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(54) Title: SARS-COV NUCLEOCAPSID PROTEIN EPITOPES AND USES THEREOF

(57) Abstract: The invention provides polypeptides, nucleic acids, antibodies, compositions, vaccines, microarrays and uses thereof for the prevention, treatment of SARS and SARS-CoV infection. The invention further provides uses of the above-noted products for the detection and diagnosis of SARS and SARS-CoV infection. The invention further provides corresponding methods and commercial packages relating to such uses.

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SARS-CoV NUCLEOCAPSID PROTEIN EPITOPES AND USES THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit, under 35 U.S.C. § 119(e), of US provisional application No. 60/564,984 filed April 26, 2004 and US provisional application No. 60/643,574 filed January 14, 2005. Both applications are herein incorporated by reference in their entirety.

FIELD OF THE INVENTION

The invention relates to peptides and corresponding nucleic acids and uses thereof for prevention, treatment and diagnosis of SARS, and particularly relates to peptides and corresponding nucleic acids derived from the SARS coronavirus nucleocapsid protein, and uses thereof for prevention, treatment and diagnosis of SARS.

BACKGROUND OF THE INVENTION

Severe acute respiratory syndrome (SARS) is a pneumonia-like disease of a previously unknown etiology that emerged and spread globally affecting countries in Asia, Europe, and North America in early 2003. According to the World Health Organization, the fatality rate of SARS is 14-15% overall and >50% in persons over the age of 65 (www.who.int/csr/sars/en/). Simultaneously, two groups identified a novel coronavirus as the etiological agent responsible for the cause of SARS designating it the SARS coronavirus (SARS-CoV). Subsequent infection of non-human primates with SARS-CoV led to similar pathological and clinical features of severe acute respiratory syndrome, confirming that the SARS-CoV was the etiological agent [1]. As

with other members of the coronavirus family, the SARS-CoV genome encodes 5 proteins of predicted function; a membrane protein (M protein), envelope protein (small E protein), surface glycoprotein (Spike) and nucleocapsid (N protein), as well as open reading frames of unknown predicted function, however it does lack a haemagluttinin protein (HA) [2,3].

Coronaviruses have a crown-like morphology attributed to the surface-expressed Spike protein. The SARS-CoV Spike protein is a glycoprotein of approximately 180 kDa that is composed of two subunits S1 and S2 [4]. The function of the Spike protein in coronavirus infection is to act as the fusogen aiding in viral attachment and entry into host cells [5]. The cellular receptor for the Spike protein of the SARS-CoV has been identified as angiotensin-converting enzyme-2 [6], with the binding domain localized to the S1 subunit [7]. Studies have been published regarding the ability of Spike to elicit neutralizing antibody responses and provide protection during challenge experiments in animal models of coronavirus infection [8-10]. These studies show that there is a strong antibody response elicited from inoculation with the Spike protein, and this antibody response is able to provide neutralizing activity against viral infection. The course of SARS-CoV infection is marked by a significant SARS specific IgM response within the first 8-14 days of onset of symptoms with the generation of an IgG response later on in the infection [11]. Inoculation of mice with a plasmid encoding the Spike gene from the SARS-CoV into mice was capable of eliciting an antibody response against the protein and prevented pulmonary viral replication in the absence of T lymphocytes [12].

The N protein of the SARS-CoV consists of 422 amino acids, of which there is a unique basic sequence located near the carboxy terminus [3]. There are no known post-translational

modifications of the protein. Functionally, the N protein is predicted to associate with the genomic DNA and contains an RNA-binding domain. Moreover, the N protein has been shown to interact with the M protein playing a role in viral assembly [13]. The nucleoprotein has been shown to localize to the host cell nucleolus where it is postulated to promote translation of viral mRNA [14].

Certain viral proteins of the types noted above have been shown to be involved in eliciting immune responses. For example, inoculation of chickens with plasmid DNA encoding the carboxyl terminus of the infection bronchitis virus (IBV) N protein led to the induction of a cytotoxic T lymphocyte population capable of recognizing two distinct IBV strains. Additionally, the adoptive transfer of T cells from animals inoculated with IBV to naïve chicks provided CD8+ $\alpha\beta$ specific protection [15]. Rhesus macaques immunized with a cocktail of adenoviral vectors encoding S1 fragment of Spike, M protein and N protein of the SARS-CoV led to the generation of antibody responses against the S1 fragment of Spike protein and T-cell responses against the N protein [16]. The injection of a T helper type 1 (Th1) T cell line resistant to MHV into susceptible mice led to a marked increase in IFNγ expression with a decrease in IL-4 production concomitant with complete protection against infection [17]. Demonstration that the immunity against MHV is a CD8+, perforin, IFNγ dependent process in the absence of CD4+ T cells [18] and the generation of IgG2a antibodies following DNA immunization of N protein [19] suggests that there is a significant Th1 type response in coronavirus infection. Further, after surveying the sera of over 400 probable SARS patients, Liu et al found that more than 90% of these patients generated an antibody response against the N protein 14 days after the onset of symptoms [20], indicative of an adaptive immune response to foreign antigen.

The reemergence of SARS in early January 2004 indicates that there is a reservoir for the virus and the reentry of the virus into a large population is probable.

There is therefore a need to develop methods and agents for the prevention and treatment of SARS.

SUMMARY OF THE INVENTION

The invention relates to epitopes derived from the SARS-CoV nucleocapsid protein (N protein) and uses thereof.

Accordingly, the invention provides an isolated immunogenic polypeptide derived from the SARS-CoV nucleocapsid protein.

In an embodiment, the polypeptide comprises an epitope of at least 8, in a further embodiment at least 9, contiguous amino acids of SEQ ID NO: 496, wherein said polypeptide is not the full length SARS CoV N protein set forth in SEQ ID NO: 496. In embodiments, the epitope is selected from the epitopes defined by the start and end positions within SEQ ID NO: 496 set forth in Table 5.

In a further embodiment, the polypeptide comprises an epitope of at least 8, in a further embodiment at least 9, contiguous amino acids of an amino acid sequence selected from SEQ ID NOs: 499-505.

In an embodiment, the isolated polypeptide is selected from: (a) a polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384,

386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505; and (b) a functional variant or fragment of (a), wherein said functional variant or fragment has an immune system-related activity.

In an embodiment, the immune response related activity is selected from: induction of T-cell activation or proliferation; an induction in T-cell lytic activity; binding to an MHC class I molecule; an alteration in cytokine or chemokine expression or production; and an alteration in expression of immunoregulatory cell surface molecules.

In an embodiment, the isolated polypeptide is 50 amino acids or less in length.

In an embodiment, the T-cell is selected from a $CD8^+$ T-cell and a $CD4^+$ T-cell.

In an embodiment, the cytokine is selected from IFNγ, IL-2,4, 5, 6, 10, 12, 13, TGF-β, and TNF-α.

In embodiments, the functional variant comprises 1-6, 1-15 or 1-30 amino acid additions to an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

In embodiments, the polypeptide consists essentially of an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-

75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

In embodiments, the polypeptide consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 44, 66, 70, 186, 303, 412, 426 and 432.

The invention further provides an isolated SARS-CoV N protein peptide epitope, wherein said peptide epitope has an immune-related activity, with the proviso that said peptide epitope is not the full length SARS-CoV N protein set forth in SEQ ID NO: 496. In embodiments, the epitope is selected from the epitopes defined by the start and end positions within SEQ ID NO: 496 set forth in Table 5.

In an embodiment, the immune-related activity is selected from: induction of T-cell activation or proliferation; an induction in T-cell lytic activity; binding to an MHC class I molecule; an alteration in cytokine or chemokine expression or production; and an alteration in expression of immunoregulatory cell surface molecules.

In an embodiment, the peptide epitope comprises of 8 to about 50, 8 to about 12, 8, 9, 10 or 11 contiguous amino acids of the SARS-CoV N protein set forth in SEQ ID NO: 496.

In an embodiment, the peptide epitope consists essentially of 8 to about 50, 8 to about 12, 8, 9, 10 or 11 contiguous amino acids of the SARS-CoV N protein set forth in SEQ ID NO: 496.

The invention further provides a pharmaceutical composition comprising the above-mentioned isolated polypeptide and a pharmaceutically acceptable carrier.

In an embodiment, the composition further comprises an adjuvant.

In an embodiment, the composition further comprises an MHC molecule.

The invention further provides a composition comprising a multimer of two or more MHC peptide complex monomers, each of said monomers comprising a polypeptide of the invention and an MHC molecule (e.g. an MHC class I heavy chain or fusion protein thereof, a β2 microglobulin or fusion protein thereof).

In an embodiment, the monomers are joined together into said multimer by virtue of a multivalent entity. In embodiments, monomers are associated with said multivalent entity by virtue of an interaction chosen from biotin-avidin interactions, biotin-streptavidin interactions, coiled-coil domain interactions, and liposome-monomer cross-linking.

In an embodiment, the above-mentioned pharmaceutical composition further comprises a second polypeptide (e.g. an additional SARS-CoV polypeptide) different from said isolated polypeptide, wherein said second polypeptide is capable of inducing a SARS-CoV immune response.

The invention further provides an antibody (e.g. monoclonal, polyclonal, recombinant, and fragments thereof) capable of specifically binding to the above mentioned polypeptide.

The invention further provides an isolated nucleic acid encoding the above-mentioned polypeptide, wherein said nucleic acid does not encode the full length SARS-CoV protein set forth in SEQ ID NO: 496. In an embodiment, the nucleic acid comprises a fragment of a nucleotide sequence capable of

encoding the amino acid sequence of SEQ ID NO: 496. In an embodiment, the nucleic acid comprises a fragment of the nucleotide sequence of SEQ ID NO: 495.

The invention further provides a vector comprising the above-noted nucleic acid operably-linked to a transcriptional regulatory sequence.

The invention further provides a host cell transformed or transfected with the above-mentioned vector.

The invention further provides a method of producing the above-mentioned polypeptide, said method comprising culturing the above-mentioned host cell under conditions permitting expression of said polypeptide.

The invention further provides a method of preventing or treating SARS, or for inducing an immunological or protective immune response against SARS-CoV, in an animal, said method comprising administering to said animal an agent selected from the above mentioned polypeptide, pharmaceutical composition and vector.

In an embodiment, the animal is a mammal, in a further embodiment, a human.

The invention further provides a use of the above-mentioned polypeptide for the preparation of a medicament.

The invention further provides a use of an agent selected from the above-mentioned polypeptide, pharmaceutical composition, and vector, for preventing or treating SARS, or for inducing an immunological or protective immune response against SARS-CoV.

The invention further provides a kit or commercial package comprising an agent selected from the above-mentioned polypeptide, pharmaceutical composition, and vector, together with instructions for preventing or treating SARS, or for inducing an immunological or protective immune response against SARS-CoV.

The invention further provides a method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising assaying a biological sample of said animal with the above-mentioned polypeptide, antibody, and/or composition comprising a multimer.

The invention further provides a method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising: contacting a biological sample of said animal with the above-mentioned polypeptide, antibody, and/or composition comprising a multimer; and

determining the binding of a constituent of the biological sample to said the above-mentioned polypeptide, antibody, and/or composition comprising a multimer; wherein said binding is indicative of SARS or SARS-CoV infection.

In an embodiment, the biological sample is a tissue or body fluid (e.g. blood, plasma, lymphocytes, etc.) of said animal.

The invention further provides a use of a complex comprising the above-mentioned polypeptide and an MHC molecule for labelling, detecting or isolating T-cells; or for detecting, selecting, sorting, or identifying T cell epitopes and/or amino acid sequences.

In an embodiment, the above-mentioned composition is an immunogenic or vaccine composition.

The invention further provides a polypeptide microarray comprising an isolated polypeptide of the invention bound to a substrate. In an embodiment, the microarray further comprises an MHC molecule bound to said substrate.

The invention further provides a polypeptide microarray comprising the above-mentioned antibody bound to a substrate.

The invention further provides a polypeptide microarray comprising an MHC complex bound to a substrate,

said complex comprising the above-mentioned polypeptide and an MHC molecule.

The invention further provides a method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising: contacting a biological sample of said animal with the above-mentioned polypeptide microarray; and determining the binding of a constituent of the biological sample to said polypeptide microarray;
wherein said binding is indicative of SARS or SARS-CoV infection.

The invention further provides a kit or commercial package comprising a component selected from the above-mentioned polypeptide, antibody and/or polypeptide microarray, together with instructions for detecting or diagnosing SARS or SARS-CoV infection.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: *Activation of immunological responses of a convalescent SARS patient from stimulation with peptides of N protein of SARS-CoV.* Representative responses of CD4+ and CD8+ peripheral blood leukocytes to sequential overlapping 15 amino acid peptides (see Figure 5). Fold proliferation (relative to nonstimulated patient cells) of leukocytes pools of ten 15 amino acid peptides *A)* or individual 15 amino acid peptides *B)* were incubated with $1x10^6$ peripheral blood leukocytes for 7 days and analysed for expression of CD4+ and CD8+ cell surface receptors. B), left panel: Proliferation of blood leukocytes from SARS convalescent patient 6 and healthy donors stimulated with nucleocapsid protein peptides; B), right panel: Proliferation of blood leukocytes from SARS convalescent patient 6 stimulated with nucleocapsid protein peptides. The inflammatory cytokine, IFNγ production was measured from

culture media of patient (patient 6) cells stimulated with N peptides *C), left panel*. Representative dot plot displaying proliferative responses of CD4+ or CD8+ peripheral blood leukocytes *C), right panel*.

Figure 2: *Activation of immunological responses of a convalescent SARS patient from stimulation with peptides of N protein of SARS-CoV*. Representative responses of CD4+ and CD8+ peripheral blood leukocytes to sequential overlapping 15 amino acid peptides (see Figure 5). Fold proliferation (relative to nonstimulated patient cells) of leukocytes pools of ten 15 amino acid peptides *A)* or individual 15 amino acid peptides *B)* were incubated with $1x10^6$ peripheral blood leukocytes for 7 days and analysed for expression of CD4+ and CD8+ cell surface receptors. The inflammatory cytokine, IFNγ production was measured from culture media of patient cells stimulated with N peptides *(C, left panel)*. Representative dot plot displaying proliferative responses of CD4+ or CD8+ peripheral blood leukocytes *(C, right panel)*. A) Proliferation of CD4+/CD8+ peripheral blood leukocytes from SARS convalescent patient 8 stimulated with N protein peptides; B) Proliferation of peripheral blood leukocytes from SARS convalescent patient 8 stimulated with N protein peptides; C) IFNγ production from SARS convalescent patient stimulated with N protein peptides.

Figure 3: *Binding Affinity and off rate of overlapping 9 amino acid peptides of the SARS-CoV,N protein to various major histocompatibility complex class I alleles*. Nonameric peptides (see Figure 6) were incubated for the binding affinity and rate of dissociation to HLA alleles A2 *A)*, A3 *B)*, A11 *C)*, and A24 *D)*. Binding affinity (*left panels of subfigures*) of the 9 amino acid peptides that displayed higher affinity as compared to positive control for the alleles had an effective dose

(ED50) less than $5x10^{-6}$ M following incubation of allele complexes with sequentially diluted peptides. Rate of dissociation (*right panels of subfigures*) of 9 amino acid peptides from the allele complexes was assayed by incubating peptides with a specific allele complex over an 8-hour period.

Figure 4: *Frequency of SARS convalescent patients exhibiting 2 fold or greater proliferation to immunogenic 15 amino acid peptides of the SARS-CoV N protein.* Percent of patients responding to stimulation with identified target N protein polypeptides. CD4+ and CD8+ proliferation induced by identified individual overlapping 15 amino acid peptides (Figure 5) were assessed against 12 patients. Those patients demonstrating 2 fold proliferation (relative to nonstimulated patient cells) were classified as positive responders.

Figure 5: List in tabular format of sequential overlapping 15 amino acid peptides derived from SARS-CoV N protein (SEQ ID NOs: 1-80) which were analyzed according to the Examples below.

Figure 6: List in tabular format of sequential overlapping 9 amino acid peptides derived from SARS-CoV N protein (SEQ ID NOs: 81-494) which were analyzed according to the Examples below.

Figure 7: DNA (SEQ ID NO: 495) and amino acid (SEQ ID NO: 496) sequences of SARS-CoV N protein (Genbank Accession No. NC_004718; nucleotides 28120-29388 and corresponding translated sequence).

Figure 8: Schematic overview of iTopia™ assay system (Beckman Coulter, Inc. Fullerton, CA).

Figures 9 to 11: Results of SARS N-protein HLA-A*0101 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 8 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 12: Results of SARS N-protein HLA-A*0101 - peptide binding studies. Cluster effect of peptides - HLA-A*0101 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figure 13: Results of affinity ED50 studies of SARS N-protein peptide - HLA-A*0101 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 14: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-A*0101 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 15: Summary of results of SARS N-protein peptide - HLA-A*0101 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6. BIMAS rank determined via BIMAS (BioInformatics & Molecular Analysis Section) analysis (for reference, see e.g., http://bimas.cit.nih.gov/). SYFPEITHI rank determined via SYFPEITHI analysis (for reference, see, e.g., http://www.syfpeithi.de/scripts/MHCServer.dll/home.htm).

Figure 16: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-A*0101. Peptide numbers

indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 17: Summary of results of SARS N-protein peptide - HLA-A*0101 studies. Six epitopes (listed in table) were identified in respect of A*0101. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 18 to 20: Results of SARS N-protein HLA-A*0201 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 31 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 21: Results of SARS N-protein HLA-A*0201 - peptide binding studies. Cluster effect of peptides - HLA-A*0201 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figures 22 to 25: Results of affinity ED50 studies of SARS N-protein peptide - HLA-A*0201 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 26 and 27: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-A*0201 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 28: Summary of results of SARS N-protein peptide - HLA-A*0201 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 29: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-A*0201. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 30: Summary of results of SARS N-protein peptide - HLA-A*0201 studies. 30 epitopes (listed in table) were identified in respect of A*0201. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 31 to 33: Results of SARS N-protein HLA-A*0301 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 21 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 34: Results of SARS N-protein HLA-A*0301 - peptide binding studies. Cluster effect of peptides - HLA-A*0301 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figures 35 to 37: Results of affinity ED50 studies of SARS N-protein peptide - HLA-A*0301 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 38 to 40: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-A*0301 binding. For Figure 38, T1/2 of positive control is 17.3 hrs. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 41: Summary of results of SARS N-protein peptide - HLA-A*0301 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 42: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-A*0301. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 43: Summary of results of SARS N-protein peptide - HLA-A*0301 studies. 18 epitopes (listed in table) were identified in respect of A*0301. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 44 to 46: Results of SARS N-protein HLA-A*1101 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 28 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 47: Results of SARS N-protein HLA-A*1101 - peptide binding studies. Cluster effect of peptides - HLA-A*1101 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figure 48: Comparison of cluster effect of SARS N-protein peptides - HLA-A*0301 and HLA-A*1101. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figures 49 to 51: Results of affinity ED50 studies of SARS N-protein peptide - HLA-A*1101 binding. Peptide numbers

indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 52 to 54: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-A*1101 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 55: Summary of results of SARS N-protein peptide - HLA-A*1101 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 56: Rank comparison of iTopia vs. BIMAS for SARS N-protein peptide - HLA-A*1101. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 57: Summary of results of SARS N-protein peptide - HLA-A*1101 studies. 28 epitopes (listed in table) were identified in respect of A*1101. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 58 to 60: Results of SARS N-protein HLA-A*2402 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. For this analysis, cutoff was adjusted to >40%, and a total of 55 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 61 to 66: Results of affinity ED50 studies of SARS N-protein peptide - HLA-A*2402 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 67 to 72: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-A*2402 binding. For Figure 67, T1/2 of positive control is 3.3 hrs. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 73 and 74: Summary of results of SARS N-protein peptide - HLA-A*2402 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 75 and 76: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-A*2402. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 77: Summary of results of SARS N-protein peptide - HLA-A*2402 studies. 37 epitopes (listed in table) were identified in respect of A*2402. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 78 to 80: Results of SARS N-protein HLA-B*0702 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 55 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 81: Results of SARS N-protein HLA-B*0702 - peptide binding studies. Cluster effect of peptides - HLA-B*0702 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figures 82 to 87: Results of affinity ED50 studies of SARS N-protein peptide - HLA-B*0702 binding. Peptide numbers

indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 88 to 93: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-B*0702 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 94 and 95: Summary of results of SARS N-protein peptide - HLA-B*0702 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 96 and 97: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-B*0702. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 98: Summary of results of SARS N-protein peptide - HLA-B*0702 studies. 18 epitopes (listed in table) were identified in respect of B*0702. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 99 to 101: Results of SARS N-protein HLA-B*0801 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure 6. Total of 8 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 102: Results of SARS N-protein HLA-B*0801 - peptide binding studies. Cluster effect of peptides - HLA-B*0801 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figure 103: Comparison of cluster effect of SARS N-protein peptides - HLA-B*0801 and HLA-A*0101. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figure 104: Results of affinity ED50 studies of SARS N-protein peptide - HLA-B*0801 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 105: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-B*0801 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 106: Summary of results of SARS N-protein peptide - HLA-B*0801 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 107: Rank comparison of iTopia vs. BIMAS vs. SYFPEITHI for SARS N-protein peptide - HLA-B*0801. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 108: Summary of results of SARS N-protein peptide - HLA-B*0801 studies. 7 epitopes (listed in table) were identified in respect of B*0801. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figures 109 to 111: Results of SARS N-protein HLA-B*1501 - peptide binding studies. Peptide numbers indicated in X-axes and table correspond to 9-mer peptide numbers listed in Figure

6. Total of 35 binding peptides were identified, which were further analyzed for ED50 and off-rate half life.

Figure 112: Results of SARS N-protein HLA-B*1501 - peptide binding studies. Cluster effect of peptides - HLA-B*1501 is examined. Peptide numbers indicated in X-axes correspond to 9-mer peptide numbers listed in Figure 6.

Figures 113 to 116: Results of affinity ED50 studies of SARS N-protein peptide - HLA-B*1501 binding. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figures 117 to 120: Results of off-rate half life (t½ or t1/2; hrs) studies of SARS N-protein peptide - HLA-B*1501 binding. For Figure 117, T1/2 of positive control is 4.2 hrs. Peptide numbers indicated in X-axes and tables correspond to 9-mer peptide numbers listed in Figure 6.

Figure 121: Summary of results of SARS N-protein peptide - HLA-B*1501 binding. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 122: Rank comparison of iTopia vs. SYFPEITHI for SARS N-protein peptide - HLA-B*1501. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

Figure 123: Summary of results of SARS N-protein peptide - HLA-B*1501 studies. 27 epitopes (listed in table) were identified in respect of B*1501. Peptide numbers indicated correspond to 9-mer peptide numbers listed in Figure 6.

DETAILED DESCRIPTION OF THE INVENTION

In the studies described herein, HLA class I alleles were studied for binding of SARS N peptides (i.e. peptides derived from the SARS-CoV nucleocapsid protein) and convalescent SARS patient peripheral blood mononuclear cells were used to demonstrate functional CD4 and CD8 reactivity to N protein epitopes.

As a result, a number of immunodominant peptides were identified that elicit proliferative and functional responses from convalescent SARS patient peripheral blood leukocytes. The peptides identified also showed high affinity binding to MHC class I alleles and reactivity among various HLA groups inducing T cell proliferation and cytokine production. Additionally, these identified peptides correspond to peptides sharing overlapping amino acid sequences which exhibit high affinity for HLA class I alleles.

Accordingly, in a first aspect, the invention relates to an epitope of the SARS-CoV N protein, i.e. an immunogenic polypeptide or fragment derived from the SARS-CoV N protein, as well as to variants or fragments of the polypeptide. In embodiments, the polypeptide or variants or fragments thereof have or are capable of effecting or eliciting an activity including but not limited to an induction of lymphocyte (e.g. T-cell [e.g. CD8+ or CD4+]) activation or proliferation, induction of T-cell lytic activity, binding to an MHC class I molecule, induction of cytokine (e.g. IFNγ, IL-2,4, 5, 6, 10, 12, 13, TGF-β, and TNF-α) or chemokine expression or production, an alteration in the expression or an immunoregulatory surface molecule, or any combination thereof. Examples of methods to determine such activities are set forth in the Examples below.

In embodiments, the polypeptide may be less than 50, 45, 40, 35, 30, 25, 20, 15 or 10 amino acids in length. In embodiments the polypeptide is greater than or equal to 5, 8 or 9 amino acids in length. In embodiments the polypeptide is 9 or 15 amino acids in length.

In embodiments, the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505; or a functional (e.g. immunogenic) variant or fragment thereof, with the proviso that the polypeptide is not the full length SARS CoV N-protein set forth in SEQ ID NO: 496. In embodiments, the polypeptide comprises 1-5, 1-6, 1-10, 1-11, 1-15, 1-16, 1-21, 1-30 or 1-36 amino acid additions to an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505. In a further embodiment, the polypeptide consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62,

64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505. In a further embodiment, the polypeptide consists essentially of an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 44,66, 70, 186, 303, 412, 426 and 432.

In embodiments, the polypeptide consists essentially of 5-10, 9, 5-15, 15, 5-20, 5-25, 5-30, 30, 5-35, 5-40, 5-45, 45 or 5-50 contiguous amino acids of SEQ ID NO: 496.

The invention further provides a pharmaceutical composition, such as a vaccine or immunogenic composition, comprising the polypeptide and a pharmaceutically acceptable carrier. In a further embodiment, the composition further comprises an adjuvant. In a further embodiment, the composition further comprises an MHC molecule.

The invention further provides a multimer (i.e. 2 or more) of MHC peptide complexes, whereby each MHC complex comprises a polypeptide of the invention and an MHC molecule. In an embodiment, the MHC complex comprises a polypeptide of the invention, an MHC class I heavy chain and β2 microglobulin. Such multimer systems are known in the art, and the complexes may for example be associated together via suitable interactions with a multivalent entity, e.g. biotin-(strept)avidin (which are tetravalent thus resulting in a tetramer) interactions (see US patent 5,635,363 [June 3, 1997]; Altman JD, Moss PA, Goulder PJ, Barouch DH, McHeyzer-Williams MG, Bell JI, McMichael AJ, Davis MM. Phenotypic analysis of antigen-specific T lymphocytes.Science. 1996 Oct

4;274(5284):94-6. Erratum in: Science 1998 Jun 19;280(5371):1821.). Such multimers can also be used to label, detect, isolate, and stimulate T cells, as well as to discover other epitopes.

In an embodiment, a composition (e.g. a vaccine or immunogenic composition) of the invention may comprise a plurality of the peptides of the invention. In an embodiment the composition may comprise a second polypeptide capable of eliciting a SAR-CoV immune response, such as an additional SARS-CoV polypeptide or fragment thereof.

The invention further provides an antibody against, or which recognizes, or is capable of specifically binding to a polypeptide of the invention.

The invention further provides an isolated nucleic acid or polynucleotide which encodes the polypeptide of the invention (such as a fragment of SEQ ID NO: 495 or a sequence which differs therefrom but still encodes the same polypeptide by virtue of the degeneracy of the genetic code).

The invention further provides a vector comprising the nucleic acid operably linked to a transcriptional regulatory or expression control sequence (e.g. a promoter). The invention further provides a host cell comprising the nucleic acid or vector.

The invention further provides prophylactic and therapeutic methods, for preventing or treating SARS or SARS-CoV infection, comprising administering a polypeptide, composition, or MHC complex (comprising a polypeptide of the invention and one or more MHC molecules [e.g. MHC class I heavy chain, β2 microglobulin]) or vector of the invention to an animal (e.g., a mammal, e.g., a human). In embodiments, such methods comprise using administering a polypeptide, composition or vector of the invention to vaccinate or immunize (i.e. generate an immune response) in an animal.

The invention further provides diagnostic methods for the diagnosis and detection of SARS or SARS-CoV infection. Such methods may utilize as a reagent a polypeptide of the invention, a multimer comprising 2 or more MHC peptide complexes as noted above, or an antibody which binds specifically to a polypeptide of the invention. In embodiments, the method comprises contacting a tissue or body fluid (e.g. blood, lymphocytes) of an animal with the reagent. The invention further provides a peptide array or microarray comprising a polypeptide of the invention, and optionally other components such as an MHC molecule, which may be used in the just-noted diagnostic methods.

The invention further provides a use of the polypeptide, MHC complex (comprising a polypeptide of the invention and one or more MHC molecules [e.g. MHC class I heavy chain, β2 microglobulin]) or vector of the invention for the preparation of a medicament or vaccine, e.g. for the prevention or treatment of SARS or SARS-CoV infection. The invention further provides a use of the polypeptide, composition or vector of the invention for the prevention or treatment of SARS or SARS-CoV infection.

The invention further provides a commercial package comprising a polypeptide, composition or vector of the invention together with instructions for the prevention or treatment of SARS or SARS-CoV infection.

The invention further provides a commercial package comprising a polypeptide, composition or antibody of the invention together with instructions for the diagnosis and detection of SARS or SARS-CoV infection.

The invention further relates to a fusion polypeptide. As used herein, a fusion polypeptide is one that contains a polypeptide or a polypeptide derivative of the

invention fused at the N- or C-terminal end to any other polypeptide (hereinafter referred to as a peptide tail). A simple way to obtain such a fusion polypeptide is by translation of an in-frame fusion of the polynucleotide sequences, *i.e.*, a hybrid sequence. The hybrid sequence encoding the fusion polypeptide is inserted into an expression vector which is used to transform or transfect a host cell. Alternatively, the polynucleotide sequence encoding the polypeptide or polypeptide derivative is inserted into an expression vector in which the polynucleotide encoding the peptide tail is already present. Such vectors and instructions for their use are commercially available, *e.g.* the pMal-c2 or pMal-p2 system from New England Biolabs, in which the peptide tail is a maltose binding protein, the glutathione-S-transferase system of Pharmacia, or the His-Tag system available from Novagen. These and other expression systems provide convenient means for further purification of polypeptides and derivatives of the invention. An advantageous example of a fusion polypeptide is one where the polypeptide or homolog or fragment of the invention is fused to a polypeptide having adjuvant activity, such as subunit B of either cholera toxin or *E. coli* heat-labile toxin.

To effect fusion, the polypeptide of the invention is fused to the N-, or preferably, to the C-terminal end of the polypeptide having adjuvant activity. Alternatively, a polypeptide fragment of the invention is inserted internally within the amino acid sequence of the polypeptide having adjuvant activity.

Consistent with the above, the polynucleotides of the invention also encode hybrid precursor polypeptides containing heterologous signal peptides, which mature into polypeptides of the invention. By "heterologous signal peptide" is meant a signal peptide that is not found in

naturally-occurring precursors of polypeptides of the invention.

Polynucleotide molecules according to the invention, including RNA, DNA, or modifications or combinations thereof, have various applications. A DNA molecule is used, for example, (i) in a process for producing the encoded polypeptide in a recombinant host system, (ii) in the construction of vaccine vectors such as poxviruses, which are further used in methods and compositions for preventing and/or treating SARS or SARS-CoV infection, and (iii) as a vaccine agent (as well as an RNA molecule), in a naked form or formulated with a delivery vehicle.

Accordingly, a further aspect of the invention encompasses (i) an expression cassette containing a DNA molecule of the invention placed under the control of the elements required for expression, in particular under the control of an appropriate promoter; (ii) an expression vector containing an expression cassette of the invention; (iii) a procaryotic or eucaryotic cell transformed or transfected with an expression cassette and/or vector of the invention, as well as (iv) a process for producing a polypeptide or polypeptide derivative encoded by a polynucleotide of the invention, which involves culturing a procaryotic or eucaryotic cell transformed or transfected with an expression cassette and/or vector of the invention, under conditions that allow expression of the DNA molecule of the invention and, recovering the encoded polypeptide or polypeptide derivative from the cell culture.

Various genes and nucleic acid sequences of the invention may be recombinant sequences. The term "recombinant" means that something has been recombined, so that when made in reference to a nucleic acid construct the term refers to a molecule that is comprised of nucleic acid sequences that are

joined together or produced by means of molecular biological techniques. The term "recombinant" when made in reference to a protein or a polypeptide refers to a protein or polypeptide molecule which is expressed using a recombinant nucleic acid construct created by means of molecular biological techniques. The term "recombinant" when made in reference to genetic composition refers to a gamete or progeny or cell or genome with new combinations of alleles that did not occur in the parental genomes. Recombinant nucleic acid constructs may include a nucleotide sequence which is ligated to, or is manipulated to become ligated to, a nucleic acid sequence to which it is not ligated in nature, or to which it is ligated at a different location in nature. Referring to a nucleic acid construct as 'recombinant' therefore indicates that the nucleic acid molecule has been manipulated using genetic engineering, i.e. by human intervention. Recombinant nucleic acid constructs may for example be introduced into a host cell by transformation. Such recombinant nucleic acid constructs may include sequences derived from the same host cell species or from different host cell species, which have been isolated and reintroduced into cells of the host species. Recombinant nucleic acid construct sequences may become integrated into a host cell genome, either as a result of the original transformation of the host cells, or as the result of subsequent recombination and/or repair events.

In another aspect of the invention, an isolated nucleic acid, for example a nucleic acid sequence encoding a polypeptide of the invention, or homolog, fragment or variant thereof, may further be incorporated into a recombinant expression vector. In an embodiment, the vector will comprise transcriptional regulatory sequences or a promoter operably-linked to a nucleic acid comprising a sequence capable of encoding a peptide compound, polypeptide or domain of the

invention. A first nucleic acid sequence is "operably-linked" with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably-linked to a coding sequence if the promoter affects the transcription or expression of the coding sequences. Generally, operably-linked DNA sequences are contiguous and, where necessary to join two protein coding regions, in reading frame. However, since for example enhancers generally function when separated from the promoters by several kilobases and intronic sequences may be of variable lengths, some polynucleotide elements may be operably-linked but not contiguous. "Transcriptional regulatory element" is a generic term that refers to DNA sequences, such as initiation and termination signals, enhancers, and promoters, splicing signals, polyadenylation signals which induce or control transcription of protein coding sequences with which they are operably-linked.

A recombinant expression system is selected from procaryotic and eucaryotic hosts. Eucaryotic hosts include yeast cells (*e.g.*, *Saccharomyces cerevisiae* or *Pichia pastoris*), mammalian cells (*e.g.*, COS1, NIH3T3, or JEG3 cells), arthropods cells (*e.g.*, *Spodoptera frugiperda* (SF9) cells), and plant cells. A preferred expression system is a procaryotic host such as *E. coli*. Bacterial and eucaryotic cells are available from a number of different sources including commercial sources to those skilled in the art, *e.g.*, the American Type Culture Collection (ATCC; Rockville, Maryland). Commercial sources of cells used for recombinant protein expression also provide instructions for usage of the cells.

The choice of the expression system depends on the features desired for the expressed polypeptide. For example,

it may be useful to produce a polypeptide of the invention in a particular lipidated form or any other form.

One skilled in the art would readily understand that not all vectors and expression control sequences and hosts would be expected to express equally well the polynucleotides of this invention. With the guidelines described below, however, a selection of vectors, expression control sequences and hosts may be made without undue experimentation and without departing from the scope of this invention.

In selecting a vector, the host must be chosen that is compatible with the vector which is to exist and possibly replicate in it. Considerations are made with respect to the vector copy number, the ability to control the copy number, expression of other proteins such as antibiotic resistance. In selecting an expression control sequence, a number of variables are considered. Among the important variables are the relative strength of the sequence (*e.g.* the ability to drive expression under various conditions), the ability to control the sequence's function, compatibility between the polynucleotide to be expressed and the control sequence (*e.g.* secondary structures are considered to avoid hairpin structures which prevent efficient transcription). In selecting the host, unicellular hosts are selected which are compatible with the selected vector, tolerant of any possible toxic effects of the expressed product, able to secrete the expressed product efficiently if such is desired, to be able to express the product in the desired conformation, to be easily scaled up, and to which ease of purification of the final product.

The choice of the expression cassette depends on the host system selected as well as the features desired for the expressed polypeptide. Typically, an expression cassette includes a promoter that is functional in the selected host

system and can be constitutive or inducible; a ribosome binding site; a start codon (ATG) if necessary; a region encoding a signal peptide, *e.g.*, a lipidation signal peptide; a DNA molecule of the invention; a stop codon; and optionally a 3' terminal region (translation and/or transcription terminator). The signal peptide encoding region is adjacent to the polynucleotide of the invention and placed in proper reading frame. The signal peptide-encoding region is homologous or heterologous to the DNA molecule encoding the mature polypeptide and is compatible with the secretion apparatus of the host used for expression. The open reading frame constituted by the DNA molecule of the invention, solely or together with the signal peptide, is placed under the control of the promoter so that transcription and translation occur in the host system. Promoters and signal peptide encoding regions are widely known and available to those skilled in the art and include, for example, the promoter of *Salmonella typhimurium* (and derivatives) that is inducible by arabinose (promoter araB) and is functional in Gram-negative bacteria such as *E. coli* (as described in U.S. Patent No. 5,028,530 and in Cagnon *et al.*, (Cagnon *et al.*, Protein Engineering (1991) 4(7):843)); the promoter of the gene of bacteriophage T7 encoding RNA polymerase, that is functional in a number of *E. coli* strains expressing T7 polymerase (described in U.S. Patent No. 4,952,496); OspA lipidation signal peptide ; and RlpB lipidation signal peptide (Takase *et al.*, J. Bact. (1987) 169:5692).

The expression cassette is typically part of an expression vector, which is selected for its ability to replicate in the chosen expression system. Expression vectors (*e.g.*, plasmids or viral vectors) can be chosen, for example, from those described in Pouwels *et al.* (Cloning Vectors: A

Laboratory Manual 1985, Supp. 1987). Suitable expression vectors can be purchased from various commercial sources.

Methods for transforming/transfecting host cells with expression vectors are well-known in the art and depend on the host system selected as described in Ausubel *et al.*, (Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons Inc., 1994).

Upon expression, a recombinant polypeptide of the invention (or a polypeptide derivative) is produced and remains in the intracellular compartment, is secreted/excreted in the extracellular medium or in the periplasmic space, or is embedded in the cellular membrane. The polypeptide is recovered in a substantially purified form from the cell extract or from the supernatant after centrifugation of the recombinant cell culture. Typically, the recombinant polypeptide is purified by antibody-based affinity purification or by other well-known methods that can be readily adapted by a person skilled in the art, such as fusion of the polynucleotide encoding the polypeptide or its derivative to a small affinity binding domain. Antibodies useful for purifying by immunoaffinity the polypeptides of the invention are obtained as described below.

In an aspect, a polypeptide of the invention is substantially purified. A "substantially purified polypeptide" as used herein is defined as a polypeptide that is separated from the environment in which it naturally occurs and/or that is free of the majority of the polypeptides that are present in the environment in which it was synthesized. For example, a substantially purified polypeptide is free from cytoplasmic polypeptides. Those skilled in the art would readily understand that the polypeptides of the invention may be chemically synthesized, produced by recombinant means, or generated from a natural source.

As used herein, the immunogenic or vaccine compositions of the invention are administered by conventional routes known the vaccine field, in such as to a mucosal (*e.g.*, ocular, intranasal, pulmonary, oral, gastric, intestinal, rectal, vaginal, or urinary tract) surface, via a parenteral (*e.g.*, subcutaneous, intradermal, intramuscular, intravenous, or intraperitoneal) route, or topical administration (e.g. via a patch). The choice of administration route depends upon a number of parameters, such as the adjuvant associated with the polypeptide. If a mucosal adjuvant is used, the intranasal or oral route is preferred. If a lipid formulation or an aluminum compound is used, the parenteral route is preferred with the sub-cutaneous or intramuscular route being most preferred. The choice also depends upon the nature of the vaccine agent.

For use in a composition of the invention, a polypeptide or derivative thereof is formulated into or with liposomes, preferably neutral or anionic liposomes, microspheres, ISCOMS, or virus-like-particles (VLPs) to facilitate delivery and/or enhance the immune response. These compounds are readily available to one skilled in the art; for example, see Liposomes: A Practical Approach, RCP New Ed, IRL press (1990).

Adjuvants other than liposomes and the like are also used and are known in the art. Adjuvants may protect the antigen from rapid dispersal by sequestering it in a local deposit, or they may contain substances that stimulate the host to secrete factors that are chemotactic for macrophages and other components of the immune system. An appropriate selection can conventionally be made by those skilled in the art, for example, from those described below.

A polynucleotide of the invention can also be useful as a vaccine. There are two major routes, either using a

viral or bacterial host as gene delivery vehicle (live vaccine vector) or administering the gene in a free form, *e.g.*, inserted into a plasmid. Therapeutic or prophylactic efficacy of a polynucleotide of the invention is evaluated as described below.

Accordingly, a further aspect of the invention provides (i) a vaccine vector such as a poxvirus, containing a DNA molecule of the invention, placed under the control of elements required for expression; (ii) a composition of matter comprising a vaccine vector of the invention, together with a diluent or carrier; specifically (iii) a pharmaceutical composition containing a therapeutically or prophylactically effective amount of a vaccine vector of the invention; (iv) a method for inducing an immune response against SARS-CoV in a mammal (*e.g.*, a human; alternatively, the method can be used in veterinary applications for treating or preventing SARS-CoV infection of non-human animals), which involves administering to the mammal an immunogenically effective amount of a vaccine vector of the invention to elicit a protective or therapeutic immune response to SARS-CoV; and particularly, (v) a method for preventing and/or treating a SARS-CoV infection and SARS, which involves administering a prophylactic or therapeutic amount of a vaccine vector of the invention to an infected individual. Additionally, the invention further provides a use of a vaccine vector of the invention in the preparation of a medicament for preventing and/or treating SARS-CoV infection and SARS.

As used herein, a vaccine vector expresses one or several polypeptides or derivatives of the invention. The vaccine vector may express additionally a cytokine, such as interleukin-2 (IL-2) or interleukin-12 (IL-12), that enhances the immune response (adjuvant effect). It is understood that each of the components to be expressed is placed under the

control of elements required for expression in a mammalian cell.

The invention further provides a composition comprising several polypeptides or derivative thereof of the invention or vaccine vectors (each of them capable of expressing a polypeptide or derivative of the invention). A composition may also comprise an additional SARS-CoV antigen, or a subunit, fragment, homolog, mutant, or derivative thereof; optionally together with or a cytokine such as IL-2 or IL-12 (or vaccine vector(s) capable of their expression).

"Vaccine" as used herein refers to a composition or formulation comprising one or more polypeptides of the invention, or a vaccine vector of the invention. Vaccination methods for treating or preventing infection in a mammal comprises use of a vaccine or vaccine vector of the invention to be administered by any conventional route.

Treatment may be effected in a single dose or repeated at intervals. The appropriate dosage depends on various parameters understood by skilled artisans such as the vaccine or vaccine vector itself, the route of administration or the condition of the mammal to be vaccinated (weight, age and the like).

Live vaccine vectors available in the art include viral vectors such as adenoviruses and poxviruses as well as bacterial vectors, *e.g.*, *Shigella*, *Salmonella*, *Vibrio cholerae*, *Lactobacillus*, Bacille bilié de Calmette-Guérin (BCG), and *Streptococcus*.

An example of an adenovirus vector, as well as a method for constructing an adenovirus vector capable of expressing a DNA molecule of the invention, are described in U.S. Patent No. 4,920,209. Poxvirus vectors include vaccinia and canary pox virus, described in U.S. Patent No. 4,722,848 and U.S. Patent No. 5,364,773, respectively. (Also see, *e.g.*,

Tartaglia *et al.*, Virology (1992) 188:217) for a description of a vaccinia virus vector and Taylor *et al*, Vaccine (1995) 13:539 for a reference of a canary pox.) Poxvirus vectors capable of expressing a polynucleotide of the invention are obtained by homologous recombination as described in Kieny *et al.*, Nature (1984) 312:163 so that the polynucleotide of the invention is inserted in the viral genome under appropriate conditions for expression in mammalian cells. Generally, the dose of vaccine viral vector, for therapeutic or prophylactic use, can be of from about $1x10^4$ to about $1x10^{11}$, advantageously from about $1x10^7$ to about $1x10^{10}$, preferably of from about $1x10^7$ to about $1x10^9$ plaque-forming units per kilogram. Preferably, viral vectors are administered parenterally; for example, in 3 doses, 4 weeks apart. It is preferable to avoid adding a chemical adjuvant to a composition containing a viral vector of the invention and thereby minimizing the immune response to the viral vector itself.

Non-toxicogenic *Vibrio cholerae* mutant strains that are useful as a live oral vaccine are known. Mekalanos *et al.*, Nature (1983) 306:551 and U.S. Patent No. 4,882,278 describe strains which have a substantial amount of the coding sequence of each of the two *ctxA* alleles deleted so that no functional *cholerae* toxin is produced. WO 92/11354 describes a strain in which the *irgA* locus is inactivated by mutation; this mutation can be combined in a single strain with *ctxA* mutations. WO 94/01533 describes a deletion mutant lacking functional *ctxA* and *attRS1* DNA sequences. These mutant strains are genetically engineered to express heterologous antigens, as described in WO 94/19482. An effective vaccine dose of a *Vibrio cholerae* strain capable of expressing a polypeptide or polypeptide derivative encoded by a DNA molecule of the invention contains about $1x10^5$ to about $1x10^9$, preferably about $1x10^6$ to about $1x10^8$, viable bacteria in a

volume appropriate for the selected route of administration. Preferred routes of administration include all mucosal routes; most preferably, these vectors are administered intranasally or orally.

Attenuated *Salmonella typhimurium* strains, genetically engineered for recombinant expression of heterologous antigens or not, and their use as oral vaccines are described in Nakayama *et al.* (Bio/Technology (1988) 6:693) and WO 92/11361. Preferred routes of administration include all mucosal routes; most preferably, these vectors are administered intranasally or orally.

Other bacterial strains used as vaccine vectors in the context of the present invention are described for *Shigella flexneri* in High *et al.*, EMBO (1992) 11:1991 and Sizemore *et al.*, Science (1995) 270:299; for *Streptococcus gordonii* in Medaglini *et al.*, Proc. Natl. Acad. Sci. USA (1995) 92:6868; and for Bacille Calmette Guerin in Flynn J.L., Cell. Mol. Biol. (1994) 40 (suppl. I):31, WO 88/06626, WO 90/00594, WO 91/13157, WO 92/01796, and WO 92/21376.

In bacterial vectors, the polynucleotide of the invention is inserted into the bacterial genome or remains in a free state as part of a plasmid.

The composition comprising a polypeptide or vaccine vector of the present invention may further contain an adjuvant. A number of adjuvants are known to those skilled in the art. Preferred adjuvants are selected as provided below.

Accordingly, a further aspect of the invention provides (i) a composition of matter comprising a polypeptide or polynucleotide of the invention, together with a diluent or carrier; (ii) a pharmaceutical composition comprising a therapeutically or prophylactically effective amount of a polypeptide or polynucleotide of the invention; (iii) a method for inducing an immune response against SARS-CoV in a mammal

by administration of an immunogenically effective amount of a polypeptide or polynucleotide of the invention to elicit a protective immune response to SARS-CoV; and particularly, (iv) a method for preventing and/or treating a SARS-CoV infection or SARS, by administering a prophylactic or therapeutic amount of a polypeptide or polynucleotide of the invention to an infected individual. Additionally, the invention further provides a use of a polypeptide or polynucleotide of the invention in the preparation of a medicament for preventing and/or treating SARS-CoV infection or SARS.

Use of the polynucleotides of the invention include their administration to a mammal as a vaccine, for therapeutic or prophylactic purposes. Such polynucleotides are used in the form of DNA as part of a plasmid that is unable to replicate in a mammalian cell and unable to integrate into the mammalian genome. Typically, such a DNA molecule is placed under the control of a promoter suitable for expression in a mammalian cell. The promoter functions either ubiquitously or tissue-specifically. Examples of non-tissue specific promoters include the early Cytomegalovirus (CMV) promoter (described in U.S. Patent No. 4,168,062) and the Rous Sarcoma Virus promoter (described in Norton & Coffin, Molec. Cell Biol. (1985) 5:281). An example of a tissue-specific promoter is the desmin promoter which drives expression in muscle cells (Li *et al.*, Gene (1989) 78:243, Li & Paulin, J. Biol. Chem. (1991) 266:6562 and Li & Paulin, J. Biol. Chem. (1993) 268:10403). Use of promoters is well-known to those skilled in the art. Useful vectors are described in numerous publications, specifically WO 94/21797 and Hartikka *et al.*, Human Gene Therapy (1996) 7:1205.

Polynucleotides of the invention which are used as vaccines encode either a precursor or a mature form of the corresponding polypeptide. In the precursor form, the signal

peptide is either homologous or heterologous. In the latter case, a eucaryotic leader sequence such as the leader sequence of the tissue-type plasminogen factor (tPA) is preferred.

Standard techniques of molecular biology for preparing and purifying polynucleotides are used in the preparation of polynucleotide therapeutics of the invention. For use as a vaccine, a polynucleotide of the invention is formulated according to various methods outlined below.

One method utililizes the polynucleotide in a naked form, free of any delivery vehicles. Such a polynucleotide is simply diluted in a physiologically acceptable solution such as sterile saline or sterile buffered saline, with or without a carrier. When present, the carrier preferably is isotonic, hypotonic, or weakly hypertonic, and has a relatively low ionic strength, such as provided by a sucrose solution, *e.g.*, a solution containing 20% sucrose.

An alternative method utilizes the polynucleotide in association with agents that assist in cellular uptake. Examples of such agents are (i) chemicals that modify cellular permeability, such as bupivacaine (see, *e.g.*, WO 94/16737), (ii) liposomes for encapsulation of the polynucleotide, or (iii) cationic lipids or silica, gold, or tungsten microparticles which associate themselves with the polynucleotides.

Anionic and neutral liposomes are well-known in the art (see, *e.g.*, Liposomes: A Practical Approach, RPC New Ed, IRL press (1990), for a detailed description of methods for making liposomes) and are useful for delivering a large range of products, including polynucleotides.

Cationic lipids are also known in the art and are commonly used for gene delivery. Such lipids include Lipofectin™ also known as DOTMA (N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride), DOTAP (1,2-bis(oleyloxy)-3-

(trimethylammonio)propane), DDAB (dimethyldioctadecylammonium bromide), DOGS (dioctadecylamidologlycyl spermine) and cholesterol derivatives such as DC-Chol (3 beta-(N-(N',N'-dimethyl aminomethane)-carbamoyl) cholesterol). A description of these cationic lipids can be found in EP 187,702, WO 90/11092, U.S. Patent No. 5,283,185, WO 91/15501, WO 95/26356, and U.S. Patent No. 5,527,928. Cationic lipids for gene delivery are preferably used in association with a neutral lipid such as DOPE (dioleyl phosphatidylethanolamine), as described in WO 90/11092 as an example.

Formulation containing cationic liposomes may optionally contain other transfection-facilitating compounds. A number of them are described in WO 93/18759, WO 93/19768, WO 94/25608, and WO 95/02397. They include spermine derivatives useful for facilitating the transport of DNA through the nuclear membrane (see, for example, WO 93/18759) and membrane-permeabilizing compounds such as GALA, Gramicidine S, and cationic bile salts (see, for example, WO 93/19768).

Gold or tungsten microparticles are used for gene delivery, as described in WO 91/00359, WO 93/17706, and Tang *et al.* Nature (1992) 356:152. The microparticle-coated polynucleotide is injected *via* intradermal or intraepidermal routes using a needleless injection device ("gene gun"), such as those described in U.S. Patent No. 4,945,050, U.S. Patent No. 5,015,580, and WO 94/24263.

The amount of DNA to be used in a vaccine recipient depends, *e.g.*, on the strength of the promoter used in the DNA construct, the immunogenicity of the expressed gene product, the condition of the mammal intended for administration (*e.g.*, the weight, age, and general health of the mammal), the mode of administration, and the type of formulation. In general, a therapeutically or prophylactically effective dose from about 1 µg to about 1 mg, preferably, from about 10 µg to about 800

μg and, more preferably, from about 25 μg to about 250 μg, can be administered to human adults. The administration can be achieved in a single dose or repeated at intervals.

Although not absolutely required, such a composition can also contain an adjuvant. If so, a systemic adjuvant that does not require concomitant administration in order to exhibit an adjuvant effect is preferable such as, *e.g.*, QS21, which is described in U.S. Patent No. 5,057,546.

Treatment is achieved in a single dose or repeated as necessary at intervals, as can be determined readily by one skilled in the art. For example, a priming dose is followed by three booster doses at weekly or monthly intervals. An appropriate dose depends on various parameters including the recipient (*e.g.*, adult or infant), the particular vaccine antigen, the route and frequency of administration, the presence/absence or type of adjuvant, and the desired effect (*e.g.*, protection and/or treatment), as can be determined by one skilled in the art. In an embodiment, a polypeptide of the invention, administered as a vaccine, is administered by a mucosal route in an amount from about 10 μg to about 500 mg, preferably from about 1 mg to about 200 mg. For the parenteral route of administration, the dose usually does not exceed about 1 mg, preferably about 100 μg.

When used as vaccine agents, polypeptides and polynucleotides of the invention may be used sequentially as part of a multistep immunization process. For example, a mammal is initially primed with a vaccine vector of the invention such as a pox virus, *e.g.*, *via* the parenteral route, and then boosted twice with the polypeptide encoded by the vaccine vector, *e.g.*, *via* the mucosal route. In another example, liposomes associated with a polypeptide or derivative of the invention is also used for priming, with boosting being carried out mucosally using a soluble polypeptide or

derivative of the invention in combination with a mucosal adjuvant (*e.g.*, LT).

A polypeptide or variant or derivative thereof of the invention is also used in accordance with a further aspect of the invention as a diagnostic reagent for detecting the presence of anti-SARS-CoV antibodies, *e.g.*, in a blood sample. Such polypeptides are about 5 to about 80, preferably about 10 to about 50 amino acids in length. They are either labeled or unlabeled, depending upon the diagnostic method. Diagnostic methods involving such a reagent are described below.

Adjuvants useful in any of the vaccine compositions described above are as follows.

Adjuvants for parenteral administration include aluminum compounds, such as aluminum hydroxide, aluminum phosphate, and aluminum hydroxy phosphate. The antigen is precipitated with, or adsorbed onto, the aluminum compound according to standard protocols. Other adjuvants, such as RIBI (ImmunoChem, Hamilton, MT), are used in parenteral administration.

Adjuvants for mucosal administration include bacterial toxins, *e.g.*, the cholera toxin (CT), the *E. coli* heat-labile toxin (LT), the *Clostridium difficile* toxin A and the *pertussis* toxin (PT), or combinations, subunits, toxoids, or mutants thereof such as a purified preparation of native cholera toxin subunit B (CTB). Fragments, homologs, derivatives, and fusions to any of these toxins are also suitable, provided that they retain adjuvant activity. Preferably, a mutant having reduced toxicity is used. Suitable mutants are described, *e.g.*, in WO 95/17211 (Arg-7-Lys CT mutant), WO 96/06627 (Arg-192-Gly LT mutant), and WO 95/34323 (Arg-9-Lys and Glu-129-Gly PT mutant). Additional LT mutants that are used in the methods and compositions of the invention include, *e.g.*, Ser-63-Lys, Ala-69Gly, Glu-110-Asp,

and Glu-112-Asp mutants. Other adjuvants, such as a bacterial monophosphoryl lipid A (MPLA) of, *e.g.*, *E. coli*, *Salmonella minnesota*, *Salmonella typhimurium*, or *Shigella flexneri*; saponins, or polylactide glycolide (PLGA) microspheres, is also be used in mucosal administration.

Adjuvants useful for both mucosal and parenteral administrations include polyphosphazene (WO 95/02415), DC-chol (3 b-(N-(N',N'-dimethyl aminomethane)-carbamoyl) cholesterol; U.S. Patent No. 5,283,185 and WO 96/14831) and QS-21 (WO 88/09336).

Any pharmaceutical composition of the invention containing a polypeptide, a polypeptide derivative, a polynucleotide or an antibody of the invention, is manufactured in a conventional manner. In particular, it is formulated with a pharmaceutically acceptable diluent or carrier, *e.g.*, water or a saline solution such as phosphate buffer saline. In general, a diluent or carrier is selected on the basis of the mode and route of administration, and standard pharmaceutical practice. Suitable pharmaceutical carriers or diluents, as well as pharmaceutical necessities for their use in pharmaceutical formulations, are described in *Remington's Pharmaceutical Sciences*, a standard reference text in this field and in the USP/NF.

A "therapeutically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic result, such as a reduction of SARS disease symptoms and in turn a reduction in SARS-related disease progression and an improvement in SARS prognosis. A therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the compound to elicit a desired response in the individual. Dosage regimens may be adjusted to provide the optimum therapeutic response. A

therapeutically effective amount is also one in which any toxic or detrimental effects of the compound are outweighed by the therapeutically beneficial effects. A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result, such as preventing or inhibiting SARS onset or progression. A prophylactically effective amount can be determined as described above for the therapeutically effective amount. For any particular subject, specific dosage regimens may be adjusted over time according to the individual need and the professional judgement of the person administering or supervising the administration of the compositions.

As used herein "pharmaceutically acceptable carrier" or "excipient" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible. In one embodiment, the carrier is suitable for parenteral administration. Alternatively, the carrier can be suitable for intravenous, intraperitoneal, intramuscular, sublingual or oral administration. Pharmaceutically acceptable carriers include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the pharmaceutical compositions of the invention is contemplated. Supplementary active compounds can also be incorporated into the compositions.

Therapeutic compositions typically must be sterile and stable under the conditions of manufacture and storage.

The composition can be formulated as a solution, microemulsion, liposome, or other ordered structure suitable to high drug concentration. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, monostearate salts and gelatin. Moreover, a polypeptide of the invention can be administered in a time release formulation, for example in a composition which includes a slow release polymer. The active compounds can be prepared with carriers that will protect the compound against rapid release, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, polylactic acid and polylactic, polyglycolic copolymers (PLG). Many methods for the preparation of such formulations are patented or generally known to those skilled in the art.

A further aspect of the invention provides an antibody that recognizes the polypeptide of the invention.

An antibody of the invention is either polyclonal or monoclonal. Antibodies may be recombinant, *e.g.*, chimeric (*e.g.*, constituted by a variable region of murine origin

associated with a human constant region), humanized (a human immunoglobulin constant backbone together with hypervariable region of animal, *e.g.*, murine, origin), and/or single chain. Both polyclonal and monoclonal antibodies may also be in the form of immunoglobulin fragments, *e.g.*, F(ab)'$_2$, Fab or Fab' fragments. The antibodies of the invention are of any isotype, *e.g.*, IgG or IgA, and polyclonal antibodies are of a single isotype or a mixture of isotypes.

Antibodies against the polypeptide of the present invention are generated by immunization of a mammal with a partially purified fraction comprising the polypeptide. Such antibodies may be polyclonal or monoclonal. Methods to produce polyclonal or monoclonal antibodies are well known in the art. For a review, see Harlow and Lane (1988) and Yelton *et al.* (1981), both of which are herein incorporated by reference. For monoclonal antibodies, see Kohler and Milstein (1975), herein incorporated by reference.

The antibodies of the invention, which are raised to a partially purified fraction comprising the polypeptide of the invention, are produced and identified using standard immunological assays, *e.g.*, Western blot analysis, dot blot assay, or ELISA (see, *e.g.*, Coligan *et al.* (1994), herein incorporated by reference). The antibodies are used in diagnostic methods to detect the presence of a SARS-CoV N protein or fragment thereof or SARS-CoV in a sample, such as a tissue or body fluid. The antibodies are also used in affinity chromatography for obtaining a purified fraction comprising the polypeptide of the invention.

Accordingly, a further aspect of the invention provides (i) a reagent for detecting the presence of a SARS-CoV N protein polypeptide or fragment thereof and/or SARS-CoV in a tissue or body fluid; and (ii) a diagnostic method for

detecting the presence of a SARS-CoV N protein polypeptide or fragment thereof and SARS-CoV in a tissue or body fluid, by contacting the tissue or body fluid with an antibody of the invention, such that an immune complex is formed, and by detecting such complex to indicate the presence of a SARS-CoV N protein polypeptide or fragment thereof and/or SARS-CoV in the sample or the organism from which the sample is derived.

Those skilled in the art will readily understand that the immune complex is formed between a component of the sample and the antibody, and that any unbound material is removed prior to detecting the complex. It is understood that an antibody of the invention is used for screening a sample, such as, for example, blood, plasma, lymphocytes, cerebrospinal fluid, urine, saliva, epithelia and fibroblasts, for the presence of a SARS-CoV N protein polypeptide or fragment thereof and/or SARS-CoV.

Similarly, a polypeptide of the invention may be used as a reagent to detect the presence of an antibody to a SARS-CoV N protein or fragment thereof and/or SARS-CoV in a tissue or body fluid, and therefore the invention further provides such a reagent, as well as a diagnostic method for detecting the presence of a an antibody to a SARS-CoV N protein or fragment thereof and/or SARS-CoV, by contacting the tissue or body fluid with a polypeptide of the invention, such that an immune complex is formed, and by detecting such complex to indicate the presence of a SARS-CoV N protein or fragment thereof and/or SARS-CoV in the sample or the organism from which the sample is derived.

For diagnostic applications, the reagent (*e.g*, the polypeptide or antibody of the invention) is either in a free state or immobilized on a solid support, such as a tube, a bead, a plate or well thereof, or any other conventional

support used in the field (such as a peptide microarray). Immobilization is achieved using direct or indirect means. Direct means include passive adsorption (non-covalent binding) or covalent binding between the support and the reagent. By "indirect means" is meant that an anti-reagent compound that interacts with a reagent is first attached to the solid support. Indirect means may also employ a ligand-receptor system, for example, where a molecule such as a vitamin is grafted onto the reagent and the corresponding receptor immobilized on the solid phase. This is illustrated by the biotin-streptavidin system. Alternatively, a peptide tail is added chemically or by genetic engineering to the reagent and the grafted or fused product immobilized by passive adsorption or covalent linkage of the peptide tail.

Such diagnostic agents may be included in a kit which also comprises instructions for use. The reagent is labeled with a detection means which allows for the detection of the reagent when it is bound to its target. The detection means may be a fluorescent agent such as fluorescein isocyanate or fluorescein isothiocyanate, or an enzyme such as horseradish peroxidase or luciferase or alkaline phosphatase, or a radioactive element such as ^{125}I or ^{51}Cr.

Although various embodiments of the invention are disclosed herein, many adaptations and modifications may be made within the scope of the invention in accordance with the common general knowledge of those skilled in this art. Such modifications include the substitution of known equivalents for any aspect of the invention in order to achieve the same result in substantially the same way. Numeric ranges are inclusive of the numbers defining the range. In the claims, the word "comprising" is used as an open-ended term, substantially equivalent to the phrase "including, but not limited to". The following examples are illustrative of

various aspects of the invention, and do not limit the broad aspects of the invention as disclosed herein.

Throughout this application, various references are referred to describe more fully the state of the art to which this invention pertains. The disclosures of these references are hereby incorporated by reference into the present disclosure.

EXAMPLES

Example 1: Materials and Methods

Generation of Peptides

For the T cell proliferation assay (see below), we utilized 15-mer peptides overlapping by 10 amino acids of the N protein (see Figure 5) synthesized by AnaSpec International (Kelowna, Taiwan, R.O.C.). The peptides were generated using solid phase peptide synthesis using F-moc chemistry and was conducted on an automated peptide synthesizer symphony according to the manufacturer's standard protocols. The peptides were cleaved from the solid support by treatment with liquid trifluoroacetic acid (TFA) in the presence of phenol, thiocresole, anisole, and methyl sulfide. The crude products had been extracted with TFA and precipitated with diethyl ether. All peptides are analyzed by HPLC and Mass spectroscopy (MS) to verify their identity, and then stored in lyophilized form at -20°C. Peptides were dissolved in DMSO and diluted to 5% DMSO in ddH_2O.

For the Affinity Binding assays (see below), we utilized 9-mer peptides overlapping by 8 amino acid of the N protein (see Figure 6) synthesized by SynPep Corporation (Dublin, CA). The peptides were generated using Fmoc chemistry prepared by 9-fluoronylmethoxycarbonyl synthesis on

Rainin/PTI Symphony™ automated machines. Peptide identity was verified by HPLC and MS analysis. For confirmation of binding results, fifteen of the 9-mer peptides were synthesized by New England Peptide Inc. (Gardner, MA) and tested for affinity to HLA class I complexes.

For the studies corresponding to the results presented in Figures 9 to 123, overlapping 9-mer peptides of the N-protein (see Figure 6) were synthesized using standard methods by Jerini AG (Berlin , Germany (http://www.jerini.de/)).

Cloning, expression and purification of recombinant SARS-CoV Nucleocapsid gene

The single stranded RNA sequence of the SARS coronavirus nucleocapsid gene was obtained from genbank (accession number: NC_04718 region: 28120-28388). Forward (GGA ATT CCA TAT GTC TGA TAA TGG ACC CA; SEQ ID NO: 497) and reverse (TAT CGC GGA TCC TTA TGC CTG AGT TGA ATC A; SEQ ID NO: 498) PCR primers were designed to amplify the open reading frame (1258 base pairs) of the nucleocapsid gene and incorporate restriction endonuclease sites *Nde*1 and *Bam*H1 respectively. Primers were synthesized at McMaster University's central molecular biology facility. The nucleocapsid gene was amplified from reverse-transcribed SARS RNA and separated by agarose gel electrophoreses to confirm the presence of the amplified gene. PCR products were purified (QIAgen, Valencia, CA), digested and ligated into the pET-28a (+) plasmid (Novagen, Madison, WI). Competent JM109 cells (Promega, Madison, WI) were transformed with 10 ng of plasmid DNA by the Promega heat shock method. Plasmid containing bacteria were selected on kanamycin (34 μg /mL) containing LB agar plates. Colonies were verified to contain the nucleocapsid gene by PCR amplification using T7 forward and

reverse primers. A single nucleocapsid-containing colony was grown in 9 mL of LB broth (34 μg/mL kanamycin) overnight at 37°C, and plasmid DNA was isolated by the mini-prep procedure (QIAgen, Valencia, CA). Rosetta DE3 (BL21) pLysS cells (Novagen) were transformed with 10 ng of plasmid DNA by the heat shock method, and selected on LB agar plates containing kanamycin (34 μg/mL) and choramphenicol (30 μg /mL). A single colony was placed in 3 mL of starter LB broth (containing kanamycin and chloramphenicol), grown overnight and used to seed 1 L of LB broth with antibiotics until A_{600} was between 0.6-0.8. IPTG (Sigma-Aldrich, St. Louis, MO.) was added to obtain a concentration of 1 mM, and the culture was incubated for 2 hours at 37°C. Cells were pelleted by centrifugation at 6000 X g for 20 minutes at 4 °C, resuspended in binding buffer (0.02 M sodium phosphate buffer, 0.5 M NaCl, pH=7.4) before being lysed in a French press (Spectronic instruments, Madison, WI). Lysates were centrifuged at 50 000 X g for 45 minutes to separate insoluble material, and applied to a 5 mL Ni charged Hi-trap Chelating HP column (Amersham-Pharmacia, Uppsala, Sweden) at 4 mL/min. Proteins were eluted in binding buffer with an imidazole gradient from 0-300 mM. Fractions were analyzed for the presence of Nucleocapsid protein by SDS-PAGE and coomassie blue staining against a size specific protein standard, followed by western blot analysis using an anti-His primary antibody at a dilution of 1:10 000 (Stressgen, Santa Cruz, CA). Nucleocapsid protein was purified using an Äkta Prime HPLC (Amersham-Pharmacia) equipped with a SP Sepharose Fast Flow cation exchange column (Amersham-Pharmacia). Proteins were eluted in modified binding buffer (0.02 M sodium phosphate, pH=7.4, 0.5 mM DTT) with a salt gradient from 0-1 M. Presence of Nucleocapsid protein was confirmed in individual fractions using coomassie staining of SDS-PAGE gels and western blot using an anti-His (Stressgen,

Santa Cruz, CA) primary antibody. Fractions containing Nucleocapsid protein were concentrated in pH=7.4 phosphate-buffered saline (PBS) using Amicon ultra centrifugal filter devices (Millipore, Bedford, MA). Concentrated samples were stored at -80°C in 15% glycerol with EDTA-free complete protease inhibitors (Roche, Laval, Quebec, Canada) prior to use.

PBMC isolation and storage

Consenting convalescent Toronto SARS patients donated 60-80ml of blood drawn into heparin CPT tubes (Bd Biosciences, San Jose,CA). Peripheral blood mononuclear cells (PBMCs) were isolated according to manufacturer's protocol. Briefly, following blood collection, CPT tubes were centrifuged in an Allegra 6R centrifuge (Beckman Coulter, Inc., Fullerton, CA) at 1800 X g for 20 minutes at room temperature. Buffy coat layer was removed, washed once in 50 ml of 1x PBS, pH 7.4. PBMCs were frozen in 2ml of 12.5% DMSO, 12.5% Human Serum Albumin (Sigma-Aldrich, St. Louis, MO) RPMI and cryopreserved in liquid nitrogen.

Proliferation Assay

The proliferation assays were carried out according to the methods utilized by Younes *et. al.*, 2003 [21]. Briefly, convalescent PBMCs were labeled with 1.5 uM 5-6-Carboxyfluorescein diacetate succinimidyl ester (CFSE) (Molecular Probes, Eugene, OR) for 20 minutes at room temperature. The labeling reaction was quenched with one volume of 10% Human AB serum RPMI. The cells were washed in 1x phosphate-buffered saline (PBS), resuspended at $1x10^6$/ml in 10% Human AB serum RPMI and 1 ml of cell suspension was distributed into 96 Deep well pates (BD Biosciences, San Jose, CA). Cells were incubated at 37°C for 7 days in the presence of

10 µg of 15-mer peptides or 6 µg of whole protein. After 7 days of culture cells were stained for CD4 and CD8 expression. Cells were washed twice in 1xPBS containing 2% fetal calf serum and stained with anti-human CD4-APC and CD8-PerCP, and analysed using a FACSCalibur™ flow cytometer (BD Biosciences, San Jose, CA).

Cytokine Analysis

To analyze the concentration of cytokines we utilized the human Th1/Th2 and Chemokine Cytometric Bead Arrays™ (BD Biosciences, San Jose, CA) according to the manufacturer's specifications. Briefly, Specific capture beads for cytokines and multiple phycoerythrin-conjugated detection antibodies were incubated at room temperature for 3 hours with 50 µl of culture supernatants of the proliferation assay taken at day 4 or day 7 of incubation. Following acquisition of sample data using a FACSCalibur™ flow cytometer and the results were analyzed using the BD CBA Analysis Software™.

HLA-Typing

Peripheral blood collected into blood collection tubes containing EDTA were obtained from convalescent patients. Genomic DNA was isolated using the QIAamp 96 DNA Blood DNA isolation kit (Qiagen, Valencia, CA). Typing was performed by the Canadian Network for Vaccine and Immunotherapeutics (CANVAC) HLA typing core. High resolution, four digit HLA class I (ABC) typing was determined by PCR-SSO, using the INNOLiPA™ reverse dot-blot hybridization method according to manufacturer's specifications (Innogenetics, Gent, Belgium).

Affinity binding and Off rate assay nonameric Nucleocapsid peptides to HLA class I complexes

Binding affinity and rate of dissociation of overlapping 9-mer peptides of N protein was assessed by using the iTopia™ Epitope Discovery System (Beckman Coulter, Inc., Fullerton, CA) to screen 8 major histocompatibility complex class I alleles, according to the manufacturer's instructions. Alleles tested were A*0101, A*0201, A*0301, A*1101, A*2402, B*0702, B*0801 and B*1501. These eight alleles represent close to 90% of the human population (March, S. et al, *HLA Facts Book*, Academic Press, 2000). The estimated gene frequencies of these HLA alleles is shown in Table 1.

Table 1: Estimated gene frequencies of HLA antigens included in this study*

	Caucasian	African	Asian	Latino
A1	15.18	5.72	4.48	7.40
A2	28.65	18.88	24.63	28.11
A3	13.38	8.44	2.64	8.07
A11	6.17	1.58	17.31	4.83
A24	9.32	2.96	22.03	13.26
B7	12.17	10.59	4.26	6.44
B8	9.40	3.83	1.33	3.82
B15	6.49	3.52	12.21	5.29

*From: http://www.ashi-hla.org/publicationfiles/archives/prepr/motomi.htm ; HLA Gene and Haplotype Frequencies in the North American Population: The National Marrow Donor Program Donor Registry

Briefly, this system entails the binding of a properly folded and biotinylated MHC class I monomer containing a bound peptide to an avidin-coated well of a microtiter plate. The buffer conditions are then changed to allow the dissociation of the folded complex, whereby the initial peptide and β2 microglobulin protein are washed away, however the MHC heavy chain remains bound to the well by

virtue of the avidin-biotin interaction. The test peptide of interest is then added with additional β2 microglobulin and a labeled anti-HLA class I detector antibody. The sample wells are then incubated, washed and subjected to detection of the label. As the detector antibody binds to a properly folded complex, antibody binding indicates that the test peptide is capable of binding to the MHC molecule (see Figure 8).

Identified binding peptides were diluted 1:90 and 20ul added to allele specific plates. The plates were incubated at 21°C for 18 hours. After 18 hours plates were washed and placed at 37°C to begin the time course. The off rate of the identified peptides was determined by measurement of the decay of association at 0, 0.5, 1, 1.5, 2, 4, 6 and 8 hours. Identified peptides are also tested at decreasing peptide concentration in order to evaluate relative affinity.

In respect of the results of Figures 9 to 123, peptide binding was studied as follows, testing the 414 N-protein 9-mers across the eight alleles noted above. Positive control peptides were provided in the iTopia™ Epitope Discovery system (Beckman Coulter, Inc., Fullerton, CA). The protocol was followed according to manufacturer's instructions:

Binding: 1:90 dilutions for each peptide were prepared. The allele coated plate was stripped and the peptide dilution was added with renaturation buffer provided by the manufacturer. Plates were then incubated for 18 hrs at 21°C with shaking. Subsequently, the plates were washed and read, and the % binding was calculated using iTopia™ software (iTopia™ Epitope Discovery System, Beckman Coulter, Inc., Fullerton, CA).

Affinity assay: 8 serial dilutions were prepared for each peptide. The allele coated plate was stripped and the serial

dilutions were added with renaturation buffer provided by the manufacturer. Plates were then incubated for 18 hrs at 21°C with shaking. Subsequently, the plates were washed and read, and the ED50 (concentration at which 50% of peptide is bound) was calculated using iTopia™ software.

Off rate assay: 1:90 dilutions for each peptide were prepared. The allele coated plate was stripped and the peptide dilution was added with renaturation buffer provided by manufacturer. Plates were then incubated for 18 hrs at 21°C with shaking. Subsequently, the plates were washed and a time decay study was performed: plates were read at T=0, 0.5hr, 1.0hr, 1.5hrs, 2.0hrs, 4.0hrs, 6.0hrs and 8.0hrs, and the % binding was calculated using iTopia™ software.

iScore: Using iTopia™ software, % binding, ED50 and off rate T1/2 were utilized to generate an iScore for each peptide. iScore was in turn used to rank peptides.

Example 2: Results

To determine T cell immune responses mounted against the SARS coronavirus proteins in patients who had contracted SARS, we examined peripheral blood mononuclear cells from convalescent probable SARS patients for CD4 and CD8 positive T cell proliferative responses to the N protein and N peptides generated from the SARS Tor2 strain. We initially screened seven patients for reactivity against pools of N peptides or the entire N protein. The peptide pools consisted of 10 consecutive overlapping 15 amino acid peptides (Figure 5) encompassing the entire N protein. We found that all patients showed a two fold or greater proliferative response to one or more of the peptide pools, 3, 5, 7 and 8 (Figure 1A and 2A).

The proliferative responses of CD4 and CD8 positive cells from two patients, 6 and 8, to N pools are shown in figure 1 and 2 respectively. Individual peptides from pools that stimulated proliferative responses were examined for their ability to stimulate CD4 and CD8 proliferative responses. We screened two 15-mer peptide pools, 3 and 7, for the ability to induce proliferative responses (Figure 1B). Of the constituting peptides of pools 3 and 7, a significant proliferative response from both CD8 and CD4 cells was elicited by peptide 70 (SEQ ID NO: 70; Figure 1B, right panel). CD4 and CD8 from patient 8 robustly proliferated when challenged with peptide 44 from pool 5 (Figure 2B left panel). A modest CD8 proliferative response was observed when peptides 72 (SEQ ID NO: 72) and 73 (SEQ ID NO: 73) in pool 7 were used to stimulate PBMCs from patient 8 (Figure 2 B, left panel). Many of the peptides that induced T cell proliferation in patients 6 and 8 could also induce IFN-γ expression (Fig. 1 C and Fig. 2 C). The screening of the seven SARS patients identified eighteen peptides that were able to stimulate CD4 or CD8 proliferation in PBMCs from one or more patients (Table 2). Of these 18 peptides ten could also induce expression of IFN-γ. We also screened PBMCs from four healthy volunteers. No peptides or pools of peptides were able to stimulate a two fold or greater proliferative response in PBMCs from healthy controls. We next screened an additional six patients with the ten peptides that induced proliferative responses of CD4 or CD8 cells in SARS PBMCs and cytokine stimulation. All of the additional patients showed functional responses to one or more of these peptides (Table 2, patients 12, 14, 15, 17, 19 and 20). Interestingly patient 19 did not show a CD4 proliferative responses to any of these ten peptides.

Table 2: Assessment of proliferative responses of PBMCs from SARS patients to 15-mer peptides

		Reactive 15-mer Peptides		MHC Class I	
Patient ID	**Pools Screened**	**CD8+**	**CD4+**	**A1 allele**	**A2 allele**
3	3,7	21-25, 27, 30, 61, 64-70	22, 66, 67, 69, 70		
5	5,8	43	43	A01	A02
6	3,7	21, 27, 61, 69, 70	21-24, 27, 29, 30, 61, 66, 67, 69, 70	A11	A11
7	3,7	22, 30, 61, 70	21, 61, 62, 70	A02	A24
8	5,8	43, 44, 45, 72, 73	44,45,	A11	A26
9	N/A			A01	A02
10	6,8	52, 53, 71, 72, 74, 78	54, 72, 78	A02	A03
11	5,8	41, 44, 71, 73, 78, 79	41, 44, 71, 75 , 78, 79	A11	A02
12	N/A	22, 79	22, 79	A01	A01
14	N/A	43, 66, 79	43, 79	A03	A03
15	N/A	43, 44, 66, 70	43, 44, 66	A11	A02
17	N/A	22, 43. 44, 67, 78, 79	43, 44	A24	A3401
19	N/A	23, 67	No reactive peptide	A26	A30
20	N/A	66	66	A2	A3
C1	N/A	No reactive peptide	No reactive peptide	A02	A02
C3	N/A	No reactive peptide	No reactive peptide	A02	A31
C4	N/A	No reactive peptide	No reactive peptide	A11	A3401
C5	N/A	No reactive peptide	No reactive peptide	A01	A23

To identify HLA Class I epitopes in the N protein we screened a library of N peptides composed of 9-mer peptides overlapping by 8 amino acids (Figure 6) for affinity and dissociation to six HLA class I alleles, A2, A3, A11, A24, B7 and B15. Fifteen peptides were identified in the preliminary screen (Table 3). Affinity and on off rates for A2, A3, A11 and A24 are shown in Figure 3. Interestingly, the sequence of all of the fifteen 9- mer peptides identified in the affinity and dissociation screen corresponded to 15 mer peptides that elicited CD8 proliferation (Table 2). Two 9-mer peptides showing affinity for the A2 allele, 223 and 332 (sequences LLLDRLNQL [SEQ ID NO:303] and LTYHGAIKL [SEQ ID NO:412], respectively) corresponded to the 15-mer peptides 44/45 and 66/67 (Table 3), three patients (#11, 15, and 20) with HLA A2 alleles showed reactivity to these peptides (Table 3).

Table 3: Assessment of affinity and dissociation of 9-mer peptides to HLA class I alleles

Allele	Peptide (9-mer)	Sequence (9-mer)	Corresponding Functional 15-mer Peptide	Sequence of 15-mer
A2	352	ILLNKHIDA	70,71	QFKDNV**ILLNKHIDA**, V**ILLNKHIDA**YKTFP
A2	332	LTYHGAIKL	66,67	TPSGTW**LTYHGAIKL**, W**LTYHGAIKL**DDKDP
A2	131	IVWVATEGA	27	**IVWVATEGA**LNTPKD
A2	223	LLLDRLNQL	44, 45	GETALA**LLLLDRLNQ**, A**LLLLDRLNQL**ESKV
A3	120	ASLPYGANK	24	TGPE**ASLPYGANK**EG
A3	362	KTFPPTEPK	73	Y**KTFPPTEPK**KDKKK
A3	331	WLTYHGAIK	66, 67	TPSGT**WLTYHGAIK**L, **WLTYHGAIK**LDDKDP
A3	230	QLESKVSGK	46	DRLN**QLESKVSGK**GQ
A11	120	ASLPYGANK	24	TGPE**ASLPYGANK**EG
A11	362	KTFPPTEPK	73	Y**KTFPPTEPK**KDKKK
A11	331	WLTYHGAIK	66, 67	TPSGT**WLTYHGAIK**L, **WLTYHGAIK**LDDKDP
A11	230	QLESKVSGK	46	DRLN**QLESKVSGK**GQ
A24	307	QFAPSASAF	61, 62	HWPQIA**QFAPSASAF**, A**QFAPSASAF**FGMSR
A24	346	QFKDNVILL	69, 70	DDKDP**QFKDNVILL**N, **QFKDNVILL**NKHIDA
B7	258	KPRQKRTAT	52	SK**KPRQKRTAT**KQYN
B7	67	FPRGQGVPI	14	R**FPRGQGVPI**NTNSG
B7	94	RVRGGDGKM	19	ATR**RVRGGDGKM**KEL
B7	106	SPRWYFYYL	22	**SPRWYFYYL**GTGPEA
B15	267	KQYNVTQAF	54	T**KQYNVTQAF**GRRGP

The 15-mer peptides 66 (SEQ ID NO: 66) and 67 (SEQ ID NO: 67) elicited CD8 proliferation in two patients (patient 14 and 20) with A3 alleles (Table 2 and 3).

The A11 class I allele displayed similar affinity to N peptides as A3 allele. The 9-mer peptides 120 (ASLPYGANK [SEQ

ID NO: 200]) and 362 (KTFPPTEPK [SEQ ID NO: 442]) showed high affinity for the A11 allele and maintained stable association with the complex over the 8 hour dissociation assay (Figure 3c, right panel). Two A11 patients showed CD8+ reactivity towards 15-mer peptide 73 (SEQ ID NO: 73) which corresponds to the 9 mer 362 (SEQ ID NO: 442). Furthermore, 3 patients had CD8+ and CD4+ reactivity towards 15-mer peptide 66 (SEQ ID NO: 66) or 67 (SEQ ID NO: 67).

One A24 patient displayed reactivity toward the 15-mer peptides corresponding to the A24 binding 9-mer peptides 307 (SEQ ID NO: 387) and 346 (SEQ ID NO: 426) (15 mer peptide 61 [SEQ ID NO: 61] and 70 [SEQ ID NO: 70], respectively).

To verify the identity of the N protein peptides capable of eliciting strong CD8+ and CD4+ responses, we tested the response to N peptides of PBMCs of 9 additional SARS convalescent patients. Of the ten 15-mer peptides that we originally identified the peptides that induced significant responses from different patients were 15mer peptides 22, 43, 44, 66 and 70 (SEQ ID NOs: 22, 43, 44, 66 and 70, respectively) (Figure 4).

The demonstration of high affinity binding coupled with the functional proliferation and cytokine production from convalescent SARS patient PBMCs stimulated with the identified peptides indicates that several CD8 N epitopes are recognized across various HLA A alleles and elicit functional T cell responses. The data herein demonstrates that immunodominant epitopes of the SARS-CoV reside in the N protein.

As noted above, the binding affinity and rate of dissociation of the 414 N-protein derived peptide 9-mers (see Figure 6) was assessed across the eight major histocompatibility complex class I alleles using the iTopia™ Epitope Discovery System (Beckman Coulter, Inc., Fullerton, CA). A schematic representation of the assay is shown in

Figure 8 and results are shown in Figures 9 to 123. The correspondence of the epitopes identified with MHC class I alleles is shown in Table 4.

Table 4: Correspondence of 9-mer epitopes identified with MHC class I alleles tested

Allele	Total Epitopes Identified	% of Total Protein
A*0101	6	1
A*0201	30	7
A*0301	18	4
A*1101	28	7
A*2402	37	9
B*0702	18	4
B*0801	7	2
B*1501	27	7

The N-protein peptides/epitopes identified in the studies described herein are summarized in Table 5:

Table 5: SARS N-protein peptides/epitopes identified herein

9-mer peptide	15-mer peptide	Sequence	Start Position*	End position*	SEQ ID NO:
5	-	See Figure 6	5	13	85
7	-		7	15	87
10	-		10	18	90
13	-		13	21	93
31	-		31	39	111
37	-		37	45	117
39	-		39	47	119
42	-		42	50	122
45	-		45	53	125
46	-		46	54	126
49	-		49	57	129
50	-		50	58	130
52	-		52	60	132
54	-		54	62	134
65	-		65	73	145
-	14	See Figure 5	66	80	14
67	-	See Figure 6	67	75	147
84	-		84	92	164
85	-		85	93	165
86	-		86	94	166
87	-		87	95	167
-	19	See Figure 5	91	105	19
94	-	See Figure 6	94	102	174
95	-		95	103	175
101	-		101	109	181
-	21	See Figure 5	101	115	21
102	-	See Figure 6	102	110	182
103	-		103	111	183
104	-		104	112	184
105	-		105	113	185
106	-		106	114	186
-	22	See Figure 5	106	120	22
111	-	See Figure 6	111	119	191
-	23	See Figure 5	111	125	23
112	-	See Figure 6	112	120	192
113	-		113	121	193
-	24	See Figure 5	116	130	24
120	-	See Figure 6	120	128	200
	25	See Figure 5	121	135	25

123	-	See Figure 6	123	131	203
131	-		131	139	211
-	27	See Figure 5	131	145	27
132	-	See Figure 6	132	140	212
136	-		136	144	216
139	-		139	147	219
-	29	See Figure 5	141	155	29
-	30		146	160	30
151	-	See Figure 6	151	159	231
160	-		160	168	240
161	-		161	169	241
162	-		162	170	242
165	-		165	173	245
166	-		166	174	246
167	-		167	175	247
168	-		168	176	248
170	-		170	178	250
182	-		182	190	262
184	-		184	192	264
188	-		188	196	268
-	41	See Figure 5	201	215	41
202	-	See Figure 6	202	210	282
210	-		210	218	290
-	43	See Figure 5	211	225	43
216	-	See Figure 6	216	224	296
-	44	See Figure 5	216	230	44
220	-	See Figure 6	220	228	300
221	-		221	229	301
-	45	See Figure 5	221	235	45
222	-	See Figure 6	222	230	302
223	-		223	231	303
224	-		224	232	304
-	46	See Figure 5	226	240	46
227	-	See Figure 6	227	235	307
239	-		239	247	319
241	-		241	249	321
242	-		242	250	322
250	-		250	258	330
255	-		255	263	335
-	52	See Figure 5	256	270	52
258	-	See Figure 6	258	266	338
261	-		261	269	341
-	53	See Figure 5	261	275	53
263	-	See Figure 6	263	271	343
-	54	See Figure 5	266	280	54
267	-	See Figure 6	267	275	347
268	-		268	276	348
270	-		270	278	350

271	–		271	279	351
272	–		272	280	352
286	–		286	294	366
292	–		292	300	372
294	–		294	302	374
296	–		296	304	376
297	–		297	305	377
300	–		300	308	380
301	–		301	309	381
–	61	See Figure 5	301	315	61
302	–	See Figure 6	302	310	382
304	–		304	312	384
306	–		306	314	386
–	62	See Figure 5	306	320	62
307	–	See Figure 6	307	315	387
308	–		308	316	388
309	–		309	317	389
310	–		310	318	390
312	–		312	320	392
313	–		313	321	393
314	–		314	322	394
315	–		315	323	395
316	–		316	324	396
–	64	See Figure 5	316	330	64
317	–	See Figure 6	317	325	397
320	–		320	328	400
325	–		325	333	405
–	66	See Figure 5	326	340	66
329	–	See Figure 6	329	337	409
330	–		330	338	410
331	–		331	339	411
–	67	See Figure 5	331	345	67
332	–	See Figure 6	332	340	412
339	–		339	347	419
–	69	See Figure 5	341	355	69
346	–	See Figure 6	346	354	426
–	70	See Figure 5	346	360	70
–	71		351	365	71
352	–	See Figure 6	352	360	432
353	–		353	361	433
354	–		354	362	434
356	–		356	364	436
–	72	See Figure 5	356	370	72
–	73		361	375	73
362	–	See Figure 6	362	370	442
363	–		363	371	443
–	74	See Figure 5	366	380	74
–	75		371	385	75

380	-	See Figure 6	380	388	460
386	-		386	394	466
-	78	See Figure 5	386	400	78
-	79		391	405	79
404	-	See Figure 6	404	412	484
406	-		406	414	486
407	-		407	415	487
408	-		408	416	488
Peptides/epitopes defined by overlapping and adjacent peptides/epitopes above		GPQSNQRSAPRITFGGP	5	21	499
		GGRNGARPKQRRPQGLPN NTASWFTALTQHGK	31	62	500
		LRFPRGQGVPI	65	80	501
		QIGYYRRATRRVRGGDGK MKELSPRWYFYYLGTGPE ASLPYGANKEGIVWVATE GALNTPKDHIGTRNPNNN AATVL QLPQGTTLPKGFYAEGSR	84	178	502
		QASSRSSSRSRGNSR	182	196	503
		GSSRGNSPARMASGGGET ALALLLLDRLNQLESKVS GKGQQQQGQTVTKKSAAE ASKKPRQKRTATKQYNVT QAFGRRGP	201	280	504
		NFGDQDLIRQGTDYK HWPQIAQFAPSASAFFGM SRIGMEVTPSGTWLTYHG AIKLDDKDPQFKDNVILL NKHIDAYKTFPPTEPKKD KKKKTDEAQPLPQRQKKQ PTVTLLPAADMDDFSRQL QNSMSGAS	286	416	505

*Start and end positions are in reference to N protein amino acid sequence set forth in Figure 7.

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WHAT IS CLAIMED IS:

1. An isolated immunogenic polypeptide comprising an epitope of at least 8 contiguous amino acids of SEQ ID NO: 496, wherein said polypeptide is not SEQ ID NO: 496.

2. The isolated polypeptide of claim 1, comprising an epitope of at least 9 contiguous amino acids of SEQ ID NO: 496.

3. The isolated polypeptide of claim 2, wherein said epitope is selected from the epitopes defined by the start and end positions within SEQ ID NO: 496 set forth in Table 5.

4. The isolated polypeptide of claim 1, comprising an epitope of at least 8 contiguous amino acids of an amino acid sequence selected from SEQ ID NOs: 499-505.

5. The isolated polypeptide of claim 4, comprising an epitope of at least 9 contiguous amino acids of an amino acid sequence selected from SEQ ID NOs: 499-505.

6. The isolated polypeptide of claim 1, selected from:

(a) a polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505; and

(b) a functional variant or fragment of (a), wherein said functional variant or fragment has an immune system-related activity.

7. The isolated peptide of claim 6, wherein said immune response related activity is selected from:

(i) induction of T-cell activation or proliferation;

(ii) an induction in T-cell lytic activity;

(iii) binding to an MHC class I molecule;

(iv) an alteration in cytokine or chemokine expression or production; and

(v) an alteration in expression of immunoregulatory cell surface molecules.

8. The isolated polypeptide of claim 1, wherein said polypeptide is 50 amino acids or less in length.

9. The isolated polypeptide of claim 7, wherein said T-cell is selected from a $CD8^+$ T-cell and a $CD4^+$ T-cell.

10. The isolated polypeptide of claim 7, wherein said cytokine is selected from IFNγ, IL-2,4, 5, 6, 10, 12, 13, TGF-β, and TNF-α.

11. The isolated polypeptide of claim 6, wherein said functional variant comprises 1-30 amino acid additions to an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330,

335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

12. The isolated polypeptide of claim 11, wherein said functional variant comprises 1-15 amino acid additions to an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

13. The isolated polypeptide of claim 12, wherein said functional variant comprises 1-6 amino acid additions to an amino acid sequence selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

14. The isolated polypeptide of claim 1, wherein said polypeptide consists essentially of an amino acid sequence

selected from SEQ ID NOs: 14, 19, 21-25, 27, 29, 30, 41, 43-46, 52-54, 61, 62, 64, 66, 67, 69-75, 78, 79, 85, 87, 90, 93, 111, 117, 119, 122, 125, 126, 129, 130, 132, 134, 145,147, 164-167, 174, 175, 181-186, 191-193, 200, 203, 211, 212, 216, 219, 231, 240-242, 245-248, 250, 262, 264, 268, 282, 290, 296, 300-304, 307, 319, 321, 322, 330, 335, 338, 341, 343, 347, 348, 350-352, 366, 372, 374, 376, 377, 380-382, 384, 386-390, 392-397, 400, 405, 409, 410, 411, 412, 419, 426, 432-434, 436, 442, 443, 460, 466, 484, 486-488 and 499-505.

15. The isolated peptide of claim 1, wherein said polypeptide consists essentially of an amino acid sequence selected from SEQ ID NOs: 22, 44, 66, 70, 186, 303, 412, 426 and 432.

16. An isolated SARS-CoV N protein peptide epitope, wherein said peptide epitope has an immune-related activity, with the proviso that said peptide epitope is not the full length SARS-CoV N protein set forth in SEQ ID NO: 496.

17. The isolated peptide epitope of claim 16, wherein said epitope is selected from the epitopes defined by the start and end positions within SEQ ID NO: 496 set forth in Table 5.

18. The isolated peptide epitope of claim 16, wherein said immune-related activity is selected from:

(i) induction of T-cell activation or proliferation;

(ii) an induction in T-cell lytic activity;

(iii) binding to an MHC class I molecule;

(iv) an alteration in cytokine or chemokine expression or production; and

(v) an alteration in expression of immunoregulatory cell surface molecules.

19. The isolated peptide epitope of claim 16, consisting essentially of 8 to about 50 contiguous amino acids of the SARS-CoV N protein set forth in SEQ ID NO: 496.

20. The isolated peptide epitope of claim 19, consisting essentially of 8 to about 12 contiguous amino acids of the SARS-CoV N protein set forth in SEQ ID NO: 496.

21. The isolated peptide epitope of claim 20, consisting essentially of 8, 9, 10 or 11 contiguous amino acids of the SARS-CoV N protein set forth in SEQ ID NO: 496.

22. A pharmaceutical composition comprising the isolated polypeptide of claim 1 and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition of claim 22, further comprising an adjuvant.

24. The pharmaceutical composition of claim 22, further comprising an MHC molecule.

25. A composition comprising a multimer of two or more MHC peptide complex monomers, each of said monomers comprising a polypeptide of claim 1 and an MHC molecule.

26. The composition of claim 25, wherein said MHC molecule comprises an MHC class I heavy chain or fusion protein thereof and a β2 microglobulin or fusion protein thereof.

27. The composition of claim 25, wherein said monomers are joined together into said multimer by virtue of a multivalent entity.

28. The composition of claim 27, wherein said monomers are associated with said multivalent entity by virtue of an interaction chosen from biotin-avidin interactions, biotin-streptavidin interactions, coiled-coil domain interactions, and liposome-monomer cross-linking.

29. The pharmaceutical composition of claim 22, further comprising a second polypeptide different from said isolated polypeptide, wherein said second polypeptide is capable of inducing a SARS-CoV immune response.

30. The pharmaceutical composition of claim 29, wherein said second polypeptide is an additional SARS-CoV polypeptide.

31. An antibody capable of specifically binding to the polypeptide of claim 1.

32. An isolated nucleic acid encoding the polypeptide of claim 1, wherein said nucleic acid does not encode SEQ ID NO: 496.

33. The isolated nucleic acid of claim 32, wherein the nucleic acid comprises a fragment of a nucleotide sequence capable of encoding the amino acid sequence of SEQ ID NO: 496.

34. The isolated nucleic acid of claim 33, wherein the nucleic acid comprises a fragment of the nucleotide sequence of SEQ ID NO: 495.

35. A vector comprising the nucleic acid of claim 32 operably-linked to a transcriptional regulatory sequence.

36. A host cell transformed or transfected with the vector of claim 35.

37. A method of producing a polypeptide of claim 1, said method comprising culturing the host cell of claim 36 under conditions permitting expression of said polypeptide.

38. A method of preventing or treating SARS, or for inducing an immunological or protective immune response against SARS-CoV, in an animal, said method comprising administering to said animal an agent selected from the polypeptide of claim 1, the pharmaceutical composition of claim 22, and the vector of claim 35.

39. The method of claim 38, wherein the animal is a mammal.

40. The method of claim 39, wherein the mammal is a human.

41. Use of the polypeptide of claim 1 for the preparation of a medicament.

42. Use of an agent selected from the polypeptide of claim 1, the pharmaceutical composition of claim 22, and the vector of claim 35, for preventing or treating SARS, or for

inducing an immunological or protective immune response against SARS-CoV.

43. A commercial package comprising an agent selected from the polypeptide of claim 1, the pharmaceutical composition of claim 22, and the vector of claim 35, together with instructions for preventing or treating SARS, or for inducing an immunological or protective immune response against SARS-CoV.

44. A method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising assaying a biological sample of said animal with a polypeptide of claim 1.

45. The method of claim 44, wherein said biological sample is a tissue or body fluid of said animal.

46. A method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising:

(a) contacting a biological sample of said animal with a polypeptide of claim 1; and

(b) determining the binding of a constituent of the biological sample to said polypeptide;

wherein said binding is indicative of SARS or SARS-CoV infection.

47. A method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising assaying a biological sample of said animal with the antibody of claim 31.

48. A method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising assaying a biological sample of said animal with the composition of claim 22.

49. Use of a complex comprising a polypeptide of claim 1 and an MHC molecule for labelling, detecting or isolating T-cells.

50. Use of a complex comprising a polypeptide of claim 1 and an MHC molecule for detecting, selecting, sorting, or identifying T cell epitopes and/or amino acid sequences.

51. The composition of claim 22, wherein said composition is an immunogenic or vaccine composition.

52. A polypeptide microarray comprising an isolated polypeptide of claim 1 bound to a substrate.

53. The polypeptide microarray of claim 52, further comprising an MHC molecule bound to said substrate.

54. A polypeptide microarray comprising an antibody of claim 31 bound to a substrate.

55. A polypeptide microarray comprising an MHC complex bound to a substrate, said complex comprising a polypeptide of claim 1 and an MHC molecule.

56. A method of detecting or diagnosing SARS or SARS-CoV infection in an animal, said method comprising:

(a) contacting a biological sample of said animal with the polypeptide microarray according to any one of claims 52 to 55; and

(b) determining the binding of a constituent of the biological sample to said polypeptide microarray;

wherein said binding is indicative of SARS or SARS-CoV infection.

57. A commercial package comprising a component selected from a polypeptide of claim 1, the antibody of claim 31 and the polypeptide microarray according to any one of claims 52 to 55, together with instructions for detecting or diagnosing SARS or SARS-CoV infection.

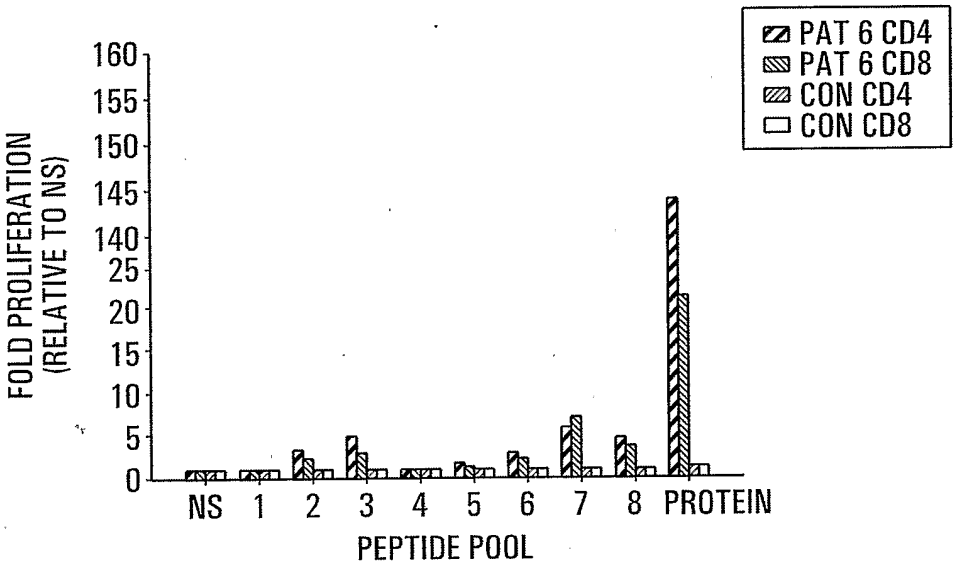
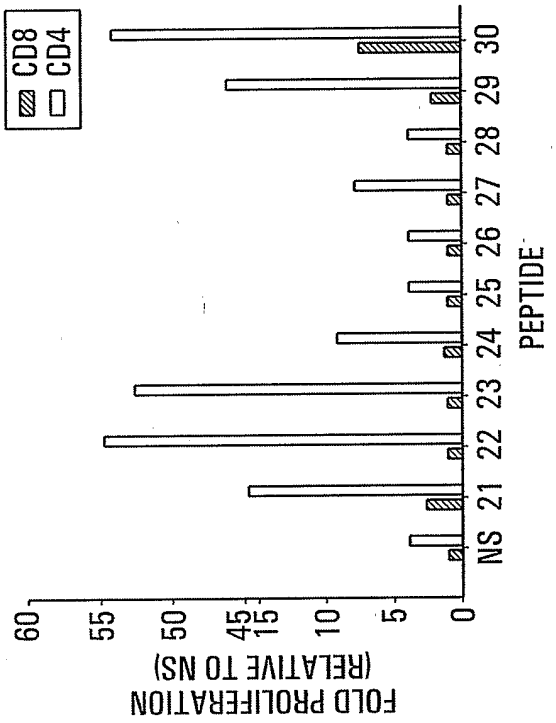

PAT 6 CD4
PAT 6 CD8
CON CD4
CON CD8
FOLD PROLIFERATION (RELATIVE TO NS)
160
155
150
145
140
25
20
15
10
5
0
NS 1 2 3 4 5 6 7 8 PROTEIN
PEPTIDE POOL

FIG. 1A


CD8
CD4
FOLD PROLIFERATION
(RELATIVE TO NS)
0
5
10
15
45
50
55
60
NS 21 22 23 24 25 26 27 28 29 30
PEPTIDE

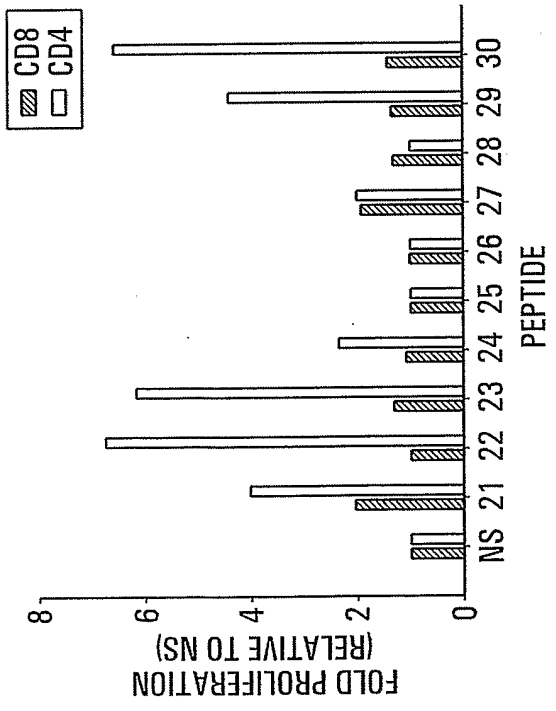

CD8
CD4
FOLD PROLIFERATION
(RELATIVE TO NS)
0
2
4
6
8
NS 21 22 23 24 25 26 27 28 29 30
PEPTIDE

FIG. 1B

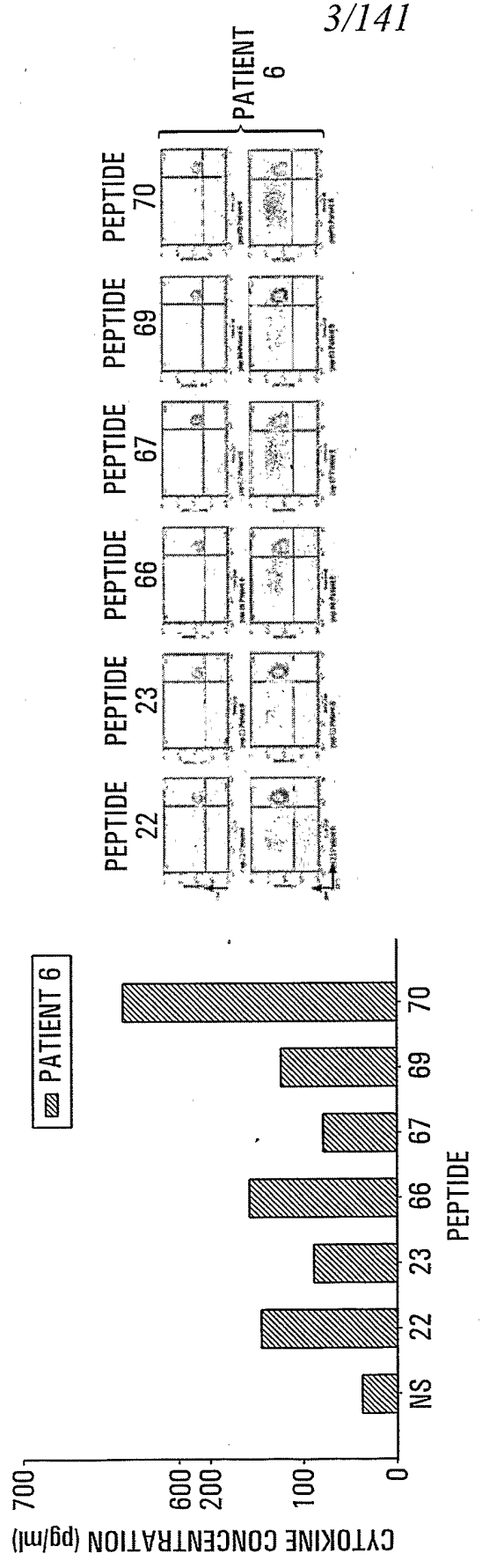

PATIENT 6
PEPTIDE 70
PEPTIDE 69
PEPTIDE 67
PEPTIDE 66
PEPTIDE 23
PEPTIDE 22
PATIENT 6
CYTOKINE CONCENTRATION (pg/ml)
700
600
200
100
0
NS
22
23
66
67
69
70
PEPTIDE

FIG. 1C

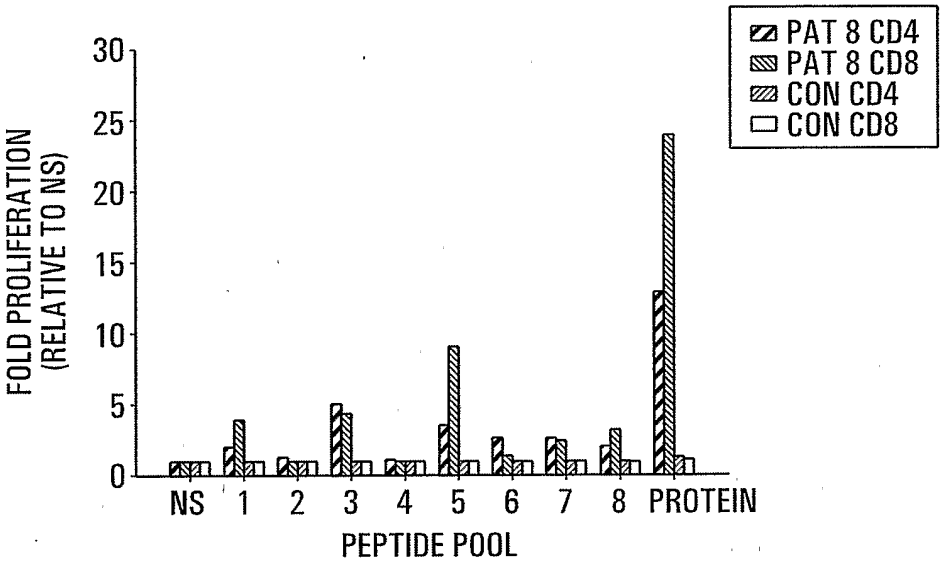
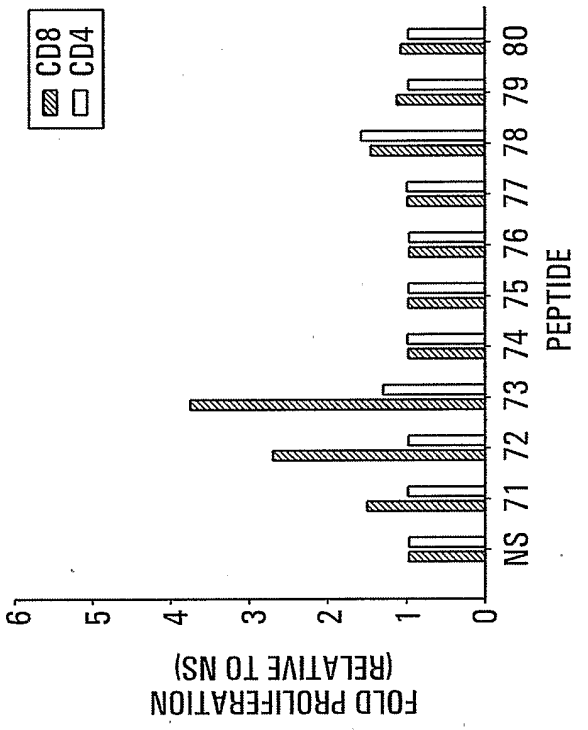

PAT 8 CD4
PAT 8 CD8
CON CD4
CON CD8
FOLD PROLIFERATION (RELATIVE TO NS)
30
25
20
15
10
5
0
NS 1 2 3 4 5 6 7 8 PROTEIN
PEPTIDE POOL

FIG. 2A


CD8
CD4
FOLD PROLIFERATION
(RELATIVE TO NS)
0
1
2
3
4
5
6
NS 71 72 73 74 75 76 77 78 79 80
PEPTIDE

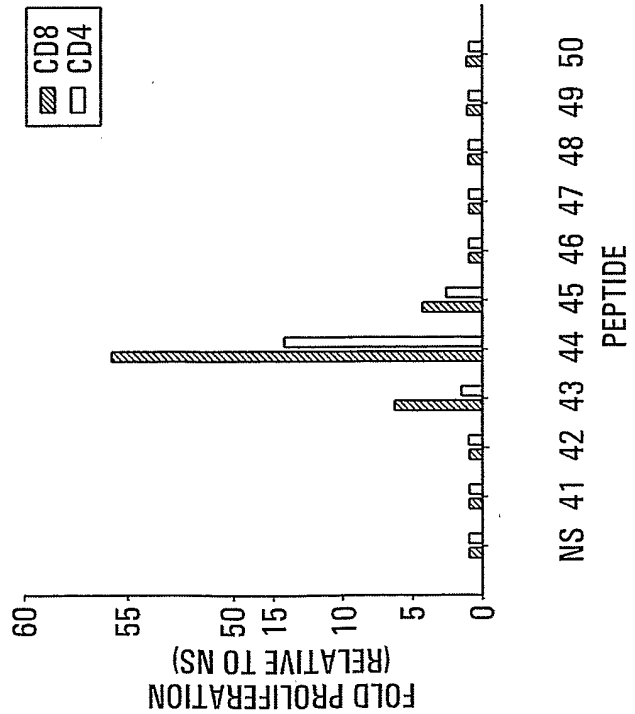

CD8
CD4
FOLD PROLIFERATION
(RELATIVE TO NS)
0
5
10
15
50
55
60
NS 41 42 43 44 45 46 47 48 49 50
PEPTIDE

FIG. 2B

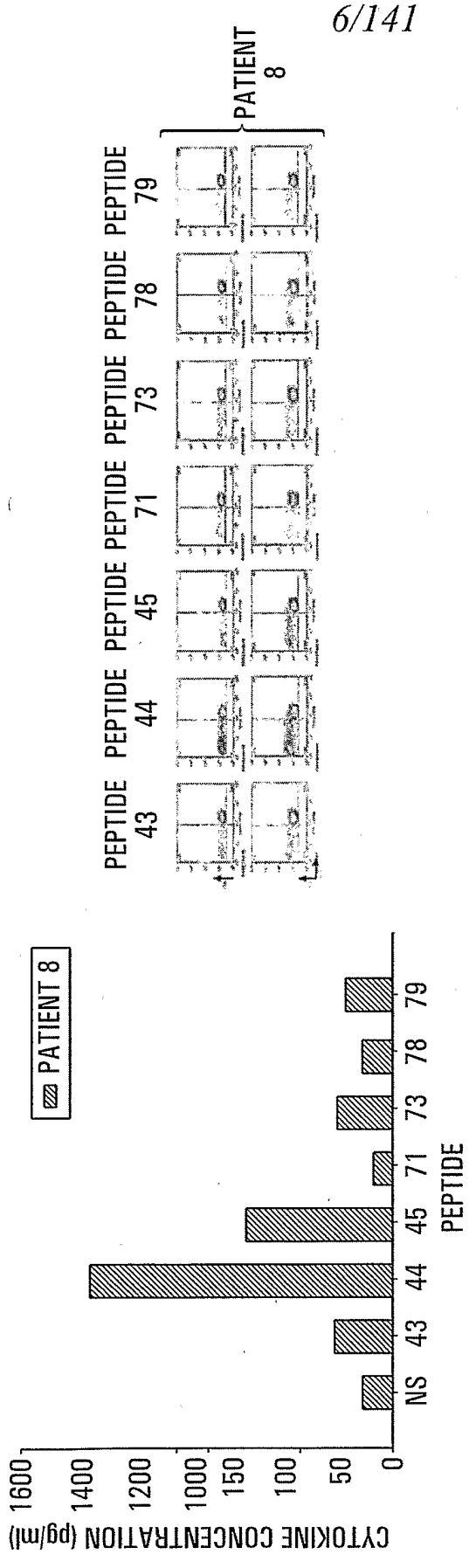
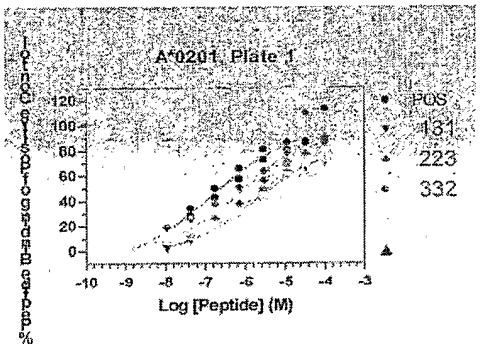
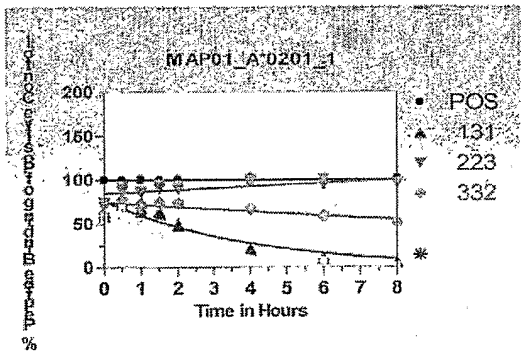

PATIENT 8
PEPTIDE 43
PEPTIDE 44
PEPTIDE 45
PEPTIDE 71
PEPTIDE 73
PEPTIDE 78
PEPTIDE 79
PATIENT 8
CYTOKINE CONCENTRATION (pg/ml)
1600
1400
1200
1000
150
100
50
0
NS
43
44
45
71
73
78
79
PEPTIDE

FIG. 2C

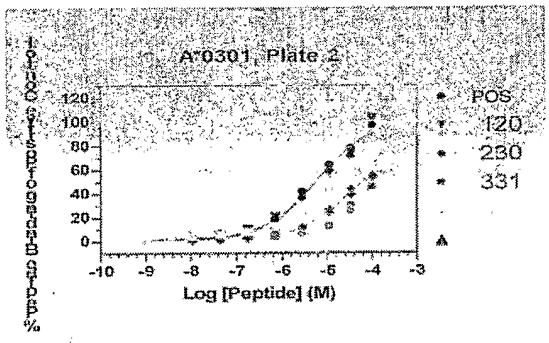


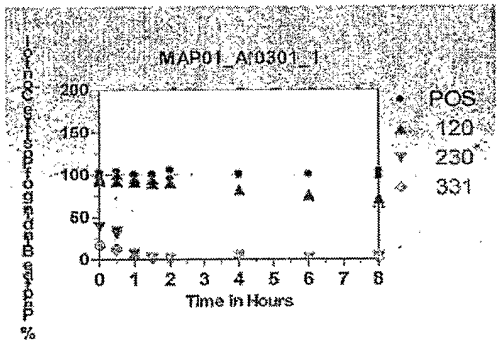


Allele	Peptide ID	ED50	R2	Sequence
A*0201	POS	1.42E-07	0.963	FLPSSDFFSV
A*0201	131	1.78E-06	0.996	IVWVATEGA
A*0201	223	9.46E-07	0.939	LLLDRLNQL
A*0201	332	3.08E-06	0.995	LTYHGAIKL
A*0201	352	4.86E-06	0.993	ILLNKHIDA

Allele	Peptide ID	R2	T1/2	iScore	Rank
A*0201	POS	0.000	21.288	2.30	High
A*0201	131	0.893	2.42	0.50	High
A*0201	223	0.439	62.866	2.84	High
A*0201	332	0.6	9.752	0.91	High
A*0201	352	0.919	1.573	0.34	Mid

FIG. 3A

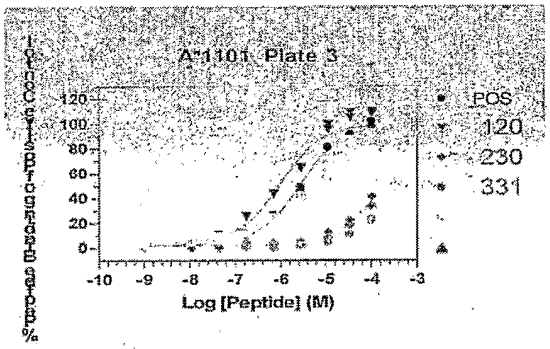


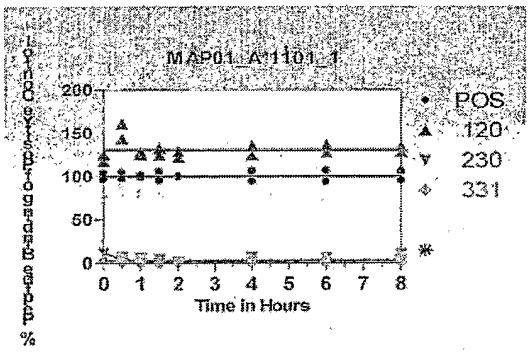


Allele	Peptide ID	ED50	R2	Sequence
A*0301	POS	5.84E-06	0.982	KVFPCALINK
A*0301	120	5.90E-06	0.979	ASLPYGANK
A*0301	230	2.38E-05	0.992	QLESKVSGK
A*0301	331	5.05E-05	0.990	WLTYHGAIK
A*0301	362	1.70E-05	0.997	KTFPPTEPK

Allele	Peptide ID	R2	T1/2	iScore	Rank
A*0301	POS	0.000	17.325	1.08	High
A*0301	120	0.94	8.375	0.75	High
A*0301	230	0.891	0.51	0.15	Low
A*0301	331	0.898	0.479	0.12	Low
A*0301	362	0.043	15.151	0.84	High

FIG. 3B

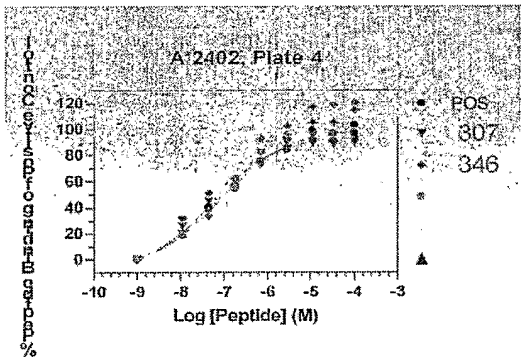


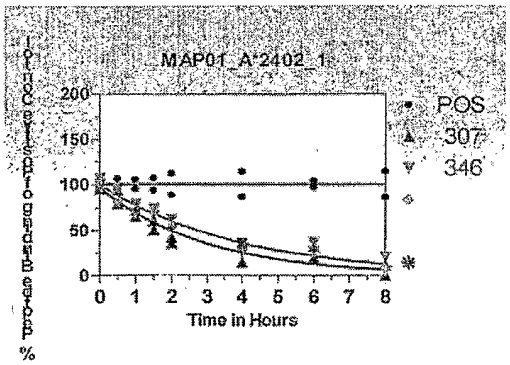


Allele	Peptide ID	ED50	R2	Sequence
A*1101	POS	2.78E-06	0.995	AVFDRKSDAK
A*1101	120	9.82E-07	0.975	ASLPYGANK
A*1101	230	1.02E-04	0.948	QLESKVSGK
A*1101	331	6.86E-05	0.976	WLTYHGAIK
A*1101	362	5.24E-06	0.991	KTFPPTEPK

Allele	Peptide ID	R2	T1/2	iScore	Rank
A*1101	POS	0.000	7.492	0.81	High
A*1101	120	0	7.443	0.97	High
A*1101	230	0.202	0.392	0.10	Low
A*1101	331	0.004	10.451	0.55	High
A*1101	362	0.079	6.811	0.69	High

FIG. 3C





Allele	Peptide ID	ED50	R2	Sequence
A*2402	POS	7.50E-08	0.990	RYLKDQQLL
A*2402	307	5.04E-08	0.989	QFAPSASAF
A*2402	346	7.79E-08	0.928	QFKDNVILL

Allele	Peptide ID	R2	T1/2	iScore	Rank
A*2402	POS	0	3.30	1.01	High
A*2402	307	0.919	1.27	0.67	High
A*2402	346	0.937	1.468	0.68	High

FIG. 3D

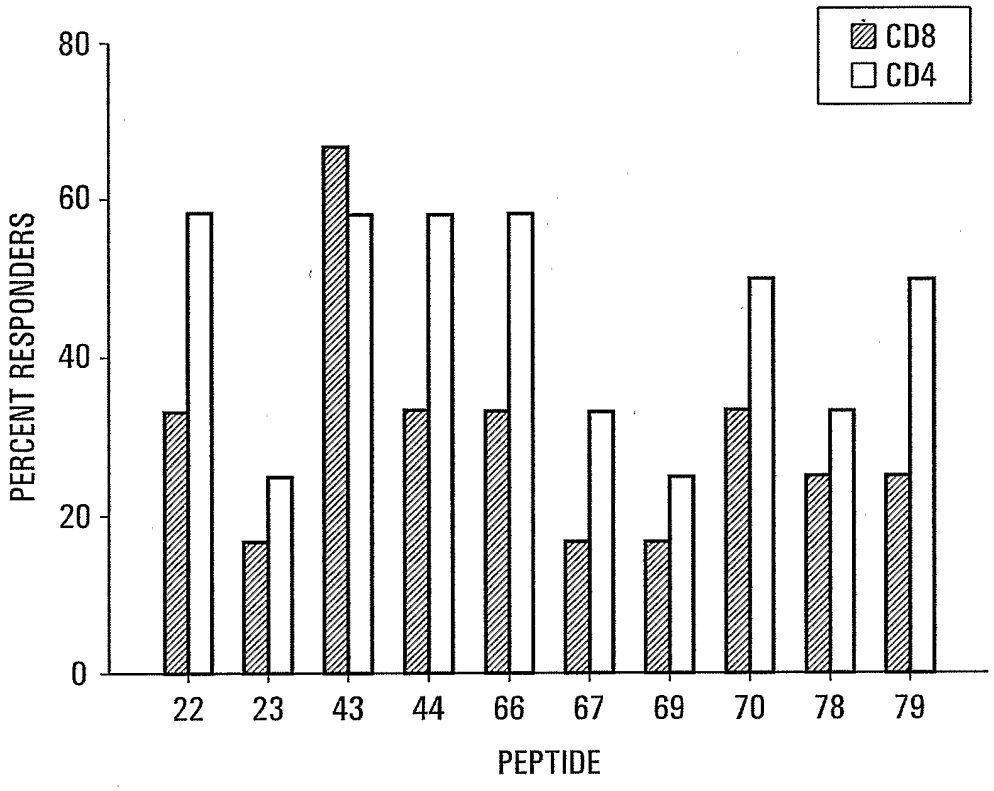

CD8
CD4
80
60
40
20
0
PERCENT RESPONDERS
22
23
43
44
66
67
69
70
78
79
PEPTIDE

FIG. 4

15-mer Peptide Sequence	SEQ-ID No:	15-mer Sequence	Pool	Start Position	End Position
1	1	MSDNGPQSNQRSAPR	1	1	15
2	2	PQSNQRSAPRITFGG	1	6	20
3	3	RSAPRITFGGPTDST	1	11	25
4	4	ITFGGPTDSTDNNQN	1	16	30
5	5	PTDSTDNNQNGGRNG	1	21	35
6	6	DNNQNGGRNGARPKQ	1	26	40
7	7	GGRNGARPKQRRPQG	1	31	45
8	8	ARPKQRRPQGLPNNT	1	36	50
9	9	RRPQGLPNNTASWFT	1	41	55
10	10	LPNNTASWFTALTQH	1	46	60
11	11	ASWFTALTQHGKEEL	2	51	65
12	12	ALTQHGKEELRFPRG	2	56	70
13	13	GKEELRFPRGQGVPI	2	61	75
14	14	RFPRGQGVPINTNSG	2	66	80
15	15	QGVPINTNSGPDDQI	2	71	85
16	16	NTNSGPDDQIGYYRR	2	76	90
17	17	PDDQIGYYRRATRRV	2	81	95
18	18	GYYRRATRRVRGGDG	2	86	100
19	19	ATRRVRGGDGKMKEL	2	91	105
20	20	RGGDGKMKELSPRWY	2	96	110
21	21	KMKELSPRWYFYYLG	3	101	115
22	22	SPRWYFYYLGTGPEA	3	106	120
23	23	FYYLGTGPEASLPYG	3	111	125
24	24	TGPEASLPYGANKEG	3	116	130
25	25	SLPYGANKEGIVWVA	3	121	135
26	26	ANKEGIVWVATEGAL	3	126	140
27	27	IVWVATEGALNTPKD	3	131	145
28	28	TEGALNTPKDHIGTR	3	136	150
29	29	NTPKDHIGTRNPNNN	3	141	155
30	30	HIGTRNPNNNAATVL	3	146	160
31	31	NPNNNAATVLQLPQG	4	151	165
32	32	AATVLQLPQGTTLPK	4	156	170
33	33	QLPQGTTLPKGFYAE	4	161	175
34	34	TTLPKGFYAEGSRGG	4	166	180

FIG. 5A

35	35	GFYAEGSRGGSQASS	4	171	185
36	36	GSRGGSQASSRSSSR	4	176	190
37	37	SQASSRSSSRSRGNS	4	181	195
38	38	RSSSRSRGNSRNSTP	4	186	200
39	39	SRGNSRNSTPGSSRG	4	191	205
40	40	RNSTPGSSRGNSPAR	4	196	210
41	41	GSSRGNSPARMASGG	5	201	215
42	42	NSPARMASGGGETAL	5	206	220
43	43	MASGGGETALALLLL	5	211	225
44	44	GETALALLLLDRLNQ	5	216	230
45	45	ALLLLDRLNQLESKV	5	221	235
46	46	DRLNQLESKVSGKGQ	5	226	240
47	47	LESKVSGKGQQQQGQ	5	231	245
48	48	SGKGQQQQGQTVTKK	5	236	250
49	49	QQQGQTVTKKSAAEA	5	241	255
50	50	TVTKKSAAEASKKPR	5	246	260
51	51	SAAEASKKPRQKRTA	6	251	265
52	52	SKKPRQKRTATKQYN	6	256	270
53	53	QKRTATKQYNVTQAF	6	261	275
54	54	TKQYNVTQAFGRRGP	6	266	280
55	55	VTQAFGRRGPEQTQG	6	271	285
56	56	GRRGPEQTQGNFGDQ	6	276	290
57	57	EQTQGNFGDQDLIRQ	6	281	295
58	58	NFGDQDLIRQGTDYK	6	286	300
59	59	DLIRQGTDYKHWPQI	6	291	305
60	60	GTDYKHWPQIAQFAP	6	296	310
61	61	HWPQIAQFAPSASAF	7	301	315
62	62	AQFAPSASAFFGMSR	7	306	320
63	63	SASAFFGMSRIGMEV	7	311	325
64	64	FGMSRIGMEVTPSGT	7	316	330
65	65	IGMEVTPSGTWLTYH	7	321	335
66	66	TPSGTWLTYHGAIKL	7	326	340
67	67	WLTYHGAIKLDDKDP	7	331	345
68	68	GAIKLDDKDPQFKDN	7	336	350

FIG. 5B

69	69	DDKDPQFKDNVILLN	7	341	355
70	70	QFKDNVILLNKHIDA	7	346	360
71	71	VILLNKHIDAYKTFP	8	351	365
72	72	KHIDAYKTFPPTEPK	8	356	370
73	73	YKTFPPTEPKKDKKK	8	361	375
74	74	PTEPKKDKKKKTDEA	8	366	380
75	75	KDKKKKTDEAQPLPQ	8	371	385
76	76	KTDEAQPLPQRQKKQ	8	376	390
77	77	QPLPQRQKKQPTVTL	8	381	395
78	78	RQKKQPTVTLLPAAD	8	386	400
79	79	PTVTLLPAADMDDFS	8	391	405
80	80	LPAADMDDFSRQLQN	8	396	410

FIG. 5C

9-mer Peptide Number	SEQ. ID NO:	9-mer Sequence	Start Position
1	81	MSDNGPQSN	1
2	82	SDNGPQSNQ	2
3	83	DNGPQSNQR	3
4	84	NGPQSNQRS	4
5	85	GPQSNQRSA	5
6	86	PQSNQRSAP	6
7	87	QSNQRSAPR	7
8	88	SNQRSAPRI	8
9	89	NQRSAPRIT	9
10	90	QRSAPRITF	10
11	91	RSAPRITFG	11
12	92	SAPRITFGG	12
13	93	APRITFGGP	13
14	94	PRITFGGPT	14
15	95	RITFGGPTD	15
16	96	ITFGGPTDS	16
17	97	TFGGPTDST	17
18	98	FGGPTDSTD	18
19	99	GGPTDSTDN	19
20	100	GPTDSTDNN	20
21	101	PTDSTDNNQ	21
22	102	TDSTDNNQN	22
23	103	DSTDNNQNG	23
24	104	STDNNQNGG	24
25	105	TDNNQNGGR	25
26	106	DNNQNGGRN	26
27	107	NNQNGGRNG	27
28	108	NQNGGRNGA	28
29	109	QNGGRNGAR	29
30	110	NGGRNGARP	30
31	111	GGRNGARPK	31
32	112	GRNGARPKQ	32
33	113	RNGARPKQR	33
34	114	NGARPKQRR	34
35	115	GARPKQRRP	35

FIG. 6A

36	116	ARPKQRRPQ	36
37	117	RPKQRRPQG	37
38	118	PKQRRPQGL	38
39	119	KQRRPQGLP	39
40	120	QRRPQGLPN	40
41	121	RRPQGLPNN	41
42	122	RPQGLPNNT	42
43	123	PQGLPNNTA	43
44	124	QGLPNNTAS	44
45	125	GLPNNTASW	45
46	126	LPNNTASWF	46
47	127	PNNTASWFT	47
48	128	NNTASWFTA	48
49	129	NTASWFTAL	49
50	130	TASWFTALT	50
51	131	ASWFTALTQ	51
52	132	SWFTALTQH	52
53	133	WFTALTQHG	53
54	134	FTALTQHGK	54
55	135	TALTQHGKE	55
56	136	ALTQHGKEE	56
57	137	LTQHGKEEL	57
58	138	TQHGKEELR	58
59	139	QHGKEELRF	59
60	140	HGKEELRFP	60
61	141	GKEELRFPR	61
62	142	KEELRFPRG	62
63	143	EELRFPRGQ	63
64	144	ELRFPRGQG	64
65	145	LRFPRGQGV	65
66	146	RFPRGQGVP	66
67	147	FPRGQGVPI	67
68	148	PRGQGVPIN	68
69	149	RGQGVPINT	69
70	150	GQGVPINTN	70
71	151	QGVPINTNS	71
72	152	GVPINTNSG	72

FIG. 6B

73	153	VPINTNSGP	73
74	154	PINTNSGPD	74
75	155	INTNSGPDD	75
76	156	NTNSGPDDQ	76
77	157	TNSGPDDQI	77
78	158	NSGPDDQIG	78
79	159	SGPDDQIGY	79
80	160	GPDDQIGYY	80
81	161	PDDQIGYYR	81
82	162	DDQIGYYRR	82
83	163	DQIGYYRRA	83
84	164	QIGYYRRAT	84
85	165	IGYYRRATR	85
86	166	GYYRRATRR	86
87	167	YYRRATRRV	87
88	168	YRRATRRVR	88
89	169	RRATRRVRG	89
90	170	RATRRVRGG	90
91	171	ATRRVRGGD	91
92	172	TRRVRGGDG	92
93	173	RRVRGGDGK	93
94	174	RVRGGDGKM	94
95	175	VRGGDGKMK	95
96	176	RGGDGKMKE	96
97	177	GGDGKMKEL	97
98	178	GDGKMKELS	98
99	179	DGKMKELSP	99
100	180	GKMKELSPR	100
101	181	KMKELSPRW	101
102	182	MKELSPRWY	102
103	183	KELSPRWYF	103
104	184	ELSPRWYFY	104
105	185	LSPRWYFYY	105
106	186	SPRWYFYYL	106
107	187	PRWYFYYLG	107
108	188	RWYFYYLGT	108
109	189	WYFYYLGTG	109

FIG. 6C

110	190	YFYYLGTGP	110
111	191	FYYLGTGPE	111
112	192	YYLGTGPEA	112
113	193	YLGTGPEAS	113
114	194	LGTGPEASL	114
115	195	GTGPEASLP	115
116	196	TGPEASLPY	116
117	197	GPEASLPYG	117
118	198	PEASLPYGA	118
119	199	EASLPYGAN	119
120	200	ASLPYGANK	120
121	201	SLPYGANKE	121
122	202	LPYGANKEG	122
123	203	PYGANKEGI	123
124	204	YGANKEGIV	124
125	205	GANKEGIVW	125
126	206	ANKEGIVWV	126
127	207	NKEGIVWVA	127
128	208	KEGIVWVAT	128
129	209	EGIVWVATE	129
130	210	GIVWVATEG	130
131	211	IVWVATEGA	131
132	212	VWVATEGAL	132
133	213	WVATEGALN	133
134	214	VATEGALNT	134
135	215	ATEGALNTP	135
136	216	TEGALNTPK	136
137	217	EGALNTPKD	137
138	218	GALNTPKDH	138
139	219	ALNTPKDHI	139
140	220	LNTPKDHIG	140
141	221	NTPKDHIGT	141
142	222	TPKDHIGTR	142
143	223	PKDHIGTRN	143
144	224	KDHIGTRNP	144
145	225	DHIGTRNPN	145
146	226	HIGTRNPNN	146

FIG. 6D

147	227	IGTRNPNNN	147
148	228	GTRNPNNNA	148
149	229	TRNPNNNAA	149
150	230	RNPNNNAAT	150
151	231	NPNNNAATV	151
152	232	PNNNAATVL	152
153	233	NNNAATVLQ	153
154	234	NNAATVLQL	154
155	235	NAATVLQLP	155
156	236	AATVLQLPQ	156
157	237	ATVLQLPQG	157
158	238	TVLQLPQGT	158
159	239	VLQLPQGTT	159
160	240	LQLPQGTTL	160
161	241	QLPQGTTLP	161
162	242	LPQGTTLPK	162
163	243	PQGTTLPKG	163
164	244	QGTTLPKGF	164
165	245	GTTLPKGFY	165
166	246	TTLPKGFYA	166
167	247	TLPKGFYAE	167
168	248	LPKGFYAEG	168
169	249	PKGFYAEGS	169
170	250	KGFYAEGSR	170
171	251	GFYAEGSRG	171
172	252	FYAEGSRGG	172
173	253	YAEGSRGGS	173
174	254	AEGSRGGSQ	174
175	255	EGSRGGSQA	175
176	256	GSRGGSQAS	176
177	257	SRGGSQASS	177
178	258	RGGSQASSR	178
179	259	GGSQASSRS	179
180	260	GSQASSRSS	180
181	261	SQASSRSSS	181
182	262	QASSRSSSR	182
183	263	ASSRSSSRS	183

FIG. 6E

184	264	SSRSSSRSR	184
185	265	SRSSSRSRG	185
186	266	RSSSRSRGN	186
187	267	SSSRSRGNS	187
188	268	SSRSRGNSR	188
189	269	SRSRGNSRN	189
190	270	RSRGNSRNS	190
191	271	SRGNSRNST	191
192	272	RGNSRNSTP	192
193	273	GNSRNSTPG	193
194	274	NSRNSTPGS	194
195	275	SRNSTPGSS	195
196	276	RNSTPGSSR	196
197	277	NSTPGSSRG	197
198	278	STPGSSRGN	198
199	279	TPGSSRGNS	199
200	280	PGSSRGNSP	200
201	281	GSSRGNSPA	201
202	282	SSRGNSPAR	202
203	283	SRGNSPARM	203
204	284	RGNSPARMA	204
205	285	GNSPARMAS	205
206	286	NSPARMASG	206
207	287	SPARMASGG	207
208	288	PARMASGGG	208
209	289	ARMASGGGE	209
210	290	RMASGGGET	210
211	291	MASGGGETA	211
212	292	ASGGGETAL	212
213	293	SGGGETALA	213
214	294	GGGETALAL	214
215	295	GGETALALL	215
216	296	GETALALLL	216
217	297	ETALALLLL	217
218	298	TALALLLLD	218
219	299	ALALLLLDR	219
220	300	LALLLLDRL	220

FIG. 6F

221	301	ALLLLDRLN	221
222	302	LLLLDRLNQ	222
223	303	LLLDRLNQL	223
224	304	LLDRLNQLE	224
225	305	LDRLNQLES	225
226	306	DRLNQLESK	226
227	307	RLNQLESKV	227
228	308	LNQLESKVS	228
229	309	NQLESKVSG	229
230	310	QLESKVSGK	230
231	311	LESKVSGKG	231
232	312	ESKVSGKGQ	232
233	313	SKVSGKGQQ	233
234	314	KVSGKGQQQ	234
235	315	VSGKGQQQQ	235
236	316	SGKGQQQQG	236
237	317	GKGQQQQGQ	237
238	318	KGQQQQGQT	238
239	319	GQQQQGQTV	239
240	320	QQQQGQTVT	240
241	321	QQQGQTVTK	241
242	322	QQGQTVTKK	242
243	323	QGQTVTKKS	243
244	324	GQTVTKKSA	244
245	325	QTVTKKSAA	245
246	326	TVTKKSAAE	246
247	327	VTKKSAAEA	247
248	328	TKKSAAEAS	248
249	329	KKSAAEASK	249
250	330	KSAAEASKK	250
251	331	SAAEASKKP	251
252	332	AAEASKKPR	252
253	333	AEASKKPRQ	253
254	334	EASKKPRQK	254
255	335	ASKKPRQKR	255
256	336	SKKPRQKRT	256
257	337	KKPRQKRTA	257

FIG. 6G

258	338	KPRQKRTAT	258
259	339	PRQKRTATK	259
260	340	RQKRTATKQ	260
261	341	QKRTATKQY	261
262	342	KRTATKQYN	262
263	343	RTATKQYNV	263
264	344	TATKQYNVT	264
265	345	ATKQYNVTQ	265
266	346	TKQYNVTQA	266
267	347	KQYNVTQAF	267
268	348	QYNVTQAFG	268
269	349	YNVTQAFGR	269
270	350	NVTQAFGRR	270
271	351	VTQAFGRRG	271
272	352	TQAFGRRGP	272
273	353	QAFGRRGPE	273
274	354	AFGRRGPEQ	274
275	355	FGRRGPEQT	275
276	356	GRRGPEQTQ	276
277	357	RRGPEQTQG	277
278	358	RGPEQTQGN	278
279	359	GPEQTQGNF	279
280	360	PEQTQGNFG	280
281	361	EQTQGNFGD	281
282	362	QTQGNFGDQ	282
283	363	TQGNFGDQD	283
284	364	QGNFGDQDL	284
285	365	GNFGDQDLI	285
286	366	NFGDQDLIR	286
287	367	FGDQDLIRQ	287
288	368	GDQDLIRQG	288
289	369	DQDLIRQGT	289
290	370	QDLIRQGTD	290
291	371	DLIRQGTDY	291
292	372	LIRQGTDYK	292
293	373	IRQGTDYKH	293
294	374	RQGTDYKHW	294

FIG. 6H

295	375	QGTDYKHWP	295
296	376	GTDYKHWPQ	296
297	377	TDYKHWPQI	297
298	378	DYKHWPQIA	298
299	379	YKHWPQIAQ	299
300	380	KHWPQIAQF	300
301	381	HWPQIAQFA	301
302	382	WPQIAQFAP	302
303	383	PQIAQFAPS	303
304	384	QIAQFAPSA	304
305	385	IAQFAPSAS	305
306	386	AQFAPSASA	306
307	387	QFAPSASAF	307
308	388	FAPSASAFF	308
309	389	APSASAFFG	309
310	390	PSASAFFGM	310
311	391	SASAFFGMS	311
312	392	ASAFFGMSR	312
313	393	SAFFGMSRI	313
314	394	AFFGMSRIG	314
315	395	FFGMSRIGM	315
316	396	FGMSRIGME	316
317	397	GMSRIGMEV	317
318	398	MSRIGMEVT	318
319	399	SRIGMEVTP	319
320	400	RIGMEVTPS	320
321	401	IGMEVTPSG	321
322	402	GMEVTPSGT	322
323	403	MEVTPSGTW	323
324	404	EVTPSGTWL	324
325	405	VTPSGTWLT	325
326	406	TPSGTWLTY	326
327	407	PSGTWLTYH	327
328	408	SGTWLTYHG	328
329	409	GTWLTYHGA	329
330	410	TWLTYHGAI	330
331	411	WLTYHGAIK	331

FIG. 6I

332	412	LTYHGAIKL	332
333	413	TYHGAIKLD	333
334	414	YHGAIKLDD	334
335	415	HGAIKLDDK	335
336	416	GAIKLDDKD	336
337	417	AIKLDDKDP	337
338	418	IKLDDKDPQ	338
339	419	KLDDKDPQF	339
340	420	LDDKDPQFK	340
341	421	DDKDPQFKD	341
342	422	DKDPQFKDN	342
343	423	KDPQFKDNV	343
344	424	DPQFKDNVI	344
345	425	PQFKDNVIL	345
346	426	QFKDNVILL	346
347	427	FKDNVILLN	347
348	428	KDNVILLNK	348
349	429	DNVILLNKH	349
350	430	NVILLNKHI	350
351	431	VILLNKHID	351
352	432	ILLNKHIDA	352
353	433	LLNKHIDAY	353
354	434	LNKHIDAYK	354
355	435	NKHIDAYKT	355
356	436	KHIDAYKTF	356
357	437	HIDAYKTFP	357
358	438	IDAYKTFPP	358
359	439	DAYKTFPPT	359
360	440	AYKTFPPTE	360
361	441	YKTFPPTEP	361
362	442	KTFPPTEPK	362
363	443	TFPPTEPKK	363
364	444	FPPTEPKKD	364
365	445	PPTEPKKDK	365
366	446	PTEPKKDKK	366
367	447	TEPKKDKKK	367
368	448	EPKKDKKKK	368

FIG. 6J

369	449	PKKDKKKKT	369
370	450	KKDKKKKTD	370
371	451	KDKKKKTDE	371
372	452	DKKKKTDEA	372
373	453	KKKKTDEAQ	373
374	454	KKKTDEAQP	374
375	455	KKTDEAQPL	375
376	456	KTDEAQPLP	376
377	457	TDEAQPLPQ	377
378	458	DEAQPLPQR	378
379	459	EAQPLPQRQ	379
380	460	AQPLPQRQK	380
381	461	QPLPQRQKK	381
382	462	PLPQRQKKQ	382
383	463	LPQRQKKQP	383
384	464	PQRQKKQPT	384
385	465	QRQKKQPTV	385
386	466	RQKKQPTVT	386
387	467	QKKQPTVTL	387
388	468	KKQPTVTLL	388
389	469	KQPTVTLLP	389
390	470	QPTVTLLPA	390
391	471	PTVTLLPAA	391
392	472	TVTLLPAAD	392
393	473	VTLLPAADM	393
394	474	TLLPAADMD	394
395	475	LLPAADMDD	395
396	476	LPAADMDDF	396
397	477	PAADMDDFS	397
398	478	AADMDDFSR	398
399	479	ADMDDFSRQ	399
400	480	DMDDFSRQL	400
401	481	MDDFSRQLQ	401
402	482	DDFSRQLQN	402
403	483	DFSRQLQNS	403
404	484	FSRQLQNSM	404
405	485	SRQLQNSMS	405

FIG. 6K

406	486	RQLQNSMSG	406
407	487	QLQNSMSGA	407
408	488	LQNSMSGAS	408
409	489	QNSMSGASA	409
410	490	NSMSGASAD	410
411	491	SMSGASADS	411
412	492	MSGASADST	412
413	493	SGASADSTQ	413
414	494	GASADSTQA	414

FIG. 6L

SARS-CoV N protein DNA sequence (SEQ ID NO: 495; Genbank Accession No. NC_004718; nucleotides 28120-29388)

atgtctgataatggaccccaatcaaaccaacgtagtgccccccgcattacatttggtggaccca
cagattcaactgacaataaccagaatggaggacgcaatggggcaaggccaaaacagcgccgacc
ccaaggtttacccaataatactgcgtcttggttcacagctctcactcagcatggcaaggaggaa
cttagattccctcgaggccagggcgttccaatcaacaccaatagtggtccagatgaccaaattg
gctactaccgaagagctacccgacgagttcgtggtggtgacggcaaaatgaaagagctcagccc
cagatggtacttctattacctaggaactggcccagaagcttcacttccctacggcgctaacaaa
gaaggcatcgtatgggttgcaactgagggagccttgaatacacccaaagaccacattggcaccc
gcaatcctaataacaatgctgccaccgtgctacaacttcctcaaggaacaacattgccaaaagg
cttctacgcagagggaagcagaggcggcagtcaagcctcttctcgctcctcatcacgtagtcgc
ggtaattcaagaaattcaactcctggcagcagtaggggaaattctcctgctcgaatggctagcg
gaggtggtgaaactgccctcgcgctattgctgctagacagattgaaccagcttgagagcaaagt
ttctggtaaaggccaacaacaacaaggccaaactgtcactaagaaatctgctgctgaggcatct
aaaaagcctcgccaaaaacgtactgccacaaaacagtacaacgtcactcaagcatttgggagac
gtggtccagaacaaacccaaggaaatttcggggaccaagacctaatcagacaaggaactgatta
caaacattggccgcaaattgcacaatttgctccaagtgcctctgcattctttggaatgtcacgc
attggcatggaagtcacaccttcgggaacatggctgacttatcatggagccattaaattggatg
acaaagatccacaattcaaagacaacgtcatactgctgaacaagcacattgacgcatacaaaac
attcccaccaacagagcctaaaaaggacaaaaagaaaaagactgatgaagctcagcctttgccg
cagagacaaaagaagcagcccactgtgactcttcttcctgcggctgacatggatgatttctcca
gacaacttcaaaattccatgagtggagcttctgctgattcaactcaggcataa

SARS-CoV N protein amino acid sequence (SEQ ID NO: 496; Genbank Accession No. NC_004718; translation of coding sequence defined by nucleotides 28120-29388)

MSDNGPQSNQRSAPRITFGGPTDSTDNNQNGGRNGARPKQRRPQGLPNNTASWFTALTQHGKEE
LRFPRGQGVPINTNSGPDDQIGYYRRATRRVRGGDGKMKELSPRWYFYYLGTGPEASLPYGANK
EGIVWVATEGALNTPKDHIGTRNPNNNAATVLQLPQGTTLPKGFYAEGSRGGSQASSRSSSRSR
GNSRNSTPGSSRGNSPARMASGGGETALALLLLDRLNQLESKVSGKGQQQQGQTVTKKSAAEAS
KKPRQKRTATKQYNVTQAFGRRGPEQTQGNFGDQDLIRQGTDYKHWPQIAQFAPSASAFFGMSR
IGMEVTPSGTWLTYHGAIKLDDKDPQFKDNVILLNKHIDAYKTFPPTEPKKDKKKKTDEAQPLP
QRQKKQPTVTLLPAADMDDFSRQLQNSMSGASADSTQA

FIG. 7

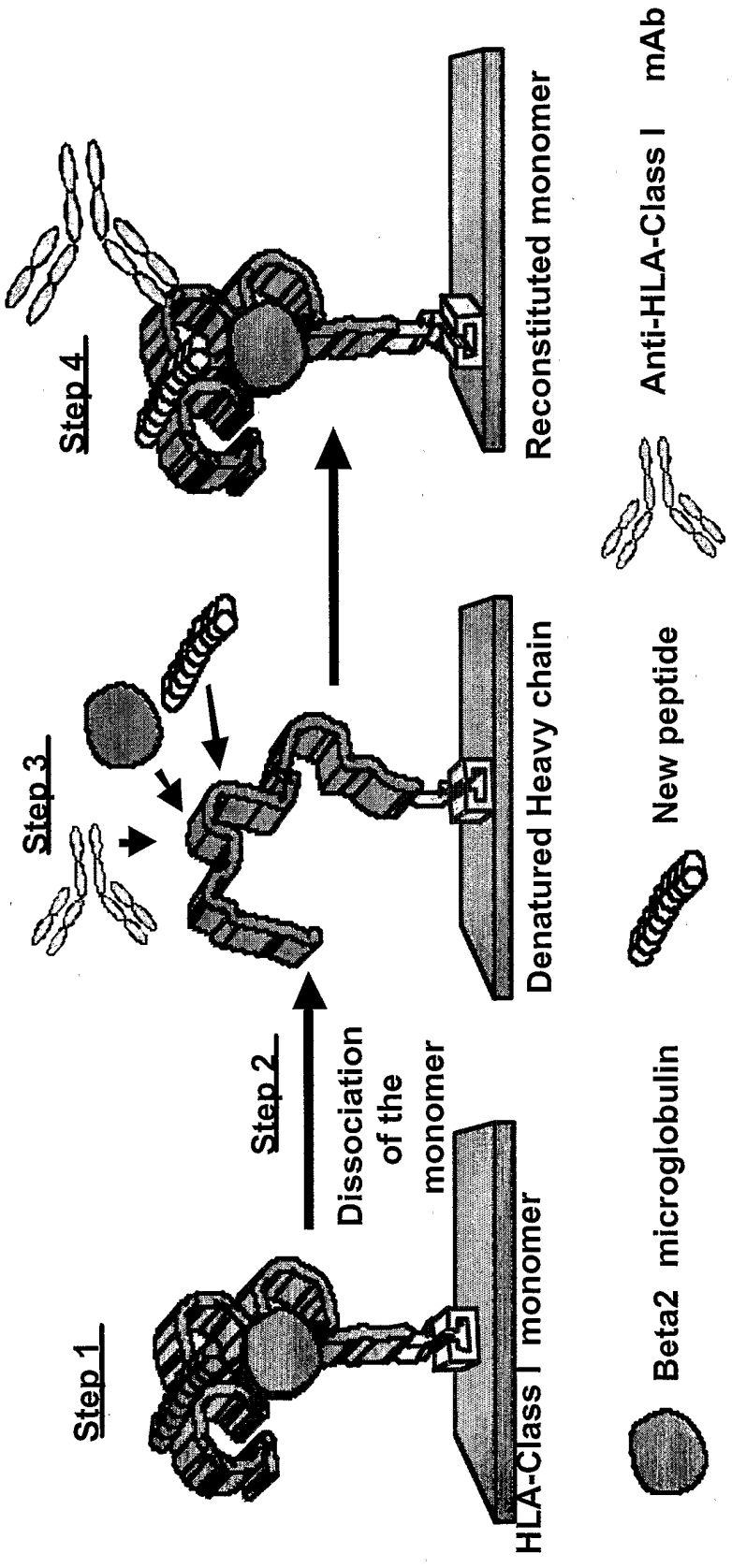

Step 1
HLA-Class I monomer
Step 2
Dissociation of the monomer
Step 3
Denatured Heavy chain
Step 4
Reconstituted monomer
Beta2 microglobulin
New peptide
Anti-HLA-Class I mAb

FIG. 8

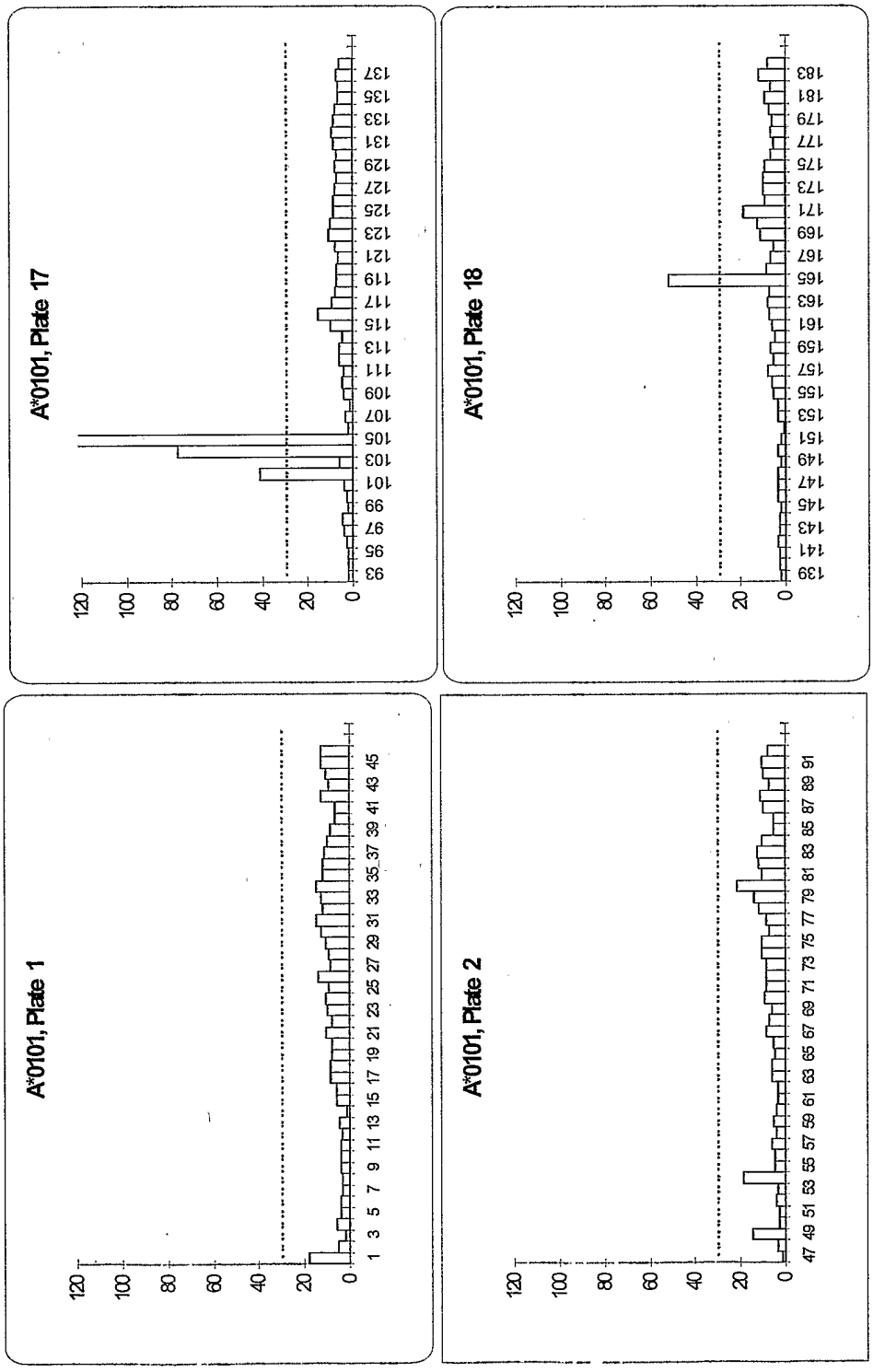


FIG. 9

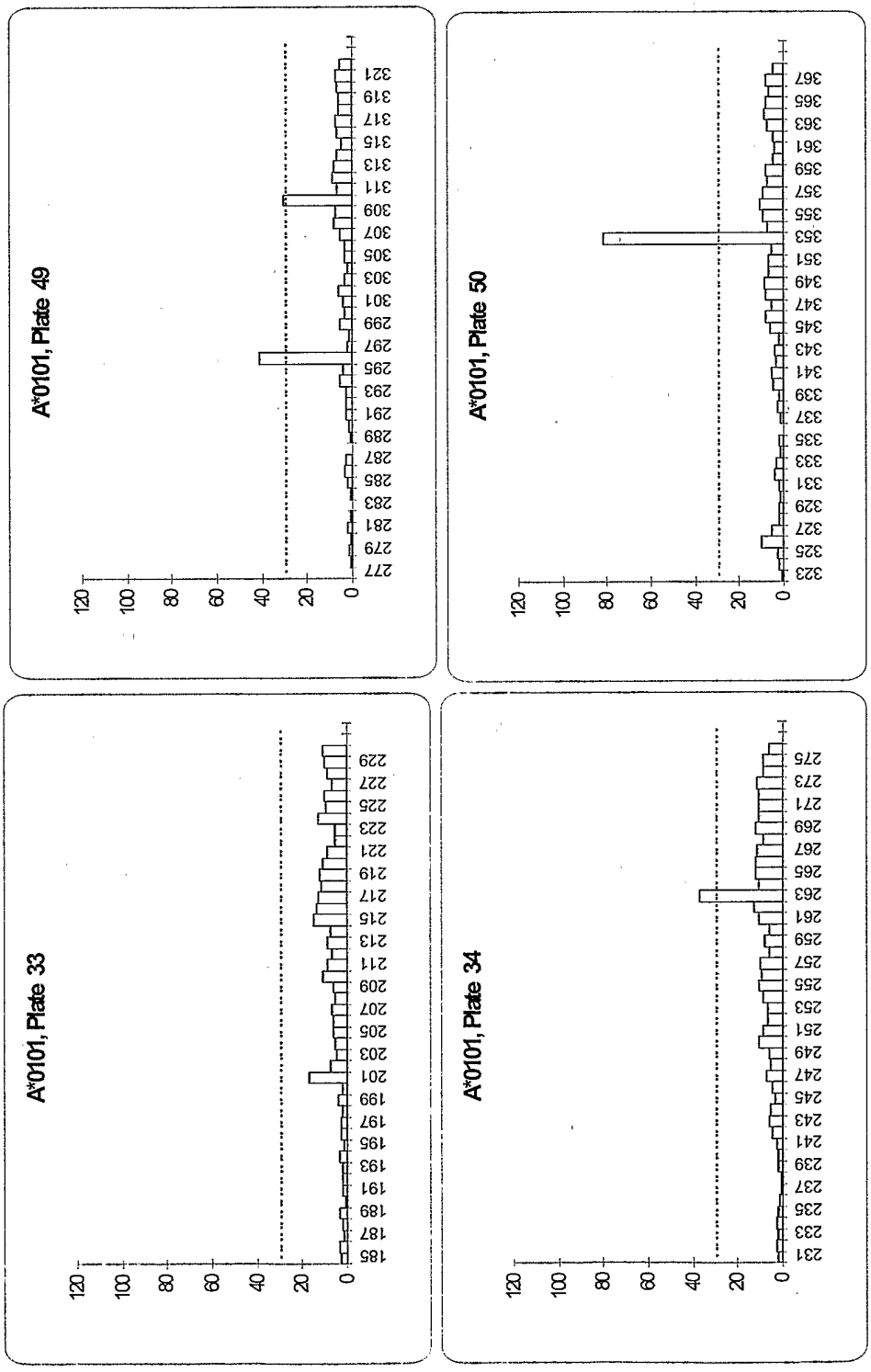


FIG. 10

Peptide ID	% Binding
102	40.9
104	77.9
105	122.2
165	52.2
263	37.4
296	41
310	30.5
353	81.3

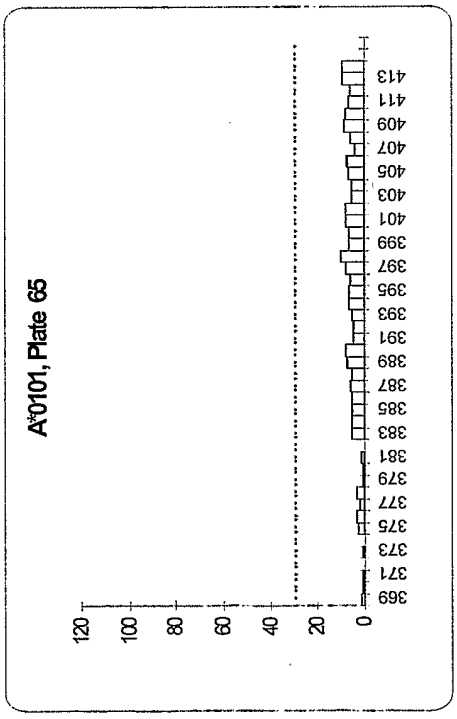


FIG. 11

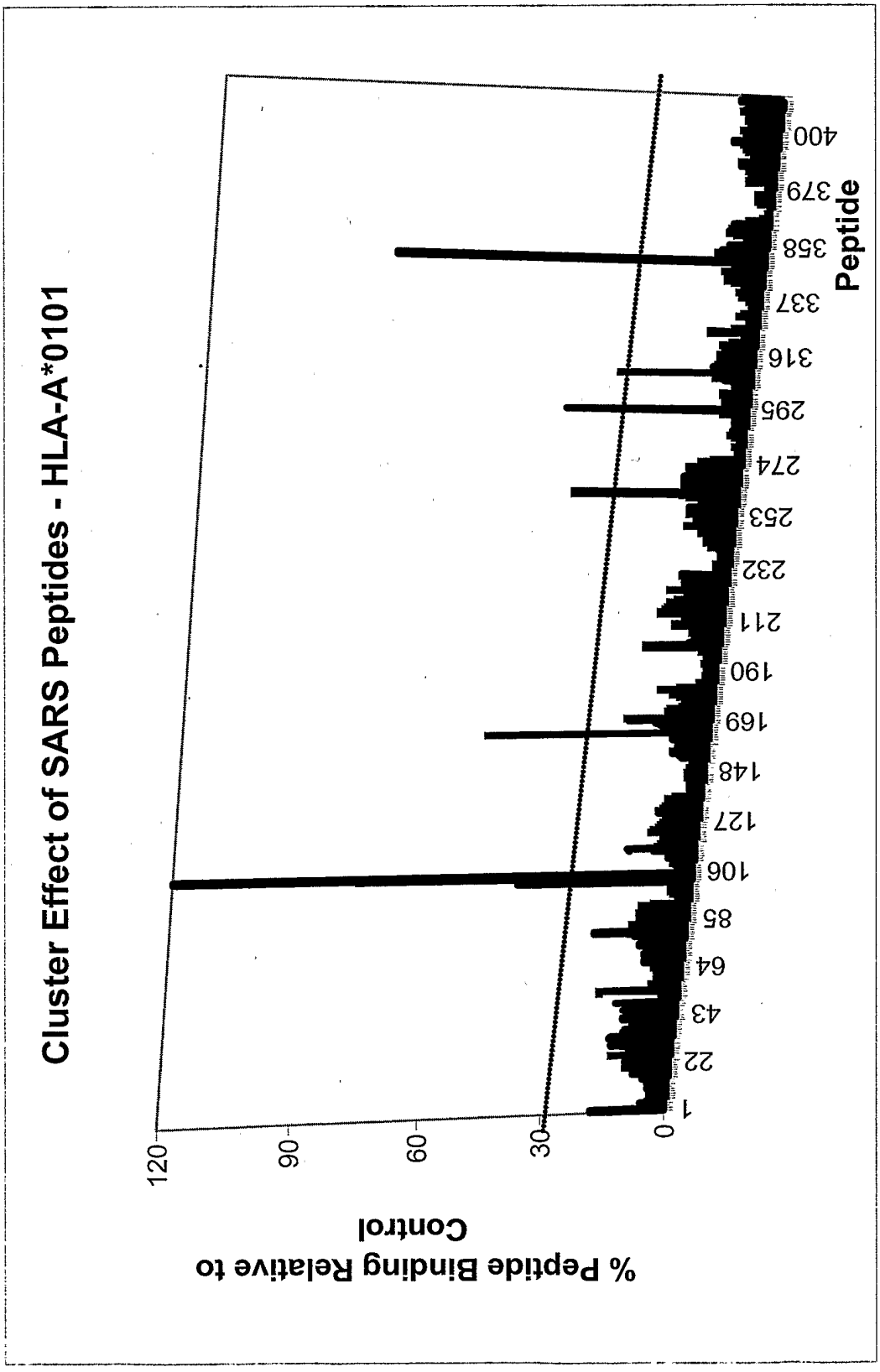
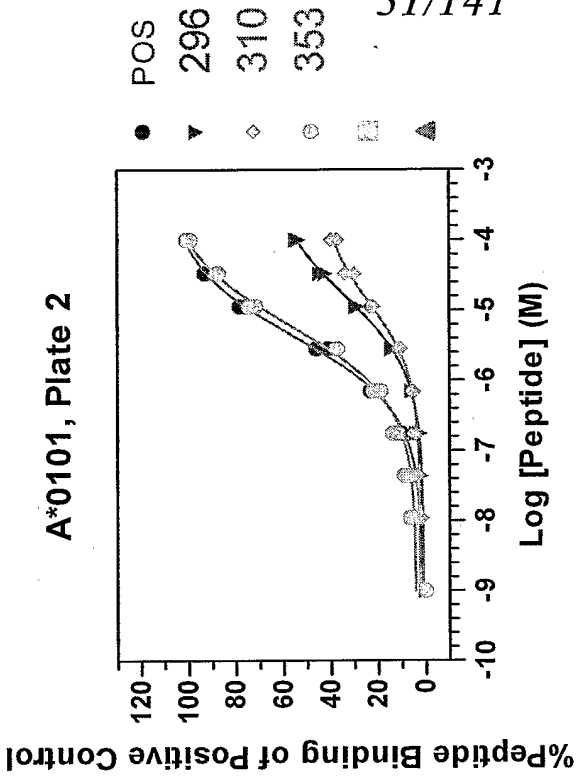
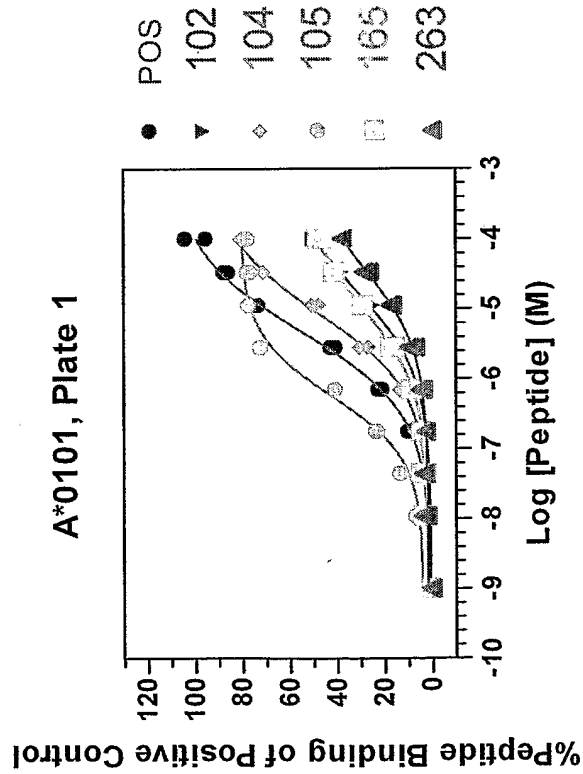

Cluster Effect of SARS Peptides - HLA-A*0101
% Peptide Binding Relative to Control
120
90
60
30
0
1
22
43
64
85
106
127
148
169
190
211
232
253
274
295
316
337
358
379
400
Peptide

FIG. 12



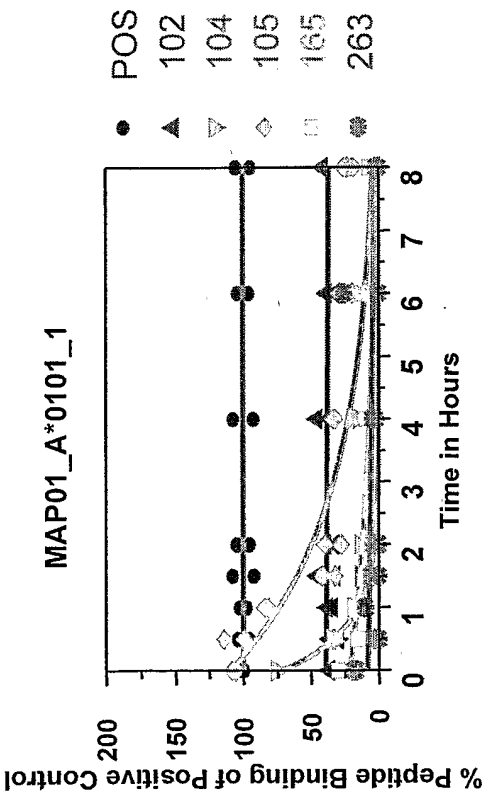
Peptide ID	Affinity ED50 x 10-6M
296	15.80
310	12.70
353	6.14



Peptide ID	Affinity ED50 x 10-6M
102	18.40
104	8.39
105	0.56
165	9.56
263	35.90

FIG. 13

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
102	4.52	38.6
104	0.41	73.4
105	1.27	106.7
165	1.62	29.6
263	2.57	17.6



Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
296	0.25	25.9
310	3.17	19.2
353	0.61	84.4

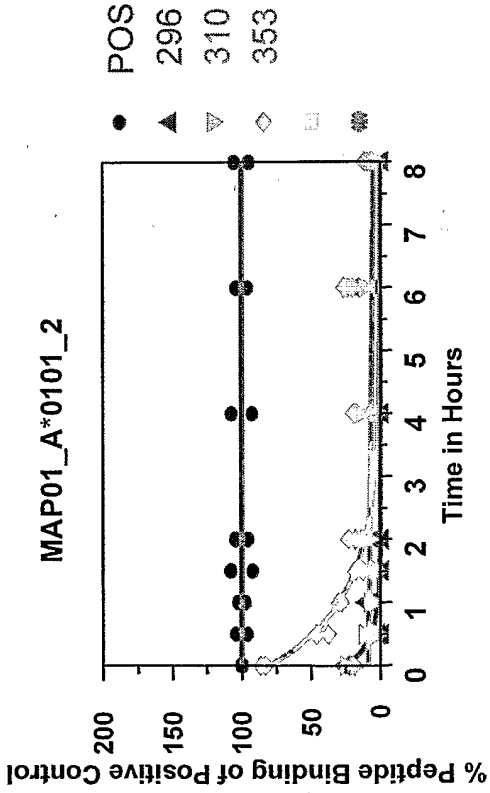


FIG. 14

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
A*0101	105	LSPRWYFYY	122.2	0.56	1.3	106.7	0.466	1	31	10
A*0101	102	MKELSPRWY	40.9	18.40	4.5	38.6	0.211	2	12	2
A*0101	353	LLNKHIDAY	81.3	6.14	0.6	84.4	0.176	3	67	20
A*0101	104	ELSPRWYFY	77.9	8.39	0.4	73.4	0.122	4	4	9
A*0101	165	GTTLPKGFY	52.2	9.56	1.6	29.6	0.115	5	14	3
A*0101	296	GTDYKHWPQ	41.0	15.80	0.2	25.9	0.037	6	16	19
A*0101	310	PSASAFFGM	30.5	12.70	3.2	**19.2**	0.000	7	162	97
A*0101	263	RTATKQYNV	37.4	35.90	2.6	**17.6**	0.000	8	61	114

FIG. 15

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
A*0101	105	LSPRWYFYY	122.2	0.56	1.3	106.7	0.466	1	31	10
A*0101	**102**	**MKELSPRWY**	**40.9**	**18.40**	**4.5**	**38.6**	**0.211**	**2**	**12**	**2**
A*0101	353	LLNKHIDAY	81.3	6.14	0.6	84.4	0.176	3	67	20
A*0101	**104**	**ELSPRWYFY**	**77.9**	**8.39**	**0.4**	**73.4**	**0.122**	**4**	**4**	**9**
A*0101	**165**	**GTTLPKGFY**	**52.2**	**9.56**	**1.6**	**29.6**	**0.115**	**5**	**14**	**3**
A*0101	296	GTDYKHWPQ	41.0	15.80	0.2	25.9	0.037	6	16	19
A*0101	310	PSASAFFGM	30.5	12.70	3.2	19.2	0.000	7	162	97
A*0101	263	RTATKQYNV	37.4	35.90	2.6	17.6	0.000	8	61	114

FIG. 16

Allele	Peptide ID	Peptide Sequence
A*0101	105	LSPRWYFYY
A*0101	102	MKELSPRWY
A*0101	353	LLNKHIDAY
A*0101	104	ELSPRWYFY
A*0101	165	GTTLPKGFY
A*0101	296	GTDYKHWPQ

FIG. 17

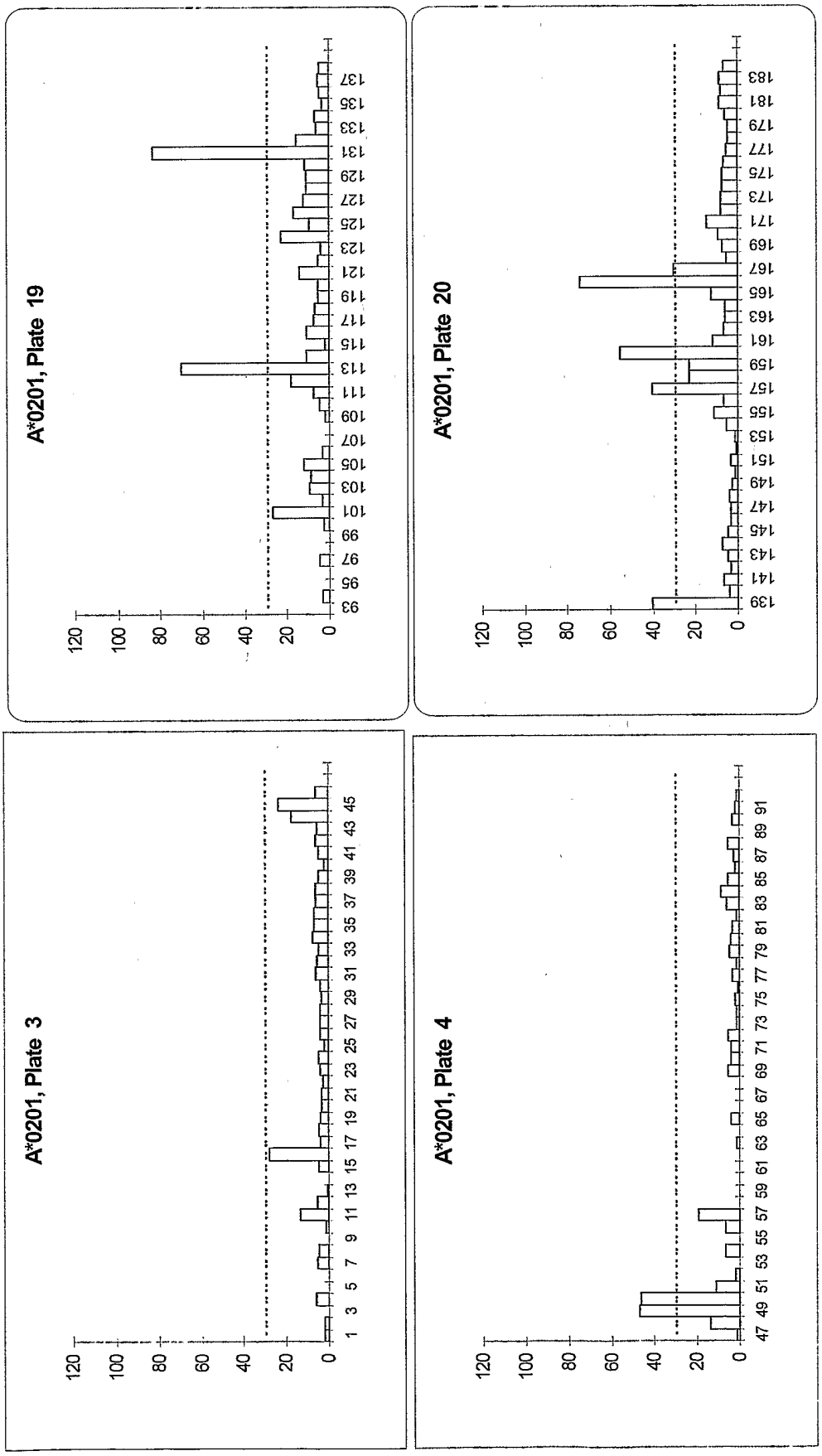


FIG. 18

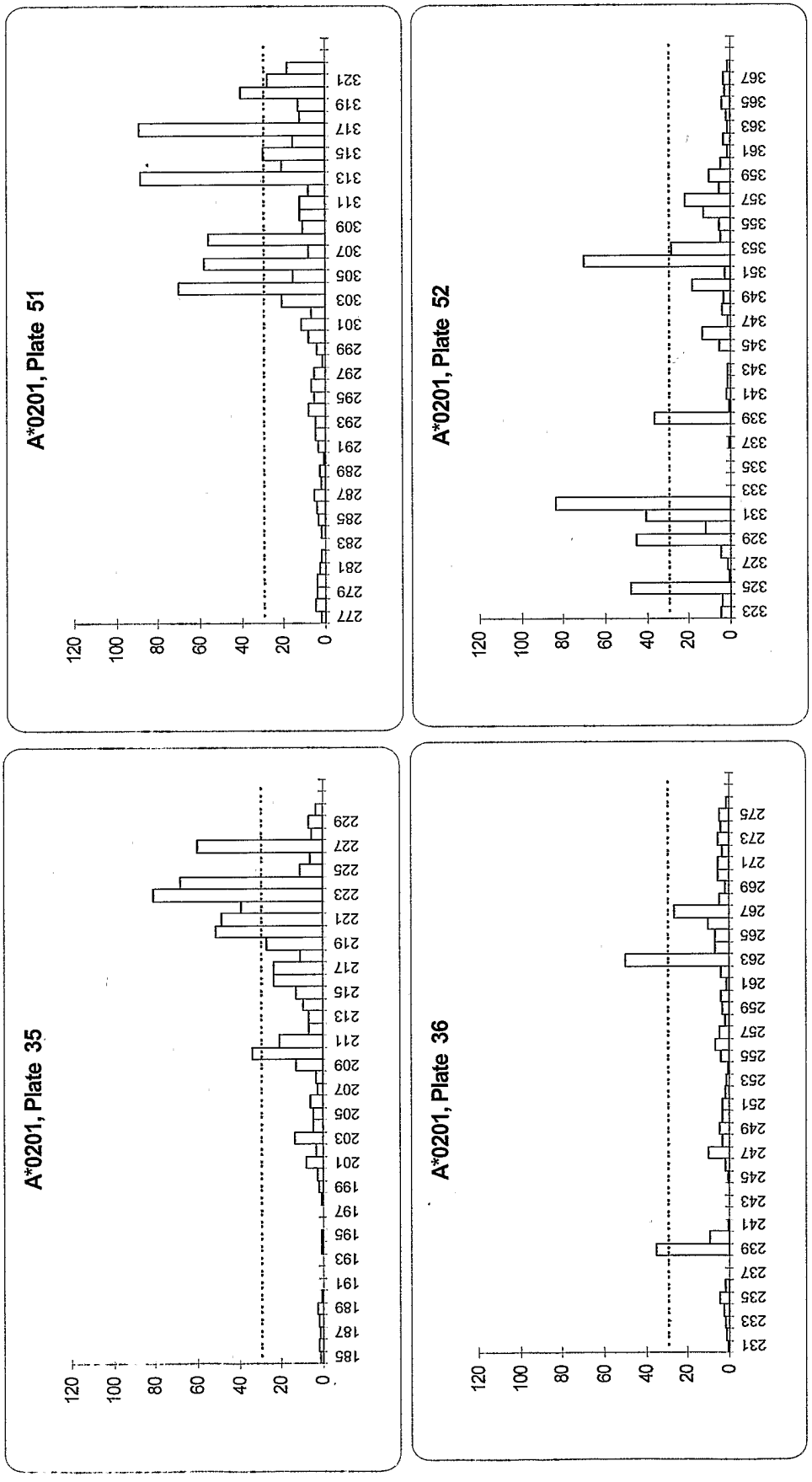


FIG. 19

Peptide ID	% Binding
49	46.8
50	46.2
113	69.8
131	83.8
139	40.6
157	40.6
160	55.2
166	73.9
167	30.2
210	33.8
220	51.1
221	48.8
222	39.3
223	81.1
224	68.0
227	60.3

Peptide ID	% Binding
239	35.1
263	49.6
304	70.4
306	58.3
308	55.6
313	88.3
317	88.8
320	40.7
325	47.9
329	45.0
331	40.2
332	83.5
339	36.6
352	70.2
407	76.3

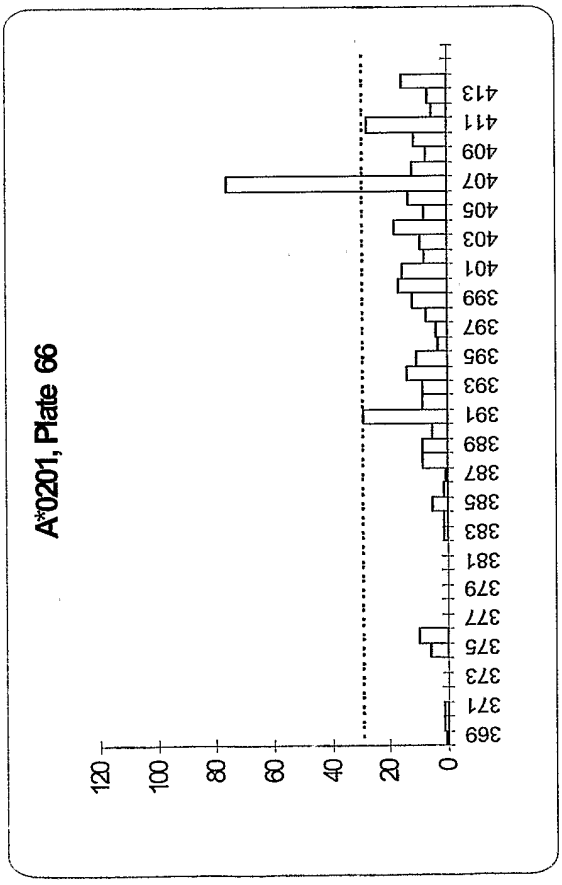


FIG. 20

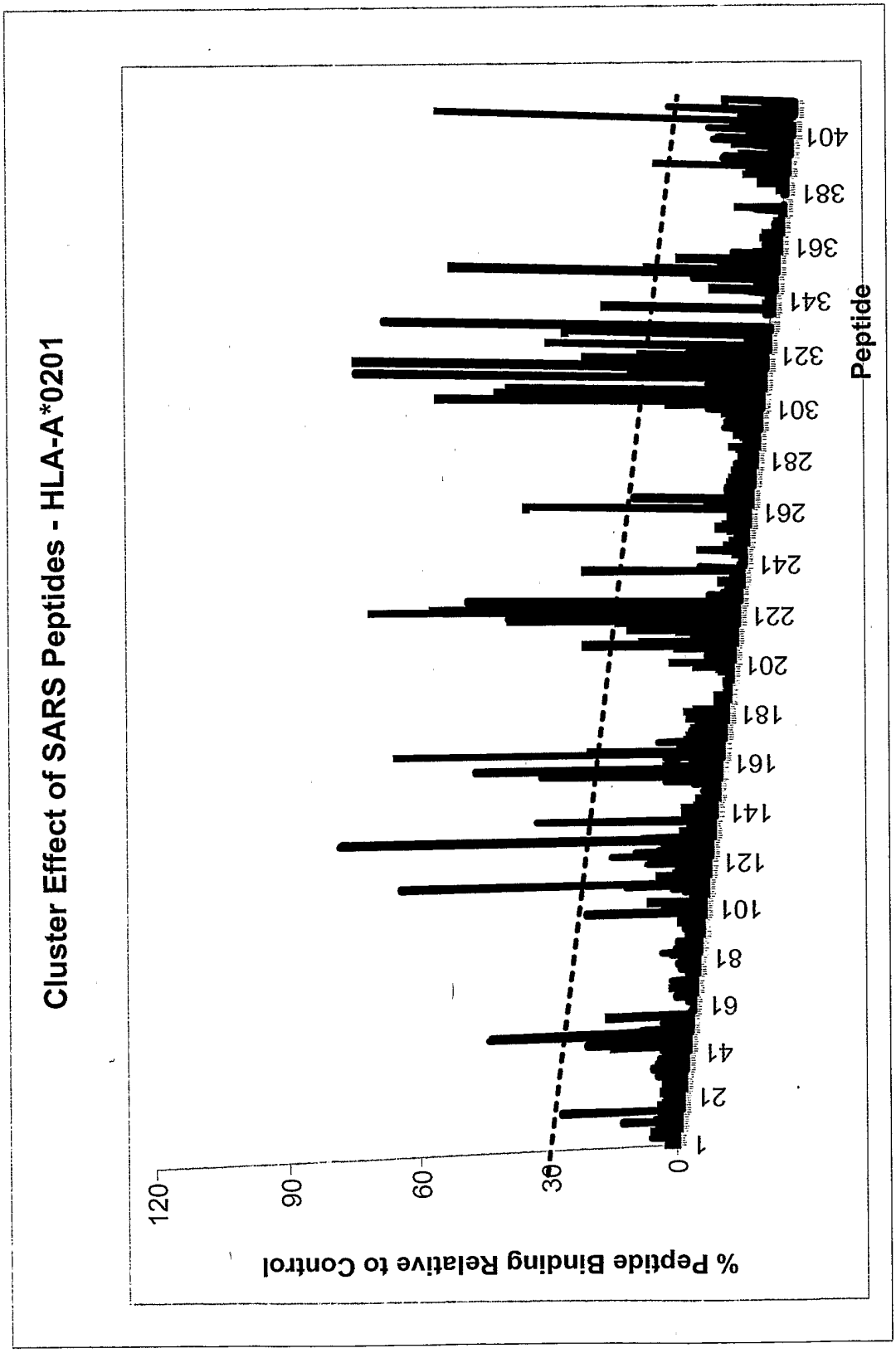
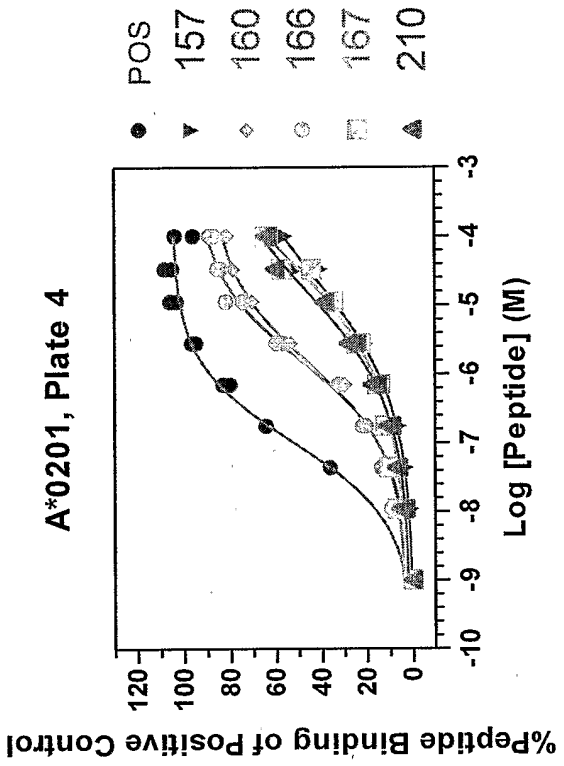
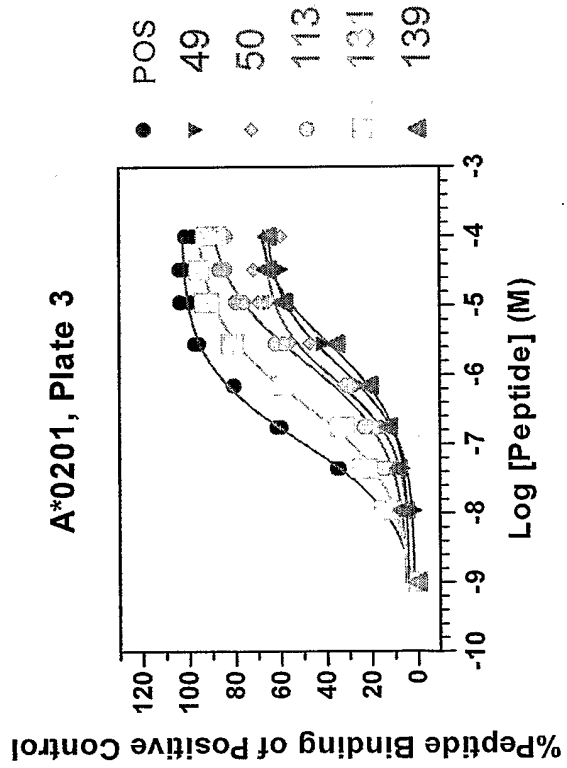

Cluster Effect of SARS Peptides - HLA-A*0201
% Peptide Binding Relative to Control
0
30
60
90
120
1
21
41
61
81
101
121
141
161
181
201
221
241
261
281
301
321
341
361
381
401
Peptide

FIG. 21

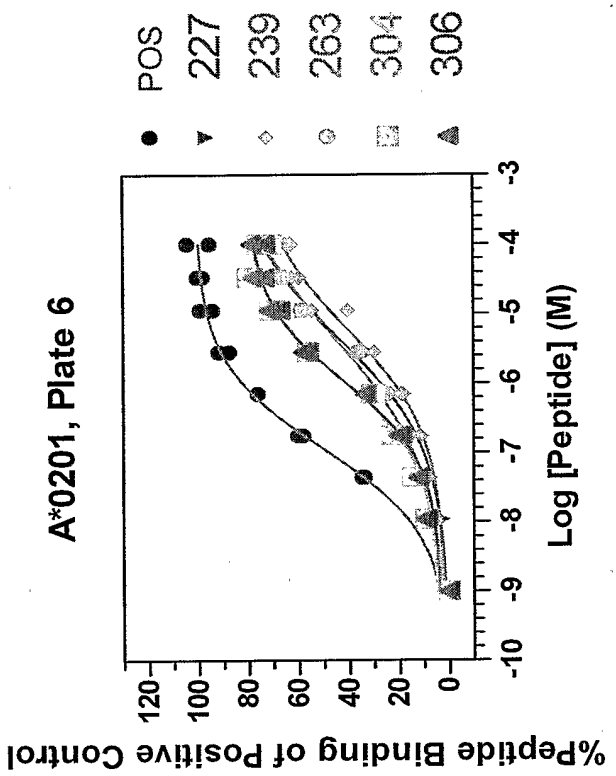


Peptide ID	Affinity ED50 x 10-6M
157	23.90
160	1.41
166	1.57
167	98.60
210	15.80

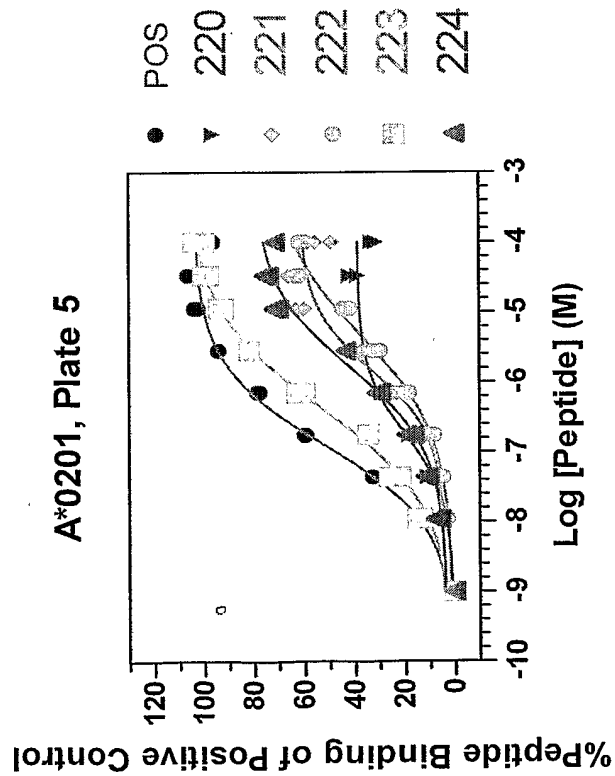


Peptide ID	Affinity ED50 x 10-6M
49	1.31
50	0.81
113	1.49
131	0.38
139	2.56

FIG. 22

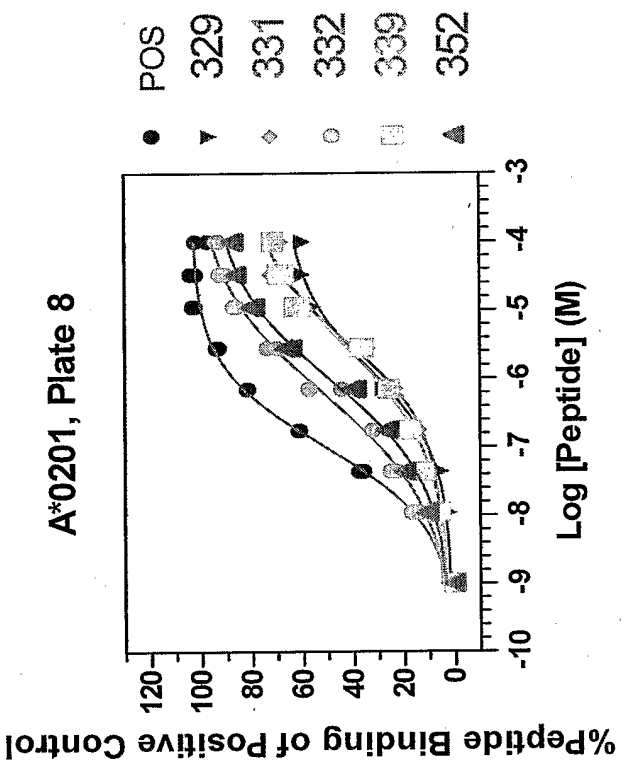


Peptide ID	Affinity ED50 x 10-6M
227	4.36
239	5.65
263	4.96
304	1.13
306	1.04

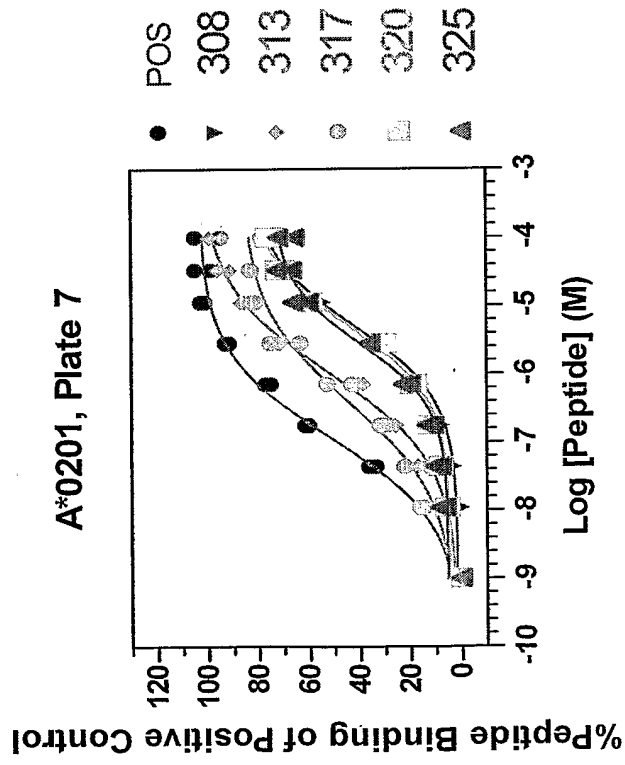


Peptide ID	Affinity ED50 x 10-6M
220	0.18
221	1.45
222	4.47
223	0.44
224	1.59

FIG. 23

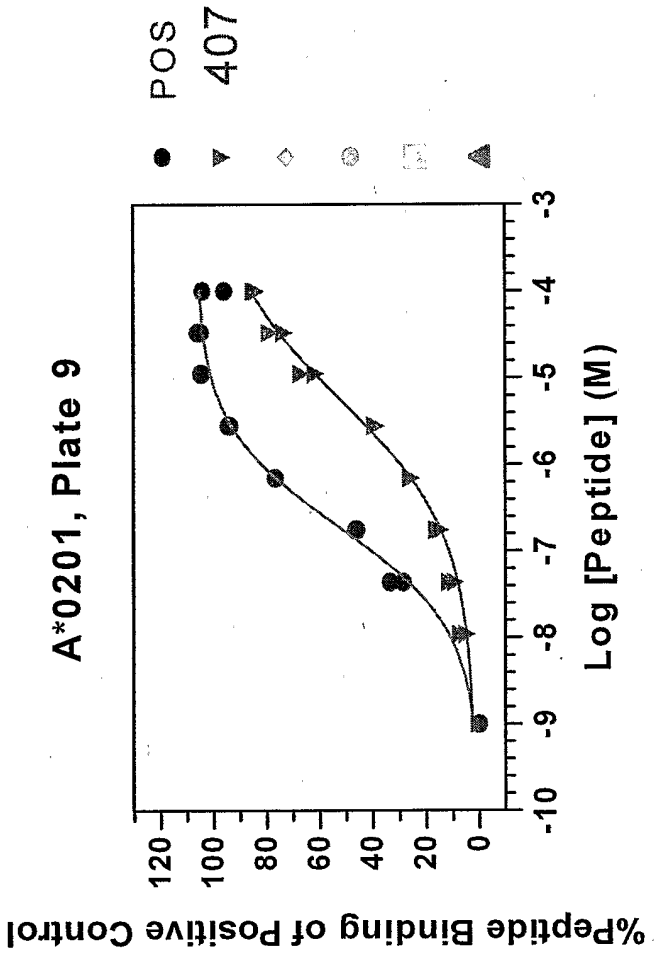


Peptide ID	Affinity ED50 x 10-6M
329	1.45
331	3.45
332	0.59
339	3.29
352	0.96



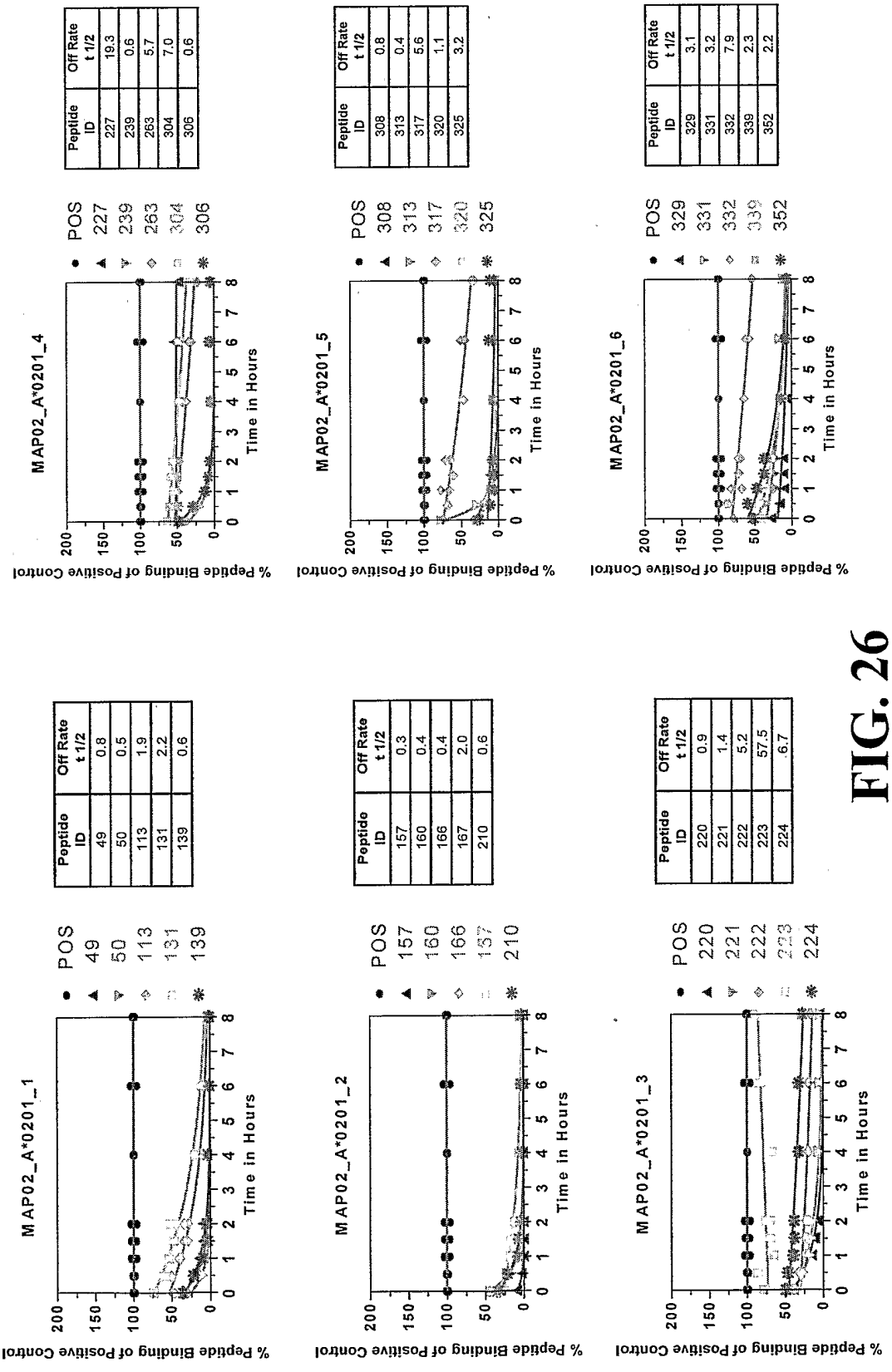
Peptide ID	Affinity ED50 x 10-6M
308	5.04
313	1.03
317	0.38
320	4.98
325	2.72

FIG. 24



Peptide ID	Affinity ED50 x 10-6M
407	5.64

FIG. 25



Peptide ID	Off Rate t 1/2
49	0.8
50	0.5
113	1.9
131	2.2
139	0.6

Peptide ID	Off Rate t 1/2
157	0.3
160	0.4
166	0.4
167	2.0
210	0.6

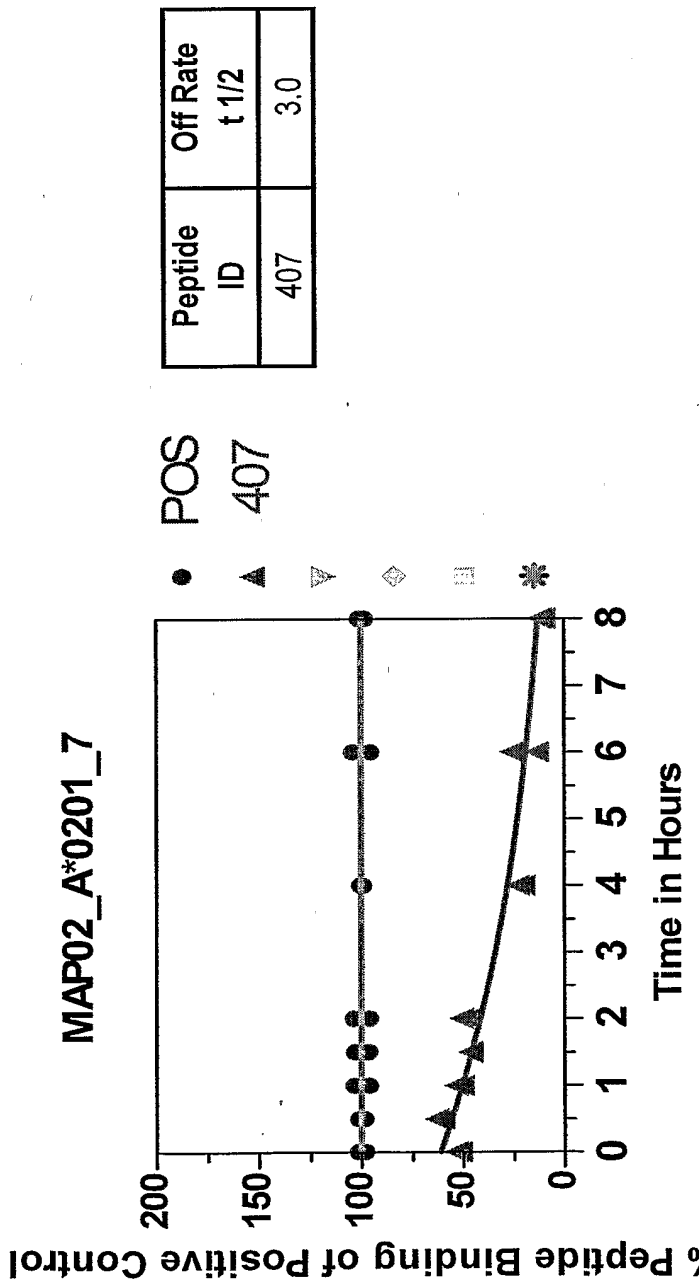
Peptide ID	Off Rate t 1/2
220	0.9
221	1.4
222	5.2
223	57.5
224	6.7

Peptide ID	Off Rate t 1/2
227	19.3
239	0.6
263	5.7
304	7.0
306	0.6

Peptide ID	Off Rate t 1/2
308	0.8
313	0.4
317	5.6
320	1.1
325	3.2

Peptide ID	Off Rate t 1/2
329	3.1
331	3.2
332	7.9
339	2.3
352	2.2

FIG. 26



Peptide ID	Off Rate t 1/2
407	3.0

FIG. 27

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
A*0201	223	LLLDRLNQL	81.1	0.44	57.5	78.9	2.57
A*0201	332	LTYHGAIKL	83.5	0.59	7.9	80.0	0.91
A*0201	317	GMSRIGMEV	88.8	0.38	5.6	74.5	0.79
A*0201	227	RLNQLESKV	60.3	4.36	19.3	48.2	0.67
A*0201	304	QIAQFAPSA	70.4	1.13	7.0	63.8	0.64
A*0201	131	IVWVATEGA	83.8	0.38	2.2	73.7	0.48
A*0201	224	LLDRLNQLE	68.0	1.59	6.7	49.3	0.48
A*0201	263	RTATKQYNV	49.6	4.96	5.7	48.7	0.36
A*0201	352	ILLNKHIDA	70.2	0.96	2.2	52.5	0.31
A*0201	222	LLLLDRLNQ	39.3	4.47	5.2	38.1	0.29
A*0201	407	QLQNSMSGA	76.3	5.64	3.0	52.5	0.27
A*0201	113	YLGTGPEAS	69.8	1.49	1.9	47.9	0.25
A*0201	331	WLTYHGAIK	40.2	3.45	3.2	39.9	0.24
A*0201	339	KLDDKDPQF	36.6	3.29	2.3	41.0	0.22
A*0201	220	LALLLLDRL	51.1	0.18	0.9	39.4	0.21
A*0201	329	GTWLTYHGA	45.0	1.45	3.1	27.9	0.21
A*0201	325	VTPSGTWLT	47.9	2.72	3.2	27.2	0.19
A*0201	221	ALLLLDRLN	48.8	1.45	1.4	34.9	0.17
A*0201	313	SAFFGMSRI	88.3	1.03	0.4	74.4	0.17
A*0201	306	AQFAPSASA	58.3	1.04	0.6	48.2	0.15
A*0201	49	NTASWFTAL	46.8	1.31	0.8	36.0	0.13
A*0201	160	LQLPQGTTL	55.2	1.41	0.4	44.1	0.12
A*0201	166	TTLPKGFYA	73.9	1.57	0.4	45.1	0.11
A*0201	320	RIGMEVTPS	40.7	4.98	1.1	29.3	0.11
A*0201	308	FAPSASAFF	55.6	5.04	0.8	34.7	0.10
A*0201	139	ALNTPKDHI	40.6	2.56	0.6	35.6	0.10
A*0201	239	GQQQQGQTV	35.1	5.65	0.6	35.4	0.09
A*0201	50	TASWFTALT	46.2	0.81	0.5	27.1	0.09
A*0201	167	TLPKGFYAE	30.2	98.60	2.0	26.2	0.08
A*0201	210	RMASGGGET	33.8	15.80	0.6	33.3	0.07
A*0201	**157**	**ATVLQLPQG**	**40.6**	**23.90**	**0.3**	**9.2**	0.00

FIG. 28

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t1/2 (hrs)	Off Rate T0 % Peptide Binding	iScore	iScore RANK	BIMAS RANK	SYFPEITHI RANK
A*0201	**223**	**LLLDRLNQL**	**81.1**	**0.44**	**57.5**	**78.9**	**2.57**	**1**	**1**	**1**
A*0201	332	LTYHGAIKL	83.5	0.59	7.9	80.0	0.91	2	16	7
A*0201	**317**	**GMSRIGMEV**	**88.8**	**0.38**	**5.6**	**74.5**	**0.79**	**3**	**3**	**6**
A*0201	**227**	**RLNQLESKV**	**60.3**	**4.36**	**19.3**	**48.2**	**0.67**	**4**	**2**	**2**
A*0201	304	QIAQFAPSA	70.4	1.13	7.0	63.8	0.64	5	11	18
A*0201	131	IVWVATEGA	83.8	0.38	2.2	73.7	0.48	6	10	42
A*0201	224	LLDRLNQLE	68.0	1.59	6.7	49.3	0.48	7	116	61
A*0201	263	RTATKQYNV	49.6	4.96	5.7	48.7	0.36	8	20	17
A*0201	352	ILLNKHIDA	70.2	0.96	2.2	52.5	0.31	9	4	10
A*0201	222	LLLLDRLNQ	39.3	4.47	5.2	38.1	0.29	10	58	36
A*0201	407	QLQNSMSGA	76.3	5.64	3.0	52.5	0.27	11	6	38
A*0201	113	YLGTGPEAS	69.8	1.49	1.9	47.9	0.25	12	48	31
A*0201	331	WLTYHGAIK	40.2	3.45	3.2	39.9	0.24	13	88	106
A*0201	339	KLDDKDPQF	36.6	3.29	2.3	41.0	0.22	14	36	48
A*0201	**220**	**LALLLLDRL**	**51.1**	**0.18**	**0.9**	**39.4**	**0.21**	**15**	**13**	**3**
A*0201	329	GTWLTYHGA	45.0	1.45	3.1	27.9	0.21	16	23	78
A*0201	325	VTPSGTWLT	47.9	2.72	3.2	27.2	0.19	17	18	64
A*0201	221	ALLLLDRLN	48.8	1.45	1.4	34.9	0.17	18	70	35
A*0201	**313**	**SAFFGMSRI**	**88.3**	**1.03**	**0.4**	**74.4**	**0.17**	**19**	**19**	**28**
A*0201	306	AQFAPSASA	58.3	1.04	0.6	48.2	0.15	20	14	75
A*0201	49	NTASWFTAL	46.8	1.31	0.8	36.0	0.13	21	31	21
A*0201	160	LQLPQGTTL	55.2	1.41	0.4	44.1	0.12	22	5	14
A*0201	166	TTLPKGFYA	73.9	1.57	0.4	45.1	0.11	23	7	60
A*0201	320	RIGMEVTPS	40.7	4.98	1.1	29.3	0.11	24	95	76
A*0201	308	FAPSASAFF	55.6	5.04	0.8	34.7	0.10	25	92	174
A*0201	139	ALNTPKDHI	40.6	2.56	0.6	35.6	0.10	26	9	4
A*0201	239	GQQQQGQTV	35.1	5.65	0.6	35.4	0.09	27	8	62
A*0201	50	TASWFTALT	46.2	0.81	0.5	27.1	0.09	28	39	55
A*0201	167	TLPKGFYAE	30.2	98.60	2.0	26.2	0.08	29	87	45
A*0201	**210**	**RMASGGGET**	**33.8**	**15.80**	**0.6**	**33.3**	**0.07**	**30**	**28**	**15**
A*0201	157	ATVLQLPQG	40.6	23.90	0.3	9.2	0.00	31	151	92

FIG. 29

Allele	Peptide ID	Peptide Sequence
A*0201	223	LLLDRLNQL
A*0201	332	LTYHGAIKL
A*0201	317	GMSRIGMEV
A*0201	227	RLNQLESKV
A*0201	304	QIAQFAPSA
A*0201	131	IVWVATEGA
A*0201	224	LLDRLNQLE
A*0201	263	RTATKQYNV
A*0201	352	ILLNKHIDA
A*0201	222	LLLLDRLNQ
A*0201	407	QLQNSMSGA
A*0201	113	YLGTGPEAS
A*0201	331	WLTYHGAIK
A*0201	339	KLDDKDPQF
A*0201	220	LALLLLDRL

Allele	Peptide ID	Peptide Sequence
A*0201	329	GTWLTYHGA
A*0201	325	VTPSGTWLT
A*0201	221	ALLLLDRLN
A*0201	313	SAFFGMSRI
A*0201	306	AQFAPSASA
A*0201	49	NTASWFTAL
A*0201	160	LQLPQGTTL
A*0201	166	TTLPKGFYA
A*0201	320	RIGMEVTPS
A*0201	308	FAPSASAFF
A*0201	139	ALNTPKDHI
A*0201	239	GQQQQGQTV
A*0201	50	TASWFTALT
A*0201	167	TLPKGFYAE
A*0201	210	RMASGGGET

FIG. 30

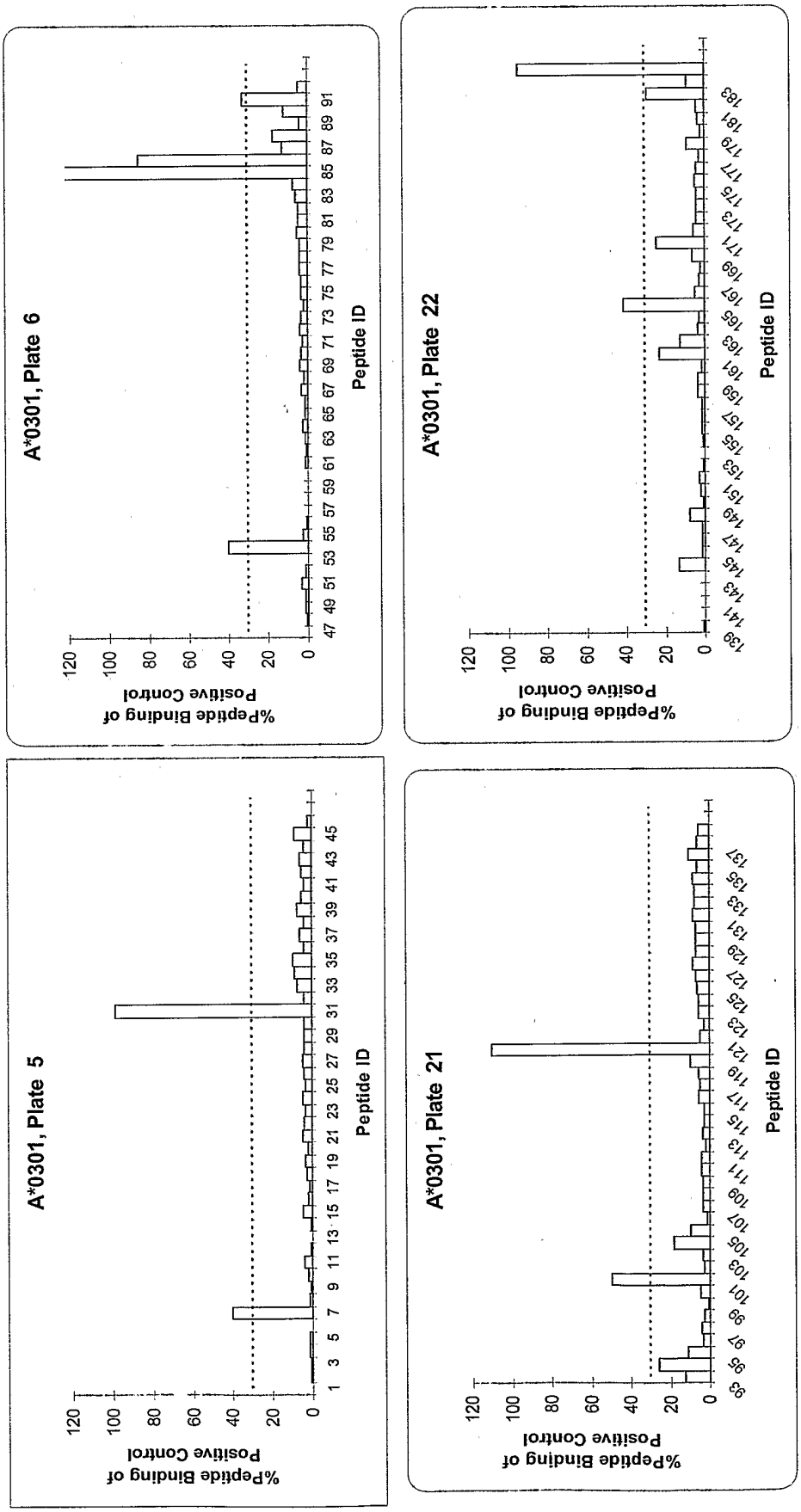

A*0301, Plate 6
%Peptide Binding of Positive Control
Peptide ID
A*0301, Plate 22
%Peptide Binding of Positive Control
Peptide ID
A*0301, Plate 5
%Peptide Binding of Positive Control
Peptide ID
A*0301, Plate 21
%Peptide Binding of Positive Control
Peptide ID

FIG. 31

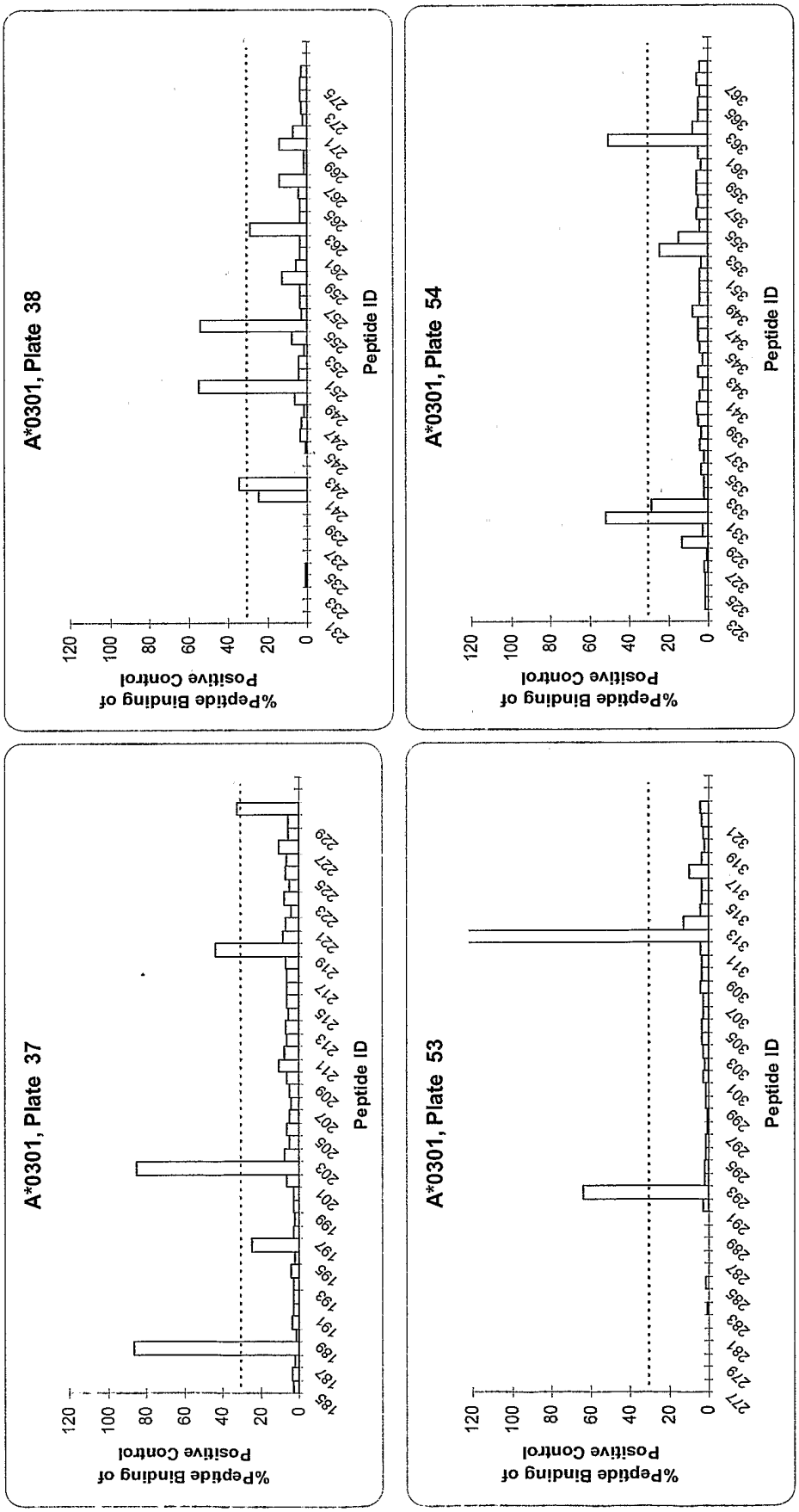

A*0301, Plate 38
A*0301, Plate 54
A*0301, Plate 37
A*0301, Plate 53
%Peptide Binding of Positive Control
Peptide ID
0
20
40
60
80
100
120

FIG. 32

Allele	Peptide ID	% Peptide Binding
A*0301	7	40.3
A*0301	31	98.5
A*0301	54	40.2
A*0301	85	122.9
A*0301	86	85.1
A*0301	91	33.0
A*0301	101	49.8
A*0301	120	110.4
A*0301	165	41.7
A*0301	184	94.8
A*0301	188	86.4
A*0301	202	85.1
A*0301	219	43.8
A*0301	230	32.2
A*0301	242	34.3
A*0301	250	54.6
A*0301	255	54.1
A*0301	292	63.6
A*0301	312	122.2
A*0301	331	52.1
A*0301	362	50.4

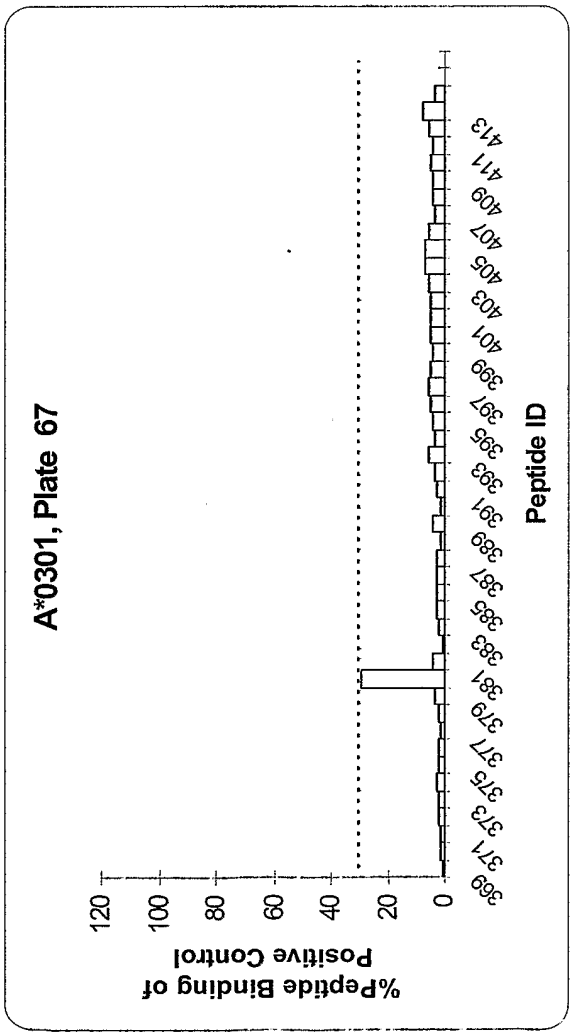


FIG. 33

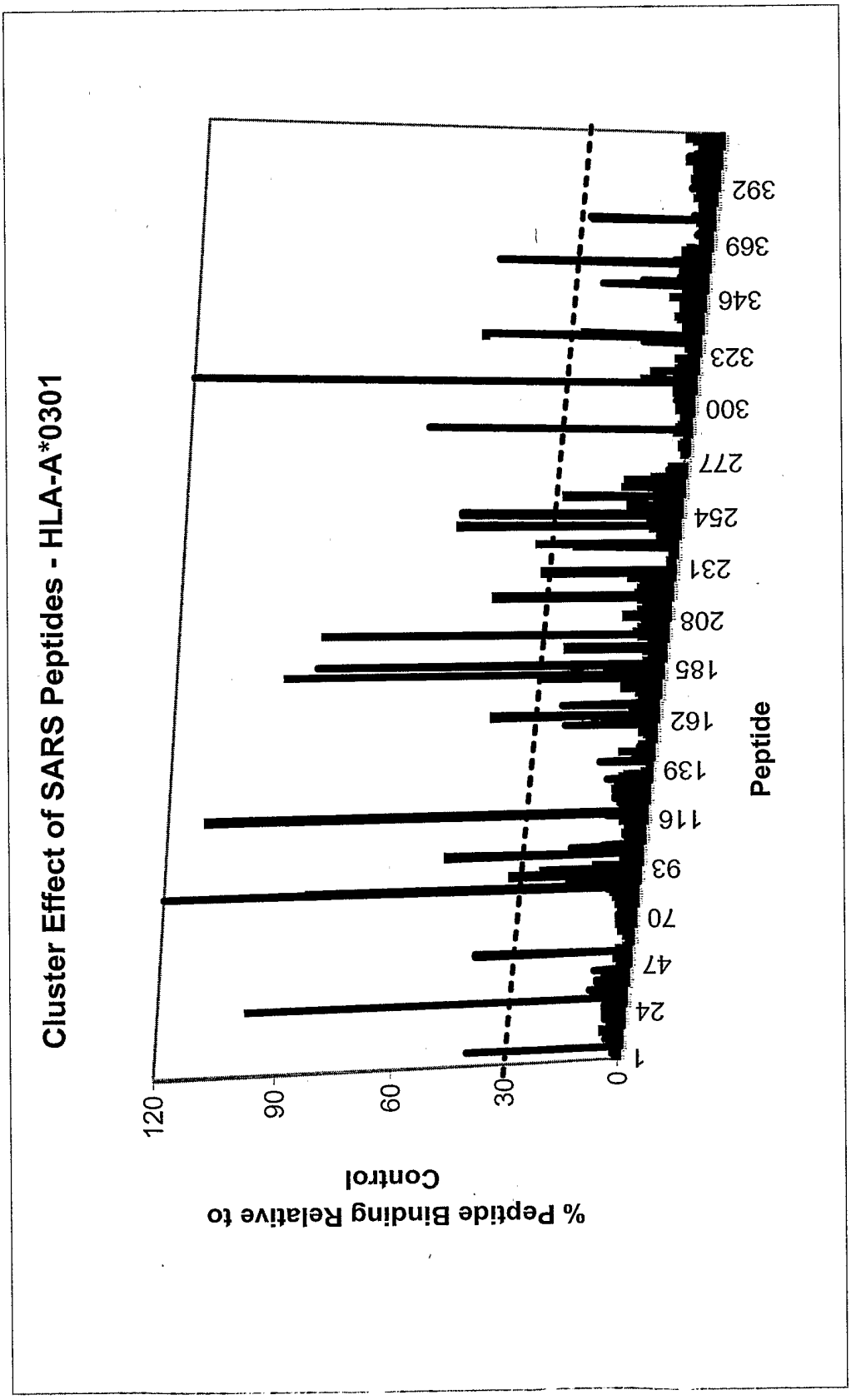
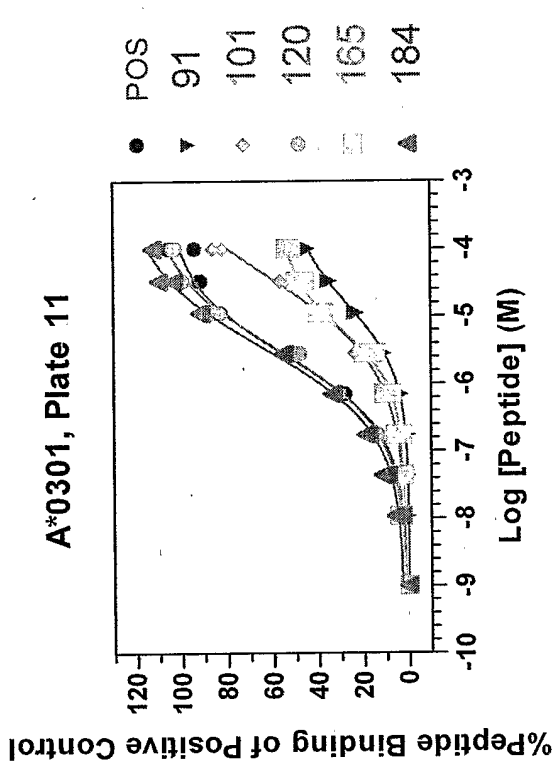
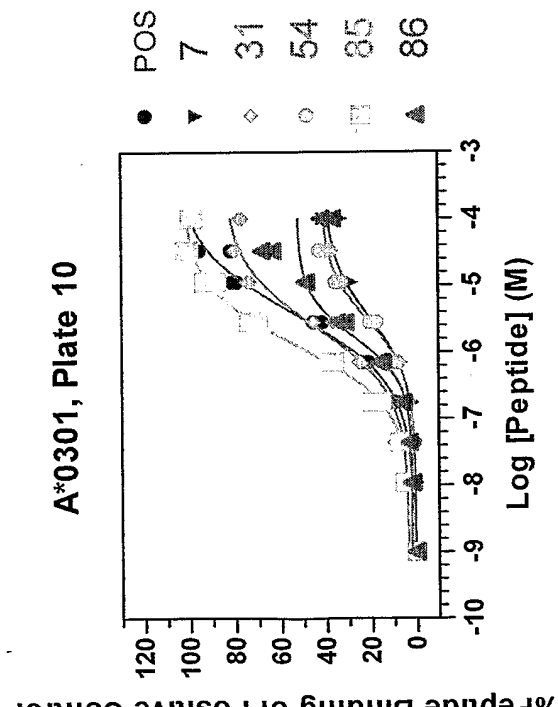

Cluster Effect of SARS Peptides - HLA-A*0301
% Peptide Binding Relative to Control
120
90
60
30
0
Peptide
1
24
47
70
93
116
139
162
185
208
231
254
277
300
323
346
369
392

FIG. 34

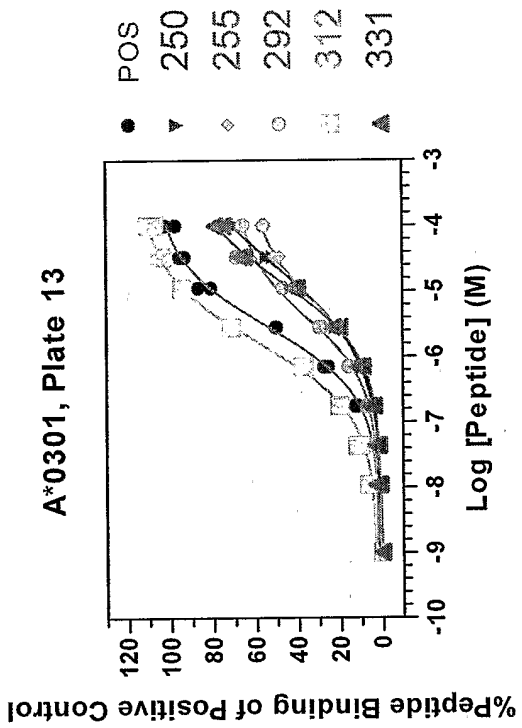


Peptide ID	Affinity ED50 x 10-6M
91	14.90
101	41.90
120	3.27
165	6.15
184	3.36

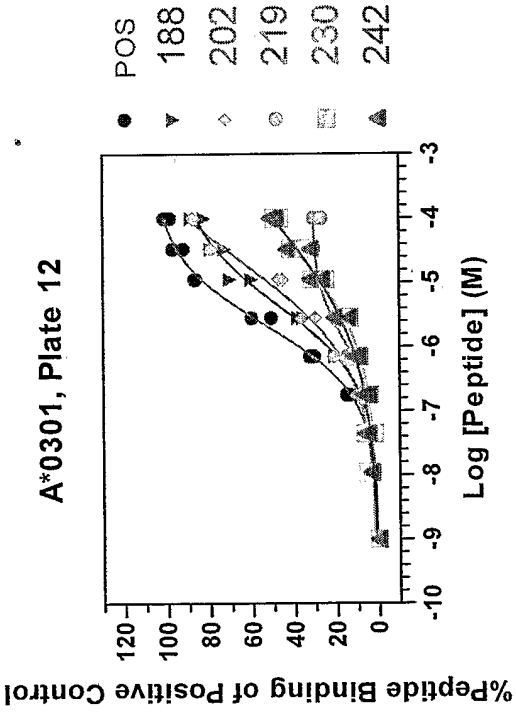


Peptide ID	Affinity ED50 x 10-6M
7	3.22
31	2.35
54	3.02
85	1.25
86	1.66

FIG. 35

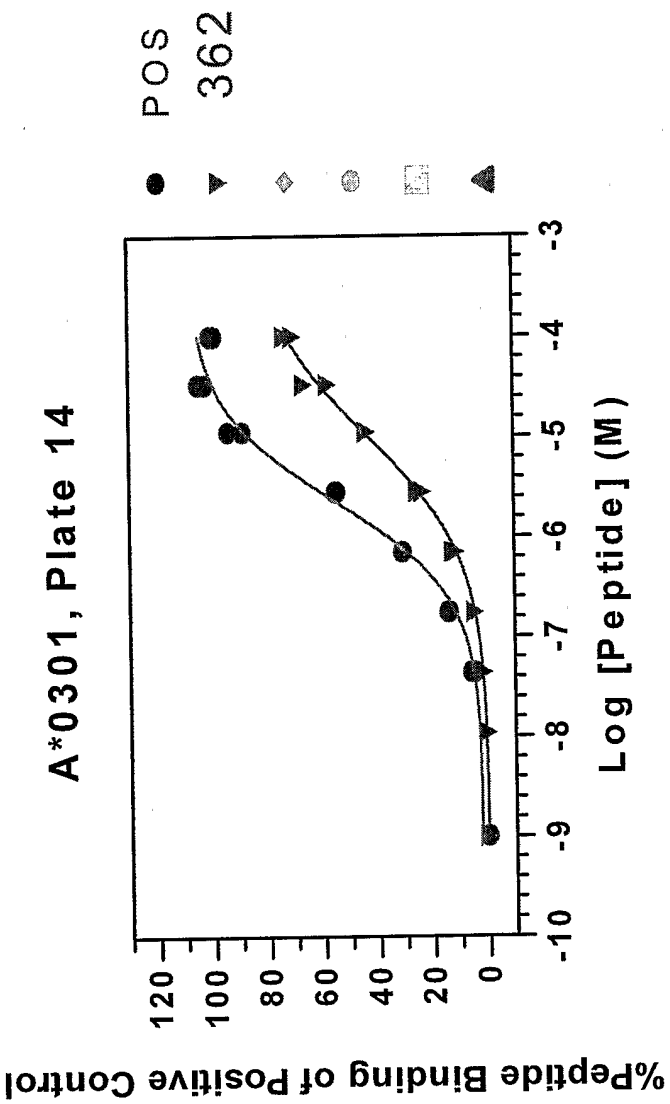


Peptide ID	Affinity ED50 x 10-6M
250	24.50
255	6.52
292	3.99
312	1.61
331	13.80



Peptide ID	Affinity ED50 x 10-6M
188	4.41
202	19.30
219	1.30
230	18.60
242	106.00

FIG. 36

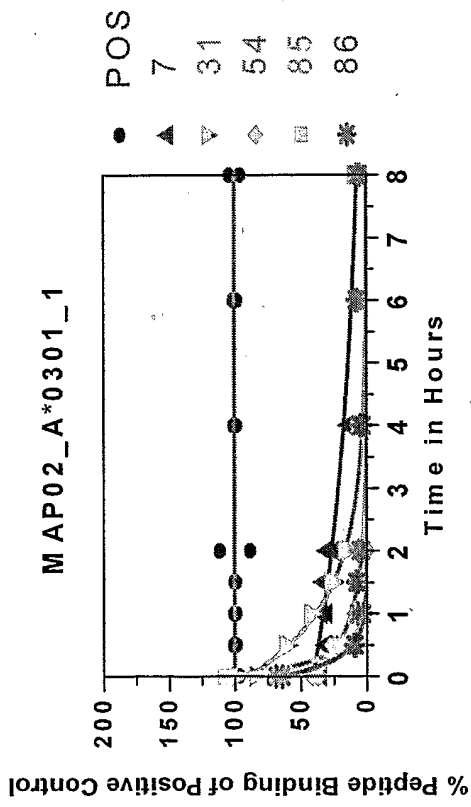


Peptide ID	Affinity ED50 x 10-6M
362	10.40

FIG. 37

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
7	2.7	39.5
31	0.8	89.9
54	0.6	38.8
85	0.2	106.1
86	0.2	66.1

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
91	0.3	22.0



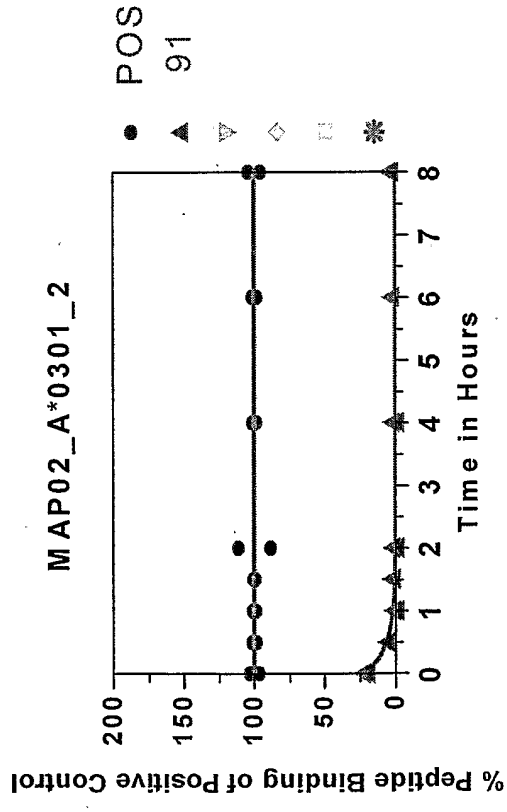
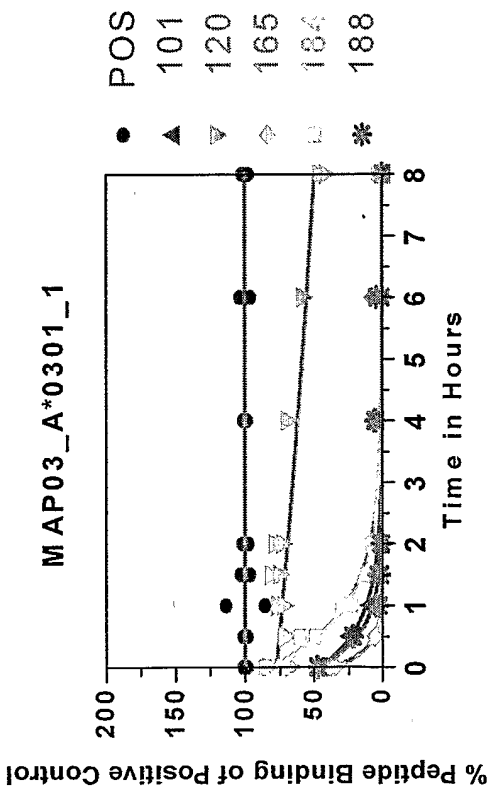


FIG. 38

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
101	0.5	44.7
120	7.2	73.6
165	0.2	35.9
184	0.6	79.2
188	0.4	47.4

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
202	0.7	49.7
219	1.0	22.8
230	0.6	23.3
242	2.0	29.3
250	6.8	40.3



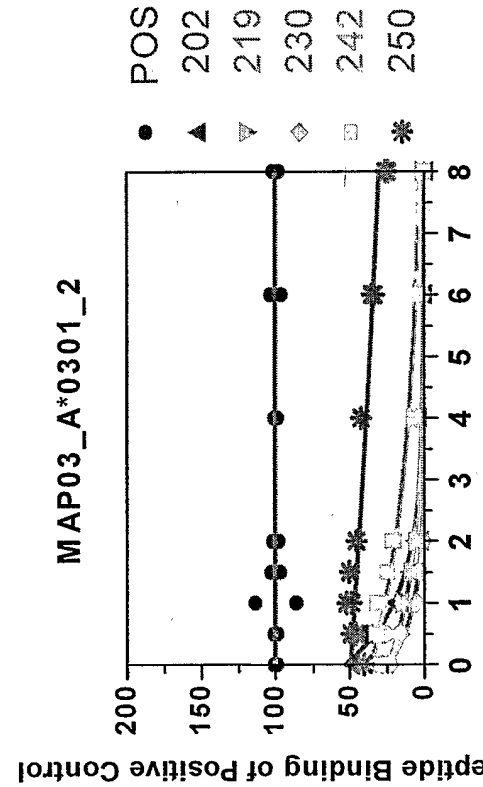


FIG. 39

Peptide ID	Off Rate t 1/2	% Peptide Binding at T0
255	0.3	33.3
292	2.2	51.7
312	0.8	88.9
331	0.4	39.1
362	11.6	37.9

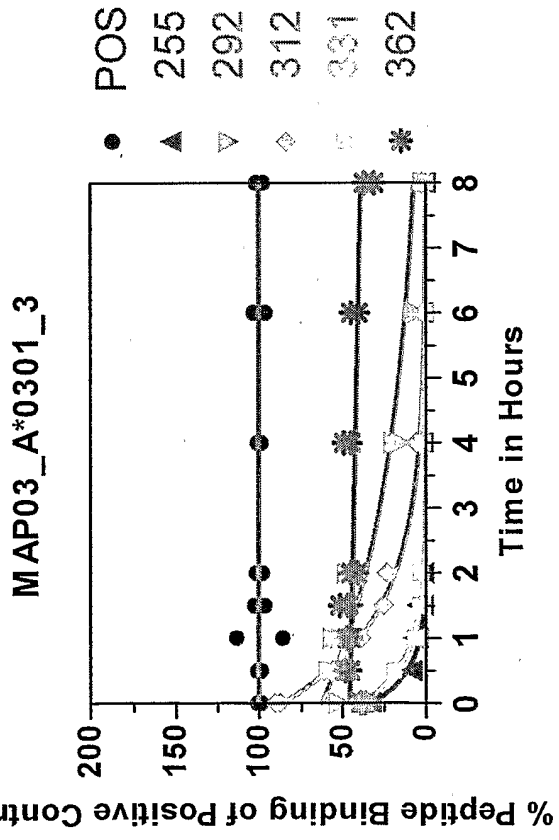


FIG. 40

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
A*0301	120	ASLPYGANK	110.4	3.27	7.2	73.6	0.61
A*0301	362	KTFPPTEPK	50.4	10.40	11.6	37.9	0.37
A*0301	312	ASAFFGMSR	122.2	1.61	0.8	88.9	0.27
A*0301	250	KSAAEASKK	54.6	24.50	6.8	40.3	0.26
A*0301	31	GGRNGARPK	98.5	2.35	0.8	89.9	0.25
A*0301	292	LIRQGTDYK	63.6	3.99	2.2	51.7	0.25
A*0301	7	QSNQRSAPR	40.3	3.22	2.7	39.5	0.23
A*0301	184	SSRSSSRSR	94.8	3.36	0.6	79.2	0.19
A*0301	85	IGYYRRATR	122.9	1.25	0.2	106.1	0.15
A*0301	54	FTALTQHGK	40.2	3.02	0.6	38.8	0.10
A*0301	86	GYYRRATRR	85.1	1.66	0.2	66.1	0.10
A*0301	202	SSRGNSPAR	85.1	19.30	0.7	49.7	0.10
A*0301	188	SSRSRGNSR	86.4	4.41	0.4	47.4	0.09
A*0301	242	QQGQTVTKK	34.3	106.00	2.0	29.3	0.08
A*0301	101	KMKELSPRW	49.8	41.90	0.5	44.7	0.07
A*0301	331	WLTYHGAIK	52.1	13.80	0.4	39.1	0.07
A*0301	255	ASKKPRQKR	54.1	6.52	0.3	33.3	0.06
A*0301	165	GTTLPKGFY	41.7	6.15	0.2	35.9	0.05
A*0301	91	ATRRVRGGD	33.0	14.90	0.3	**22.0**	0.00
A*0301	219	ALALLLLDR	43.8	1.30	1.0	**22.8**	0.00
A*0301	230	QLESKVSGK	32.2	18.60	0.6	**23.3**	0.00

FIG. 41

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	T0 % Peptide Binding	iScore	iTopia Rank	BIMAS Rank	SYFPEITHI Rank
A*0301	120	ASLPYGANK	110.4	3.27	7.2	73.6	0.61	1	18	4
A*0301	**362**	**KTFPPTEPK**	**50.4**	**10.40**	**11.6**	**37.9**	**0.37**	**2**	**2**	**44**
A*0301	312	ASAFFGMSR	122.2	1.61	0.8	88.9	0.27	3	39	63
A*0301	250	KSAAEASKK	54.6	24.50	6.8	40.3	0.26	4	24	11
A*0301	31	GGRNGARPK	98.5	2.35	0.8	89.9	0.25	5	126	17
A*0301	**292**	**LIRQGTDYK**	**63.6**	**3.99**	**2.2**	**51.7**	**0.25**	**6**	**8**	**5**
A*0301	7	QSNQRSAPR	40.3	3.22	2.7	39.5	0.23	7	93	101
A*0301	184	SSRSSSRSR	94.8	3.36	0.6	79.2	0.19	8	176	131
A*0301	85	IGYYRRATR	122.9	1.25	0.2	106.1	0.15	9	90	15
A*0301	**54**	**FTALTQHGK**	**40.2**	**3.02**	**0.6**	**38.8**	**0.10**	**10**	**14**	**88**
A*0301	86	GYYRRATRR	85.1	1.66	0.2	66.1	0.10	11	47	24
A*0301	202	SSRGNSPAR	85.1	19.30	0.7	49.7	0.10	12	74	108
A*0301	188	SSRSRGNSR	86.4	4.41	0.4	47.4	0.09	13	85	49
A*0301	242	QQGQTVTKK	34.3	106.00	2.0	29.3	0.08	14	9	80
A*0301	101	KMKELSPRW	49.8	41.90	0.5	44.7	0.07	15	16	278
A*0301	331	WLTYHGAIK	52.1	13.80	0.4	39.1	0.07	16	3	3
A*0301	255	ASKKPRQKR	54.1	6.52	0.3	33.3	0.06	17	75	163
A*0301	165	GTTLPKGFY	41.7	6.15	0.2	35.9	0.05	18	28	183
A*0301	91	ATRRVRGGD	33.0	14.90	0.3	22.0	0.00	19	240	92
A*0301	219	ALALLLLDR	43.8	1.30	1.0	22.8	0.00	20	4	8
A*0301	230	QLESKVSGK	32.2	18.60	0.6	23.3	0.00	21	1	1

FIG. 42

FIG. 43

Allele	Peptide ID	Peptide Sequence
A*0301	120	ASLPYGANK
A*0301	362	KTFPPTEPK
A*0301	312	ASAFFGMSR
A*0301	250	KSAAEASKK
A*0301	31	GGRNGARPK
A*0301	292	LIRQGTDYK
A*0301	7	QSNQRSAPR
A*0301	184	SSRSSSRSR
A*0301	85	IGYYRRATR
A*0301	54	FTALTQHGK
A*0301	86	GYYRRATRR
A*0301	202	SSRGNSPAR
A*0301	188	SSRSRGNSR
A*0301	242	QQGQTVTKK
A*0301	101	KMKELSPRW
A*0301	331	WLTYHGAIK
A*0301	255	ASKKPRQKR
A*0301	165	GTTLPKGFY

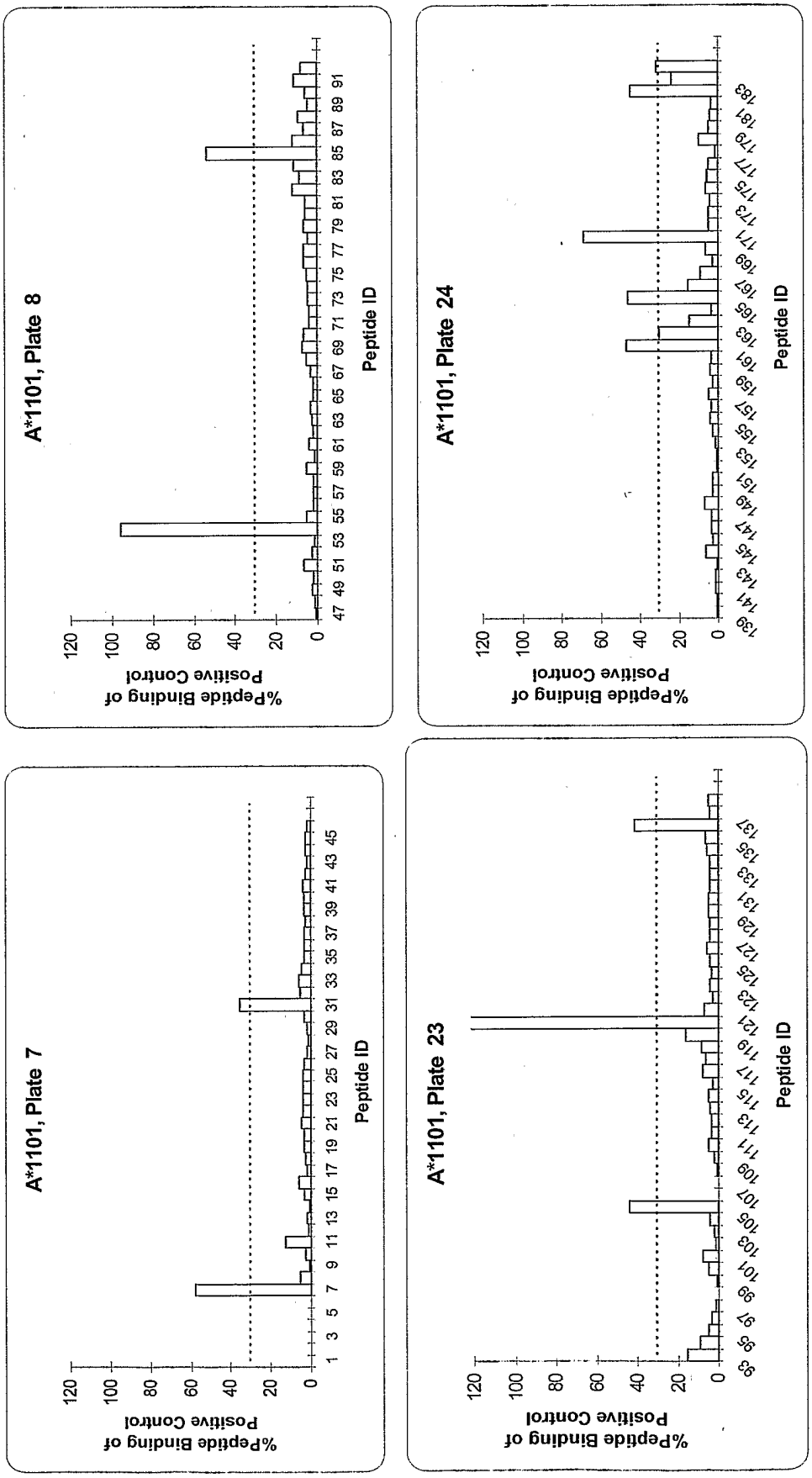

A*1101, Plate 8
A*1101, Plate 24
A*1101, Plate 7
A*1101, Plate 23
%Peptide Binding of Positive Control
Peptide ID

FIG. 44

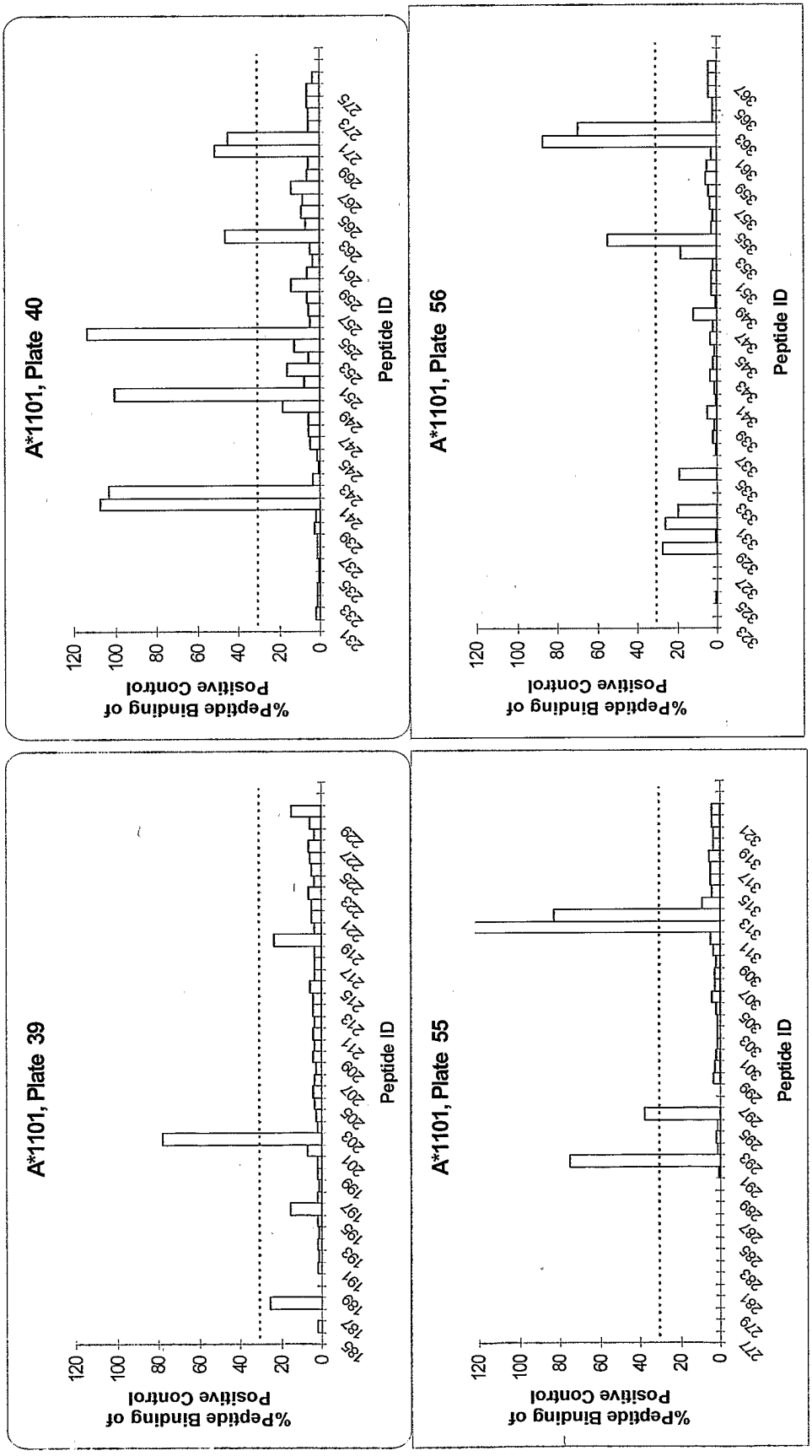

A*1101, Plate 40
%Peptide Binding of Positive Control
Peptide ID
A*1101, Plate 56
%Peptide Binding of Positive Control
Peptide ID
A*1101, Plate 39
%Peptide Binding of Positive Control
Peptide ID
A*1101, Plate 55
%Peptide Binding of Positive Control
Peptide ID

FIG. 45

Allele	Peptide ID	% Peptide Binding
A*1101	7	57.8
A*1101	31	35.2
A*1101	54	95.9
A*1101	85	53.6
A*1101	105	44.0
A*1101	120	126.0
A*1101	136	41.2
A*1101	161	47.2
A*1101	165	46.1
A*1101	170	69.0
A*1101	182	45.2
A*1101	184	31.5
A*1101	202	78.2
A*1101	241	107.1
A*1101	242	103.4
A*1101	250	100.4
A*1101	255	113.4
A*1101	263	46.6
A*1101	270	51.4
A*1101	271	44.7
A*1101	292	74.8
A*1101	296	37.9
A*1101	312	131.0
A*1101	313	82.6
A*1101	354	55.0
A*1101	362	87.2
A*1101	363	69.7
A*1101	380	88.6

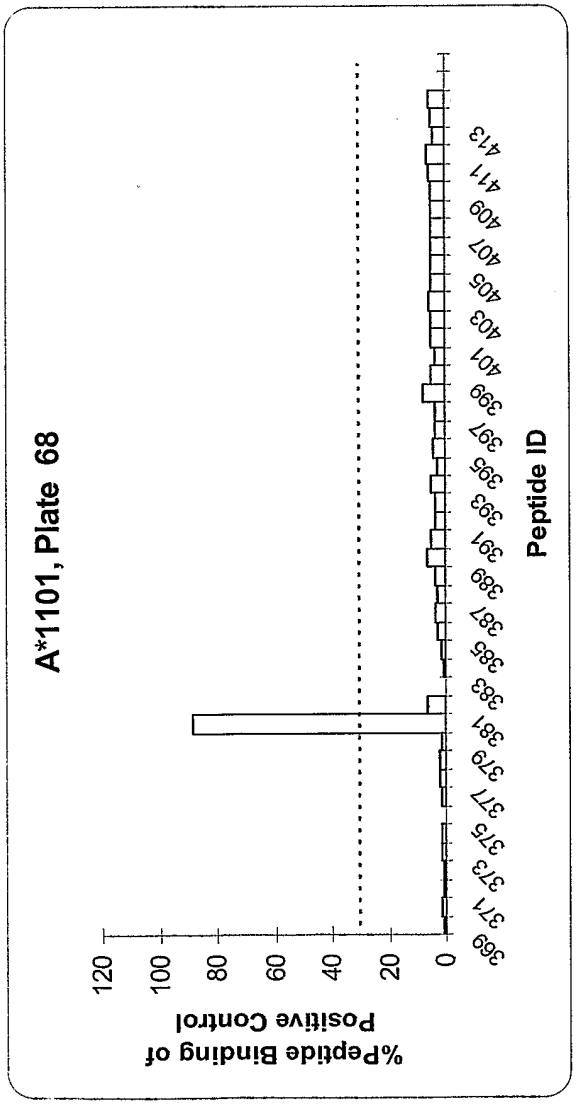


FIG. 46

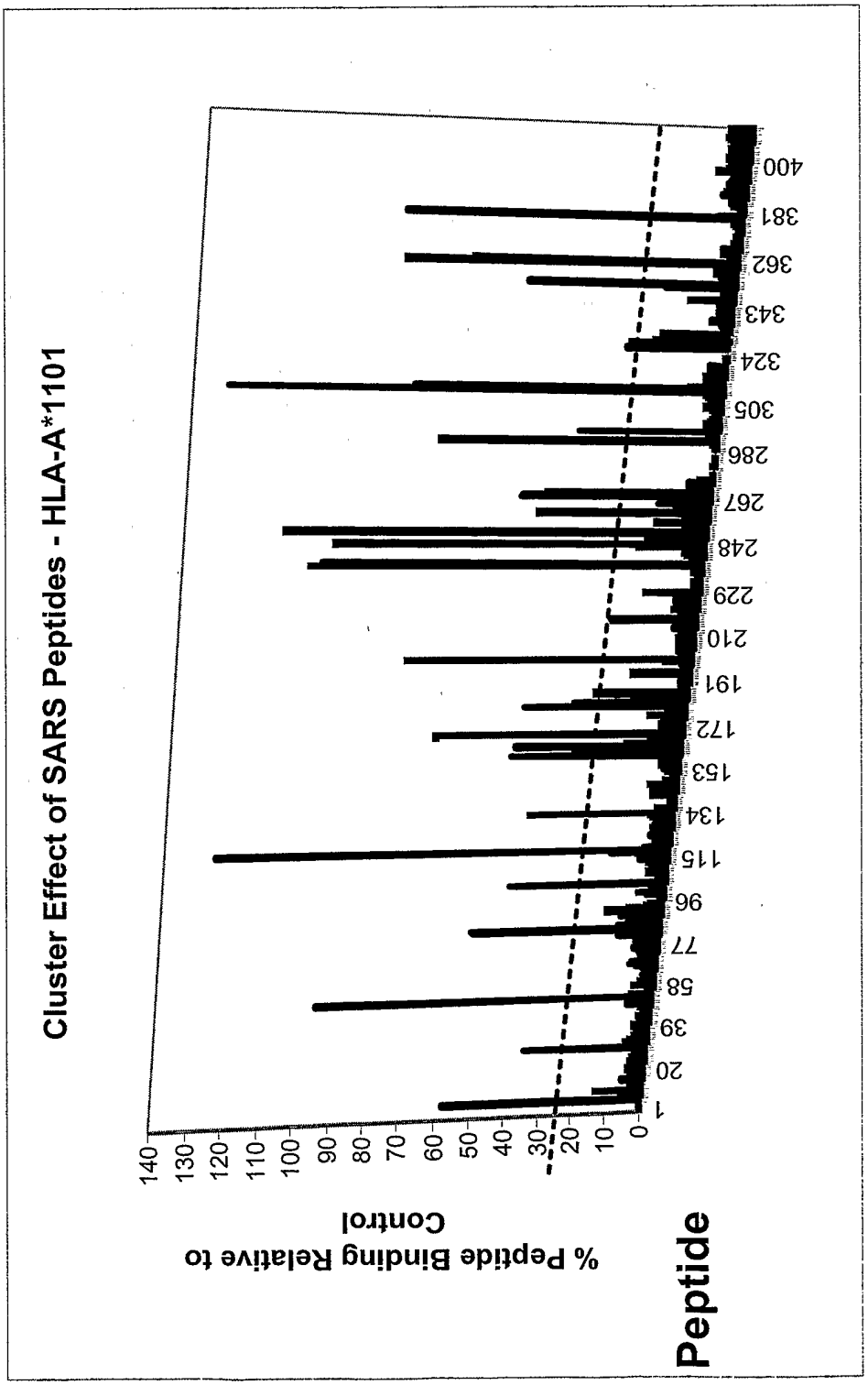

Cluster Effect of SARS Peptides - HLA-A*1101
% Peptide Binding Relative to Control
Peptide
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
1
20
39
58
77
96
115
134
153
172
191
210
229
248
267
286
305
324
343
362
381
400

FIG. 47

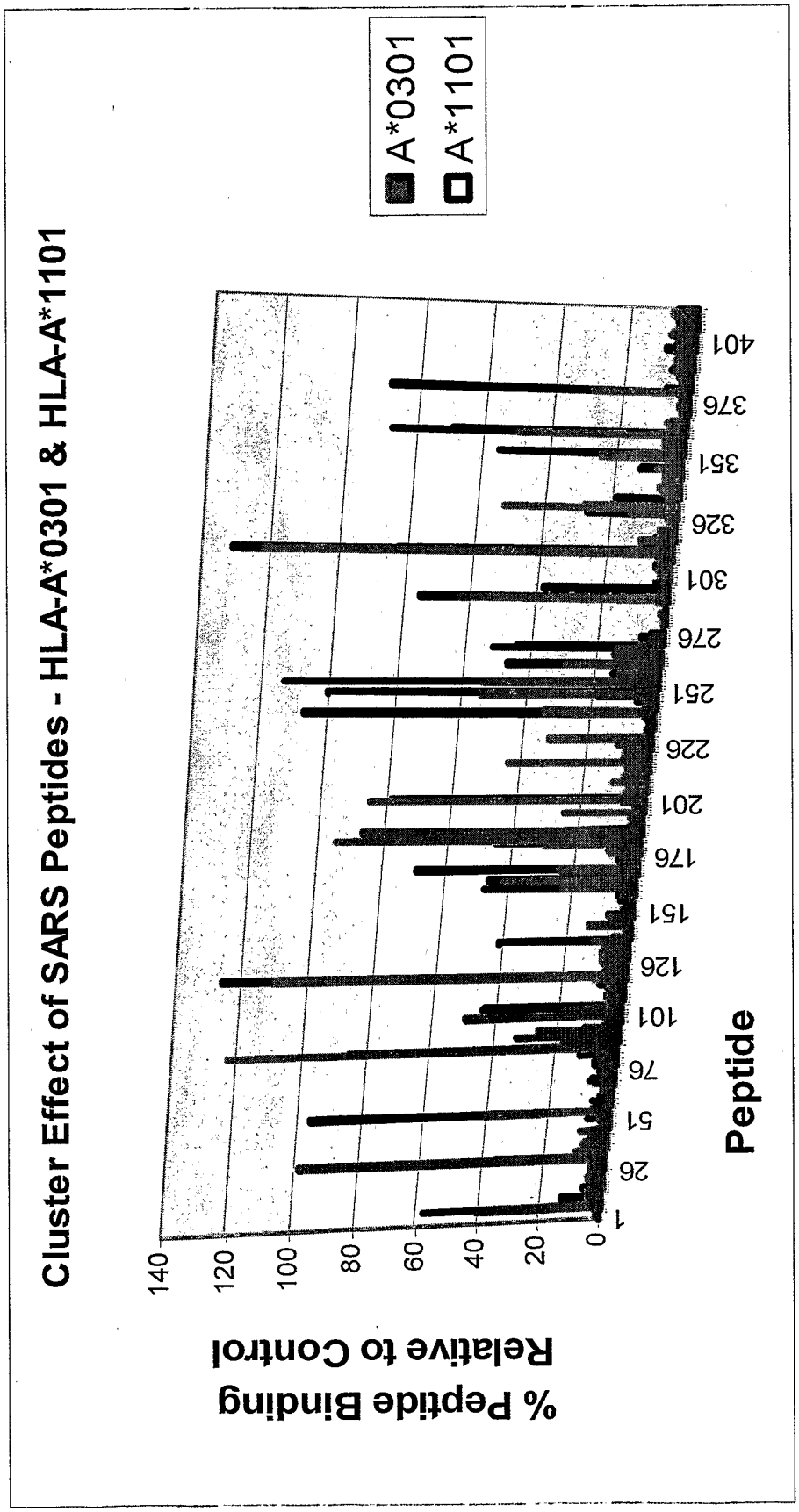
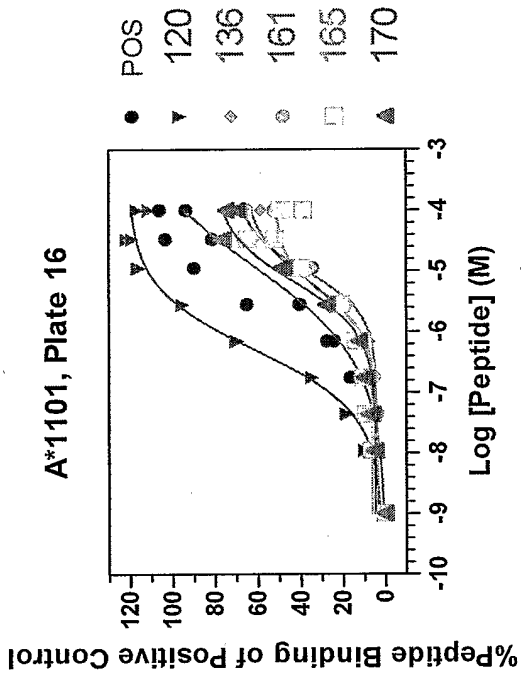
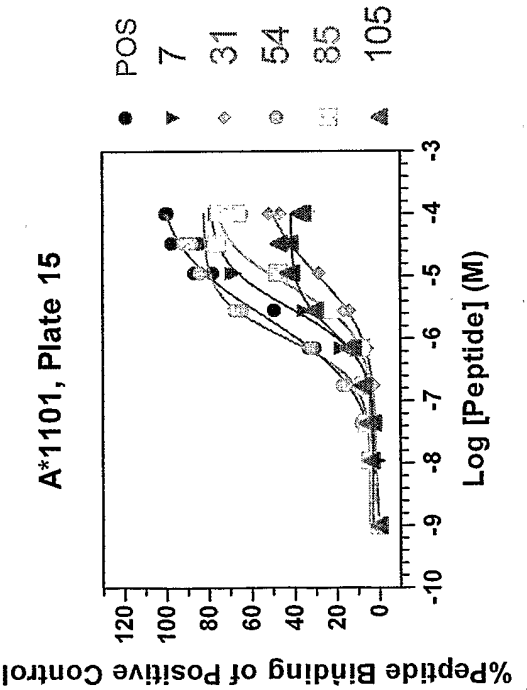

Cluster Effect of SARS Peptides - HLA-A*0301 & HLA-A*1101
A*0301
A*1101
% Peptide Binding Relative to Control
0
20
40
60
80
100
120
140
Peptide
1
26
51
76
101
126
151
176
201
226
251
276
301
326
351
376
401

FIG. 48

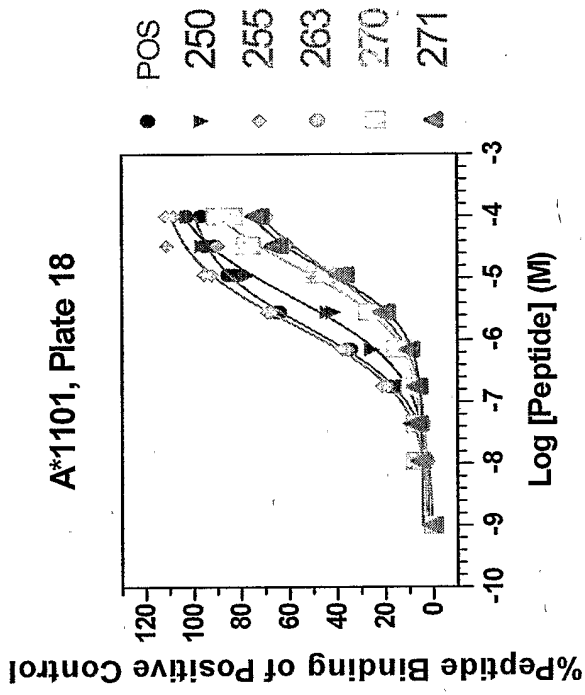


Peptide ID	Affinity ED50 x 10-6M
120	0.50
136	9.91
161	6.42
165	4.09
170	6.44

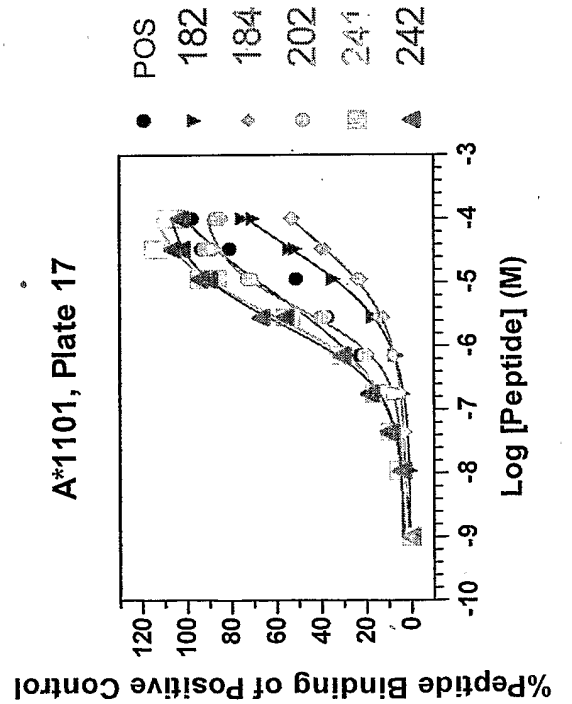


Peptide ID	Affinity ED50 x 10-6M
7	2.91
31	10.40
54	0.98
85	6.67
105	1.33

FIG. 49

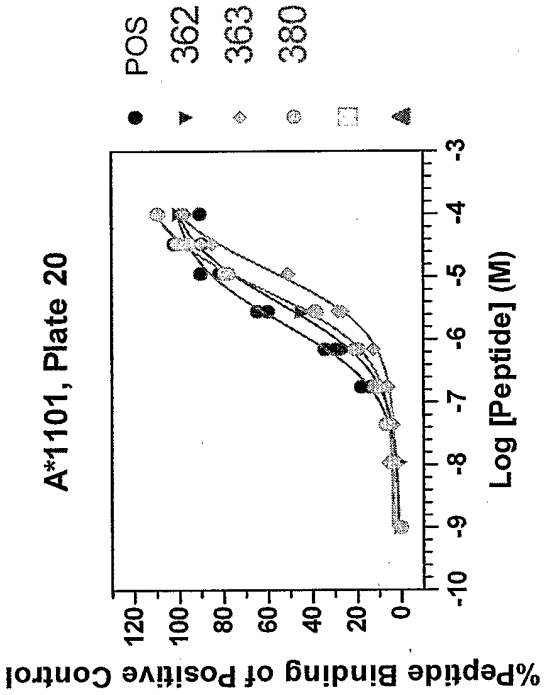


Peptide ID	Affinity ED50 x 10-6M
250	4.87
255	1.76
263	14.60
270	14.20
271	13.20

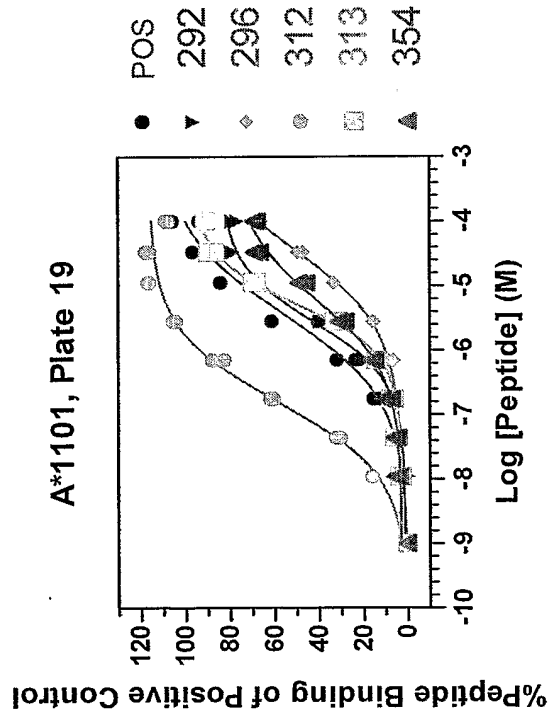


Peptide ID	Affinity ED50 x 10-6M
182	35.50
184	6.33
202	3.66
241	2.99
242	2.09

FIG. 50



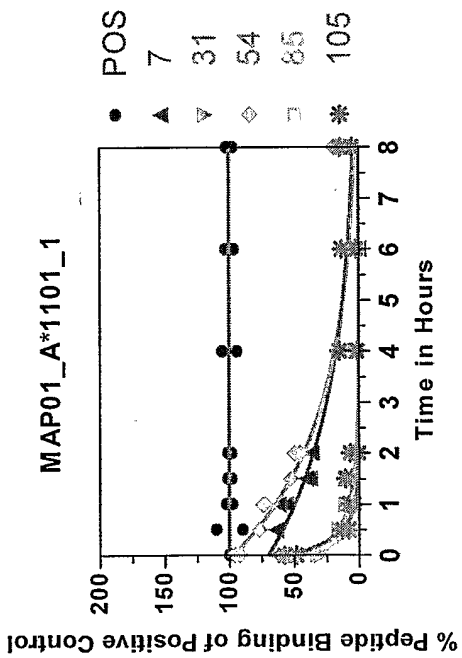
Peptide ID	Affinity ED50 x 10-6M
362	3.75
363	12.70
380	6.16



Peptide ID	Affinity ED50 x 10-6M
292	2.77
296	40.80
312	0.15
313	5.16
354	5.99

FIG. 51

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
7	1.6	61.5
31	0.5	30.4
54	1.4	93.8
85	0.2	54.1
105	0.3	52.8



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
120	7.4	112.8
136	3.4	26.9
161	1.8	36.8
165	0.3	36.8
170	0.3	48.8

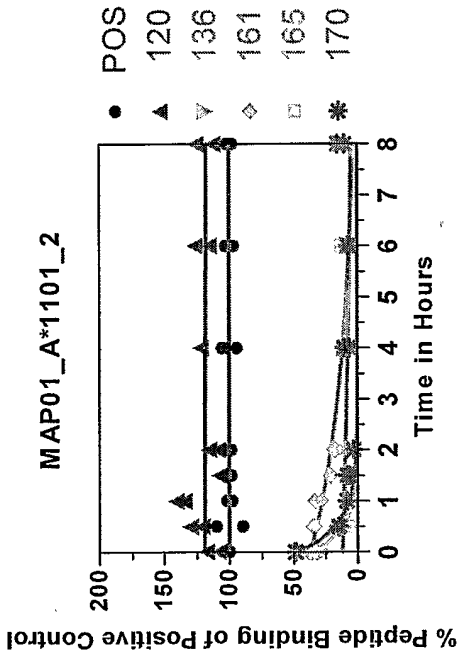
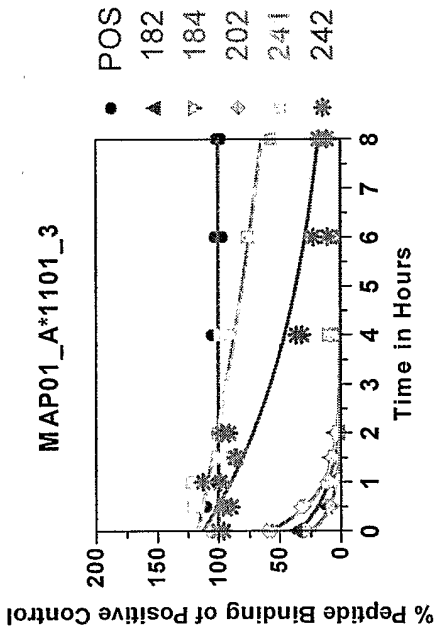


FIG. 52

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
182	0.5	37.3
184	0.3	25.3
202	0.5	58.5
241	4.1	105.4
242	2.2	98.4



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
250	3.1	82.4
255	1.4	101.9
263	1.6	39.0
270	0.7	48.1
271	1.1	35.0

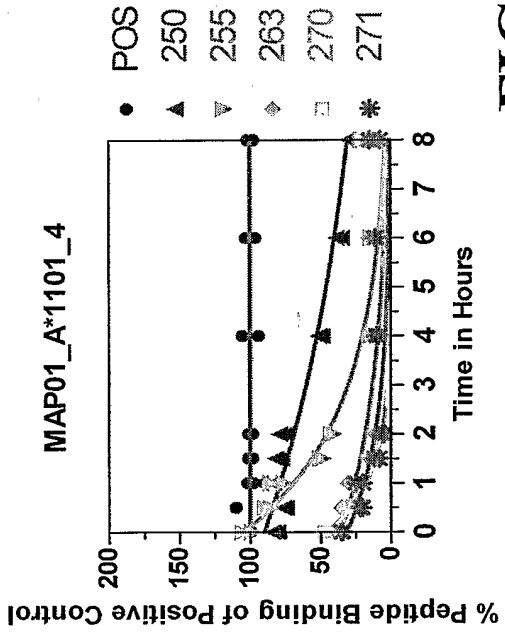
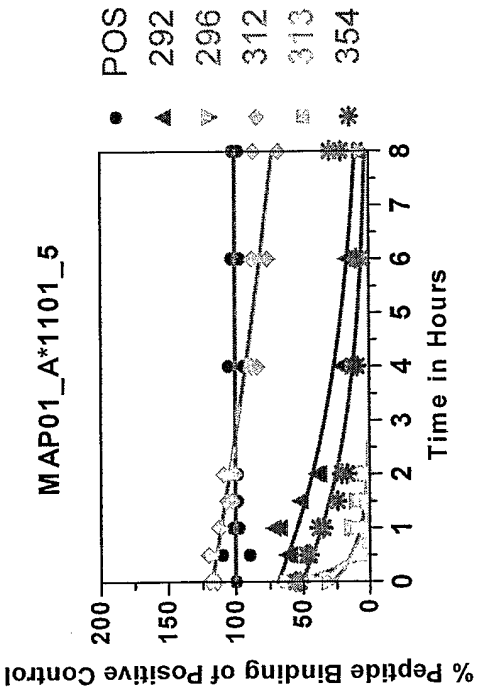


FIG. 53

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
292	2.1	59.5
296	0.5	30.1
312	4.5	117.3
313	0.2	60.6
354	1.6	54.0



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
362	7.4	71.1
363	0.5	54.2
380	1.2	92.2

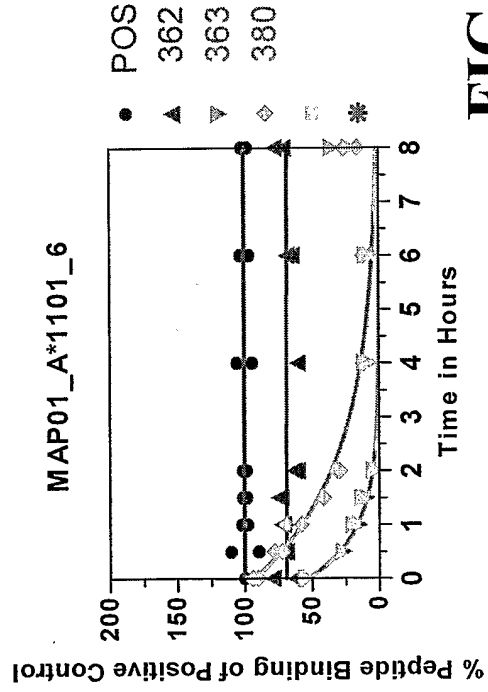


FIG. 54

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
A*1101	120	ASLPYGANK	126.0	0.5	7.4	112.8	1.20
A*1101	312	ASAFFGMSR	131.0	0.2	4.5	117.3	1.19
A*1101	241	QQQGQTVTK	107.1	3.0	4.1	105.4	0.62
A*1101	362	KTFPPTEPK	87.2	3.8	7.4	71.1	0.58
A*1101	242	QQGQTVTKK	103.4	2.1	2.2	98.4	0.45
A*1101	250	KSAAEASKK	100.4	4.9	3.1	82.4	0.40
A*1101	54	FTALTQHGK	95.9	1.0	1.4	93.8	0.40
A*1101	255	ASKKPRQKR	113.4	1.8	1.4	101.9	0.38
A*1101	292	LIRQGTDYK	74.8	2.8	2.1	59.5	0.28
A*1101	380	AQPLPQRQK	88.6	6.2	1.2	92.2	0.27
A*1101	7	QSNQRSAPR	57.8	2.9	1.6	61.5	0.25
A*1101	354	LNKHIDAYK	55.0	6.0	1.6	54.0	0.20
A*1101	161	QLPQGTTLP	47.2	6.4	1.8	36.8	0.16
A*1101	136	TEGAINTPK	41.2	9.9	3.4	26.9	0.15
A*1101	263	RTATKQYNV	46.6	14.6	1.6	39.0	0.13
A*1101	202	SSRGNSPAR	78.2	3.7	0.5	58.5	0.13
A*1101	271	VTQAFGRRG	44.7	13.2	1.1	35.0	0.10
A*1101	363	TFPPTEPKK	69.7	12.7	0.5	54.2	0.10
A*1101	105	LSPRWYFYY	44.0	1.3	0.3	52.8	0.10
A*1101	270	NVTQAFGRR	51.4	14.2	0.7	48.1	0.10
A*1101	170	KGFYAEGSR	69.0	6.4	0.3	48.8	0.08
A*1101	313	SAFFGMSRI	82.6	5.2	0.2	60.6	0.08
A*1101	165	GTTLPKGFY	46.1	4.1	0.3	36.8	0.07
A*1101	31	GGRNGARPK	35.2	10.4	0.5	30.4	0.06
A*1101	85	IGYYRRATR	53.6	6.7	0.2	54.1	0.06
A*1101	182	QASSRSSSR	45.2	35.5	0.5	37.3	0.06
A*1101	296	GTDYKHWPQ	37.9	40.8	0.5	30.1	0.05
A*1101	184	SSRSSSRSR	31.5	6.3	0.3	25.3	0.03

FIG. 55

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK
A*1101	120	ASLPYGANK	126.0	0.5	7.4	112.8	1.20	1	36
A*1101	312	ASAFFGMSR	131.0	0.2	4.5	117.3	1.19	2	71
A*1101	**241**	**QQQGQTVTK**	**107.1**	**3.0**	**4.1**	**105.4**	**0.62**	**3**	**4**
A*1101	**362**	**KTFPPTEPK**	**87.2**	**3.8**	**7.4**	**71.1**	**0.58**	**4**	**1**
A*1101	**242**	**QQGQTVTKK**	**103.4**	**2.1**	**2.2**	**98.4**	**0.45**	**5**	**3**
A*1101	250	KSAAEASKK	100.4	4.9	3.1	82.4	0.40	6	22
A*1101	54	FTALTQHGK	95.9	1.0	1.4	93.8	0.40	7	2
A*1101	255	ASKKPRQKR	113.4	1.8	1.4	101.9	0.38	8	93
A*1101	**292**	**LIRQGTDYK**	**74.8**	**2.8**	**2.1**	**59.5**	**0.28**	**9**	**10**
A*1101	380	AQPLPQRQK	88.6	6.2	1.2	92.2	0.27	10	20
A*1101	7	QSNQRSAPR	57.8	2.9	1.6	61.5	0.25	11	96
A*1101	354	LNKHIDAYK	55.0	6.0	1.6	54.0	0.20	12	29
A*1101	161	QLPQGTTLP	47.2	6.4	1.8	36.8	0.16	13	198
A*1101	136	TEGALNTPK	41.2	9.9	3.4	26.9	0.15	14	26
A*1101	263	RTATKQYNV	46.6	14.6	1.6	39.0	0.13	15	25
A*1101	202	SSRGNSPAR	78.2	3.7	0.5	58.5	0.13	16	103
A*1101	271	VTQAFGRRG	44.7	13.2	1.1	35.0	0.10	17	> 250
A*1101	363	TFPPTEPKK	69.7	12.7	0.5	54.2	0.10	18	12
A*1101	105	LSPRWYFYY	44.0	1.3	0.3	52.8	0.10	19	177
A*1101	270	NVTQAFGRR	51.4	14.2	0.7	48.1	0.10	20	8
A*1101	170	KGFYAEGSR	69.0	6.4	0.3	48.8	0.08	21	41
A*1101	313	SAFFGMSRI	82.6	5.2	0.2	60.6	0.08	22	100
A*1101	165	GTTLPKGFY	46.1	4.1	0.3	36.8	0.07	23	38
A*1101	31	GGRNGARPK	35.2	10.4	0.5	30.4	0.06	24	73
A*1101	85	IGYYRRATR	53.6	6.7	0.2	54.1	0.06	25	72
A*1101	182	QASSRSSSR	45.2	35.5	0.5	37.3	0.06	26	31
A*1101	296	GTDYKHWPQ	37.9	40.8	0.5	30.1	0.05	27	83
A*1101	184	SSRSSSRSR	31.5	6.3	0.3	25.3	0.03	28	191

FIG. 56

Allele	Peptide ID	Peptide Sequence
A*1101	120	ASLPYGANK
A*1101	312	ASAFFGMSR
A*1101	241	QQQGQTVTK
A*1101	362	KTFPPTEPK
A*1101	242	QQGQTVTKK
A*1101	250	KSAAEASKK
A*1101	54	FTALTQHGK
A*1101	255	ASKKPRQKR
A*1101	292	LIRQGTDYK
A*1101	380	AQPLPQRQK
A*1101	7	QSNQRSAPR
A*1101	354	LNKHIDAYK
A*1101	161	QLPQGTTLP
A*1101	136	TEGALNTPK

Allele	Peptide ID	Peptide Sequence
A*1101	263	RTATKQYNV
A*1101	202	SSRGNSPAR
A*1101	271	VTQAFGRRG
A*1101	363	TFPPTEPKK
A*1101	105	LSPRWYFYY
A*1101	270	NVTQAFGRR
A*1101	170	KGFYAEGSR
A*1101	313	SAFFGMSRI
A*1101	165	GTTLPKGFY
A*1101	31	GGRNGARPK
A*1101	85	IGYYRRATR
A*1101	182	QASSRSSSR
A*1101	296	GTDYKHWPQ
A*1101	184	SSRSSSRSR

FIG. 57

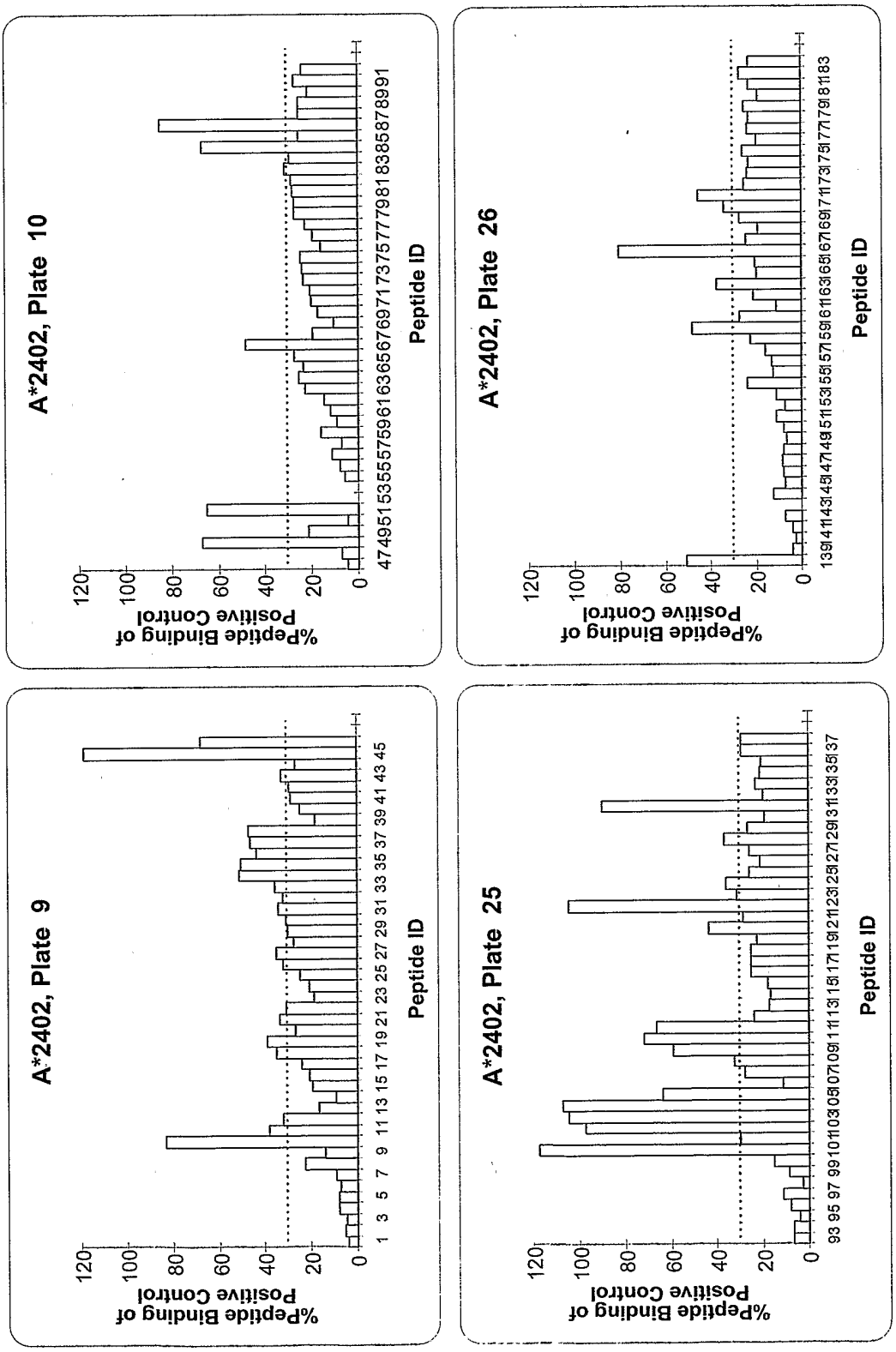

A*2402, Plate 10
%Peptide Binding of Positive Control
Peptide ID
A*2402, Plate 26
%Peptide Binding of Positive Control
Peptide ID
A*2402, Plate 9
%Peptide Binding of Positive Control
Peptide ID
A*2402, Plate 25
%Peptide Binding of Positive Control
Peptide ID

FIG. 58

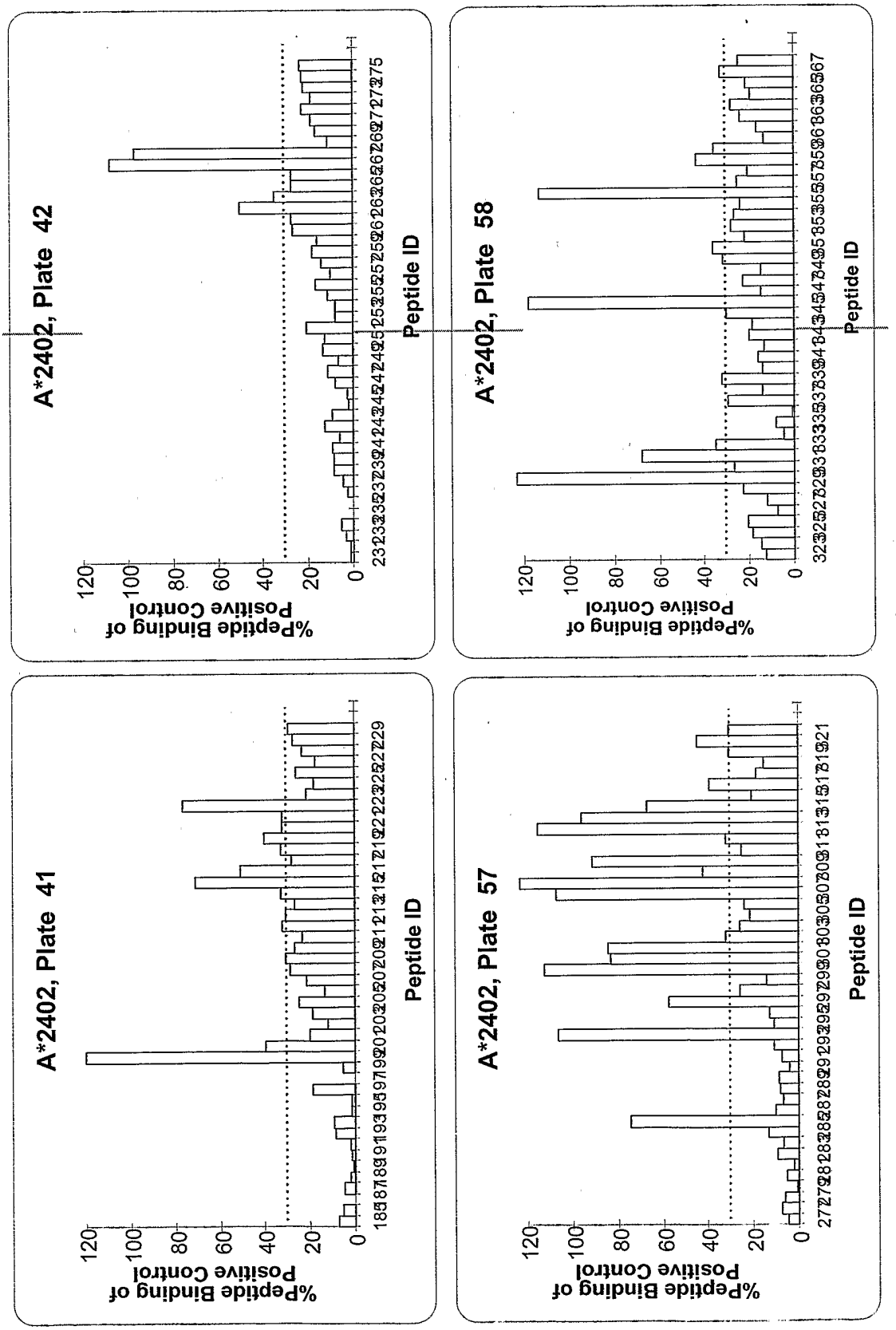

A*2402, Plate 42
A*2402, Plate 58
A*2402, Plate 41
A*2402, Plate 57
%Peptide Binding of Positive Control
Peptide ID
0
20
40
60
80
100
120

FIG. 59

Allele	Peptide ID	% Peptide Binding
A*2402	10	83.2
A*2402	34	50.7
A*2402	35	50.4
A*2402	36	43.9
A*2402	37	46.2
A*2402	38	46.7
A*2402	45	118.5
A*2402	46	67.7
A*2402	49	67.1
A*2402	52	65.2
A*2402	67	48.5
A*2402	85	66.8
A*2402	87	85.2
A*2402	101	117.1
A*2402	103	97.4
A*2402	104	104.6
A*2402	105	107.3
A*2402	106	63.6
A*2402	110	58.8
A*2402	111	71.9
A*2402	112	66.6
A*2402	121	43.5
A*2402	123	104.6
A*2402	132	89.8
A*2402	139	50.9
A*2402	160	48.5
A*2402	167	80.6

Allele	Peptide ID	% Peptide Binding
A*2402	172	45.8
A*2402	200	207.4
A*2402	216	71.1
A*2402	217	51
A*2402	220	40.1
A*2402	223	76.1
A*2402	263	50.2
A*2402	267	107.7
A*2402	268	97.2
A*2402	286	74.4
A*2402	294	106.6
A*2402	297	57.8
A*2402	300	112.7
A*2402	301	82.9
A*2402	302	84.5
A*2402	307	107.6
A*2402	308	123.2
A*2402	309	42.5
A*2402	310	91.2
A*2402	313	115.4
A*2402	314	96
A*2402	315	67.2
A*2402	321	45
A*2402	330	123.6
A*2402	332	67.8
A*2402	346	117.9
A*2402	356	113.6
A*2402	359	43.6

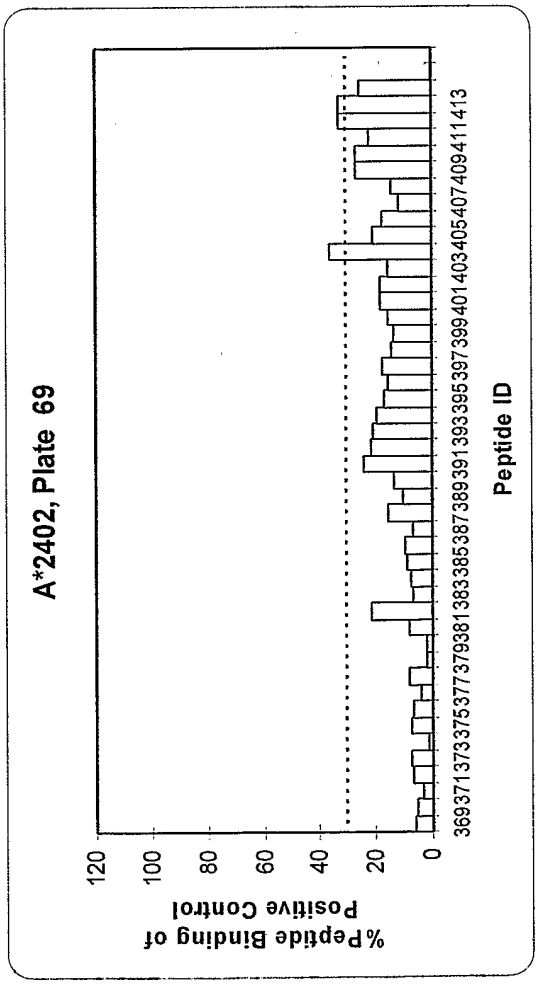
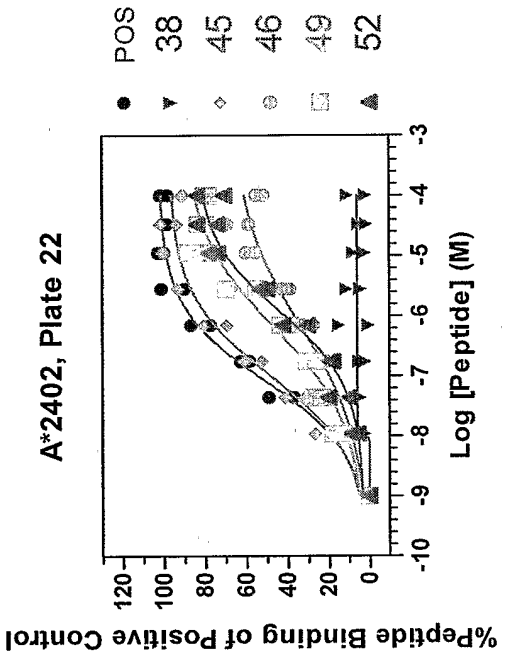
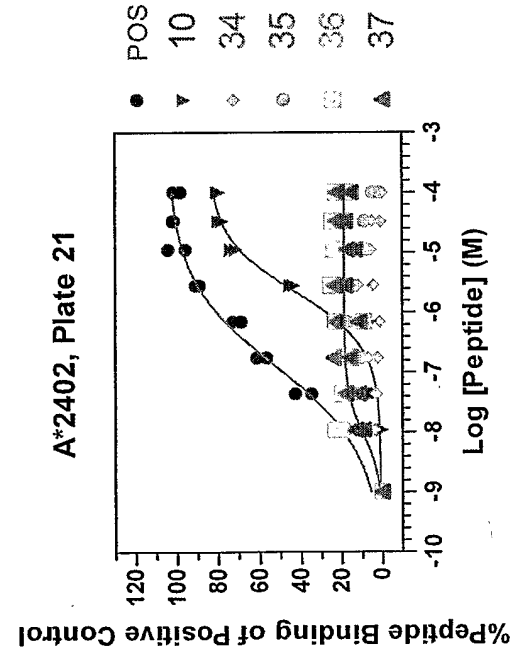


FIG. 60

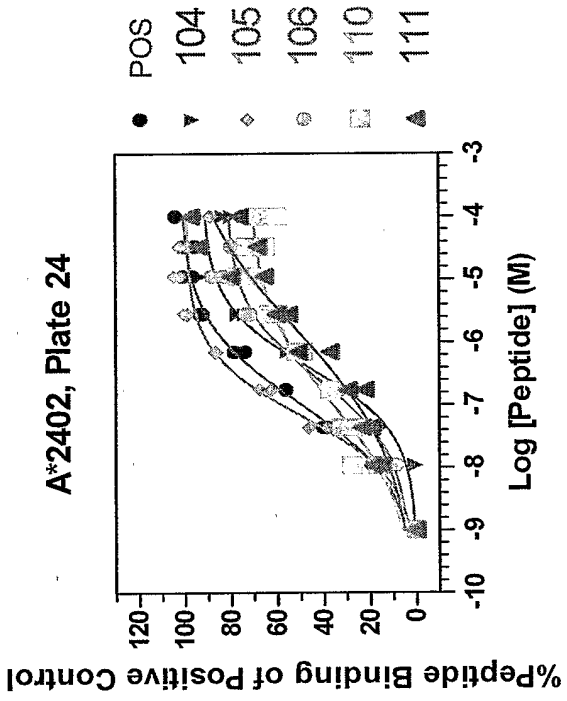


Peptide ID	Affinity ED50 x 10-6M
38	0.01
45	0.10
46	0.66
49	0.64
52	1.17

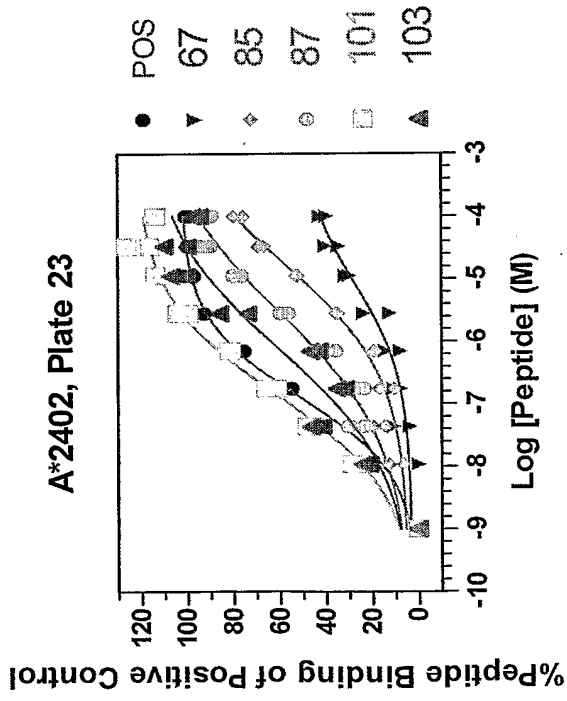


Peptide ID	Affinity ED50 x 10-6M
10	2.20
34	
35	
36	
37	0.01

FIG. 61

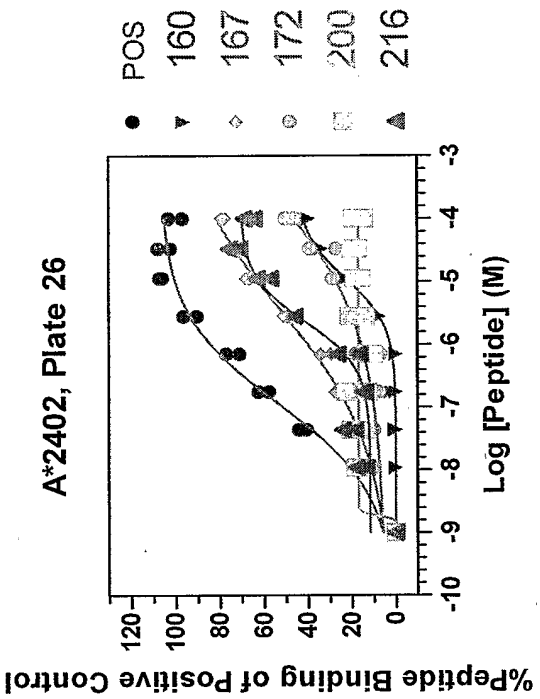


Peptide ID	Affinity ED50 x 10-6M
104	0.39
105	0.07
106	0.26
110	0.10
111	1.66

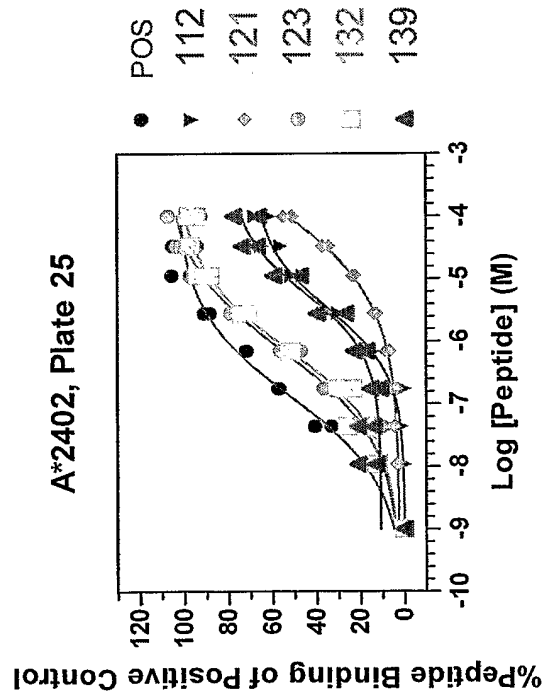


Peptide ID	Affinity ED50 x 10-6M
67	8.35
85	16.80
87	2.96
101	0.14
103	0.75

FIG. 62

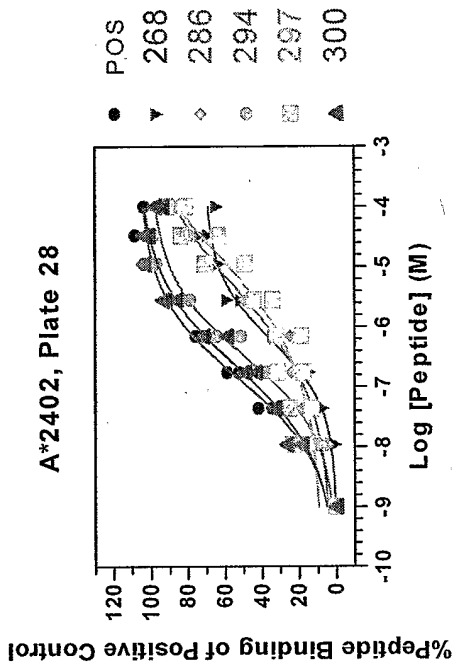


Peptide ID	Affinity ED50 x 10-6M
160	10.90
167	3.47
172	587.00
200	0.00
216	2.29

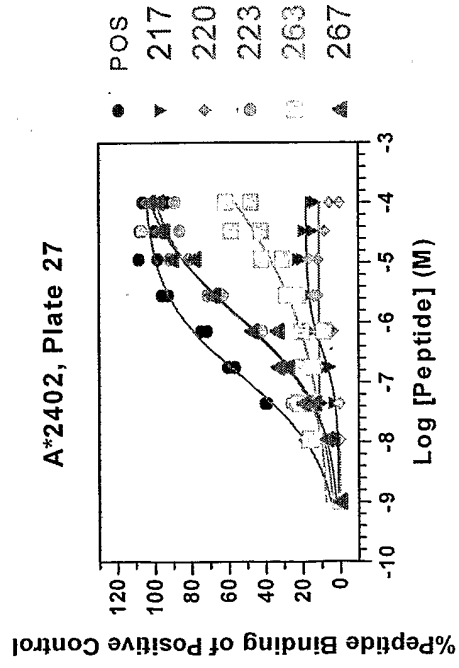


Peptide ID	Affinity ED50 x 10-6M
112	3.23
121	193.00
123	0.70
132	0.75
139	5.83

FIG. 63

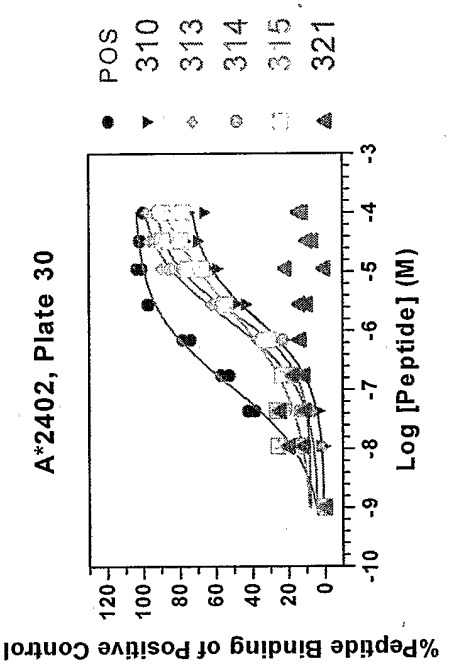


Peptide ID	Affinity ED50 x 10-6M
268	0.61
286	4.47
294	0.33
297	20.40
300	0.21

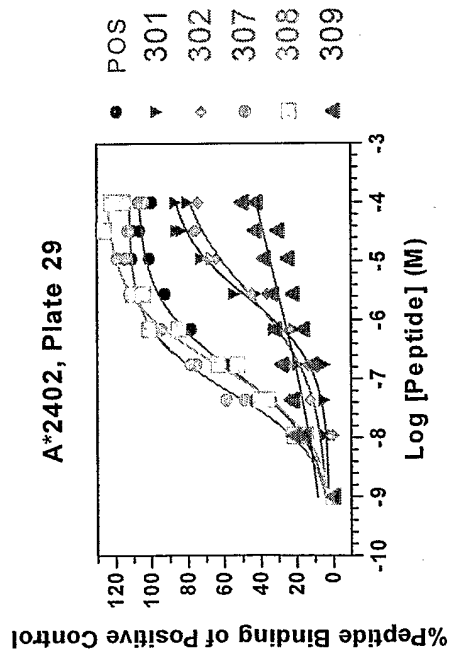


Peptide ID	Affinity ED50 x 10-6M
217	0.32
220	0.01
223	1.15
263	251.00
267	1.39

FIG. 64

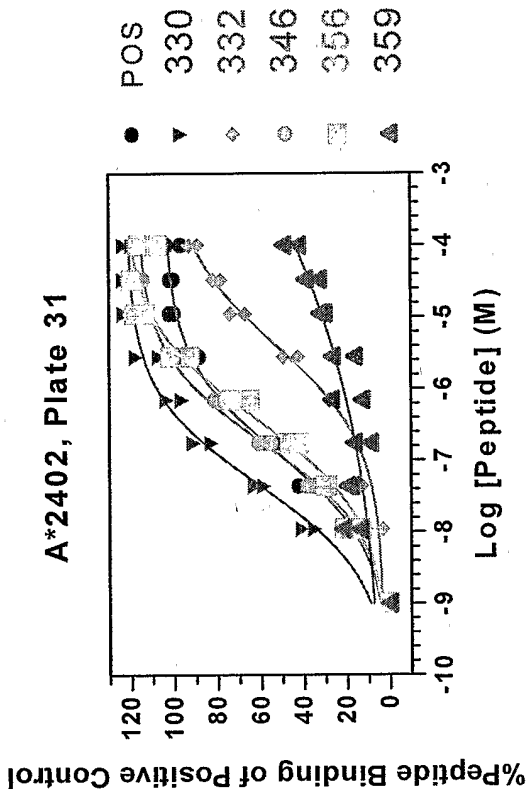


Peptide ID	Affinity ED50 x 10-6M
310	1.64
313	1.56
314	2.04
315	2.89
321	-



Peptide ID	Affinity ED50 x 10-6M
301	2.41
302	2.86
307	0.06
308	0.17
309	3.79

FIG. 65

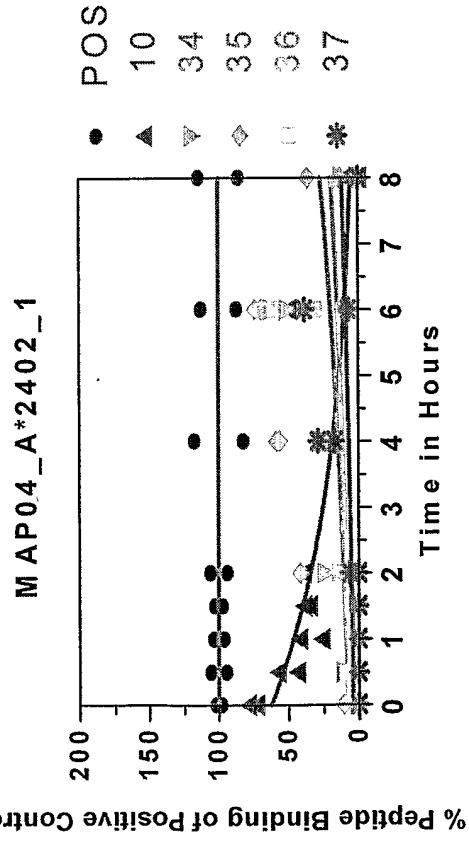


Peptide ID	Affinity ED50 x 10-6M
330	0.04
332	4.02
346	0.17
356	0.39
359	2210.00

FIG. 66

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
10	1.4	76.2
34	12.1	0.0
35	CurveErr	6.1
36	9.2	0.0
37	8.5	0.0

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
38	11.9	0.0
45	0.0	71.0
46	0.4	36.0
49	16.8	51.1
52	5.0	67.6



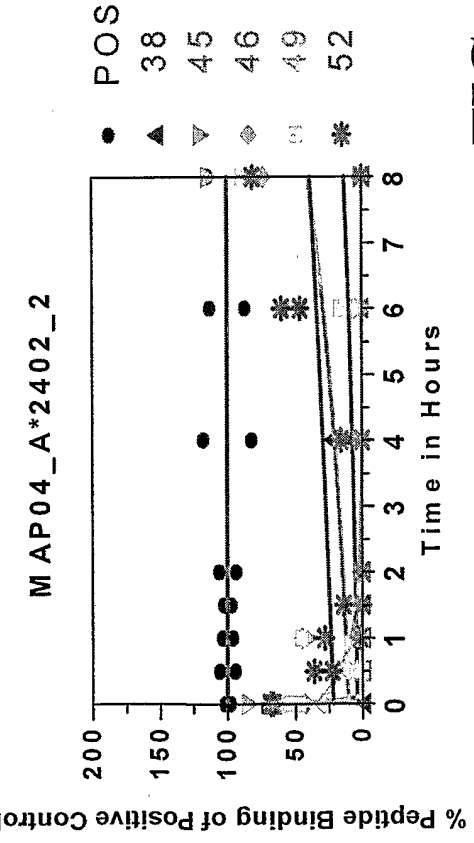
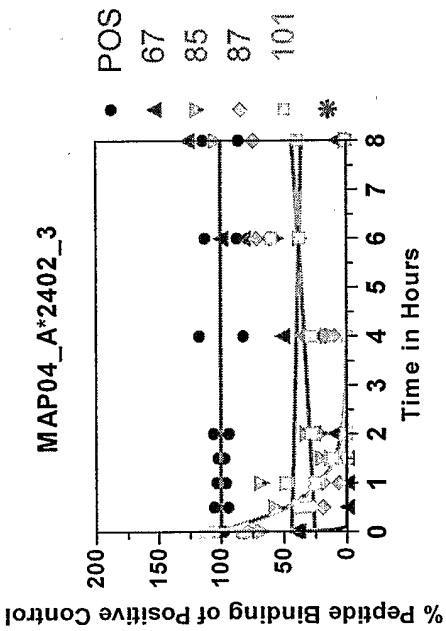
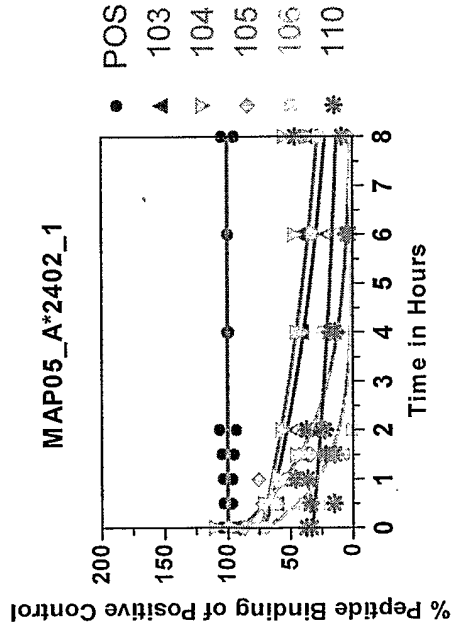


FIG. 67



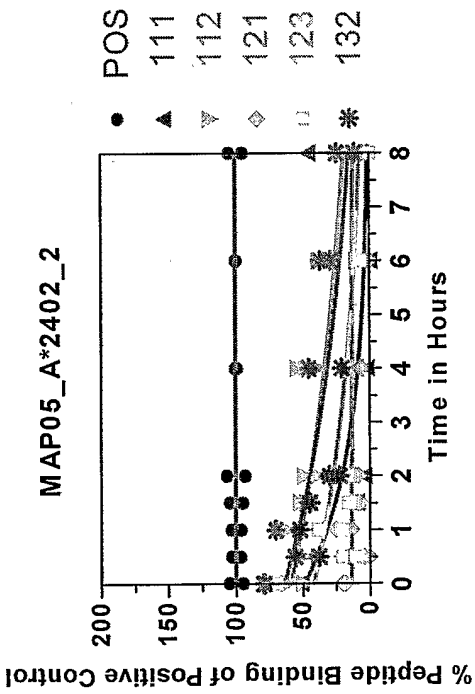
Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
67	0.0	40.0
85	2.9	71.0
87	4.8	83.9
101	0.4	110.2



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
103	1.9	94.1
104	2.1	102.0
105	1.0	93.3
106	0.6	74.4
110	2.1	35.2

FIG. 68

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
111	1.1	52.1
112	2.0	55.4
121	3.1	19.2
123	1.6	73.4
132	1.8	79.4



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
139	2.0	38.6
160	1.8	31.2
167	1.6	71.4
172	1.2	16.5
200	4.5	0.6

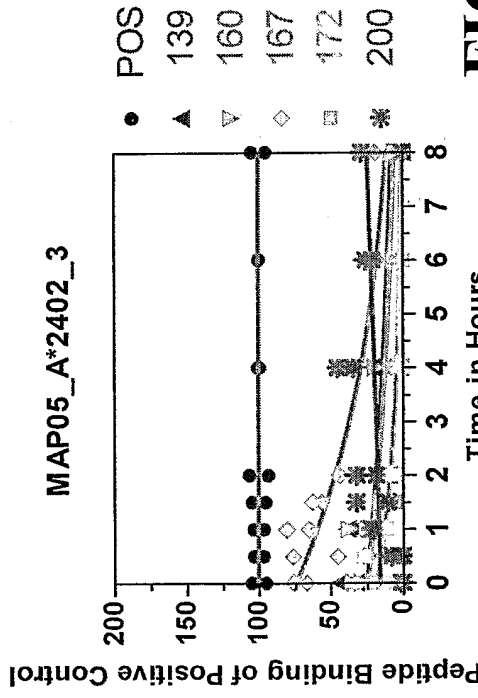
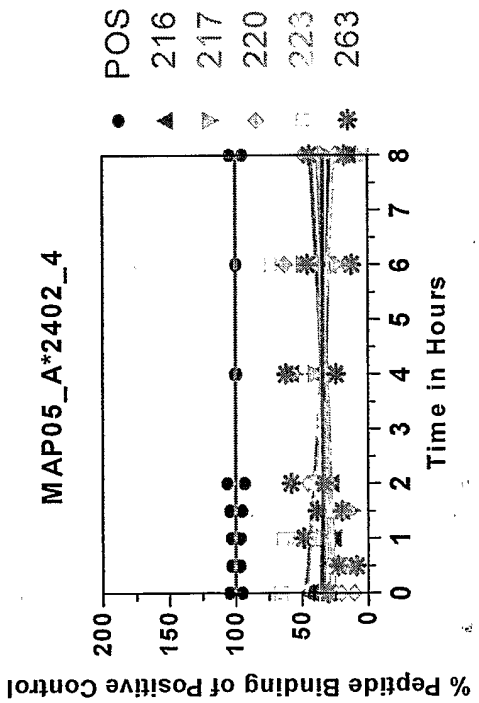


FIG. 69

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
216	2.9	45.3
217	4.3	23.4
220	4.5	15.0
223	2.4	66.3
263	3.3	29.9



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
267	2.5	87.1
268	2.6	68.4
286	2.7	77.8
294	2.9	85.5
297	4.0	57.9

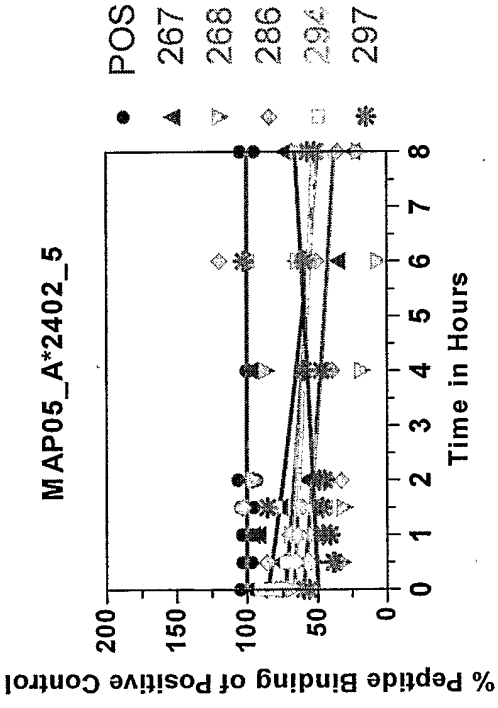
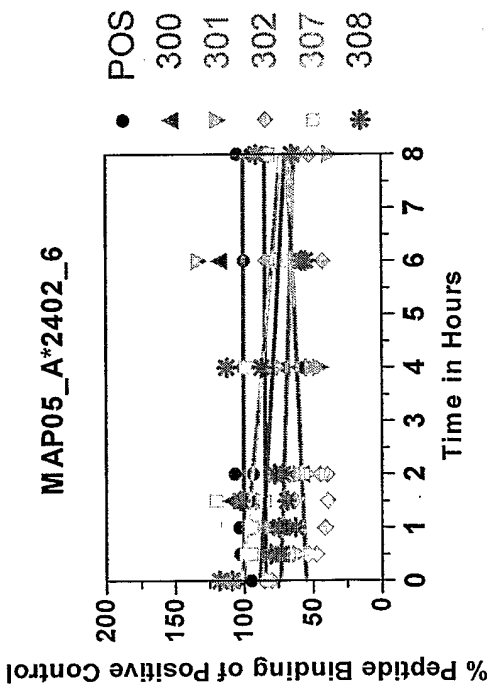


FIG. 70

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
300	3.3	118.0
301	3.0	79.8
302	3.8	82.2
307	2.7	113.0
308	2.9	113.3



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
309	7.3	49.3
310	6.2	74.7
313	4.5	112.7
314	4.4	101.3
315	5.3	68.8

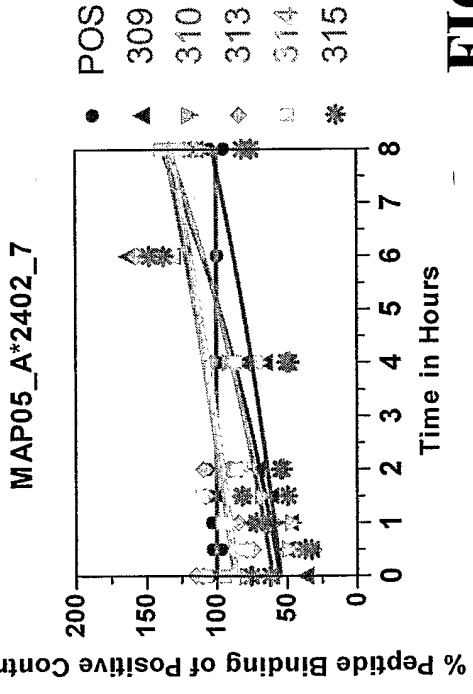
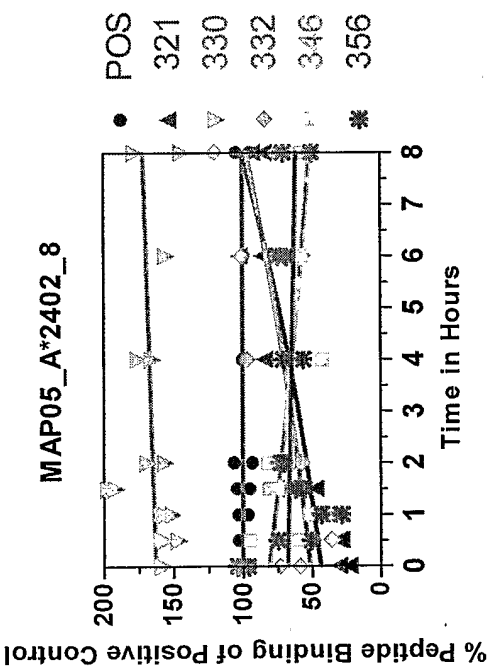


FIG. 71

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
321	6.6	26.7
330	3.4	157.1
332	5.3	65.6
346	2.6	104.6
356	3.1	100.1



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
359	5.1	34.2

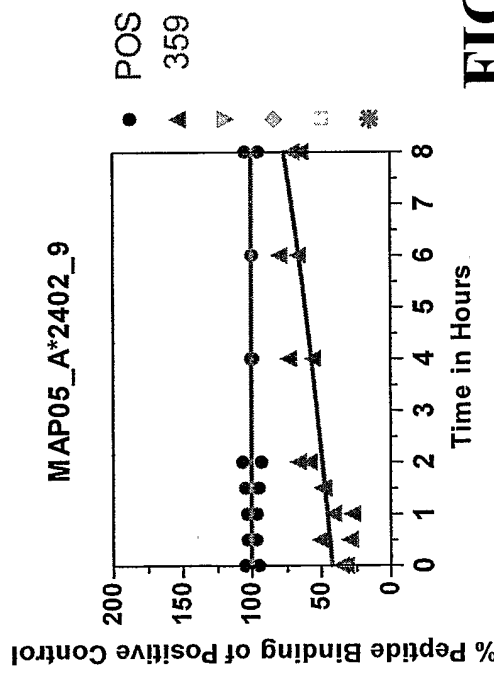


FIG. 72

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
A*2402	330	TWLTYHGAI	123.6	0.04	3.4	157.1	1.62
A*2402	307	QFAPSASAF	107.6	0.06	2.7	113.0	1.07
A*2402	300	KHWPQIAQF	112.7	0.21	3.3	118.0	0.97
A*2402	49	NTASWFTAL	67.1	0.64	16.8	51.1	0.92
A*2402	308	FAPSASAFF	123.2	0.17	2.9	113.3	0.91
A*2402	346	QFKDNVILL	117.9	0.17	2.6	104.6	0.81
A*2402	313	SAFFGMSRI	115.4	1.56	4.5	112.7	0.76
A*2402	356	KHIDAYKTF	113.6	0.39	3.1	100.1	0.74
A*2402	314	AFFGMSRIG	96	2.04	4.4	101.3	0.67
A*2402	294	RQGTDYKHW	106.6	0.33	2.9	85.5	0.65
A*2402	310	PSASAFFGM	91.2	1.64	6.2	74.7	0.64
A*2402	104	ELSPRWYFY	104.6	0.39	2.1	102.0	0.62
A*2402	52	SWFTALTQH	65.2	1.17	5.0	67.6	0.57
A*2402	87	YYRRATRRV	85.2	2.96	4.8	83.9	0.56
A*2402	105	LSPRWYFYY	107.3	0.07	1.0	93.3	0.53
A*2402	315	FFGMSRIGM	67.2	2.89	5.3	68.8	0.50
A*2402	103	KELSPRWYF	97.4	0.75	1.9	94.1	0.50
A*2402	302	WPQIAQFAP	84.5	2.86	3.8	82.2	0.49
A*2402	267	KQYNVTQAF	107.7	1.39	2.5	87.1	0.47
A*2402	268	QYNVTQAFG	97.2	0.61	2.6	68.4	0.46
A*2402	332	LTYHGAIKL	67.8	4.02	5.3	65.6	0.46
A*2402	301	HWPQIAQFA	82.9	2.41	3.0	79.8	0.44
A*2402	309	APSASAFFG	42.5	3.79	7.3	49.3	0.43
A*2402	132	VWVATEGAL	89.8	0.75	1.8	79.4	0.42
A*2402	223	LLLDRLNQL	76.1	1.15	2.4	66.3	0.39
A*2402	123	PYGANKEGI	104.6	0.70	1.6	73.4	0.38
A*2402	286	NFGDQDLIR	74.4	4.47	2.7	77.8	0.37
A*2402	101	KMKELSPRW	117.1	0.14	0.4	110.2	0.34

FIG. 73

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	T0 % Peptide Binding	iScore
A*2402	10	QRSAPRITF	83.2	2.20	1.4	76.2	0.29
A*2402	85	IGYYRRATR	66.8	16.80	2.9	71.0	0.28
A*2402	106	SPRWYFYYL	63.6	0.26	0.6	74.4	0.28
A*2402	216	GETALALLL	71.1	2.29	2.9	45.3	0.28
A*2402	167	TLPKGFYAE	80.6	3.47	1.6	71.4	0.27
A*2402	297	TDYKHWPQI	57.8	20.40	4.0	57.9	0.27
A*2402	112	YYLGTGPEA	66.6	3.23	2.0	55.4	0.25
A*2402	111	FYYLGTGPE	71.9	1.66	1.1	52.1	0.20
A*2402	45	GLPNNTASW	118.5	0.10	0.0	71.0	0.07
A*2402	110	YFYYLGTGP	58.8	0.10	2.1	**35.2**	0.00
A*2402	139	ALNTPKDHI	50.9	5.83	2.0	**38.6**	0.00
A*2402	160	LQLPQGTTL	48.5	10.90	1.8	**31.2**	0.00
A*2402	46	LPNNTASWF	67.7	0.66	0.4	**36.0**	0.00
A*2402	263	RTATKQYNV	50.2	251.00	3.3	**29.9**	0.00
A*2402	359	DAYKTFPPT	43.6	2210.00	5.1	**34.2**	0.00
A*2402	67	FPRGQGVPI	48.5	8.35	0.0	**40.0**	0.00
A*2402	34	NGARPKQRR	50.7		12.1	**0.0**	0.00
A*2402	35	GARPKQRRP	50.4		CurveErr	**6.1**	0.00
A*2402	36	ARPKQRRPQ	43.9		9.2	**0.0**	0.00
A*2402	37	RPKQRRPQG	46.2	0.01	8.5	**0.0**	0.00
A*2402	38	PKQRRPQGL	46.7	0.01	11.9	**0.0**	0.00
A*2402	121	SLPYGANKE	43.5	193.00	3.1	**19.2**	0.00
A*2402	172	FYAEGSRGG	45.8	587.00	1.2	**16.5**	0.00
A*2402	200	PGSSRGNSP	207.4	0.00	4.5	**0.6**	0.00
A*2402	217	ETALALLLL	51	0.32	4.3	**23.4**	0.00
A*2402	220	LALLLLDRL	40.1	0.01	4.5	**15.0**	0.00
A*2402	321	IGMEVTPSG	45		6.6	**26.7**	0.00

FIG. 74

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
A*2402	330	TWLTYHGAI	123.6	0.04	3.4	157.1	1.62	1	36	6
A*2402	**307**	**QFAPSASAF**	**107.6**	**0.06**	**2.7**	**113.0**	**1.07**	**2**	**2**	**3**
A*2402	300	KHWPQIAQF	112.7	0.21	3.3	118.0	0.97	3	59	11
A*2402	49	NTASWFTAL	67.1	0.64	16.8	51.1	0.92	4	15	30
A*2402	308	FAPSASAFF	123.2	0.17	2.9	113.3	0.91	5	28	26
A*2402	346	QFKDNVILL	117.9	0.17	2.6	104.6	0.81	6	1	2
A*2402	313	SAFFGMSRI	115.4	1.56	4.5	112.7	0.76	7	42	56
A*2402	356	KHIDAYKTF	113.6	0.39	3.1	100.1	0.74	8	47	7
A*2402	314	AFFGMSRIG	96	2.04	4.4	101.3	0.67	9	178	72
A*2402	294	RQGTDYKHW	106.6	0.33	2.9	85.5	0.65	10	76	280
A*2402	310	PSASAFFGM	91.2	1.64	6.2	74.7	0.64	11	176	190
A*2402	104	ELSPRWYFY	104.6	0.39	2.1	102.0	0.62	12	123	158
A*2402	52	SWFTALTQH	65.2	1.17	5.0	67.6	0.57	13	>250	319
A*2402	87	YYRRATRRV	85.2	2.96	4.8	83.9	0.56	14	13	60
A*2402	105	LSPRWYFYY	107.3	0.07	1.0	93.3	0.53	15	110	114
A*2402	315	FFGMSRIGM	67.2	2.89	5.3	68.8	0.50	16	30	73
A*2402	103	KELSPRWYF	97.4	0.75	1.9	94.1	0.50	17	51	8
A*2402	302	WPQIAQFAP	84.5	2.86	3.8	82.2	0.49	18	>250	282
A*2402	267	KQYNVTQAF	107.7	1.39	2.5	87.1	0.47	19	8	24
A*2402	268	QYNVTQAFG	97.2	0.61	2.6	68.4	0.46	20	45	52
A*2402	332	LTYHGAIKL	67.8	4.02	5.3	65.6	0.46	21	21	27
A*2402	301	HWPQIAQFA	82.9	2.41	3.0	79.8	0.44	22	71	131
A*2402	309	APSASAFFG	42.5	3.79	7.3	49.3	0.43	23	>250	284
A*2402	132	VWVATEGAL	89.8	0.75	1.8	79.4	0.42	24	12	17
A*2402	223	LLLDRLNQL	76.1	1.15	2.4	66.3	0.39	25	3	5
A*2402	123	PYGANKEGI	104.6	0.70	1.6	73.4	0.38	26	14	1
A*2402	286	NFGDQDLIR	74.4	4.47	2.7	77.8	0.37	27	174	66
A*2402	101	KMKELSPRW	117.1	0.14	0.4	110.2	0.34	28	70	157

FIG. 75

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
A*2402	10	QRSAPRITF	83.2	2.20	1.4	76.2	0.29	29	78	44
A*2402	85	IGYYRRATR	66.8	16.80	2.9	71.0	0.28	30	>250	232
A*2402	106	SPRWYFYYL	63.6	0.26	0.6	74.4	0.28	31	19	46
A*2402	216	GETALALLL	71.1	2.29	2.9	45.3	0.28	32	60	21
A*2402	167	TLPKGFYAE	80.6	3.47	1.6	71.4	0.27	33	224	78
A*2402	297	TDYKHWPQI	57.8	20.40	4.0	57.9	0.27	34	160	10
A*2402	112	YYLGTGPEA	66.6	3.23	2.0	55.4	0.25	35	4	16
A*2402	111	EYYLGTGPE	71.9	1.66	1.1	52.1	0.20	36	53	48
A*2402	45	GLPNNTASW	118.5	0.10	0.0	71.0	0.07	37	113	148
A*2402	110	YFYYLGTGP	58.8	0.10	2.1	35.2	0.00	38	175	69
A*2402	139	ALNTPKDHI	50.9	5.83	2.0	38.6	0.00	39	35	36
A*2402	160	LQLPQGTTL	48.5	10.90	1.8	31.2	0.00	40	5	9
A*2402	46	LPNNTASWF	67.7	0.66	0.4	36.0	0.00	41	27	45
A*2402	263	RTATKQYNV	50.2	251.00	3.3	29.9	0.00	42	79	269
A*2402	359	DAYKTFPPT	43.6	2210.00	5.1	34.2	0.00	43	122	198
A*2402	**67**	**FPRGQGVPI**	**48.5**	**8.35**	**0.0**	**40.0**	**0.00**	**44**	**44**	**59**
A*2402	34	NGARPKQRR	50.7		12.1	0.0	0.00	45	>250	313
A*2402	35	GARPKQRRP	50.4		CurveErr	6.1	0.00	46	>250	222
A*2402	36	ARPKQRRPQ	43.9		9.2	0.0	0.00	47	>250	106
A*2402	37	RPKQRRPQG	46.2	0.01	8.5	0.0	0.00	48	204	314
A*2402	38	PKQRRPQGL	46.7	0.01	11.9	0.0	0.00	49	172	15
A*2402	121	SLPYGANKE	43.5	193.00	3.1	19.2	0.00	50	212	89
A*2402	**172**	**FYAEGSRGG**	**45.8**	**587.00**	**1.2**	**16.5**	**0.00**	**51**	**52**	**18**
A*2402	200	PGSSRGNSP	207.4	0.00	4.5	0.6	0.00	52	>250	256
A*2402	217	ETALALLLL	51	0.32	4.3	23.4	0.00	53	26	22
A*2402	220	LALLLLDRL	40.1	0.01	4.5	15.0	0.00	54	6	23
A*2402	321	IGMEVTPSG	45		6.6	26.7	0.00	55	190	133

FIG. 76

Allele	Peptide ID	Peptide Sequence
A*2402	330	TWLTYHGAI
A*2402	307	QFAPSASAF
A*2402	300	KHWPQIAQF
A*2402	49	NTASWFTAL
A*2402	308	FAPSASAFF
A*2402	346	QFKDNVILL
A*2402	313	SAFFGMSRI
A*2402	356	KHIDAYKTF
A*2402	314	AFFGMSRIG
A*2402	294	RQGTDYKHW
A*2402	310	PSASAFFGM
A*2402	104	ELSPRWYFY
A*2402	52	SWFTALTQH
A*2402	87	YYRRATRRV
A*2402	105	LSPRWYFYY
A*2402	315	FFGMSRIGM
A*2402	103	KELSPRWYF
A*2402	302	WPQIAQFAP
A*2402	267	KQYNVTQAF

Allele	Peptide ID	Peptide Sequence
A*2402	268	QYNVTQAFG
A*2402	332	LTYHGAIKL
A*2402	301	HWPQIAQFA
A*2402	309	APSASAFFG
A*2402	132	VWVATEGAL
A*2402	223	LLLDRLNQL
A*2402	123	PYGANKEGI
A*2402	286	NFGDQDLIR
A*2402	101	KMKELSPRW
A*2402	10	QRSAPRITF
A*2402	85	IGYYRRATR
A*2402	106	SPRWYFYYL
A*2402	216	GETALALLL
A*2402	167	TLPKGFYAE
A*2402	297	TDYKHWPQI
A*2402	112	YYLGTGPEA
A*2402	111	FYYLGTGPE
A*2402	45	GLPNNTASW

FIG. 77

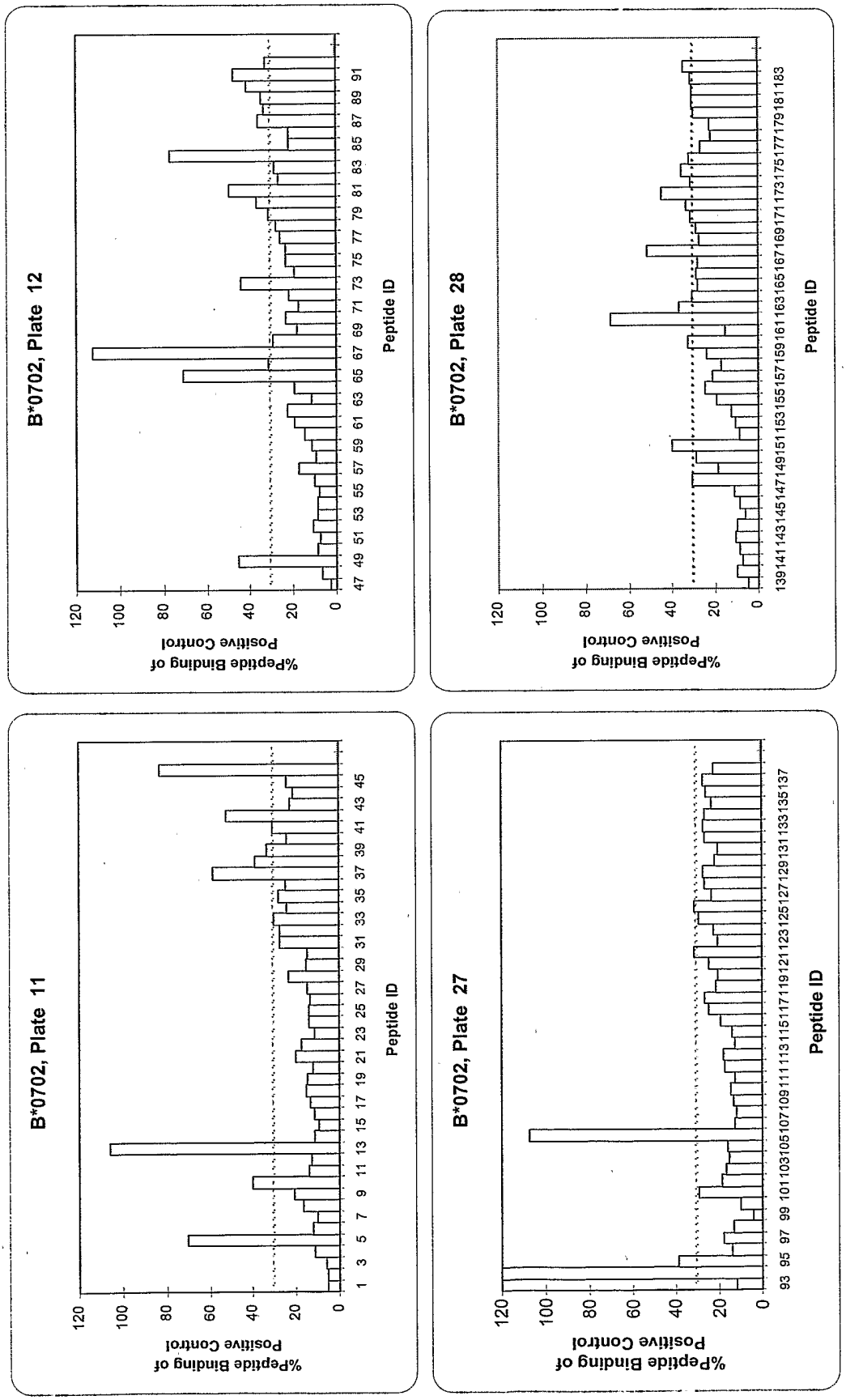

B*0702, Plate 12
%Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 28
%Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 11
%Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 27
%Peptide Binding of Positive Control
Peptide ID

FIG. 78

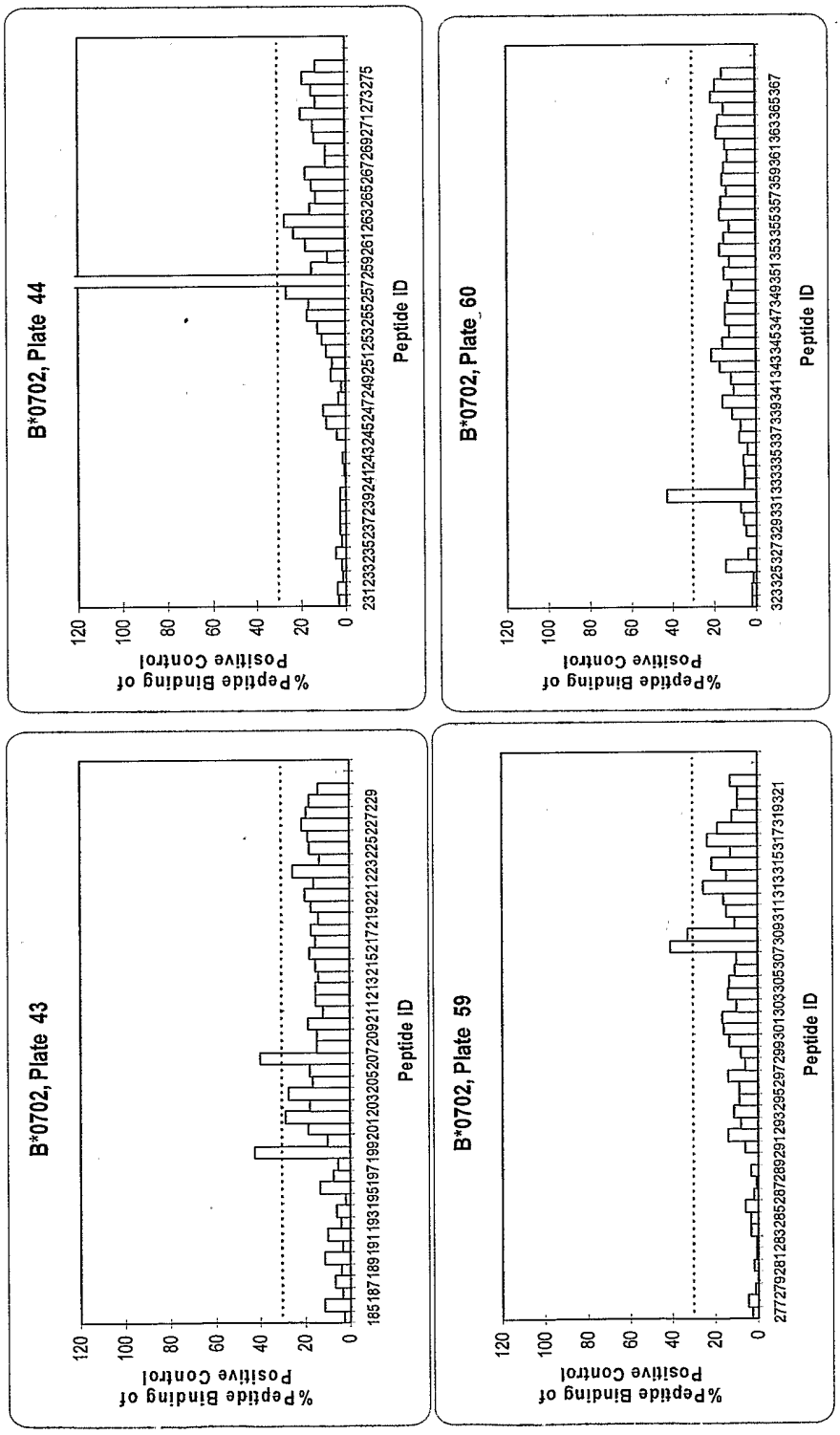
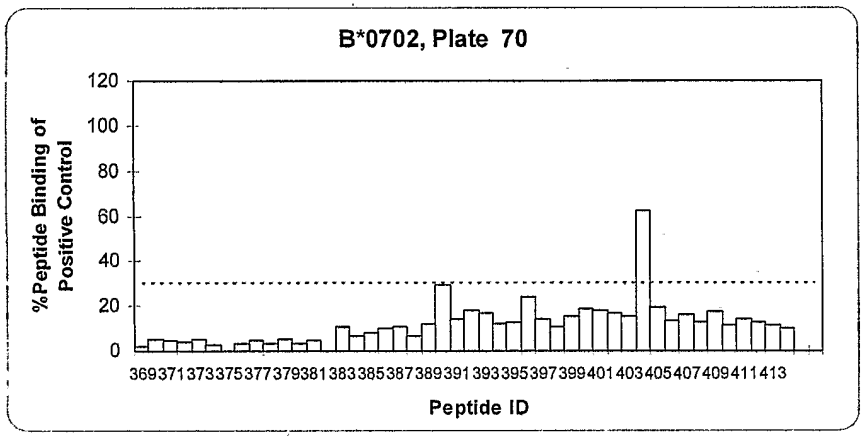

B*0702, Plate 44
% Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 60
% Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 43
% Peptide Binding of Positive Control
Peptide ID
B*0702, Plate 59
% Peptide Binding of Positive Control
Peptide ID

FIG. 79



Allele	Peptide ID	% Peptide Binding
B*0702	5	70.6
B*0702	10	40.1
B*0702	13	105.8
B*0702	33	30.2
B*0702	37	58.5
B*0702	38	38.8
B*0702	39	33.7
B*0702	41	30.9
B*0702	42	52.6
B*0702	46	83.1
B*0702	49	45.5
B*0702	65	70.8
B*0702	66	31.8
B*0702	67	112.6
B*0702	73	44.4
B*0702	79	31.4
B*0702	80	37.1
B*0702	81	49.8
B*0702	84	76.9
B*0702	87	35.9
B*0702	88	33.8
B*0702	89	35.1
B*0702	90	41.5
B*0702	91	47.5
B*0702	92	32.9
B*0702	94	144.8
B*0702	95	38.7

Allele	Peptide ID	% Peptide Binding
B*0702	106	107.2
B*0702	122	31.5
B*0702	126	31.7
B*0702	148	30.9
B*0702	151	40.0
B*0702	160	32.6
B*0702	162	68.7
B*0702	163	36.8
B*0702	164	31.0
B*0702	168	51.7
B*0702	171	31.3
B*0702	172	33.6
B*0702	173	45.2
B*0702	174	31.5
B*0702	175	35.6
B*0702	176	32.2
B*0702	180	30.0
B*0702	181	30.6
B*0702	182	31.0
B*0702	183	31.3
B*0702	184	34.8
B*0702	199	43.0
B*0702	207	40.0
B*0702	258	125.7
B*0702	308	40.7
B*0702	309	32.8
B*0702	332	42.6
B*0702	404	62.3

FIG. 80

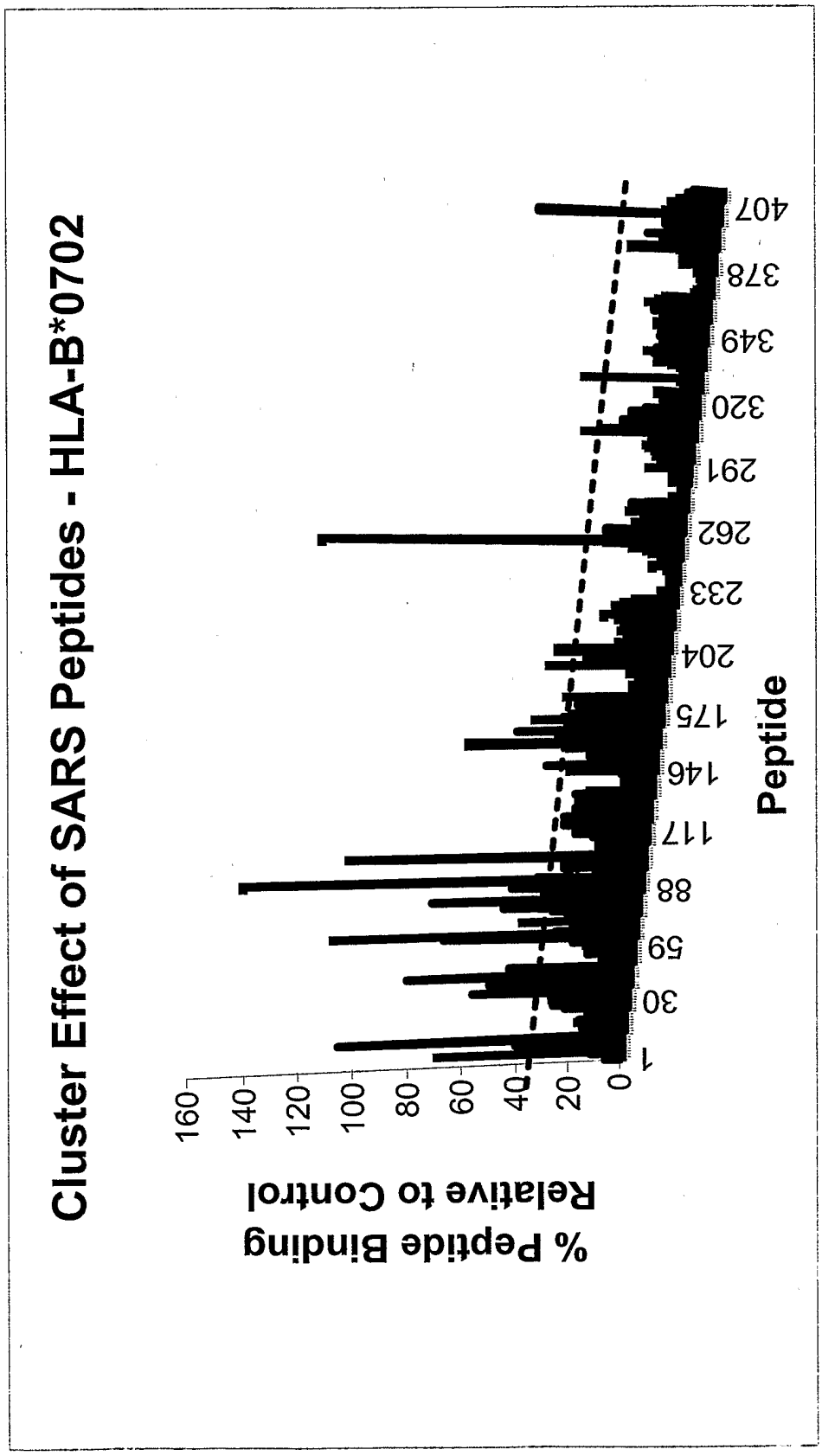
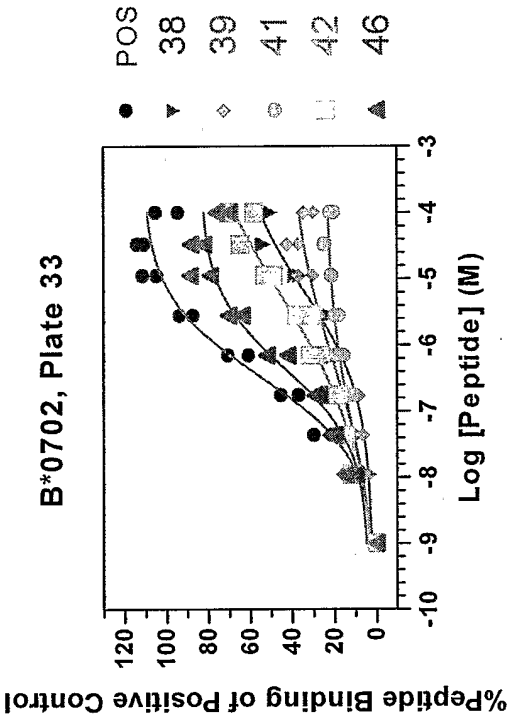
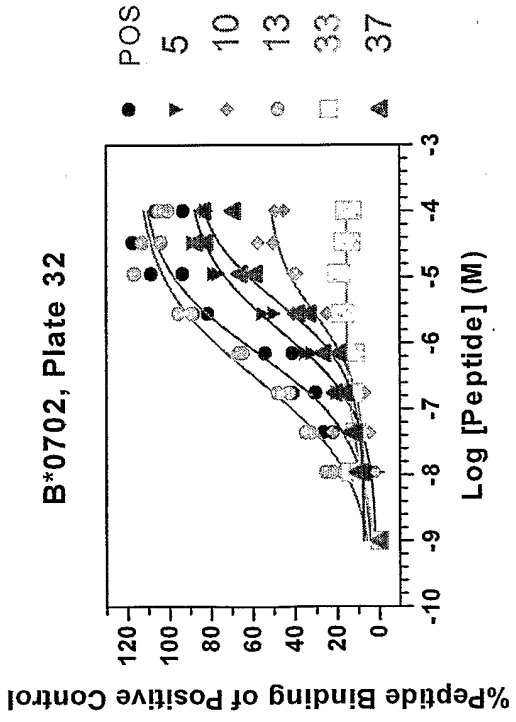

Cluster Effect of SARS Peptides - HLA-B*0702
% Peptide Binding Relative to Control
0
20
40
60
80
100
120
140
160
Peptide
1
30
59
88
117
146
175
204
233
262
291
320
349
378
407

FIG. 81

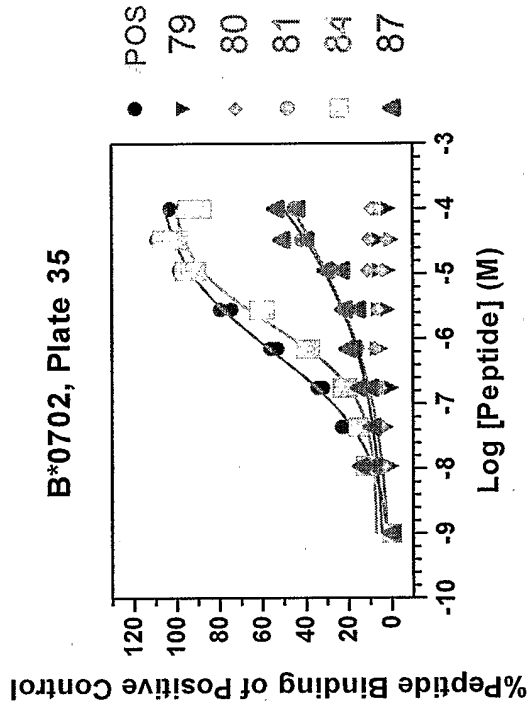


Peptide ID	Affinity ED50 x 10-6M
38	6.84
39	-0.56
41	0.07
42	6.40
46	0.45

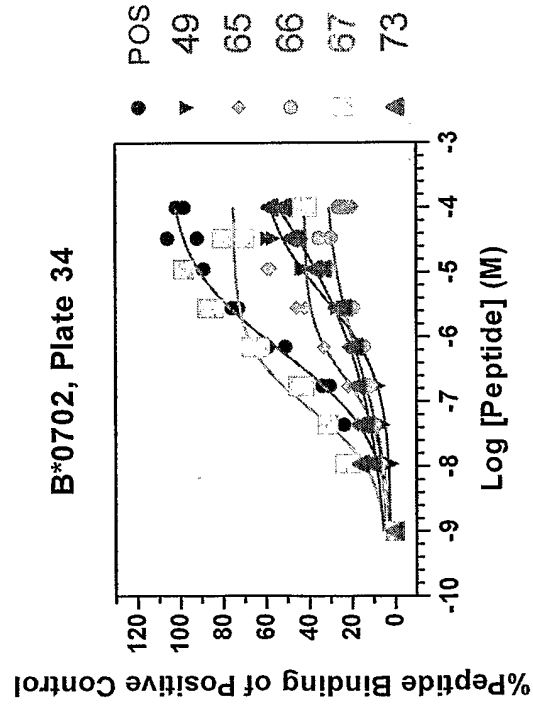


Peptide ID	Affinity ED50 x 10-6M
5	1.53
10	2.63
13	0.30
33	0.01
37	4.26

FIG. 82

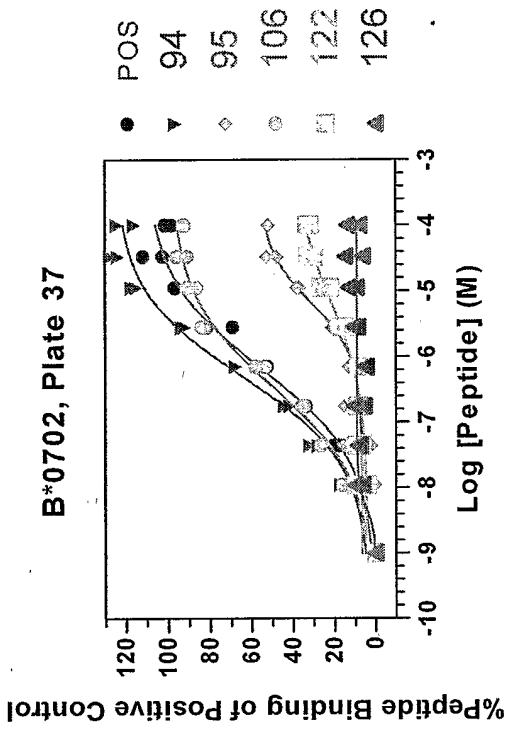


Peptide ID	Affinity ED50 x 10-6M
79	
80	
81	54.90
84	1.57
87	427.00

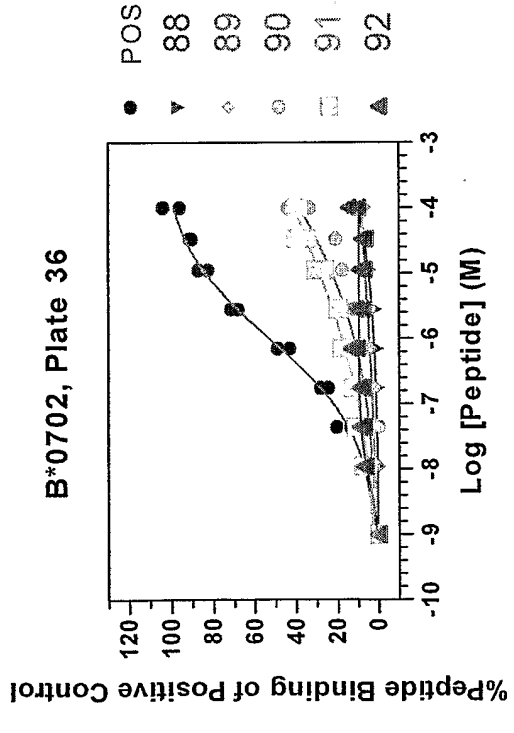


Peptide ID	Affinity ED50 x 10-6M
49	4.15
65	0.24
66	0.43
67	0.08
73	302.00

FIG. 83

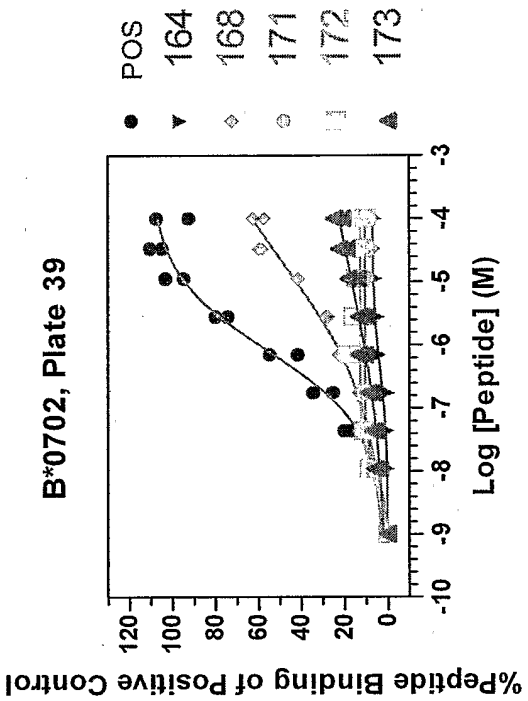


Peptide ID	Affinity ED50 x 10-6M
94	0.48
95	6.72
106	0.35
122	6.92
126	0.00

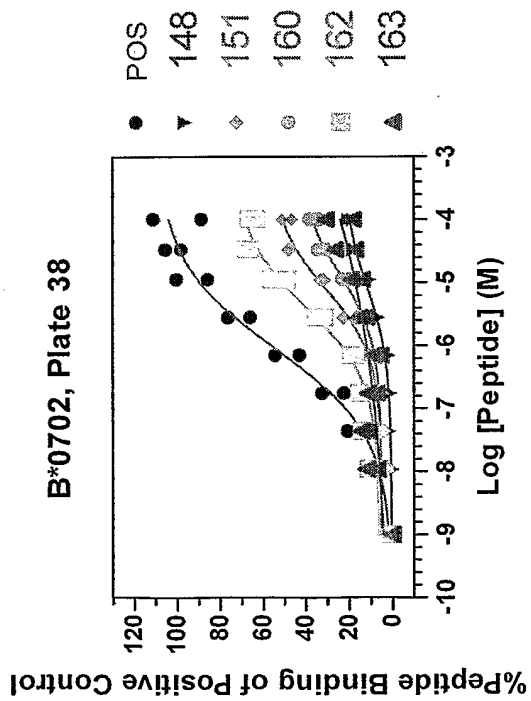


Peptide ID	Affinity ED50 x 10-6M
88	169000.00
89	3.72
90	190.00
91	21.70
92	0.01

FIG. 84

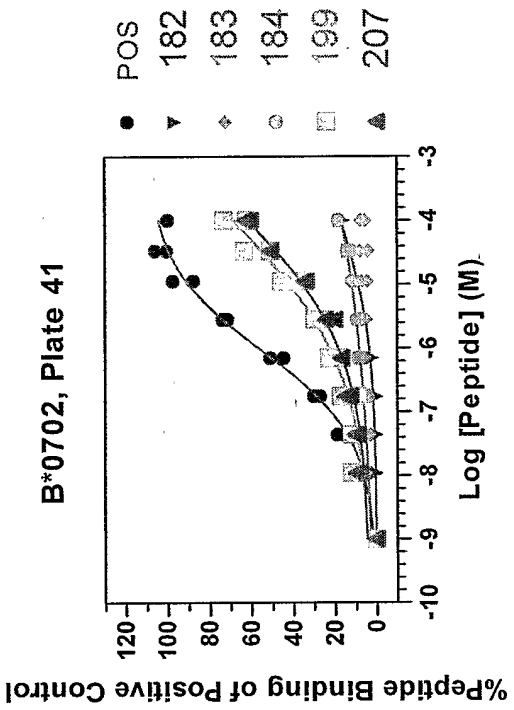


Peptide ID	Affinity ED50 x 10-6M
164	0.40
168	20.20
171	0.01
172	0.01
173	21.00

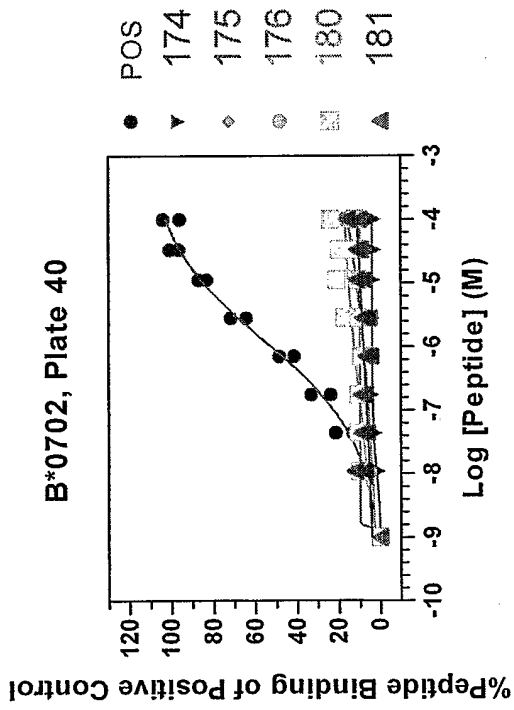


Peptide ID	Affinity ED50 x 10-6M
148	8.77
151	8.08
160	13.40
162	4.13
163	249000.00

FIG. 85

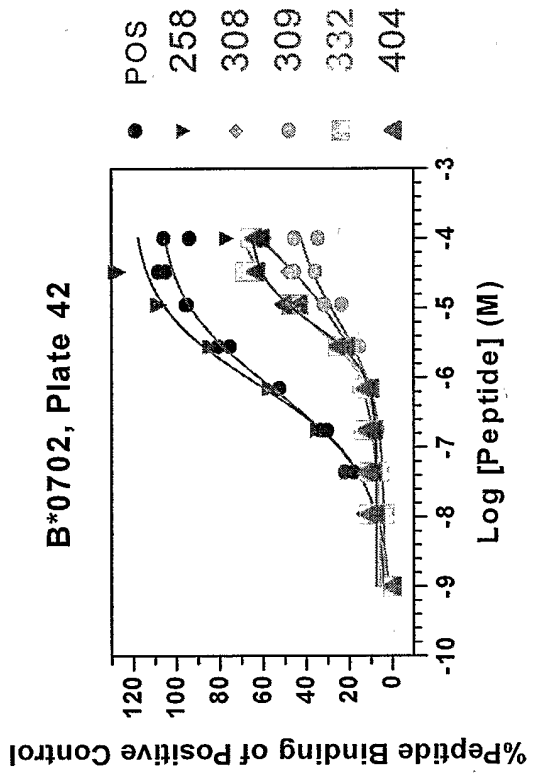


Peptide ID	Affinity ED50 x 10-6M
182	59.80
183	
184	0.00
199	70.60
207	125.00



Peptide ID	Affinity ED50 x 10-6M
174	0.01
175	0.00
176	44700.00
180	0.09
181	

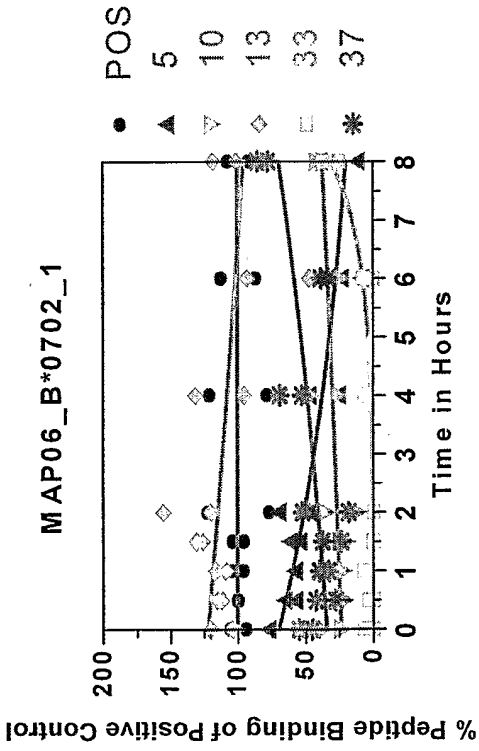
FIG. 86



Peptide ID	Affinity ED50 x 10-6M
258	0.79
308	87.90
309	7.15
332	6.74
404	5.86

FIG. 87

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
5	1.5	67.5
10	2.9	29.8
13	2.1	111.8
33	-1.7	3.6
37	3.4	49.8



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
38	33.1	16.9
39	3.7	14.7
41	5.3	7.9
42	3.4	37.5
46	0.9	85.3

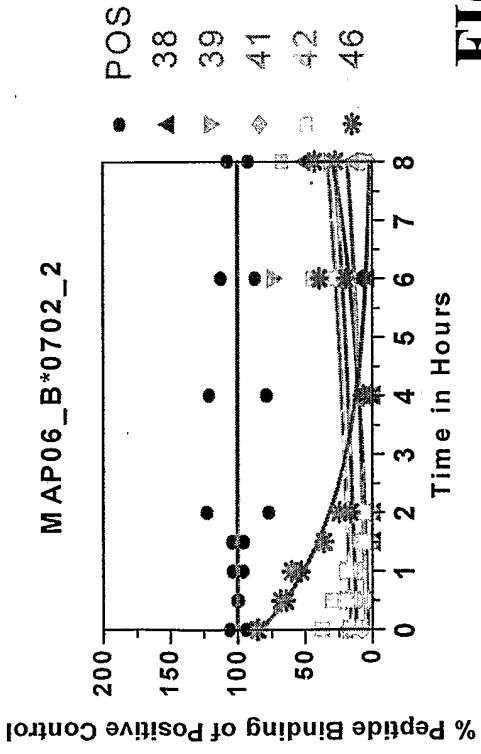
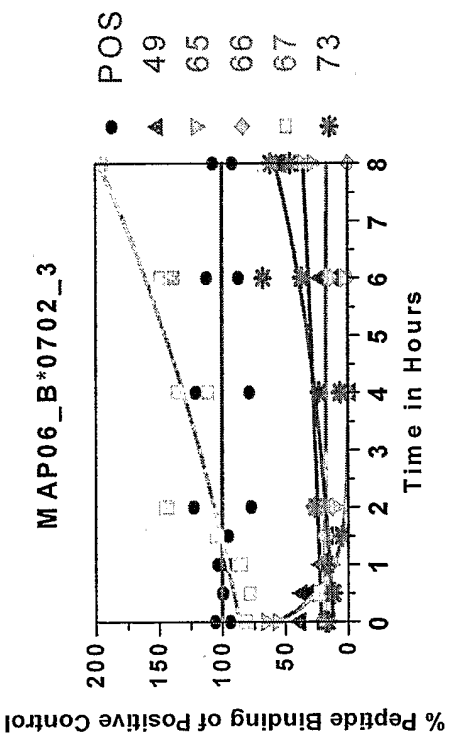


FIG. 88

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
49	3.0	40.4
65	0.4	59.0
66	2.3	21.2
67	3.6	82.1
73	6.9	17.4



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
79	13.0	0.9
80	140.4	5.0
81	6.6	29.9
84	19.1	87.6
87	-63.2	19.9

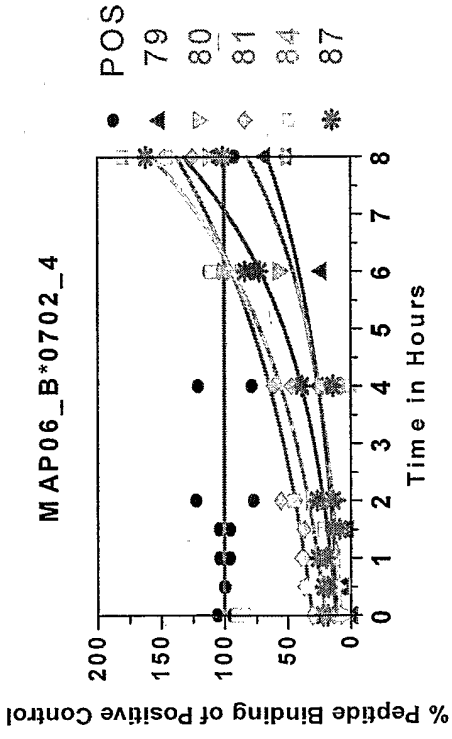
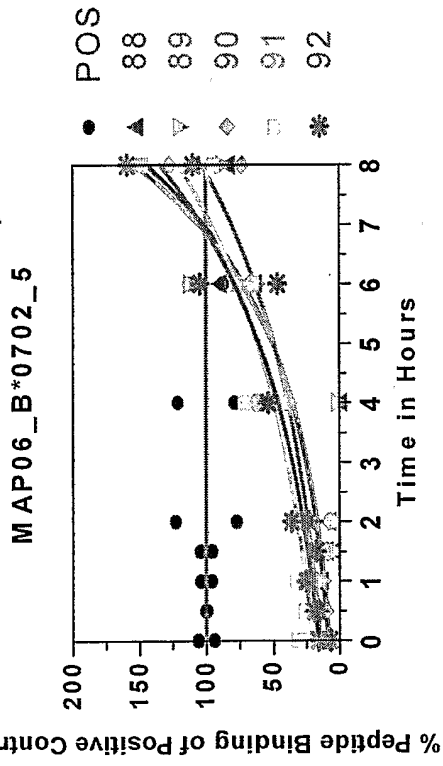


FIG. 89

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
88	-12.2	14.5
89	-9.2	8.7
90	14.0	12.8
91	9.9	28.0
92	25.0	11.3



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
94	4.5	161.5
95	10.1	44.7
106	4.6	124.4
122	11.9	24.1
126	20.1	11.2

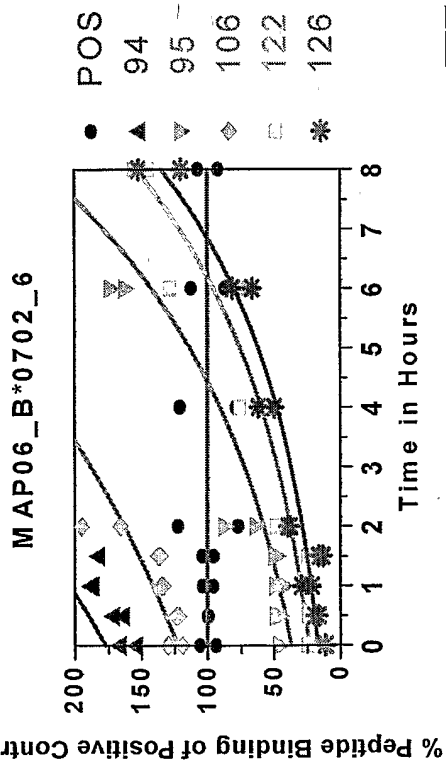
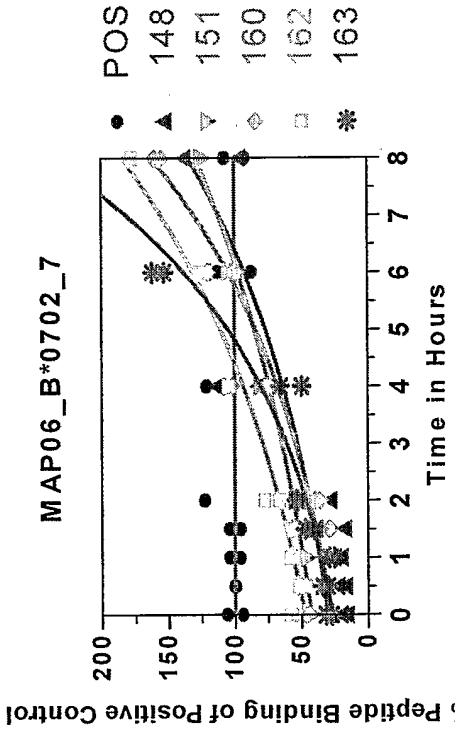


FIG. 90

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
148	6.5	18.9
151	4.5	42.2
160	9.3	29.5
162	5.6	57.8
163	33.3	29.5



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
164	31.2	17.1
168	36.8	41.3
171	-1898.6	8.0
172	11.3	3.1
173	9.3	13.7

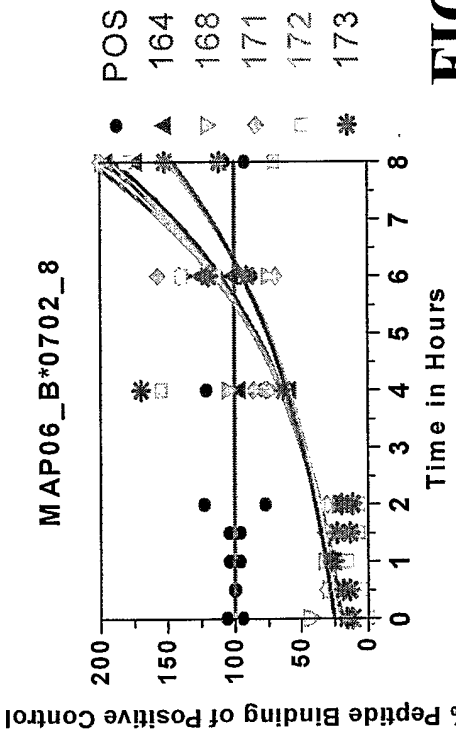
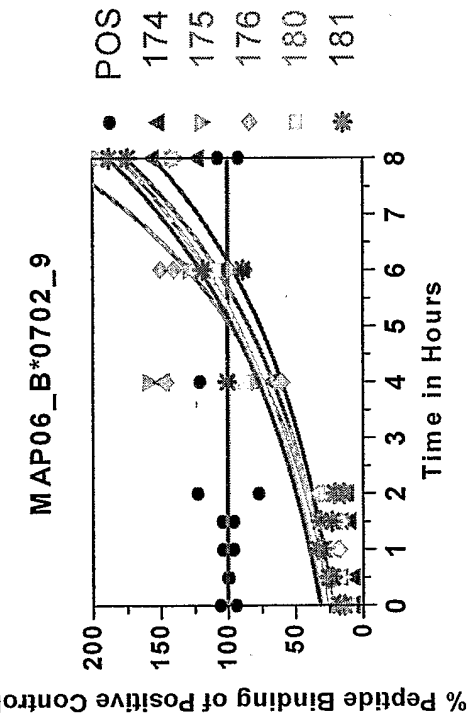


FIG. 91

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
174	12.3	8.8
175	13.8	12.1
176	56.2	18.8
180	9.6	13.5
181	9.8	16.0



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
182	9.2	12.8

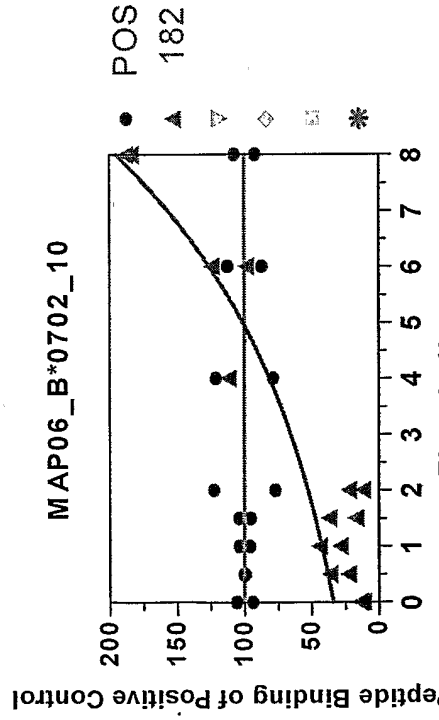
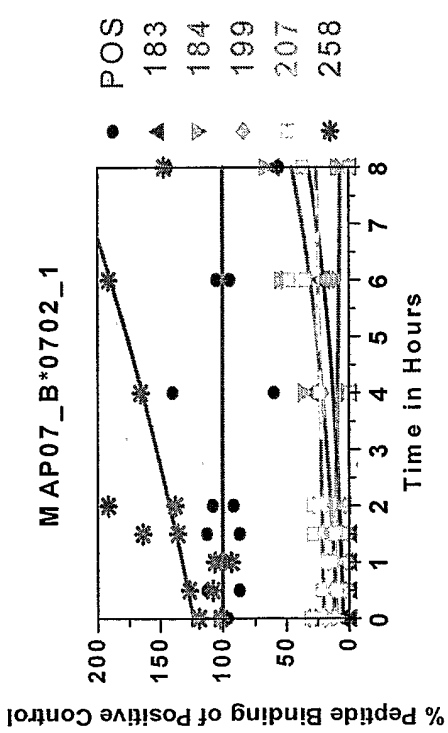


FIG. 92

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
183	12.5	3.6
184	6.9	10.8
199	1.9	29.3
207	2.6	27.5
258	3.1	110.3



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
308	3.1	25.5
309	10.7	22.9
332	8.1	34.8
404	7.0	37.5

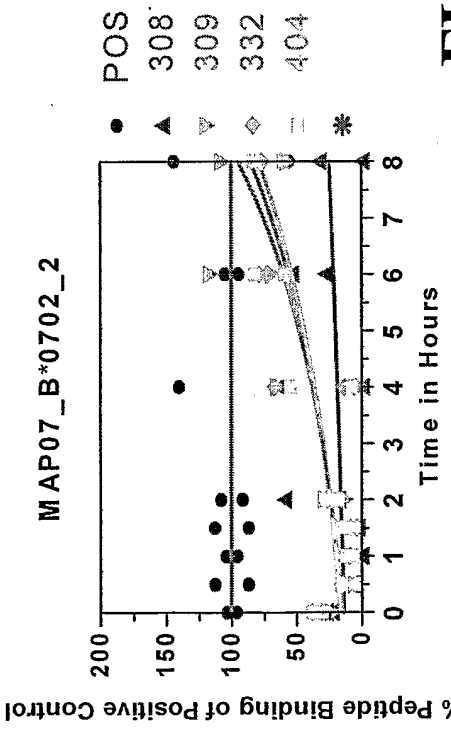


FIG. 93

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
B*0702	84	QIGYYRRAT	76.9	1.57	19.1	87.6	1.29
B*0702	94	RVRGGDGKM	144.8	0.48	4.5	161.5	1.26
B*0702	106	SPRWYFYYL	107.2	0.35	4.6	124.4	1.09
B*0702	67	FPRGQGVPI	112.6	0.08	3.6	82.1	0.91
B*0702	258	KPRQKRTAT	125.7	0.79	3.1	110.3	0.71
B*0702	13	APRITFGGP	105.8	0.30	2.1	111.8	0.70
B*0702	168	LPKGFYAEG	51.7	20.20	36.8	41.3	0.63
B*0702	95	VRGGDGKMK	38.7	6.72	10.1	44.7	0.42
B*0702	162	LPQGTTLPK	68.7	4.13	5.6	57.8	0.42
B*0702	46	LPNNTASWF	83.1	0.45	0.9	85.3	0.34
B*0702	404	FSRQLQNSM	62.3	5.86	7.0	37.5	0.32
B*0702	332	LTYHGAIKL	42.6	6.74	8.1	34.8	0.31
B*0702	5	GPQSNQRSA	70.6	1.53	1.5	67.5	0.30
B*0702	37	RPKQRRPQG	58.5	4.26	3.4	49.8	0.29
B*0702	151	NPNNNAATV	40.0	8.08	4.5	42.2	0.26
B*0702	49	NTASWFTAL	45.5	4.15	3.0	40.4	0.23
B*0702	42	RPQGLPNNT	52.6	6.40	3.4	37.5	0.22
B*0702	65	LRFPRGQGV	70.8	0.24	0.4	59.0	0.18
B*0702	171	GFYAEGSRG	31.3	0.01	-1898.6	**8.0**	**0.00**
B*0702	175	EGSRGGSQA	35.6	0.00	13.8	**12.1**	**0.00**
B*0702	92	TRRVRGGDG	32.9	0.01	25.0	**11.3**	**0.00**
B*0702	126	ANKEGIVWV	31.7	0.00	20.1	**11.2**	**0.00**
B*0702	164	QGTTLPKGF	31.0	0.40	31.2	**17.1**	**0.00**
B*0702	174	AEGSRGGSQ	31.5	0.01	12.3	**8.8**	**0.00**
B*0702	38	PKQRRPQGL	38.8	6.84	33.1	**16.9**	**0.00**
B*0702	180	GSQASSRSS	30.0	0.09	9.6	**13.5**	**0.00**
B*0702	122	LPYGANKEG	31.5	6.92	11.9	**24.1**	**0.00**
B*0702	87	YYRRATRRV	35.9	427.00	-63.2	**19.9**	**0.00**

FIG. 94

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
B*0702	160	LQLPQGTTL	32.6	13.40	9.3	29.5	0.00
B*0702	309	APSASAFFG	32.8	7.15	10.7	22.9	0.00
B*0702	91	ATRRVRGGD	47.5	21.70	9.9	28.0	0.00
B*0702	10	QRSAPRITF	40.1	2.63	2.9	29.8	0.00
B*0702	66	RFPRGQGVP	31.8	0.43	2.3	21.2	0.00
B*0702	172	FYAEGSRGG	33.6	0.01	11.3	3.1	0.00
B*0702	41	RRPQGLPNN	30.9	0.07	5.3	7.9	0.00
B*0702	81	PDDQIGYYR	49.8	54.90	6.6	29.9	0.00
B*0702	39	KQRRPQGLP	33.7	0.56	3.7	14.7	0.00
B*0702	148	GTRNPNNNA	30.9	8.77	6.5	18.9	0.00
B*0702	173	YAEGSRGGS	45.2	21.00	9.3	13.7	0.00
B*0702	89	RRATRRVRG	35.1	3.72	-9.2	8.7	0.00
B*0702	176	GSRGGSQAS	32.2	44700.00	56.2	18.8	0.00
B*0702	90	RATRRVRGG	41.5	190.00	14.0	12.8	0.00
B*0702	182	QASSRSSSR	31.0	59.80	9.2	12.8	0.00
B*0702	308	FAPSASAFF	40.7	87.90	3.1	25.5	0.00
B*0702	163	PQGTTLPKG	36.8	249000.00	33.3	29.5	0.00
B*0702	207	SPARMASGG	40.0	125.00	2.6	27.5	0.00
B*0702	199	TPGSSRGNS	43.0	70.60	1.9	29.3	0.00
B*0702	73	VPINTNSGP	44.4	302.00	6.9	17.4	0.00
B*0702	33	RNGARPKQR	30.2	0.01	-1.7	3.6	0.00
B*0702	88	YRRATRRVR	33.8	169000.00	-12.2	14.5	0.00
B*0702	184	SSRSSSRSR	34.8	0.00	6.9	10.8	0.00
B*0702	79	SGPDDQIGY	31.4		13.0	0.9	0.00
B*0702	80	GPDDQIGYY	37.1		140.4	5.0	0.00
B*0702	181	SQASSRSSS	30.6		9.8	16.0	0.00
B*0702	183	ASSRSSSRS	31.3		12.5	3.6	0.00

FIG. 95

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
B*0702	84	QIGYYRRAT	76.9	1.57	19.1	87.6	1.29	1	89	83
B*0702	**94**	**RVRGGDGKM**	**144.8**	**0.48**	**4.5**	**161.5**	**1.26**	**2**	**3**	**46**
B*0702	**106**	**SPRWYFYYL**	**107.2**	**0.35**	**4.6**	**124.4**	**1.09**	**3**	**1**	**2**
B*0702	**67**	**FPRGQGVPI**	**112.6**	**0.08**	**3.6**	**82.1**	**0.91**	**4**	**2**	**1**
B*0702	**258**	**KPRQKRTAT**	**125.7**	**0.79**	**3.1**	**110.3**	**0.71**	**5**	**4**	**3**
B*0702	**13**	**APRITFGGP**	**105.8**	**0.30**	**2.1**	**111.8**	**0.70**	**6**	**10**	**18**
B*0702	168	LPKGFYAEG	51.7	20.20	36.8	41.3	0.63	7	85	31
B*0702	95	VRGGDGKMK	38.7	6.72	10.1	44.7	0.42	8	>250	193
B*0702	162	LPQGTTLPK	68.7	4.13	5.6	57.8	0.42	9	81	13
B*0702	46	LPNNTASWF	83.1	0.45	0.9	85.3	0.34	10	56	11
B*0702	**404**	**FSRQLQNSM**	**62.3**	**5.86**	**7.0**	**37.5**	**0.32**	**11**	**8**	**124**
B*0702	332	LTYHGAIKL	42.6	6.74	8.1	34.8	0.31	12	19	73
B*0702	5	GPQSNQRSA	70.6	1.53	1.5	67.5	0.30	13	24	10
B*0702	37	RPKQRRPQG	58.5	4.26	3.4	49.8	0.29	14	63	27
B*0702	**151**	**NPNNNAATV**	**40.0**	**8.08**	**4.5**	**42.2**	**0.26**	**15**	**15**	**7**
B*0702	**49**	**NTASWFTAL**	**45.5**	**4.15**	**3.0**	**40.4**	**0.23**	**16**	**17**	**20**
B*0702	42	RPQGLPNNT	52.6	6.40	3.4	37.5	0.22	17	22	4
B*0702	65	LRFPRGQGV	70.8	0.24	0.4	59.0	0.18	18	205	99
B*0702	171	GFYAEGSRG	31.3	0.01	-1898.6	8.0	0.00	19	>250	303
B*0702	175	EGSRGGSQA	35.6	0.00	13.8	12.1	0.00	20	105	174
B*0702	92	TRRVRGGDG	32.9	0.01	25.0	11.3	0.00	21	>250	237
B*0702	126	ANKEGIVWV	31.7	0.00	20.1	11.2	0.00	22	40	65
B*0702	164	QGTTLPKGF	31.0	0.40	31.2	17.1	0.00	23	216	153
B*0702	174	AEGSRGGSQ	31.5	0.01	12.3	8.8	0.00	24	>250	68
B*0702	38	PKQRRPQGL	38.8	6.84	33.1	16.9	0.00	25	146	58
B*0702	180	GSQASSRSS	30.0	0.09	9.6	13.5	0.00	26	184	366
B*0702	122	LPYGANKEG	31.5	6.92	11.9	24.1	0.00	27	76	37
B*0702	87	YYRRATRRV	35.9	427.00	-63.2	19.9	0.00	28	77	84

FIG. 96

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
B*0702	160	LQLPQGTTL	32.6	13.40	9.3	29.5	0.00	29	14	30
B*0702	309	APSASAFFG	32.8	7.15	10.7	22.9	0.00	30	39	15
B*0702	91	ATRRVRGGD	47.5	21.70	9.9	28.0	0.00	31	44	170
B*0702	10	QRSAPRITF	40.1	2.63	2.9	29.8	0.00	32	>250	25
B*0702	66	RFPRGQGVP	31.8	0.43	2.3	21.2	0.00	33	>250	285
B*0702	172	FYAEGSRGG	33.6	0.01	11.3	3.1	0.00	34	>250	365
B*0702	41	RRPQGLPNN	30.9	0.07	5.3	7.9	0.00	35	>250	280
B*0702	81	PDDQIGYYR	49.8	54.90	6.6	29.9	0.00	36	>250	288
B*0702	39	KQRRPQGLP	33.7	0.56	3.7	14.7	0.00	37	87	151
B*0702	148	GTRNPNNNA	30.9	8.77	6.5	18.9	0.00	38	28	50
B*0702	173	YAEGSRGGS	45.2	21.00	9.3	13.7	0.00	39	178	200
B*0702	89	RRATRRVRG	35.1	3.72	-9.2	8.7	0.00	40	>250	169
B*0702	176	GSRGGSQAS	32.2	44700.00	56.2	18.8	0.00	41	72	366
B*0702	90	RATRRVRGG	41.5	190.00	14.0	12.8	0.00	42	154	289
B*0702	182	QASSRSSSR	31.0	59.80	9.2	12.8	0.00	43	155	307
B*0702	308	FAPSASAFF	40.7	87.90	3.1	25.5	0.00	44	136	118
B*0702	163	PQGTTLPKG	36.8	249000.00	33.3	29.5	0.00	45	>250	302
B*0702	207	SPARMASGG	40.0	125.00	2.6	27.5	0.00	46	79	51
B*0702	199	TPGSSRGNS	43.0	70.60	1.9	29.3	0.00	47	38	40
B*0702	73	VPINTNSGP	44.4	302.00	6.9	17.4	0.00	48	71	63
B*0702	33	RNGARPKQR	30.2	0.01	-1.7	3.6	0.00	49	>250	229
B*0702	88	YRRATRRVR	33.8	169000.00	-12.2	14.5	0.00	50	218	168
B*0702	184	SSRSSSRSR	34.8	0.00	6.9	10.8	0.00	51	124	308
B*0702	79	SGPDDQIGY	31.4		13.0	0.9	0.00	52	191	396
B*0702	80	GPDDQIGYY	37.1		140.4	5.0	0.00	53	93	45
B*0702	181	SQASSRSSS	30.6		9.8	16.0	0.00	54	164	306
B*0702	183	ASSRSSSRS	31.3		12.5	3.6	0.00	55	130	202

FIG. 97

Allele	Peptide ID	Peptide Sequence
B*0702	84	QIGYYRRAT
B*0702	94	RVRGGDGKM
B*0702	106	SPRWYFYYL
B*0702	67	FPRGQGVPI
B*0702	258	KPRQKRTAT
B*0702	13	APRITFGGP
B*0702	168	LPKGFYAEG
B*0702	95	VRGGDGKMK
B*0702	162	LPQGTTLPK
B*0702	46	LPNNTASWF
B*0702	404	FSRQLQNSM
B*0702	332	LTYHGAIKL
B*0702	5	GPQSNQRSA
B*0702	37	RPKQRRPQG
B*0702	151	NPNNNAATV
B*0702	49	NTASWFTAL
B*0702	42	RPQGLPNNT
B*0702	65	LRFPRGQGV

FIG. 98

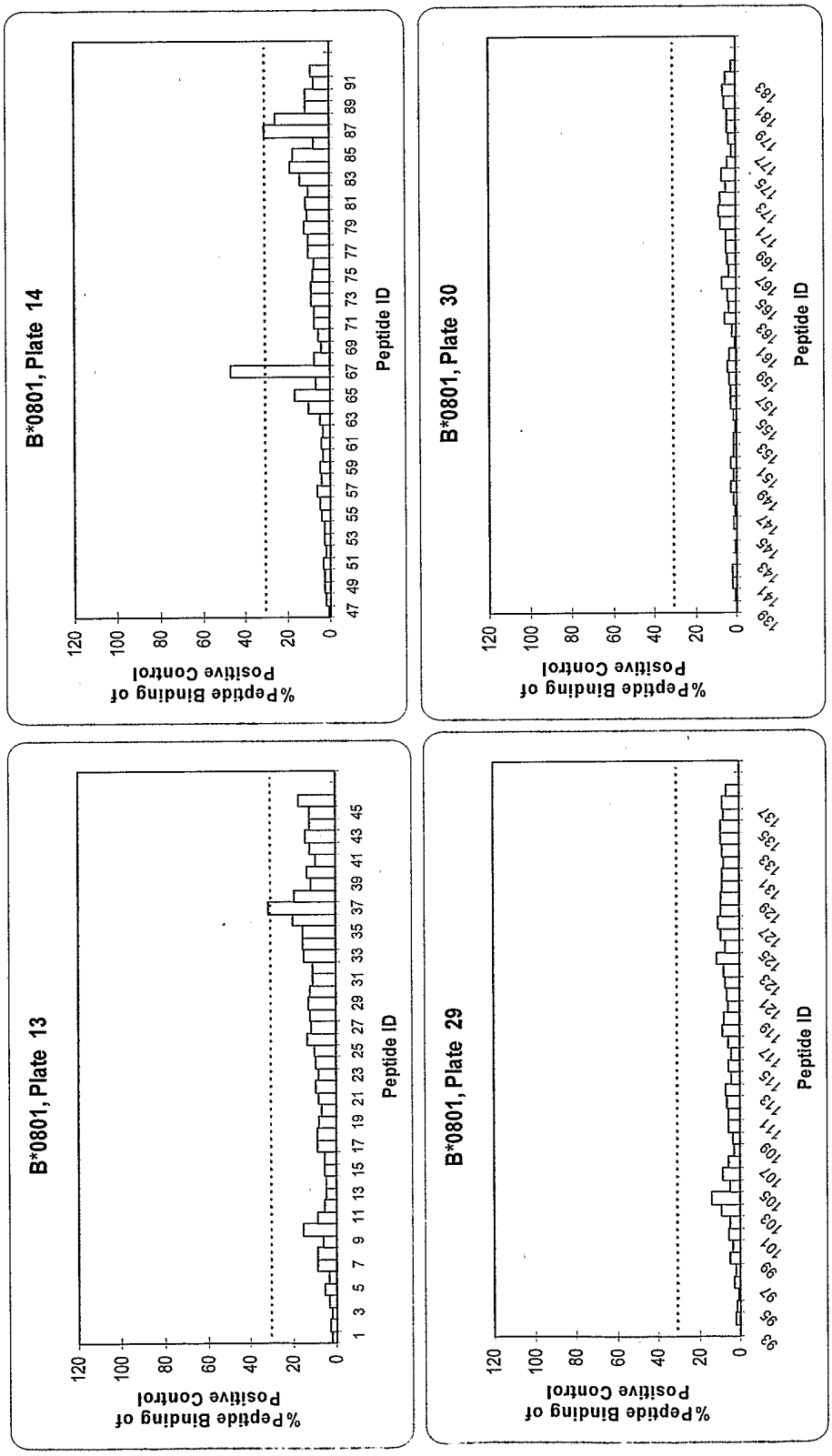

B*0801, Plate 14
B*0801, Plate 30
B*0801, Plate 13
B*0801, Plate 29
% Peptide Binding of Positive Control
Peptide ID

FIG. 99

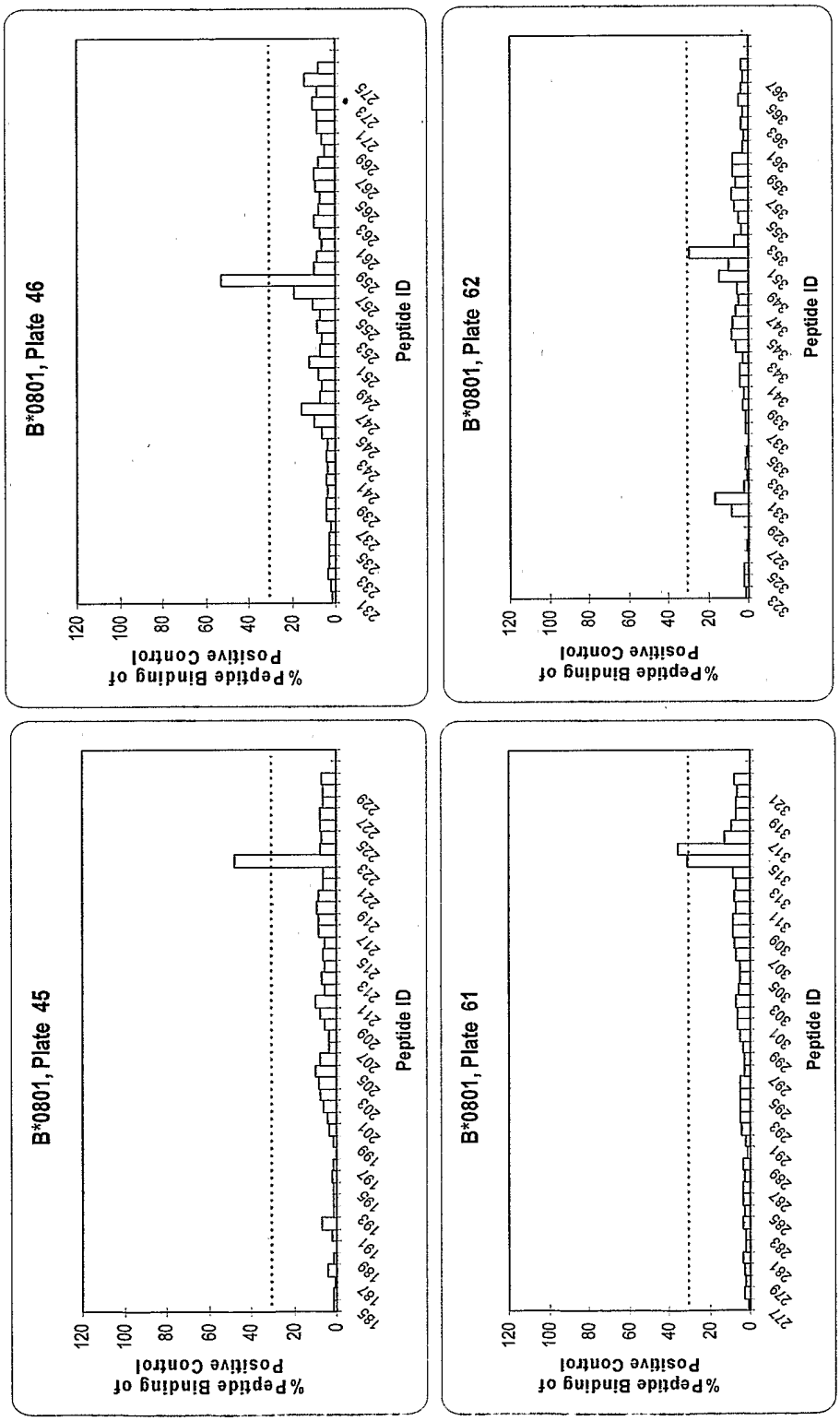

B*0801, Plate 46
B*0801, Plate 62
B*0801, Plate 45
B*0801, Plate 61
% Peptide Binding of Positive Control
Peptide ID
0
20
40
60
80
100
120

FIG. 100

Allele	Peptide ID	Peptide Sequence	% Peptide Binding
B*0801	37	RPKQRRPQG	31.3
B*0801	67	FPRGQGVPI	47.1
B*0801	87	YYRRATRRV	30.6
B*0801	223	LLLDRLNQL	47.6
B*0801	258	KPRQKRTAT	52.4
B*0801	315	FFGMSRIGM	30.9
B*0801	316	FGMSRIGME	35.7
B*0801	404	FSRQLQNSM	31.3

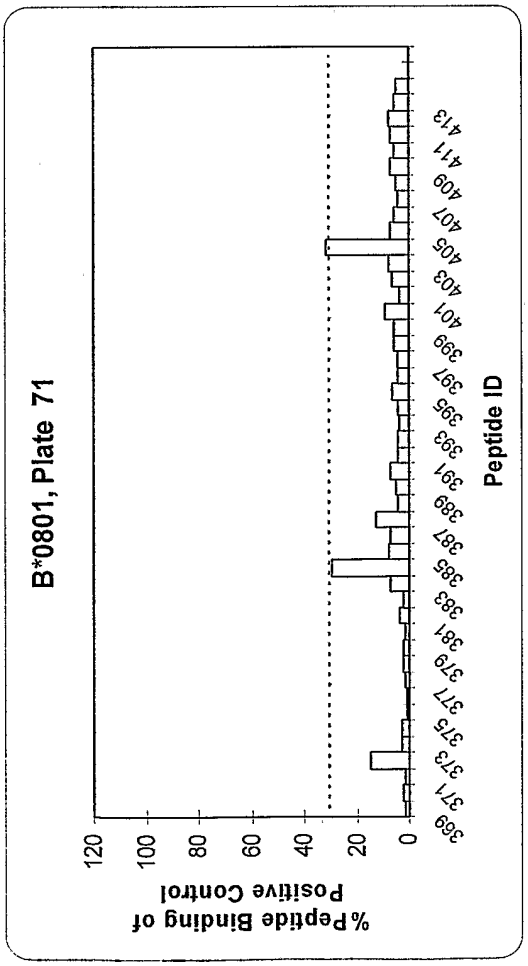


FIG. 101

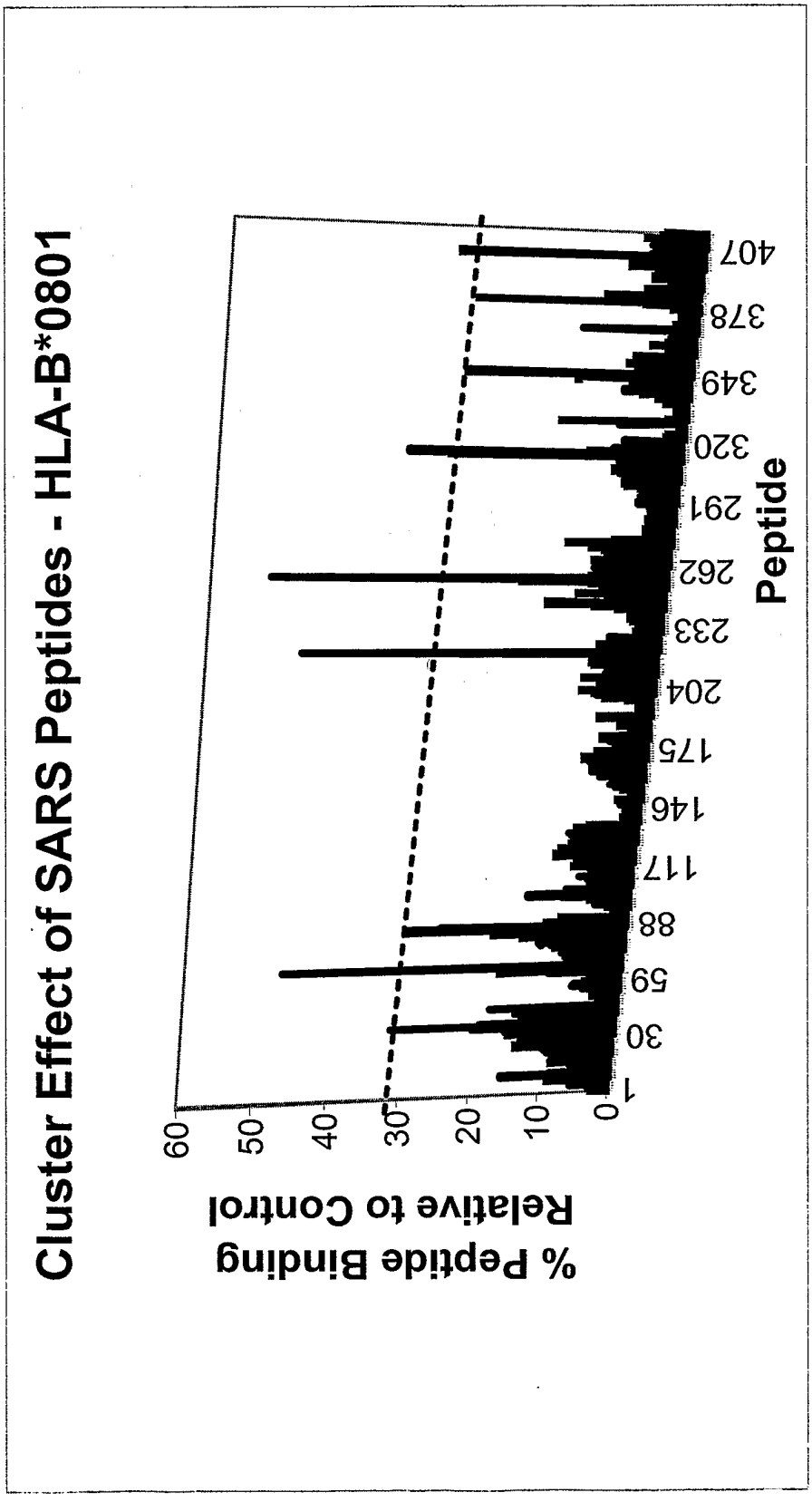

Cluster Effect of SARS Peptides - HLA-B*0801
% Peptide Binding Relative to Control
0
10
20
30
40
50
60
1
30
59
88
117
146
175
204
233
262
291
320
349
378
407
Peptide

FIG. 102

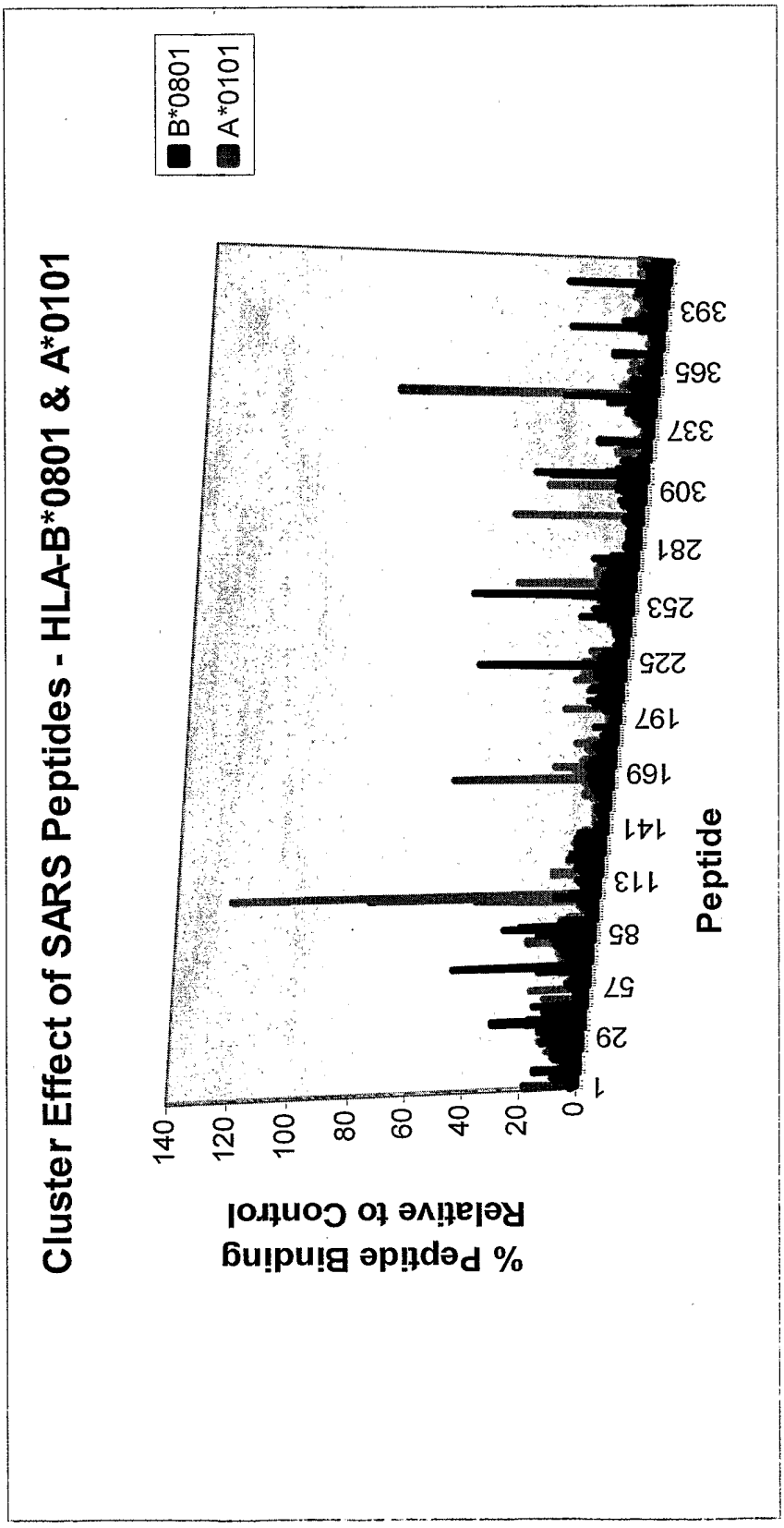
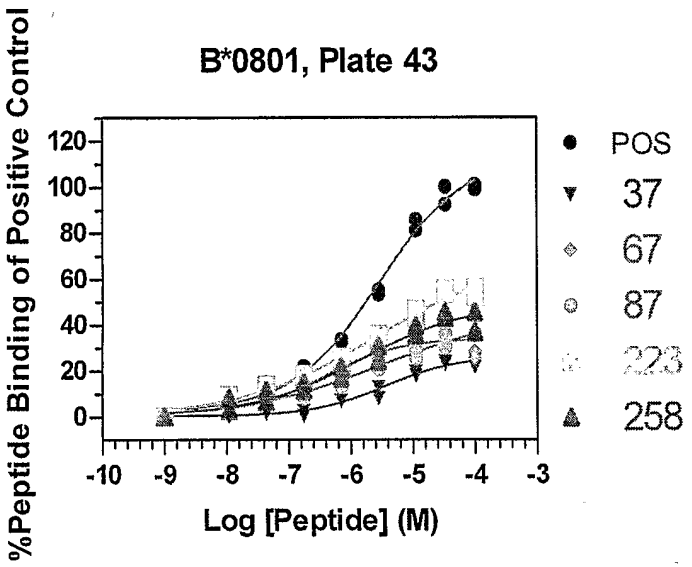
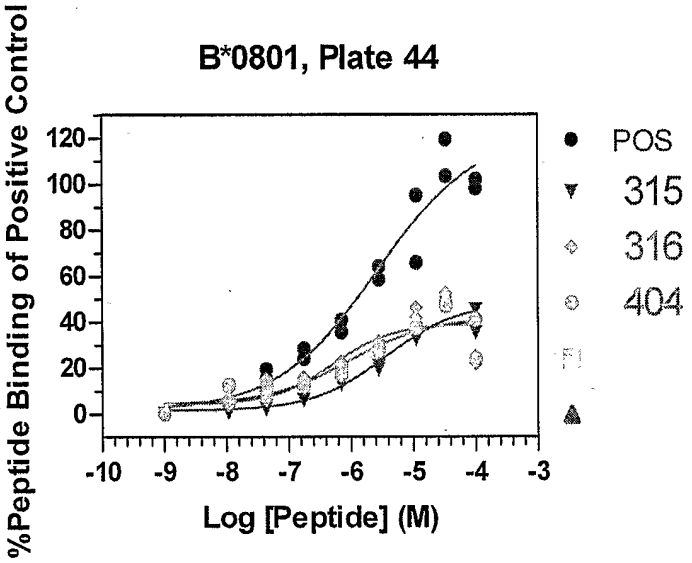

Cluster Effect of SARS Peptides - HLA-B*0801 & A*0101
B*0801
A*0101
% Peptide Binding
Relative to Control
140
120
100
80
60
40
20
0
1
29
57
85
113
141
169
197
225
253
281
309
337
365
393
Peptide

FIG. 103



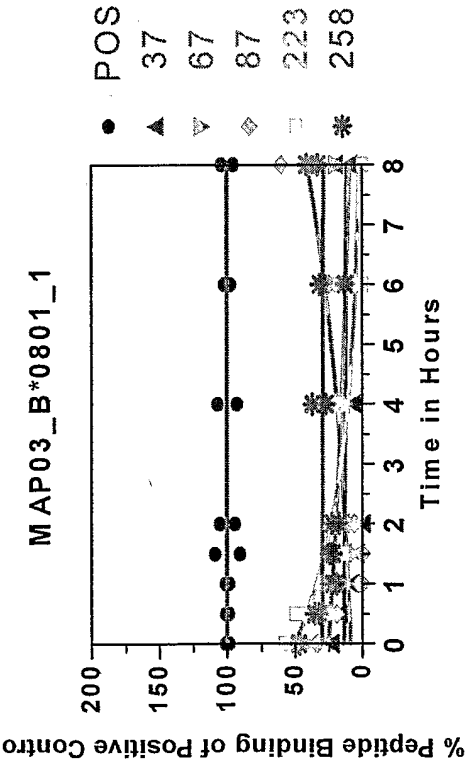
Peptide ID	Affinity ED50 x 10-6M
37	3.54
67	0.40
87	3.25
223	2.76
258	1.40



Peptide ID	Affinity ED50 x 10-6M
315	3.55
316	0.51
404	0.92

FIG. 104

Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
37	2.2	23.4
67	1.7	41.1
87	7.1	34.0
223	1.0	56.8
258	2.3	46.9



Peptide ID	Off Rate t 1/2 (Hrs)	% Peptide Binding at T0
315	0.3	31.6
316	4.6	35.7
404	2.9	31.2

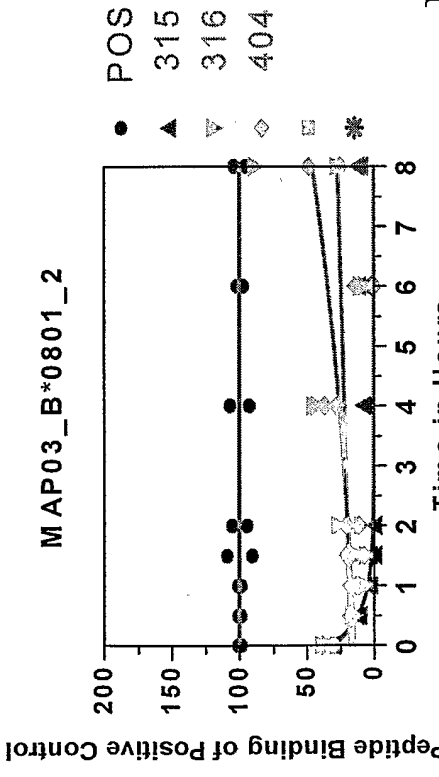


FIG. 105

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
B*0801	316	FGMSRIGME	35.7	0.51	4.6	35.7	0.38
B*0801	87	YYRRATRRV	30.6	3.25	7.1	34.0	0.32
B*0801	258	KPRQKRTAT	52.4	1.40	2.3	46.9	0.28
B*0801	67	FPRGQGVPI	47.1	0.40	1.7	41.1	0.27
B*0801	404	FSRQLQNSM	31.3	0.92	2.9	31.2	0.24
B*0801	223	LLLDRLNQL	47.6	2.76	1.0	56.8	0.19
B*0801	315	FFGMSRIGM	30.9	3.55	0.3	31.6	0.06
B*0801	37	RPKQRRPQG	31.3	3.54	2.2	**23.4**	**0.0**

FIG. 106

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	BIMAS RANK	SYFPEITHI RANK
B*0801	316	FGMSRIGME	35.7	0.51	4.6	35.7	0.38	1	200	89
B*0801	87	YYRRATRRV	30.6	3.25	7.1	34.0	0.32	2	57	171
B*0801	**258**	**KPRQKRTAT**	**52.4**	**1.40**	**2.3**	**46.9**	**0.28**	**3**	**3**	**5**
B*0801	**67**	**FPRGQGVPI**	**47.1**	**0.40**	**1.7**	**41.1**	**0.27**	**4**	**5**	**14**
B*0801	**404**	**FSRQLQNSM**	**31.3**	**0.92**	**2.9**	**31.2**	**0.24**	**5**	**7**	**161**
B*0801	**223**	**LLLDRLNQL**	**47.6**	**2.76**	**1.0**	**56.8**	**0.19**	**6**	**2**	**3**
B*0801	315	FFGMSRIGM	30.9	3.55	0.3	31.6	0.06	7	163	321
B*0801	37	RPKQRRPQG	31.3	3.54	2.2	23.4	0.00	8	11	1

FIG. 107

Allele	Peptide ID	Peptide Sequence
B*0801	316	FGMSRIGME
B*0801	87	YYRRATRRV
B*0801	258	KPRQKRTAT
B*0801	67	FPRGQGVPI
B*0801	404	FSRQLQNSM
B*0801	223	LLLDRLNQL
B*0801	315	FFGMSRIGM

FIG. 108

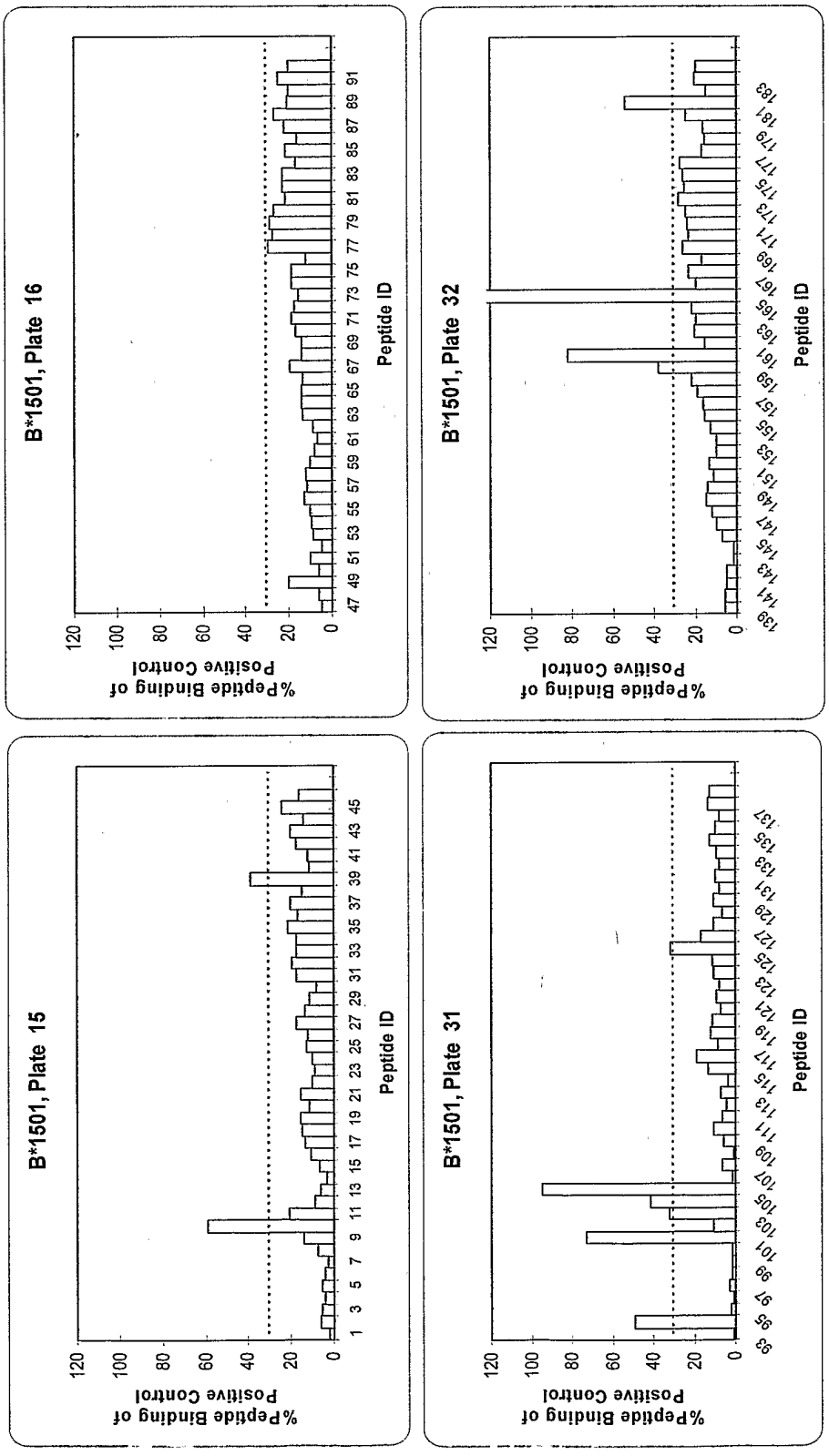

B*1501, Plate 16
B*1501, Plate 32
B*1501, Plate 15
B*1501, Plate 31
% Peptide Binding of Positive Control
Peptide ID

FIG. 109

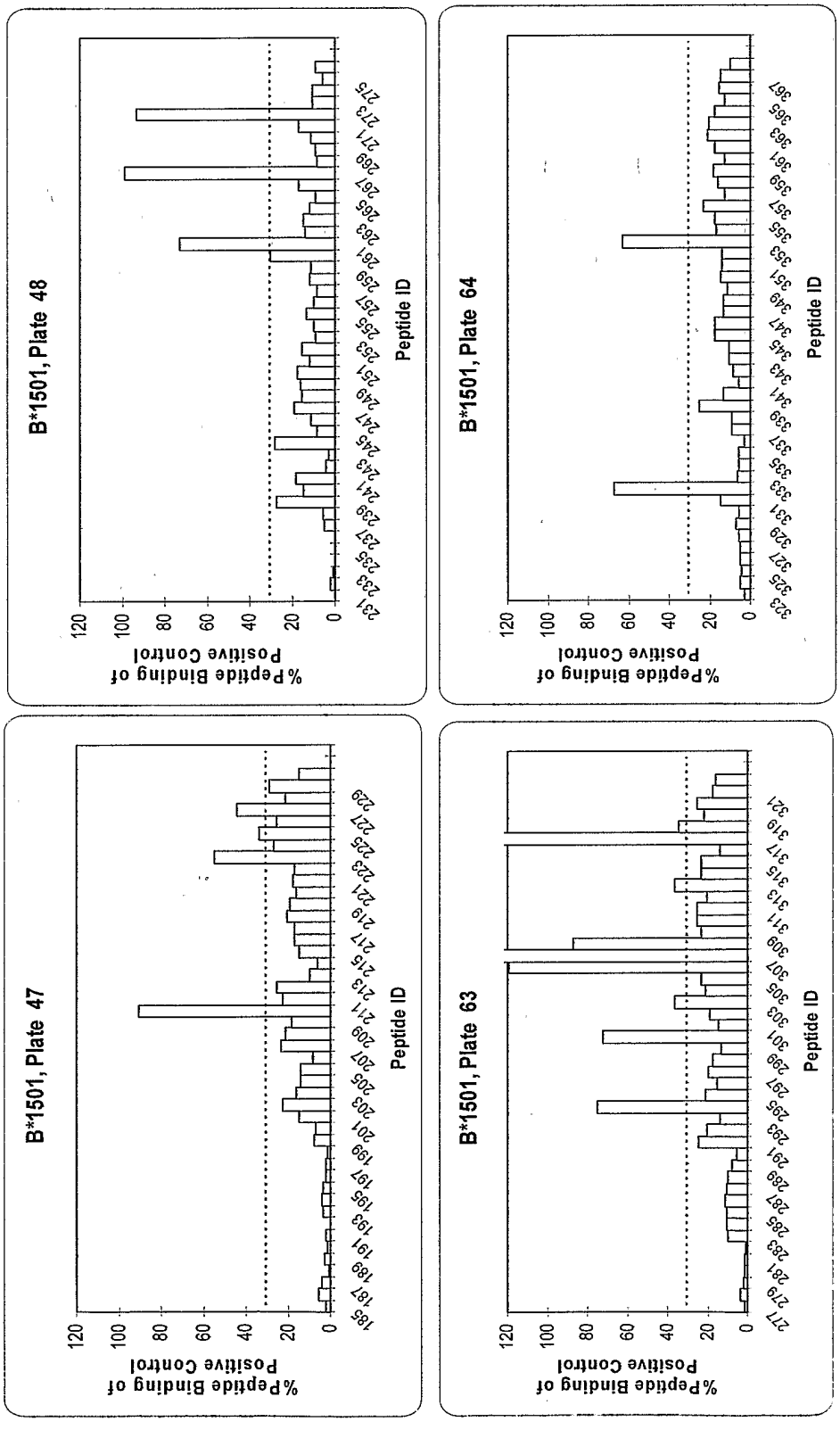

B*1501, Plate 48
B*1501, Plate 64
B*1501, Plate 47
B*1501, Plate 63
% Peptide Binding of Positive Control
Peptide ID
0
20
40
60
80
100
120

FIG. 110

Allele	Peptide ID	Peptide Sequence	% Peptide Binding
B*1501	10	QRSAPRITF	59.2
B*1501	39	KQRRPQGLP	38.7
B*1501	94	RVRGGDGKM	49.0
B*1501	101	KMKELSPRW	72.6
B*1501	103	KELSPRWYF	32.1
B*1501	104	ELSPRWYFY	41.2
B*1501	105	LSPRWYFYY	94.6
B*1501	125	GANKEGIVW	31.8
B*1501	159	VLQLPQGTT	38.2
B*1501	160	LQLPQGTTL	82.4
B*1501	165	GTTLPKGFY	134.5
B*1501	181	SQASSRSSS	54.0
B*1501	210	RMASGGGET	90.7
B*1501	223	LLLDRLNQL	54.6
B*1501	225	LDRLNQLES	33.4
B*1501	227	RLNQLESKV	44.0
B*1501	261	QKRTATKQY	73.0
B*1501	267	KQYNVTQAF	99.2
B*1501	272	TQAFGRRGP	93.6
B*1501	294	RQGTDYKHW	75.4
B*1501	300	KHWPQIAQF	72.1
B*1501	303	PQIAQFAPS	36.7
B*1501	306	AQFAPSASA	119.2
B*1501	307	QFAPSASAF	147.0
B*1501	308	FAPSASAFF	87.3
B*1501	313	SAFFGMSRI	36.7
B*1501	317	GMSRIGMEV	123.1
B*1501	318	MSRIGMEVT	34.5
B*1501	332	LTYHGAIKL	67.1
B*1501	353	LLNKHIDAY	63.4
B*1501	386	RQKKQPTVT	46.4
B*1501	404	FSRQLQNSM	106.8
B*1501	406	RQLQNSMSG	39.8
B*1501	407	QLQNSMSGA	39.9
B*1501	408	LQNSMSGAS	49.2

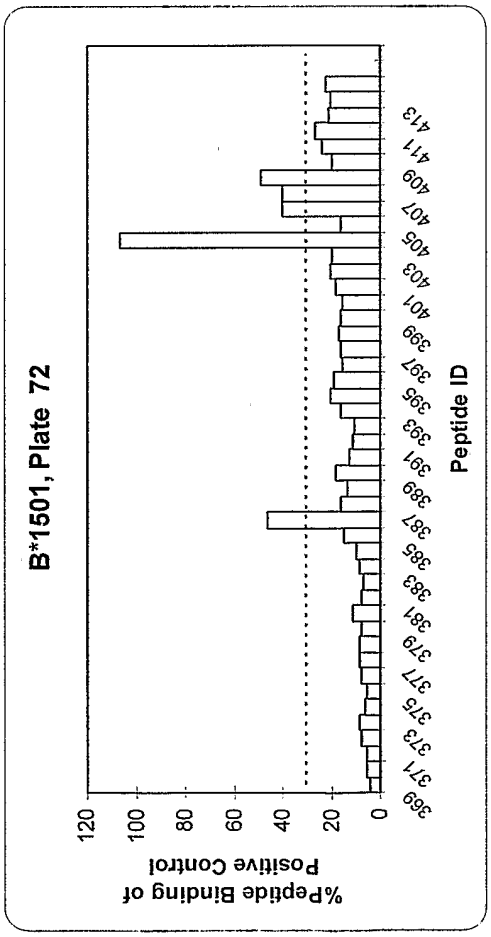


FIG. 111

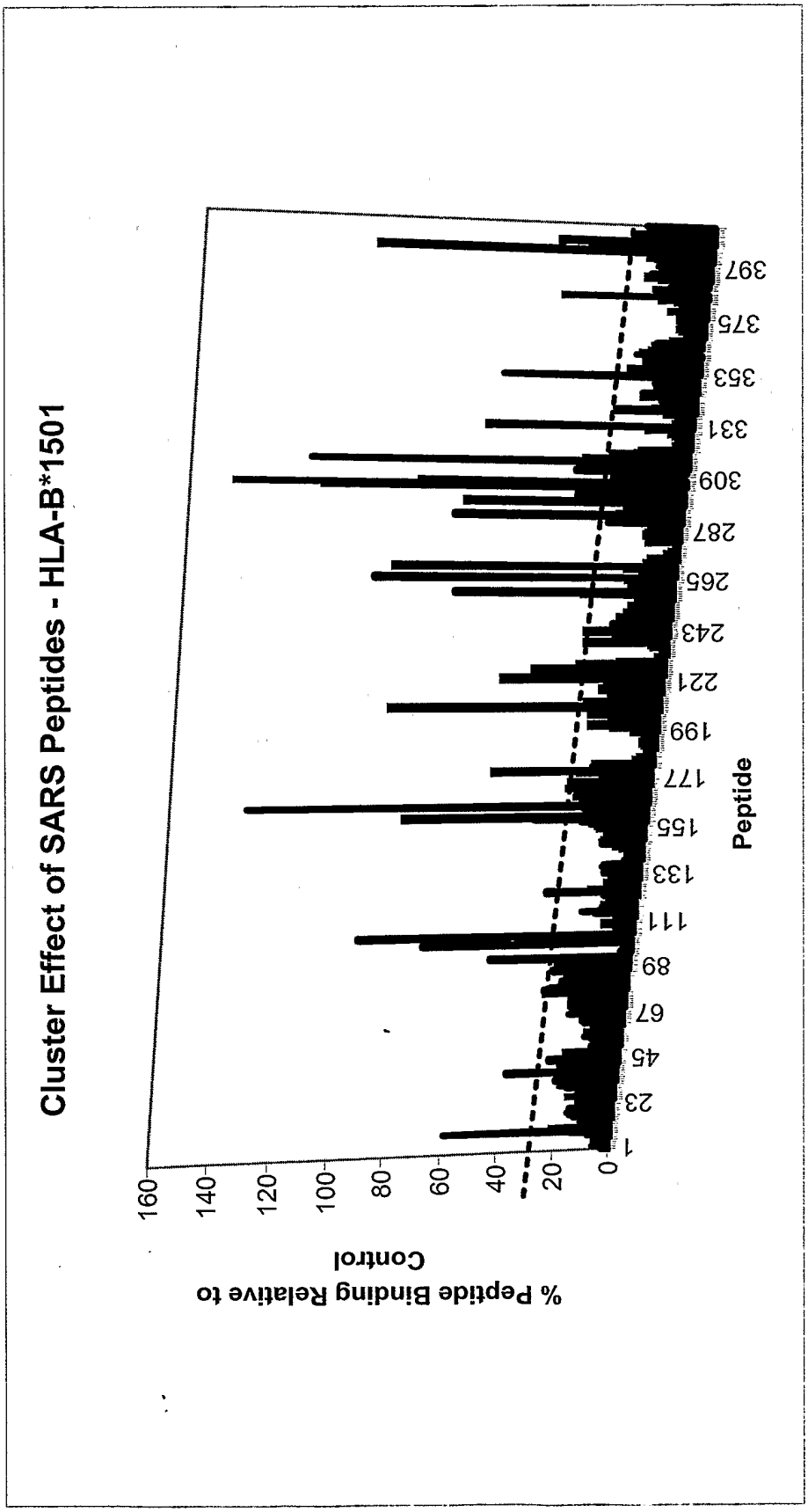
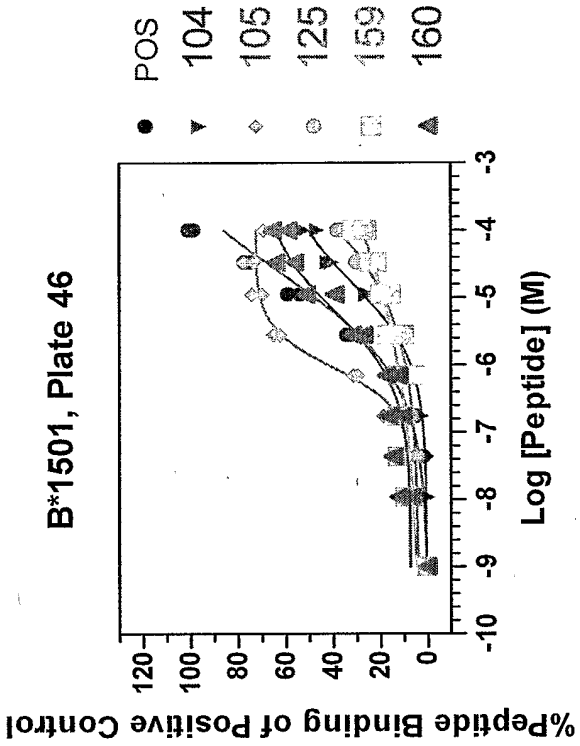
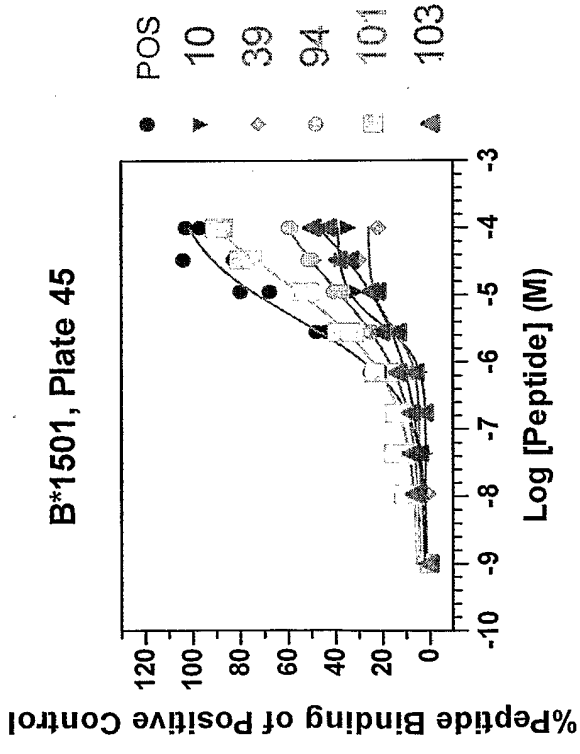

Cluster Effect of SARS Peptides - HLA-B*1501
% Peptide Binding Relative to Control
0
20
40
60
80
100
120
140
160
1
23
45
67
89
111
133
155
177
199
221
243
265
287
309
331
353
375
397
Peptide

FIG. 112

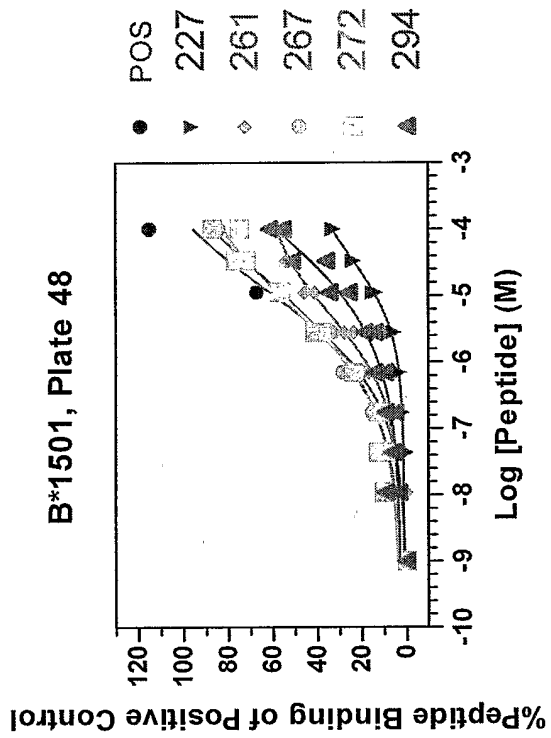


Peptide ID	Affinity ED50 x 10-6M
104	16.10
105	0.92
125	780.00
159	39000.00
160	6.33

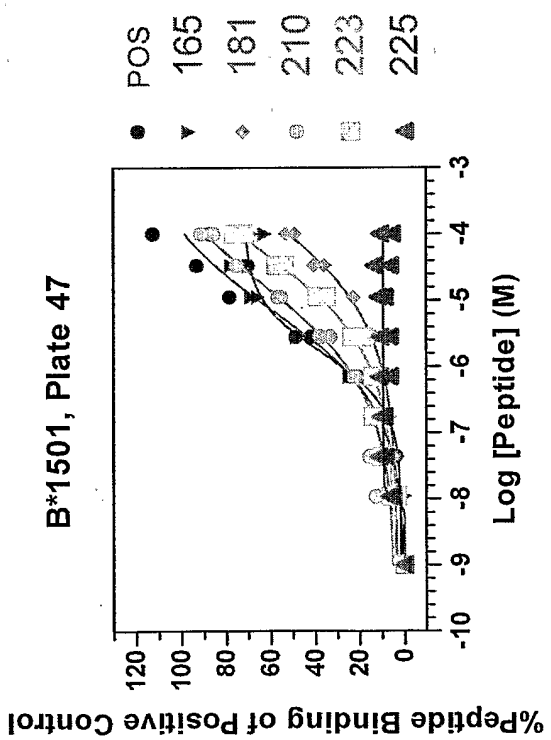


Peptide ID	Affinity ED50 x 10-6M
10	3.59
39	3.07
94	12.50
101	19.80
103	378.00

FIG. 113

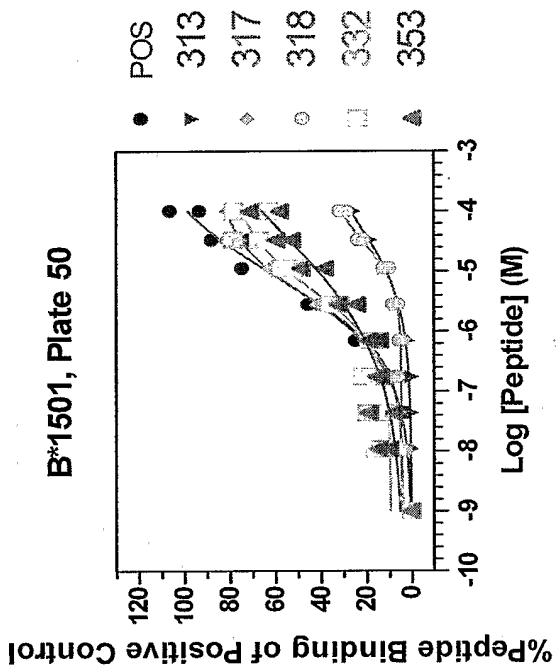


Peptide ID	Affinity ED50 x 10-6M
227	38.30
261	5.11
267	18.20
272	7.08
294	141.00

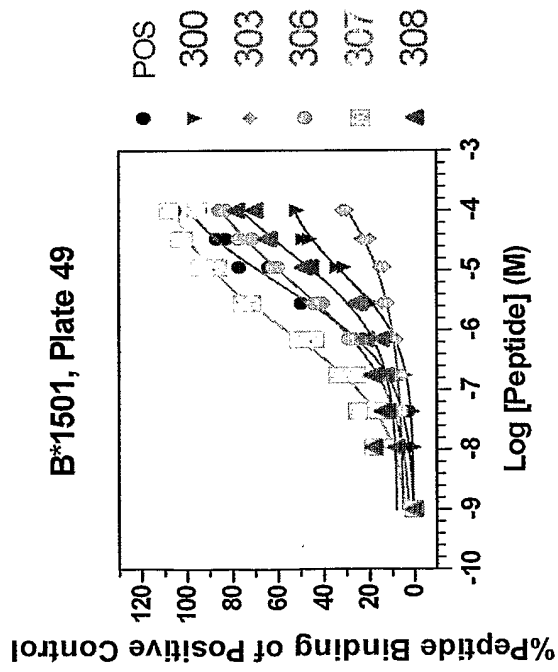


Peptide ID	Affinity ED50 x 10-6M
165	1.58
181	224.00
210	19.10
223	59.50
225	0.01

FIG. 114

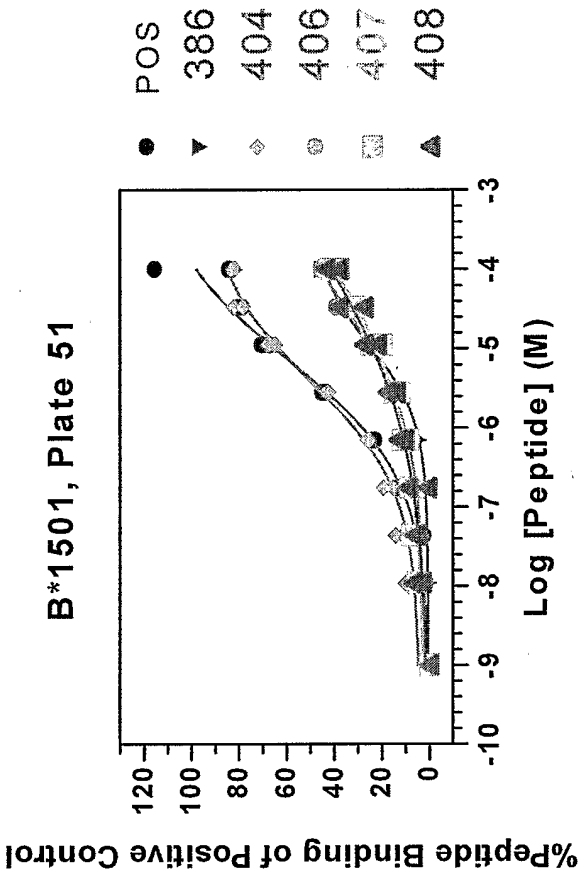


Peptide ID	Affinity ED50 x 10-6M
313	55.70
317	3.60
318	28.20
332	5.11
353	62.00



Peptide ID	Affinity ED50 x 10-6M
300	8.17
303	3630.00
306	6.43
307	6.43
308	19.70

FIG. 115

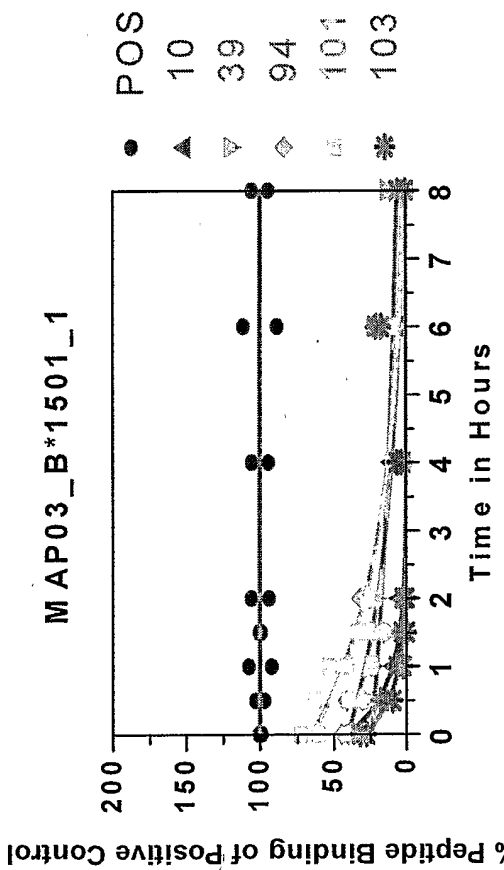


Peptide ID	Affinity ED50 x 10-6M
386	11.20
404	3.73
406	38.80
407	865.00
408	147.00

FIG. 116

Peptide ID	Off Rate t 1/2
10	0.4
39	2.1
94	1.3
101	1.2
103	0.4

Peptide ID	Off Rate t 1/2
104	0.5



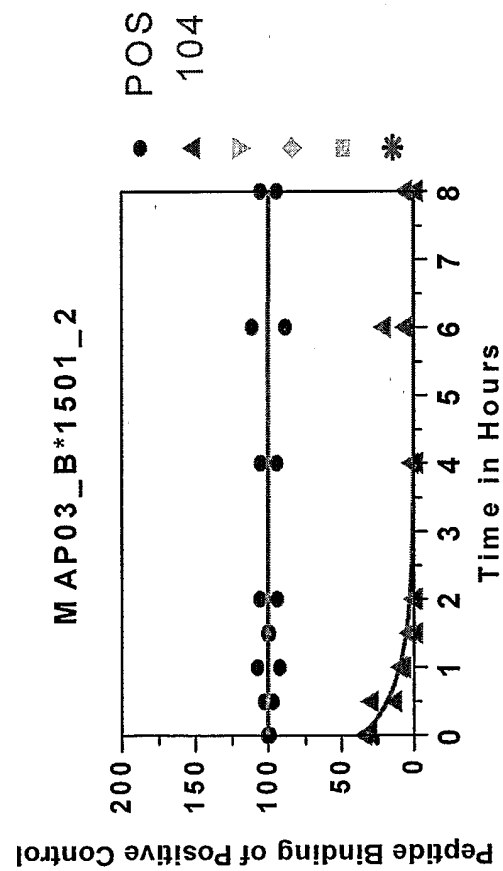
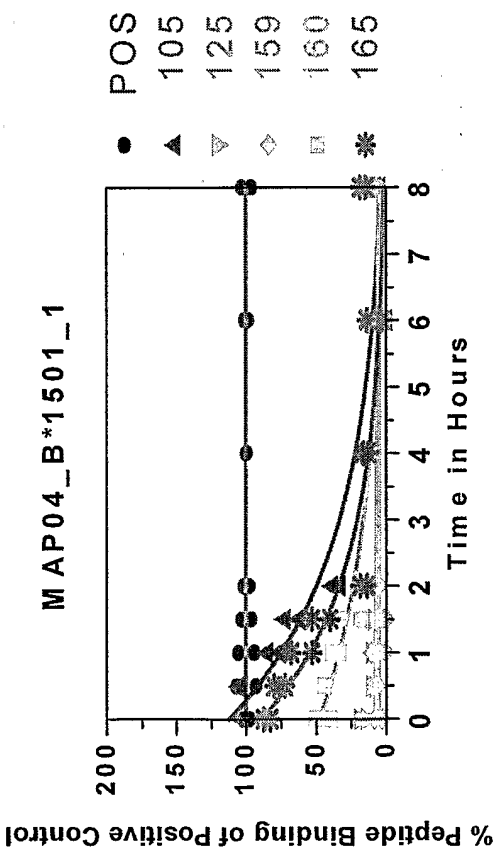


FIG. 117

Peptide ID	Off Rate t 1/2
105	1.2
125	3.2
159	3.9
160	1.3
165	1.1



Peptide ID	Off Rate t 1/2
181	0.4
210	1.2
223	0.6
225	-10.1
227	1.9

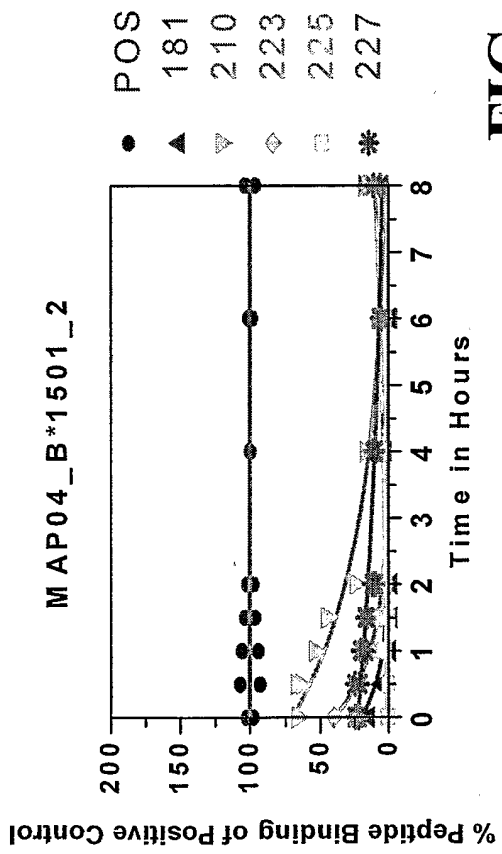
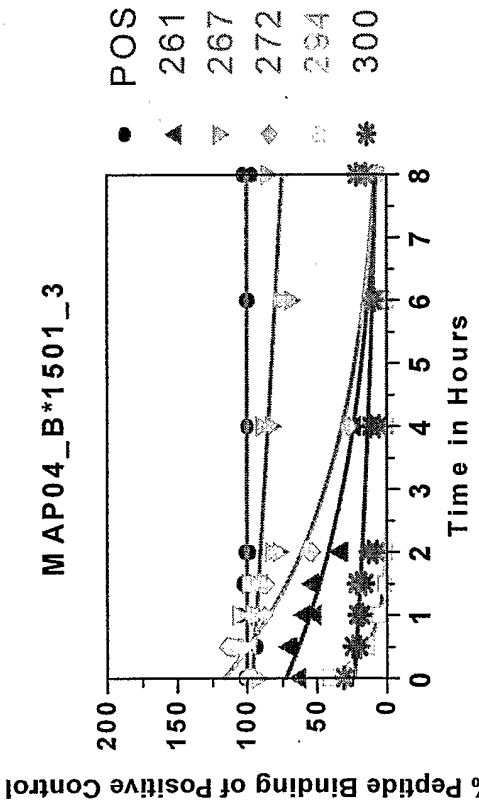


FIG. 118

Peptide ID	Off Rate t 1/2
261	1.6
267	3.6
272	1.4
294	0.3
300	2.3



Peptide ID	Off Rate t 1/2
303	21.2
306	2.3
307	3.3
308	1.8
313	20.2

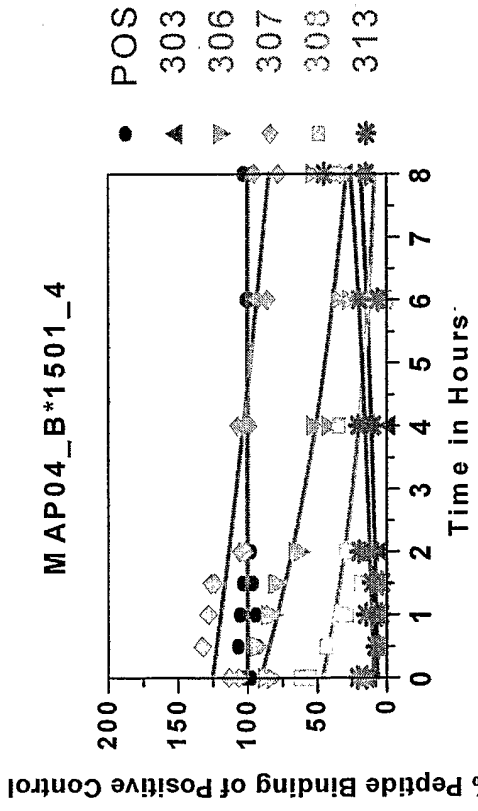
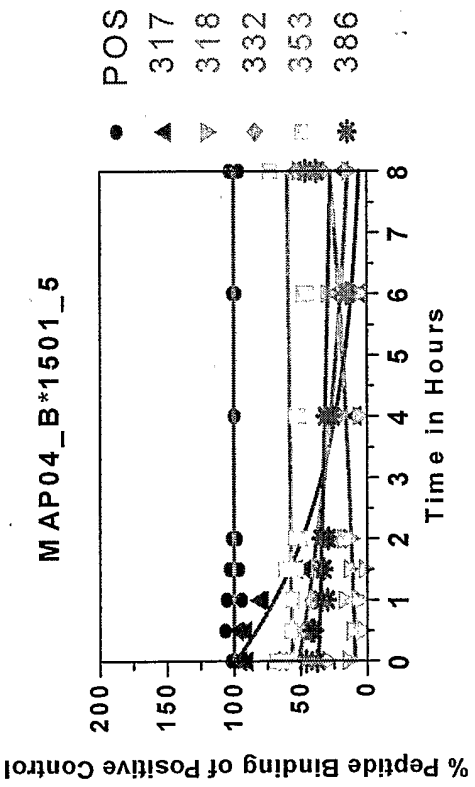


FIG. 119

Peptide ID	Off Rate t 1/2
317	1.3
318	33.3
332	2.1
353	4.4
386	3.5



Peptide ID	Off Rate t 1/2
404	2.6
406	2.6
407	4.5
408	3.2

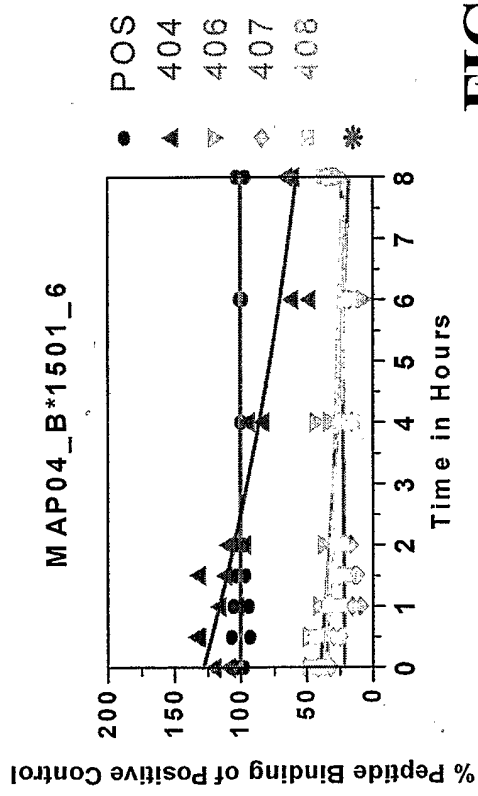


FIG. 120

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore
B*1501	307	QFAPSASAF	147.0	6.43	3.27	109.7	0.68
B*1501	404	FSRQLQNSM	106.8	3.73	2.63	115.6	0.51
B*1501	105	LSPRWYFYY	94.6	0.92	1.22	98.2	0.39
B*1501	267	KQYNVTQAF	99.2	18.20	3.56	91.2	0.38
B*1501	306	AQFAPSASA	119.2	6.43	2.26	83.5	0.33
B*1501	317	GMSRIGMEV	123.1	3.60	1.34	94.0	0.31
B*1501	165	GTTLPKGFY	134.5	1.58	1.06	84.8	0.30
B*1501	272	TQAFGRRGP	93.6	7.08	1.43	97.7	0.30
B*1501	332	LTYHGAIKL	67.1	5.11	2.14	63.6	0.27
B*1501	353	LLNKHIDAY	63.4	62.00	4.43	66.0	0.26
B*1501	261	QKRTATKQY	73.0	5.11	1.58	64.6	0.24
B*1501	386	RQKKQPTVT	46.4	11.20	3.47	41.4	0.22
B*1501	308	FAPSASAFF	87.3	19.70	1.84	59.1	0.19
B*1501	101	KMKELSPRW	72.6	19.80	1.21	66.8	0.17
B*1501	210	RMASGGGET	90.7	19.10	1.24	64.5	0.17
B*1501	160	LQLPQGTTL	82.4	6.33	1.33	45.3	0.16
B*1501	406	RQLQNSMSG	39.8	38.80	2.63	41.0	0.15
B*1501	300	KHWPQIAQF	72.1	8.17	2.33	31.0	0.15
B*1501	39	KQRRPQGLP	38.7	3.07	2.11	26.1	0.14
B*1501	408	LQNSMSGAS	49.2	147.00	3.18	44.4	0.14
B*1501	94	RVRGGDGKM	49.0	12.50	1.34	42.2	0.13
B*1501	407	QLQNSMSGA	39.9	865.00	4.48	36.7	0.10
B*1501	10	QRSAPRITF	59.2	3.59	0.44	41.9	0.09
B*1501	104	ELSPRWYFY	41.2	16.10	0.49	33.7	0.06
B*1501	223	LLLDRLNQL	54.6	59.50	0.57	40.1	0.06
B*1501	294	RQGTDYKHW	75.4	141.00	0.34	40.3	0.04
B*1501	103	KELSPRWYF	32.1	378.00	0.37	30.0	0.03
B*1501	318	MSRIGMEVT	34.5	28.20	33.26	**20.5**	0.00
B*1501	313	SAFFGMSRI	36.7	55.70	20.18	**17.7**	0.00
B*1501	303	PQIAQFAPS	36.7	3630.00	21.17	**14.1**	0.00
B*1501	227	RLNQLESKV	44.0	38.30	1.91	**23.2**	0.00
B*1501	225	LDRLNQLES	33.4	0.01	-10.12	**0.9**	0.00
B*1501	125	GANKEGIVW	31.8	780.00	3.19	**14.4**	0.00
B*1501	181	SQASSRSSS	54.0	224.00	0.41	**21.3**	0.00
B*1501	159	VLQLPQGTT	38.2	39000.00	3.88	**5.6**	0.00

FIG. 121

Allele	Peptide ID	Peptide Sequence	% Peptide Binding	Affinity ED50 x 10-6M	Off Rate t 1/2 (Hrs)	Off Rate T0 % Peptide Binding	iScore	iTopia RANK	SYFPEITHI RANK
B*1501	307	QFAPSASAF	147.0	6.43	3.27	109.7	0.68	1	33
B*1501	404	FSRQLQNSM	106.8	3.73	2.63	115.6	0.51	2	46
B*1501	105	LSPRWYFYY	94.6	0.92	1.22	98.2	0.39	3	381
B*1501	267	KQYNVTQAF	99.2	18.20	3.56	91.2	0.38	4	42
B*1501	306	AQFAPSASA	119.2	6.43	2.26	83.5	0.33	5	351
B*1501	317	GMSRIGMEV	123.1	3.60	1.34	94.0	0.31	6	179
B*1501	165	GTTLPKGFY	134.5	1.58	1.06	84.8	0.30	7	153
B*1501	272	TQAFGRRGP	93.6	7.08	1.43	97.7	0.30	8	52
B*1501	332	LTYHGAIKL	67.1	5.11	2.14	63.6	0.27	9	29
B*1501	353	LLNKHIDAY	63.4	62.00	4.43	66.0	0.26	10	181
B*1501	261	QKRTATKQY	73.0	5.11	1.58	64.6	0.24	11	395
B*1501	386	RQKKQPTVT	46.4	11.20	3.47	41.4	0.22	12	122
B*1501	308	FAPSASAFF	87.3	19.70	1.84	59.1	0.19	13	53
B*1501	101	KMKELSPRW	72.6	19.80	1.21	66.8	0.17	14	82
B*1501	210	RMASGGGET	90.7	19.10	1.24	64.5	0.17	15	164
B*1501	160	LQLPQGTTL	82.4	6.33	1.33	45.3	0.16	16	7
B*1501	406	RQLQNSMSG	39.8	38.80	2.63	41.0	0.15	17	286
B*1501	300	KHWPQIAQF	72.1	8.17	2.33	31.0	0.15	18	2
B*1501	39	KQRRPQGLP	38.7	3.07	2.11	26.1	0.14	19	296
B*1501	408	LQNSMSGAS	49.2	147.00	3.18	44.4	0.14	20	370
B*1501	94	RVRGGDGKM	49.0	12.50	1.34	42.2	0.13	21	36
B*1501	407	QLQNSMSGA	39.9	865.00	4.48	36.7	0.10	22	369
B*1501	10	QRSAPRITF	59.2	3.59	0.44	41.9	0.09	23	31
B*1501	104	ELSPRWYFY	41.2	16.10	0.49	33.7	0.06	24	84
B*1501	223	LLLDRLNQL	54.6	59.50	0.57	40.1	0.06	25	27
B*1501	294	RQGTDYKHW	75.4	141.00	0.34	40.3	0.04	26	398
B*1501	103	KELSPRWYF	32.1	378.00	0.37	30.0	0.03	27	37
B*1501	318	MSRIGMEVT	34.5	28.20	33.26	20.5	0.00	28	112
B*1501	313	SAFFGMSRI	36.7	55.70	20.18	17.7	0.00	29	111
B*1501	303	PQIAQFAPS	36.7	3630.00	21.17	14.1	0.00	30	399
B*1501	227	RLNQLESKV	44.0	38.30	1.91	23.2	0.00	31	333
B*1501	225	LDRLNQLES	33.4	0.01	-10.12	0.9	0.00	32	242
B*1501	125	GANKEGIVW	31.8	780.00	3.19	14.4	0.00	33	88
B*1501	181	SQASSRSSS	54.0	224.00	0.41	21.3	0.00	34	236
B*1501	159	VLQLPQGTT	38.2	39000.00	3.88	5.6	0.00	35	233

FIG. 122

Allele	Peptide ID	Peptide Sequence
B*1501	307	QFAPSASAF
B*1501	404	FSRQLQNSM
B*1501	105	LSPRWYFYY
B*1501	267	KQYNVTQAF
B*1501	306	AQFAPSASA
B*1501	317	GMSRIGMEV
B*1501	165	GTTLPKGFY
B*1501	272	TQAFGRRGP
B*1501	332	LTYHGAIKL
B*1501	353	LLNKHIDAY
B*1501	261	QKRTATKQY
B*1501	386	RQKKQPTVT
B*1501	308	FAPSASAFF
B*1501	101	KMKELSPRW
B*1501	210	RMASGGGET
B*1501	160	LQLPQGTTL
B*1501	406	RQLQNSMSG
B*1501	300	KHWPQIAQF
B*1501	39	KQRRPQGLP
B*1501	408	LQNSMSGAS
B*1501	94	RVRGGDGKM
B*1501	407	QLQNSMSGA
B*1501	10	QRSAPRITF
B*1501	104	ELSPRWYFY
B*1501	223	LLLDRINQL
B*1501	294	RQGTDYKHW
B*1501	103	KELSPRWYF

FIG. 123

SEQUENCE LISTING

<110> University Health Network
Beckman Coulter Inc.
Université de Montréal
National Health Research Institutes
KELVIN, David
PERSAD, Desmond
CAMERON, Cheryl
BRAY, Kurtis R
LOFARO, Lori R
JOHNSON, Camille
SEKALY, Rafick-Pierre
YOUNES, Souheil-Antoine
CHONG, Pele

<120> SARS-CoV NUCLEOCAPSID PROTEIN EPITOPES AND USES THEREOF

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cgccgacccc aaggtttacc caataatact gcgtcttggt tcacagctct cactcagcat 180

ggcaaggagg aacttagatt ccctcgaggc cagggcgttc caatcaacac caatagtggt 240

ccagatgacc aaattggcta ctaccgaaga gctacccgac gagttcgtgg tggtgacggc 300

aaaatgaaag agctcagccc cagatggtac ttctattacc taggaactgg cccagaagct 360

tcacttccct acggcgctaa caaagaaggc atcgtatggg ttgcaactga gggagccttg 420

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caacaacaag gccaaactgt cactaagaaa tctgctgctg aggcatctaa aaagcctcgc 780

caaaaacgta ctgccacaaa acagtacaac gtcactcaag catttgggag acgtggtcca 840

gaacaaaccc aaggaaattt cggggaccaa gacctaatca gacaaggaac tgattacaaa 900

cattggccgc aaattgcaca atttgctcca agtgcctctg cattctttgg aatgtcacgc 960

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Leu Arg Phe Pro Arg Gly Gln Gly Val Pro Ile Asn Thr Asn Ser Gly
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Gly Gly Asp Gly Lys Met Lys Glu Leu Ser Pro Arg Trp Tyr Phe Tyr
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Asp His Ile Gly Thr Arg Asn Pro Asn Asn Asn Ala Ala Thr Val Leu
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Gln Leu Pro Gln Gly Thr Thr Leu Pro Lys Gly Phe Tyr Ala Glu Gly
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Leu Asp Arg Leu Asn Gln Leu Glu Ser Lys Val Ser Gly Lys Gly Gln
225 230 235 240

Gln Gln Gln Gly Gln Thr Val Thr Lys Lys Ser Ala Ala Glu Ala Ser
245 250 255

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Lys Lys Pro Arg Gln Lys Arg Thr Ala Thr Lys Gln Tyr Asn Val Thr
260 265 270

Gln Ala Phe Gly Arg Arg Gly Pro Glu Gln Thr Gln Gly Asn Phe Gly
275 280 285

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Asp Gln Asp Leu Ile Arg Gln Gly Thr Asp Tyr Lys His Trp Pro Gln
290 295 300

Ile Ala Gln Phe Ala Pro Ser Ala Ser Ala Phe Phe Gly Met Ser Arg
305 310 315 320

Ile Gly Met Glu Val Thr Pro Ser Gly Thr Trp Leu Thr Tyr His Gly
325 330 335

Ala Ile Lys Leu Asp Asp Lys Asp Pro Gln Phe Lys Asp Asn Val Ile
340 345 350

Leu Leu Asn Lys His Ile Asp Ala Tyr Lys Thr Phe Pro Pro Thr Glu
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Pro Lys Lys Asp Lys Lys Lys Lys Thr Asp Glu Ala Gln Pro Leu Pro
370 375 380

Gln Arg Gln Lys Lys Gln Pro Thr Val Thr Leu Leu Pro Ala Ala Asp
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Thr Gly Pro Glu Ala Ser Leu Pro Tyr Gly Ala Asn Lys Glu Gly Ile
35 40 45

Val Trp Val Ala Thr Glu Gly Ala Leu Asn Thr Pro Lys Asp His Ile
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Gly Thr Arg Asn Pro Asn Asn Asn Ala Ala Thr Val Leu Gln Leu Pro
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Met Ser Arg Ile Gly Met Glu Val Thr Pro Ser Gly Thr Trp Leu Thr
35 40 45

Tyr His Gly Ala Ile Lys Leu Asp Asp Lys Asp Pro Gln Phe Lys Asp
50 55 60

Asn Val Ile Leu Leu Asn Lys His Ile Asp Ala Tyr Lys Thr Phe Pro
65 70 75 80

Pro Thr Glu Pro Lys Lys Asp Lys Lys Lys Lys Thr Asp Glu Ala Gln
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Pro Leu Pro Gln Arg Gln Lys Lys Gln Pro Thr Val Thr Leu Leu Pro
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Ala Ala Asp Met Asp Asp Phe Ser Arg Gln Leu Gln Asn Ser Met Ser
115 120 125

Gly Ala Ser
130

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2005/000632

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7): C12N 15/50, C07K 14/165, C07K 7/04, A61K 39/215, C07K 16/10, C12N 15/11, A61P 31/14, A61K 48/00, G01N 33/569, C07K 17/00

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(7): C12N 15/50, C07K 14/165, C07K 7/04, A61K 39/215, C07K 16/10, C12N 15/11, A61P 31/14, A61K 48/00, G01N 33/569, C07K 17/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Epodoc, STN, Canadian Patent Database, Medline. Keywords: SARS, Severe Acute Respiratory Syndrome, SARS-CoV, coronavirus, nucleocapsid, epitope, vaccine, (poly)peptide, (micro)array.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIN, Y ET AL. *Identification of an epitope of SARS-coronavirus nucleocapsid protein.* Cell Research (2003) Vol. 13, No. 3, pp. 141-145. Whole document.	1-5, 8, 16, 19-21, 35-37 and 44-48 (partially) 1-57
X	LI, S ET AL., *The Epitope Study on the SARS-CoV Nucleocapsid Protein.* Geno., Prot. & Bioinfo. (2003) Vol. 1, No. 3, pp. 198-206. Whole document.	1-5, 8, 16, 19-21, 35-37 and 44-48 (partially) 1-57
X	HE, Q ET AL., *Development of a Western Blot Assay for Detection of Antibodies against Coronavirus Causing Severe Acute Respiratory Syndrome.* Clinical and Diagnostic Laboratory Immunology (2004), Vol. 11, No. 2, pp. 417-422. Whole document.	1-5, 8, 16, 19-21, 35-37 and 44-48 (partially) 1-57
X	CHEN, Z ET AL., *Antigenicity Analysis of Different Regions of the Severe Acute Respiratory Syndrome Coronavirus Nucleocapsid Protein.* Clinical Chemistry (March 30, 2004) Vol. 50, No. 6, pp. 988-995. Whole document.	1-5, 8, 16, 19-21, 35-37, 44-48, 52, 56 and 57 (partially) 1-57

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 August 2005 (21-08-2005)	29 August 2005 (29-08-2005)

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	André Pilon (819) 997-2996

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2005/000632

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 38-40

because they relate to subject matter not required to be searched by this Authority, namely :

Although claims 38-40 are directed to a method for treatment of the human or animal body, which the Authority is not required to search under Rule 39.1(iv) of the PCT, the search has been carried out and based on the alleged effects of the composition.

2. [X] Claim Nos. : 1-6 and 11-15

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

The wording used in the claims, "an isolated polypeptide comprising an epitope of at least (x) amino acids of SEQ ID NO..." yields a multitude of polypeptide sequences that cannot be effectively searched. Therefore, the search was limited to SEQ ID NO: 496.

3. [ ] Claim Nos. :

because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	HE, Y ET AL., *Mapping of Antigenic Sites on the Nucleocapsid Protein of the Severe Acute Respiratory Syndrome Coronavirus*. Journal of Clinical Microbiology (November, 2004) Vol. 42, No. 11, pp. 5309-5314. Whole document.	1-5, 8, 16, 19-21, 35-37 and 44-48 (partially) 1-57