttgacc	ctggtttttg	gattaaatta	gtttgtgaag	3240
gattatggaa	aaataaaaact	gtcactgttg	gacgtcagca	agttcacatg	gaggcattga	3300

ADS5001.ST25.txt

tgcatgctat	tcacaattat	tccaaaccaa	attttaattt	ttgcttttag	aaaagggagt	3360
ttaaaaatgg	tatcaaaatt	acatatacta	cagtcaagat	agaaaggggtg	ctgccacgga	3420
gtggtgaggt	accgtctaca	tttcacatta	ttctgggcac	cacaaaatat	acaaaacttt	3480
atcagggaaa	ctaagattct	tttaaattag	aaaatattct	ctatttgaat	tatttctgtc	3540
acagtaaaaa	taaaataact	tgagttttga	gctactggat	tcttattagt	tccccaata	3600
caaagttaga	gaactaaact	agtttttcct	atcatgttaa	cctctgcttt	tatctcagat	3660
gttaaaataa	atggtttggt	gctttttata	aaaagataat	ctcagtgcct	tcctccttca	3720
ctgtttcatc	taagtgcctc	acattttttt	ctacctataa	cactctagga	tgtatatttt	3780
atataaagta	ttctttttct	tttttaaatt	aatatctttc	tgcacacaaa	tattatttgt	3840
gtttcctaaa	tccaaccaat	tttcattaat	tcaggcatat	tttaactcca	ctgcttacct	3900
actttcttca	ggtaaaaggg	caaataatga	tcgaaaaaat	aattatttat	tacataattt	3960
agttgtttct	agactataaa	tggtgctatg	tgccttatgt	tgaaaaaatt	taaaagtaaa	4020
atgtctttcc	aaattatttc	ttaattatta	taaaaatatt	aagacaatag	cacttaaatt	4080
cctcaacagt	gttttcagaa	gaaataaata	taccactctt	tacctttatt	gatatctcca	4140
tgatgatagt	tgaatgttgc	aatgtgaaaa	atctgctggt	aactgcaacc	ttgtttatta	4200
aattgcaaga	agctttattt	ctagcttttt	aattaagcaa	agcaccatt	tcaatgtgta	4260
taaattgtct	ttaaaaactg	ttttagacct	ataatccttg	ataatatatt	gtgttgactt	4320
tataaatttc	gcttcttaga	acagtggaaa	ctatgtgttt	ttctcatatt	tgaggagtgt	4380
taagattgca	gatagcaagg	tttggtgcaa	agtattgtaa	tgagtgaatt	gaatggtgca	4440
ttgtatagat	ataatgaaca	aaattatttg	taagatattt	gcagtttttc	attttaaaaa	4500
gtccatacct	tatatatgca	cttaatttgt	tggggcttta	catactttat	caatgtgtct	4560
ttctaagaaa	tcaagtaatg	aatccaactg	cttaaagttg	gtattaataa	aaagacaacc	4620
acatagttcg	tttaccttca	aacttttaggt	ttttttaatg	atatactgat	cttcattacc	4680
aataggcaaa	ttaatcacc	taccaacttt	actgtcctaa	catggacttt	caaaaagaaa	4740
aaatgacacc	atcttttatt	cttttttttt	tttttttttt	gagagagagt	cttactctgc	4800
cgcccaaact	ggagtgcagt	ggcacaaatct	tggctcactg	caacctctac	ctcctggggt	4860
caagtgattc	tcttgccctca	gcctcccagag	ttgctgggat	tgcgggcatg	gtggcgtgag	4920
cctgtagtcc	tagctactcg	ggaggctgag	gcaggagaat	agcctgaacc	tgggaatcgg	4980
aggttgcagg	gccaagatcg	ccccactgca	ctccagcctg	gcaatagacc	gagctccgtc	5040
tccaaaaaaa	aaaataacaat	ttttatttct	tttacttttt	ttagtaagtt	aatgtatata	5100
aaaatggctt	cggacaaaat	atctctgagt	tctgtgtatt	ttcagtcaaa	actttaaac	5160
tgtagaatca	atttaagtgt	tgaaaaaaat	ttgtctgaaa	catttcataa	tttgtttcca	5220

ADS5001.ST25.txt

gcatgaggta tctaaggatt tagaccagag gtctagatta atactctatt tttacattta	5280
aaccttttat tataagtctt acataaacca tttttgttac tctcttcac atgttactgg	5340
ataaattggt tagtggaata taggcttttt aatcatgaat atgatgacaa tcagttatac	5400
agttataaaa ttaaaagttt gaaaagcaat attgtatatt tttatctata taaaataact	5460
aaaatgtatc taagaataat aaaatcacgt taaacc	5496

<210> 2
 <211> 1737
 <212> DNA
 <213> Human

<400> 2	
gtggtcacct tccccagcta gaaagccttc tttttatata aacttccttt taattatgaa	60
gtattacaat caagcataaa gacataataa atgttaacat ctttcctttg tgtctgttta	120
aaaaatgttt cttattacag aaaatttcaa atagatttaa agtagagaaa tgcacgtgat	180
gaaaccccat gcacttgcca ttccatttca atagttatta cttcacggaa gagttggcaa	240
tgatgagaac atgtcaaaca cctggaaatt cctgtctcat tcaacagact cactaaataa	300
aatcagcaag gtcaatgagt caacagaatc acttactgat gagggtagag acatgaatga	360
aggacaacta ctgggagact ttgagattga gtccaaacag ctggaagcag agtcttggag	420
tcggataata gacagcaagt ttctaaaaca gcaaaagaaa gatgtggtca aacggcaaga	480
agtaatatat gagttgatgc agacagagtt tcatcatgtc cgactctca agatcatgag	540
tggtgtgtac agccagggga tgatggcaga tctgcttttt gagcagcaga tggtagaaaa	600
gctgttcccc tgtttggtatg agctgatcag tatccatagc caattcttcc agaggattct	660
ggagcggag aaggagtctc tgggtggataa aagtgaaaag aactttctca tcaagaggat	720
aggggatgtg cttgtaaatc agttttcagg tgagaatgca gaacgtttaa agaagacata	780
tggcaagttt tgtgggcaac ataaccagtc tgtaaaactac ttcaaagacc tttatgccaa	840
ggataagcgt tttcaagcct ttgtaaagaa gaagatgagc agttcagttg ttagaaggct	900
tggaattcca gagtgcataat tgcttgtaac tcagcggatt accaagtacc cagttttatt	960
ccaaagaata ttgcagtgtc ccaaagacaa tgaagtggag caggaagatc tagcacagtc	1020
cttgagcctg gtgaaggatg tgattggagc tgtagacagc aaagtggcaa gttatgaaaa	1080
gaaagtgcgt ctcaatgaga tttatacaaa gacagatagc aagtcaatca tgaggatgaa	1140
gagtggtcag atgtttgcca aggaagattt gaaacggaag aagcttgtag gtgatgggag	1200
tgtgtttctg aagaatgcag caggaagggtt gaaagagggt caagcagttc ttctcactga	1260
catttttagtt ttcttcaag aaaaagacca gaagtacatc tttgcatcat tggaccagaa	1320
gtcaacagtg atctctttaa agaagctgat tgtgagagaa gtggcacatg aggagaaagg	1380

ADS5001.ST25.txt

tttattcctg atcagcatgg ggatgacaga tccagagatg gtagaagtcc atgccagctc	1440
caaagaggaa cgaaacagct ggattcagat cattcaggac acaatcaaca ccctttccgg	1500
gaatggatgg aggtgcttta actgatgcga gtctcacaga gtcctatttc agcaccagct	1560
ttattggagt caatggattt ggaagccctg tagaaacaaa gtatcccttg atgcagtaca	1620
ctctggttgt cttccaacgt cttcgggtct gcacctctgg attcagcaat accaaaaaca	1680
ccggccccc aacttcccac ctacttgaac caataaactt cctcttgtgt ttaaact	1737

<210> 3
 <211> 1051
 <212> DNA
 <213> Human

<220>
 <221> misc_feature
 <222> (23)..(23)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (26)..(26)
 <223> n=any nucleotide

<400> 3	
agtaaatacag gtaggaaatc acnttngwyt twkcttccag tagtcattac caccttttac	60
tgcacaattc acaagcatgt tttcctggtg aattggactg aaaattacat tttgacaact	120
ttttttcctt ttatcccaa cttttgccag aaagcagaaa aatgctctat tttataaag	180
aaagattaaa ttctccaatg atattttaaa aaatatcaac ctacatgccc tttagaatgt	240
taaataacaa tgactatttt aagactcgaa gaccactat tttgagtatt ttttatagac	300
tttaaatact gggttttttt cctccttcaa tctcaggctt ttctccatct ttttaagcggc	360
ctctgtkact cccttttgtc catagggtgtt gcgtgcctct catctgtggg gaagtattat	420
ttaataaaat ttatgttaca ggataacttt attttaatgg gcatgggctt gtctatacac	480
aaaggatatgt atattttcat tataaaaaac cagtttaaaa ttttttctta ttttaattgt	540
ttgaaatttt tctagagcca aagaagctct ttaaagaagt tgtttcttcc aaagaacaaa	600
gccagggttaa tgacattcaa ttctaaatga tacattggaa ttgtgccttt tctaccacac	660
tggattaaat aaacttgtca aaatatgggt ttgtcatttt ctgagacact tggtaatttg	720
ctgttctttc tttcatgtgc ccgtagtac atttggccaa ctgamcdkct gtaacaggga	780
ggctctcatgt ttgttagtag atacgcagggt aagggraactt gaattcatcc tctcctcggc	840
tcaggctcttt gcttttcttt taatatatgc atataaaata gtaggcattt gattctgcsa	900
aggcactaga ctacttgaaw ttaacattct gtccagaggg ataataccag gctttccttt	960
tccttcatct gttgtaagtt tcaggtcctt gacagaaata gctggactat tccaaatttg	1020

ADS5001.ST25.txt

ctcagtgcac caaatgtgma aagggagcgg a 1051

<210> 4
 <211> 1098
 <212> DNA
 <213> Human

<400> 4
 ggccgcgtcg aagccgaaat gccgccaccc cggaccggcc gaggccttct ctggctgggt 60
 ctggttctga gctccgtctg cgtcgccctc ggatccgaaa cgcaggccaa ctcgaccaca 120
 gatgctctga acgttcttct catcatcgtg gatgacctgc gccctccctt gggctgttat 180
 ggggataagc tgggtgaggtc cccaaatatt gaccaactgg catcccacag cctcctcttc 240
 cagaatgcct ttgctgcagca agcagtgtgc gccccgagcc gcgtttcttt cctcactggc 300
 aggagacctg acaccacccg cctgtacgac ttcaactcct actggagggt gcacgctgga 360
 aacttctcca ccatcccccga gtacttcaag gagaatggct atgtgaccat gtcgggtggga 420
 aaagtctttc accctgggtac tgctccatgt ccagagtctg ggttctcttg gtttgtgggtg 480
 tctgaatcca gcattcccat cctgggggatg gggctgtctt tgcagagccc tcttctggct 540
 gggcgagtcc ctcgctagtc agtgcttcct ttctaaaaaa ctgacttgtc aaccagcca 600
 cgtttttcacc caaagtgaaa aagggtagaa agagctttgc ttcctttcag aaaccactga 660
 ggggtgtgctg ttgggtcttt cagctcctcg ggtggtaggg aggacacagg ctggggaggt 720
 ggcagtgttg ggtggagtcc agctcagggc cccaccctct cccctgcagg gtacctgtca 780
 gtaaacctag ggggtgggtg aggacacctg agggcctccc gtgtggccag cattgctgtt 840
 gctgacttat tgcccaatga gggggctgtg cttaggtagg ggctgctatc cactctggaa 900
 attaagtcag aaagatgagt gtaatctggt acccaggatc tatagggtcc cagagacgga 960
 cattccttac ctcaaagtct gcctgataaa ctggctctct ttaatgcaa tatggggata 1020
 gtgaaaagca aacaaacttt aaaacttttt atttatagaa gtaatgcatg agtatttgag 1080
 aaaaaaaaaa aaaaaaaaaa 1098

<210> 5
 <211> 2110
 <212> DNA
 <213> Human

<400> 5
 cgagccccgc cgcaagctga gcgcctccgc ccgccaggcg cgccggcgcc gggccatgta 60
 ctcggggaac cgcagcggcg gccacggcta ctgggacggc ggcggggccg cgggcgctga 120
 ggggccggcg ccggcgggga cactgagccc cgcgcccctc ttcagccccg gcacctacga 180
 gcgcctggcg ctgctgctgg gctccattgg gctgctgggc gtcggcaaca acctgctggt 240
 gctcgtcctc tactacaagt tccagcggct ccgcactccc actcacctcc tcctgggtcaa 300

ADS5001.ST25.txt

catcagcctc agcgacctgc tgggtgtccct cttcgggggtc accttttacct tcgtgtcctg	360
cctgaggaac ggctgggtgt gggacaccgt gggctgcgtg tgggacgggt ttagcggcag	420
cctcttcggg attgtttcca ttgccaccct aaccgtgctg gcctatgaac gttacattcg	480
cgtgggtccat gccagagtga tcaatttttc ctgggcctgg agggccatta cctacatctg	540
gctctactca ctggcgtggg caggagcacc tctcctggga tggaacaggt acatcctgga	600
cgtacacgga ctaggctgca ctgtggactg gaaatccaag gatgccaacg attcctcctt	660
tgtgcttttc ttattttctg gctgcctggg ggtgcccctg ggtgtcatag cccattgcta	720
tggccatatt ctatattcca ttcgaatgct tcgttgtgtg gaagatcttc agacaattca	780
agtgatcaag attttaaaat atgaaaagaa actggccaaa atgtgctttt taatgatatt	840
caccttcctg gtctgttgga tgccttatat cgtgatctgc ttcttggtgg ttaatgggtca	900
tggtcacctg gtcactccaa caatatctat tgtttcgtac ctctttgcta aatcgaacac	960
tgtatacaat ccagtgattt atgtcttcat gatcagaaag tttcgaagat cccttttgca	1020
gcttctgtgc ctccgactgc tgaggtgcca gaggcctgct aaagacctac cagcagctgg	1080
aagtgaaatg cagatcagac ccattgtgat gtcacagaaa gatggggaca ggccaaagaa	1140
aaaagtgact ttcaactctt cttccatcat ttttatcatc accagtgatg aatcactgtc	1200
agttgacgac agcgacaaaa ccattggggg ccaaagtttg atgttaatcc aagttcgtcc	1260
tttgtaggaa tgaaggatgg caacgaaagg tggggcctta aattggatgc cacttttgga	1320
ctttcatcat cctcctgaag aagaagtgtc tggaataccc gttctatgta atatcaacag	1380
aaccttgtgg tccagcagga aatccgaatt gcccatatgc tcttgggcct caggaagagg	1440
ttgaacaaaa acaaattctt ttaattcaac ggggtgcttta cataatgaaa aaaccacttg	1500
tgcacacgat gggcatctaa catcatcatc ttctaattgtg ttggagattt tcatttcaaa	1560
tatatTTTTT aaattactct attttccaaa acacgtaatg catttttctc gaaaatacct	1620
tactgtaaaa ataactgtcg cgtacacatg tgtgaagtag ctagaacata ctgaattttt	1680
tttgtactgt tggactctat tcagtgtcat gtcctatatc tgatcaagtt atcaaggaga	1740
taattctaga atgaaaaaga aaatcctctt gttggaaaca aaagacgttt tatatgtgca	1800
gtatgacaaa gaggagtttc agagacaact ttgaatcctt gtcagcctgg agaccagcac	1860
cagaggaatc tacaaggcaa actcccatat atttgcttcc ccaaattgc tgcccctaca	1920
gactcaaagc tctttttctt tgttttgttg tttctctaaa aatttactgt tctttgtcga	1980
tgctatataa gccagggagt tctaagacgc cagctctttg agatttgctc attcccctgt	2040
atttcccaca tatatattac atatacccg c taataaattt atgtttgttt taaaaaaaaa	2100
aaaaaaaaaa	2110

ADS5001.ST25.txt

<210> 6
 <211> 2416
 <212> DNA
 <213> Human

<400> 6
 gaacagtgtt accttggagc ctacaatgag aggtatttca aaatgagtga agcatgactc 60
 tcacagatga aggcctagac gcaggatctt taatggaaaa acacttgggc cacttcaaga 120
 cgacaaacgc tcaactgggca aaacaccttc actgaaaaga gacctcatat tatgcaaaaa 180
 aaatcttaag aggcctctgc cttcagaagt tacaagatga tcaattcaac ctccacacag 240
 cctccagatg aatcctgctc tcagaacctc ctgatcactc agcagatcat tcctgtgctg 300
 tactgtatgg tcttcattgc gggaatccta ctcaatggag tgtcaggatg gatattcttt 360
 tacgtgccca gctctaagag tttcatcatc tatctcaaga acattgttat tgctgacttt 420
 gtgatgagcc tgacttttcc tttcaagatc cttggtgact caggccttgg tccctggcag 480
 ctgaacgtgt ttgtgtgcag ggtctctgcc gtgctcttct acgtcaacat gtacgtcagc 540
 attgtgttct ttgggctcat cagctttgac aggtattata aaattgtaaa gcctctttgg 600
 acttctttca tccagtcagt gagttacagc aaacttctgt cagtgatagt atggatgctc 660
 atgctcctcc ttgctgttcc aaatattatt ctaccaacc agagtgttag ggaggttaca 720
 caaataaaat gtatagaact gaaaagtga ctgggacgga agtggcacia agcatcaaac 780
 tacatcttcg tggccatctt ctggattgtg tttcttttgt taatcgtttt ctatactgct 840
 atcaciaaga aaatctttta gtcccacctt aagtcaagtc ggaattccac ttcggtcaaa 900
 aagaaatcta gccgcaacat attcagcatc gtgtttgtgt tttttgtctg ttttgtacct 960
 taccatattg ccagaatccc ctacacaaag agtcagaccg aagctcatta cagctgccag 1020
 tcaaaagaaa tcttgcggtg tatgaaagaa ttcactctgc tactatctgc tgcaaatgta 1080
 tgcttggacc ctattattta tttctttcta tgccagccgt ttagggaaat cttatgtaag 1140
 aaattgcaca ttccattaaa agctcagaat gacctagaca tttccagaat caaaagagga 1200
 aatacaacac ttgaaagcac agatactttg tgagttccta ccctcttcca aagaaagacc 1260
 acgtgtgcat gttgtcatct tcaattacat aacagaaatc aataagatat gtgccctcat 1320
 cataaatatc atctctagca ctgccatcca atttagttca ataaaattca aatataagtt 1380
 tccatgcttt tttgtaacat caaagaaaac atacccatca gtaattttct taatactgac 1440
 ctttctattc tctattaata aaaaattaat acatacaatt attcaattct attatattaa 1500
 aataagttaa agtttataac cactagtctg gtcagttaat gtagaaattt aaatagtaaa 1560
 taaaacacaa cataatcaaa gacaactcac tcaggcatct tctttctcta aataccagaa 1620
 tctagtatgt aattgttttc aacactgtcc ttaaagacta acttgaaagc aggcacagtt 1680
 tgatgaaggg ctagagagct gtttgcaata aaaagtcagg ttttttctct gatttgaaga 1740

ADS5001.ST25.txt

```

agcaggaaaa gctgacaccc agacaatcac ttaagaaacc ccttattgat gtattttcatg 1800
gcactgcaaa ggaagaggaa tattaattgt atacttagca agaaaatttt ttttttctga 1860
tagcactttg aggatattag atacatgcta aatatgtttt ctacaaagac ttacgtcatt 1920
taatgagcct ggggttctgg tgttagaata tttttaagta ggctttactg agagaaacta 1980
aatattggca tacgttatca gcaacttccc ctgttcaata gtatgggaaa aataagatga 2040
ctgggaaaaa gacacacca caccgtagaa catatattaa tctactggcg aatgggaaag 2100
gagaccatth tcttagaaag caaataaact tgattttttt aaatctaaaa tttacattaa 2160
tgagtgcaaa ataacacata aaatgaaaat tcacacatca catttttctg gaaaacagac 2220
ggattttact tctggagaca tggcatacgg ttactgactt atgagctacc aaaactaaat 2280
tcttttctctg ctattaactg gctagaagac attcatctat ttttcaaag ttctttcaaa 2340
acatttttat aagtaatgtt tgtatctatt tcatgcttta ctgtctatat actaataaag 2400
aatgttttta atactg 2416

```

```

<210> 7
<211> 3763
<212> DNA
<213> Human

```

```

<400> 7
acttccaagt tctggtacaa ggcggatatt tcaagagaac aagccatcgc catgttgaag 60
gacaaggagc cgggctcatt cattgttcga gacagccatt ccttccgagg ggcttatggc 120
ctggccatga aggtggccac gccccacct tcagtcctgc agctgaacaa gaaagctgga 180
gatttgcca atgaactcgt ccggcacttt ttgatcgagt gtaccccgaa gggagtgcgg 240
ttgaaagggg gctcgaatga accatatttc gggagcctga cggccttggt gtgccagcat 300
tccatcacgc ccttggcctt gccgtgcaag ctgcttatcc cagagagaga tccattggag 360
gaaatagcag aaagtctctc ccagacggca gccaattcag cagctgagct gttgaagcag 420
ggggcagcct gcaacgtgtg gtacttgaac tctgtggaga tggagtccct caccggccac 480
caggcgatcc agaaggccct gagcatcacc ctggtccagg agcctccacc tgtgtccaca 540
gttgtgcact tcaaggtgtc agcccagggc atcaccctga cagacaatca gaggaagctc 600
ttcttccgga ggcattaccc cgtgaacagt gtgattttct gtgccttgga cccacaagac 660
aggaagtgga tcaaagatgg cccttcctca aaagtctttg gatttgtggc ccggaagcag 720
ggcagtgcc cggataatgt gtgccacctg tttgcagagc atgaccctgt gcagcctgcc 780
agtgccattg tcaacttcgt atcaaaggtc atgattgggt ccccaaagaa ggtctgagaa 840
ctccccctcc tccctggacc caccgatgcc tctcgaagcc ctggagacag ccgttgggtg 900
agggtggggc cccactttt taccaaacta gtaaacctga cattccaggc ccatgagggg 960
aaagaggatc ttccagctct gcaaaaacaa gaacaaacaa catcaccgtg aattggcctt 1020

```

ADS5001.ST25.txt

tcctgaaagt gacttatctg acacatctct gtagccacat gctttttggg tagaagaagc	1080
tgggcatggg tgcacccccc cccctagggg ccccatggga aagggacatg caaggaaaca	1140
gcacagaaca cgagggtggc cccatgtccc tggcacacta gcattctggg ggatgaggaa	1200
tccccagccc ttgaggcaga ggtgccgagt gactgccatg cttcgcccgt ccgcatgggc	1260
gcttctgtcc agctgcaccc gagggccggg gtttccctca cctcgggtctt cccaagatgg	1320
agatgctaac gaaactgaga agggggcgta tgtttgacga aggtttgtgc aagtcaggcc	1380
cttctggaac acagcagggc ctacaacgag gggcctttgc gatgggctgt gaggatgggg	1440
gtggtgggaa gaattggcca cgtagagac cccatgccac cccaccatgg tgagtgtctt	1500
gtgcctcctg ctcacctgtg gtgagctggg cgagctgggc gagctgggcg agctgggctg	1560
gggagagcct gtgaggaccg agaggagaaa tgagaagaag gaacaaaaat attatttcta	1620
tgtaatttat attttactta tgccaaatta tttatgataa tttgccattg ctatactgta	1680
ccagtgtcaa atgctgcagc ctgccaagct gtgattttgt gaggcttgtc cctatgtagg	1740
atgcaccgca ggccccctgg cactgaaaga gtgtgcagtg gactgtgggt ctcccatatg	1800
cggtgccgcc caaagggtgg tttgcctcaa gcaacctacc ctgatgtttt actcattgga	1860
atgtttttcc ccgattgtgg atgacttctt ttctgatgga gagagtccag gagggatgga	1920
aaactcctgg atttaagctc agcatcccc acatgggctt ttcgatcatc ttcaggcctg	1980
aagctgcacg acctgaagtt cgctgcatt tatcagccct tttgtgctgc tccttgccac	2040
cttgggggtc ctgctgggga ccatgtgtgg ttgtggcatg tgtgagcaga agggaggatg	2100
aggaaaaaga gaagaaaccc cggtactgac aagctgtttt tgagtgccac tgtttgccat	2160
catctaagcc actgaatcaa gtgtatttca ggcttatttc aacattccaa tgccctgggt	2220
ttcctgcttg aatctgttcg tggtaaagg tttgggggaa tttgtgacct tggaccatcc	2280
ccagagtgaag agatggagct gggccacatc agaataaggc cttggcccca tcctctcaca	2340
gcctaggtgc tctgcaggca tactgactgt cctgattgcg atccagcccc aaattccctc	2400
ctctgctttc aaaagtcaaa tccccattc ttaggccaca ctggtgtcac aagctcctgt	2460
caggagctg gggtttggga atgtgctttg tgaactctgc tttaaagtga ggggcccagg	2520
aaaacttaga aacaggcaga gttggaagca gccaaatcac agtgggtgtt gtgtgtgtgt	2580
gcgtgtgtgc atgcgtgct gtatgcgtgt gtgaaagcag gtggaccatt ccacttttta	2640
gctcctattg atgcaccaa ccaagtgcct ctttctgtg ccaaagtgtt gccttggtcg	2700
tcgtggacct ctttctctaa cttgagggtg catgactgtc aggaggtgct ggcattttca	2760
gcagatcctc atgtgttgac cctgatgtct ttagcagagg cctctagcat ctcggttttt	2820
catccactgc aggaatgtgg ccacaggag cagaggtttg tactttccc aagaggtcct	2880
catcctgaga cggctctctac ccatgtttta ccaaagagt gcaggccagg ttccttatcc	2940

ADS5001.ST25.txt

```

ttctgatgaa ggatgagaga gctcatttag aagtcagagc aaactagggt ctcagtattg 3000
agaaacgcag cctgccaggg aatcacagag acatcggggg gcccgcgatg gccctcatga 3060
agccatgcct cgacggcatt caggaagccc tgcaaactg ctttttgaac tcattggcca 3120
ggtgtgattt ttacacaagg taaacgtggt caagggcatc ggggaatttg ctccaagcag 3180
atagctccct ctgaggaacc aaaggaagca agtttccatg atttctgaag agctggtata 3240
ggaagtttct ttcttccttt tgtgttacat gtgcattaaa cagaacaagc tgtgtgtcat 3300
cacagattgt actgtgggct cagaaaccgt gagagagccc ccaccgtgga caccggctct 3360
atggccacag gaaaaggaac gtttccaggg attttgtctc cagggctccc gctggacagg 3420
cacgtactgc cccggggagt aaatgcggag agttcacgaa ctgtgcccaa cgcattgttat 3480
agccagggtc ctactaacta ctcagtaaaa gaacgtattg ttgtattcct ccagtgttaa 3540
gctatagcca tgttaaaagt cactgtgcat ttattctcag catcaaatac cttgtaacgt 3600
cttctctgcc ttgttagtgc atatttttac ttttctgata ctgtaaagaa tatatccagt 3660
atgtaaata gaatgttctata aatcttttgt atagtcattt tctctgctcc ttaaataatca 3720
tctctattca gagtataata aaattatgaa cttggttaagc ctc 3763

```

```

<210> 8
<211> 1684
<212> DNA
<213> Human

```

```

<400> 8
cgacggagtg ccaggagcac taacagtacc cttagcttgc tttcctcctc cctccttttt 60
attttcaagt tcctttttat ttctccttgc gtaacaacct tcttcccttc tgcaccactg 120
cccgtaccct taccgcgccc gccacctct tgctacccca ctcttgaaac cacagctgtt 180
ggcagggtcc ccagctcatg ccagcctcat ctcttttctt gctagcccc aaagggcctc 240
caggcaacat gggggggcca gtcagagagc cggcactctc agttgccctc tggttgagtt 300
ggggggcagc tctgggggccc gtggcttgtg ccatggctct gctgacccaa caaacagagc 360
tgcagagcct caggagagag gtgagccggc tgcaggggac aggaggcccc tcccagaatg 420
gggaagggtg tccctggcag agtctcccgg agcagagtcc cgatgccctg gaagcctggg 480
agaatgggga gagatcccgg aaaaggagag cagtgtcac ccaaaaacag aagaatgact 540
ccgatgtgac agaggtgatg tggcaaccag ctcttaggcg tgggagaggc ctacaggccc 600
aaggatatgg tgtccgaatc caggatgctg gagtttatct gctgtatagc caggctcctgt 660
ttcaagacgt gactttcacc atgggtcagg tgggtgtctcg agaaggccaa ggaaggcagg 720
agactctatt ccgatgtata agaagtatgc cctcccaccc ggaccgggcc tacaacagct 780
gctatagcgc aggtgtcttc catttacacc aaggggatat tctgagtgtc ataattcccc 840

```

ADS5001.ST25.txt

```

gggcaagggc gaaacttaac ctctctccac atggaacctt cctgggggttt gtgaaactgt    900
gatttgtgta taaaaagtgg ctcccagctt ggaagaccag ggtgggtaca tactggagac    960
agccaagagc tgagtatata aaggagaggg aatgtgcagg aacagaggcg tcttcctggg   1020
tttggtcccc cgttcctcac ttttcccttt tcattcccac cccctagact ttgattttac   1080
ggatatcttg cttctgttcc ccatggagct ccgaattctt gcgtgtgtgt agatgagggg   1140
cgggggacgg gcgccaggca ttgttcagac ctggtcgggg cccactggaa gcatccagaa   1200
cagcaccacc atctagcggc cgctcgaggg aagcaccgcg cggttgggcg aagtccacga   1260
agccgccctc tgctagggaa aacccttggg tctccatgcc acacctctct ccaggtgccc   1320
tctgcctctt caccacacaa gaagccttat cctacgtcct tctctccatc tatcggaccc   1380
cagtttccat cactatctcc agagatgtag ctattatgcg cccgtctaca gggggtgccc   1440
gacgatgacg gtgccttcgc agtcaaatta ctcttcgggt cccaagggtt ggctttcacg   1500
cgctccattg ccccggcgtg gcaggccatt ccaagccctt ccgggctgga actggtgtcg   1560
gaggagcctc ggggtgtatcg tacgccctgg tgttgggtgt gcctcactcc tctgagctct   1620
tctttctgat caagccctgc ttaaagttaa ataaaataga atgaatgata aaaaaaaaaa   1680
aaaa                                           1684

```

```

<210> 9
<211> 6719
<212> DNA
<213> Human

```

```

<400> 9
tcggcgggaa gcggcgatcc tgccaccggg aggtgtggaa gagccgggta gattctggct    60
acattggaga ttggttgctt tctaaaactg aaggagaagc ccatgaagag atggtggatt   120
ctcactgagt tttgactagc ggaagaaaag agagagttca agtggatggc cttgaggact   180
tgaaaagctg agatatgatg attttgaagt catttcacat cgaagccatg atttaaatat   240
cggcgттаag atttcaacaa gaaaaactta agcttccttg gattcccacg tcaaaggaaa   300
gtttcaagct ttcagaagga gttctcactc gaagataaag aacagctcgc taaccacgaa   360
agaggaatcg atgctcagct tttagttgca cttcctaaag ttgcagaatt aagacaaatc   420
tttgaaccaa agaagaaaga attcttagaa atgaaaagaa aagaaagaat tgccaggcgc   480
ctggaagggg ttgaaaatga cactcagccc atcctcttgc agagctgcac aggattggtg   540
actcaccgcc tgctggagga agacaccctt cgatacatga gagccagcga ccctgccagc   600
ccccacatcg gccgatcaaa tgaagaggag gaaacttctg attcttctct agaaaagcaa   660
actcgatcca aatactgcac agaaacctcc ggtgtccacg gtgactcacc ctatggttcg   720
ggtaccatgg acaccacag tctggagtcc aaagccgaaa gaattgcaag gtacaaagca   780
gaaagaaggc gacagctggc agagaagtat gggctgactc tggatcccga ggccgactcc   840

```

ADS5001.ST25.txt

gagtatttat	cccgctatac	caagtccagg	aaggagcctg	atgctgtcga	gaagcgggga	900
ggaaaaagtg	acaaacagga	agagtcaagc	agagatgcga	gttctctgta	ccccgggacc	960
gagacgatgg	ggctcaggac	ctgtgccggt	gaatccaagg	actatgccct	ccatgtgggt	1020
gacggctctt	ccgacccgga	ggtgctgctg	aacatagaaa	accaaagacg	aggtcaagag	1080
ctgagtgcc	cccggcaggc	ccatgacctg	tccccagcag	ccgagagttc	ctcgaccttc	1140
tctttctctg	ggcgagactc	ctccttcact	gaagtgccac	ggtcccccaa	gcacgcccac	1200
agctcctccc	tgcagcaggc	agcctcccgg	agccccctct	ttggtgacct	acagctatcc	1260
cctgaggccc	gacccagggtg	catttcacat	tcagaaacgc	caactgtcga	tgatgaagaa	1320
aagggtggatg	aacgagccaa	gctgagcgtc	gccgccaaga	ggttgctttt	caggagatg	1380
gaaaaatctt	ttgatgaaca	aaatgttcca	aagcgacgct	caagaaacac	agctgtggag	1440
cagaggctac	gccgtctgca	ggacagggtcc	ctcaccacgc	ccatcaccac	tgaagagggtg	1500
gtcatcgcag	ccacattgca	ggcctctgct	caccaaagg	ccttagccaa	ggaccagaca	1560
aatgagggca	aagagcttgc	tgagcaagga	gaacctgatt	cctccactct	aagcttggcc	1620
gaaaagttag	ccttgtttaa	caaattgtcc	cagccagtct	caaaagcgat	ttctacccgg	1680
aacagaatag	acacgagaca	gaggagaatg	aacgctcgct	atcaaactca	gccagtcaca	1740
ctgggagagg	tggagcaggt	gcagagtgg	aagctcattc	ctttctcacc	tgccgtgaac	1800
acatcagtgt	ctaccgtagc	atccacgggt	gctccaatgt	atgccggaga	tcttcgcaca	1860
aagccacctc	ttgaccacaa	tgcaagtgcc	actgactata	agttttcttc	ttcaatagaa	1920
aattcggact	ctccagttag	aagcattctg	aaatcgcaag	cttggcagcc	tttggttagag	1980
ggtagcgaga	acaaggggaat	gttgagagaa	tatggagaga	cagaaagcaa	gagagctttg	2040
acaggtcgag	acagtgggat	ggagaagtat	gggtcctttg	aggaagcaga	agcatcctac	2100
cccatcctga	accgagccag	ggaaggagac	agccataagg	aatctaaata	tgctgttccc	2160
agaagaggaa	gcctggaacg	ggcgaaccct	cccatcacc	acctcgggga	tgaaccgaag	2220
gaattttcca	tggctaaaat	gaatgcacaa	ggaaacttgg	acttgaggga	caggctgccc	2280
tttgaagaga	aggtggaggt	ggagaatgtt	atgaaaagga	agttttcact	aagagcggca	2340
gagttcgggg	agcccacttc	cgagcagacg	gggacagctg	ctgggaaaac	tattgctcaa	2400
accacagccc	ccgtgtcctg	gaagccccag	gattcttcgg	aacagccaca	ggagaagctc	2460
tgcaagaatc	catgtgcgat	gtttgctgct	ggagagatca	aaacgccgac	aggggagggc	2520
cttcttgact	caccagcaa	aaccatgtct	attaaagaaa	gattggcact	gttgaagaaa	2580
agcggggagg	aagattggag	aaacagactc	agcaggaggc	aggagggcgg	caaggcgccg	2640
gccagcagcc	tgacaccca	ggaagcaggg	cggtccctca	tcaagaagcg	ggtcacagaa	2700
agtcgagaga	gccaaatgac	gattgaggag	aggaagcagc	tcactactgt	gagagaggag	2760

ADS5001.ST25.txt

gcctggaaga	cgagaggcag	aggagcggcc	aacgactcga	cccagttcac	tgtggctggc	2820
aggatggtga	agaaaggttt	ggcgtcacct	actgccataa	ccccagtagc	ctcagccatt	2880
tgcggtaaaa	caagaggcac	cacacccgtt	tccaaacccc	tggaagatat	cgaagccaga	2940
ccagatatgc	agttagaatc	ggacctgaag	ttggacaggc	tggaaacctt	tctaagaagg	3000
ctgaataaca	aagttggcgg	gatgcacgaa	acggtgctca	ctgtcaccgg	caaattctgtg	3060
aaggaggtga	tgaagccaga	tgatgatgaa	acctttgcc	aattttaccg	cagcgtggat	3120
tataatatgc	caagaagtcc	tgtggagatg	gatgaggact	tcgatgtcat	tttcgatcct	3180
tatgcacca	aattgacgtc	ttccgtggcc	gagcacaagc	gggcagttag	gccaagcgc	3240
cgggttcagg	cctccaaaaa	ccccctgaaa	atgctggcgg	caagagaaga	tctccttcag	3300
gaatacactg	agcagagatt	aaacgttgcc	ttcatggagt	caaagcggat	gaaagtagaa	3360
aagatgtctt	ccaactccaa	cttctcagaa	gtcaccctgg	cgggttttagc	cagtaaagaa	3420
aacttcagca	acgtcagcct	gcggagcgtc	aacctgacgg	aacagaactc	taacaacagc	3480
gccgtgccct	acaagaggct	gatgctggtg	cagattaaag	gaagaagaca	tgtgcagacc	3540
aggctggtgg	aacctcgagc	ttcggcgctc	aacagtgggg	actgcttcct	cctgctctct	3600
ccccactgct	gcttcctgtg	ggtaggagag	tttgcaaacg	tcatagaaaa	ggcgaaggcc	3660
tcagaacttg	caactttaat	tcagacaaag	agggaacttg	gttgtagagc	tacttatatc	3720
caaaccattg	aagaaggaat	taatacacac	actcatgcag	ccaagactt	ctggaagctt	3780
ctgggtggcc	aaaccagtta	ccaatctgct	ggagacccaa	aagaagatga	actctatgaa	3840
gcagccataa	tagaaactaa	ctgcatttac	cgtctcatgg	atgacaaact	tgttcctgat	3900
gacgactact	gggggaaaat	tccgaagtgc	tcccttctgc	aacccaaaga	ggtactggtg	3960
tttgattttg	gtagtgaagt	ttacgtatgg	catgggaaag	aagtcacatt	agcacaacga	4020
aaaatagcat	ttcagctggc	aaagcactta	tggaatggaa	cctttgacta	tgagaactgt	4080
gacatcaatc	ccctggatcc	tggagaatgc	aatccgctta	tccccagaaa	aggacagggg	4140
cggcccgaact	gggcgatatt	tgggagactt	actgaacaca	atgagacgat	tttgttcaaa	4200
gagaagtttc	tggattggac	ggaactgaag	agatcgaatg	agaagaaccc	cggggaactt	4260
gcccagcaca	aggaagaccc	caggactgat	gtcaaggcat	acgatgtgac	acggatggtg	4320
tccatgcccc	agacgacagc	aggcaccatc	ctggacggag	tgaacgtcgg	ccgtggctat	4380
ggcctggtgg	aaggacacga	caggaggcag	tttgagatca	ccagcgtttc	cgtggatgtc	4440
tggcacatcc	tggaattcga	ctatagcagg	ctccccaac	aaagcatcgg	gcagttccat	4500
gaggggggatg	cctatgtggt	caagtggaag	ttcatggtga	gcacggcagt	gggaagtcgc	4560
cagaagggag	agcactcggt	gagggcagcc	ggcaaagaga	agtgcgtcta	cttcttctgg	4620
caaggccggc	actccaccgt	gagtgagaag	ggcacgtcgg	cgctgatgac	ggtggagctg	4680

ADS5001.ST25.txt

gacgaggaaa ggggggcccc ggtccagggt ctccagggaa aggagcccc ctgtttcctg	4740
cagtgtttcc aggggggggat ggtggtgcac tcggggaggc ggaagagga agaagaaat	4800
gtgcaaagtg agtggcggct gtactgcgtg cgtggagagg tgcccgtgga agggaatttg	4860
ctggaagtgg cctgtcactg tagcagcctg aggtccagaa cttccatggt ggtgcttaac	4920
gtcaacaagg ccctcatcta cctgtggcac ggatgcaaag cccaggcccc cacgaaggag	4980
gtcgggaagga ccgctgcgaa caagatcaag gaacaatgtc ccctggaagc aggactgcat	5040
agtagcagca aagtcacaat acacgagtgt gatgaaggct ccgagccact cggattctgg	5100
gatgccttag gaaggagaga caggaaagcc tacgattgca tgcttcaaga tcctggaagt	5160
tttaacttcg cggccgcct gttcatcctc agcagctcct ctggggattt tgcagccaca	5220
gagtttgtgt accctgcccc agccccctct gtggtcagtt ccatgccctt cctgcaggaa	5280
gatctgtaca gcgcgccccca gccagcactt ttccttgttg acaatcacca cgaggtgtac	5340
ctctggcaag gctggtggcc catcgagaac aagatcactg gttccgcccc catccgctgg	5400
gcctccgacc ggaagagtgc gatggagact gtgctccagt actgcaaagg aaaaaatctc	5460
aagaaaccag cccccaagtc ttaccttate cacgctggtc tggagcccct gacattcacc	5520
aatatgtttc ccagctggga gcacagagag gacatcgctg agatcacaga gatggacacg	5580
gaagtttcca atcagatcac cctcgtggaa gacgtcttag ccaagctctg taaaaccatt	5640
tacccgctgg ccgacctcct ggccaggcca ctcccggagg gggtcgatcc tctgaagctt	5700
gagatctatc tcaccgacga agacttcgag tttgcactag acatgacgag ggatgaatac	5760
aacgccctgc ccgcctggaa gcaggtgaac ctgaagaaag caaaaggcct gttctgagt	5820
gggagacgcc agaggagcct cacggtcacg tccaacaaca ccactgcacc agggaaatgg	5880
atatatatat ttggactggt gtttttcaca aagtattttt caatcagagt tttcagaacc	5940
tgacattggt aaagatactg cttgtcccgg agttgtgtat tttgtaaatg ttcaagggaa	6000
ctgtttggaa acttctttcc accattcagg aggttatcag aattaataaa agtatctgtt	6060
atgtgcactt aagccgcagc tgctatagat agcactgcct tcttgttcca gctaggcaat	6120
gccttttttt ttttttttga agcagttctc tttataaagt gttattttga tagtttgtgg	6180
attctaaaat atatatatat ttatataaac accatataag tcaaataatg atttaacaaa	6240
gcaatatgta ttcattcact ttcaagattt gttttggtgt caaaataaca tgaaaaggta	6300
gatggagttg cttctgttga attagctctg ccaccaatat gtatcttcat acacgtttgg	6360
aatgtttcc tgcagcatta ggtatgactt gttctgagta ctgcttccgg tgctaaaatg	6420
aacaaagaat ttgtacttaa tggcatggac tctggagaat ctatgcgaat caacctttct	6480
accttaatat ctccccaaaa atgtatagtg cttgtttttt atgtacagtt tatatacaga	6540
aaagtttgct ctgcattttt gatgatggtt tggaacatta tctacaattt tactctcaaa	6600

ADS5001.ST25.txt

tagtcaaaat aaaaacatct caattttctaa taccggttgt aaacaaacag tacacatgtc 6660
 attttgtgat ataggactcc caaataaaag tatcagaata aacacaacaa ttaactggt 6719

<210> 10
 <211> 1460
 <212> DNA
 <213> Human

<400> 10
 gcacacggga agatatcaga aacatcctag gatcaggaca cccagatct tctcaactgg 60
 aaccacgaag gctgttttctt ccacacagca ctttgatctc catttaagca ggcacctctg 120
 tcctgcgttc cggagctgcg ttcccgatgg tcctcctttg gctcacgctg ctctgatcg 180
 ccctgccctg tctcctgcaa acgaaggaag atccaaaccc accaatcacg aacctaagga 240
 tgaaagcaaa ggctcagcag ttgacctggg accttaacag aaatgtgacc gatatcgagt 300
 gtgttaaaga tgccgactat tctatgccgg cagtgaacaa tagctattgc cagtttgag 360
 caatttcctt atgtgaagtg accaactaca ccgtccgagt ggccaacca ccattctcca 420
 cgtggatcct cttccctgag aacagtggga agccttgggc aggtgcggag aatctgacct 480
 gctggattca tgacgtggat ttcttgagct gcagctgggc ggtaggcccg ggggcccccg 540
 cggacgtcca gtacgacctg tacttgaacg ttgccaacag gcgtcaacag tacgagtgtc 600
 ttcactacaa aacggatgct cagggaacac gtatcgggtg tcgtttcgat gacatctctc 660
 gactctccag cggttctcaa agttcccaca tcctggtgcg gggcaggagc gcagccttcg 720
 gtatcccctg cacagataag tttgtcgtct tttcacagat tgagatatta actccacca 780
 acatgactgc aaagtgtaat aagacacatt cctttatgca ctggaaaatg agaagtcatt 840
 tcaatcgcaa atttcgctat gagcttcaga tacaaaagag aatgcagcct gtaatcacag 900
 aacaggtcag agacagaacc tccttccagc tactcaatcc tggaacgtac acagtacaaa 960
 taagagcccc ggaaagagtg tatgaattct tgagcgcctg gagcaccccc cagcgcttcg 1020
 agtgcgacca ggaggagggc gcaaacacac gtgcctggcg gacgtcgctg ctgatcgcg 1080
 tggggacgct gctggccctg gtctgtgtct tcgtgatctg cagaaggat ctggtgatgc 1140
 agagactctt tccccgcac cctcacatga aagaccccat cggtgacagc ttccaaaacg 1200
 acaagctggg ggtctgggag gcgggcaaag ccggcctgga ggagtgtctg gtgactgaag 1260
 tacaggctcg gcagaaaact tgagactggg gttcagggct tgtgggggtc tgcctcaatc 1320
 tccctggccg ggccaggcgc ctgcacagac tggctgctgg acctgcgcac gcagcccagg 1380
 aatggacatt cctaacgggt ggtgggcatg ggagatgcct gtgtaatttc gtccgaagct 1440
 gccaggaaga agaacagaac 1460

<210> 11

ADS5001.ST25.txt

<211> 4318
 <212> DNA
 <213> Human

<400> 11
 gcttcccggc tgccaggcta cagaactcgc ctgccactc ctgagacatg gacaacgccg 60
 ttgacggact ggacaaagct tctatagcaa actcagatgg cccacacagca gggtcccaaa 120
 cacctccctt caaaagaaag gggaaactat ccaccattgg taaaatcttt aagccttgga 180
 aatggaggaa aaagaagacc agcgacaaat ttagagaaac ctgggcagta ttagaaagga 240
 agatatccac acgacaaagt agagaggagc tgataagaag gggagtgcctt aaggaattgc 300
 ctgatcaaga tggagatgta acagttaact ttgaaaattc aaacgggcac atgataccca 360
 tcggagagga atctacccga gaggaaaatg tagtaaagtc tgaagaagggt aatggctctg 420
 tatctgaaaa aacaccacct ctggagggaac aggcagaaga taagaaagag aacactgaaa 480
 accactctga aacaccggca gctcctgctc tacctccttc tgctcctcct aagcctagat 540
 ccaaacctaa acccaaaaaa tcacctgtgc ctccgaaagg ggccactgct ggggccagcc 600
 acaaagggtga tgaagtgcct cccattaaaa aaaataccaa ggctcctggt aagcaggccc 660
 ccgtccctcc acccaagcca gcaagccgaa acacgacccg agaggctgct ggctcctctc 720
 attcaaaaaa aacaactggc tctaaagcat cagcttcgcc atccacttca tccacctcat 780
 ctcgccccaa agcttcaaag gagacagttt ctagcaaagc agggacagtg gggaccacca 840
 agggcaagag aaaaactgac aagcagccaa taactttctca cctgtcctca gacacaacaa 900
 cttctggcac atccgacctg aaaggagagc ctgcagagac cagagtggag agtttcaaac 960
 tcgaacagac tgtccctgga gctgaggagc agaacacagg caaattcaag tccatggtcc 1020
 ctccaccccc tgtggctcca gcaccttctc ctctggcccc ccctctccct cttgaggatc 1080
 agtgcattac tgcctcagac actccagttg tcctcgtcag cgttggagct gacctgcccg 1140
 tctctgcctt agaccaagt cagcttcttt gggctgaaga gccgacgaac agaaccactc 1200
 tctactcagg cactggctta agtgттаaca gagaaaatgc aaaatgtttc acaaccaaaag 1260
 aggagctggg gaagacagtg cctcagctac tgactcctgg gctgatgggc gaatcttcag 1320
 aatccttttag tgcctcagaa gatgaaggcc acaggggaata ccaagccaat gactctgact 1380
 cggacgggccc tatcttgtac accgatgatg aggacgaaga cgaagatgag gatggcagtg 1440
 gagaaagtgc tttggcaagt aaaatacgcc ggaggggatac tcttgctatc aaacttggca 1500
 acagaccatc taagaaagaa ctagaggaca aaaacatctt gcagcgtaca tctgaagaag 1560
 agaggcagga aatccgacaa caaattggaa ccaagttagt caggaggctg agccagaggc 1620
 ccacaactga agaattagag caaagaaaca tcctaaaaca aaagaatgaa gaagaggaac 1680
 aagaagcaaa aatggaactt aaacgcagac tcagcagaaa gctcagcctg agaccacag 1740
 tggcagagct acaagctcga aggatcctgc gatttaacga gtatgtagaa gtcacggatt 1800

ADS5001.ST25.txt

ctcctgacta	tgaccgccga	gcagacaagc	cctggggccag	gttaacacct	gcagacaagg	1860
cagcaataag	gaaagaacta	aatgaattta	aaagcacaga	aatggaagtt	catgaagaga	1920
gtcgacagtt	tacaaggttt	catcgtccat	aacgaagagt	gagactattt	ggaaacagag	1980
actgatcatc	tttgggggaa	gccctgcttc	ctgaaaacct	gatattgcac	tgggatttga	2040
atgtgtgtgt	ttccgtttta	cttgtggtga	aggaagtgtg	tgactcagct	tggctgggaa	2100
gtgctcctca	cctgtgtggc	ccagatggct	ccaacaagca	aaaggaagga	tgcagtgact	2160
cttgctgccc	agaatgcaca	gcgatggtaa	gagacaccgt	ggatattctt	catcagaagc	2220
tttaataaaa	gaagatgagc	agaagacaat	cactggctcc	ctgttaccag	aaagccaaat	2280
tttataatgc	gggtgaaaga	aaaatataga	ttaaaattgc	tgggcactga	aaaggggtgg	2340
gagttggaag	tcagaaagaa	agagaaatat	ttcattatgt	taatgaagaa	aagagaaaat	2400
tgaagcataa	atgtattttt	gaagtagtta	ttcggtagct	gagaacttat	taagggattt	2460
aggaatttaa	cctcctgatg	tggattcctc	aaagacttga	tcggagaata	ctcttgtttc	2520
accattatgt	tggtagagta	tagtaccatt	attttatggt	gtgccagtga	atccagttgc	2580
cagaaataag	tctgaatggt	ttcatgcatc	tttttcttaa	atgcaagagc	ttctactgac	2640
tcttaacaag	catgcttacc	caaattttgt	tgcattgctt	taagtagcat	tagctatgca	2700
cacttgacat	ttttaaatat	ccctttccta	gtgtaccagc	cttcacagga	taagaggact	2760
gggaataaag	tcagatgtaa	tgtgacccta	gaaaactgta	gcaagcttca	gaaataaatc	2820
ttttgatctt	tccctatctt	gattagatcc	aaagtcaaag	caaccatact	tcacctagag	2880
aagacagtat	tggcaatcat	gacacctgta	ataaaaactt	gaatccaaag	tcaaaaactta	2940
agcaagatac	aaatgtgctg	cctgcagtta	gtcctgcatg	ggaataagga	ctagttattt	3000
ttttagtgtg	gcattttttt	aaagttggat	tgctgctatt	taaaaaaaaa	aaaaggacac	3060
agatcaaaaa	aacacccaaa	ggcttaacag	aacatggaaa	gttcccacta	agttgtgtgt	3120
gaggaaatcc	tcatcttgta	ttttaagaat	ctgcagatgg	catccataga	tacagtacag	3180
tatttactgt	caatgcaaaa	gaatcagtga	ggttaaagta	gtggaagttt	tccctatgag	3240
cctacagtct	gtattgttta	cattaagaaa	ctctctatta	ttgtgttgct	attttccatg	3300
gagtcacagg	cacactatga	cttctgctcc	caaatacata	tgaccatatg	taaataccac	3360
cttgcatctc	attgttcttc	acaagtgttc	tgtgcccctt	taattaaaaa	cacatgaaat	3420
gaataacaaa	acaagacca	aatagagttt	attttattct	cagagtttgg	actacaattt	3480
tctaagatgt	ttctggttca	agactgtcat	tttctatttc	aaccgaaaag	taagcattta	3540
acccggtgaa	taaatgtaga	tcctgccatt	cattgggtatt	ttaaagaacc	acttgaaatc	3600
ggatcatttt	atttaaaaa	aaaaaatgtt	aatgccagtt	ggcctactat	aaaaagccag	3660
gaccatgtta	gaattaggaa	aagtaaccag	cattactgca	cctcttggtta	gactctgtgc	3720

ADS5001.ST25.txt

attaataaaa	cacacctaga	gtctgttgtc	atttcactaa	taggataaga	caaatttttt	3780
gctttgaaaa	aatttttctg	catgcccagg	tgtctgtctc	tggctgaggt	tttgtctatt	3840
ttacagtgtt	tcaatccagc	cataaaaatt	aacttgtgat	tttttttttc	ccaaagtcac	3900
gcttttcctt	aattatat	ttattttatt	atttttagtgt	cttgagaaaa	ataccaagag	3960
atataatgtt	tcttttaatt	gtctatgctt	aatcatcttt	aaacactttt	taaatttcta	4020
accacaagac	ctctctataa	tggtaaattgt	aagacatcac	catttttatca	ctcaaagtac	4080
gttattgaaa	gtttctattt	ggttgataaa	aggaacaatt	ttttcccact	tttgatgcct	4140
gtgatgcaat	tttttattgc	ctacaatgag	atacacttag	tacaaaaaat	gaaaatctgg	4200
tattttcaaaa	ttgcatttct	tgtataatag	gtcagattta	ttaactactc	atactttttc	4260
tttacactaa	tcgatacatt	tagaaaaaat	tttctaagtt	agagacaagt	ttaaaagt	4318

<210> 12
 <211> 3015
 <212> DNA
 <213> Human

<400> 12						
gggagcaaat	tcattccctt	gctgggttgc	tgggctctgg	cactgcgctg	gccctcgttg	60
gaggtctgca	gaagtgcaca	gaaagtgtgg	gcaatggact	ggccatttcc	acagttttgg	120
aaacttttaa	aaatccatat	tcttgctggg	attacagatg	tgagccatcg	tgcccagccc	180
accactttg	ttaatcatga	tcagagcagg	ggtgccattc	taccaccttg	gcacacctgc	240
ctagaggagt	gagtggcgct	gggagcagac	tgaggaacat	cttagctgag	cagtgaatcc	300
agcactgttc	taaggaagct	cagatggtct	gtgactcatc	cctgtcctct	ggactgaatc	360
tgaggccttg	gaactcacc	agggcttag	tggaggcaca	gctctgagct	atgggtgaag	420
agcatctgaa	cccatctaca	cattgaccaa	acacaggcag	gttccagtct	gcgggggaga	480
tggagaaggt	gccaccatgc	tgctgcacaa	atcccaggat	agctggggaa	tgagaatcca	540
gcactttggg	cctaggacct	ggaaggagag	gtcttttggg	agaggtatgg	ggacatctga	600
aggaggactt	cttggaaagg	gaggggctgg	agcagaggca	agagtgattt	tgtcagatgg	660
agagaagggt	ctccacatgg	gcggggctgg	cagaggcaga	tgcccagaca	ggtcacaact	720
ctctaggtgc	ccaattacct	gccctcggtg	agctcagcca	tcggcgggga	ggtgccccag	780
cgctacgtgt	ggcgtttctg	catcggcctg	cactcggcgc	ctcgcttctt	ggtggccttc	840
gcctactgga	accactacct	cagctgcacc	tccccgtgtt	cctgctatcg	cccgtctgc	900
cgcttcaact	tcggcctcaa	tgtcgtggag	aacctcgcgt	tgctagtgtc	cacttatgtc	960
tcctcctccg	aggacttcag	tgggtgcctg	gatgaggagg	gagtggggaa	gtgttccctg	1020
aggggacggg	cctgccccta	ccacattcgg	accttcctac	ttcgtggtgt	gggcactccc	1080

ADS5001.ST25.txt

tgcaatgtgg	ctcccaatcc	tctttccctc	cagccatcca	cgaaaatgct	ttcattgtgt	1140
tcattgcctc	atccctcggg	cacatgctcc	tcacctgcat	tctctggcgg	ttgaccaaga	1200
agcacacagt	aagtcaggag	gtacggtcta	tccctagcgg	gggctccaag	gcagcccaga	1260
agaaaatcaa	ggacatctgt	cctcaggatt	cgggtaatgg	tgagggtggga	actgagttct	1320
aatgggaacc	ctggcagagg	ggtgctgggg	ttggggctgg	ggcttgaggaa	caaactgagg	1380
gtgggttggtc	agaatctagg	actatagcac	tgtgtttggg	tagtgtggga	gactggagaa	1440
tagaagagat	ggaggctgca	aatggggata	gaatgaggag	tcgcatctag	gcggcagtga	1500
gttaggaaca	gtgtcagagg	actggtctgt	cataattcca	gcgccccacc	catgtacatg	1560
ggtttctttt	ccccacagt	atttgagggt	ggggttggtg	ggtgactcca	tgtaactttc	1620
atactccatc	cccctgaagt	ggaagcggca	ggaataccac	tgctcctcgg	cccatcactc	1680
ccccagaggc	agggacgtga	acacatagtc	gtcattcttg	ctgccccctgc	ctgtgctccc	1740
ttccatgacc	gctagtggga	gccaagggag	ataaggccca	gcccttagga	gttagggctg	1800
agagggggagc	ccacgctctc	ataccagca	agctgcagag	tgatcagaca	gcccattccc	1860
taggatcgca	agtcctacag	ctggaaacag	cggctcttca	tcatcaactt	catctccttc	1920
ttctcggcgc	tggctgtcta	ctttcggcac	aacatgtatt	gtgaggctgg	agtgtacacc	1980
atctttgccca	tcctggagta	cactgtttgtc	ttaaccaaca	tggcgttcca	catgacggcc	2040
tggtgggact	tcgggaacaa	ggagctgctc	ataacctctc	agcctgagga	aaagcgattc	2100
tgaacccttc	agtcctgctt	gggaggacgc	agcccactgc	ccagaaacaa	gaaacacgat	2160
accattctgg	ccttccccac	cccacatcct	ctcttggcct	tactgaagat	gggggaaggg	2220
taagaaggaa	gggtgtaggc	caaggctcac	cccagtgtg	ctggcttctc	ctctccaccc	2280
ctcatatggg	cgtgggggtcc	tcaaacatca	cctttacctg	agaggcccca	agaagctgag	2340
ctggcagaga	gctctaccat	ttggtgctaa	aaaaaaaaaa	acgtcctgag	gttcatgacc	2400
accatccagt	ttctggcctt	tacacagtca	cctttcactg	aggtcaggag	cccctgagca	2460
gtggctgctc	cctgacaacc	acagccattt	ctctgcgcgg	gggtcattca	taggactaat	2520
gtatttcatg	atctactgtg	cacatccagg	cctgtggcca	cagtcccctg	ctaaagttgc	2580
tcagggtgttc	tagtcctgac	ttcacctttt	tgatttggtg	tgtgccctag	ggtatgtacc	2640
cttccccatc	tgagcctcgg	tgtgtccatg	tgtctgggtg	gggatgggtg	gactgtatga	2700
tttccaagga	ctctaccagt	cagtggttct	gatgtcatcg	ggtggagggtg	gtgttctata	2760
cctaaaggat	gacctgctcc	agaaacagca	ccagcacagc	atgtattttc	ttctcttctg	2820
aaagttctgg	cttgtagacc	cctcccctcc	tttgcaaagg	tatgggatag	aggggtcaga	2880
tgcagatctc	tactgtaaaa	tgggctccct	ggtatctcct	gtcttcccta	ctgctccaaa	2940
ccctaaattt	tggttgtaca	ttttatttga	aaggaaaata	aatttttttt	ttgggccaaa	3000

ADS5001.ST25.txt

aaaaaaaaaa aaaaa

3015

<210> 13
 <211> 558
 <212> DNA
 <213> Human

<220>
 <221> misc_feature
 <222> (252)..(252)
 <223> n=any nucleotide

<400> 13
 tttttttataa ttaaataaat aacttttattt atgatacttc agattttata aatgccaaact 60
 acatagcaaa gtcccataaa ttttaaccga gacacaacca ccaatcaagg ccctttgaaa 120
 aatcaaagat aataaagtgt caagggagaa aagttttgtt ctcccaacag agaatttaat 180
 caatgaactt acttctctga tcatttaagg ttcacaatgg gaaaacttct tttcttttaa 240
 gggtagcctg anatcaatta acagtcaatc aaccacatt tagaaaaata aaccccatag 300
 ttaagaaaaa tatatcaaata gcccttcaca cccataatgt aacaaaactt tgacaccaga 360
 atgaaaaact tctcagtctc tgtaccaaac caggtgtagg tccacccatg agcaagttcg 420
 cctgaataac agcatctata caccatgatg tagctgagaa ctacagctga tctcctttta 480
 ttgcctgtgg ctcggaactga agccaatact ataaatacca cagtgaattc caatggtgaa 540
 gagcagcagt gtagatgt 558

<210> 14
 <211> 5481
 <212> DNA
 <213> Human

<400> 14
 ccgctggtcc gagctgtctg gcctcagttt ccctccgact tttctccgct ctgccagccc 60
 tcactgctgc ccgtcattgt tctcgcagtt agatgggggt gctttgtgac ggctgccaag 120
 ttgggggtgtg ttctcttttat tccgtttttc aaacagaaca aggcctccaa ggctgacccc 180
 agacaacca cccctcggga ccctaattca cttattgca ctgatttttt ttatcaagtc 240
 gtattttatt gtacaggagc cagccctga tttcttaaag gcgccttgca ctctggccat 300
 gtgttatctc tgcagccggt gtgtgggagg cctcttgtag gccagttggt ttcccgcctc 360
 caccacccc ctcgaagatt tagggatgcc aggggggaag aaggtggctg ggggtggcag 420
 cagcggtgcc actccaacgt ccgctgcggc caccgcccc tctggggtca ggcgtttgga 480
 gaccagcgaa ggaacctcag cccagagaga tgaggagcca gaagaggaag gggaagagga 540
 cctgagagac ggaggcgtcc cttctttgt caaccggggt gggctacctg tggatgaggc 600
 cacctgggaa aggatgtgga aacacgtggc caagatccac cccgatggag agaaggtggc 660

ADS5001.ST25.txt

gcaacggatc	cgtggggcca	cagacctgcc	caagatcccc	ataccgagtg	tgccctacgtt	720
ccagccgtct	acacctgtcc	ctgagcgcct	ggaagctgtg	cagcgctata	tcagagagct	780
gcagtacaat	cacacagggg	cacagttctt	tgaaattaag	aagagcagac	ctctgacagg	840
gctgatggac	ctggccaagg	aaatgaccaa	agaggccctg	ccaatcaaat	gcctggaagc	900
cgtgatcctg	ggaatttacc	tcaccaacag	catgcccacc	ctggagcgct	tccccatcag	960
cttcaagacc	tacttctcag	ggaactactt	ccgccacatc	gtgctggggg	tgaacttcgc	1020
gggccgctac	ggtgcgctgg	gcatgagtcg	gcgcgaggac	ctgatgtaca	agccgcccgc	1080
cttccgcacg	ctcagcgagc	tcgtgctgga	cttcgaggcc	gcctacggcc	gctgctggca	1140
cgtgctcaag	aaggtgaagc	tgggccagag	cgtgtcacac	gacccgcaca	gcgtggagca	1200
gatcgagtgg	aagcactcgg	tgctggacgt	ggagcgcctg	ggccgcgatg	acttccgcaa	1260
ggagctggag	cgccacgccc	gcgacatgcg	gctcaagatt	ggcaaaggga	cgggcccctc	1320
cttccccacc	aaggaccgga	agaaggatgt	ttcttccccg	cagcgggccc	agtccagccc	1380
ccaccgcagg	aacagccgca	gtgaaagacg	gccctcgggt	gacaagaaga	cttccgagcc	1440
caaagccatg	ccagacctta	acgggtacca	gatccgggtc	tgaggcggat	gccagcaccc	1500
caggccccac	ccactcttgg	gggccaggat	ccacctgctg	gaaccagcct	tatgcatggg	1560
gaaggcgggg	ctggtgacaa	ggcaggggcaa	gaggctgcag	gaagagtgtg	ttccagctca	1620
gccccccaag	ctgctctcgc	tcccactgag	ccaagcccc	taactttggg	cctagaggcc	1680
gttagtattt	tatttggagt	ttttaactct	acaactgaag	tttaagggtat	ttggggaaaa	1740
cttagtccaa	atggatctgc	tgatggtggg	aaggccagtg	cttaacaaat	ccatgtgtca	1800
tggggccagg	tgagggaaac	tgctggttct	gctggtgcct	ctgcccctgg	cttctctctg	1860
ggagttaggt	gcatcttatc	agtgggaaat	ctcccagcct	taccaggcct	gtgatggggg	1920
gtgggggtgg	ggtggagatg	tttctccagt	tctgcctgcc	ctggcagaat	cttgacccag	1980
ggaaagggaa	gcagggtagg	agtccttctg	agaaaggctt	gtgtagccca	ttaaccagga	2040
gcttggcaca	ggccacatct	gccccaaagag	catgagctcg	tggctcagga	gagccttcag	2100
gcccttgagg	cccccatggg	cagtgctgtg	tgggcagagg	aggggtgata	tgagagcgag	2160
cccagggaag	gacctctggg	caaaaagttc	ccaggcccta	actgcgtcta	cttgctcagt	2220
cccagctctg	cctgttgctc	tagccccacag	gctccctgcg	gagggtctgg	gcttggcgga	2280
ggacccagaa	tggcactgag	gccagcatgg	ctgtgggagt	tgagcaaacc	ctgggtgcca	2340
gtccaggagc	tgtggctgga	catgggggtga	tggggcgggg	tgcttggggc	tgggtctctc	2400
cgccagcagt	gccaggagcc	cttgctgggg	aaatcaagac	cagactagga	tgcttctgcc	2460
ccaggcctgc	cttccattct	ttaacagccc	atcttggctt	ggggttgcaa	tgatggctgg	2520
gccagtcact	tgtggcaggg	catcaggggc	ctggcagggg	agaacctagg	cacctggggg	2580

ADS5001.ST25.txt

tgtccccagc	ctgcccgtca	gcatgagata	cccagtggga	aagtgagagg	atgcggagag	2640
gttggcagag	ccaggggtag	gttctggagg	ctcaagcaac	aaggagggtgc	aggtaaaggg	2700
tgcagtgcag	ccactgaggg	acagctggga	actgggggat	gcaagtgaga	aagggatgtg	2760
ggggagagtt	caggatcagg	ctgcttgagg	agtaatgggt	tacctacagc	agagacgaga	2820
tggctgtttg	tcaggaggcg	gtagaaaggt	agaaaggatt	cagattgtgg	aagggtaa	2880
ggatgagatg	accattaagg	ttttgtttta	ctgagaggct	gtaagtctgc	cagggacagc	2940
tgtcagtaag	gctgcagaag	ggctgggggg	ctacacaagg	aagagcagaa	ctagggttgt	3000
aagctcaaat	gacgagcaaa	cggtgagaag	gaggcctgaa	gggctgtgtg	gggactatgg	3060
ctacctgaag	agggcacacc	ctgttaaagg	ggccacagct	gctcagctgt	tcttacagtg	3120
ccggccctgt	gttgccagat	tgtctgcttt	gtcagaggcc	agaattctga	ctttttatgt	3180
gaaataggat	ttttaaatgc	tggtgatcac	ttaaaaaaaaa	cttaaaaacc	caatactggc	3240
aaaagaggat	gccagtttgc	aatccctgaa	gtagagagag	ctcgtgctgg	ggagaagtcc	3300
accaagatgc	tttgaggcgg	gctgtagcaa	agtcctgttt	ctcagagctg	ggctgggctg	3360
gggtaggatc	cttgcagctg	aggaggagga	aaagccactg	agtctcctcc	cagagcggga	3420
caaaccagag	gccctttgca	gttgctgggt	caccagcggg	ggtggcgcac	ggagtacaga	3480
cagtgtagct	cttggcctgc	caggagagacg	gatggtgcct	ttgaagcaaa	gaggaaggga	3540
aggcagaacc	agggatgcct	ttgctgatga	gagtgcctgt	caggaaggc	gccacaggct	3600
ggcagctctt	caaaccagca	gcgcttgacc	cagagccaga	tccagcatgg	cctggccaga	3660
ggcaccctgg	gaggccagct	ggtcagtccc	ttgcctcccc	aagttcccc	tgggggtcaat	3720
gagccctggg	aggatgccta	acctaactcc	agccagacta	ataggggcat	ggtgaccctt	3780
gactcaccat	cccatcccag	ctttcaggga	gtgggggtag	tgtggtctcc	atgttcctac	3840
tatgcctaag	aagagatggc	tcaccttggg	aggtgccagg	ctgaaactag	gtcctttccg	3900
ggtctggatg	ctgccgctca	ggagcagggg	cgtggcctca	gctgcctctg	ggagcttccc	3960
gggaatgaca	gggtttgagg	ggagtagata	tgagagggag	ccgctcctgg	ttctggagtc	4020
ttaggagggt	ccaacttgca	ggatcctttc	ccagagccct	ccatggagaa	aacagcaaaa	4080
tgaagccctt	acctgcttgc	tgtctgcaag	ggagggagcc	gagccccagc	tgataatccc	4140
ccagcactca	cccttcctga	gctgagactt	cggggctgtg	gagaccagca	caggacatag	4200
tggtgctttt	taaatttatt	tttaactgtt	tctcatatgt	agcaaccctt	cctcccctcc	4260
tgggcatgtt	tacacaggct	ctgctctggg	ggctggcctg	gctgtgaggt	ttctggggag	4320
gcagagaggc	agggactttg	gggccttagt	caccatccat	ggtatcacct	catctcactt	4380
cctgtgaggg	acagggcctg	gctgatgtga	tcccagctcc	ccccagttca	ggactgtctt	4440
tcagctcctt	tgcccctgga	ggtgggggct	gctggctgag	gaggggtcaa	ggtgagttca	4500

ADS5001.ST25.txt

```

agaaagctac ctgtggaaaa tggaccaggt tggggggggtg attgcaaagt ctccccaag 4560
cctggctcct catgctcagt gccaggggca gaacactggg gagccaggta tagagagcct 4620
tcctgtcata actgccagtc ctcttcctcc aaggcctctg catattctca tgttcccctc 4680
acccatcatg ccagccaccc ctatccctct tctagcaggg ccaagatggg gacagcagca 4740
gccctctggc cttgggatgt gatgataaag caagcctagg gccagggttt ggggagcaga 4800
gagagccaag aagttgacca cgtgtgattt ccagcccttc ccactgggac ttgacttccc 4860
aggtcaagga gtccgtctca ttctggctgg tcgagtgacc agaggcctgt gtgaatgtgt 4920
gcacctgctt ttctgcctg gaatgttttc tggtcagct gcagcaacat ctgtgagccc 4980
agtgtctgcc ctgtgtccct gggctcgctc caagtgcagg aacatacatg cagggcccaa 5040
catgatgatg gtgtgaaggg caggaaacag tcctctgaag gagtggggag gtgggcagtc 5100
tgcccccgcc aggtaccatc gcctcctgcc agcttcctta gaccaggcag ggctgccatg 5160
gtgctagctg caagtccatc agtattgacc gtctcgctcc atcttggtcc tccggagtcc 5220
caagtttcct tttcatcaaa tctgacaaga gagaagaaac atgggtgtgc ttggcccaca 5280
gggcctgggtg gtgatggacc tccccgctcc ctcaagctct ggatggctgc agtgttgtac 5340
tagactttgt tcaggctggt ctcattctag tattgcccct tcctttcact ttcacacttc 5400
atctcattcc tgttgtcact ttccccgaaa cgaataaagt ctccccagct cctgctgtgt 5460
aggctgggca gaaaccacaa c 5481

```

```

<210> 15
<211> 743
<212> DNA
<213> Human

```

```

<220>
<221> misc_feature
<222> (531)..(531)
<223> n=any nucleotide

```

```

<220>
<221> misc_feature
<222> (655)..(655)
<223> n=any nucleotide

```

```

<220>
<221> misc_feature
<222> (657)..(657)
<223> n=any nucleotide

```

```

<220>
<221> misc_feature
<222> (658)..(658)
<223> n=any nucleotide

```

ADS5001.ST25.txt

<220>
 <221> misc_feature
 <222> (665)..(665)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (667)..(667)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (672)..(672)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (673)..(673)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (702)..(702)
 <223> n=any nucleotide

<220>
 <221> misc_feature
 <222> (736)..(736)
 <223> n=any nucleotide

<400> 15
 ttgcatgc cactaactat tttttatttg caactacatg atggcacaca attctcttaa 60
 acaacgacat aaaatagatt tccttggtata taaataactt acatacgctc cataaagtaa 120
 attctcaaag gtgctagaac aaatcgtcca cttctacagt gttctcgtat ccaacagagt 180
 tgatgcacaa tatataaata ctcaagtcca atattaaaaa cttaggcact tgactaactt 240
 taataaaatt tctcaaacta tatcaatatc taaagggcat atatttttta agaaagatta 300
 ttctcaataa cttctataaa aataagtttg atggtttggc ccatctaact tcactactat 360
 tagtaagaac ttttaacttt taatgtgtag taaggtttat tctacctttt tctcaacatg 420
 acaccaacac aatcaaaaac gaagttagtg aggtgctaac atgtgaggat taatccagtg 480
 attccggtca caatgcattc caggaggagg tacccatgct actggaattg ngcgatatgg 540
 tttatttttt cttccctgat ttggataacc aaatggaaca ggaggaggat agtgattctg 600
 atggccattc cctcgataca ttcctggctt ttttctgggc aagggtgccc acatngnnag 660
 agtgnanata tnnagtctga aatctggtac acaggacttg cngctgcagt caccgaactg 720
 ggttcacttt catttncttt act 743

ADS5001.ST25.txt

<210> 16
 <211> 4701
 <212> DNA
 <213> Human

<400> 16
 gcggccgcca caccagcac cacaggcacc aagtccaaca cgccacatc ctccgtgccc 60
 tcggccgccc tcacaccct caacgagagc ctgcagcccc tgggggacta tggcgtgggc 120
 tccaagaaca gcaagcgtgc ccgggagaag cgcgacagcc gcaacatgca agtacaggtc 180
 acccaggaga tgcgcaacgt cagtataggc atgggcagca gtgacgagtg gtctgatgtt 240
 caagacatta ttgactccac gccagagctg gacatgtgtc cagagacccg cctggaccgc 300
 acaggaagca gccaaccca gggcatcgtg aacaaagctt tcggcatcaa caccgactcc 360
 ctgtaccatg agctgtcgac ggcaggggtct gaggtcatcg gggatgtgga cgaaggggccc 420
 gacctcctag gggagttctc aggaatgggc aaagaagtgg ggaatctgct actggaaaac 480
 tcacagcttc tggaaaccaa aaacgccttg aatgtggtga agaattgacct gattgccaag 540
 gtcgaccagc tgtccgggga gcaggagggtg ctgaggggagc agttggaggc tgctaagcag 600
 gccaaagtca agctggaaaa ccgtatcaag gagctggaag aggaactgaa aagagtgaag 660
 tccgaggcca tcatcgcccg ccgtgaaccc aaagaagagg cggaggatgt aagcagctat 720
 ctctgtacag aatcggacaa aatcccatg gccagcgcc gccgcttcac gcgggtggag 780
 atggcccgtg tgctcatgga gcggaaccag tacaaggagc ggctgatgga gctgcaggag 840
 gctgtgcggt ggactgagat gatcagagcg tcccgagagc acccatccgt ccaggagaag 900
 aagaagtcga ccatctggca gttcttcagc cgcctcttca gctcttcctc cagccccctt 960
 ccggccaagc gcccctatcc ctcggtgaac atccactaca agtcacccac cactgccggc 1020
 ttcagccagc gccgcaacca tgccatgtgc ccgatctcgg caggcagccg gcccctggaa 1080
 ttcttccttg acgacgactg cacgtcctcc gcccgtcgag agcagaagcg cgagcagtac 1140
 cgccagggtg gtgagcacgt gcgtaacgac gacggccgtc tgcaggcctg cggctggagc 1200
 ctgcccgcca agtacaagca gctgagtccc aacggggggc aggaggacac gcggatgaag 1260
 aacgtgccgg tgccggtgta ctgccgccct ctggtggaga aggacccac catgaagctg 1320
 tgggtgtgccg cgggcgtcaa cctgagcggg tggaggccca atgaggacga cgctgggaat 1380
 ggagtcaagc cagcgccagg ccgcatccc ctgacctgag accgcgaagg agacggcgag 1440
 cccaagagcg ccacgcgtc tcccgagaag aagaaggcca aggagctccc tgaaatggac 1500
 gccacctcca gccgggtgtg gatcctgacc agcaccctga ccaccagcaa ggtggtgatc 1560
 atcgacgcca accagccggg cacggtggtg gaccagttca ccgtctgcaa cgcgcacgtg 1620
 ctgtgcatct ccagcatccc cgcggccagc gacagcgact accctcccgg ggagatgttc 1680
 ctggacagcg acgtgaaccc agaggacccg ggcgcagatg gcgtgctggc cggtatcacc 1740

ADS5001.ST25.txt

ctggtgggct	gtgccacccg	ctgcaacgtg	ccgcggagca	actgctcctc	ccgagggggac	1800
accccagtgc	tagacaaggg	gcagggggag	gtggccacca	tcgccaacgg	gaaggtcaac	1860
ccgtcccagt	ccacagagga	ggccacagag	gccacggagg	tgccagaccc	tgggcccagc	1920
gagccagaga	cagccacatt	gcggccccgg	cctctcacag	agcacgtctt	cactgaccca	1980
gccccgaccc	cgctctctgg	ccccagcct	ggcagcgaga	acgggcccaga	gcctgacagc	2040
agcagcacac	ggccagagcc	agagcccagc	ggggacccca	cgggagcagg	cagcagtgct	2100
gcacccacca	tgtggctggg	agcccagaac	ggctggctct	atgtgcactc	ggctgtggcc	2160
aactggaaga	agtgcctgca	ctccatcaag	ctgaaggatt	ctgtgctgag	cctggtgcat	2220
gtcaaaggcc	gtgtgctggg	ggctctggcg	gacgggaccc	tggccatctt	ccaccgtggt	2280
gaagatggcc	agtgggatct	gagcaactat	cacctaattg	acctgggcca	cccgcaccac	2340
tccatccgct	gcatggctgt	tgtgtacgac	cgcggtggtg	gtggctacaa	gaacaagggtg	2400
cacgtcatcc	agcccaagac	catgcagata	gagaagtcac	ttgacgcca	cccgcggcgg	2460
gagagccagg	tgcggcagct	ggcgtggatc	ggcgatggcg	tatgggtgtc	catccgcctg	2520
gactccaccc	tgaggctcta	ccatgcacac	acgcaccagc	atctacagga	cgtggacatt	2580
gagccctacg	tcagcaagat	gctaggcact	ggcaagctgg	gtttctcctt	cgtacgcatc	2640
acggccctgc	ttgtcgcggg	cagccggctc	tgggtgggca	ccggcaacgg	agtggtcac	2700
tccatcccc	tgacagagac	tgtggctcctg	caccgaggcc	agctcctggg	gctccgagcc	2760
aataagacat	ccccacctc	tggggagggc	gcccgtccc	ggggcatcat	ccacgtgtat	2820
ggcgatgaca	gcagtgcag	ggcggccagc	agcttcatcc	cctactgctc	catggcccag	2880
gcccagctat	gcttccatgg	gcaccgcgat	gccgtgaagt	tctttgtctc	ggtgccaggg	2940
aacgtgctgg	ccaccctgaa	tggcagtgtg	ctggacagcc	cagccgaggg	ccctgggcca	3000
gctgcccctg	cctcggaggt	cgagggccag	aagctgcgga	acgtgctggg	gctgagcggc	3060
ggggagggct	acatcgactt	ccgcattgga	gacggagagg	acgacgagac	ggaggagggc	3120
gcaggggaca	tgagccaggt	gaagcccgtg	ctgtccaagg	cagagcgag	tcacatcatc	3180
gtgtggcagg	tgtcctacac	ccccgagtga	agctgctgcc	ctgcctggcc	cgacctgtac	3240
ataggacccc	cgaccacctg	acccccgccc	ggcccgcggg	gtagccagcc	aggcgccgcc	3300
gcccctcttc	taacctctca	acctgcagct	ttcacctgag	tctggcccct	ccagcgggca	3360
gggagtgcgg	ggatgcggat	cagctgggag	gaggagggga	ggggtgcttc	cacccgaggg	3420
gaagatgctc	tcgggacagt	ttcccgggca	gctcctggcc	agcttccagc	ccagagtcct	3480
caagtccagg	gcaccttggg	cccagcgag	gcagaatccg	aggtggtcct	ggctctaccc	3540
tgggcctcct	actccccagc	acccctggag	gaggcagggg	ctccccgccg	ccgaggctgc	3600
ctgccctggg	cccacctctg	catgctgctc	atggggccac	cctgcctcct	gggccctcac	3660

ADS5001.ST25.txt

tctgcctagg ggagctgggc caggcactag cctttgcccc gggagggtggg cctcaggctg 3720
 cccagggtgcc tgcaccccag ccggccttct ctggggcctc cccgtcgtca agcctctatc 3780
 ctgtctgtcc ccaccccagc tgtcccctgc ccaggggagct ggcataaaag cacgaggccc 3840
 ggctccctgg ggcagctgct tgagaacaga gactgctacc ccatcctgcc catgcaggca 3900
 ggctcttgcc agccccgttc tgacccgtgt cccccaggc tctgcctggg cagaagactc 3960
 accttgaggg agtggggcct ggagtcctgt ccctcccaga agccccagg gtgggatttc 4020
 tcaggctgcc agggcaggcc caggcctcag gaagaagggg aggcccctgg cctctccggg 4080
 atcagtccta ggacacaggc tcagcctcag gttgatgggg gatgatgtgc tcccggggcc 4140
 tgcctcctgc acggggctcc acggagccca gctcccagac acgctactaa gtgcctaggg 4200
 ttgcccgtg tggcctgctc ccaggggagca acagagaggc caccaagcag aggcccgtgg 4260
 ggctgaggat ggagccgccc ccagccgact ccaagcccgc agagggcaga cgccaccctg 4320
 gactgctctc cctgcccagc tgggcctctc tggcctattc ctaccttcca ggcccactgc 4380
 actcctgtct gggaggccct tatgagggca gcccagcccc cgcacccacc cccaaccaga 4440
 gaagcacaga tcttggggag ctgccccaca agccccgtg gccaccgagg gctgcagccg 4500
 ctgcgctgcc ggcttctccc caccaccctg ccacctccac tgtgatgtat gtccgctccc 4560
 tcgtctgttc ccccaggatc tcgaagtgac tccgggctga gcagtggggc ggctggggga 4620
 ggggtgacga ttctcctcag gctttggccc tgcaagcaaa cccacatatc tgctctgtat 4680
 gtaataaatg tcttaacgtc g 4701

<210> 17
 <211> 1445
 <212> DNA
 <213> Human

<400> 17
 ctgccccaca cacactaacc caaccatctt ggggtggact ccctgccagc ccaactgttg 60
 tattttcagt tcttccagtg tgaatcagtt aatattctcg ggaacgaggg agaggttgat 120
 cctatgagga aatcaaccac agtgaaaagg cttggggccgc ttttgttttc gcctcctttt 180
 gttgaacaaa tttgatttcc ggagtcagtc attttactgt caagacattt cttcggcatt 240
 ctgcaacagt ttccaacatg gctagatcca tcagaaactg aagccgtgga gaacgctctc 300
 ggggcctttg ccacttcttg gagtagaagc cgacagagag ctgtttggaa acttctcctt 360
 cacacaccag ttgaagacta ggctttggag gttttcaaag cagacggtgc ttggatgggc 420
 agggagaagt aacattctgc aaatcgccgt cagaggctct gaggacacag acctacctgg 480
 cttgcattcc ccttgctgaa tggcgtgtgc tgcagctgcc cactgagggc tcttttccct 540
 gggattctgg acttcagagt aggacagcag gctgggaaga tgctgagttc catcaagtgc 600
 gtgttggtgg gcgactctgc tgtggggaaa acctctctgt tgggtgcgctt cacctccgag 660

ADS5001.ST25.txt

```

accttcccgg aggcctacaa gcccacagtg tacgagaaca caggggtgga cgtcttcatg 720
gatggcatcc agatcagcct gggcctctgg gacacagccg gcaatgacgc cttcagaagc 780
atccggcccc tgtcctacca gcaggcagac gtggtgctga tgtgctactc tgtggccaac 840
cataactcat tcctgaactt gaagaacaag tggattggtg aaattaggag caacttgccc 900
tgtacccttg tgctggtggt ggccacccag actgaccagc gggagatggg gccccacagg 960
gcctcctgcg tcaatgccat ggaagggaag aaactggccc aggatgtcag agccaagggc 1020
tacctggagt gctcagccct tagcaatcgg ggagtacagc aggtgtttga gtgcgccgtc 1080
cgaactgccg tcaaccaggc caggagacga aacagaagga ggctcttctc catcaatgag 1140
tgcaagatct tctaaacccc aagagacttc acacaacact tatgtatgca ccccaaagac 1200
taatggggag agggagggcc gggaagccag gaaagcttgg tgttttctct gggtagaccc 1260
caagcagcgt ctccgttttg gatacagtta ttgatgaggc ttggccactg gatgttttca 1320
ctaactacac tctacaagtg aactccttgc ccaggccagt tagaaaatcc cttggggaac 1380
tgtgatgaat attccatctt tgattaaaaa agtgaaatag tctccataaa aaaaaaaaaa 1440
aaaaa 1445

```

```

<210> 18
<211> 2429
<212> DNA
<213> Human

```

```

<400> 18
ggcgggtgcac gccggctgcc cgctgcccgc gatgcccattg cagggcgggc cgcagagtcc 60
cgaggaggag ctgagggccg cggtgctgca gctgcgcgag accgtcgtgc agcagaagga 120
gacgctggcc agcgcgaggg ccatccgcga gctcacgggc aagctagcgc gctgcgaggg 180
gctggcgggc ggcaaggcgc gcggcgcggg ggccacgggc aaggacacta tgggcgacct 240
gccgcgggac cccggccacg tcgtggagca gctcagccgc tcgctgcaga ccctcaagga 300
ccgcctggag agcctcgagc accagctcag agcaaactg tccaatgctg ggctgcccgg 360
cgacttccgc gaggtgctcc agcagcggct gggggagctg gagaggcagc ttctgcgcaa 420
gggtggcagag ctggaggacg agaagtcctt gctgcacaat gagacctcgg ctcaccggca 480
gaagaccgag agcaccctga acgcgctgct gcagagggtc accgagctgg agcgaggcaa 540
tagcgccttt aagtcaccag atgcgttcaa ggtgtccctc cactccgca caaactacct 600
atacggcaag atcaagaaga cgctgcctga gctgtacgcc ttcaccatct gcctgtggct 660
gcggtccagc gcctcaccag gcattggcac ccccttctcc tatgcggtgc cagggcaggg 720
caacgagatc ttgctgatcg agtggggcaa caacccatc gagctgctca tcaacgacaa 780
ggttgcgcag ctgcccctgt ttgtcagtga cggcaagtgg caccacatct gtgtcacctg 840

```

ADS5001.ST25.txt

gacgacacgg gatggcatgt gggagggcatt ccaggacgga gagaagctgg gcactgggga 900
 gaacctggcc ccctggcacc ccatcaagcc cgggggctgt ctgatccttg gacaagagca 960
 ggacaccgtg gggggtaggt ttgatgccac tcaggcattt gtcggggagc tcagccagtt 1020
 caacatatgg gaccgcgtcc ttcgcgcaca agaaattgtc aacatcgcca actgctccac 1080
 aaacatgccg ggcaacatca tcccgtgggt ggacaataac gtcgatgtgt tcggaggggc 1140
 ctccaagtgg cccgtggaga cgtgtgagga ggctctcctt gacttgtagc cgccttctcc 1200
 tctgtccagg aggccgggat caggctgttg ccatggaagt tcagggccat agactgcccc 1260
 acttaaactc ttgtcagtct gggctcaggg ttcccagagc tcattcccca ggaatctcta 1320
 agaccagggc tggggcagtg tctgtcactg gcttgtttgt tccctaccaa tattctgttg 1380
 ctgtttgaag tagtgccagg gtcccctggg aagatgcccc caagacacct gcccgaagtg 1440
 ggtggatatc tgccttcctg ctgcaagtgg aggcaggctc agcagcccct cttcagagcc 1500
 cctgtaaagt ctatcgagc ctgagtcctg ccgccttcca gttccttggt gtcccgtgca 1560
 ccccttctgt ctgtcccctt tcatgctgtg cagccgtccc gctggagtgg ccatgtccct 1620
 tgtgcattga gtgcatcccc gctgggtgact aagctcgag caagcgctac ccccgatctg 1680
 caaaagggcc tctccctttg tgttctatac attgtgaatc ttcccgtctg aagaacgccc 1740
 agcctgcca gacaaagccc cgccttcccc aaagcagagg ggctgtctgt gtctccagaa 1800
 aggggacatc ggggggggag gggggctcag aaaggagaag ggctgtgatc tccggtccct 1860
 tccccatca tccttcctta gactgatgct ttgactgaat catcactagc tatggcatta 1920
 aaaggcctct cttctcatct ggtgccaaag gttccgttgc agctttttac aaccatccgg 1980
 tgtggtttgg aggatttgtt tttttttttt cccaacagaa aagaacagcc attagaagaa 2040
 ggctcccatt ttctgatgtt ccgccccact gtgaagagtg tgctcgtttt aaattcatgt 2100
 tgattcttgt aagcactgga ctgtcttcat caagtatttc ccctacagaa ctctcaaga 2160
 aaaacagaga tcatttggct agagattgtc tgagtgactc caagctactc actgtattgg 2220
 acgggagtag taatttatat taaagataaa gtgactaagt ggggaaattt ataaagctaa 2280
 atattatata ttttattttt catacatgtt tgaagtgcaa atctgtggat attccatttg 2340
 taggaccaag tcgacatgcc catcctgaca ttgtatgcta cgagaactct tctgatgatg 2400
 gaatttcgat taaagtgcac tgaaagatg 2429

<210> 19
 <211> 21
 <212> DNA
 <213> Primer

<400> 19
 ggtcagatgt ttgccaagga a

21

ADS5001.ST25.txt

<210> 20
 <211> 24
 <212> DNA
 <213> Primer

<400> 20
 tcttcagaaa cacactccca tcac

24

<210> 21
 <211> 20
 <212> DNA
 <213> Probe

<400> 21
 tgaaacggaa gaagcttgta

20

<210> 22
 <211> 8081
 <212> DNA
 <213> Human

<400> 22
 gtctaaaact ctcttttctc ttggctcttc ttattcgagt gatgaggagg aggagttgca 60
 taattcacgg cccttccaca gtaccttcca caataccagt gctaactctga ctgagagtat 120
 aacagaagag aactataatt tcctgccaca tagccccctcc aagaaagatt ctgaatggaa 180
 gagtggaaca aaagtcagtc gtacattcag ctacatcaag aataaaaatgt ctagcagcaa 240
 gaagagcaaa gaaaaggaaa aagaaaaaga taagattaag gagaaggaga aagattctaa 300
 agacaaggag aaagataaga agactgtcaa cgggcacact ttcagttcca ttcctgttgt 360
 ggggtcccatc agctgtagcc agtgtatgaa gcccttcacc aacaaagatg cctatacttg 420
 tgcaaattgc agtgcttttg tccacaaagg ctgccgagaa agtctagcct cctgtgcaaa 480
 ggtcaaaatg aagcagccca aaggagagcct tcaggcacat gacacatcat cactgcccac 540
 ggtcattatg agaaacaagc cctcacagcc caaggagcgt cctcgggtccg cagtcctcct 600
 ggtggatgaa accgctacca cccaatatt tgccaataga cgatcccagc agagtgtctc 660
 gctctccaaa agtgtctcca tacagaacat tactggagtt ggcaatgatg agaacatgtc 720
 aaacacctgg aaattcctgt ctcatcaca agactcacta aataaaaatca gcaagggtcaa 780
 tgagtcaaca gaatcactta ctgatgaggg agtaggtaca gacatgaatg aaggacaact 840
 actgggagac tttgagattg agtccaaaca gctggaagca gagtcttgga gtcggataat 900
 agacagcaag tttctaaaac agcaaaaagaa agatgtgggtc aaacggcaag aagtaatata 960
 tgagttgatg cagacagagt ttcacatgt cgcactctc aagatcatga gtggtgtgta 1020
 cagccagggg atgatggcgg atctgctttt tgagcagcag atggtagaaa agctgttccc 1080
 ctgtttggat gagctgatca gtatccatag ccaattcttc cagaggattc tggagcggaa 1140
 gaaggagtct ctggtggata aaagtgaata gaactttctc atcaagagga taggggatgt 1200

ADS5001.ST25.txt

gcttgtaa	at	cagttttc	ag	gtgaga	atgc	agaacgttta	aagaagacat	atggcaagtt	1260
ttgtgggcaa	cataaccagt	ctgtaaacta	cttcaaagac	ctttatgcc	aggataagcg				1320
ttttcaagcc	tttgtaaaga	agaagatgag	cagttcagtt	gttagaaggc	ttggaattcc				1380
agagtgcata	ttgcttgtaa	ctcagcggat	taccaagtac	ccagttttat	tccaaagaat				1440
attgcagtgt	accaaagaca	atgaagtgga	gcaggaagat	ctagcacagt	ccttgagcct				1500
ggtgaaggat	gtgattggag	ctgtagacag	caaagtggca	agttatgaaa	agaaagtgcg				1560
tctcaatgag	atttatacaa	agacagatag	caagtcaatc	atgaggatga	agagtgggtca				1620
gatgtttgcc	aaggaagatt	tgaaacggaa	gaagcttgta	cgtgatggga	gtgtgtttct				1680
gaagaatgca	gcaggaaggt	tgaaagaggt	tcaagcagtt	cttctcactg	acattttagt				1740
tttccttcaa	gaaaaagacc	agaagtacat	ctttgcatca	ttggaccaga	agtcaacagt				1800
gatctcttta	aagaagctga	ttgtgagaga	agtggcacat	gaggagaaag	gtttattcct				1860
gatcagcatg	gggatgacag	atccagagat	ggtagaagtc	catgccagct	ccaaagagga				1920
acgaaacagc	tggattcaga	tcattcagga	cacaatcaac	accctgaaca	gagatgaaga				1980
tgaaggaatt	cctagtgaga	atgaggaaga	aaagaaaatg	ttggacacca	gagcccgaga				2040
attaaaagaa	caacttcacc	agaaggacca	aaaaatccta	ctcttgttgg	aagagaagga				2100
gatgattttc	cgggacatgg	ctgagtgcag	cacccctctc	ccagaggatt	gctccccaac				2160
acatagccct	agagttctct	tccgctccaa	cacagaagag	gctctcaaag	gaggaccttt				2220
aatgaaaagt	gcaataaatg	aggtggagat	ccttcagggt	ttggtgagtg	gaaatctggg				2280
aggcacactt	gggccgactg	tcagcagccc	cattgagcaa	gatgtggtcg	gtcccgtttc				2340
cctgccccgg	agagcagaga	cctttggagg	atttgacagc	catcagatga	atgcttcaaa				2400
aggaggcgag	aaggaagagg	gagatgatgg	ccaagatctt	aggagaacgg	aatcagatag				2460
tggcctaaaa	aaggggtggaa	atgctaacct	ggtatttatg	cttaaaagaa	acagtgagca				2520
ggttggtccag	agcgttggtc	atctctacga	gctcctcagc	gctctgcagg	gtgtggtgct				2580
gcagcaggac	agctacattg	aggaccagaa	actggtgctg	agcgagaggg	cgctcactcg				2640
cagcttggtc	cgcccgagct	ccctcattga	gcaggagaag	cagcgcagcc	tggagaagca				2700
gcgccaggac	ctggccaacc	tgcagaagca	gcaggcccag	tacctcgagg	agaagcgcag				2760
gcgcgagcgt	gagtgggaag	ctcgtgagag	ggagctgcgg	gagcgggagg	ccctcctggc				2820
ccagcgcgag	gaggaggtgc	agcagggggca	gcaggacctg	gaaaaggagc	gggaggagct				2880
ccagcagaag	aagggcacat	accagtatga	cctggagcga	ctgcgtgctg	cccagaaaca				2940
gcttgagagg	gaacaggagc	agctgcgccg	ggaggcagag	cggctcagcc	agcggcagac				3000
agaacggggac	ctgtgtcagg	tttcccatcc	acataccaag	ctgatgagga	tcccatcggt				3060
cttccccagt	cctgaggagc	ccccctcgcc	atctgcacct	tccatagcca	aatcagggtc				3120

ADS5001.ST25.txt

attggactca gaactttcag tgtcccaaaa aaggaacagc atctctcgga cacacaaaga	3180
taaggggcct tttcacatac tgagttcaac cagccagaca aacaaaggac cagaagggca	3240
gagccaggcc cctgcgtcca cctctgcctc taccgcctg tttgggttaa caaagccaaa	3300
ggaaaagaag gagaaaaaaa agaagaacaa aaccagccgc tctcagcccc gtgatgggtcc	3360
cgcgtcagaa gtatcagcag aggggtgaaga gatcttctgc tgaccctctt cctctctgct	3420
gaggcagctg cctcctgata ctggccagcc cacctctcct gctgtccccg cgtgcacaag	3480
tctcttacac tggacgcca ctgctcctca gcgtccagtc ctctggggcg gccccaggtc	3540
ctggacaata agcaacagat gatattgagt gtcgggtggg gaaggaggcc cagactctgc	3600
ttcggccatg atttgtgact gcccaggact ctgaggttgg gctggcccta ctcaggatta	3660
cactgaaagt aatggcctcg taagtacagg tgatggtttt ggacacgtca ggaattccta	3720
aaggctgaaa gagtgtatcc aagtaaggct tgaacctccg aatgcctttt atttggggga	3780
acacaaaacc aaacagcaga tgttttggac ttgatctgtg tacgtacatg gggacctgtc	3840
tgcatataca cacggggaat gccagaagaa ggcccagtct gcaccaggcg tctgggtcaac	3900
ttagcacaag ggcagtgctt ggacggaccc ggagcccccg catatcagca gttcacccag	3960
tactcctcag agactggttt ccctctaaac ccatcccggg cacataccac ccgtgttttg	4020
catgtatttc tcatttcatt ttagggatga caaacatttg tgaaaccagt gagagaaggc	4080
ttgatgtgta taaaagacgt gatgtgcacc acctcgatct cggtgtttca ggcactaaag	4140
caacaaaaca acccatagta tctcattctg tcatcagatc cagaagaaat atcctggttt	4200
tccagcatgt ttaccacat gttttggcca tggataaagt gaagaggcct actcaccatt	4260
atccctgcag cgtgacacct tttgattgtc actgaccact cagaaggggc cacggcctcc	4320
tggctgtgtt cctgagcccc cgtcgtgcct ctcccagaca gcagctgtct ggcccttgct	4380
gggtgagggc acaccactgc caggggtcag cctcgcaccc aggccaggca gaagctgtgc	4440
tctgaagcta ggacagctgg ctgagaagtg ggttcaggcg aagggtgaag ccatgtgtag	4500
cagttcctgc cagtgcagat ctggagagga gctggccccg aaggcgtggt tgtgaaagcg	4560
cccttcttat gttaggaggc cttggcaaaa ttggatttct tcaaaaatac atgtaaaggt	4620
ctgttgttga attgtactct gcccctggaa gcagatacag atggctgcct gctgctcggc	4680
tttgcttttg cttttccac cggtgtttca tctttgttca cttgaggctt tccccagctg	4740
gtgtgtgcag gacagttcat ggtaatgttg ccctctgagg ccccgtaac cagaaggag	4800
gccctggaaa attttgtgct tccaacgtgg ccttcaattc ttgctttttt gccctcgga	4860
agcatggggc ttttgagcac acttaaaaaa agaaaaatct gtaacttggg gcttattgat	4920
gaattgcaag ctggccttgc agatggagat atttatcttt cagtttattt gaaagaggtc	4980
tggtttaaaa tttgtagcct acatttgttt tatttattgt atttgtgtgt ttgtgtttgt	5040

ADS5001.ST25.txt

ttttttttaa	gggtgagcca	ggtctagccc	aacagtctaa	actatccagt	caataccgag	5100
tgaagtggca	gccagcactg	ttcactctgt	gtcttttgaa	gtgccttgaa	ggcccagatg	5160
aaattttaaa	gggagggggg	ccatgtcctt	ccctcccca	ccccgcctca	ttctttaatc	5220
aaaggatgtc	ttctcccttg	tttgagaatg	aagaaactcg	ccacctctga	cctacctttg	5280
cctttttctg	tcatggagaa	tactcaccct	tcagaaacag	accaaaggcc	aaaacctgct	5340
gatttttcta	ttgaaaatat	gtccccttgc	aaagacccta	aacaaaaagt	taagtttctt	5400
tctttcacct	atttgtacaa	ctccaagtta	cagctgaatc	tgtcgtgact	ttcctgagat	5460
ctaccggggg	cttggtgtgc	tgttctgggc	actggctccg	agttcccctc	ctgggatttg	5520
caggagggca	gtactgaacc	tgcattcttc	tccttgtaaa	tgtaggccgg	gtgcccctgt	5580
tctccggggt	tggaacaata	cgagggttgg	gctgatggga	tttacttgcg	tacgtgctct	5640
tcacaaaaac	accgtggatg	ctgaagttag	agcacgtcgc	cacagagctt	gacatcaatg	5700
ttagagggtc	tcttactccc	cgcccagctg	tgatgtttca	tctgctttgg	ttgttttggt	5760
ggtctttttt	aaaaatagag	atttcacatc	tgcccagacc	ccactcaaaa	cgatttggtc	5820
aggttctggt	tggacaagtt	taaaatcaaa	gtagtgcccg	gaattccctc	aaaccaccca	5880
acttcatcca	ggaatacagt	ctgcagtgca	gcaacagaac	cgcttaccaa	gaactgtgct	5940
tacatacctt	tgtcatctct	cttccccctt	tggaagtgtg	cctcaggggg	atttgttcct	6000
gtcctgggga	tttacctggg	atggtggctg	cctgtgcttt	tgctcatggc	cttgacagtg	6060
ctctagttag	tggatctaata	ggcctgtctt	ggtttctatc	acatgagaag	gggttgtttt	6120
tttggggtga	ctcggactga	attccccata	ctgtttccac	gccgggacac	catgttctcc	6180
atcaagctaa	agaaatcacg	tgccctgaaac	tgtgcttaag	ttttggggga	aagatggagt	6240
tcctatccag	agcccccaga	tttccagaat	cgagtgagct	tcctggaagg	agactgcgtc	6300
ttctctcaat	tccagtcatc	tcagtcgttg	tcgttaggtg	acatgtgcac	tttaaagtct	6360
ctcatcggtt	ggcttcattt	tcaagacaat	caaagtattt	gactgtgttt	tcttcttaga	6420
aaatggagag	ggttaaaaaac	atgcaaactg	ccactttcaa	cctttgccag	tattccctct	6480
acccccgtga	gagctatctg	gggggaagaa	tccttaccaa	ggtttttttg	gaaagggtacg	6540
aatcttaact	tttttcccct	tctgtgtctc	agggttaatac	tattcagagt	cgcccctttg	6600
ctcattttct	cccgtatttg	ttaccttcct	gaggcctcag	tattagtcgt	gagcaciaag	6660
ttttgagacc	tttggcggtg	tttcttgatg	tgggagggga	ggtgttagtg	catgcaaggg	6720
ttgaactaga	tagaccctgc	cttagtagag	ggtgggacta	taaccttaga	ggccagaact	6780
tgatccagaa	gttgctgtcc	acagaagtgc	tttctatttc	atcatttttg	tttctagggc	6840
tctttttctg	tagccaggtc	ttcccaagga	ttttagtatt	tgcattggag	ttgaggttta	6900
ctctaagtat	ggtggcccag	ctgtgcccag	aggacagcca	ggcaggccct	gggagggagt	6960

ADS5001.ST25.txt

```

ttagaaagac agtcctggtg aatgggcttc aagtgggtcac aaagaggggtg gctgtgaggt 7020
gaccccagac actgcagaac gatgtgcacc ctctgcgttt tggatgtcct tggaatgtgg 7080
gagcctagaa ataaccctgt ggatggaatt ggggcagcgg ctgctggaga tctgtgtgcc 7140
ttgccttcct tcagcaggac cgtctaggtg cgcagccacc tatggatgcg tcccagccag 7200
ccccgtcgct ctcgctccatc ctcagagaca aagaagaggg cagggagttt gggcttggtt 7260
ttgaactttc ctttcaatgt agcaaagcat tcctagttaa ccagagcctt ggaatctact 7320
gcctgctggc caggctttta aatgaaaagt gttttaatgc tgccataaaa gggaggcggg 7380
ggggaggaag ggaaaataaa ggcattcttc caagtactca tctaatttaa ttgtcaaaag 7440
attgataggc catgaattac ttctccatct cactaagggt taaaggcgtg caacccccca 7500
ctggctgtgt cccctgccac cgaagtgagt gacctgccct acaaccagggt gggaccacct 7560
gtgctgcagt ccggagggggc ttctgcagga agcactcacc ccccacacct tccccggcct 7620
gagcttcccc tacctttcgt caccacctga gggcatgagc acaggccatg gggcgtgcct 7680
ggtgagtctg cctgtggttc aggcttagcc tgtggtctcc tgtgtgctgc tgcccgcagt 7740
ggatgcgcag gggaggcgtg gggatccgca ggagggtggt tgggatacac cggatacctc 7800
tgctctcatt gcttgtttgc aaatgctcta tggacatttg tgtgctaaat cctattaaat 7860
aaaaaagacg ggttaaaacc cagatgctgt atattcattt gtaattatgt ataaagtga 7920
gcagttttaa actgtaaaga tttttttcag tgtgttttct cgaattttgc cacaacatac 7980
tggtctcgta ttttatttat ctttctttct agttaccagc ttcagaccct tgtaaagtct 8040
ccctcagccc tttcaaaaaa taataaattt cctgtgaagt t 8081

```

```

<210> 23
<211> 13290
<212> DNA
<213> Human

```

```

<400> 23
gaagcgcctg tgctctgccg agactgccgt gccattgct cgcctcgggt gccgcccgtt 60
tagccgcctc cgggggagcg gccgcctatt gtctttctcc gcggcgaagg tgaagagttg 120
tcccagctcg gcccgcgggg gagccccggg agccgcacgt gtcctgggtc atgaaactta 180
atccacagca agctccctta tatggtgatt gtgttggtac agtgctgctt gctgaagagg 240
acaaagctga agatgatgta gtgttttact tggatttttt gggttccacc ctccgtcact 300
gtacaagtac tcggaagggtc agttctgata cattggagac cattgctcct ggtcatgatt 360
gttgtgaaac agtgaagggt cagctctgtg cttccaaaga gggccttccc gtgtttgtgg 420
tggtgaaga agactttcat ttcgtccagg atgaagcgta tgatgcagct caattcctag 480
caaccagtgc tggaaatcag caggctttga actttaccgg ttttcttgac cagtcaggac 540
cccatctgg ggatgtgaat tcccttgata agaagttggt gctggcattc aggcacctga 600

```

ADS5001.ST25.txt

agctgcccac	ggagtggaat	gtattgggga	cagatcagag	tttgcattgat	gctggcccgc	660
gagagacatt	gatgcatttt	gctgtgcggc	tgggactgct	gaggttgacg	tggttcctgt	720
tgcagaagcc	aggtggccgc	ggagctctca	gtatccacaa	ccaggaagg	gcgacgcctg	780
tgagcttggc	cttggagcga	ggctatcaca	agctgcacca	gcttctaacc	gaggagaatg	840
ctggagaacc	agactcctgg	agcagtttat	cctatgaaat	accgtatgga	gactgttctg	900
tgaggcatca	tcgagagttg	gacatctata	cattaacctc	tgagtctgat	tcacatcatg	960
aacacccatt	tcctggagac	ggttgcactg	gaccaatttt	taaacttatg	aacatccaac	1020
agcaactaat	gaaaacaaac	ctcaagcaga	tggacagtct	tatgccctta	atgatgacag	1080
cacaggatcc	ttccagtgcc	ccagagacag	atggccagtt	tcttcctgt	gcaccggagc	1140
ccacggaccc	tcagcgactt	tcttcttctg	aagagactga	gagcactcag	tgctgcccag	1200
ggagccctgt	tgcacagact	gaaagtccct	gtgatttgtc	aagcatagtt	gaggaggaga	1260
atacagaccg	ttcctgtagg	aagaaaaata	aaggcgtgga	aagaaaagg	gaagaggtgg	1320
agccagcacc	tattgtggac	tctggaactg	tatctgatca	agacagctgc	cttcagagct	1380
tgccctgattg	tggagtaaag	ggcacggaag	gcctttcgtc	ctgtggaaac	agaaatgaag	1440
aaactggaac	aaaatcttct	ggaatgcca	cagaccagga	gtccctgagc	agtggagatg	1500
ctgtgcttca	gagagacttg	gtcatggagc	caggcacagc	ccagtattcc	tctggaggtg	1560
aactgggagg	catttcaaca	acaaatgtca	gtaccccaga	cactgcagg	gaaatggaac	1620
atgggctcat	gaaccagat	gccactgttt	ggaagaatgt	gcttcaggga	ggggaaagta	1680
caaaggaaag	atttgagaac	tctaattattg	gcacagctgg	agcctctgac	gtgcacgtca	1740
caagtaagcc	tgtggataaa	atcagtgttc	caaactgtgc	ccctgctgcc	agttccctgg	1800
atggtaacaa	acctgctgag	tcttcacttg	catttagtaa	tgaagaaacc	tccactgaaa	1860
aaacagcaga	aacggaaact	tcacgaagtc	gtgaggagag	tgctgatgct	ccagtagatc	1920
agaattctgt	ggtgattcca	gctgctgcaa	aagacaagat	ttcagatgga	ttagaacctt	1980
atactctctt	agcagcaggc	ataggtgagg	caatgtcacc	ctcagattta	gcccttcttg	2040
ggctggaaga	agatgtaatg	ccacaccaga	actcagaaac	aaattcatct	catgctcaaa	2100
gccaaaagg	caaatcctca	cccatttggt	ctacaactgg	agacgataaa	ctttgtgcag	2160
actctgcatg	tcaacagaac	acagtgactt	ctagtggcga	tttggttgca	aaactgtgtg	2220
ataacatagt	tagcgagtcc	gaaagcacca	cagcaaggca	accagctca	caagatccac	2280
ccgatgcctc	ccactgtgaa	gaccacagg	ctcatacagt	cacctctgac	cctgtaagg	2340
atacccagga	acgtgcggat	ttttgtcctt	tcaaagtgg	ggataacaaa	ggccaacgaa	2400
aagatgtgaa	actagataaa	cctttaacaa	atatgcttga	ggtggtttca	catccacatc	2460
cagttgtccc	taaaatggag	aaagaactgg	tgccagacca	ggcagtaata	tcagacagta	2520

ADS5001.ST25.txt

ctttctctct	ggcaaacagt	ccaggcagtg	aatcagtaac	caaggatgac	gcactttctt	2580
ttgtcccctc	ccagaaagaa	aagggaacag	caactcctga	actacataca	gctacagatt	2640
atagagatgg	cccagatgga	aattcgaatg	agcctgatac	gcggccacta	gaagacaggg	2700
cagtaggcct	gtccacatcc	tccactgctg	cagagcttca	gcacgggatg	gggaatacca	2760
gtctcacagg	acttggtgga	gagcatgagg	gtcccgcctc	tccagcaatc	ccagaagctc	2820
tgaatatcaa	ggggaacact	gactcttccc	tgcaaagtgt	gggtaaggcc	actttggctt	2880
tagattcagt	tttgactgaa	gaaggaaaac	ttctggtggt	ttcagaaagc	tctgcagctc	2940
aggaacaaga	taaggataaa	gcggtgacct	gttcctctat	taaggaaaat	gctctctctt	3000
caggaacttt	gcaggaagag	cagagaacac	cacctcctgg	acaagatact	caacaatttc	3060
atgaaaaatc	aatctcagct	gactgtgcca	aggacaaagc	acttcagcta	agtaattcac	3120
cgggtgcatc	ctctgccttt	cttaaggcag	aaactgaaca	taacaaggaa	gtggccccac	3180
aagtctcact	gctgactcaa	ggtggggctg	cccagagcct	ggtgccacca	ggagcaagtc	3240
tggccacaga	gtcaaggcag	gaagccttgg	gggcagagca	caacagctcc	gctctgttgc	3300
catgtctgtt	gccagatggg	tctgatgggt	ccgatgctct	taactgcagt	cagccttctc	3360
ctctggatgt	tggagtgaag	aacactcaat	cccagggaaa	aactagtgcc	tgtgaggtga	3420
gtggagatgt	gacggtggat	gttacagggg	ttaatgctct	acaaggatat	gctgagccca	3480
gaagagagaa	tatatcacac	aacacccaag	acatcctgat	tccaaacgtc	ttgttgagcc	3540
aagagaagaa	tgccgttcta	ggtttgccag	tggctctaca	ggacaaagct	gtgactgacc	3600
cacagggagt	tggaacccca	gagatgatac	ctcttgattg	ggagaaaggg	aagctggagg	3660
gagcagacca	cagctgtacc	atgggtgacg	ctgaggaagc	ccaaatagac	gatgaagcac	3720
atcctgtcct	actgcagcct	gttgccaagg	agctccccac	agacatggag	ctctcagccc	3780
atgatgatgg	ggccccagct	ggtgtgaggg	aagtcatgcg	agccccgcct	tcaggcaggg	3840
aaaggagcac	tccctctcta	ccttgcatgg	tctctgcccc	ggacgcacct	ctgcctaagg	3900
gggcagactt	gatagaggag	gctgccagcc	gtatagtgga	tgctgtcatc	gaacaagtca	3960
aggccgctgg	agcactgctt	actgaggggg	aggcctgtca	catgtcactg	tccagccctg	4020
agttgggtcc	tctcactaaa	ggactagaga	gtgctttttac	agaaaaagtg	agtactttcc	4080
cacctgggga	gagcctacca	atgggcagta	ctcctgagga	agccacgggg	agccttgagc	4140
gatgttttgc	tggaaggag	gagccagaga	agatcatttt	acctgtccag	gggcctgagc	4200
cagcagcaga	aatgccagac	gtgaaagctg	aagatgaagt	ggattttaga	gcaagttcaa	4260
tttctgaaga	agtggctgta	gggagcatag	ctgctacact	gaagatgaag	caaggcccaa	4320
tgacctcaggc	gataaaccga	gaaaactggg	gtacaataga	gccatgccct	gatgcagcat	4380
ctcttctggc	ttccaagcag	agcccagaat	gtgagaactt	cctggatggt	ggactgggca	4440

ADS5001.ST25.txt

gagagtgtac	ctcaaaacaa	ggtgtactta	aaagagaatc	tgggagtgat	tctgacctct	4500
ttcactcacc	cagtgatgac	atggacagca	tcattcttccc	aaagccagag	gaagagcatt	4560
tggcctgtga	tatcaccgga	tccagttcat	ccaccgatga	cacggcttca	ctggaccgac	4620
attctttctca	tggcagtgat	gtgtctctct	cccagatttt	aaagccaaac	aggtcaagag	4680
atcggcaaag	ccttgatgga	ttctacagcc	atgggatggg	agctgagggt	cgagaaagtg	4740
agagtgaagc	tgctgaccca	ggcgacgtgg	aggaggagga	gatggacagt	atcactgaag	4800
tgcctgcaaa	ctgctctgtc	ctaaggagct	ccatgcgctc	tctttctccc	ttccggaggc	4860
acagctgggg	gcctgggaaa	aatgcagcca	gcgatgcaga	aatgaaccac	cggagttaa	4920
tgcgagttct	tggggatggt	gtcaggagac	ctcccattca	taggagaagt	ttcagtctag	4980
aaggcttgac	aggaggagct	ggtgtcggaa	acaagccatc	ctcatctcta	gaagtaagct	5040
ctgcaaatgc	cgaagagctc	agacacccat	tcagtgggtga	ggaacggggt	gactctttgg	5100
tgctactttc	agaagaggat	ctggagtcag	accagagaga	acataggatg	tttgatcagc	5160
agatatgtca	cagatctaag	cagcagggat	ttaattactg	tacatcagcc	atttcctctc	5220
cattgacaaa	atccatctca	ttaatgacaa	tcagccatcc	tggattggac	aattcacggc	5280
ccttccacag	taccttccac	aataccagtg	ctaattctgac	tgagagtata	acagaagaga	5340
actataatth	cctgccacat	agccccctca	agaaagattc	tgaatggaag	agtggaacaa	5400
aagtcagtcg	tacattcagc	tacatcaaga	ataaaatgtc	tagcagcaag	aagagcaaag	5460
aaaaggaaaa	agaaaaagat	aagattaagg	agaaggagaa	agattctaaa	gacaaggaga	5520
aagataagaa	gactgtcaac	gggcacactt	tcagttccat	tcctgttggtg	ggtcccatca	5580
gctgtagcca	gtgtatgaag	cccttcacca	acaaagatgc	ctatacttgt	gcaaattgca	5640
gtgcttttgt	ccacaaaggc	tgccgagaaa	gtctagcctc	ctgtgcaaag	gtcaaaatga	5700
agcagcccaa	agggagcctt	caggcacatg	acacatcatc	actgcccacg	gtcattatga	5760
gaaacaagcc	ctcacagccc	aaggagcgtc	ctcgggtccgc	agtcctcctg	gtggatgaaa	5820
ccgctaccac	cccaatattt	gccaatagac	gatcccagca	gagtgtctcg	ctctccaaaa	5880
gtgtctccat	acagaacatt	actggagttg	gcaatgatga	gaacatgtca	aacacctgga	5940
aattcctgtc	tcattcaaca	gactcactaa	ataaaatcag	caagggtcaat	gagtcaacag	6000
aatcacttac	tgatgagggg	gtaggtacag	acatgaatga	aggacaacta	ctgggagact	6060
ttgagattga	gtccaaacag	ctggaagcag	agtcttgag	tcggataata	gacagcaagt	6120
ttctaaaaca	gcaaaagaaa	gatgtggtca	aacggcaaga	agtaatatat	gagttgatgc	6180
agacagagtt	tcatcatgtc	cgcactctca	agatcatgag	tggtgtgtac	agccagggga	6240
tgatggcgga	tctgcttttt	gagcagcaga	tggtagaaaa	gctgttcccc	tgtttgatg	6300
agctgatcag	tatccatagc	caattcttcc	agaggattct	ggagcggaag	aaggagtctc	6360

ADS5001.ST25.txt

tggtggataa	aagtgaaaag	aacttttctca	tcaagaggat	aggggatgtg	cttgtaaadc	6420
agttttcagg	tgagaatgca	gaacgtttta	agaagacata	tggcaagttt	tgtgggcaac	6480
ataaccagtc	tgtaaactac	ttcaaagacc	tttatgccaa	ggataagcgt	tttcaagcct	6540
ttgtaaagaa	gaagatgagc	agttcagttg	ttagaaggct	tggaattcca	gagtgcatac	6600
tgcttgtaac	tcagcggatt	accaagtacc	cagttttatt	ccaaagaata	ttgcagtgtc	6660
ccaaagacaa	tgaagtggag	caggaagatc	tagcacagtc	cttgagcctg	gtgaaggatg	6720
tgattggagc	tgtagacagc	aaagtggcaa	gttatgaaaa	gaaagtgcgt	ctcaatgaga	6780
tttatacaaa	gacagatagc	aagtcaatca	tgaggatgaa	gagtggtcag	atgtttgcca	6840
aggaagattt	gaaacggaag	aagcttgtag	gtgatgggag	tgtgtttctg	aagaatgcag	6900
caggaagggt	gaaagagggt	caagcagttc	ttctcactga	catttttagtt	ttccttcaag	6960
aaaaagacca	gaagtacatc	tttgcatcat	tggaccagaa	gtcaacagtg	atctctttaa	7020
agaagctgat	tgtgagagaa	gtggcacatg	aggagaaagg	tttattcctg	atcagcatgg	7080
ggatgacaga	tccagagatg	gtagaagtcc	atgccagctc	caaagaggaa	cgaaacagct	7140
ggattcagat	cattcaggac	acaatcaaca	ccctgaacag	agatgaagat	gaaggaattc	7200
ctagtgagaa	tgaggaagaa	aagaaaatgt	tggacaccag	agcccagagaa	ttaaaagaac	7260
aacttcacca	gaaggaccaa	aaaatcctac	tcttgttgga	agagaaggag	atgattttcc	7320
gggacatggc	tgagtgcagc	acccctctcc	cagaggattg	ctccccaaca	catagcccta	7380
gagttctctt	ccgctccaac	acagaagagg	ctctcaaagg	aggaccttta	atgaaaagtg	7440
caataaatga	ggtggagatc	cttcagggtt	tggtgagtgg	aaatctggga	ggcacacttg	7500
ggccgactgt	cagcagcccc	attgagcaag	atgtggtcgg	tcccgtttcc	ctgccccgga	7560
gagcagagac	ctttggagga	tttgacagcc	atcagatgaa	tgcttcaaaa	ggaggcgaga	7620
aggaagaggg	agatgatggc	caagatctta	ggagaacgga	atcagatagt	ggcctaaaaa	7680
agggtggaaa	tgctaacctg	gtatttatgc	ttaaaagaaa	cagtgagcag	gttgtccaga	7740
gcgttgttca	tctctacgag	ctcctcagcg	ctctgcaggg	tgtgggtgctg	cagcaggaca	7800
gctacattga	ggaccagaaa	ctggtgctga	gcgagagggc	gctcactcgc	agcttgctcc	7860
gcccagagctc	cctcattgag	caggagaagc	agcgcagcct	ggagaagcag	cgccaggacc	7920
tggccaacct	gcagaagcag	caggcccagt	acctcgagga	gaagcgcagg	cgcgagcgtg	7980
agtgggaagc	tcgtgagagg	gagctgcggg	agcgggaggc	cctcctggcc	cagcgcgagg	8040
aggaggtgca	gcaggggagc	caggacctgg	aaaaggagcg	ggaggagctc	cagcagaaga	8100
agggcacata	ccagtatgac	ctggagcgac	tgcgtgctgc	ccagaaacag	cttgagaggg	8160
aacaggagca	gctgcgccgg	gaggcagagc	ggctcagcca	gcggcagaca	gaacgggacc	8220
tgtgtcaggt	ttcccatcca	cataccaagc	tgatgaggat	cccatcgttc	ttccccagtc	8280

ADS5001.ST25.txt

ctgaggagcc	cccctcgcca	tctgcacctt	ccatagccaa	atcaggggtca	ttggactcag	8340
aacttttcagt	gtccccaaaa	aggaacagca	tctctcggac	acacaaagat	aaggggcctt	8400
ttcacatact	gagttcaacc	agccagacaa	acaaaggacc	agaagggcag	agccaggccc	8460
ctgcgtccac	ctctgcctct	acccgcctgt	ttgggttaac	aaagccaaag	gaaaagaagg	8520
agaaaaaaaa	gaagaacaaa	accagccgct	ctcagcccgg	tgatgggtccc	gcgtcagaag	8580
tatcagcaga	gggtgaagag	atcttctgct	gaccctcttc	ctctctgctg	aggcagctgc	8640
ctcctgatcc	tggccagccc	acctctcctg	ctgtccccgc	gtgcacaagt	ctcttacact	8700
ggacgcccac	tgctcctcag	cgtccagtcc	tcctgggcgg	ccccagggtcc	tggacaataa	8760
gcaacagatg	atattgagtg	tcgggtgggg	aaggaggccc	agactctgct	tcggccatga	8820
tttgtgactg	cccaggactc	tcagggttggg	ctggccctac	tcaggattac	actgaaagta	8880
atggcctcgt	aagtacaggt	gatgggttttg	gacacgtcag	gaattcctaa	aggctgaaag	8940
agtgtatcca	agtaagggtct	gaacctccga	atgcctttta	tttgggggaa	cacaaaacca	9000
aacagcagat	gttttggact	tgatctgtgt	acgtacatgg	ggacctgtct	gcatatacac	9060
acgggggaatg	ccagaagaag	gcccagtcctg	caccaggcgt	ctgggtcaact	tagcacaagg	9120
gcagtgcctg	gacggacccg	gagcccccg	atatcagcag	ttcaccagct	actcctcaga	9180
gactggtttc	cctctaaacc	catcccgggc	acataccacc	cgtgttttgc	atgtattttct	9240
cattttcattt	tagggatgac	aaacatttgt	gaaaccagtg	agagaaggct	tgatgtgtat	9300
aaaagacgtg	atgtgcacca	cctcgatctc	ggtgttttcag	gcactaaagc	aacaaaacaa	9360
cccatagtat	ctcattctgt	catcagatcc	agaagaaata	tcctggtttt	ccagcatggt	9420
taccacatg	ttttggccat	ggataaagtg	aagaggccta	ctcaccatta	tccctgcagc	9480
gtgacacctt	ttgattgtca	ctgaccactc	agaaggggcc	acggcctcct	ggctgtgttc	9540
ctgagcccc	gtcgtgcctc	tcccagacag	cagctgtctg	gcccttgctg	ggtgagggca	9600
caccactgcc	aggggtcagc	ctcgcaccca	ggccaggcag	aagctgtgct	ctgaagctag	9660
gacagctggc	tgagaagtg	gttcaggcga	aggggtgaagc	catgtgtagc	agttcctgcc	9720
agtgcagatc	tggagaggag	ctggccccga	aggcgtgggt	gtgaaagcgc	ccttcttatg	9780
ttaggaggcc	ttggcaaaat	tggattttctt	caaaaataca	tgtaaagggtc	tgttgttgaa	9840
ttgtactctg	cccctggaag	cagatacaga	tggtgcctg	ctgctcggct	ttgcttttgc	9900
ttttcccacc	gtgttttcat	ctttgttcac	ttgaggcttt	ccccagctgg	tgtgtgcagg	9960
acagttcatg	gtaatgttgc	cctctgaggc	cccgtacacc	agaagggagg	ccctggaaaa	10020
ttttgtgctt	ccaacgtggc	cttcaattct	tgcttttttg	cccctcggaa	gcatggggct	10080
tttgagcaca	cttaaaaaaa	gaaaaatctg	taacttggtg	cttattgatg	aattgcaagc	10140
tggccttgca	gatggagata	tttatctttc	agtttatattg	aaagagggtct	ggtttaaaat	10200

ADS5001.ST25.txt

```

ttgtagccta catttgTTTT atttattgta tttgtgtgtt tgtgtttgtt tttttttaag 10260
ggtgagccag gtctagccca acagtctaaa ctatccagtc aataccgagt gaagtggcag 10320
ccagcactgt tcactctgtg tcttttgaag tgccttgaag gcccagatga aattttaaag 10380
ggaggggggtc catgtccttc cctcccccac cccgcctcat tctttaatca aaggatgtct 10440
tctcccttgt ttgagaatga agaaactcgc cacctctgac ctaccttgc ctttttctgt 10500
catggagaat actcaccctt cagaaacaga ccaaaggcca aaacctgctg atttttctat 10560
tgaaaatatg tccccttgca aagaccctaa acaaaaagtt aagtttcttt ctttcaccta 10620
ttgtacaac tccaagttac agctgaatct gtcgtgactt tcctgagatc taccggggc 10680
ttggctgtct gttctgggca ctggctccga gttcccctcc tgggatttgc aggagggcag 10740
tactgaacct gcattcttct ccttgtaa at gtaggccggg tgcccctgtt ctccgggttt 10800
ggaacaatac gaggttggtg ctgatgggat ttacttgctg acgtgctctt cacaaaaaca 10860
ccgtggatgc tgaagttaga gcacgtcgcc acagagcttg acatcaatgt tagagggctt 10920
cttactcccc gccagctgt gatgtttcat ctgctttggt tgttttggtg gtctttttta 10980
aaaatagaga tttcacatct gccagaccc cactcaaac gatttggtca ggttctggtt 11040
ggacaagttt aaaatcaaag tagtgcccg aattccctca aaccaccaa cttcatccag 11100
gaatacagtc tgcagtgcag caacagaacc gcttaccaag aactgtgctt acataccttt 11160
gtcatctctc ttccccctt ggaagttgtc ctcaggggga tttgttctg tcctggggat 11220
ttacctggga tgggtggctgc ctgtgctttt gctcatggcc ttgacagtgc tctagtgtct 11280
ggatcta atg gcctgtcttg gtttctatca catgagaagg ggttggtttt ttgggggtgac 11340
tcggactgaa ttccccatac tgtttccacg ccgggacacc atgttctcca tcaagctaaa 11400
gaaatcacgt gcctgaaact gtgcttaagt tttgggggaa agatggagtt cctatccaga 11460
gccccagat ttccagaatc gagtgagctt cctggaagga gactgctct tctctcaatt 11520
ccagtcactc cagtcgttgt cgttaggtga catgtgcact ttaa atgctc tcatcggttg 11580
gcttcatttt caagacaatc aaatgtattg actgtgtttt cttcttagaa aatggagagg 11640
gttaaaaaca tgcaaactgc cactttcaac ctttgccagt attccctcta ccccgtgag 11700
agctatctgg ggggaagaat ccttaccaag gtttttttgg aaagggtacga atcttaactt 11760
ttttccccctt ctgtgtctca gggtaatact attcagagtc gccccttgc tcattttctc 11820
ccgtatttgt taccttctg aggcctcagt attagtcgtg agcaciaaagt tttgagacct 11880
ttggcgttgt ttcttgatgt gggaggggag gtgttagtgc atgcaagggt tgaactagat 11940
agaccctgcc ttagtagagg gtgggactat aaccttagag gccagaactt gatccagaag 12000
ttgctgtcca cagaagtgtt ttctatttca tcatttttgt ttctagggct ctttttctgt 12060
agccaggtct tccaaggat tttagtat tt gcattggagt tgaggtttac tcta atgatg 12120

```

ADS5001.ST25.txt

```

gtggcccagc tgtgcccaga ggacagccag gcaggccctg ggagggagtt tagaaagaca 12180
gtcctggtga atgggcttca agtggtcaca aagaggggtg ctgtgaggtg accccagaca 12240
ctgcagaacg atgtgcaccc tctgcgtttt ggatgtcctt ggaatgtggg agcctagaaa 12300
taaccctgtg gatggaattg gggcagcggc tgctggagat ctgtgtgcct tgccttcctt 12360
cagcaggacc gtctaggtgc gcagccacct atggatgcgt cccagccagc cccgtcgctc 12420
tcgtccatcc tcagagacaa agaagagggc agggagtttg ggcttggttt tgaactttcc 12480
tttcaatgta gcaaagcatt cctagttaac cagagccttg gaatctactg cctgctggcc 12540
aggctttaaa atgaaaagtg ttttaatgct gccataaaag ggaggcgggg gggaggaagg 12600
gaaaataaag gcatctttcc aagtactcat ctaatttaat tgtcaaaaga ttgataggcc 12660
atgaattact tctccatctc actaagggtt aaaggcgtgc aacccccac tggctgtgtc 12720
ccctgccacc gaagtgagtg acctgcccta caaccaggtg ggaccacctg tgctgcagtc 12780
cggaggggct tctgcaggaa gcactcacc cccacacctt ccccgccctg agcttcccct 12840
acctttcgtc accacctgag ggcatgagca caggccatgg ggcgtgcctg gtgagtctgc 12900
ctgtggttca ggcttagcct gtggtctcct gtgtgctgct gcccgcatgg gatgcgcagg 12960
ggaggcgtgg ggatccgcag gagggtggtt gggatacacc ggatacctct gctctcattg 13020
cttgtttgca aatgctctat ggacatttgt gtgctaaatc ctattaaata aaaaagacgg 13080
gttaaaaccc agatgctgta tattcatttg taattatgta taaagtgaag cagttttaaa 13140
ctgtaaagat ttttttcagt gtgttttctc gaattttgcc acaacatact ggcttcgtat 13200
tttatttatc tttctttcta gttaccagct tcagaccctt gtaaagtctc cctcagccct 13260
ttcaaaaaat aataaatttc ctgtgaagtt 13290

```

```

<210> 24
<211> 13302
<212> DNA
<213> Human

```

```

<400> 24
gaagcgcctg tgctctgccg agactgccgt gccattgct cgcctcggtc gccgccgctt 60
tagccgcctc cgggggagcg gccgcctatt gtctttctcc gcggcgaagg tgaagagttg 120
tcccagctcg gcccgcgggg gagccccggg agccgcacgt gtcctgggtc atgaaactta 180
atccacagca agctccccta tatggtgatt gtgttggttac agtgctgctt gctgaagagg 240
acaaagctga agatgatgta gtgttttact tggatattttt gggttccacc ctccgtcact 300
gtacaagtac tcggaagggtc agttctgata cattggagac cattgctcct ggcatgatt 360
gttgtgaaac agtgaagggtg cagctctgtg cttccaaaga gggccttccc gtgtttgtgg 420
tggctgaaga agactttcat ttcgtccagg atgaagcgta tgatgcagct caattcctag 480

```

ADS5001.ST25.txt

caaccagtgc	tggaaatcag	caggctttga	actttacccg	ttttcttgac	cagtcaggac	540
ccccatctgg	ggatgtgaat	tcccttgata	agaagttggt	gctggcattc	aggcacctga	600
agctgcccac	ggagtggaat	gtattgggga	cagatcagag	tttgcattgat	gctggcccgc	660
gagagacatt	gatgcatttt	gctgtgcggc	tgggactgct	gaggttgacg	tggttcctgt	720
tgcagaagcc	aggtggccgc	ggagctctca	gtatccacaa	ccaggaaggg	gcgacgcctg	780
tgagcttggc	cttggagcga	ggctatcaca	agctgcacca	gcttctaacc	gaggagaatg	840
ctggagaacc	agactcctgg	agcagtttat	cctatgaaat	accgtatgga	gactgttctg	900
tgaggcatca	tcgagagttg	gacatctata	cattaacctc	tgagtctgat	tcacatcatg	960
aacacccatt	tcctggagac	ggttgcaactg	gaccaatttt	taaacttatg	aacatccaac	1020
agcaactaat	gaaaacaaac	ctcaagcaga	tggacagtct	tatgccctta	atgatgacag	1080
cacaggatcc	ttccagtgcc	ccagagacag	atggccagtt	tcttccctgt	gcaccggagc	1140
ccacggaccc	tcagcgactt	tcttcttctg	aagagactga	gagcactcag	tgctgcccag	1200
ggagccctgt	tgcacagact	gaaagtcctt	gtgatttgtc	aagcatagtt	gaggaggaga	1260
atacagaccg	ttcctgtagg	aagaaaaata	aaggcgtgga	aagaaaaggg	gaagagggtg	1320
agccagcacc	tattgtggac	tctggaactg	tatctgatca	agacagctgc	cttcagagct	1380
tgcctgattg	tggagtaaag	ggcacggaag	gcctttcgtc	ctgtggaaac	agaaatgaag	1440
aaactggaac	aaaatcttct	ggaatgcca	cagaccagga	gtccctgagc	agtggagatg	1500
ctgtgcttca	gagagacttg	gtcatggagc	caggcacagc	ccagtattcc	tctggagggtg	1560
aactgggagg	catttcaaca	acaaatgtca	gtaccccaga	cactgcaggg	gaaatggaac	1620
atgggctcat	gaaccagat	gccactgttt	ggaagaatgt	gcttcaggga	ggggaaagta	1680
caaaggaaag	atttgagaac	tctaataattg	gcacagctgg	agcctctgac	gtgcacgtca	1740
caagtaagcc	tgtggataaa	atcagtgttc	caaactgtgc	ccctgctgcc	agttccctgg	1800
atggtaacaa	acctgctgag	tcttcacttg	catttagtaa	tgaagaaacc	tccactgaaa	1860
aaacagcaga	aacggaaact	tcacgaagtc	gtgaggagag	tgctgatgct	ccagtagatc	1920
agaattctgt	ggtgattcca	gctgctgcaa	aagacaagat	ttcagatgga	ttagaacctt	1980
atactctctt	agcagcaggc	ataggtgagg	caatgtcacc	ctcagattta	gcccttcttg	2040
ggctggaaga	agatgtaatg	ccacaccaga	actcagaaac	aaattcatct	catgctcaaa	2100
gccaaaaggg	caaatcctca	cccatttggt	ctacaactgg	agacgataaa	ctttgtgcag	2160
actctgcatg	tcaacagaac	acagtgactt	ctagtggcga	tttggttgca	aaactgtgtg	2220
ataacatagt	tagcgagtcc	gaaagcacca	cagcaaggca	accagctca	caagatccac	2280
ccgatgcctc	ccactgtgaa	gaccacaggg	ctcatacagt	cacctctgac	cctgtaaggg	2340
atacccagga	acgtgcggat	ttttgtcctt	tcaaagtggg	ggataacaaa	ggccaacgaa	2400

ADS5001.ST25.txt

aagatgtgaa	actagataaa	cctttaacaa	atatgcttga	ggtgggtttca	catccacatc	2460
cagttgtccc	taaaatggag	aaagaactgg	tgccagacca	ggcagtaata	tcagacagta	2520
ctttctctct	ggcaaacagt	ccaggcagtg	aatcagtaac	caaggatgac	gcactttctt	2580
ttgtcccctc	ccagaaagaa	aaggggaacag	caactcctga	actacataca	gctacagatt	2640
atagagatgg	cccagatgga	aattcgaatg	agcctgatac	gcggccacta	gaagacaggg	2700
cagtaggcct	gtccacatcc	tccactgctg	cagagcttca	gcacgggatg	gggaatacca	2760
gtctcacagg	acttgggtgga	gagcatgagg	gtcccgcctc	tccagcaatc	ccagaagctc	2820
tgaatatcaa	ggggaacact	gactcttccc	tgcaaagtgt	gggtaaggcc	actttggctt	2880
tagattcagt	tttgactgaa	gaaggaaaac	ttctggtggt	ttcagaaagc	tctgcagctc	2940
aggaacaaga	taaggataaa	gcggtgacct	gttcctctat	taaggaaaat	gctctctctt	3000
caggaacttt	gcaggaagag	cagagaacac	cacctcctgg	acaagatact	caacaatttc	3060
atgaaaaatc	aatctcagct	gactgtgcca	aggacaaagc	acttcagcta	agtaattcac	3120
cgggtgcatc	ctctgccttt	cttaaggcag	aaactgaaca	taacaaggaa	gtggccccac	3180
aagtctcact	gctgactcaa	ggtggggctg	cccagagcct	ggtgccacca	ggagcaagtc	3240
tggccacaga	gtcaaggcag	gaagccttgg	gggcagagca	caacagctcc	gctctgttgc	3300
catgtctgtt	gccagatggg	tctgatgggt	ccgatgctct	taactgcagt	cagccttctc	3360
ctctggatgt	tggagtgaag	aacactcaat	cccagggaaa	aactagtgcc	tgtgaggtga	3420
gtggagatgt	gacggtggat	gttacagggg	ttaatgctct	acaaggatg	gctgagccca	3480
gaagagagaa	tatatcacac	aacacccaag	acatcctgat	tccaaacgtc	ttgttgagcc	3540
aagagaagaa	tgccgttcta	ggtttgccag	tggtcttaca	ggacaaagct	gtgactgacc	3600
cacagggagt	tggaaaccca	gagatgatac	ctcttgattg	ggagaaaggg	aagctggagg	3660
gagcagacca	cagctgtacc	atgggtgacg	ctgaggaagc	ccaaatagac	gatgaagcac	3720
atcctgtcct	actgcagcct	gttgccaagg	agctccccac	agacatggag	ctctcagccc	3780
atgatgatgg	ggccccagct	ggtgtgaggg	aagtcatgcg	agccccgcct	tcaggcaggg	3840
aaaggagcac	tccctctcta	ccttgcatgg	tctctgcca	ggacgcacct	ctgcctaagg	3900
gggcagactt	gatagaggag	gctgccagcc	gtatagtgga	tgctgtcatc	gaacaagtca	3960
aggccgctgg	agcactgctt	actgaggggg	aggcctgtca	catgtcactg	tccagccctg	4020
agttgggtcc	tctcactaaa	ggactagaga	gtgcttttac	agaaaaagtg	agtactttcc	4080
cacctgggga	gagcctacca	atgggcagta	ctcctgagga	agccacgggg	agccttgagc	4140
gatgttttgc	tggaaaggag	gagccagaga	agatcatttt	acctgtccag	gggcctgagc	4200
cagcagcaga	aatgccagac	gtgaaagctg	aagatgaagt	ggattttaga	gcaagttcaa	4260
tttctgaaga	agtggctgta	gggagcatag	ctgctacact	gaagatgaag	caaggcccaa	4320

ADS5001.ST25.txt

tgacccaggc gataaaccga gaaaactggg gtacaataga gccatgccct gatgcagcat	4380
ctctttctggc ttccaagcag agcccagaat gtgagaactt cctggatgtt ggactgggca	4440
gagagtgtac ctcaaaacaa ggtgtactta aaagagaatc tgggagtgat tctgacctct	4500
ttcactcacc cagtgatgac atggacagca tcattcttccc aaagccagag gaagagcatt	4560
tggcctgtga tatcaccgga tccagttcat ccaccgatga cacggcttca ctggaccgac	4620
attctttctca tggcagtgat gtgtctctct cccagatttt aaagccaaac aggtcaagag	4680
atcggcaaag ccttgatgga ttctacagcc atgggatggg agctgagggt cgagaaagtg	4740
agagtgaacc tgctgaccga ggcgacgtgg aggaggagga gatggacagt atcactgaag	4800
tgcctgcaaa ctgctctgtc ctaaggagct ccatgcgctc tctttctccc ttccggaggc	4860
acagctgggg gcctgggaaa aatgcagcca gcgatgcaga aatgaaccac cggagtatga	4920
gctgggtgccc ctctgggtgtg cagtactctg ctggcctgag tgctgacttt aattacagaa	4980
gtttcagtct agaaggcttg acaggaggag ctgggtgtcg aaacaagcca tcctcatctc	5040
tagaagtaag ctctgcaaat gccgaagagc tcagacaccc attcagtggg gaggaacggg	5100
ttgactcttt ggtgtcactt tcagaagagg atctggagtc agaccagaga gaacatagga	5160
tgtttgatca gcagatatgt cacagatcta agcagcaggg atttaattac tgtacatcag	5220
ccatttcctc tccattgaca aaatccatct cattaatgac aatcagccat cctggattgg	5280
acaattcacg gcccttccac agtaccttcc acaataccag tgctaattctg actgagagta	5340
taacagaaga gaactataat ttcttgccac atagcccctc caagaaagat tctgaatgga	5400
agagtggaac aaaagtcagt cgtacattca gctacatcaa gaataaaatg tctagcagca	5460
agaagagcaa agaaaaggaa aaagaaaaag ataagattaa ggagaaggag aaagattcta	5520
aagacaagga gaaagataag aagactgtca acgggcacac tttcagttcc attcctgttg	5580
tgggtcccat cagctgtagc cagtgtatga agcccttcac caacaaagat gcctatactt	5640
gtgcaaattg cagtgccttt gtccacaaag gctgccgaga aagtctagcc tcctgtgcaa	5700
aggtcaaaat gaagcagccc aaagggagcc ttcaggcaca tgacacatca tcaactgcca	5760
cggtcattat gagaaacaag ccctcacagc ccaaggagcg tcctcgggtcc gcagtcctcc	5820
tggtggatga aaccgctacc accccaatat ttgccaatag acgatcccag cagagtgtct	5880
cgctctccaa aagtgtctcc atacagaaca ttactggagt tggcaatgat gagaacatgt	5940
caaacacctg gaaattcctg tctcattcaa cagactcact aaataaaatc agcaagggtca	6000
atgagtcaac agaatacatt actgatgagg gagtaggtac agacatgaat gaaggacaac	6060
tactgggaga ctttgagatt gagtccaaac agctggaagc agagtcttgg agtcggataa	6120
tagacagcaa gtttctaaaa cagcaaaaga aagatgtggg caaacggcaa gaagtaatat	6180
atgagttgat gcagacagag tttcatcatg tccgcactct caagatcatg agtggtgtgt	6240

ADS5001.ST25.txt

acagccaggg gatgatggcg gatctgcttt ttgagcagca gatggtagaa aagctgttcc 6300
cctgttttga tgagctgac agtatccata gccaatctt ccagaggatt ctggagcgga 6360
agaaggagtc tctggtggat aaaagtgaag agaactttct catcaagagg ataggggatg 6420
tgcttgtaaa tcagttttca ggtgagaatg cagaacgttt aaagaagaca tatggcaagt 6480
tttgtgggca acataaccag tctgtaaact acttcaaaga cttttatgcc aaggataagc 6540
gttttcaagc ctttgtaaag aagaagatga gcagttcagt tgtagaagg cttggaattc 6600
cagagtgcac attgcttgta actcagcgga ttaccaagta cccagtttta ttccaaagaa 6660
tattgcagtg taccaaagac aatgaagtgg agcaggaaga tctagcacag tccttgagcc 6720
tggtgaagga tgtgattgga gctgtagaca gcaaagtggc aagttatgaa aagaaagtgc 6780
gtctcaatga gatttataca aagacagata gcaagtcaat catgaggatg aagagtggtc 6840
agatgtttgc caaggaagat ttgaaacgga agaagcttgt acgtgatggg agtgtgtttc 6900
tgaagaatgc agcaggaagg ttgaaagagg ttcaagcagt tcttctcact gacattttag 6960
ttttccttca agaaaaagac cagaagtaca tctttgcac attggaccag aagtcaacag 7020
tgatctcttt aaagaagctg attgtgagag aagtggcaca tgaggagaaa ggttttattcc 7080
tgatcagcat ggggatgaca gatccagaga tggtagaagt ccatgccagc tccaaagagg 7140
aacgaaacag ctggattcag atcattcagg acacaatcaa caccctgaac agagatgaag 7200
atgaaggaat tcctagttag aatgaggaag aaaagaaaat gttggacacc agagcccgag 7260
aattaaaaga acaacttcac cagaaggacc aaaaaatcct actcttggtg gaagagaagg 7320
agatgatttt ccgggacatg gctgagtgca gcacccctct cccagaggat tgctcccaa 7380
cacatagccc tagagttctc ttccgctcca acacagaaga ggctctcaaa ggaggacctt 7440
taatgaaaag tgcaataaat gaggtggaga tccttcaggg tttggtgagt ggaaatctgg 7500
gaggcacact tgggccgact gtcagcagcc ccattgagca agatgtggtc ggtcccgttt 7560
ccctgccccg gagagcagag acctttggag gatttgacag ccatcagatg aatgcttcaa 7620
aaggaggcga gaaggaagag ggagatgatg gccaatctt taggagaacg gaatcagata 7680
gtggcctaaa aaaggggtga aatgctaacc tggtatttat gcttaaaaga aacagtgagc 7740
aggttgtcca gagcgttggt catctctacg agctcctcag cgctctgcag ggtgtggtgc 7800
tgcagcagga cagctacatt gaggaccaga aactggtgct gagcgagagg gcgctcactc 7860
gcagcttgct ccgcccagac tccctcattg agcaggagaa gcagcgcagc ctggagaagc 7920
agcgccagga cctggccaac ctgcagaagc agcaggccca gtacctcgag gagaagcgca 7980
ggcgcgagcg tgagtgggaa gctcgtgaga gggagctgcg ggagcgggag gccctcctgg 8040
cccagcgca ggaggaggtg cagcaggggc agcaggacct ggaaaaggag cgggaggagc 8100
tccagcagaa gaagggcaca taccagtatg acctggagcg actgcgtgct gccagaaac 8160

ADS5001.ST25.txt

agcttgagag ggaacaggag cagctgcgcc gggaggcaga gcggctcagc cagcggcaga	8220
cagaacggga cctgtgtcag gtttcccatc cacataccaa gctgatgagg atcccatcgt	8280
tcttccccag tcctgaggag cccccctcgc catctgcacc ttccatagcc aaatcagggt	8340
cattggactc agaactttca gtgtcccca aaaggaacag catctctcgg acacacaaag	8400
ataaggggcc ttttcacata ctgagttcaa ccagccagac aaacaaagga ccagaagggc	8460
agagccaggc ccctgcgtcc acctctgcct ctacccgcct gtttggttta acaaagccaa	8520
aggaaaagaa ggagaaaaaa aagaagaaca aaaccagccg ctctcagccc ggtgatggtc	8580
ccgcgtcaga agtatcagca gaggggtgaag agatcttctg ctgaccctct tcctctctgc	8640
tgaggcagct gcctcctgat cctggccagc ccacctctcc tgctgtcccc gcgtgcacaa	8700
gtctcttaca ctggacgccc actgctcctc agcgtccagt cctcctgggc ggccccagg	8760
cctggacaat aagcaacaga tgatattgag tgtcgggtgg ggaaggaggc ccagactctg	8820
cttcggccat gatttgtgac tgcccaggac tctcagggtg ggctggccct actcaggatt	8880
acactgaaag taatggcctc gtaagtacag gtgatggttt tggacacgtc aggaattcct	8940
aaaggctgaa agagtgtatc caagtaaggc ctgaacctcc gaatgccttt tatttggggg	9000
aacacaaaac caaacagcag atgttttgga cttgatctgt gtacgtacat ggggacctgt	9060
ctgcatatac acacggggaa tgccagaaga aggcccagtc tgcaccaggc gtctggtcaa	9120
cttagcaciaa gggcagtgcc tggacggacc cggagcccc gcatacagc agttcaccca	9180
gtactcctca gagactgggt tccctctaaa cccatcccgg gcacatacca cccgtgtttt	9240
gcatgtattt ctcatctcat tttagggatg acaaacattt gtgaaaccag tgagagaagg	9300
cttgatgtgt ataaaagacg tgatgtgcac cacctcgatc tcggtgtttc aggcactaaa	9360
gcaacaaaac aaccatagc atctcattct gtcacagat ccagaagaaa tatcctgggt	9420
ttccagcatg ttaccacaca tgttttggcc atggataaag tgaagaggcc tactcaccat	9480
tatccctgca gcgtgacacc ttttgattgt cactgaccac tcagaagggg ccacggcctc	9540
ctggctgtgt tcctgagccc ccgtcgtgcc tctcccagac agcagctgtc tggcccttgc	9600
tgggtgaggg cacaccactg ccaggggtca gcctcgcacc caggccaggc agaagctgtg	9660
ctctgaagct aggacagctg gctgagaagt gggttcaggc gaagggtgaa gccatgtgta	9720
gcagttcctg ccagtgcaga tctggagagg agctggcccc gaaggcgtgg ttgtgaaagc	9780
gcccttctta tgtaggagg ccttggcaaa attggatttc ttcaaaaata catgtaaagg	9840
tctgttggtg aattgtactc tgcccctgga agcagataca gatggctgcc tgctgctcgg	9900
ctttgctttt gcttttccca ccgtgttttc atctttgttc acttgaggct ttccccagct	9960
ggtgtgtgca ggacagttca tggtaatgtt gccctctgag gccccgtaca ccagaaggga	10020
ggccctggaa aattttgtgc ttccaacgtg gccttcaatt cttgcttttt tgcccctcgg	10080

ADS5001.ST25.txt

aagcatgggg cttttgagca cacttaaaaa aagaaaaatc tgtaacttgg tgcttattga 10140
tgaattgcaa gctggccttg cagatggaga tatttatctt tcagtttatt tgaaagaggt 10200
ctggtttaaa atttgtagcc tacatttggt ttatttattg tatttggtgtg tttgtgtttg 10260
ttttttttta agggtagacc aggtctagcc caacagtcta aactatccag tcaataaccga 10320
gtgaagtggc agccagcact gttcactctg tgtcttttga agtgccttga aggcccagat 10380
gaaattttaa agggaggggg tccatgtcct tccctcccc accccgcctc attctttaat 10440
caaaggatgt cttctccctt gtttgagaat gaagaaactc gccacctctg acctaccttt 10500
gcctttttct gtcattggaga atactcacc ttcagaaaca gaccaaaggc caaacctgc 10560
tgatttttct attgaaaata tgtccccttg caaagaccct aaacaaaaag ttaagtttct 10620
ttctttcacc tatttgtaga actccaagtt acagctgaat ctgtcgtgac tttcctgaga 10680
tctaccggg gcttggctgt ctgttctggg cactggctcc gagttcccct cctgggattt 10740
gcaggagggc agtactgaac ctgcattctt ctcttgtaa atgtaggccg ggtgcccctg 10800
ttctccgggt ttggaacaat acgaggttgg tgctgatggg atttacttgc gtacgtgctc 10860
ttcacaaaa caccgtggat gctgaagtta gagcacgtcg ccacagagct tgacatcaat 10920
gttagagggg ctcttactcc ccgcccagct gtgatgtttc atctgctttg gttgttttgg 10980
tggtcttttt taaaaataga gatttcacat ctgcccagac cccactcaaa acgatttggt 11040
caggttctgg ttggacaagt ttaaaatcaa agtagtgccc ggaattccct caaaccaccc 11100
aacttcatcc aggaatacag tctgcagtgc agcaacagaa ccgcttacca agaactgtgc 11160
ttacatacct ttgtcatctc tcttcccccc ttggaagttg tcctcagggg gatttgttcc 11220
tgtcctgggg atttacctgg gatgggtggc gcctgtgctt ttgctcatgg ccttgacagt 11280
gctctagttg ctggatctaa tggcctgtct tggtttctat cacatgagaa ggggttggtt 11340
ttttgggggtg actcggactg aattccccat actgtttcca cgccgggaca ccatgttctc 11400
catcaagcta aagaaatcac gtgcctgaaa ctgtgcttaa gttttggggg aaagatggag 11460
ttcctatcca gagccccag atttccagaa tcgagtgagc ttcttggag gagactgcgt 11520
cttctctcaa ttccagtcac ctgagtcgtt gtcgttaggt gacatgtgca ctttaaagtc 11580
tctcatcggt tggcttcatt ttcaagacaa tcaaagtgtat tgactgtgtt ttcttcttag 11640
aaaatggaga gggttaaaaa catgcaaact gccactttca acctttgcca gtattccctc 11700
taccctcggt agagctatct ggggggaaga atccttacca aggttttttt ggaaagggtac 11760
gaatcttaac ttttttcccc ttctgtgtct cagggttaata ctattcagag tcgccccttt 11820
gctcattttc tcccgtattt gttaccttcc tgaggcctca gtattagtcg tgagcacaaa 11880
gttttgagac ctttggcgtt gtttcttgat gtgggagggg aggtgttagt gcatgcaagg 11940
gttgaactag atagaccctg ccttagtaga ggggtgggact ataaccttag aggccagaac 12000

ADS5001.ST25.txt

```

ttgatccaga agttgctgtc cacagaagtg ctttctatatt catcatatttt gtttctaggg 12060
ctcttttttct gtagccaggt cttcccaagg attttagtat ttgcattgga gttgagggtt 12120
actctaataga tgggtggccca gctgtgccca gaggacagcc aggcaggccc tgggagggag 12180
tttagaaaga cagtcctggt gaatgggctt caagtgggtca caaagagggt ggctgtgagg 12240
tgaccccaga cactgcagaa cgatgtgcac cctctgcgtt ttggatgtcc ttggaatgtg 12300
ggagcctaga aataaccctg tggatggaat tggggcagcg gctgctggag atctgtgtgc 12360
cttgcccttcc ttcagcagga ccgtctaggt gcgcagccac ctatggatgc gtcccagcca 12420
gccccgtcgc tctcgtccat cctcagagac aaagaagagg gcagggagtt tgggcttggt 12480
tttgaacttt cctttcaatg tagcaaagca ttcctagtta accagagcct tggaatctac 12540
tgcctgctgg ccaggcttta aaatgaaaag tgttttaatg ctgccataaa agggaggcgg 12600
gggggaggaa gggaaaataa aggcattctt ccaagtactc atctaattta attgtcaaaa 12660
gattgatagg ccatgaatta cttctccatc tcactaagggt ttaaaggcgt gcaaccccc 12720
actggctgtg tcccctgcca ccgaagtgag tgacctgccc tacaaccagg tgggaccacc 12780
tgtgctgcag tccggagggg cttctgcagg aagcactcac ccccccacacc ttccccggcc 12840
tgagcttccc ctacctttcg tcaccacctg agggcatgag cacaggccat ggggcgtgcc 12900
tgggtgagtct gcctgtggtt caggcttagc ctgtggtctc ctgtgtgctg ctgcccgcgt 12960
gggatgcgca ggggaggcgt ggggatccgc aggagggtgg ttgggataca ccggatacct 13020
ctgctctcat tgcttgtttg caaatgctct atggacattt gtgtgctaaa tcctattaaa 13080
taaaaaagac ggggttaaac ccagatgctg tatattcatt tgtaattatg tataaagtga 13140
agcagtttta aactgtaaag atttttttca gtgtgttttc tcgaattttg ccacaacata 13200
ctggcttcgt attttattta tctttctttc tagttaccag cttcagacct ttgtaaagtc 13260
tccctcagcc ctttcaaaaa ataataaatt tcctgtgaag tt 13302

```

```

<210> 25
<211> 8442
<212> DNA
<213> Human

```

```

<400> 25
atgaaactta atccacagca agctccctta tatggtgatt gtgttggttac agtgctgctt 60
gctgaagagg acaaagctga agatgatgta gtgttttact tggatattttt gggttccacc 120
ctccgtcact gtacaagtac tcggaaggct agttctgata cattggagac cattgctcct 180
ggtcatgatt gttgtgaaac agtgaagggt cagctctgtg cttccaaaga gggccttccc 240
gtgtttgtgg tggctgaaga agactttcat ttcgtccagg atgaagcgta tgatgcagct 300
caattcctag caaccagtgc tggaaatcag caggctttga actttacccg ttttcttgac 360
cagtcaggac ccccatctgg ggatgtgaat tcccttgata agaagttggt gctggcattc 420

```

ADS5001.ST25.txt

aggcacctga agctgcccac ggagtggaaat gtattgggga cagatcagag tttgcatgat	480
gctggcccg c gagagacatt gatgcatttt gctgtgcggc tgggactgct gaggttgacg	540
tggttcctgt tgcagaagcc aggtggccgc agagctctca gtatccacaa ccaggaagg	600
gcgacgcctg tgagcttggc cttggagcga ggctatcaca agctgcacca gcttctaacc	660
gaggagaatg ctggagaacc agactcctgg agcagtttat cctatgaaat accgtatgga	720
gactgttctg tgaggcatca tcgagagttg gacatctata cattaacctc tgagtctgat	780
tcacatcatg aacacccatt tcctggagac ggttgcactg gaccaatttt taaacttatg	840
aacatccaac agcaactaat gaaaacaaac ctcaagcaga tggacagtct tatgccctta	900
atgatgacag cacaggatcc ttccagtgcc ccagagacag atggccagtt tcttcctgt	960
gcaccggagc ccacggaccc tcagcgactt tcttcttctg aagagactga gagcactcag	1020
tgctgcccag ggagccctgt tgcacagact gaaagtcccc gtgatttgtc aagcatagtt	1080
gaggaggaga atacagaccg ttcctgtagg aagaaaaata aaggcgtgga aagaaaagg	1140
gaagaggtgg agccagcacc tattgtggac tctggaactg tatctgatca agacagctgc	1200
cttcagagct tgcctgattg tggagtaaag ggcacggaag gcctttcgtc ctgtggaaac	1260
agaaatgaag aaactggaac aaaatcttct ggaatgcca cagaccagga gtccctgagc	1320
agtggagatg ctgtgcttca gagagacttg gtcattggagc caggcacagc ccagtattcc	1380
tctggaggtg aactgggagg catttcaaca acaaatgtca gtaccccaga cactgcagg	1440
gaaatggaac atgggctcat gaaccagat gccactgttt ggaagaatgt gcttcaggga	1500
ggggaaagta caaaggaaag atttgagaac tctaataattg gcacagctgg agcctctgac	1560
gtgcacgtca caagtaagcc tgtggataaa atcagtgttc caaactgtgc ccctgccgcc	1620
agttccctgg atggtaacaa acctgctgag tcttcacttg catttagtaa tgaagaaacc	1680
tccactgaaa aaacagcaga aacggaaact tcacgaagtt gtgaggagag tgctgatgct	1740
ccagtagatc agaattctgt ggtgattcca gctgctgcaa aagacaagat ttcagatgga	1800
ttagaacctt atactctctt agcagtaggc ataggtgaga caatgtcacc cccagattta	1860
gcccttcttg ggctggaaga agatgtaatg ccacaccaga actcagaaac aaattcatct	1920
catgctcaaa gccaaaaggg caaatcctca cccatttggt ctacaactgg agacgataaa	1980
ctttgtgcag actctgcatg tcaacagaac acagtgactt ctagtggcga tttggttgca	2040
aaactgtgtg ataacatagt tagcgagtcc gaaagcacca cagcaaggca acccagctca	2100
caagatccac ccgatgcctc cactgtgaa gaccacagg ctatacagt cacctctgac	2160
cctgtaaggg ataccagga acgtgcggat ttttgtcctt tcaaagtggg ggataacaaa	2220
ggccaacgaa aagatgtgaa actagataaa cctttaacaa atatgcttga ggtggtttca	2280
catccacatc cagttgtccc taaaatggag aaagaactgg tgccagacca ggcagtaata	2340

ADS5001.ST25.txt

tcagacagta ctttctctct ggcaaacagt ccaggcagtg aatcagtaac caaggatgac	2400
gcactttctt ttgtcccctc ccagaaagaa aagggaacag caactcctga actacataca	2460
gctacagatt atagagatgg cccagatgga aattcgaatg agcctgatac gcggccacta	2520
gaagacaggg cagtaggcct gtccacatcc tccactgctg cagagcttca gcacgggatg	2580
gggaatacca gtctcacagg acttggtgga gagcatgagg gtcccgcccc tccagcaatc	2640
ccagaagctc tgaatatcaa ggggaacact gactcttccc tgcaaagtgt gggtaaggcc	2700
actttggctt tagattcagt tttgactgaa gaaggaaaac ttctggtggt ttcagaaagc	2760
tctgcagctc aggaacaaga taaggataaa gcggtgacct gttcctctat taaggaaaat	2820
gctctctctt caggaacttt gcaggaagag cagagaacac cacctcctgg acaagatact	2880
caacaatttc atgaaaaatc aatctcagct gactgtgcca aggacaaagc acttcagcta	2940
agtaattcac cgggtgcatc ctctgccttt ctttaaggcag aaactgaaca taacaaggaa	3000
gtggccccac aagtctcact gctgactcaa ggtggggctg cccagagcct ggtgccacca	3060
ggagcaagtc tggccacaga gtcaaggcag gaagccttgg gggcagagca caacagctcc	3120
gctctgttgc catgtctgtt gccagatggg tctgatgggt ccgatgctct taactgcagt	3180
cagccttctc ctctggatgt tggagtgaag aacactcaat cccagggaaa aactagtgcc	3240
tgtgaggtga gtggagatgt gacggtggat gttacagggg ttaatgctct acaaggatatg	3300
gctgagccca gaagagagaa tatatcacac aacacccaag acatcctgat tccaaacgtc	3360
ttgttgagcc aagagaagaa tgccgttcta ggtttgccag tggctctaca ggacaaagct	3420
gtgactgacc cacagggagt tggaaccca gagatgatac ctcttgattg ggagaaaggg	3480
aagctggagg gagcagacca cagctgtacc atgggtgacg ctgaggaagc ccaaatagac	3540
gatgaagcac atcctgtcct actgcagcct gttgccaagg agctccccac agacatggag	3600
ctctcagccc atgatgatgg ggccccagct ggtgtgaggg aagtcatgcg agccccgcct	3660
tcaggcaggg aaaggagcac tccctctcta ctttgcattg tctctgcca ggacgcacct	3720
ctgcctaagg gggcagactt gatagaggag gctgccagcc gtatagtgga tgctgtcatc	3780
gaacaagtca aggccgctgg agcactgctt actgaggggg aggcctgtca catgtcactg	3840
tccagccctg agttgggtcc tctcactaaa ggactagaga gtgcttttac agaaaaagtg	3900
agtactttcc cacctgggga gagcctacca atgggcagta ctctgagga agccacgggg	3960
agccttgacg gatgttttgc tggaaggag gagccagaga agatcatttt acctgtccag	4020
gggcctgagc cagcagcaga aatgccagac gtgaaagctg aagatgaagt ggattttaga	4080
gcaagttcaa tttctgaaga agtggctgta gggagcatag ctgctacact gaagatgaag	4140
caaggcccaa tgaccagggc gataaaccga gaaaactggt gtacaataga gccatgccct	4200
gatgcagcat ctcttctggc ttccaagcag agcccagaat gtgagaactt cctggatggt	4260

ADS5001.ST25.txt

ggactgggca	gagagtgtac	ctcaaaacaa	ggtgtactta	aaagagaatc	tgggagtgat	4320
tctgacctct	ttcactcacc	cagtgatgac	atggacagca	tcattcttccc	aaagccagag	4380
gaagagcatt	tggcctgtga	tatcaccgga	tccagttcat	ccaccgatga	cacggcttca	4440
ctggaccgac	attctttctca	tggcagtgat	gtgtctctct	cccagatttt	aaagccaaac	4500
aggtcaagag	atcggcaaag	ccttgatgga	ttctacagcc	atgggatggg	agctgagggt	4560
cgagaaagtg	agagtgaacc	tgctgacca	ggcgacgtgg	aggaggagga	gatggacagt	4620
atcactgaag	tgcctgcaaa	ctgctctgtc	ctaaggagct	ccatgcgctc	tctttctccc	4680
ttccggaggc	acagctgggg	gcctgggaaa	aatgcagcca	gcgatgcaga	aatgaaccac	4740
cggagttcaa	tgcgagttct	tggggatggt	gtcaggagac	ctccattca	taggagaagt	4800
ttcagtctag	aaggcttgac	aggaggagct	ggtgtcggaa	acaagccatc	ctcatctcta	4860
gaagtaagct	ctgcaaatgc	cgaagagctc	agacacccat	tcagtgggtga	ggaacggggt	4920
gactcttttg	tgtcactttc	agaagaggat	ctggagtcag	accagagaga	acataggatg	4980
tttgatcagc	agatatgtca	cagatctaag	cagcagggat	ttaattactg	tacatcagcc	5040
atttcctctc	cattgacaaa	atccatctca	ttaatgacaa	tcagccatcc	tggattggac	5100
aattcacggc	ccttccacag	taccttccac	aataccagtg	ctaattctgac	tgagagtata	5160
acagaagaga	actataatth	cctgccacat	agcccctcca	agaaagattc	tgaatggaag	5220
agtggaacaa	aagtcagtcg	tacattcagc	tacatcaaga	ataaaatgtc	tagcagcaag	5280
aagagcaaa	aaaaggaaaa	agaaaaagat	aagattaagg	agaaggagaa	agattctaaa	5340
gacaaggaga	aagataagaa	gactgtcaac	gggcacactt	tcagttccat	tcctgttggtg	5400
ggtcccatca	gctgtagcca	gtgtatgaag	cccttcacca	acaaagatgc	ctatacttgt	5460
gcaaattgca	gtgcttttgt	ccacaaaggc	tgccgagaaa	gtctagcctc	ctgtgcaaag	5520
gtcaaaatga	agcagcccaa	agggagcctt	caggcacatg	acacatcatc	actgcccacg	5580
gtcattatga	gaaacaagcc	ctcacagccc	aaggagcgtc	ctcgggtccgc	agtcctcctg	5640
gtggatgaaa	ccgctaccac	cccaatatth	gccaatagac	gatcccagca	gagtgtctcg	5700
ctctccaaaa	gtgtctccat	acagaacatt	actggagttg	gcaatgatga	gaacatgtca	5760
aacacctgga	aattcctgtc	tcattcaaca	gactcactaa	ataaaatcag	caagggtcaat	5820
gagtcaacag	aatcacttac	tgatgaggga	gtaggtacag	acatgaatga	aggacaacta	5880
ctgggagact	ttgagattga	gtccaaacag	ctggaagcag	agtcttgag	tcggataata	5940
gacagcaagt	ttctaaaaca	gcaaaagaaa	gatgtgggtca	aacggcaaga	agtaatatat	6000
gagttgatgc	agacagagtt	tcattcatgtc	cgcactctca	agatcatgag	tgggtgtgtac	6060
agccagggga	tgatggcaga	tctgcttttt	gagcagcaga	tggtagaaaa	gctgttcccc	6120
tgtttgatg	agctgatcag	tatccatagc	caattcttcc	agaggattct	ggagcggaag	6180

ADS5001.ST25.txt

aaggagtctc	tggtggataa	aagtgaaaag	aacttttctca	tcaagaggat	aggggatgtg	6240
cttgtaaadc	agtttttcagg	tgagaatgca	gaacgtttta	agaagacata	tggcaagttt	6300
tgtgggcaac	ataaccagtc	tgtaaactac	ttcaaagacc	tttatgccaa	ggataagcgt	6360
tttcaagcct	ttgtaaagaa	gaagatgagc	agttcagttg	ttagaaggct	tggaattcca	6420
gagtgcatac	tgcttgtaac	tcagcggatt	accaagtacc	cagttttatt	ccaaagaata	6480
ttgcagtgtg	ccaaagacaa	tgaagtggag	caggaagatc	tagcacagtc	cttgagcctg	6540
gtgaaggatg	tgattggagc	tgtagacagc	aaagtggcaa	gttatgaaa	gaaagtgcgt	6600
ctcaatgaga	tttatacaaa	gacagatagc	aagtcaatca	tgaggatgaa	gagtggtcag	6660
atgttttgcca	aggaagattt	gaaacggaag	aagcttgtag	gtgatgggag	tgtgtttctg	6720
aagaatgcag	caggaagggt	gaaagagggt	caagcagttc	ttctcactga	catttttagtt	6780
ttccttcaag	aaaaagacca	gaagtacatc	tttgcatcat	tggaccagaa	gtcaacagtg	6840
atctctttta	agaagctgat	tgtgagagaa	gtggcacatg	aggagaaagg	tttattcctg	6900
atcagcatgg	ggatgacaga	tccagagatg	gtagaagtcc	atgccagctc	caaagaggaa	6960
cgaaacagct	ggattcagat	cattcaggac	acaatcaaca	ccctgaacag	agatgaagat	7020
gaaggaattc	ctagtgagaa	tgaggaagaa	aagaaaatgt	tggacaccag	agcccagagaa	7080
ttaaaagaac	aacttcacca	gaaggaccaa	aaaatcctac	tcttgttgga	agagaaggag	7140
atgattttcc	gggacatggc	tgagtgcagc	accctctctc	cagaggattg	ctccccaaca	7200
catagcccta	gagtttctct	ccgctccaac	acagaagagg	ctctcaaagg	aggaccttta	7260
atgaaaagtg	caataaatga	ggtggagatc	cttcagggtt	tggtgagtgg	aaatctggga	7320
ggcacacttg	ggccgactgt	cagcagcccc	attgagcaag	atgtggtcag	tcccgtttcc	7380
ctgccccgga	gagcagagac	ctttggagga	tttgacagcc	atcagatgaa	tgcttcaaaa	7440
ggaggcgaga	aggaagaggg	agatgatggc	caagatctta	ggagaacgga	atcagatagt	7500
ggcctaataa	aggggtgaaa	tgctaacctg	gtatttatgc	ttaaaagaaa	cagtgcagcag	7560
gttggtccaga	gcgttggtca	tctctacgag	ctcctcagcg	ctctgcaggg	tgtggtgctg	7620
cagcaggaca	gctacattga	ggaccagaaa	ctgggtgctga	gcgagagggc	gctcactcgc	7680
agcttggtccc	gcccagagctc	cctcattgag	caggagaagc	agcgcagcct	ggagaagcag	7740
cgccaggacc	tggccaacct	gcagaagcag	caggcccagt	acctcgagga	gaagcgcagg	7800
cgcgagcgtg	agtgggaagc	tcgtgagagg	gagctgcggg	acgggaggcc	ctcctggccc	7860
agcgcgagga	ggagggtgcag	caggggcagc	aggacctgga	aaaggagcgg	gaggagctcc	7920
agcagaagaa	gggcacatag	ccagtatgac	ctggagcgac	tgcgtgctgc	ccagaaacag	7980
cttgagaggg	aacaggagca	gctgcgccgg	gaggcagagc	ggctcagcca	gcggcagaca	8040
gaacgggacc	tgtgtcaggt	ttcccatcca	cataccaagc	tgatgaggat	cccatcgttc	8100

ADS5001.ST25.txt

ttccccagtc ctgaggagcc cccctcgcca tctgcacctt ccatagccaa atcaggggtca 8160
 ttggactcag aacttttcagt gtccccaaaa aggaacagca tctctcggac acacaaagat 8220
 aaggggcctt ttcacatact gagttcaacc agccagacaa acaaaggacc agaagggcag 8280
 agccaggccc ctgcgccac ctctgcctct acccgctgt ttgggttaac aaagccaaag 8340
 gaaaagaagg agaaaaaaaa gaagaacaaa accagccgct ctcagcccgg tgatgggtccc 8400
 gcgtcagaag tatcagcaga ggggtgaagag atcttctgct ga 8442

<210> 26
 <211> 3777
 <212> DNA
 <213> Human

<400> 26
 gaagcgcctg tgctctgccg agactgccgt gccattgct cgcctcggtc gccgccgctt 60
 tagccgcctc cgggggagcg gccgcctatt gtctttctcc gcggcgaagg tgaagagttg 120
 tcccagctcg gcccgcgggg gagccccggg agccgcacgt gtcctgggtc atgaaactta 180
 atccacagca agctccctta tatggtgatt gtgttggttac agtgctgctt gctgaagagg 240
 acaaagctga agatgatgta gtgttttact tggatattttt gggttccacc ctccgtcact 300
 gtacaagtac tcggaagggtc agttctgata cattggagac cattgctcct ggtcatgatt 360
 gttgtgaaac agtgaagggtg cagctctgtg ctcccaaaga gggccttccc gtgtttgtgg 420
 tggctgaaga agactttcat ttcgtccagg atgaagcgta tgatgcagct caattcctag 480
 caaccagtgc tggaaatcag caggctttga actttacccg ttttcttgac cagtcaggac 540
 ccccatctgg ggatgtgaat tcccttgata agaagttggt gctggcattc aggcacctga 600
 agctgcccac ggagtggaat gtattgggga cagatcagag tttgcatggt gagaatttat 660
 atgatctaca aacacacttt aagtttgtga tatttctact ttttttttaa tggggctact 720
 tttctatggt catcatattc aggtcttcca cagaggctgc gtaaatctta gaattactgt 780
 aggaaagtgg cctcaatggc atctcttcta ggttcttcaa ttgagctgtt aagcatgttg 840
 ttgcagcgaa atgaccctag ggattacca aggagagtgg cacgtcacct tcctgtgggt 900
 ctggatttca gatattgatct ctcaagtgtg gaaagtgaca cgctcttcat gaggagagta 960
 gcagagttac tttttgggtgt ttaatgatca aagacatggt tttcattatt gtattctgaa 1020
 gttctctaaa gatagcctgg aagtgaagga gaggaaagat tgggcagtga gtgggaggag 1080
 catgagaaca ggggtgtgctc tgagaaacca cacacttcct taaccagggt agtgtcactc 1140
 ttactgactt tatctgttgg ccctccctat gagagttcac tgaagaaagg actttttgtt 1200
 tgttttttgt ttttttttga gaacgggctt tcaactctgt agtccaggct ggagtgcagt 1260
 ggcattgatct cggctcactg cagcctccac ctctggggtt cagggtgattc tgctgcctca 1320

ADS5001.ST25.txt

gcctcccaaa tagctgggat tacaggcatg taccaccatg cctagcaa	at	tttttttttt	1380
ttttaattag agacaggggt tcaccgtgtt agtcaggctg gtctcgaact	cctgacctca		1440
ggtaatctac ccacctcggc ctcccaaagt gctgggatta taggcatgag	ccactgcgcc		1500
cggccagaac tccacttttt caaaaatatt tacatagtaa gtcctcttac	tcaaacaagg		1560
gttttcccac ataattctag tagccaatga catctacttg atgtcataat	tgtatagata		1620
ttttttaatg aacataatg tgtacctgga gttcaataag taacatccag	tttcccttct		1680
gagttcaagt ccaattgaac gatttgggag tcctgagata gaaacaaaa	tgtttattac		1740
tgatgaaatc tagattggaa gcctgatgtt agagctcctg ccagaagggt	ctgcttgtac		1800
tttctatgtc ttcaatgaaa gagctgggtc gtcacaccat tgccctgtag	agtccacca		1860
gccttgagta ttgaattatt ttgggtaagc agaccacaag tcaactctcc	cacagggtgag		1920
cagttcctga ggagaaatac ccagaggggc ctgagccata gcatagttag	tttctacact		1980
cagatgaatt ttgtcttctt ccatggaaga atggtaaaga ggtctttgcc	agctttgatt		2040
ctcttaaadc tacactaaat ttaacagtta aacctgtggt cagccgtcag	aacgggtgtc		2100
catactgtca ggtgcatact gtcagattct acctggatag tcctgcccag	gtaaaacctg		2160
aaaggaagta tcaaatcaag gaagaaagga tttatccttt tcttcttctt	tttttaagta		2220
tagtgtccaa gaaacttctg tcttgctaata atttagagat cagaatattt	gacattctga		2280
aaaggcactc atgccttata taaacctggt gatgggcctt aatacctcta	gctcctccta		2340
tttctgtatt gatacaggaa tgtttattct ggctgccttt cacaaatcag	tgtcaagata		2400
gtactgcatt agttatttgt ggggcttatg gtgttttatg gttttgtttt	gtcttgttta		2460
aagaggggccc caggagttgg atagttttat gttgccatga ttaaaaacaa	ctattagaaa		2520
aagcaaacat ctgaaacttt ggacatatca cttcctcttt ctctctcttt	tttttttttt		2580
ttttgagata gagtcttgct ctgtcgccca ggctggagtg caatggtgca	atctcggctc		2640
actgcaacct gcatctcctg gggtgaagcg attctcctgc cttagcctcc	caagtagctg		2700
ggaatacagg cacatgccac cacaccctgc tgcttttttg tgtgttttag	tagagacggg		2760
gtttcaccat gttgcccagg ctggtcctga actcctgagc tcaggcaatc	cacccgcctc		2820
agcctcccaa agtgctagga ttacaggcgt gagccactgt gcccgccac	ttcctctctt		2880
tgggccttaa cttccttgct tttaatagga gggaattggc cagctttaat	ttttttttgt		2940
actgtcagtg tactggtaaa ttttctgttg cacaaaattg ctcaagcagt	gctaacaaag		3000
gccaaaccaa atttgaacac ttgaggaagg aaatacatat taaaaccaca	atgagatatc		3060
attacacatt tatcataatg gctaagatga agaataccaa gtgctggcaa	agatgaagaa		3120
catatcatat gttgcttgta ggaatgcaaa atgtataacc actctagaaa	tatttggcag		3180
tttcttgtaa agttaaacat acacttagcg tatgaccagc taatcccact	tttgggtggt		3240

ADS5001.ST25.txt

tatcctagag	aaatgaaaat	ctgtagtcac	caaaaagtct	gtgcacagac	gtgctcatag	3300
taatgttatt	cataatcttc	aaaaactgga	aataacccag	atttccctca	ctgagtgaat	3360
acagaagcac	actataatat	atccatacag	tggaatacta	ctcagcaata	aaaagaagca	3420
aactgttgac	atgtgcaaca	acttggaatg	gttttaaata	cattatgcgg	gaaaatgaag	3480
tcagtttcca	aaggttccat	actatgtgat	tctatttata	tgatattctg	gaagatgcaa	3540
aattatagaa	aaagagaaca	gatgagtagt	tgctaggggc	tgggagtggg	ggaagtctga	3600
ctggaaagag	gtatcatgag	ggaattcttt	gggttggttg	agttgttttg	tcttgttcgt	3660
ggtggtggct	gtaagaatct	atgcatgtgt	taaaactcat	aggagtgtac	atcccctaaa	3720
ggtgaatttt	attgtacata	tattttaaata	aataaaataa	caaaaaaaaa	aaaaaaa	3777

<210> 27
 <211> 4290
 <212> DNA
 <213> Human

<400> 27	
atgttgata	taaaccgaga
aaactgggtgt	acaatagagc
catgccctga	tgcagcatct
	60
cttctggctt	ccaagcagag
cccagaatgt	gagaacttcc
tggatgttgg	actgggcaga
	120
gagtgtacct	caaaacaagg
tgtacttaaa	agagaatctg
ggagtgattc	tgacctcttt
	180
cactcaccca	gtgatgacat
ggacagcatc	atcttcccaa
agccagagga	agagcatttg
	240
gcctgtgata	tcaccggatc
cagttcatcc	accgatgaca
cggcttcact	ggaccgacat
	300
tcttctcatg	gcagtgatgt
gtctctctcc	cagattttta
agccaaacag	gtcaagagat
	360
cggcaaagcc	ttgatggatt
ctacagccat	gggatgggag
ctgagggctg	agaaagtgag
	420
agtgagcctg	ctgaccagag
cgacgtggag	gaggaggaga
tggacagtat	cactgaagtg
	480
cctgcaaact	gctctgtcct
aaggagctcc	atgcgctctc
tttctccctt	ccggaggcac
	540
agctgggggc	ctgggaaaaa
tgcagccagc	gatgcagaaa
tgaaccaccg	gagttcaatg
	600
cgagttcttg	gggatgttgt
caggagacct	cccattcata
ggagaagttt	cagtctagaa
	660
ggcttgacag	gaggagctgg
tgctcgaaac	aagccatcct
catctctaga	agtaagctct
	720
gcaaattgccg	aagagctcag
acacccattc	agtgggtgagg
aacggggtga	ctctttggtg
	780
tcactttcag	aagaggatct
ggagtcagac	cagagagaac
ataggatggt	tgatcagcag
	840
atatgtcaca	gatctaagca
gcagggatgt	aattactgta
catcagccat	ttcctctcca
	900
ttgacaaaat	ccatctcatt
aatgacaatc	agccatcctg
gattggacaa	ttcacggccc
	960
ttccacagta	ccttccacaa
taccagtgtg	aatctgactg
agagtataac	agaagagaac
	1020
tataatttcc	tgccacatag
cccctccaag	aaagattctg
aatggaagag	tggaacaaaa
	1080
gtcagtcgta	cattcagcta
catcaagaat	aaaatgtcta
gcagcaagaa	gagcaaagaa
	1140
aaggaaaaag	aaaaagataa
gattaaggag	aaggagaaa
attctaaaga	caaggagaaa
	1200

ADS5001.ST25.txt

gataagaaga	ctgtcaacgg	gcacactttc	agttccattc	ctgttgtggg	tcccatcagc	1260
tgtagccagt	gtatgaagcc	cttcaccaac	aaagatgcct	atacttgtgc	aaattgcagt	1320
gcttttgtcc	acaaaggctg	ccgagaaagt	ctagcctcct	gtgcaaaggt	caaaatgaag	1380
cagcccaaag	ggagccttca	ggcacatgac	acatcatcac	tgcccacggt	cattatgaga	1440
aacaagccct	cacagcccaa	ggagcgtcct	cgggtccgcag	tcctcctggg	ggatgaaacc	1500
gctaccaccc	caatatttgc	caatagacga	tcccagcaga	gtgtctcgct	ctccaaaagt	1560
gtctccatac	agaacattac	tggagttggc	aatgatgaga	acatgtcaaa	cacctggaaa	1620
ttcctgtctc	attcaacaga	ctcactaaat	aaaatcagca	agggtcaatga	gtcaacagaa	1680
tcacttactg	atgagggagt	aggtacagac	atgaatgaag	gacaactact	gggagacttt	1740
gagattgagt	ccaaacagct	ggaagcagag	tcttggagtc	ggataataga	cagcaagttt	1800
ctaaaacagc	aaaagaaaga	tgtgggtcaaa	cggcaagaag	taatatatga	gttgatgcag	1860
acagagtttc	atcatgtccg	cactctcaag	atcatgagtg	gtgtgtacag	ccaggggatg	1920
atggcggatc	tgctttttga	gcagcagatg	gatgaaaagc	tgttcccctg	tttgatgag	1980
ctgatcagta	tccatagcca	attcttccag	aggattctgg	agcggaaaga	ggagtctctg	2040
gtggataaaa	gtgaaaagaa	ctttctcatc	aagaggatag	gggatgtgct	tgtaaatacag	2100
ttttcagggtg	agaatgcaga	acgttttaaag	aagacatatg	gcaagttttg	tgggcaacat	2160
aaccagtctg	taaactactt	caaagacctt	tatgccaagg	ataagcgttt	tcaagccttt	2220
gtaaagaaga	agatgagcag	ttcagttggt	agaaggcttg	gaattccaga	gtgcatattg	2280
cttgtaactc	agcggattac	caagtaccca	gttttattcc	aaagaatatt	gcagtgtacc	2340
aaagacaatg	aagtggagca	ggaagatcta	gcacagtcct	tgagcctggg	gaaggatgtg	2400
attggagctg	tagacagcaa	agtggcaagt	tatgaaaaga	aagtgcgtct	caatgagatt	2460
tatacaaaga	cagatagcaa	gtcaatcatg	aggatgaaga	gtggtcagat	gtttgccaag	2520
gaagatttga	aacggaagaa	gcttgtacgt	gatgggagtg	tgtttctgaa	gaatgcagca	2580
ggaaggttga	aagaggttca	agcagttctt	ctcactgaca	ttttagtttt	ccttcaagaa	2640
aaagaccaga	agtacatctt	tgcattcattg	gaccagaagt	caacagtgat	ctcttttaaag	2700
aagctgattg	tgagagaagt	ggcacatgag	gagaaagggt	tattcctgat	cagcatgggg	2760
atgacagatc	cagagatggg	agaagtccat	gccagctcca	aagaggaacg	aaacagctgg	2820
attcagatca	ttcaggacac	aatcaacacc	ctgaacagag	atgaagatga	aggaattcct	2880
agtgagaatg	aggaagaaaa	gaaaatgttg	gacaccagag	cccagagaatt	aaaagaacaa	2940
cttcaccaga	aggaccaaaa	aatcctactc	ttgttggaag	agaaggagat	gattttccgg	3000
gacatggctg	agtgcagcac	ccctctccca	gaggattgct	ccccaacaca	tagccctaga	3060
gttctcttcc	gctccaacac	agaagaggct	ctcaaaggag	gacctttaat	gaaaagtgca	3120

ADS5001.ST25.txt

```

ataaatgagg tggagatcct tcagggtttg gtgagtggaa atctgggagg cacacttggg 3180
ccgactgtca gcagcccccatt tgagcaagat gtggtcagtc ccgtttccct gccccggaga 3240
gcagagacct ttggaggatt tgacagccat cagatgaatg cttcaaaagg aggcgagaag 3300
gaagagggag gtgatggcca agatcttagg agaacggaat cagatagtgg cctaaaaaag 3360
ggtggaaatg ctaacctggt atttatgctt aaaagaaaca gtgagcaggt tgtccagagc 3420
gttgttcatc tctacgagct cctcagcgct ctgcagggtg tgggtgctgca gcaggacagc 3480
tacattgagg accagaaact ggtgctgagc gagagggcgc tctctcgag cttgtcccgc 3540
ccgagctccc tcattgagca ggagaagcag cgcagcctgg agaagcagcg ccaggacctg 3600
gccaacctgc agaagcagca ggcccagtac ctcgaggaga agcgcaggcg cgagcgtgag 3660
tggaagctc gtgagagggg gctgcgggac gggaggccct cctggcccag cgcgaggagg 3720
aggtgcagca ggggcagcag gacctggaaa aggagcggga ggagctccag cagaagaagg 3780
gcacatagcc agtatgacct ggagcgactg cgtgctgccc agaaacagct tgagagggaa 3840
caggagcacg tgcgccggga ggcagagcgg ctcagccagc ggcagacaga acgggacctg 3900
tgtcaggttt cccatccaca taccaagctg atgaggatcc catcgttctt ccccagtcct 3960
gaggagcccc cctcgccatc tgcaccttcc atagccaaat cagggtcatt ggactcagaa 4020
ctttcagtgt ccccaaaaag gaacagcatc tctcggacac acaaagataa ggggcctttt 4080
cacatactga gttcaaccag ccagacaaac aaaggaccag aagggcagag ccaggcccct 4140
gcgtccacct ctgcctctac ccgcctgttt ggggtaacaa agccaaagga aaagaaggag 4200
aaaaaaaaaga agaacaaaac cagccgctct cagcccgggtg atggtcccgc gtcagaagta 4260
tcagcagagg gtgaagagat cttctgctga 4290

```

<210> 28
 <211> 424
 <212> PRT
 <213> Human

<400> 28

Met Ser Asn Thr Trp Lys Phe Leu Ser His Ser Thr Asp Ser Leu Asn
 1 5 10 15

Lys Ile Ser Lys Val Asn Glu Ser Thr Glu Ser Leu Thr Asp Glu Gly
 20 25 30

Thr Asp Met Asn Glu Gly Gln Leu Leu Gly Asp Phe Glu Ile Glu Ser
 35 40 45

Lys Gln Leu Glu Ala Glu Ser Trp Ser Arg Ile Ile Asp Ser Lys Phe
 50 55 60

ADS5001.ST25.txt

Leu Lys Gln Gln Lys Lys Asp Val Val Lys Arg Gln Glu Val Ile Tyr
 65 70 75 80
 Glu Leu Met Gln Thr Glu Phe His His Val Arg Thr Leu Lys Ile Met
 85 90 95
 Ser Gly Val Tyr Ser Gln Gly Met Met Ala Asp Leu Leu Phe Glu Gln
 100 105 110
 Gln Met Val Glu Lys Leu Phe Pro Cys Leu Asp Glu Leu Ile Ser Ile
 115 120 125
 His Ser Gln Phe Phe Gln Arg Ile Leu Glu Arg Lys Lys Glu Ser Leu
 130 135 140
 Val Asp Lys Ser Glu Lys Asn Phe Leu Ile Lys Arg Ile Gly Asp Val
 145 150 155 160
 Leu Val Asn Gln Phe Ser Gly Glu Asn Ala Glu Arg Leu Lys Lys Thr
 165 170 175
 Tyr Gly Lys Phe Cys Gly Gln His Asn Gln Ser Val Asn Tyr Phe Lys
 180 185 190
 Asp Leu Tyr Ala Lys Asp Lys Arg Phe Gln Ala Phe Val Lys Lys Lys
 195 200 205
 Met Ser Ser Ser Val Val Arg Arg Leu Gly Ile Pro Glu Cys Ile Leu
 210 215 220
 Leu Val Thr Gln Arg Ile Thr Lys Tyr Pro Val Leu Phe Gln Arg Ile
 225 230 235 240
 Leu Gln Cys Thr Lys Asp Asn Glu Val Glu Gln Glu Asp Leu Ala Gln
 245 250 255
 Ser Leu Ser Leu Val Lys Asp Val Ile Gly Ala Val Asp Ser Lys Val
 260 265 270
 Ala Ser Tyr Glu Lys Lys Val Arg Leu Asn Glu Ile Tyr Thr Lys Thr
 275 280 285
 Asp Ser Lys Ser Ile Met Arg Met Lys Ser Gly Gln Met Phe Ala Lys
 290 295 300
 Glu Asp Leu Lys Arg Lys Lys Leu Val Arg Asp Gly Ser Val Phe Leu
 305 310 315 320

ADS5001.ST25.txt

Lys Asn Ala Ala Gly Arg Leu Lys Glu Val Gln Ala Val Leu Leu Thr
 325 330 335

Asp Ile Leu Val Phe Leu Gln Glu Lys Asp Gln Lys Tyr Ile Phe Ala
 340 345 350

Ser Leu Asp Gln Lys Ser Thr Val Ile Ser Leu Lys Lys Leu Ile Val
 355 360 365

Arg Glu Val Ala His Glu Glu Lys Gly Leu Phe Leu Ile Ser Met Gly
 370 375 380

Met Thr Asp Pro Glu Met Val Glu Val His Ala Ser Ser Lys Glu Glu
 385 390 395 400

Arg Asn Ser Trp Ile Gln Ile Ile Gln Asp Thr Ile Asn Thr Leu Ser
 405 410 415

Gly Asn Gly Trp Arg Cys Phe Asn
 420

Claims

I claim:

5

1. A method of determining whether a patient will respond to treatment with an FTI by analyzing the presence or expression of the lbc oncogene.

10

2. The method of claim 1 further including the analysis of the expression of a gene that is differentially modulated in the presence of an FTI.

3. The method of claim 2 wherein the analysis is of the expression of more than one genes in addition to the lbc oncogene.

15

4. The method of claim 2 wherein the gene is selected from the group consisting of Seq. ID No 1-18.

5. The method of claim 1 wherein a patient in whom the lbc oncogene is determined to be absent or is not expressed is treated with an FTI.

20

6. The method of claim 1 wherein a patient in whom the lbc oncogene is determined to be present or express is treated with an agent other than an FTI.

25

7. The method of claim 1 further comprising the step of determining whether the patient samples used to determine response to the FTI includes cell surface antigens selected from the group consisting of CD33 and CD34.

8. The method of claim 7 wherein the presence of cells having said surface antigens is prognostic of response to FTI treatment.

9. The method of claim 1 further comprising the step of determining the percentage
5 of cells in the patient sample used to determine response to the FTI that includes blast cells.

10. The method of claim 9 wherein the presence of less than 60% blast cells in said sample is prognostic of response to the FTI.

10

11. A method of monitoring the therapy of a patient being treated with an FTI by analyzing the presence or expression of the lbc oncogene.

12. The method of claim 11 further including the analysis of the expression of a gene
15 that is differentially modulated in the presence of an FTI.

13. The method of claim 11 wherein the analysis is of the expression of more than one genes in addition to the lbc oncogene.

20 14. The method of claim 13 wherein the gene is selected from the group consisting of Seq. ID No. 1 and Seq. ID No. 3-18.

15. The method of claim 11 wherein a patient in whom the lbc oncogene is determined to be absent or is not expressed is treated as patient responding to the FTI.

25

16. The method of claim 11 further comprising the step of determining whether the patient samples used to determine response to the FTI includes cell surface antigens selected from the group consisting of CD33 and CD34.
- 5 17. The method of claim 16 wherein the presence of cells having said surface antigens comprises less than 15% in the case of CD33 or less than 60% in the case of CD34 is indicative of response to FTI treatment.
18. The method of claim 16 wherein the absence of cells having said surface antigens is
10 indicative of response to FTI treatment.
19. The method of claim 11 further comprising the step of determining the percentage of cells in the patient sample used to determine response to the FTI that includes blast cells.
15
20. The method of claim 19 wherein the presence of less than or equal to 60% blast cells in said sample is indicative of response to the FTI.
21. The method of claim 20 wherein the presence of more than 60% blast cells in said
20 sample is indicative of non-response to the FTI.
22. The method of claim 11 wherein a patient in whom the lbc oncogene is determined to be present or expressed without a reduction in amount is treated as not responding to the FTI.
25
23. The method of claim 1 wherein the FTI is (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone).

24. The method of claim 11 wherein the FTI is (R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone).

5 25. A method of treating a patient comprising:

- a) analyzing the gene expression profile or the presence of lbc oncogene in said patient to determine whether the patient will respond to treatment with an FTI, and
- 10 b) treating the patient with the FTI if the analysis indicates that the patient will respond.

26. The method of claim 25 wherein the analysis is of the expression of more than one gene.

15

27. The method of claim 25 wherein the FTI is selected from the group consisting of quinolines or quinoline derivatives.

20

28. The method of claim 27 wherein the FTI is selected from the group consisting of

7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-2,3-dihydro-1H,5H-benzo[ij]quinolizin-5-one,

25

7-(3-chlorophenyl)-9-[(4-chlorophenyl)-1H-imidazol-1-ylmethyl]-1,2-dihydro-4H-pyrrolo[3,2,1-ij]quinoline-4-one,

8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl),methyl]-6-(3-chlorophen

yl)-1,2-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one,

8-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-6-(3-chlorophenyl)-
2,3-dihydro-1H,5H-benzo[ij]quinolizin-5-one, and

5

(R)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-
chlorophenyl)-1-methyl-2(1H)-quinolinone).

29. The method of claim 28 wherein the FTI is (R)-6-[amino(4-chlorophenyl)(1-
10 methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone)

30. The method of claim 26 wherein the genes correlate with one or more nucleic acid
sequences having Seq. ID No. 1-18.

15 31. The method of claim 25 wherein the treatment comprises the administration of an
FTI and another therapeutic composition.

32. The method of claim 31 wherein said another therapeutic composition modulates
MAPK/ERK signaling pathways, TGF β , WNT, Rho, or apoptotic pathways.

20

33. The method of claim 31 wherein said another composition is selected from the
group consisting of tyrosine kinase inhibitors, MEK kinase inhibitors, PI3 kinase
inhibitors, MAP kinase inhibitors, apoptosis modulators, and combinations thereof.

25 34. Articles for assessing the efficacy of treatment of a patient with an FTI comprising
a medium with which patient gene expression profiles indicative of FTI response are
determined.

35. The articles of claim 34 wherein the gene expression profiles are obtained from a group of genes correlating to more than one nucleic acid sequences of Seq. ID. No 1-18.
- 5 36. The articles of claim 34 comprising representations of gene expression profiles fixed to a medium.
37. Kits comprising reagents for determining response to FTI treatment.
- 10 38. The kits of claim 37 wherein said reagents for detecting the presence or expression of the lbc oncogene.
39. The kits of claim 38 wherein said reagents for detecting the expression of genes selected from the group consisting of Seq. ID No. 1-18 and their variants.
- 15 40. The kits of claim 37 further comprising reagents for the detection of cell surface antigens selected from the group consisting of CD33 and CD34.
41. The kits of claim 37 further comprising reagents for the detection of blast cells.
- 20 42. The kits of claim 37 wherein said reagents include PCR primers.
43. The kits of claim 43 further comprising probes.
- 25 44. Use of an FTI for the preparation of a medicament for treating a patient in whom the lbc oncogene has been, or is subsequently, determined to be absent or not expressed.

45. Use of an FTI for the preparation of a medicament for treating a patient who is subsequently monitored for the presence or expression of the lbc oncogene.

46. A diagnostic kit for analysing a sample from a patient whereby the presence or
5 expression of the lbc oncogene is determined.

47. A combination for treating a patient comprising:

10 means for determining the gene expression profile or the presence of lbc oncogene in said patient to determine whether the patient will respond to treatment with an FTI; and use of an FTI for the preparation of a pharmaceutical composition for therapeutic treatment of said patient if the analysis indicates that the patient will respond.

15

20

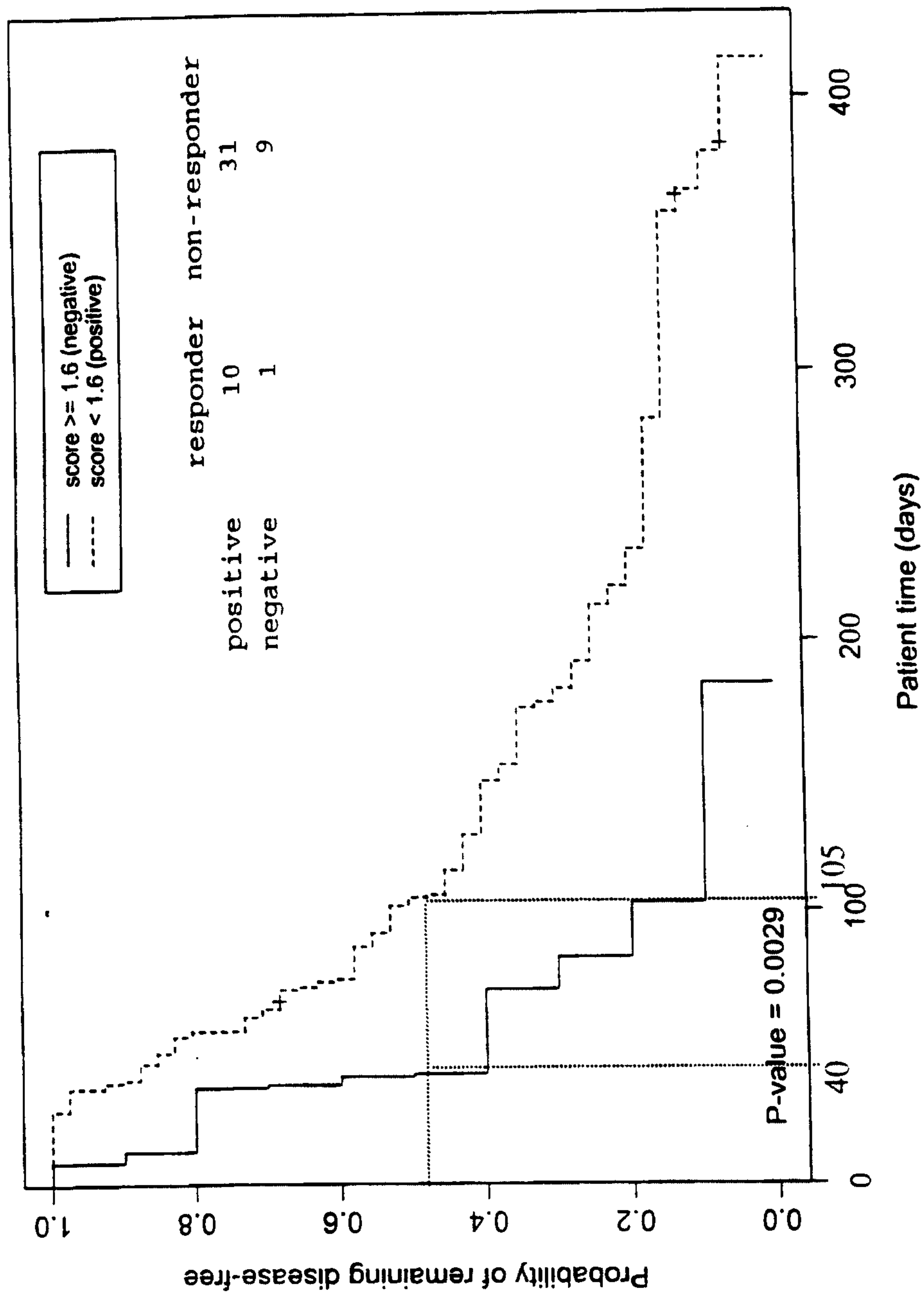


Fig 1.

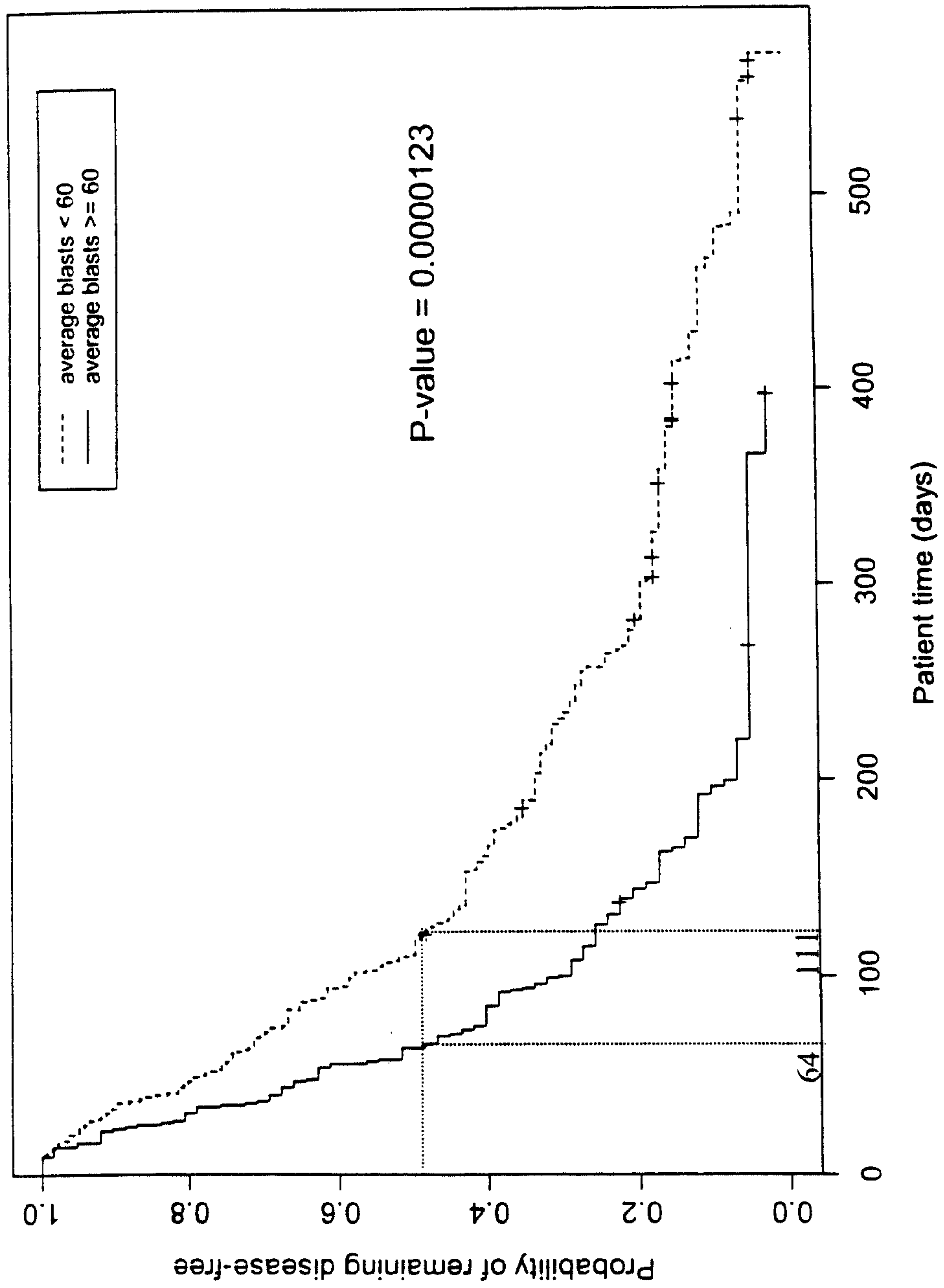


Fig 2.

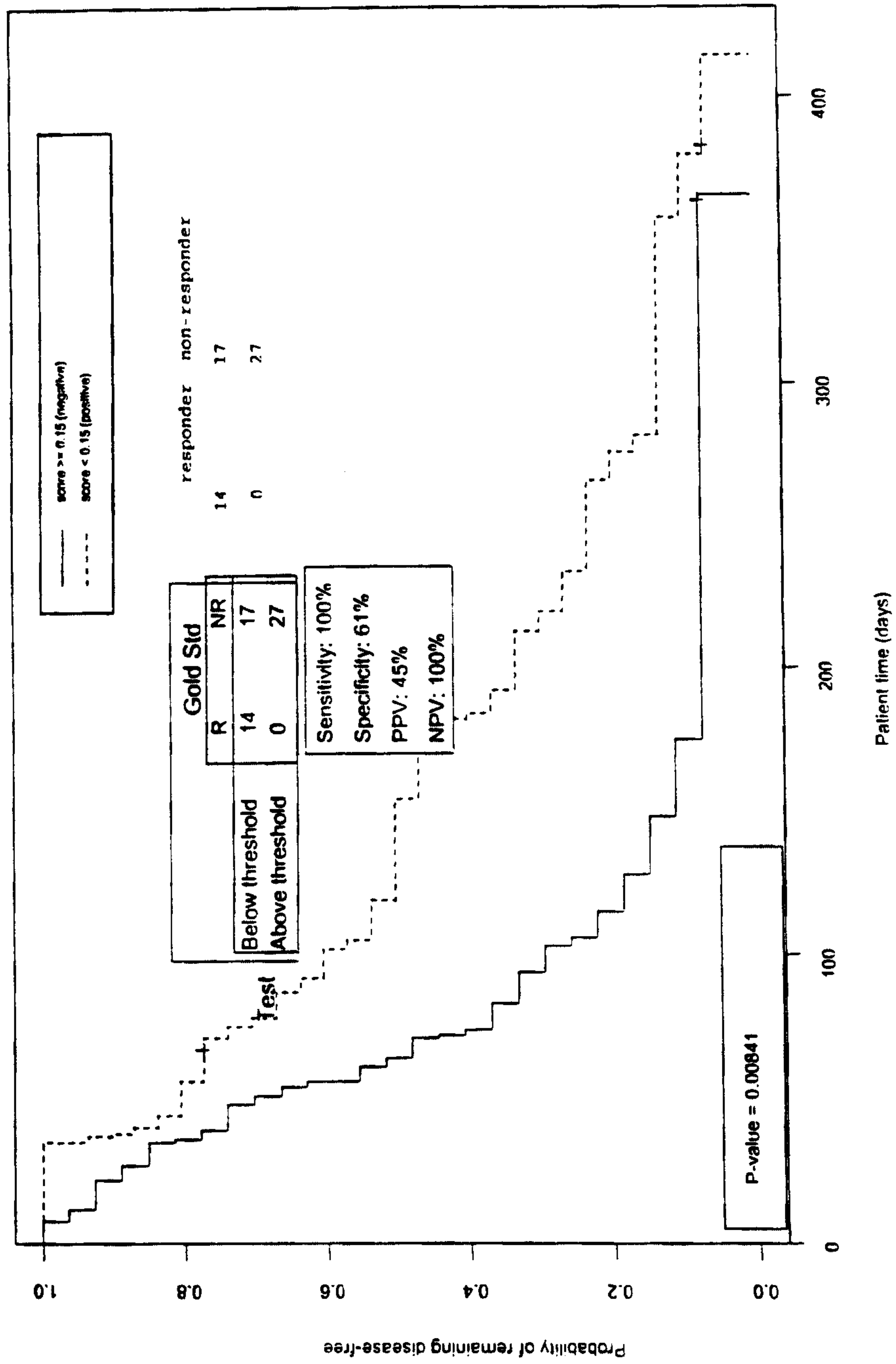


Fig. 3A

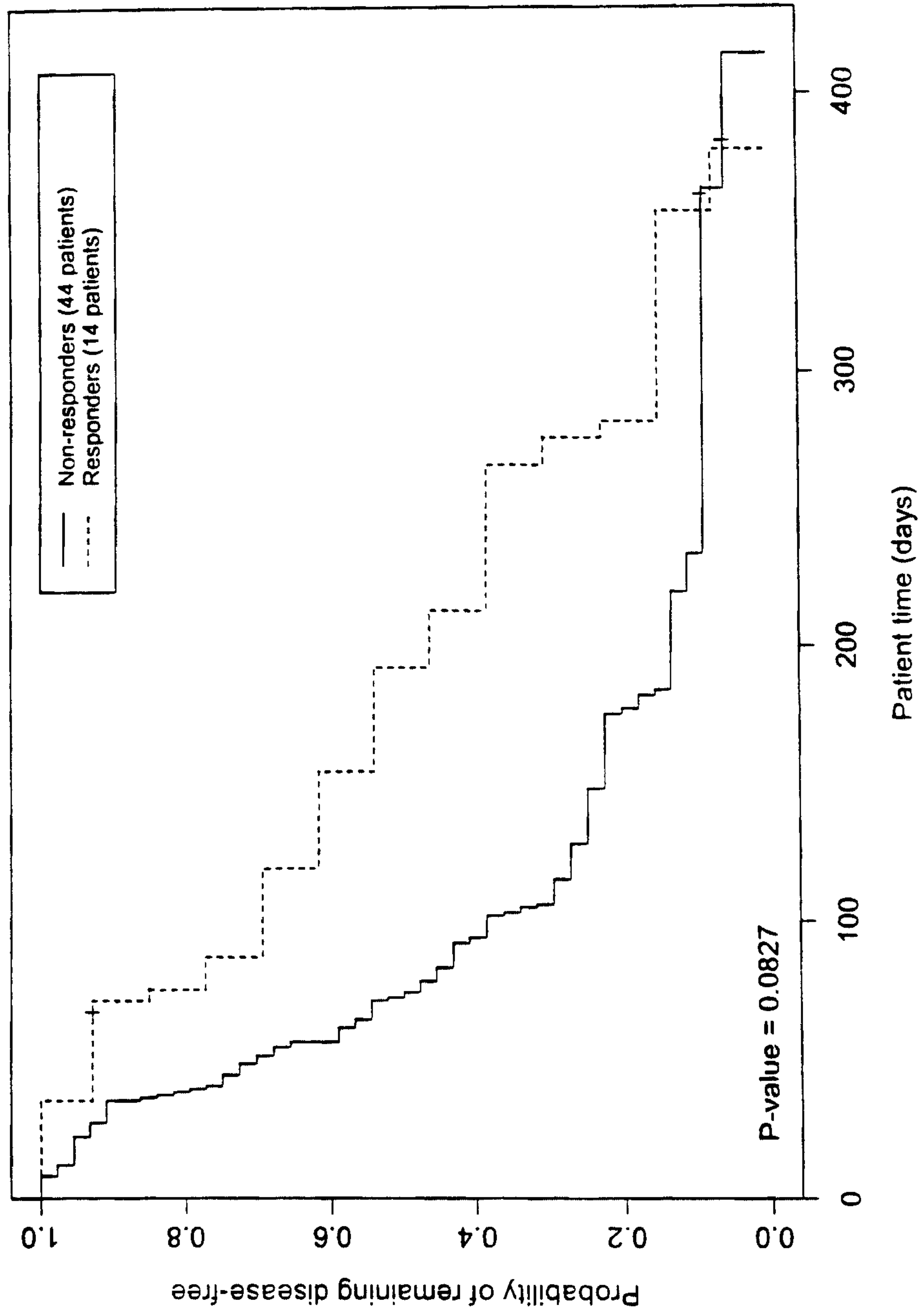


Fig. 3B

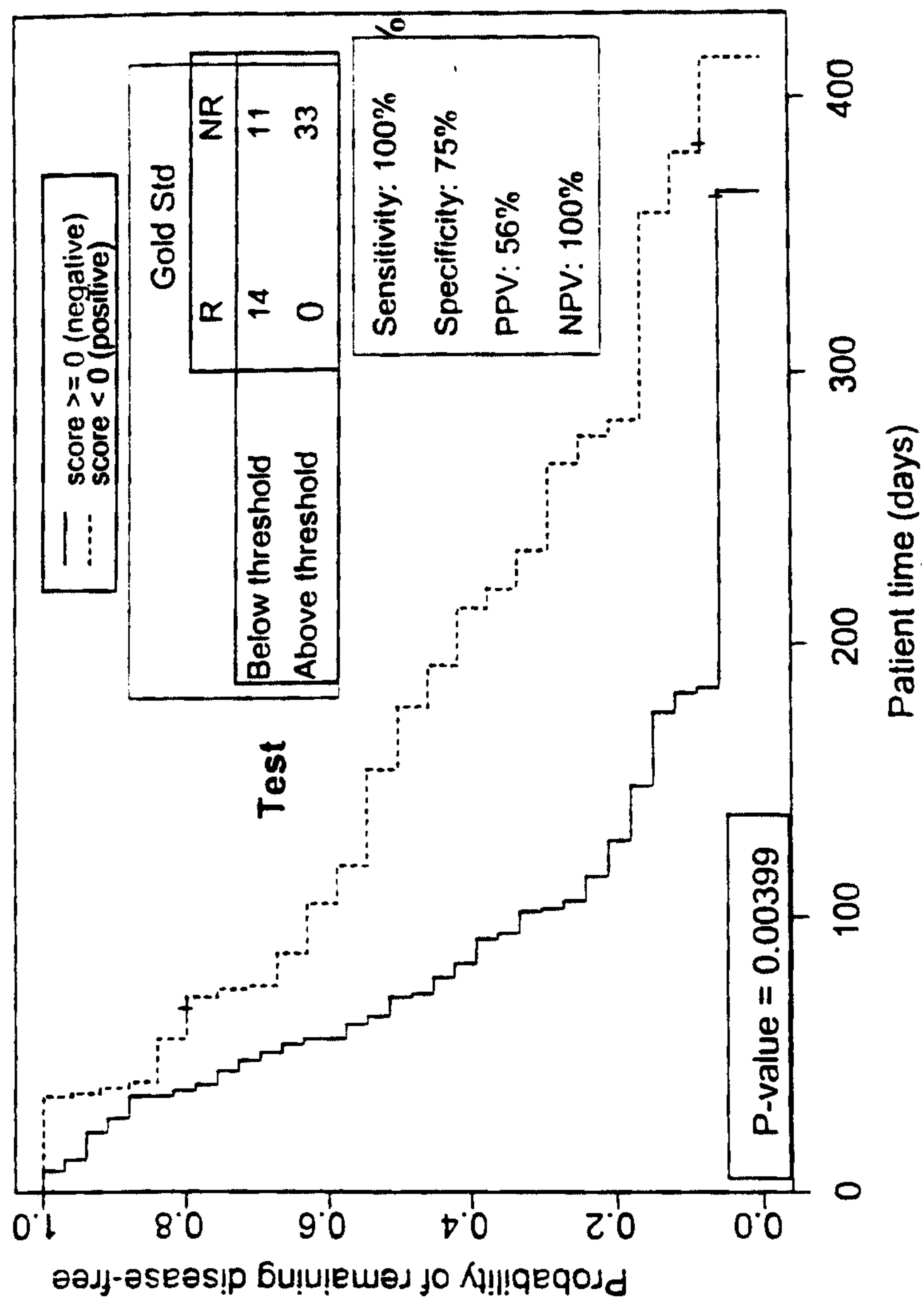


Figure 3C