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(71) Demandeur/Applicant:
BAYLOR RESEARCH INSTITUTE, US

(72) Inventeurs/Inventors:
BANCHEREAU, JACQUES F., US;
ZURAWSKI, SANDRA, US;
ZURAWSKI, GERARD, US;
KLECHEVSKY, EYNAV, IL;
OH, SANGKON, US

(74) Agent: SHAPIRO COHEN

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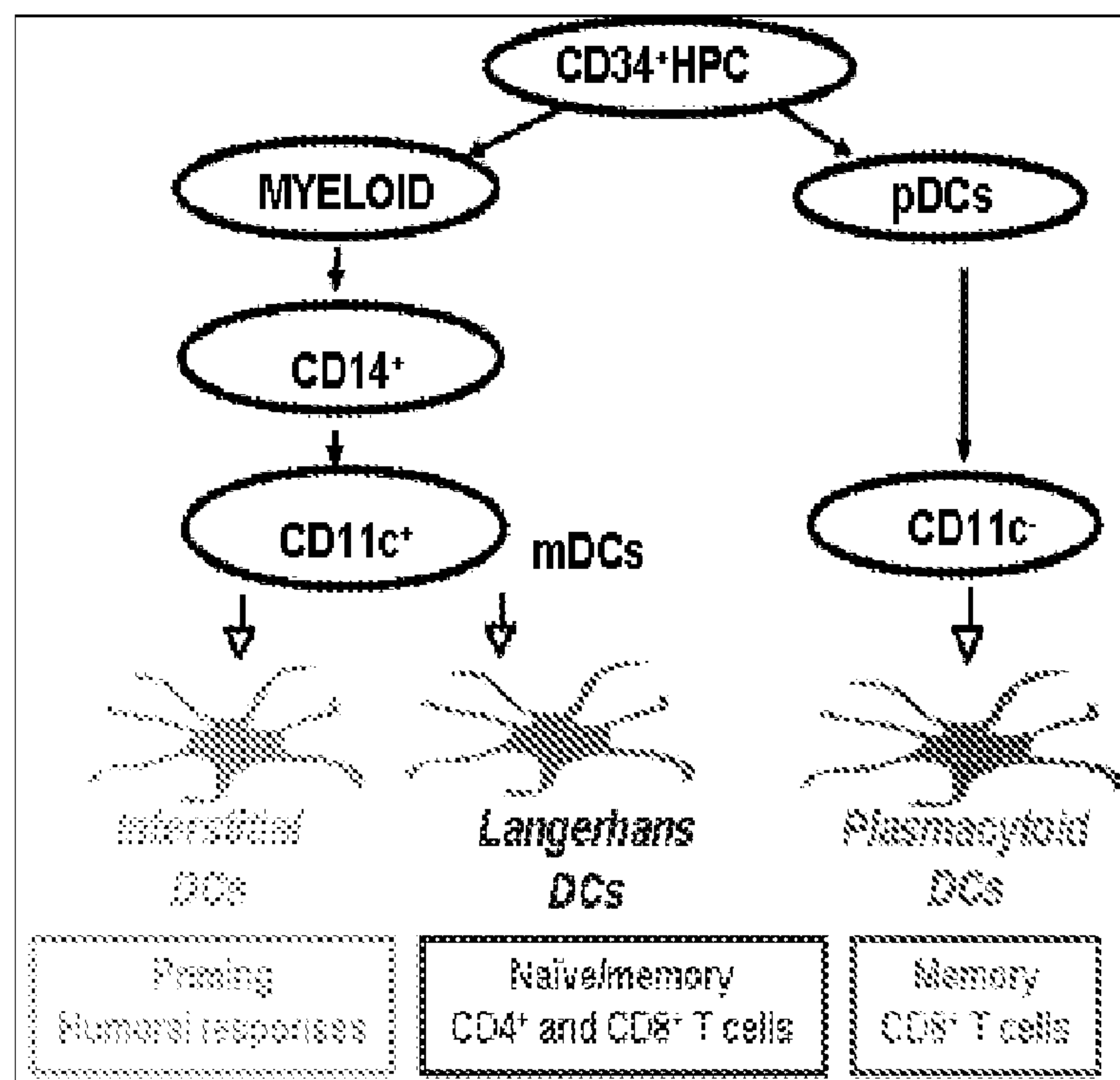


Figure 1

(57) Abrégé/Abstract:

The present invention includes isolated anti-Langerin vaccines, methods for making and using an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides at the carboxy- terminus of the isolated anti-Langerin antibody,

(57) **Abrégé(suite)/Abstract(continued):**

wherein when two or more antigenic peptides are present, the peptides are separated by the one or more linker peptides that comprise at least one glycosylation site. The present invention also includes isolated vectors for the expression of the anti-Langerin antigen delivery vectors and their manufactures and use.

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(71) Applicant (for all designated States except US): **BAY-LOR RESEARCH INSTITUTE** [US/US]; 3310 Live Oak Street, Suite 501, Dallas, TX 75201 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BANCHEREAU, Jacques, F.** [FR/US]; 6730 Northaven Road, Dallas, TX 75230 (US). **ZURAWSKI, Sandra** [US/US]; 7620 Jordan Lane, Midlothian, TX 76065 (US). **ZURAWSKI, Gerard** [AU/US]; 7620 Jordan Lane, Midlothian, TX 76065 (US). **KLECHEVSKY, Eynav** [IL/IL]; 27 Hanna Street, 34817 Haifa (IL). **OH, Sangkon** [KR/US]; 45 Caterham Court, Baltimore, MD 21237 (US).(74) Agents: **FLORES, Edwin, S.** et al.; Chalker Flores LLP, 14951 North Dallas Parkway, Suite 400, Dallas, TX 75254 (US).

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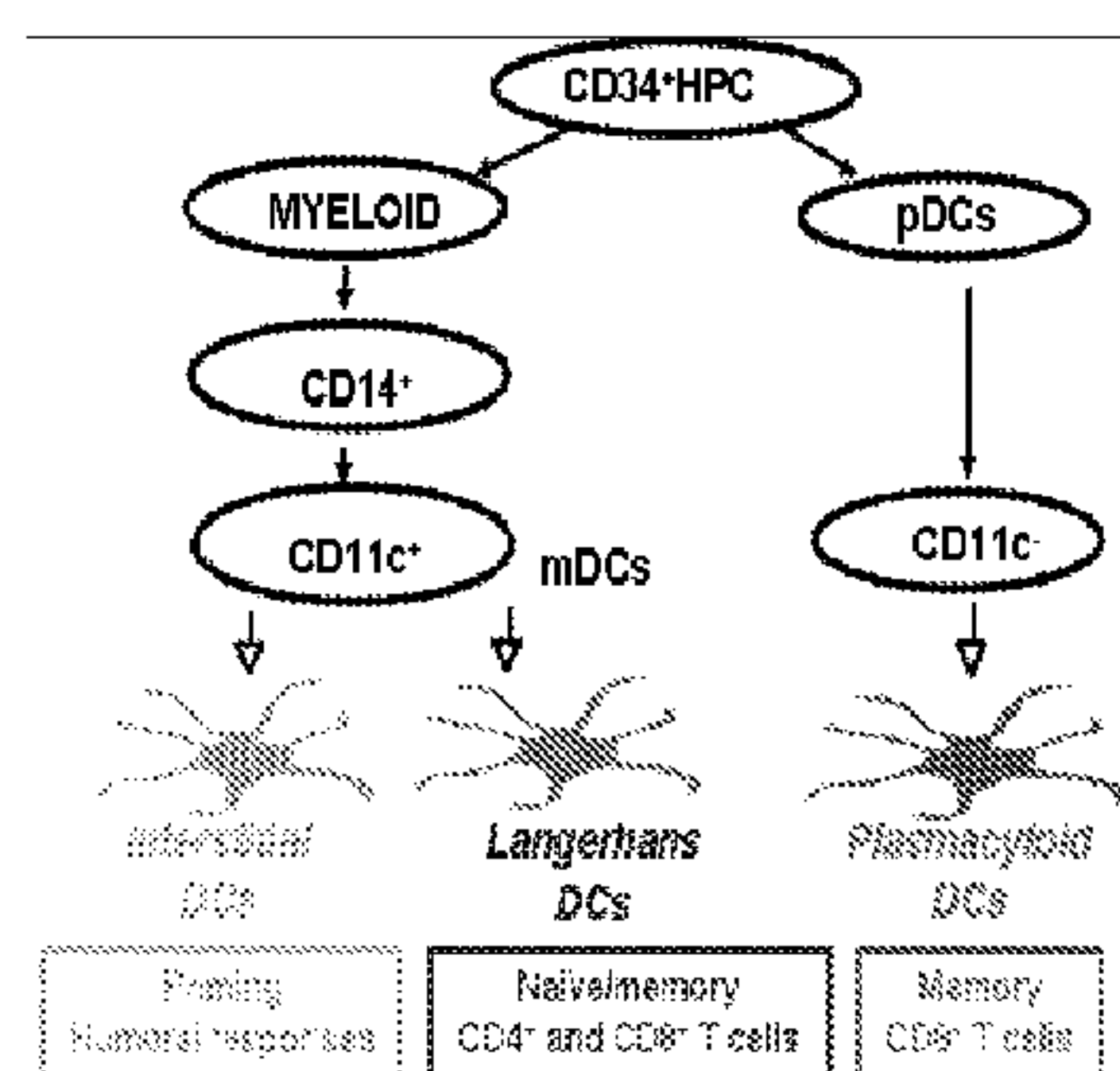
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Figure 1



(57) Abstract: The present invention includes isolated anti-Langerin vaccines, methods for making and using an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides at the carboxy- terminus of the isolated anti-Langerin antibody, wherein when two or more antigenic peptides are present, the peptides are separated by the one or more linker peptides that comprise at least one glycosylation site. The present invention also includes isolated vectors for the expression of the anti-Langerin antigen delivery vectors and their manufactures and use.

VACCINES DIRECTED TO LANGERHANS CELLS

Technical Field of the Invention

The present invention relates in general to the field of vaccines, and more particularly, to compositions and methods for targeting and delivering antigens to Langerhans cells for antigen presentation using high affinity anti-Langerin monoclonal antibodies and fusion proteins therewith.

Background Art

Without limiting the scope of the invention, its background is described in connection with antigen presentation.

Dendritic Cells (DCs) are professional antigen-presenting cells (APCs) that induce and sustain immune responses and are fundamental in establishing both tolerance and immunity. DCs capture and present antigens to CD4⁺ T cells, which then determine the quantity and quality of antigen-specific CD8⁺ T cells. There are subsets of DCs^{1,2}, including both myeloid and plasmacytoid DCs (mDCs and pDCs, respectively).

Prior Langerin related agents include those taught in United States Patent No. 6,878,528, issued to Duvert-Frances, et al., which include polynucleotides encoding a mammalian Langerhans cell antigen, including purified mammalian DC cell surface protein, designated Langerin, nucleic acids encoding Langerin, and antibodies which specifically bind Langerin.

Other anti-DC related agents are taught in, e.g., United States Patent Application Publication No. 20060257412, filed by Bowdish, et al., which includes a method of treating autoimmune disease by inducing antigen presentation by tolerance inducing antigen presenting cells. Briefly, this application teaches that antibodies to antigen presenting cells may be utilized to interfere with the interaction of the antigen presenting cell and immune cells, including T cells. Peptides may be linked to the antibodies thereby generating an immune response to such peptides, e.g., those peptides associated with autoimmunity.

Disclosure of the Invention

In one embodiment, the present invention includes compositions and methods for activating T and B cell responses by targeting antigens to antigen presenting cells along with the proper activation of the APC to activate T cell and B cells responses. One embodiment is a vaccine comprising an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides at the carboxy-terminus of the anti-Langerin antibody, wherein when two or more antigens are present, they are separated by one or more linker peptides that comprise at least one glycosylation site. In one aspect, the antibody binding fragment is selected from an Fv, Fab, Fab', F(ab')₂, Fc, or a ScFv fragment. In another aspect, the antibody comprises one or more complementarity determining regions selected from: ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVDPDRFSGSGSGGTNFTLKISRVE

AEDLGLYFCS (SEQ ID NO.: 45);
SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46);
VTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
5 EDEAIYFCA (SEQ ID NO.: 47);
SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); or a direct equivalent thereof. In another aspect, the
antigenic peptide is a cancer antigen selected from:
MWVPVVFLTLSVTWIGAAPLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWV
10 (SEQ ID NO.: 9);
LTAAHCIRNKSIVLLGRHSLFHPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHD (SEQ
ID NO.: 10);
LMLLRLSEPAELTDAVKVMDLPTQEPALGTTCYASGWGSIEPEEFLTPKKLQCVDLHVIS (SEQ
ID NO.: 11);
15 NDVCAQVHPQKVTKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERP
(SEQ ID NO.: 12); SLYTKVVHYRKWIKDTIVANP (SEQ ID NO.: 13); IMDQVPFSV (SEQ ID NO.:
14); ITDQVPFSV (SEQ ID NO.: 15); YLEPGPVTV (SEQ ID NO.: 16); YLEPGPVTA (SEQ ID NO.:
17); KTWGQYWQV (SEQ ID NO.: 18);
APLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWVLTAAHCIRNKSIVLLGRHSLF
20 HPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHDLMMLLRLSEPAELTDAVKVMDLPTQE
PALGTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKVTKFMLCAGRWTGGKST
CSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKDTIVANP (SEQ ID NO.:
19);
DTTEPATPTTPVTTPTTTKVPRNQDWLGVSRLRTKAWNRQLYPEWTEAQRLLDCWRGGQVSL
25 KVSNDGPTLIGANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVPYQETDDACIFP
DGGPCPSGSWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLGHTMEVTVYHRRGS
QSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQ (SEQ ID NO.: 20);
PLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRAXVVTHTYLEPGPVTAQVVLQAAIPLTSC
GSSPVPAS (SEQ ID NO.: 21);
30 GTTDGHRPTAEAPNTTAGQVPTTEVVGTTGQAPTAEPSTTSVQVPTTEVISTAPVQMPTAEST
GMTPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAA (SEQ ID NO.: 22);
QVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRYGS
FSVTLDIVQ (SEQ ID NO.: 23);
GIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLLCQPVLPSPACQLVLHQI
35 LKGGSGTYCLNVSLADTNSLAVVSTQLIVPGILLTGQEAGLGQ (SEQ ID NO.: 24);
MEMKILRALNFGLGRPLPLHFLRRASKIGEVDVEQHTLAKYLMELTMLDY (SEQ ID NO.: 25);
DWLVQVQMKFRLLQETMYMTVSIIDRFMQNNCVPPK (SEQ ID NO.: 26);
MEHQLLCCEVETIRRAYPDANLLNDRVLRAMLKAEETCAPSVSYFKCV (SEQ ID NO.: 27);

QKEVLPSMRKIVATWMLEVCEEQKCEEEVFPLAMNYLDRFLSLEPVKKSRLQLLGATCMFVAS
 KMKETIPLTAEKLCIYTDNSIRPEELLQMELL (SEQ ID NO.: 28);
 LVNKLKWNLAAMTPHDFIEHFLSKMPEAEENKQIRKHAQTFVALCATDVKFISNPPSMV (SEQ
 ID NO.: 29); or

5 AAGSVVAAVQGLNLRSPNNFLSYRLTRFLSRVIKCDPDCLRACQEIEALLESSLRQAQQNMD
 PKAAEEEEEEEEVDLACTPTDVRDVDI (SEQ ID NO.: 30), or binding fragments thereof. In another
 aspect, the antigenic peptide is a viral antigen selected from:
 VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL (SEQ ID NO.: 31);
 HTQGYFPDWQNYTPGPGVRYPLTFGWLYKL (SEQ ID NO.: 32); EKIRLRPGGKKKYKLKHIV
 10 (SEQ ID NO.: 33); NPPIVGEIYKRWIILGLNKIVRMYSPTSILD (SEQ ID NO.: 34);
 AIFQSSMTKILEPFRKQNPDIVIYQYMDDLY (SEQ ID NO.: 35);
 DTICIGYHANNSTDTVDTVLEKNVTVTHSVNLLED SHNGKLCRLKGIAPLQLGKCNIAGWLLGN
 PECDLLPVRSWSYIVETPNSENGICYPGDFIDYEELREQLSSVSSFERFEIFPKESSWPNHNTNGV
 TAACSHEGKSSFYRNLLWLTEKEGSYPKLKNSYVNKKGKEVLVLWGIHHPNSKEQQONLYQNE
 15 NAYVSVVTSNYYNRRFTPEIAERP KVRDQAGRMNYYWTLLKPGDTIIFEANGNLIAPMYAFALSR
 GFGSGIITSNASMHECNTKCQTPLGAINSSLPYQNIHPVTIGECPKYVRS AKLRMV (SEQ ID NO.:
 36);
 DQICIGYHANNSTEQVD TIMEKNVTVTTHAQDILEKKHNGKLCDL DGVKPLILRDCSVAGWLLGN
 PMCDEFIN VPEWSYIVEKANPVNDLCYPGDFNDYEELKHLLSRINHFEKIQIIPKSSWSSHEASLG
 20 VSSACPYQGKSSFFRN VVWLIKKNSTYPTIKRSYNNTN QEDLLVLWGIHHPNDAAEQTKLYQNP
 TTYISVGTSTLNQRLVPRIATRSKVNGQSGRMEFFWTILKPNDAINFESNGNFIAPEYAYKIVKKG
 DSTIMKSELEYGNCNTKCQTPMGAINSSMPFHNIHPLTIGECPKYVKS NRLVLA (SEQ ID NO.:
 37); or
 PIVQNIQGQM VHQAI SPRTLNAWVKVVEEKAFSPEVIPMFSALSEGATPQDLNTMLNTVGGHQA
 25 AMQMLKETINEEAAEWDRVHPVHAGPIAPGQMREPRGSDIAGTTSTLQE QIGWMTNNPPIPVGE
 IYKRWIILGLNKIVRMYSPTSILDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQN
 ANPDCKTILKALGPAATLEEMMTACQGVGGPGHKARVL (SEQ ID NO.: 38). In another aspect,
 when two or more antigens are present, the antigens are separated by one or more peptide linkers are
 selected from: SSVSPTTSVHPTPTSVPPTPTKSSP (SEQ ID NO.: 39);
 30 PTSTPADSSTITPTATPTATPTIKG (SEQ ID NO.: 40); TVTPTATATPSAIVTTITPTATTKP (SEQ ID
 NO.: 41); or TNGSITVAATAPT VTPTVNATPSAA (SEQ ID NO.: 42). In another aspect, the anti-
 Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4;
 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof. In another aspect, the anti-
 Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID
 35 NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79. In another aspect, the anti-Langerin
 antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852,
 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and humanized derivatives thereof. In

another aspect, the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein.

Another embodiment of the present invention includes an isolated nucleic acid vector that expresses an anti-Langerin antibody or binding fragment thereof and two or more antigenic peptides at the carboxy-terminus of the light chain, the heavy chain or both the light and heavy chains of the anti-Langerin antibody, wherein when two or more antigenic peptides are present, the antigenic peptides are separated by the one or more peptide linkers that comprise at least one glycosylation site. In one aspect, the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC (Mucin) (e.g., MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, and Ki-67. In another aspect, the antigenic peptides are cancer peptides are selected from tumor associated antigens comprising antigens from leukemias and lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia. In another aspect, the antigenic peptides are selected from Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain, HLA-A201-FluMP (58-66) peptide (GILGFVFTL) tetramer, Avian Flu (HA5-1), dockerin domain from *C. thermocellum* (doc), HIV gag p24 (gag), or a string of HIV peptides (Lipo5), PSA (KLQCVDLHV)-tetramer, or an HIVgag-derived p24-PLA. In another aspect, the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof. In another aspect, the anti-Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79. In another aspect, the anti-Langerin antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and humanized derivatives thereof. In another aspect, the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein.

Yet another embodiment of the present invention includes a method of enhancing T and B cell responses comprising: immunizing a subject in need of vaccination with an effective amount of a vaccine

comprising an isolated fusion protein comprising an anti-Langerin antibody or binding portion thereof and one or more antigenic peptides linked to the carboxy-terminus of the anti-Langerin antibody. In one aspect, the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC (Mucin) (e.g., MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, and Ki-67. In another aspect, the antigenic peptides are cancer peptides selected from tumor associated antigens comprising antigens from leukemias, lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia. In another aspect, the antigenic peptides are selected from Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain, HLA-A201-FluMP (58-66) peptide (GILGFVFTL) tetramer, Avian Flu (HA5-1), Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain (HA1-1), dockerin domain from *C. thermocellum* (doc), HIV gag p24 (gag), or a string of HIV peptides (Hipo5), PSA (KLQCVDLHV)-tetramer, or an HIVgag-derived p24-PLA.

Yet another embodiment is a method of making an anti-Langerin-antigen fusion protein comprising: expressing an isolated fusion protein comprising an anti-Langerin antibody or binding fragment thereof in a host cell, the fusion protein comprising one or more antigenic peptides at the carboxy-terminus of the anti-Langerin antibody or binding fragment thereof, wherein when two or more cancer peptides are present, the cancer peptides are separated by one or more linkers, at least one linker comprising a glycosylation site; and isolating the fusion protein. In one aspect, fusion protein expressed in the host is further isolated and purified. In another aspect, the host is a eukaryotic cell. In another aspect, the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC-related protein (Mucin) (MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance

protein (LRP), Bcl-2, and Ki-67. In another aspect, the antigenic peptides are cancer peptides selected from tumor associated antigens comprising antigens from leukemias and lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia. In another aspect, the cancer peptides are selected from at least one of:

- 10 MWVPVVFLTLSVTWIGAAPLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWV
(SEQ ID NO.: 9);
LTAAH CIRNKS VILLGRHSLFHPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHD (SEQ
ID NO.: 10);
LMLLRLSEPAELTDAVKVMDLPTQEPALGTTTCYASGWGSIEPEEFLTPKKLQCVDLHVIS (SEQ
15 ID NO.: 11);
NDVCAQVHPQKVTKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERP
(SEQ ID NO.: 12); SLYTKVVHYRKWIKDTIVANP (SEQ ID NO.: 13); IMDQVPFSV (SEQ ID NO.:
14); ITDQVPFSV (SEQ ID NO.: 15); YLEPGPVTV (SEQ ID NO.: 16); YLEPGPVTA (SEQ ID NO.:
17); KTWGQYWQV (SEQ ID NO.: 18);
20 APLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWVLTAAHCIRNKS VILLGRHSLF
HPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHD LMLLRLSEPAELTDAVKVMDLPTQE
PALGTTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKVTKFMLCAGRWTGGKST
CSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKDTIVANP (SEQ ID NO.:
19);
25 DTTEPATPTTPVTTPTTTKVPRNQDWLGVSRLRTKAWNRQLYPEWTEAQRLDCWRGGQVSL
KVSNDGPTLIGANASFSIALNFPQSQKVLPDGQVIWVNNTIINGSQVWGGQPVPYQETDDACIFP
DGGPCPSGWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLGHTMEVTVYHRRGS
QSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQ (SEQ ID NO.: 20);
PLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRAXVVHTHTYLEPGPVTAQVVLQAAIPLTSC
30 GSSPVPAS (SEQ ID NO.: 21);
GTTDGHRTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAEST
GMTPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAA (SEQ ID NO.: 22);
QVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRYGS
FSVTLDIVQ (SEQ ID NO.: 23);
35 GIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLPSPACQLVLHQI
LKGGSGTYCLNVSLADTNSLAVVSTQLIVPGILLTGQEAGLGQ (SEQ ID NO.: 24);
MEMKILRALNFGLGRPLPLHFLRRASKIGEVDVEQHTLAKYLMELTMLDY (SEQ ID NO.: 25);
DWLVQVQMKFRLLQETMYMTVSIIDRFMQNNCVPKK (SEQ ID NO.: 26);

MEHQLLCCEVETIRRAYPDANLLNDRVLRAMLKAEETCAPSVSYFKCV (SEQ ID NO.: 27);
 QKEVLPSMRKIVATWMLLEVCEEQKCEEEVFPLAMNYLDRFLSLEPVKKSRLLQLLGATCMFVAS
 KMKETIPLTAEKLCIYTDNSIRPEELLQMELL (SEQ ID NO.: 28);
 LVNKLKWNLAAMTPHDFIEHFLSKMPEAEENKQIIRKHAQTFVALCATDVKFISNPPSMV (SEQ
 5 ID NO.: 29); or

AAGSVVAAVQGLNLRSPNNFLSYRLTRFLSRVIKCDPDCLRACQEIEALLESSLRQAQQNMD
 PKAAEEEEEEEEVDLACTPTDVRDVDI (SEQ ID NO.: 30), or immunogenic fragments thereof.

In another embodiment, the invention includes a method of expanding antigen-specific T cells or B cells
 in vitro comprising: isolating peripheral blood mononuclear cells (PBMCs) from a cancer patient;
 10 incubating the isolated PBMCs with an immunogenic amount of an isolated anti-Langerin-(PL-Ag)_x or
 anti-Langerin-(Ag-PL)_x vaccine, wherein Ag is a tumor associated antigen and x is an integer 1 to 20;
 expanding the PBMCs in the presence of an effective amount of IL-2; harvesting the cells; and assessing
 the cytokine production by the cells to determine the presence of anti-cancer specific T cells or B cells.

In yet another embodiment, the invention includes a tumor associated antigen-specific T cell or B cell
 15 made by the method comprising: isolating peripheral blood mononuclear cells (PBMCs) from a cancer
 patient; incubating the isolated PBMCs with an immunogenic amount of an anti-Langerin-(PL-Ag)_x or
 anti-Langerin-(Ag-PL)_x vaccine, wherein Ag is a tumor associated antigen and x is an integer 1 to 20;
 expanding the PBMCs in the presence of an effective amount of IL-2; harvesting the cells; and assessing
 the cytokine production by the cells to determine the presence of tumor associated antigen-specific T
 20 cells or B cells.

Another embodiment of the invention includes a therapeutic vaccine comprising an isolated fusion
 protein comprising the formula: Ab-(PL-Ag)_x; Ab-(Ag-PL)_x; Ab-(PL-Ag-PL)_x; Ab-(Ag-PL-Ag)_x; Ab-
 (PL-Ag)_x-PL; or Ab-(Ag-PL)_x-Ag; wherein Ab is an anti-Langerin monoclonal antibody or binding
 fragment thereof; PL is at least one peptide linker comprising at least one glycosylation site; Ag is at least
 25 one infectious disease antigen; and x is an integer from 1 to 20.

Yet another embodiment includes a method of expanding antigen-specific T cells or B cells in vitro
 comprising: isolating peripheral blood mononuclear cells (PBMCs) from a patient suspected of having an
 infection; incubating the isolated PBMCs with an immunogenic amount of an isolated anti-Langerin-(PL-
 Ag)_x or α Langerin-(Ag-PL)_x vaccine, wherein Ag is an antigen of the infectious agent and x is an integer
 30 1 to 20; expanding the PBMCs in the presence of an effective amount of one or more cytokines;
 harvesting the cells; and assessing the cytokine production by the cells to determine the presence of anti-
 infections agent specific T cells or B cells. Another embodiment is a viral associated antigen-specific T
 cell or B cell made by the method comprising: isolating peripheral blood mononuclear cells (PBMCs)
 from a patient suspected of having a viral infection; incubating the isolated PBMCs with an immunogenic
 35 amount of an isolated anti-Langerin-(PL-Ag)_x or anti-Langerin-(Ag-PL)_x vaccine, wherein Ag is a viral
 associated antigen and x is an integer 1 to 20; expanding the PBMCs in the presence of an effective

amount of one or more cytokines; harvesting the cells; and assessing the cytokine production by the cells to determine the presence of viral associated antigen-specific T cells or B cells.

Another embodiment is a therapeutic vaccine comprising an isolated fusion protein comprising the formula: Ab-(PL-Ag)_x; Ab-(Ag-PL)_x; Ab-(PL-Ag-PL)_x; Ab-(Ag-PL-Ag)_x; Ab-(PL-Ag)_x-PL; or Ab-

(Ag-PL)_x-Ag; wherein Ab is an anti-Langerin monoclonal antibody or binding fragment thereof; PL is at least one peptide linker comprising at least one glycosylation site; Ag is at least one viral antigen; and x is an integer from 1 to 20. In one example, the isolated antibody comprising one or more of complementarity determining regions selected from:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTNFTLKISRVE

10 AEDLGLYFCS (SEQ ID NO.: 45);

SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNFKGKATLTADKSSTTAY

MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46);

VTLTCSRSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT

EDEAIYFCA (SEQ ID NO.: 47);

15 SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS

LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); or a direct equivalent thereof. In one aspect, the antibody is humanized. In another aspect, the antibody is 15B10 having ATCC Accession No. PTA-9852 and humanized derivatives thereof. In another aspect, the antibody is 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7, and humanized derivatives thereof.

20 Yet another embodiment is an isolated isolated nucleic acid that encodes a 15B10, 2G3, 91E7, 37C1, or 4C7 antibody, antibody binding fragment or a humanized derivative thereof. In one aspect, the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80; or binding fragments thereof respectively. In another aspect, the anti-Langerin antibody is the expression product from the following pairs of nucleic acid sequences

25 SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79; or binding fragments thereof, which are the 15B10, 2G3, 91E7, 37C1, or 4C7 antibodies, respectively.

Yet another embodiment of the present invention is a pharmaceutical composition comprising an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides attached to the anti-Langerin antibody, wherein when two or more antigens are present, they are separated by one or

30 more linker peptides that comprise at least one glycosylation site. In one aspect, the antibody binding fragment is selected from an Fv, Fab, Fab', F(ab')₂, Fc, or a ScFv fragment. In another aspect, the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof. In another aspect, the anti-Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID

35 NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79. In another aspect, the anti-Langerin antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and humanized derivatives thereof. In

another aspect, the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein. In another aspect, the composition further comprises an adjuvant. In another aspect, the composition further comprises one or more pharmaceutical excipients.

Yet another embodiment of the present invention is a therapeutic vaccine comprising a fusion protein comprising the formula: Ab-(PL-Ag)_x; Ab-(Ag-PL)_x; Ab-(PL-Ag-PL)_x; Ab-(Ag-PL-Ag)_x; Ab-(PL-Ag)_x-PL; or Ab-(Ag-PL)_x-Ag; wherein Ab is an anti-Langerin monoclonal antibody or binding fragment thereof; PL is at least one peptide linker comprising at least one glycosylation site; Ag is at least one viral antigen; and x is an integer from 1 to 20.

The invention provides a Langerin binding antibody (15B10) that comprises at least one immunoglobulin light chain variable domain (VL) which comprises the amino acid and nucleic acid sequence encoding:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTNFTLKISRVE
AEDLGLYFCS (SEQ ID NO.: 45); or and direct equivalent thereof.

Accordingly the invention provides a Langerin binding antibody (15B10) that comprises an antigen binding site comprising at least one immunoglobulin heavy chain variable domain (VH) which comprises the amino acid and nucleic acid sequence encoding:

SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46); and direct equivalents thereof.

The invention provides a Langerin binding antibody (2G3) that comprises at least one immunoglobulin light chain variable domain (VL) which comprises the amino acid and nucleic acid sequence encoding:

VTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
EDEAIYFCA (SEQ ID NO.: 47); or and direct equivalent thereof.

Accordingly the invention provides a Langerin binding antibody (2G3) that comprises an antigen binding site comprising at least one immunoglobulin heavy chain variable domain (VH) which comprises the amino acid and nucleic acid sequence encoding:

SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYCYC (SEQ ID NO.: 48); and direct equivalents thereof.

In one aspect the invention provides a single domain Langerin antibody comprising an isolated immunoglobulin light chain comprising a heavy chain variable domain (VL) as defined above. In another aspect the invention provides a single domain Langerin binding molecule comprising an isolated immunoglobulin heavy chain comprising a heavy chain variable domain (VH) as defined above.

In another aspect the invention also provides a Langerin binding antibody comprising a light chain (VL) variable domains in which the Langerin binding antibody comprises at least one antigen binding site comprising: an antibody light chain variable domain (VL) which comprises in sequence hypervariable regions obtained from the amino acid and nucleic acid sequences encoding:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTNFTLKISRVE
 AEDLGLYFCS (SEQ ID NO.: 45); or
 VTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPPARFSGSLIGDKAALTITGAQT
 EDEAIYFCA (SEQ ID NO.: 47); and direct equivalents thereof.

- 5 In another aspect the invention also provides a Langerin binding antibody comprising, the amino acid and
 nucleic acid sequences of heavy chain variable domain (VH) which comprises in sequence hypervariable
 regions obtained from:
 SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
 MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46); or
 10 SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
 LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); and direct equivalents thereof.

mAnti-Langerin15B10K – Nucleotide and mature protein amino acid sequence of the light chain of the
 mouse anti-Langerin 15B10 antibody cDNA, respectively. The variable region residues are underlined.

- 15 **ATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGGATTCTGCTTCCAGCAGTGATGTT**
 GTGATGACCCAACTCCACTCTCCCTGCCTGTCCGTCTTGGAGATCAAGCCTCCATCTCTTGC
 AGATCTAGTCAGAGCCTTGTACACAGTAATGGAAACACCTATTTACATTGGTACCTGCAGAA
 GCCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAG
 ACAGGTTCAGTGGCAGTGGATCAGGGACAAATTTCACTCAAGATCAGCAGAGTGGAGGC
 TGAGGATCTGGGACTTTATTTCTGCTCTCAAAGTACACATGTTCCGTACACGTTTCGGAGGGG
 20 GGACCAAGCTGGAAATAAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCC
 AGTGAGCAGTTAACATCTGGAGGTGCCTCAGTCGTGTGCTTCTTGAACAACTTCTACCCCAA
 AGACATCAATGTCAAGTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGT
 TGGACTGATCAGGACAGCAAAGACAGCACCTACAGCATGAACAGCACCTCACGTTGACCA
 AGGACGAGTATGAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTC
 25 ACCCATCGTCAAGAGCTTCAACAGGAATGAGTGTTAG (SEQ ID NO. 49)
DVVMQTPLSLPVRLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPD
RFSGSGSGTNFTLKISRVEAEDLGLYFCSQSTHVPYTFGGGTKLEIKRADAAPTVSIFPPSSEQLTSG
GASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDYSTYSMNSTLTTLTKDEYERHNSY
TCEATHKTSTSPIVKSFNRNEC
 30 (SEQ ID NO. 50)

mAnti-Langerin15B10H-LV-hIgG4H-C – Nucleotide and mature protein amino acid sequence of the
 heavy chain variable region of the mouse anti-Langerin 15B10 antibody fused to human IgG4,
 respectively. The variable region residues are underlined.

- 35 **ATGGAATGGAGGATCTTTCTCTTCATCCTGTCAGGAACTGCAGGTGTCCACTCCCAGGTTTCAG**
 CTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGC
 TTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGCAGAGAACTGGACAGGGCC
 TTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTCTACAATGAGAACTTCAAGG
 GCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCTACATGCAGCTCAGCAGCCTG
 ACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTATAACTACCCTTTTGCTTACTGGG
 40 GCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACGGGGCCCATCCGTCTTCCCCCTGG
 CGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGACTAC
 TTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCCTGACCAGCGGCGTGACACCTT
 CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG
 CAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGTGG
 45 ACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCCACCCTGCCCAGCACCTGAGTTCGAA

GGGGGACCATCAGTCTTCCTGTTCCCCC AAAACCCAAGGACACTCTCATGATCTCCCGGACC
 CCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTCAACTG
 GTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTTCAAC
 AGCACGTACCGTGTGGTGCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAACGGCAAGGA
 5 GTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCCTCCATCGAGAAAACCATCTCCAAAG
 CCAAAGGGCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCCCAGGAGGAGATGACC
 AAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTACCCCAGCGACATCGCCGTGGA
 GTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC
 GACGGCTCCTTCTTCTCTACAGCAGGCTAACCGTGGACAAGAGCAGGTGGCAGGAGGGGAA
 10 TGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGCCTCTC
 CCTGTCTCTGGGTAAAGCTAGCTGA (SEQ ID NO. 51)

QVQLRQSGPELVKPGASVKMSCKASGYTFD YVISWVKQRTGQGLEWIGDIYPGSGYSFY NENF
 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFPL
 APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS SSG
 15 TKTYTCNV DHKPSNTKVDKR VESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTCVV
 VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
 KGLPSSIEKTISKAKGQPREPQVYTLPPS QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
 KTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKAS (SEQ ID
 NO. 52)

20 mAnti-Langerin2G3L – Nucleotide and mature protein amino acid sequence of the light chain of the
 mouse anti-Langerin 2G3 antibody cDNA, respectively. The variable region residues are underlined.

ATGGCCTGGATTTCACTTATACTCTCTCTCCTGGCTCTCAGCTCAGGGGGCCATTTCCCAGGCT
 GTTGTGACTCAGGAATCTGCACTCACCATCATCCTGGTGAAACAGTCACACTCACTTGTCTGC
 TCAAGTACTGGGGCTGTTACAAC TAGTA ACTATGCCAACTGGGTCCAAGAAAAACCAGATCA
 25 TTTATTCACTGGTCTAATAGGTGGTACCAACAACCGAGTTTCAGGTGTTCTCCTGCCAGATTCTC
 AGGCTCCCTGATTGGAGACAAGGCTGCCCTCACCATCACAGGGGGCACAGACTGAGGATGAGG
 CAATATATTTCTGTGCTCTATGGTACAGCAACCATTGGGTGTTTCGGTGGAGGAACCAA ACTGA
 CTGTCCTAGGCCAGCCCAAGTCTTCGCCATCAGTCACCCTGTTTCCACCTTCCTCTGAAGAGC
 TCGAGACTAACAAGGCCACACTGGTGTGTACGATCACTGATTTCTACCCAGGTGTGGTGACA
 30 GTGGACTGGAAGGTAGATGGTACCCCTGTCACCTCAGGGTATGGAGACAACCCAGCCTTCCAA
 ACAGAGCAACAACAAGTACATGGCTAGCAGCTACCTGACCCTGACAGCAAGAGCATGGGAA
 AGGCATAGCAGTTACAGCTGCCAGGTCACTCATGAAGGTCACACTGTGGAGAAGAGTTTGTC
 CCGTGCTGACTGTTCTTAG (SEQ ID NO. 53)

QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGV PARFS
 35 GSLIGDKAALTITGAQTEDEAIYFCALWYSNHWVFGGGTKLTVLGQPKSSPSVTLFPPSSEETN
KATLVCTITDFYPGVVTVDWKVDGT
 PVTQGMETTQPSKQSNKYMASSYLTLTARAWERHSSYSCQVTHEGHTVEKSLSRADCS (SEQ
 ID NO. 54)

40 mAnti-Langerin2G3H – Nucleotide and mature protein amino acid sequence of the heavy chain of the
 mouse anti-Langerin 2G3 antibody cDNA, respectively. The variable region residues are underlined.

ATGACATTGAACATGCTGTTGGGGCTGAAGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
 CATTGTGAGGTGCAGCTTGTTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
 ACTCTCATGTGCAGCCTCTGGATTAACTTCAATATCTACGCCATGAACTGGGTCCGCCAGGC
 TCCAGGAAAGGGTTTGGAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAACAT
 45 ATTATGCCGATTCAGTGAAAGACAGGTTCAACATCTCCAGAGATGATTCACAAAGCTTGCTCT
 ATCTGCAAATGAACA ACTTGAAA ACTGAGGACACAGCCATGTATTACTGTGTGGGACGGGAC
 TGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACACCCCCA
 TCTGTCTATCCACTGGCCCCCTGGATCTGCTGCCCAA ACTCACTCCATGGTGACCCTGGGATGC
 CTGGTCAAGGGCTATTTCCCTGAGCCAGTGACAGTGACCTGGA ACTCTGGATCCCTGTCCAGC
 50 GGTGTGCACACCTTCCCAGCTGTCCTGCAGTCTGACCTCTACACTCTGAGCAGCTCAGTGACT
 GTCCCCTCCAGCACCTGGCCCAGCGAGACCGTCACCTGCAACGTTGCCACCCGGCCAGCAG
 CACCAAGGTGGACAAGAAAATTGTGCCCAGGGATTGTGGTTGTAAGCCTTG CATATGTACAG

TCCCAGAAAGTATCATCTGTCTTCATCTTCCCCCCTAAAGCCCAAGGATGTGCTCACCATTACTC
 TGACTCCTAAGGTCACGTGTGTTGTGGTAGACATCAGCAAGGATGATCCCGAGGTCCAGTTC
 AGCTGGTTTGTAGATGATGTGGAGGTGCACACAGCTCAGACGCAACCCCGGGAGGAGCAGTT
 CAACAGCACTTTCCGCTCAGTCAGTGAACCTCCCATCATGCACCAGGACTGGCTCAATGGCAA
 5 GGAGTTCAAATGCAGGGTCAACAGTGCAGCTTTCCCTGCCCCCATCGAGAAAACCATCTCCA
 AAACCAAAGGCAGACCGAAGGCTCCACAGGTGTACACCATTCCACCTCCCAAGGAGCAGATG
 GCCAAGGATAAAGTCAGTCTGACCTGCATGATAACAGACTTCTTCCCTGAAGACATTACTGTG
 GAGTGGCAGTGGAATGGGCAGCCAGCGGAGAACAACAAGCACTCAGCCCATCATGGACA
 CAGATGGCTCTTACTTCGTCTACAGCAAGCTCAATGTGCAGAAGAGCAACTGGGAGGCAGGA
 10 AATACTTTACCTGCTCTGTGTTACATGAGGGCCTGCACAACCACCATACTGAGAAGAGCCTC
 TCCCACTCTCCTGGTAAAGCTAGCTGA (SEQ ID NO. 55)

EVQLVESGGGLVQPKGSLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYA
 DSVKDRFTISRDDSQLLYLQMNNLKTEDTAMYYCVGRDWFYWGQGLVTVSAAKTTPPSVY
 PLAPGSAAQTNSMVTLGCLVKGYFPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSST
 15 WPSETVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLITLTPKVTCTVVV
 DISKDDPEVQFSWFVDDVEVHTAQTQPREEQFNSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFP
 APIEKTISKTKGRPKAPQVYTIPPPKEQMAKDKVSLTCMITDFFPEDITVEWQWNGQPAENYKNT
 QPIMDTDGSYFVYSKLVNPKSNWEAGNTFTCSVLHEGLHNHHTEKSLSHSPGKAS (SEQ ID NO.
 56)

20 In another embodiment the invention includes an antibody comprising one or more of the
 complementarity determining regions selected from:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVDPDRFSGSGSGTNFTLKISRVE
 AEDLGLYFCS (SEQ ID NO.: 45);

25 SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
 MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46);

VTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
 EDEAIYFCA (SEQ ID NO.: 47);

30 SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQL
 LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); or a direct equivalent thereof. In one aspect, the
 antibody is humanized. In another aspect, the antibody is 15B10, 2G3 or humanized derivatives thereof.
 In another aspect, the invention includes nucleic acids that encode the 15B10, the 2G3 antibody or
 humanized derivatives thereof.

Description of the Drawings

35 For a more complete understanding of the features and advantages of the present invention, reference is
 now made to the detailed description of the invention along with the accompanying figures and in which:

Figure 1 shows that two main DC differentiation pathways exist. A myeloid pathway generates two
 subsets: Langerhans cells (LCs) found in stratified epithelia such as the skin, and interstitial DCs
 (intDCs) found in all other tissues.

40 Figure 2 shows that recombinant anti-Langerin antibodies fused to antigens retain their ability to bind to
 cell surface Langerin.

Figure 3 is a demonstration of the ability of recombinant anti-Langerin antibody fused to the human prostate specific cancer antigen to elicit the expansion of antigen-specific CD4+ T cells from a health donor.

5 Figure 4 is a demonstration of the ability of recombinant anti-Langerin antibody fused to the human prostate specific cancer antigen to elicit the expansion of antigen-specific CD8+ T cells from a prostate cancer patient.

Figure 5 shows that anti-Langerin preferentially targets epidermal LCs.

Figure 6 shows the differential expression of Langerin by human skin DCs.

Figure 7 shows that the anti-Langerin antibody (15B10) specifically stains human Langerhans cells.

10 Figure 8 shows the binding results of the anti-Langerin antibodies against a non-human primate target.

Figure 9 shows the ability of recombinant anti-Langerin 15B10 antibody fused to Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain to evoke potent antigen-specific antibody production in NHP.

15 Figure 10 shows that recombinant fusion proteins of anti-human DC receptors and antigens induce antigen-specific immune responses in NHP.

Figure 11 shows that the Anti-Langerin G3 antibody specifically stains NHP Langerhans cells.

Figure 12 shows the antibody titers for anti-HIV-gag antibodies in NHP vaccination with a gag-microparticle, an anti-hlGG4-gag antibody, an anti-DCIR-gag vaccine and an anti-Langerin-gag-p24 vaccine, all with or without poly I:C as an adjuvant.

20 Figure 13 shows FACS analysis on Langerin clones: 293F cells were transiently transfected with vectors directing the expression of full-length (cell surface) Langerin from human, Rhesus macaque, and mouse.

Figure 14 show the results of ELISA binding analysis in two formats – direct (antigen bound to plate directly and bound antibody detected with an anti-mouse IgG-HRP conjugate) and capture (antibody bound to plate).

25 **Description of the Invention**

While the making and using of various embodiments of the present invention are discussed in detail below, it should be appreciated that the present invention provides many applicable inventive concepts that can be embodied in a wide variety of specific contexts. The specific embodiments discussed herein are merely illustrative of specific ways to make and use the invention and do not delimit the scope of the
30 invention.

To facilitate the understanding of this invention, a number of terms are defined below. Terms defined herein have meanings as commonly understood by a person of ordinary skill in the areas relevant to the present invention. Terms such as “a”, “an” and “the” are not intended to refer to only a singular entity, but include the general class of which a specific example may be used for illustration. The terminology

herein is used to describe specific embodiments of the invention, but their usage does not delimit the invention, except as outlined in the claims.

Subsets of Dendritic Cells (DCs). The present inventors have discovered that two main DC differentiation pathways exist. A myeloid pathway generates two subsets: Langerhans cells (LCs) found in stratified epithelia such as the skin, and interstitial DCs (intDCs) found in all other tissues. A plasmacytoid pathway generates plasmacytoid DCs (pDCs), which secrete large amounts of IFN $\alpha\beta$ after viral infection³ and efficiently present viral antigens in a novel mechanism⁴ (Figure 1). DCs and their precursors show remarkable functional plasticity. For example, pDCs form a first barrier to the expansion of intruding viruses, thereby acting, through the release of interferon, as part of the innate immune response^{5,6}.

Monocytes can differentiate into either macrophages, which act as scavengers, or DCs that induce specific immune responses^{7,8}. Different cytokines skew the in vitro differentiation of monocytes into DCs with different phenotypes and functions. Thus, when activated (e.g., by GM-CSF) monocytes encounter IL-4, they yield IL-4DCs⁹⁻¹¹. By contrast, after encountering IFN α , TNF α , or IL-15, activated monocytes will differentiate into IFNDCs¹²⁻¹⁵, TNFDCs⁸, or IL-15DCs¹⁶. Each of these DC subsets has common as well as unique biological functions, determined by a unique combination of cell-surface molecules and cytokines. For example, whereas IL-4DCs are a homologous population of immature cells devoid of LCs, large portions of IFNDCs express CD1a and Langerin⁸.

The invention includes also variants and other modification of an antibody (or “Ab”) or fragments thereof, e.g., anti-Langerin fusion protein (antibody is used interchangeably with the term “immunoglobulin”). As used herein, the term “antibodies or binding fragments thereof,” includes whole antibodies or binding fragments of an antibody, e.g., Fv, Fab, Fab’, F(ab’)₂, Fc, and single chain Fv fragments (ScFv) or any biologically effective fragments of an immunoglobulins that binds specifically to, e.g., Langerin. Antibodies from human origin or humanized antibodies have lowered or no immunogenicity in humans and have a lower number or no immunogenic epitopes compared to non-human antibodies. Antibodies and their fragments will generally be selected to have a reduced level or no antigenicity in humans.

As used herein, the terms “Ag” or “antigen” refer to a substance capable of either binding to an antigen binding region of an immunoglobulin molecule or of eliciting an immune response, e.g., a T cell-mediated immune response by the presentation of the antigen on Major Histocompatibility Antigen (MHC) cellular proteins. As used herein, “antigen” includes, but is not limited to, antigenic determinants, haptens, and immunogens, which may be peptides, small molecules, carbohydrates, lipids, nucleic acids or combinations thereof. The skilled immunologist will recognize that when discussing antigens that are processed for presentation to T cells, the term “antigen” refers to those portions of the antigen (e.g., a peptide fragment) that is a T cell epitope presented by MHC to the T cell receptor. When used in the context of a B cell mediated immune response in the form of an antibody that is specific for an “antigen”, the portion of the antigen that binds to the complementarity determining regions of the variable domains of the antibody (light and heavy) the bound portion may be a linear or three-

dimensional epitope. In the context of the present invention, the term antigen is used on both contexts, that is, the antibody is specific for a protein antigen (Langerin), but also carries one or more peptide epitopes for presentation by MHC to T cells. In certain cases, the antigens delivered by the vaccine or fusion protein of the present invention are internalized and processed by antigen presenting cells prior to presentation, e.g., by cleavage of one or more portions of the antibody or fusion protein.

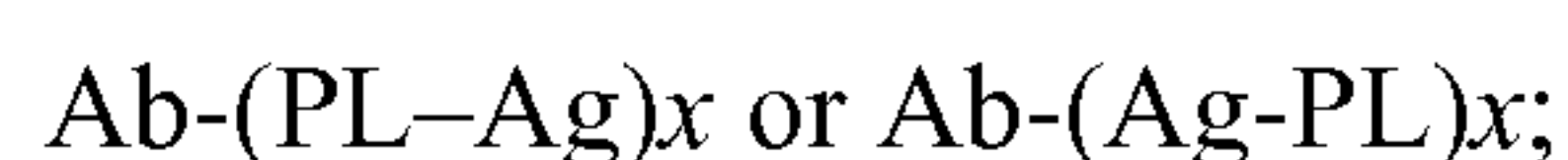
As used herein, the term “antigenic peptide” refers to that portion of a polypeptide antigen that is specifically recognized by either B-cells or T-cells. B-cells respond to foreign antigenic determinants via antibody production, whereas T-lymphocytes are the mediate cellular immunity. Thus, antigenic peptides are those parts of an antigen that are recognized by antibodies, or in the context of an MHC, by T-cell receptors.

As used herein, the term “epitope” refers to any protein determinant capable of specific binding to an immunoglobulin or of being presented by a Major Histocompatibility Complex (MHC) protein (e.g., Class I or Class II) to a T-cell receptor. Epitopic determinants are generally short peptides 5-30 amino acids long that fit within the groove of the MHC molecule that presents certain amino acid side groups toward the T cell receptor and has certain other residues in the groove, e.g., due to specific charge characteristics of the groove, the peptide side groups and the T cell receptor. Generally, an antibody specifically binds to an antigen when the dissociation constant is 1 mM, 100 nM or even 10 nM.

As used herein, the term “vector” is used in two different contexts. When using the term “vector” with reference to a vaccine, a vector is used to describe a non-antigenic portion that is used to direct or deliver the antigenic portion of the vaccine. For example, an antibody or binding fragments thereof may be bound to or form a fusion protein with the antigen that elicits the immune response. For cellular vaccines, the vector for delivery and/or presentation of the antigen is the antigen presenting cell, which is delivered by the cell that is loaded with antigen. In certain cases, the cellular vector itself may also process and present the antigen(s) to T cells and activate an antigen-specific immune response. When used in the context of nucleic acids, a “vector” refers a construct that is capable of delivering, and preferably expressing, one or more genes or polynucleotide sequences of interest in a host cell. Examples of vectors include, but are not limited to, viral vectors, naked DNA or RNA expression vectors, DNA or RNA expression vectors associated with cationic condensing agents, DNA or RNA expression vectors encapsulated in liposomes, and certain eukaryotic cells, such as producer cells.

The compositions and methods of the present invention can be used with a wide variety of peptides and/or protein in which the antibody or binding fragment thereof and the peptide linker or “PL” create a protein that is stable and/or soluble.

As used herein, the compositions and methods use an anti-Langerin antigen delivery vector comprising the formula:



wherein Ab is an anti-Langerin antibody or binding fragment thereof;

PL is at least one Peptide Linker comprising at least one glycosylation site;

Ag is at least one antigen; and

x is an integer from 1 to 20.

As used herein, the terms “stable” and “unstable” when referring to proteins is used to describe a peptide or protein that maintains its three-dimensional structure and/or activity (stable) or that loses immediately or over time its three-dimensional structure and/or activity (unstable). As used herein, the term “insoluble” refers to those proteins that when produced in a cell (e.g., a recombinant protein expressed in a eukaryotic or prokaryotic cell or in vitro) are not soluble in solution absent the use of denaturing conditions or agents (e.g., heat or chemical denaturants, respectively). The antibody or binding fragment thereof and the linkers taught herein have been found to convert antibody fusion proteins with the peptides from insoluble and/or unstable into proteins that are stable and/or soluble. Another example of stability versus instability is when the domain of the protein with a stable conformation has a higher melting temperature (T_m) than the unstable domain of the protein when measured in the same solution. A domain is stable compared to another domain when the difference in the T_m is at least about 2° C, more preferably about 4° C, still more preferably about 7° C, yet more preferably about 10° C, even more preferably about 15° C, still more preferably about 20° C, even still more preferably about 25° C, and most preferably about 30° C, when measured in the same solution.

As used herein, “polynucleotide” or “nucleic acid” refers to a strand of deoxyribonucleotides or ribonucleotides in either a single- or a double-stranded form (including known analogs of natural nucleotides). A double-stranded nucleic acid sequence will include the complementary sequence. The polynucleotide sequence may encode variable and/or constant region domains of immunoglobulin that are formed into a fusion protein with one or more linkers. For use with the present invention, multiple cloning sites (MCS) may be engineered into the locations at the carboxy-terminal end of the heavy and/or light chains of the antibodies to allow for in-frame insertion of peptide for expression between the linkers.

As used herein, the term “isolated polynucleotide” refers to a polynucleotide of genomic, cDNA, or synthetic origin or some combination thereof. By virtue of its origin the “isolated polynucleotide” (1) is not associated with all or a portion of a polynucleotide in which the “isolated polynucleotides” are found in nature, (2) is operably linked to a polynucleotide which it is not linked to in nature, or (3) does not occur in nature as part of a larger sequence. The skilled artisan will recognize that to design and implement a vector having the formula $Ab-(PL-Ag)_x$ or $Ab-(Ag-PL)_x$, can be manipulated at the nucleic acid level by using techniques known in the art, such as those taught in Current Protocols in Molecular Biology, 2007 by John Wiley and Sons, relevant portions incorporated herein by reference. Briefly, the Ab, Ag and PL encoding nucleic acid sequences can be inserted using polymerase chain reaction, enzymatic insertion of oligonucleotides or polymerase chain reaction fragments in a vector, which may be an expression vector. To facilitate the insertion of $(PL-Ag)_x$ or $(Ag-PL)_x$ at the carboxy terminus of the antibody light chain, the heavy chain, or both, a multiple cloning site (MCS) may be engineered in sequence with the antibody sequences.

As used herein, the term “polypeptide” refers to a polymer of amino acids and does not refer to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide. This term also does not refer to or exclude post expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like. Included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), polypeptides with substituted linkages, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. The term “domain,” or “polypeptide domain” refers to that sequence of a polypeptide that folds into a single globular region in its native conformation, and that may exhibit discrete binding or functional properties. As used herein, the term “fusion protein” refers to a hybrid protein expressed by a nucleic acid molecule comprising nucleotide sequences of at least two genes into a protein. For example, a fusion protein can comprise at least part of anti-Langerin antibody or binding fragment thereof fused with one or more antigen and/or one or more linkers if more than one antigen is fused with the antibody or fragment thereof.

A polypeptide or amino acid sequence “derived from” a designated nucleic acid sequence refers to a polypeptide having an amino acid sequence identical to that of a polypeptide encoded in the sequence, or a portion thereof wherein the portion consists of at least 3-5 amino acids, preferably at least 4-7 amino acids, more preferably at least 8-10 amino acids, and even more preferably at least 11-15 amino acids, or which is immunologically identifiable with a polypeptide encoded in the sequence. This terminology also includes a polypeptide expressed from a designated nucleic acid sequence.

As used herein, “pharmaceutically acceptable carrier” refers to any material that when combined with an immunoglobulin (Ig) fusion protein of the present invention allows the Ig to retain biological activity and is generally non-reactive with the subject’s immune system. Examples include, but are not limited to, standard pharmaceutical carriers such as a phosphate buffered saline solution, water, emulsions such as an oil/water emulsion, and various types of wetting agents. Certain diluents may be used with the present invention, e.g., for aerosol or parenteral administration, that may be phosphate buffered saline or normal (0.85%) saline.

The invention provides a Langerin binding antibody (15B10) that comprises at least one immunoglobulin light chain variable domain (VL) which comprises the amino acid and nucleic acid sequence encoding:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVS NRFS GVPDRFSGSGSGTNFTLKISRVE
AEDLGLYFCS (SEQ ID NO.: 45); or and direct equivalent thereof.

Accordingly the invention provides a Langerin binding antibody (15B10) that comprises an antigen binding site comprising at least one immunoglobulin heavy chain variable domain (VH) which comprises the amino acid and nucleic acid sequence encoding:
SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFY NENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46); and direct equivalents thereof.

The invention provides a Langerin binding antibody (2G3) that comprises at least one immunoglobulin light chain variable domain (VL) which comprises the amino acid and nucleic acid sequence encoding:

VTLTCSRSTGAVTTSNYANWVQEKPDLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
EDEAIYFCA (SEQ ID NO.: 47); or and direct equivalent thereof.

- 5 Accordingly the invention provides a Langerin binding antibody (2G3) that comprises an antigen binding site comprising at least one immunoglobulin heavy chain variable domain (VH) which comprises the amino acid and nucleic acid sequence encoding:
SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); and direct equivalents thereof.

- 10 In one aspect the invention provides a single domain Langerin antibody comprising an isolated immunoglobulin light chain comprising a heavy chain variable domain (VL) as defined above. In another aspect the invention provides a single domain Langerin binding molecule comprising an isolated immunoglobulin heavy chain comprising a heavy chain variable domain (VH) as defined above.

- In another aspect the invention also provides a Langerin binding antibody comprising a light chain (VL) variable domains in which the Langerin binding antibody comprises at least one antigen binding site comprising: an antibody light chain variable domain (VL) which comprises in sequence hypervariable regions obtained from the amino acid and nucleic acid sequences encoding:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVDPDRFSGSGSGTNFTLKISRVE
AEDLGLYFCS (SEQ ID NO.: 45); or

- 20 VTLTCSRSTGAVTTSNYANWVQEKPDLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
EDEAIYFCA (SEQ ID NO.: 47); and direct equivalents thereof.

In another aspect the invention also provides a Langerin binding antibody comprising, the amino acid and nucleic acid sequences of heavy chain variable domain (VH) which comprises in sequence hypervariable regions obtained from:

- 25 SVKMCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46); or
SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); and direct equivalents thereof.

- Unless otherwise indicated, any polypeptide chain is herein described as having an amino acid sequence starting at the N-terminal end and ending at the C-terminal end. When the antigen binding site comprises both the VH and VL domains, these may be located on the same polypeptide molecule or, preferably, each domain may be on a different chain, the VH domain being part of an immunoglobulin heavy chain or binding fragment thereof and the VL being part of an immunoglobulin light chain or binding fragment thereof.
- 30

As used herein, the term “Langerin binding molecule” or “Langerin binding antibody” refer to any molecule capable of binding to the Langerin antigen either alone or associated with other molecules having one or more the VL and VH CDRs taught herein, in some cases 2, 3, 4, 5, or all 6 CDRs. The binding reaction may be shown by standard methods (qualitative assays) including, for example, a bioassay for determining by blocking the binding of other molecules to Langerin or any kind of binding or activity assays (e.g., activation, reduction or modulation of an immune response), with reference to a negative control test in which an antibody of unrelated specificity but of the same isotype, e.g., an anti-CD25 or anti-CD80 antibody, is used.

The present invention may also be made into a single chain antibody having the variable domains of the heavy and light chains of an antibody covalently bound by a peptide linker usually including from 10 to 30 amino acids, preferably from 15 to 25 amino acids. Therefore, such a structure does not include the constant part of the heavy and light chains and it is believed that the small peptide spacer should be less antigenic than a whole constant part.

As used herein, the term “chimeric antibody” refers to an antibody in which the constant regions of heavy or light chains or both are of human origin while the variable domains of both heavy and light chains are of non-human (e.g., mouse, hamster or rat) origin or of human origin but derived from a different human antibody.

As used herein, the term “CDR-grafted antibody” refers to an antibody in which the hypervariable complementarity determining regions (CDRs) are derived from a donor antibody, such as a non-human (e.g., mouse) antibody or a different human antibody, while all or substantially all the other parts of the immunoglobulin (e.g., the conserved regions of the variable domains, i.e., framework regions), are derived from an acceptor antibody (in the case of a humanized antibody -an antibody of human origin). A CDR-grafted antibody may include a few amino acids of the donor sequence in the framework regions, for instance in the parts of the framework regions adjacent to the hypervariable regions.

As used herein, the term “human antibody” refers to an antibody in which the constant and variable regions of both the heavy and light chains are all of human origin, or substantially identical to sequences of human origin, not necessarily from the same antibody and includes antibodies produced by mice in which the mouse, hamster or rat immunoglobulin variable and constant part genes have been replaced by their human counterparts, e.g. as described in general terms in EP 0546073 B1, U.S. Patent No. 5,545,806, U.S. Patent No. 5,569,825, U.S. Patent No. 5,625,126, U.S. Patent No. 5,633,425, U.S. Patent No. 5,661,016, U.S. Patent No. 5,770,429, EP Patent No. 0 438474 B1 and EP Patent No. 0 463151 B1, relevant portions incorporated herein by reference.

The Langerin binding antibodies of the invention include humanized antibodies that comprise the CDRs obtained from the anti-Langerin 15B10 or 2G3 antibody. One example of a chimeric antibody includes the variable domains of both heavy and light chains are of human origin, for instance those of the anti-Langerin 15B10 or 2G3 antibody. The constant region domains preferably also comprise suitable human

constant region domains, for instance as described in “Sequences of Proteins of Immunological Interest”, Kabat E. A. et al, US Department of Health and Human Services, Public Health Service, National Institute of Health.

Hypervariable regions may be associated with any kind of framework regions, e.g., of human origin.

5 Suitable framework regions were described Kabat E. A. One heavy chain framework is a heavy chain framework, for instance those of the anti-Langerin 15B10 or 2G3 antibody, includes sequences for the light chain framework regions: FR1L, FR2L, FR3L and FR4L regions. In a similar manner, the anti-Langerin 15B10 or 2G3 heavy chain framework that includes the sequence of FR1H, FR2H, FR3H and FR4H regions. The CDRs may be added to a human antibody framework, such as those described in
10 7,456,260, issued to Rybak, et al., which teach new human variable chain framework regions and humanized antibodies comprising the framework regions, relevant portions and framework sequences incorporated herein by reference. To accomplish the engraftment at a genetic level, the present invention also includes the underlying nucleic acid sequences for the VL AND VH regions as well as the complete antibodies and the humanized versions thereof. The nucleic acid sequences of the present invention
15 include the anti-Langerin antibody light and the heavy chains, respectively, as well as those nucleic acid sequences that include variable codon usage for the same amino acid sequences and conservative variations thereof having 85, 90, 95 or 100 % sequence identity at the nucleic or amino acid level. Likewise, the CDRs may have 85, 90, 95 or 100 % sequence identity at the nucleic or amino acid level, individually, in groups or 2, 3, 4 or 5 or all together.

20 Monoclonal antibodies raised against a protein naturally found in all humans are typically developed in a non-human system e.g. in mice, and as such are typically non-human proteins. As a direct consequence of this, a xenogenic antibody as produced by a hybridoma, when administered to humans, elicits an undesirable immune response that is predominantly mediated by the constant part of the xenogenic immunoglobulin. Xenogeneic antibodies tend to elicit a host immune response, thereby limiting the use
25 of such antibodies as they cannot be administered over a prolonged period of time. Therefore, it is particularly useful to use single chain, single domain, chimeric, CDR-grafted, or especially human antibodies that are not likely to elicit a substantial allogenic response when administered to humans. The present invention includes antibodies with minor changes in an amino acid sequence such as deletion, addition or substitution of one, a few or even several amino acids which are merely allelic forms of the
30 original protein having substantially identical properties.

The inhibition of the binding of Langerin to its receptor may be conveniently tested in various assays including such assays are described hereinafter in the text. By the term “to the same extent” is meant that the reference and the equivalent molecules exhibit, on a statistical basis, essentially identical Langerin binding inhibition curves in one of the assays referred to above. For example, the assay used may be an
35 assay of competitive inhibition of binding of Langerin by the binding molecules of the invention.

Generally, the human anti-Langerin antibody comprises at least: (a) one light chain which comprises a variable domain having an amino acid sequence substantially identical to the 15B10 or 2G3 antibody

starting with the amino acid at position 1 and ending with the amino acid at position 107 and the constant part of a human light chain; and (b) one heavy chain which comprises a variable domain having an amino acid sequence substantially identical to the 15B10 or 2G3 antibody and the constant part of a human heavy chain. The constant part of a human heavy chain may be of the $\gamma 1$, $\gamma 2$, $\gamma 3$, $\gamma 4$, μ , $\beta 2$, or δ or ϵ type, preferably of the γ -type, whereas the constant part of a human light chain may be of the κ or λ type (which includes the $\lambda 1$, $\lambda 2$ and $\lambda 3$ subtypes) but is preferably of the κ type. The amino acid sequences of the general locations of the variable and constant domains are well known in the art and generally follow the Kabat nomenclature.

A Langerin binding molecule of the invention may be produced by recombinant DNA techniques. In view of this, one or more DNA molecules encoding the binding molecule must be constructed, placed under appropriate control sequences and transferred into a suitable host organism for expression.

In a very general manner, there are accordingly provided: (i) DNA molecules encoding a single domain Langerin binding molecule of the invention, a single chain Langerin binding molecule of the invention, a heavy or light chain or binding fragments thereof of a Langerin binding molecule of the invention; and (ii) the use of the DNA molecules of the invention for the production of a Langerin binding molecule of the invention by recombinant methods.

The present state of the art is such that the skilled worker in the art can synthesize the DNA molecules of the invention given the information provided herein, i.e., the amino acid sequences of the hypervariable regions and the DNA sequences coding for them. A method for constructing a variable domain gene is for example described in EPA 239 400, relevant portions incorporated herein by reference. Briefly, a gene encoding a variable domain of a MAb is cloned. The DNA segments encoding the framework and hypervariable regions are determined and the DNA segments encoding the hypervariable regions are removed so that the DNA segments encoding the framework regions are fused together with suitable restriction sites at the junctions. The restriction sites may be generated at the appropriate positions by mutagenesis of the DNA molecule by standard procedures. Double stranded synthetic CDR cassettes are prepared by DNA synthesis according to the sequences given in for 15B10 or 2G3 (amino acid and nucleic acid sequences, respectively). These cassettes are often provided with sticky ends so that they can be ligated at the junctions of the framework.

It is not necessary to have access to the mRNA from a producing hybridoma cell line in order to obtain a DNA construct coding for the Langerin binding molecules of the invention. For example, PCT application WO 90/07861 gives full instructions for the production of an antibody by recombinant DNA techniques given only written information as to the nucleotide sequence of the gene, relevant portions incorporated herein by reference. Briefly, the method comprises the synthesis of a number of oligonucleotides, their amplification by the PCR method, and their splicing to give the desired DNA sequence.

Expression vectors comprising a suitable promoter or genes encoding heavy and light chain constant parts are publicly available. Thus, once a DNA molecule of the invention is prepared it may be conveniently transferred in an appropriate expression vector. DNA molecules encoding single chain antibodies may also be prepared by standard methods, for example, as described in WO 88/1649. In view of the foregoing, no hybridoma or cell line deposit is necessary to comply with the criteria of sufficiency of description.

For example, first and second DNA constructs are made that bind specifically to Langerin. Briefly, a first DNA construct encodes a light chain of an antibody, CDRs or binding fragments thereof and comprises a) a first part which encodes a variable domain comprising alternatively framework and hypervariable regions, the hypervariable regions being in sequence CDR1L, CDR2L and CDR3L the amino acid sequences of which are found in SEQ ID NOs. 45-48; this first part starting with a codon encoding the first amino acid of the variable domain and ending with a codon encoding the last amino acid of the variable domain, and b) a second part encoding a light chain constant part or binding fragment thereof which starts with a codon encoding the first amino acid of the constant part of the heavy chain and ends with a codon encoding the last amino acid of the constant part or binding fragment thereof, followed by a stop codon.

The first part encodes a variable domain having an amino acid sequence substantially identical to the amino acid sequences of 15B10 or 2G3. A second part encodes the constant part of a human heavy chain, more preferably the constant part of the human γ 1 chain. This second part may be a DNA fragment of genomic origin (comprising introns) or a cDNA fragment (without introns).

The second DNA construct encodes a heavy chain or binding fragment thereof and comprises a) a first part which encodes a variable domain comprising alternatively framework and hypervariable regions; the hypervariable regions being CDR1H and optionally CDR2H and CDR3H, the amino acid sequences of 15B10 or 2G3; this first part starting with a codon encoding the first amino acid of the variable domain and ending with a codon encoding the last amino acid of the variable domain, and b) a second part encoding a heavy chain constant part or binding fragment thereof which starts with a codon encoding the first amino acid of the constant part of the light chain and ends with a codon encoding the last amino acid of the constant part or binding fragment thereof followed by a stop codon.

The first part encodes a variable domain having an amino acid sequence substantially identical to the amino acid sequence of 15B10 or 2G3. The first part has the nucleotide sequence of the 15B10 or 2G3 antibodies starting with the nucleotide at position 1 and ending with the nucleotide at position 321. Also preferably the second part encodes the constant part of a human light chain, more preferably the constant part of the human κ chain.

The invention also includes Langerin binding molecules in which one or more of the residues of CDR1L, CDR2L, CDR3L, CDR1H, CDR2H or CDR3H or the frameworks, typically only a few (e.g. FR1-4L or H), are changed from the residues of the 15B10 or 2G3 antibodies; by, e.g., site directed mutagenesis of

the corresponding DNA sequences. The invention includes the DNA sequences coding for such changed Langerin binding molecules. In particular the invention includes a Langerin binding molecules in which one or more residues of CDR1L, CDR2L and/or CDR3L have been changed from the residues of the 15B10 or 2G3 antibodies and one or more residues of CDR1H, CDR2H and/or CDR3H have been changed from the residues of the 15B10 or 2G3 antibodies.

Each of the DNA constructs are placed under the control of suitable control sequences, in particular under the control of a suitable promoter. Any kind of promoter may be used, provided that it is adapted to the host organism in which the DNA constructs will be transferred for expression. However, if expression is to take place in a mammalian cell, an immunoglobulin gene promoter may be used in B cells. The first and second parts may be separated by an intron, and, an enhancer may be conveniently located in the intron between the first and second parts. The presence of such an enhancer that is transcribed but not translated, may assist in efficient transcription. In particular embodiments the first and second DNA constructs comprise the enhancer of, e.g., a heavy chain human gene.

The antibody or binding fragments thereof can be isolated, purified, and stored using any method known in the art. The binding fragments retain the specific binding activity of the intact antibody, and can be used for any application that employs the intact antibody (e.g., therapeutics, diagnostic assays, competitive binding assays, etc.).

In another aspect, the invention provides an antibody or binding fragment generated by the above-described method, and may further include a half-life extending vehicle, such as those known to those skilled in the art. Such vehicles include, but are not limited to, linear polymers (e.g., polyethylene glycol (PEG), polylysine, dextran, etc.); branched-chain polymers (See, e.g., U.S. Patent No. 4,289,872; U.S. Patent No. 5,229,490; WO 93/21259); a lipid; a cholesterol group (such as a steroid); a carbohydrate or polysaccharide; or any natural or synthetic protein, polypeptide or peptide. Additionally, it will be appreciated that one or more Fc regions, can also be employed with the invention to increase half-life. It will be appreciated that the vehicle can be linked to the antibody or binding fragment by way of various techniques known in the art including, for example, covalent linkage.

The desired antibody may be produced in an animal as an ascites, in cell culture or in a transgenic animal. A suitable transgenic animal may be obtained according to standard methods that include micro injecting into eggs the first and second DNA constructs placed under suitable control sequences transferring the so prepared eggs into appropriate pseudo-pregnant females and selecting a descendant expressing the desired antibody.

The invention also provides an expression vector able to replicate in a prokaryotic or eukaryotic cell line, which comprises at least one of the DNA constructs above described. Each expression vector containing a DNA construct is then transferred into a suitable host organism. When the DNA constructs are separately inserted on two expression vectors, they may be transferred separately, i.e. one type of vector per cell, or co-transferred, this latter possibility being preferred. A suitable host organism may be a

bacterium, a yeast or a mammalian cell line, this latter being preferred. More preferably, the mammalian cell line is of lymphoid origin, e.g., a myeloma, hybridoma or a normal immortalized B-cell, which conveniently does not express any endogenous antibody heavy or light chain.

5 When the antibody chains are produced in a cell culture, the DNA constructs must first be inserted into either a single expression vector or into two separate but compatible expression vectors, the latter possibility being preferred. For expression in mammalian cells it is preferred that the coding sequence of the Langerin binding molecule is integrated into the host cell DNA within a locus which permits or favors high level expression of the Langerin binding molecule.

10 In a further aspect of the invention there is provided a process for the product of a Langerin binding molecule that comprises: (i) culturing an organism which is transformed with an expression vector as defined above; and (ii) recovering the Langerin binding molecule from the culture.

15 In accordance with the present invention it has been found that the anti-Langerin antibodies 15B10, 2G3, 91E7, 37C1, or 4C7 and humanized derivatives thereof, appear to have binding specificity for the antigenic epitope of human Langerin. It is therefore most surprising that antibodies to this epitope, e.g. the anti-Langerin 15B10, 2G3, 91E7, 37C1, or 4C7 and humanized derivatives thereof, are capable of delivering antigen efficiently into dendritic cells (DCs). Antibodies, in particular chimeric and CDR-grafted antibodies and especially human antibodies, which have binding specificity for the antigenic epitope of mature human Langerin; and use of such antibodies for DC antigen loading are novel and are included within the scope of the present invention.

20 To use the anti-Langerin antibody of the present invention for treatment indications, the appropriate dosage will, of course, vary depending upon, for example, the antibody disclosed herein to be employed, the host, the mode of administration and the nature and severity of the condition being treated. However, in prophylactic use, satisfactory results are generally found at dosages from about 0.05 mg to about 10 mg per kilogram body weight more usually from about 0.1 mg to about 5 mg per kilogram body weight.

25 The frequency of dosing for prophylactic uses will normally be in the range from about once per week up to about once every 3 months, more usually in the range from about once every 2 weeks up to about once every 10 weeks, e.g., once every 4 to 8 weeks. The anti-Langerin antibody of the present can be administered parenterally, intravenously, e.g., into the antecubital or other peripheral vein, intramuscularly, or subcutaneously.

30 Pharmaceutical compositions of the invention may be manufactured in conventional manner, e.g., in a lyophilized form. For immediate administration it is dissolved in a suitable aqueous carrier, for example sterile water for injection or sterile buffered physiological saline. If it is considered desirable to make up a solution of larger volume for administration by infusion rather as a bolus injection, it is advantageous to incorporate human serum albumin or the patient's own heparinized blood into the saline at the time of

35 formulation. The presence of an excess of such physiologically inert protein prevents loss of antibody by

adsorption onto the walls of the container and tubing used with the infusion solution. If albumin is used, a suitable concentration is from 0.5 to 4.5% by weight of the saline solution.

One embodiment of the present invention provides an immunoconjugate comprising a humanized antibody of the invention, e.g., a humanized anti-Langerin antibody, linked to one or more effector molecules, antigen(s) and/or a detectable label(s). Preferably, the effector molecule is a therapeutic molecule such as, for example, one or more peptides that comprise one or more T cell epitopes, a toxin, a small molecule, a cytokine or a chemokine, an enzyme, or a radiolabel.

Exemplary toxins include, but are not limited to, *Pseudomonas* exotoxin or diphtheria toxin. Examples of small molecules include, but are not limited to, chemotherapeutic compounds such as taxol, doxorubicin, etoposide, and bleomycin. Exemplary cytokines include, but are not limited to, IL-1, IL-2, IL-4, IL-5, IL-6, and IL-12, IL-17, and IL-25. Exemplary enzymes include, but are not limited to, RNases, DNases, proteases, kinases, and caspases. Exemplary radioisotopes include, but are not limited to, ³²P and ¹²⁵I.

As used herein, the term “epitope” refers to a molecule or substance capable of stimulating an immune response. In one example, epitopes include but are not limited to a polypeptide and a nucleic acid encoding a polypeptide, wherein expression of the nucleic acid into a polypeptide is capable of stimulating an immune response when the polypeptide is processed and presented on a Major Histocompatibility Complex (MHC) molecule. Generally, epitopes include peptides presented on the surface of cells non-covalently bound to the binding groove of Class I or Class II MHC, such that they can interact with T cell receptors and the respective T cell accessory molecules.

Proteolytic Processing of Antigens. Epitopes that are displayed by MHC on antigen presenting cells are cleavage peptides or products of larger peptide or protein antigen precursors. For MHC I epitopes, protein antigens are often digested by proteasomes resident in the cell. Intracellular proteasomal digestion produces peptide fragments of about 3 to 23 amino acids in length that are then loaded onto the MHC protein. Additional proteolytic activities within the cell, or in the extracellular milieu, can trim and process these fragments further. Processing of MHC Class II epitopes generally occurs via intracellular proteases from the lysosomal/endosomal compartment. The present invention includes, in one embodiment, pre-processed peptides that are attached to the anti-Langerin antibody (or binding fragment thereof) that directs the peptides against which an enhanced immune response is sought directly to antigen presenting cells.

To identify epitopes potentially effective as immunogenic compounds, predictions of MHC binding alone are useful but often insufficient. The present invention includes methods for specifically identifying the epitopes within antigens most likely to lead to the immune response sought for the specific sources of antigen presenting cells and responder T cells.

The present invention allows for a rapid and easy assay for the identification of those epitopes that are most likely to produce the desired immune response using the patient's own antigen presenting cells and T cell repertoire. The compositions and methods of the present invention are applicable to any protein

sequence, allowing the user to identify the epitopes that are capable of binding to MHC and are properly presented to T cells that will respond to the antigen. Accordingly, the invention is not limited to any particular target or medical condition, but instead encompasses and MHC epitope(s) from any useful source.

5 As used herein, the term “veneered” refers to a humanized antibody framework onto which antigen-binding sites or CDRs obtained from non-human antibodies (e.g., mouse, rat or hamster), are placed into human heavy and light chain conserved structural framework regions (FRs), for example, in a light chain or heavy chain polynucleotide to “graft” the specificity of the non-human antibody into a human framework from, e.g., SEQ ID NOS: 45-48 or the nucleic acids that encode those sequences, as will be
10 readily apparent to the skilled artisan. The polynucleotide expression vector or vectors that express the veneered antibodies can be transfected mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the non-human antibody and will undergo posttranslational modifications that will enhance their expression, stability, solubility, or combinations thereof.

15 Antigen.

Examples of viral antigens for use with the present invention include, but are not limited to, e.g., HIV, HCV, CMV, adenoviruses, retroviruses, picornaviruses, etc. Non-limiting example of retroviral antigens such as retroviral antigens from the human immunodeficiency virus (HIV) antigens such as gene products of the gag, pol, and env genes, the Nef protein, reverse transcriptase, and other HIV components;
20 hepatitis viral antigens such as the S, M, and L proteins of hepatitis B virus, the pre-S antigen of hepatitis B virus, and other hepatitis, e.g., hepatitis A, B, and C, viral components such as hepatitis C viral RNA; influenza viral antigens such as hemagglutinin and neuraminidase and other influenza viral components; measles viral antigens such as the measles virus fusion protein and other measles virus components; rubella viral antigens such as proteins E1 and E2 and other rubella virus components; rotaviral antigens
25 such as VP7sc and other rotaviral components; cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV fusion protein, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein D, and other herpes simplex viral antigen components; varicella zoster viral antigens such as gpI, gpII, and other varicella zoster viral antigen
30 components; Japanese encephalitis viral antigens such as proteins E, M-E, M-E-NS1, NS1, NS1-NS2A, 80% E, and other Japanese encephalitis viral antigen components; rabies viral antigens such as rabies glycoprotein, rabies nucleoprotein and other rabies viral antigen components. See Fundamental Virology, Second Edition, eds. Fields, B. N. and Knipe, D. M. (Raven Press, New York, 1991) for additional examples of viral antigens. The at least one viral antigen may be peptides from an adenovirus,
35 retrovirus, picornavirus, herpesvirus, rotaviruses, hantaviruses, coronavirus, togavirus, flavivirus, rhabdovirus, paramyxovirus, orthomyxovirus, bunyavirus, arenavirus, reovirus, papillomavirus, parvovirus, poxvirus, hepadnavirus, or spongiform virus. In certain specific, non-limiting examples, the

at least one viral antigen are peptides obtained from at least one of HIV, CMV, hepatitis A, B, and C, influenza, measles, polio, smallpox, rubella; respiratory syncytial, herpes simplex, varicella zoster, Epstein-Barr, Japanese encephalitis, rabies, flu, and/or cold viruses.

In one aspect, the one or more of the antigenic peptides are selected from at least one of: Nef (66-97):
 5 VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL (SEQ ID NO.: 31); Nef (116-145):
 HTQGYFPDWQNYTPGPGVRYPLTFGWLYKL (SEQ ID NO.: 32); Gag p17 (17-35):
 EKIRLRPGGKKKYKLKHIV (SEQ ID NO.: 33); Gag p17-p24 (253-284):
 NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD (SEQ ID NO.: 34); or Pol 325-355 (RT 158-188) is:
 AIFQSSMTKILEPFRKQNPDIVIYQYMDDLY (SEQ ID NO.: 35). In one aspect, the fusion protein
 10 peptides are separated by one or more linkers selected from: SSVSPTTSVHPTPTSPPTPTKSSP (SEQ
 ID NO.: 39); PTSTPADSSTITPTATPTATPTIKG (SEQ ID NO.: 40);
 TVTPTATATPSAIVTTITPTATTKP (SEQ ID NO.: 41); or TNGSITVAATAPTVTPTVNATPSAA
 (SEQ ID NO.: 42).

Antigenic targets that may be delivered using the anti-Langerin-antigen vaccines of the present invention
 15 include genes encoding antigens such as viral antigens, bacterial antigens, fungal antigens or parasitic
 antigens. Pathogens include trypanosomes, tapeworms, roundworms, helminthes, malaria. Tumor
 markers, such as fetal antigen or prostate specific antigen, may be targeted in this manner. Other
 examples include: HIV env proteins and hepatitis B surface antigen. Administration of a vector
 according to the present invention for vaccination purposes would require that the vector-associated
 20 antigens be sufficiently non-immunogenic to enable long-term expression of the transgene, for which a
 strong immune response would be desired. In some cases, vaccination of an individual may only be
 required infrequently, such as yearly or biennially, and provide long-term immunologic protection against
 the infectious agent. Specific examples of organisms, allergens and nucleic and amino sequences for use
 in vectors and ultimately as antigens with the present invention may be found in U.S. Patent No.
 25 6,541,011, relevant portions incorporated herein by reference, in particular, the tables that match
 organisms and specific sequences that may be used with the present invention.

Bacterial antigens for use with the anti-Langerin-antigen vaccines disclosed herein include, but are not
 limited to, e.g., bacterial antigens such as pertussis toxin, filamentous hemagglutinin, pertactin, FIM2,
 FIM3, adenylate cyclase and other pertussis bacterial antigen components; diptheria bacterial antigens
 30 such as diptheria toxin or toxoid and other diptheria bacterial antigen components; tetanus bacterial
 antigens such as tetanus toxin or toxoid and other tetanus bacterial antigen components; streptococcal
 bacterial antigens such as M proteins and other streptococcal bacterial antigen components; gram-
 negative bacilli bacterial antigens such as lipopolysaccharides and other gram-negative bacterial antigen
 components, Mycobacterium tuberculosis bacterial antigens such as mycolic acid, heat shock protein 65
 35 (HSP65), the 30 kDa major secreted protein, antigen 85A and other mycobacterial antigen components;
 Helicobacter pylori bacterial antigen components; pneumococcal bacterial antigens such as pneumolysin,
 pneumococcal capsular polysaccharides and other pneumococcal bacterial antigen components;

haemophilus influenza bacterial antigens such as capsular polysaccharides and other haemophilus influenza bacterial antigen components; anthrax bacterial antigens such as anthrax protective antigen and other anthrax bacterial antigen components; rickettsiae bacterial antigens such as rompA and other rickettsiae bacterial antigen component. Also included with the bacterial antigens described herein are
 5 any other bacterial, mycobacterial, mycoplasmal, rickettsial, or chlamydial antigens. Partial or whole pathogens may also be: haemophilus influenza; Plasmodium falciparum; neisseria meningitidis; streptococcus pneumoniae; neisseria gonorrhoeae; salmonella serotype typhi; shigella; vibrio cholerae; Dengue Fever; Encephalitides; Japanese Encephalitis; lyme disease; Yersinia pestis; west nile virus; yellow fever; tularemia; hepatitis (viral; bacterial); RSV (respiratory syncytial virus); HPIV 1 and HPIV
 10 3; adenovirus; small pox; allergies and cancers.

Fungal antigens for use with compositions and methods of the invention include, but are not limited to, e.g., candida fungal antigen components; histoplasma fungal antigens such as heat shock protein 60 (HSP60) and other histoplasma fungal antigen components; cryptococcal fungal antigens such as capsular polysaccharides and other cryptococcal fungal antigen components; coccidioides fungal antigens such as
 15 spherule antigens and other coccidioides fungal antigen components; and tinea fungal antigens such as trichophytin and other coccidioides fungal antigen components.

Examples of protozoal and other parasitic antigens include, but are not limited to, e.g., plasmodium falciparum antigens such as merozoite surface antigens, sporozoite surface antigens, circumsporozoite antigens, gametocyte/gamete surface antigens, blood-stage antigen pf 155/RESA and other plasmodial
 20 antigen components; toxoplasma antigens such as SAG-1, p30 and other toxoplasmal antigen components; schistosomae antigens such as glutathione-S-transferase, paramyosin, and other schistosomal antigen components; leishmania major and other leishmaniae antigens such as gp63, lipophosphoglycan and its associated protein and other leishmanial antigen components; and trypanosoma cruzi antigens such as the 75-77 kDa antigen, the 56 kDa antigen and other trypanosomal
 25 antigen components.

Antigen that can be targeted using the anti-Langerin-antigen vaccines of the present invention will generally be selected based on a number of factors, including: likelihood of internalization, level of immune cell specificity, type of immune cell targeted, level of immune cell maturity and/or activation and the like. In this embodiment, the antibodies may be mono- or bi-specific antibodies that include one
 30 anti-Langerin binding domain and one binding domain against a second antigen, e.g., cell surface markers for dendritic cells such as, MHC class I, MHC Class II, B7-2, CD18, CD29, CD31, CD43, CD44, CD45, CD54, CD58, CD83, CD86, CMRF-44, CMRF-56, DCIR and/or Dectin-1 and the like; while in some cases also having the absence of CD2, CD3, CD4, CD8, CD14, CD15, CD16, CD 19, CD20, CD56, and/or CD57. Examples of cell surface markers for antigen presenting cells include, but
 35 are not limited to, MHC class I, MHC Class II, CD45, B7-1, B7-2, IFN- γ receptor and IL-2 receptor, ICAM-1 and/or Fc γ receptor. Examples of cell surface markers for T cells include, but are not limited to, CD3, CD4, CD8, CD 14, CD20, CD11b, CD16, CD45 and HLA-DR.

Target antigens on cell surfaces for delivery include those characteristic of tumor antigens typically will be derived from the cell surface, cytoplasm, nucleus, organelles and the like of cells of tumor tissue. Examples of tumor targets for the antibody portion of the present invention include, without limitation, hematological cancers such as leukemias and lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors such as gastric or colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia.

Examples of antigens that may be delivered alone or in combination to immune cells for antigen presentation using the present invention includes tumor proteins, e.g., mutated oncogenes; viral proteins associated with tumors; and tumor mucins and glycolipids. The antigens may be viral proteins associated with tumors would be those from the classes of viruses noted above. Certain antigens may be characteristic of tumors (one subset being proteins not usually expressed by a tumor precursor cell), or may be a protein that is normally expressed in a tumor precursor cell, but having a mutation characteristic of a tumor. Other antigens include mutant variant(s) of the normal protein having an altered activity or subcellular distribution, e.g., mutations of genes giving rise to tumor antigens.

Specific non-limiting examples of tumor antigens for use in an anti-Langerin-fusion protein vaccine include, e.g., CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC (Mucin) (e.g., MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, MAGE, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), DAGE, EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, Ki-67, Cyclin B1, gp100, Survivin, and NYESO-1.

In addition, the immunogenic molecule can be an autoantigen involved in the initiation and/or propagation of an autoimmune disease, the pathology of which is largely due to the activity of antibodies specific for a molecule expressed by the relevant target organ, tissue, or cells, e.g., SLE or MG. In such diseases, it can be desirable to direct an ongoing antibody-mediated (i.e., a Th2-type) immune response to the relevant autoantigen towards a cellular (i.e., a Th1-type) immune response. Alternatively, it can be desirable to prevent onset of or decrease the level of a Th2 response to the autoantigen in a subject not having, but who is suspected of being susceptible to, the relevant autoimmune disease by prophylactically inducing a Th1 response to the appropriate autoantigen. Autoantigens of interest include, without limitation: (a) with respect to SLE, the Smith protein, RNP ribonucleoprotein, and the SS-A and SS-B proteins; and (b) with respect to MG, the acetylcholine receptor. Examples of other miscellaneous

antigens involved in one or more types of autoimmune response include, e.g., endogenous hormones such as luteinizing hormone, follicular stimulating hormone, testosterone, growth hormone, prolactin, and other hormones.

Antigens involved in autoimmune diseases, allergy, and graft rejection can be used in the compositions and methods of the invention. For example, an antigen involved in any one or more of the following autoimmune diseases or disorders can be used in the present invention: diabetes, diabetes mellitus, arthritis (including rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis, psoriatic arthritis), multiple sclerosis, myasthenia gravis, systemic lupus erythematosus, autoimmune thyroiditis, dermatitis (including atopic dermatitis and eczematous dermatitis), psoriasis, Sjogren's Syndrome, including keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, Crohn's disease, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, ulcerative colitis, asthma, allergic asthma, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, idiopathic bilateral progressive sensorineural hearing loss, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Stevens-Johnson syndrome, idiopathic sprue, lichen planus, Crohn's disease, Graves ophthalmopathy, sarcoidosis, primary biliary cirrhosis, uveitis posterior, and interstitial lung fibrosis. Examples of antigens involved in autoimmune disease include glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, and the thyroid stimulating hormone (TSH) receptor.

Examples of antigens involved in allergy include pollen antigens such as Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, animal derived antigens such as dust mite antigens and feline antigens, histocompatibility antigens, and penicillin and other therapeutic drugs. Examples of antigens involved in graft rejection include antigenic components of the graft to be transplanted into the graft recipient such as heart, lung, liver, pancreas, kidney, and neural graft components. The antigen may be an altered peptide ligand useful in treating an autoimmune disease.

It will be appreciated by those of skill in the art that the sequence of any protein effector molecule may be altered in a manner that does not substantially affect the functional advantages of the effector protein. For example, glycine and alanine are typically considered to be interchangeable as are aspartic acid and glutamic acid and asparagine and glutamine. One of skill in the art will recognize that many different variations of effector sequences will encode effectors with roughly the same activity as the native effector. The effector molecule and the antibody may be conjugated by chemical or by recombinant means as described above. Chemical modifications include, for example, derivitization for the purpose of linking the effector molecule and the antibody to each other, either directly or through a linking compound, by methods that are well known in the art of protein chemistry. Both covalent and noncovalent attachment methods may be used with the humanized antibodies of the present invention.

The procedure for attaching an effector molecule to an antibody will vary according to the chemical structure of the moiety to be attached to the antibody. Polypeptides typically contain a variety of functional groups; e.g., carboxylic acid (COOH), free amine ($--NH_2$) or sulfhydryl ($--SH$) groups, which are available for reaction with a suitable functional group on an antibody to result in the binding of the effector molecule. Alternatively, the antibody can be derivatized to expose or to attach additional reactive functional groups, e.g., by attachment of any of a number of linker molecules such as those available from Pierce Chemical Company, Rockford Ill.

The linker is capable of forming covalent bonds to both the antibody and to the effector molecule. Suitable linkers are well known to those of skill in the art and include, but are not limited to, straight or branched-chain carbon linkers, heterocyclic carbon linkers, or peptide linkers. Where the antibody and the effector molecule are polypeptides, the linkers may be joined to the constituent amino acids through their side groups (e.g., through a disulfide linkage to cysteine). However, in a preferred embodiment, the linkers will be joined to the alpha carbon amino and carboxyl groups of the terminal amino acids.

In some circumstances, it is desirable to free the effector molecule from the antibody when the immunoconjugate has reached its target site. Therefore, in these circumstances, immunoconjugates will comprise linkages that are cleavable in the vicinity of the target site. Cleavage of the linker to release the effector molecule from the antibody may be prompted by enzymatic activity or conditions to which the immunoconjugate is subjected either inside the target cell or in the vicinity of the target site. When the target site is a tumor, a linker that is cleavable under conditions present at the tumor site (e.g. when exposed to tumor-associated enzymes or acidic pH) may be used.

Exemplary chemical modifications of the effector molecule and the antibody of the present invention also include derivitization with polyethylene glycol (PEG) to extend time of residence in the circulatory system and reduce immunogenicity, according to well known methods (See for example, Lisi, et al., *Applied Biochem.* 4:19 (1982); Beauchamp, et al., *Anal Biochem.* 131:25 (1982); and Goodson, et al., *Bio/Technology* 8:343 (1990)).

The present invention contemplates vaccines for use in both active and passive immunization embodiments. Immunogenic compositions, proposed to be suitable for use as a vaccine, may be prepared most readily directly from immunogenic T-cell stimulating peptides prepared in a manner disclosed herein. The final vaccination material is dialyzed extensively to remove undesired small molecular weight molecules and/or lyophilized for more ready formulation into a desired vehicle. In certain embodiment of the present invention, the compositions and methods of the present invention are used to manufacture a cellular vaccine, e.g., the antigen-delivering anti-Langerin binding portion of the antibody is used to direct the antigen(s) to an antigen presenting cell, which then "loads" the antigen onto MHC proteins for presentation. The cellular vaccine is, therefore, the antigen presenting cell that has been loaded using the compositions of the present invention to generate antigen-loaded antigen presenting cells.

When the vaccine is the anti-Langerin binding protein itself, e.g., a complete antibody or binding fragments thereof, then these “active ingredients” can be made into vaccines using methods understood in the art, e.g., U.S. Patent Nos. 4,608,251; 4,601,903; 4,599,231; 4,599,230; and 4,578,770, relevant portions incorporated herein by reference. Typically, such vaccines are prepared as injectables, e.g., as liquid solutions or suspensions or solid forms suitable for re-suspension in liquid prior to injection. The preparation may also be emulsified. The active immunogenic ingredient is often mixed with excipients which are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, or adjuvants that enhance the effectiveness of the vaccines.

The vaccines are administered in a manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and immunogenic. The quantity to be administered depends on the subject to be treated, including, e.g., the capacity of the individual's immune system to generate an immune response. Precise amounts of cells or active ingredient required to be administered depend on the judgment of the practitioner. However, suitable dosage ranges are of the order of a few thousand cells (to millions of cells) for cellular vaccines. For standard epitope or epitope delivery vaccines then the vaccine may be several hundred micrograms active ingredient per vaccination. Suitable regimes for initial administration and booster shots are also variable, but are typified by an initial administration followed by subsequent inoculations or other administrations.

The manner of application may vary widely, however, certain embodiments herein will most likely be delivered intravenously or at the site of a tumor or infection directly. Regardless, any of the conventional methods for administration of a vaccine are applicable. The dosage of the vaccine will depend on the route of administration and will vary according to the size of the host.

In many instances, it will be desirable to have multiple administrations of the vaccine, e.g., four to six vaccinations provided weekly or every other week. A normal vaccination regimen will often occur in two to twelve week intervals or from three to six week intervals. Periodic boosters at intervals of 1-5 years, usually three years, may be desirable to maintain protective levels of the immune response or upon a likelihood of a remission or re-infection. The course of the immunization may be followed by assays for, e.g., T cell activation, cytokine secretion or even antibody production, most commonly conducted *in vitro*. These immune response assays are well known and may be found in a wide variety of patents and as taught herein.

The vaccine of the present invention may be provided in one or more “unit doses” depending on whether the nucleic acid vectors are used, the final purified proteins, or the final vaccine form is used. Unit dose is defined as containing a predetermined-quantity of the therapeutic composition calculated to produce the desired responses in association with its administration, i.e., the appropriate route and treatment regimen. The quantity to be administered, and the particular route and formulation, are within the skill of those in the clinical arts. The subject to be treated may also be evaluated, in particular, the state of the

subject's immune system and the protection desired. A unit dose need not be administered as a single injection but may include continuous infusion over a set period of time. Unit dose of the present invention may conveniently be described in terms of DNA/kg (or protein/Kg) body weight, with ranges between about 0.05, 0.10, 0.15, 0.20, 0.25, 0.5, 1, 10, 50, 100, 1,000 or more mg/DNA or protein/kg body weight are administered.

Likewise, the amount of anti-Langerin-antigen vaccine delivered can vary from about 0.2 to about 8.0 mg/kg body weight. Thus, in particular embodiments, 0.4 mg, 0.5 mg, 0.8 mg, 1.0 mg, 1.5 mg, 2.0 mg, 2.5 mg, 3.0 mg, 4.0 mg, 5.0 mg, 5.5 mg, 6.0 mg, 6.5 mg, 7.0 mg and 7.5 mg of the vaccine may be delivered to an individual in vivo. The dosage of vaccine to be administered depends to a great extent on the weight and physical condition of the subject being treated as well as the route of administration and the frequency of treatment. A pharmaceutical composition that includes a naked polynucleotide prebound to a liposomal or viral delivery vector may be administered in amounts ranging from 1 µg to 1 mg polynucleotide to 1 µg to 100 mg protein. Thus, particular compositions may include between about 1 µg, 5 µg, 10 µg, 20 µg, 30 µg, 40 µg, 50 µg, 60 µg, 70 µg, 80 µg, 100 µg, 150 µg, 200 µg, 250 µg, 500 µg, 600 µg, 700 µg, 800 µg, 900 µg or 1,000 µg polynucleotide or protein that is bound independently to 1 µg, 5 µg, 10 µg, 20 µg, 3.0 µg, 40 µg 50 µg, 60 µg, 70 µg, 80 µg, 100 µg, 150 µg, 200 µg, 250 µg, 500 µg, 600 µg, 700 µg, 800 µg, 900 µg, 1 mg, 1.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg or 100 mg vector.

Antibodies of the present invention may optionally be covalently or non-covalently linked to a detectable label. Detectable labels suitable for such use include any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical methods. Useful labels in the present invention include magnetic beads (e.g. DYNABEADS™), fluorescent dyes (e.g., fluorescein isothiocyanate, Texas red, rhodamine, green fluorescent protein, and the like), radiolabels (e.g., ³H, ¹²⁵I, ³⁵S, ¹⁴C, or ³²P), enzymes (e.g., horse radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), and colorimetric labels such as colloidal gold or colored glass or plastic (e.g. polystyrene, polypropylene, latex, etc.) beads.

Methods of detecting such labels are well known to those of skill in the art. Thus, for example, radiolabels may be detected using photographic film or scintillation counters, fluorescent markers may be detected using a photodetector to detect emitted illumination. Enzymatic labels are typically detected by providing the enzyme with a substrate and detecting the reaction product produced by the action of the enzyme on the substrate, and colorimetric labels are detected by simply visualizing the colored label.

The antibody and/or immunoconjugate compositions of this invention are particularly useful for parenteral administration, such as intravenous administration or administration into a body cavity. The compositions for administration will commonly comprise a solution of the antibody and/or immunoconjugate dissolved in a pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers can be used, e.g., buffered saline and the like. These solutions are sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well-known

sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, for example, sodium acetate, sodium chloride, potassium chloride, calcium chloride, sodium lactate and the like. The concentration of fusion protein in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight and the like in accordance with the particular mode of administration selected and the patient's needs.

Thus, a typical pharmaceutical immunoconjugate composition of the present invention for intravenous administration would be about 0.1 to 10 mg per patient per day. Dosages from 0.1 up to about 100 mg per patient per day may be used. Actual methods for preparing administrable compositions will be known or apparent to those skilled in the art and are described in more detail in such publications as REMINGTON'S PHARMACEUTICAL SCIENCE, 19TH ED., Mack Publishing Company, Easton, Pa. (1995).

The compositions of the present invention can be administered for therapeutic treatments. In therapeutic applications, compositions are administered to a patient suffering from a disease, in an amount sufficient to cure or at least partially arrest the disease and its complications. An amount adequate to accomplish this is defined as a "therapeutically effective dose." Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's health. An effective amount of the compound is that which provides either subjective relief of a symptom(s) or an objectively identifiable improvement as noted by the clinician or other qualified observer.

Single or multiple administrations of the compositions are administered depending on the dosage and frequency as required and tolerated by the patient. In any event, the composition should provide a sufficient quantity of the proteins of this invention to effectively treat the patient. Preferably, the dosage is administered once but may be applied periodically until either a therapeutic result is achieved or until side effects warrant discontinuation of therapy. Generally, the dose is sufficient to treat or ameliorate symptoms or signs of disease without producing unacceptable toxicity to the patient.

Controlled release parenteral formulations of the immunoconjugate compositions of the present invention can be made as implants, oily injections, or as particulate systems. For a broad overview of protein delivery systems see, Banga, A. J., THERAPEUTIC PEPTIDES AND PROTEINS: FORMULATION, PROCESSING, AND DELIVERY SYSTEMS, Technomic Publishing Company, Inc., Lancaster, Pa., (1995) incorporated herein by reference. Particulate systems include microspheres, microparticles, microcapsules, nanocapsules, nanospheres, and nanoparticles. Microcapsules contain the therapeutic protein as a central core. In microspheres the therapeutic is dispersed throughout the particle. Particles, microspheres, and microcapsules smaller than about 1 μm are generally referred to as nanoparticles, nanospheres, and nanocapsules, respectively. Capillaries have a diameter of approximately 5 μm so that only nanoparticles are administered intravenously. Microparticles are typically around 100 μm in diameter and are administered subcutaneously or intramuscularly.

Polymers can be used for ion-controlled release of immunoconjugate compositions of the present invention. Various degradable and non-degradable polymeric matrices for use in controlled drug delivery are known in the art (Langer, R., *Accounts Chem. Res.* 26:537-542 (1993)). For example, the block copolymer, poloxamer 407® exists as a viscous yet mobile liquid at low temperatures but forms a semisolid gel at body temperature, hydroxyapatite has been used as a microcarrier for controlled release of proteins, and/or liposomes may be used for controlled release as well as drug targeting of the lipid-capsulated drug. Numerous additional systems for controlled delivery of therapeutic proteins are known. See, e.g., U.S. Patent Nos. 5,055,303, 5,188,837, 4,235,871, 4,501,728, 4,837,028 4,957,735 and 5,019,369, 5,055,303; 5,514,670; 5,413,797; 5,268,164; 5,004,697; 4,902,505; 5,506,206, 5,271,961; 5,254,342 and 5,534,496, relevant portions of each of which are incorporated herein by reference.

Among various uses of the immunoconjugates of the invention are included a variety of disease conditions caused by specific human cells that may be eliminated by the toxic action of the fusion protein. For example, for the humanized Anti-Langerin antibodies, e.g., 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and binding fragments thereof, disclosed herein. For example, one application for immunoconjugates is the treatment of malignant cells expressing Langerin. Exemplary malignant cells include those of chronic lymphocytic leukemia and hairy cell leukemia.

In another embodiment, this invention provides kits for the delivery of antigens, e.g., Langerin or an immunoreactive fragment thereof, conjugated or in the form of a fusion protein with one or more T cell or B cell epitopes. A “biological sample” as used herein is a sample of biological tissue or fluid that contains the antigen. Such samples include, but are not limited to, tissue from biopsy, blood, and blood cells (e.g., white cells). Preferably, the cells are lymphocytes, e.g., dendritic cells. Biological samples also include sections of tissues, such as frozen sections taken for histological purposes. A biological sample is typically obtained from a multicellular eukaryote, preferably a mammal such as rat, mouse, cow, dog, guinea pig, or rabbit, and more preferably a primate, such as a macaque, chimpanzee, or human. Most preferably, the sample is from a human. The antibodies of the invention may also be used in vivo, for example, as a diagnostic tool for in vivo imaging.

Kits will typically comprise a nucleic acid sequence that encodes an antibody of the present invention (or binding fragment thereof) with one or more framework portions or multiple cloning sites at the carboxy-terminal end into which the coding sequences for one or more antigens may be inserted. In some embodiments, the antibody will be a humanized anti-Langerin Fv fragment, such as an scFv or dsFv fragment. In addition the kits will typically include instructional materials disclosing methods of use of an antibody of the present invention (e.g. for loading into dendritic cells prior to immunization with the dendritic cells, which can be autologous dendritic cells). The kits may also include additional components to facilitate the particular application for which the kit is designed. Thus, for example, the kit may additionally contain methods of detecting the label (e.g. enzyme substrates for enzymatic labels, filter sets to detect fluorescent labels, appropriate secondary labels such as a sheep anti-mouse-HRP, or the like).

The kits may additionally include buffers and other reagents routinely used for the practice of a particular method. Such kits and appropriate contents are well known to those of skill in the art.

In another set of uses for the invention, immunoconjugates targeted by antibodies of the invention can be used to purge targeted cells from a population of cells in a culture. For example, if a specific population of T cells is preferred, the immunoconjugates of the present invention may be used to enrich a population of T cells having the opposite effect of the on-going immune response. Thus, for example, cells cultured from a patient having a cancer can be purged of cancer cells by providing the patient with dendritic cells that were antigen loaded using the antibodies of the invention as a targeting moiety for the antigens that will trigger an immune response against the cancer, virus or other pathogen. Likewise, the immunoconjugates can be used to increase the population of regulatory T cells or drive the immune response toward or away from a cytotoxic T cell response or even drive a B cell response.

Differential functions of DC subsets: The present inventors have demonstrated that LCs and intDCs derived from CD34+ hematopoietic progenitor cells differ in their capacity to activate lymphocytes (Figure 1). IntDCs induce the differentiation of naïve B cells into immunoglobulin-secreting plasma cells and differentiation of CD4+ T cells into follicular helper T cells (TFH)^{17,18}, while LCs are particularly efficient activators of cytotoxic CD8+ lymphocytes (CTLs). In addition, only interstitial DCs produce IL-10 and their enzymatic activity, which might be fundamental for the selection of peptides that will be presented to T cells, is not the same. Indeed, different enzymes are likely to degrade an antigen into different peptide repertoires, as shown for HIV nef protein¹⁹. This will lead to different sets of MHC/peptide complexes being presented and to a distinct antigen-specific T-cell repertoire. Dudziak, et al.²⁰ have shown that antigens delivered to DCs through the subset-specific lectin Dectin-1 were presented differentially on MHC class II, while those presented through DEC-205 were mostly on MHC Class I and this difference was intrinsic to the DC subsets.

DC subsets play an important role in determining CD4+ T cell responses. Either polarized DCs or distinct DC subsets provide T cells with different signals that determine the types of immune response (Type 1 versus Type 2)²¹. Thus, in mice, splenic CD8+ DCs prime naïve CD4+ T cells to make Th1 cytokines in a process involving IL-12, whereas splenic CD8+ DCs prime naïve CD4+ T cells to make Th2 cytokines^{22,23}. Furthermore, different signals from the same DCs can induce different T-cell polarization, as shown by the induction of IL-12 production and Th1-cell polarization when DCs are activated with *Escherichia coli* lipopolysaccharide (LPS), but no IL-12 production and Th2-cell polarization when DCs are exposed to LPS from *Porphyromonas gingivalis*²⁴. CD40-ligand (CD40L)-activated DCs prime Th1 responses through an IL-12-dependent mechanism, whereas pDCs activated with IL-3 and CD40L have been shown to secrete negligible amounts of IL-12 and prime Th2 responses²⁵. Soares, et al. also reported that two DC subsets that express different lectins have innate propensities to differentially affect the Th1/Th2 balance in vivo by distinct mechanisms. More interestingly, we have found that delivering the same antigens to the same type of DCs, but through different DC-receptors, induces a different quality of CD4+ T cell

responses (see preliminary data). Thus, both DC subsets and activation signals to which DCs are exposed are important factors determining the nature of immune outcome.

Figure 2 – Recombinant anti-Langerin antibodies fused to antigens retain their ability to bind to cell surface Langerin. CHO-S cells were stably transfected with a plasmid directing the expression of full-length human Langerin. Pure recombinant anti-Langerin 2G3 or 15B10 mouse V region-human IgG4 chimeric antibodies or the same antibodies with C-terminal fusions to Influenza A Hemagglutinin HA-1 domain from Avian Flu (HA5-1), Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain (HA1-1), dockerin domain from *C. thermocellum* (doc), HIV gag p24 (gag), or a string of HIV peptides (Hipo5), were titrated against the Langerin-CHO cells. After incubation on ice, the cells were washed and treated with an anti-human Fc-PE reagent. After further incubation on ice, the cells were washed and analyzed on a FACS Array instrument to determine the amount of cell-bound fluorescence (expressed as %MFI compared to untransfected CHO-S cells).

This data shows that addition of antigen to the H-chain C-termini does not affect the binding of the antibody to cell surface Langerin and also demonstrates that these anti-Langerin antibodies serve as effective vehicles to bring antigen to the surface of cells bearing human Langerin.

Figure 3– demonstration of the ability of recombinant anti-Langerin antibody fused to the human prostate specific cancer antigen to elicit the expansion of antigen-specific CD4⁺ T cells from a health donor. Figure 3a compares delivering PSA to DCs through CD40 and Langerin induces IFN γ -producing PSA-specific CD4⁺ T cells. CD4⁺ T cells from healthy donors were co-cultured with IFNDCs targeted with anti-CD40-PSA or anti-Langerin-PSA for 8 days. Cells were stimulated with individual peptides (59 peptides of 15-mers) of PSA (5 μ M). After 2 days, culture supernatants were analyzed for measuring IFN γ . Dotted lines represent upper limits of average $\pm$ SD for no peptides and responses above this line are considered significant. Figure 3b shows that CD4⁺ T cells were stained for measuring the frequency of peptide-specific intracellular IFN γ ⁺ cells.

These data show that an anti-Langerin vaccine bearing a cancer antigen can prime a potent antigen-specific anti-CD4⁺ T cell response in vitro using immune cells from a normal individual. In this in vitro culture system this agent is as potent as an anti-CD40 based vaccine – these DCs express both receptors. In vivo, an anti-Langerin-based vaccine would target antigen only to Langerhans cells (LCs), and based on recent research [Immunity, Volume 29, Issue 3, 497-510, 19 September 2008] LCs preferentially induce the differentiation of CD4⁺ T cells secreting T helper 2 (Th2) cell cytokines and are particularly efficient at priming and cross priming naive CD8⁺ T cells – the latter characteristic is particularly desirable for evoking anti-cancer CTL responses. In contrast, anti-CD40 targeting agents would deliver antigen to a much broader array of APC in vivo.

Figure 4– demonstration of the ability of recombinant anti-Langerin antibody fused to the human prostate specific cancer antigen to elicit the expansion of antigen-specific CD8⁺ T cells from a prostate cancer patient. DCs targeted with anti-CD40-PSA and anti-Langerin-PSA targeted to DCs induces PSA-specific

CD8⁺ T cell responses. (a) IFNDCs were targeted with 1 mg mAb fusion proteins with PSA. Purified autologous CD8⁺ T cells were co-cultured for 10 days. Cells were stained with anti-CD8 and PSA (KLQCVDLHV)-tetramer. Cells are from HLA-A*0201 positive prostate cancer patients. The PSA tetramer reagent identified T cells bearing T cell receptors specifically reactive with HLA-A*0201 complexes bearing the PSA KLQCVDLHV peptide.

These data show that an anti-Langerin vaccine bearing a cancer antigen can prime a potent antigen-specific anti-CD8⁺ T cell response in vitro using immune cells from a prostate cancer. In this in vitro culture system this agent is as potent as a anti-CD40 based vaccine – these DCs express both receptors. In vivo, an anti-Langerin-based vaccine would target antigen only to Langerhans cells (LCs), and based on recent research [Immunity, Volume 29, Issue 3, 497-510, 19 September 2008] LCs preferentially induce the differentiation of CD4⁺ T cells secreting T helper 2 (Th2) cell cytokines and are particularly efficient at priming and cross priming naive CD8⁺ T cells – the latter characteristic is particularly desirable for evoking anti-cancer CTL responses. In contrast, anti-CD40 targeting agents would deliver antigen to a much broader array of APC in vivo.

Figure 5 – Anti-Langerin preferentially targets epidermal LCs. Purified skin DC subsets (Epidermal LCs, dermal CD1a⁺ DCs and CD14⁺ DCs) from HLA-A201 donor were cultured with 8 nM anti-Langerin, IgG4 conjugates mAbs, free FluMP or without antigen for 3 h. Syngeneic purified CD8⁺ T cells were cultured with the antigen-pulsed DCs at a DC/T ratio 1:20. CD40L (100 ng/ml; R&D) was added to the culture after 24 h. CD40-ligation enhances crosspresentation by DCs. The cocultures were incubated at 37°C for 8 -10 days. IL-2 (10 U/ml) was added at day 3. The response of FluMP-specific CD8⁺ T cells was evaluated using HLA-A201-FluMP (58-66) peptide (GILGFVFTL) tetramer.

The data in panel Figure 5A : 2D FACs-plots showing FluMP-specific CD8⁺ T cell expansion as evaluated by specific HLA-A201-FluMP (58-66) tetramer staining demonstrating that targeting antigen via anti-Langerin elicits antigen-specific CD8⁺ T cell expansion only through LCs, which is more robust than other methods of antigen delivery such as free FluMP. Some response is induced by the dermal CD1a⁺ DCs, in concordance with the ability of these cells to upregulate Langerin in culture. Figure 5B summarizes the data in a graph shows mean $\pm$ sd, N=3. Figure 5C. IFN- γ levels in the culture supernatants of human LCs that were culture for 8 days with either Langerin-FluMP, control IgG4-FluMP, free FluMP or no antigen after 8 days.

Figure 6 shows the differential expression of Langerin by human skin DCs. Figure 6A shows the expression of Langerin on isolated human skin DC subsets. Data show restricted expression of Langerin on human LCs, but not on dermal CD1a⁺ or CD14⁺ DCs. Figure 6B show a gene expression analysis of Langerin by skin DCs isolated from 3 different specimens. RNA was prepared from sorted migrated skin mDC subsets: epidermal LCs, dermal CD1a⁺ DCs and CD14⁺ DCs. Figure 6C shows the immunofluorescent staining of normal human skin using Langerin and HLA-DR mAbs.

Figure 7 – Anti-Langerin 15B10 antibody (produced by hybridoma ATCC Accession No. PTA-9852) specifically stains human Langerhans cells. Human epithelial sheet was prepared and stained with Alexa568 [red]-labeled anti-Langerin 15B10 and a commercial anti-HLA antibody labeled green. The top image shows the red and green image superimposed highlighting the co-localization of these two markers.

Constructs.

mAnti-Langerin15B10K – Nucleotide and mature protein amino acid sequence of the light chain of the mouse anti-Langerin 15B10 antibody cDNA, respectively. The variable region residues are underlined.

10 **ATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGGATTCTGCTTCCAGCAGTGATGTT**
 GTGATGACCCAAACTCCACTCTCCCTGCCTGTCCGTCTTGGAGATCAAGCCTCCATCTCTTGC
 AGATCTAGTCAGAGCCTTGTACACAGTAATGGAAACACCTATTTACATTGGTACCTGCAGAA
 GCCAGGCCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAGA
 CAGGTTTCAGTGGCAGTGGATCAGGGACAAATTTCACTCAAGATCAGCAGAGTGGAGGCTG
 AGGATCTGGGACTTTATTTCTGCTCTCAAAGTACACATGTTCCGTACACGTTCCGGAGGGGGGA
 15 CCAAGCTGGAAATAAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCCAGT
 GAGCAGTTAACATCTGGAGGTGCCTCAGTCGTGTGCTTCTTGAACAACTTCTACCCCAAAGAC
 ATCAATGTCAAGTGGAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGTTGGAC
 TGATCAGGACAGCAAAGACAGCACCTACAGCATGAACAGCACCCCTCACGTTGACCAAGGAC
 GAGTATGAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTCACCCAT
 20 CGTCAAGAGCTTCAACAGGAATGAGTGTTAG (SEQ ID NO. 1)

DVVMTQTPLSLPVRLGDQASISCRSSQSLVHSNGNTYLHWYLOKPGQSPKLLIYKVSNNRFSGVDP
RFSGSGSGTNFTLKISRVEAEDLGLYFCSQSTHVPYTFGGGTKLEIKRADAAPT
VSIFPPSSEQLTSG
 GASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDYSTYSMNSTLT
 25 TCEATHKTSTSPIVKSFNRNEC (SEQ ID NO. 2)

mAnti-Langerin15B10H-LV-hIgG4H-C – Nucleotide and mature protein amino acid sequence of the heavy chain variable region of the mouse anti-Langerin 15B10 antibody fused to human IgG4, respectively. The variable region residues are underlined.

30 **ATGGAATGGAGGATCTTTCTCTTCATCCTGTCAGGAACTGCAGGTGTCCACTCCCAGGTTTCAG**
 CTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGC
 TTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGCAGAGAACTGGACAGGGCC
 TTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTCTACAATGAGAACTTCAAGG
 GCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCTACATGCAGCTCAGCAGCCTG
 35 ACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTATAACTACCCTTTTGCTTACTGGG
 GCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACGGGGCCCATCCGTCTTCCCCCTGG
 CGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAAGGACTAC
 TTCCCCGAACCGGTGACGGTGTGCTGGAACCTCAGGCGCCCTGACCAGCGGCGTGACACCTT
 CCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAG
 40 CAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAACACCAAGGTGG
 ACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCCCACCCTGCCAGCACCTGAGTTTCGAA
 GGGGGACCATCAGTCTTCCTGTTCCCCCAAAACCCAAGGACACTCTCATGATCTCCCGGACC
 CCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTCAACTG
 GTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTTCAAC
 45 AGCACGTACCGTGTGGTCAGCGTCCTACCGTCCTGCACCAGGACTGGCTGAACGGCAAGGA
 GTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCCTCCATCGAGAAAACCATCTCCAAAG
 CCAAGGGCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCCCAGGAGGAGATGACC
 AAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTACCCAGCGACATCGCCGTGGA
 GTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTGGACTCC

GACGGCTCCTTCTTCTCTACAGCAGGCTAACCGTGGACAAGAGCAGGTGGCAGGAGGGGAA
TGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGCCTCTC
CCTGTCTCTGGGTAAAGCTAGCTGA (SEQ ID NO. 3)

5 QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFPL
APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLG
TKTYTCNVDPHKPSNTKVDKRVESKYGPPCPPPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
10 KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKAS (SEQ ID
NO. 4)

mAnti-Langerin2G3L (produced by hybridoma ATCC Accession No. PTA-9853)– Nucleotide and
15 mature protein amino acid sequence of the light chain of the mouse anti-Langerin 2G3 antibody cDNA,
respectively. The variable region residues are underlined.

ATGGCCTGGATTTCACTTATACTCTCTCTCCTGGCTCTCAGCTCAGGGGCCATTTCCCAGGCT
GTTGTGACTCAGGAATCTGCACTCACCATCACCTGGTGAAACAGTCACACTCACTTGTCTGC
TCAAGTACTGGGGCTGTTACAAGTAACTATGCCAACTGGGTCCAAGAAAAACCAGATCA
20 TTTATTCACTGGTCTAATAGGTGGTACCAACAACCGAGTTTCAGGTGTTCTCCTGCCAGATTCTC
AGGCTCCCTGATTGGAGACAAGGCTGCCCTCACCATCACAGGGGGCACAGACTGAGGATGAGG
CAATATATTTCTGTGCTCTATGGTACAGCAACCATTGGGTGTTCTGGTGGAGGAACCAAAGTGA
CTGTCCTAGGCCAGCCCAAGTCTTCGCCATCAGTCACCCTGTTTCCACCTTCCTCTGAAGAGC
TCGAGACTAACAAGGCCACACTGGTGTGTACGATCACTGATTTCTACCCAGGTGTGGTGACA
25 GTGGACTGGAAGGTAGATGGTACCCCTGTCCTCAGGGTATGGAGACAACCCAGCCTTCCAA
ACAGAGCAACAACAAGTACATGGCTAGCAGCTACCTGACCCTGACAGCAAGAGCATGGGAA
AGGCATAGCAGTTACAGCTGCCAGGTCACTCATGAAGGTCACACTGTGGAGAAGAGTTTGTC
CCGTGCTGACTGTTCTAG (SEQ ID NO. 5)

30 QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFS
GSLIGDKAALTITGAQTEDEAIYFCALWYSNHWVFGGGTKLTVLGQPKSSPSVTLFPPSSEELETN
KATLVCTITDFYPGVVTVDWKVDGTPVTQGMETTQPSKQSNKYMSSYLTLTARAWERHSSY
SCQVTHEGHTVEKSLSRADCS (SEQ ID NO. 6)

35 mAnti-Langerin2G3H – Nucleotide and mature protein amino acid sequence of the heavy chain of the
mouse anti-Langerin 2G3 antibody cDNA, respectively. The variable region residues are underlined.

ATGACATTGAACATGCTGTTGGGGCTGAAGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
CATTGTGAGGTGCAGCTTGTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
40 ACTCTCATGTGCAGCCTCTGGATTAACCTTCAATATCTACGCCATGAACTGGGTCCGCCAGGC
TCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAACAT
ATTATGCCGATTCAGTGAAAGACAGGTTACCATCTCCAGAGATGATTCACAAAGCTTGCTCT
ATCTGCAAATGAACAACCTGAAAACCTGAGGACACAGCCATGTATTACTGTGTGGGACGGGAC
TGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACACCCCCA
45 TCTGTCTATCCACTGGCCCCTGGATCTGCTGCCCAAACCTCACTCCATGGTGACCCTGGGATGC
CTGGTCAAGGGCTATTTCCCTGAGCCAGTGACAGTGACCTGGAACCTCTGGATCCCTGTCCAGC
GGTGTGCACACCTTCCCAGCTGTCCTGCAGTCTGACCTCTACACTCTGAGCAGCTCAGTGACT
GTCCCCTCCAGCACCTGGCCCAGCGAGACCGTCACCTGCAACGTTGCCACCCGGCCAGCAG
CACCAAGGTGGACAAGAAAATTGTGCCAGGGATTGTGGTTGTAAGCCTTGCAATATGTACAG
50 TCCCAGAAGTATCATCTGTCTTCATCTTCCCCCAAAGCCCAAGGATGTGCTCACCATTACTC
TGACTCCTAAGGTCACGTGTGTTGTGGTAGACATCAGCAAGGATGATCCCGAGGTCCAGTTC
AGCTGGTTTGTAGATGATGTGGAGGTGCACACAGCTCAGACGCAACCCCGGGAGGAGCAGTT

CAACAGCACTTTCCGCTCAGTCAGTGAACCTTCCCATCATGCACCAGGACTGGCTCAATGGCAA
 GGAGTTCAAATGCAGGGTCAACAGTGCAGCTTTCCCTGCCCCCATCGAGAAAACCATCTCCA
 AAACCAAAGGCAGACCGAAGGCTCCACAGGTGTACACCATCCACCTCCCAAGGAGCAGATG
 5 GCCAAGGATAAAGTCAGTCTGACCTGCATGATAACAGACTTCTTCCCTGAAGACATTACTGTG
 GAGTGGCAGTGGAATGGGCAGCCAGCGGAGAACTACAAGAACAACACTCAGCCCATCATGGACA
 CAGATGGCTCTTACTTCGTCTACAGCAAGCTCAATGTGCAGAAGAGCAACTGGGAGGCAGGA
 AATACTTTCACCTGCTCTGTGTTACATGAGGGCCTGCACAACCACCATACTGAGAAGAGCCTC
 TCCCACTCTCCTGGTAAAGCTAGCTGA (SEQ ID NO. 7)

10 EVQLVESGGGLVQPKGSLKLSCAASGLTFENIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYA
DSVKDRFTISRDDSQSLLYLQMNNLKTEDTAMYCYCVGRDWF~~FDYWGQGT~~LVTVSAAKTPPSVY
 PLAPGSAAQTNSMVTLGCLVKGYFPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLSSSVTVPSST
 WPSETVTCNVAHPASSTKVDDKKIVPRDCGCKPCICTVPEVSSVFIFPPKPKDVLITITLTPKVTCTVTV
 DISKDDPEVQFSWFVDDVEVHTAQTQPREEQFNSTFRSVSELPIMHQDWLNGKEFKCRVNSAAFP
 15 APIEKTISKTKGRPKAPQVYTIPPPKEQMAKDKVSLTCMITDFFPEDITVEWQWNGQPAENYKNT
 QPIMDTDGSYFVYSKLVNPKSNWEAGNTFTCSVLHEGLHNHHTEKSLSHSPGKAS (SEQ ID NO.
 8)

C84 rAB-pIRES2 [mAnti-Langerin2G3H-LV-hIgG4H-C-Dockerin] The coding region for this H chain-
 20 dockerin fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGC
 restriction site.

ATGACATTGAACATGCTGTTGGGGCTGAGGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
 CATTGTGAGGTGCAGCTTGTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
 25 ACTCTCATGTGCAGCCTCTGGATTAACCTTCAATATCTACGCCATGAACTGGGTCCGCCAGG
 CTCCAGGAAAGGGTTTGGGAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAAC
 ATATTATGCCGATTCAGTGAAAGACAGGTTCAACCATCTCCAGAGATGATTCACAAAGCTTGC
 TCTATCTGCAAATGAACAACCTTGAAAACCTGAGGACACAGCCATGTATTACTGTGTGGGACG
 GGACTGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGAAG
 30 GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCT
 GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCC
 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 35 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCCCTCAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACAGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 40 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTACAGCCTGACCTGCCTGGTC
 AAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 45 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**CTAGCAATTCT**
CCTCAAAATGAAGTACTGTACGGAGATGTGAATGATGACGGAAAAGTA**AACTCCACTGACT**
TGACTTTGTTAAAAAGATATGTTCTTAAAGCCGTCTCAACTCTCCCTTCTTCCAAAGCTGAAA
AGAACGCAGATGTAAATCGTGACGGAAGAGTTAATTCCAGTGATGTCACAATACTTTCAAG
ATATTTGATAAGGGTAATCGAGAAATTACCAATATAA (SEQ ID NO. 57)

50 The mature H chain sequence for C84 heavy chain is shown below. Joining sequence AS is bold and
 dockerin is underlined.

EVQLVESGGGLVQPKGSLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYY
 ADSVKDRFTISRDDSQSLLYLQMNNLKTEDTAMYYCVGRDWFYWGQGTLLTVSAAKTKGPS
 VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
 5 SSLGKTKYTCNVDPHKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEV
 TCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNGKLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
 PENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASN
 10 SPQNEVLYGDVNDDGKVNSTDLTLLKRYVLKAVSTLPSSKAENADVNRDGRVNSSDVILSR
YLIRVIEKLPI (SEQ ID NO. 58)

C85 rAB-pIRES2 [mAnti-Langerin2G3H-LV-hIgG4H-C-Flex-FluHA1-1-6xHis] The coding region for this H chain-Flu HA1-1 fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGC restriction site.

15 **ATG**ACATTGAACATGCTGTTGGGGCTGAGGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
 CATTGTGAGGTGCAGCTTGTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
 ACTCTCATGTGCAGCCTCTGGATTAACCTTCAATATCTACGCCATGAACTGGGTCCGCCAGG
 CTCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAAC
 ATATTATGCCGATTCAGTGAAAGACAGGTTCAACATCTCCAGAGATGATTCACAAAGCTTGC
 20 TCTATCTGCAAATGAACAACCTGAAAACCTGAGGACACAGCCATGTATTACTGTGTGGGACG
 GGACTGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGAAG
 GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCT
 GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCC
 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 25 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCCCTAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACAGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 30 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTACAGCCTGACCTGCCTGGTC
 AAAGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 35 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**GCTAGCG**GATAC
 AACAGAACCTGCAACACCTACAACACCTGTAACAACAGACACAATATGTATAGGCTACCAT
 GCGAACAATTCAACCGACACTGTTGACACAGTACTCGAGAAGAATGTGACAGTGACACACT
 40 CTGTAAACCTGCTCGAAGACAGCCACAACGGAAACTATGTAGATTAAGGAATAGCCCC
 ACTACAATTGGGGAAATGTAACATCGCCGGATGGCTCTTGGGAAACCCAGAATGCGACCCA
 CTGCTTCCAGTGAGATCATGGTCCTACATTGTAGAAACACCAAACCTCTGAGAATGGAATATG
 TTATCCAGGAGATTTTCATCGACTATGAGGAGCTGAGGGAGCAATTGAGCTCAGTGTCATCAT
 TCGAAAGATTTCGAAATATTTCCCAAAGAAAGCTCATGGCCCAACCACAACACAACGGAGT
 45 AACGGCAGCATGCTCCCATGAGGGGAAAAGCAGTTTTTACAGAAATTTGCTATGGCTGACG
 GAGAAGGAGGGCTCATACCCAAAGCTGAAAAATTCTTATGTGAACAAAAAAGGGAAAGAA
 GTCCTTGTACTGTGGGGTATTCATCACCCGCCTAACAGTAAGGAACAACAGAATCTCTATCA
 GAATGAAAATGCTTATGTCTCTGTAGTGACTTCAAATTATAACAGGAGATTTACCCCGGAAA
 TAGCAGAAAGACCCAAAGTAAGAGATCAAGCTGGGAGGATGAACTATTACTGGACCTTGCT
 50 AAAACCCGGAGACACAATAATATTTGAGGCAAATGGAAATCTAATAGCACCAATGTATGCT
 TTCGCACTGAGTAGAGGCTTTGGGTCCGGCATCATCACCTCAAACGCATCAATGCATGAGTG
 TAACACGAAGTGTCAAACACCCCTGGGAGCTATAAACAGCAGTCTCCCTTACCAGAATATA
 CACCAGTCACAATAGGAGAGTGCCCAAATACGTCAGGAGTGCCAAATTGAGGATGGTTC
 ACCATCACCATCACCAT**TGA** (SEQ ID NO. 59)

The mature H chain sequence for C85 heavy chain is shown below. Joining sequence AS is bold and Flu HA1-1 is underlined. A flexible linker joining sequence is italicized.

5 EVQLVESGGGLVQPKGSLKLSAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYY
 ADSVKDRFTISRDDSQSLLYLQMNNLKTEDTAMYYCVGRDWFYWGQGLVTVSAAKTKGPS
 VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
 SSLGTKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEV
 TCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 10 KVSNGKLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
 PENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLKASD
TTEPATPTTPVTTDTICIGYHANNSTDVDTVLEKNVTVTHSVNLLLED SHNGKLCRLKGIAPLQLG
KCNIAGWLLGNPECDPLLPVRSWSYIVETPNSENGICYPGDFIDYEELREQLSSVSSFERFEIFPKE
SSWPNHNTNGVTAACSHGKSSFYRNLLWLTEKEGSYPKLKNSYVNKKGKEVLVLWGIHHPN
 15 *SKEQQNLYQENAYVSVVTSNYNRRFTPEIAERPVRDQAGRMNYYWTLLKPGDTIIFEANGNL*
IAPMYAFALSRGFGSGIITSNASMHECNTKCQTPLGAINSSLPYQNIHPVTIGECPKYVRSACLRLM
VHHHHHHH (SEQ ID NO. 60)

20 C86 rAB-pIRES2 [mAnti-Langerin2G3H-LV-hIgG4H-C-Flex-FluHA5-1-6xHis] The coding region for
 this H chain-Flu HA5-1 fusion protein is shown below. Start and stop codons are in bold, as is the joining
 GCTAGC restriction site.

ATGACATTGAACATGCTGTTGGGGCTGAGGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
 CATTGTGAGGTGCAGCTTGTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
 25 ACTCTCATGTGCAGCCTCTGGATTAACCTTCAATATCTACGCCATGAACTGGGTCCGCCAGG
 CTCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAAC
 ATATTATGCCGATTCAGTGAAAGACAGGTTCCACCATCTCCAGAGATGATTCACAAAGCTTGC
 TCTATCTGCAAATGAACAACCTTGAAAACCTGAGGACACAGCCATGTATTACTGTGTGGGACG
 GGACTGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGAAG
 30 GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCT
 GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACCTCAGGCGCC
 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 35 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCTGTTCCCCCCCCAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 40 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTACAGCCTGACCTGCCTGGTC
 AAAGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 45 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**GCTAGCG**GATAC
AACAGAACCTGCAACACCTACAACACCTGTAACAACAGATCAGATTTGCATTGGTTACCATG
CAAACAACCTCGACAGAGCAGGTTGACACAATAATGGAAAAGAACGTTACTGTTACACATGC
CCAAGACATACTGGAAAAGAAACACAACGGGAAGCTCTGCGATCTAGATGGAGTGAAGCCT
CTAATTTTGAGAGATTGTAGCGTAGCTGGATGGCTCCTCGGAAACCAATGTGTGACGAATT
 50 CATCAATGTGCCGGAATGGTCTTACATAGTGGAGAAGGCCAATCCAGTCAATGACCTCTGTT
ACCCAGGGGATTTCAATGACTATGAAGAATTGAAACACCTATTGAGCAGAATAAACCATTTT
GAGAAAATTCAGATCATCCCCAAAAGTTCTTGGTCCAGTCATGAAGCCTCATTAGGGGTGAG

CTCAGCATGTCCATACCAGGGAAAGTCCTCCTTTTTTCAGAAATGTGGTATGGCTTATCAAAA
 AGAACAGTACATACCCAACAATAAAGAGGAGCTACAATAATACCAACCAAGAAGATCTTTT
 GGTACTGTGGGGGATTACCATCCTAATGATGCGGCAGAGCAGACAAAGCTCTATCAAAAC
 CCAACCACCTATATTTCCGTTGGGACATCAACACTAAACCAGAGATTGGTACCAAGAATAGC
 5 TACTAGATCCAAAGTAAACGGGGCAAAGTGGAAGGATGGAGTTCTTCTGGACAATTTTAAAG
 CCGAATGATGCAATCAACTTCGAGAGTAATGGAAATTTTCATTGCTCCAGAATATGCATACAA
 AATTGTCAAGAAAGGGGACTCAACAATTATGAAAAGTGAATTGGAATATGGTAACTGCAAC
 ACCAAGTGTCAAACCTCCAATGGGGGCGATAAACTCTAGCATGCCATTCCACAATATACACCC
 TCTCACCATTGGGGGAATGCCCCAAATATGTGAAATCAAACAGATTAGTCCTTGCGCACCATC
 10 ACCATCACCATTGA (SEQ ID NO. 61)

The mature H chain sequence for C86 heavy chain is shown below. Joining sequence AS is bold and Flu HA5-1 is underlined. A flexible linker joining sequence is italicized.

EVQLVESGGGLVQPKGSLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYY
 ADSVKDRFTISRDDSQSLLYLQMNNLKTEDTAMYYCVGRDWFYWGQGTLLTVSAAKTKGPS
 15 VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
 SSLGTKTYTCNVDHKPSNTKVDKRVESKYGPCCPPAPEFEFGGPSVFLFPPKPKDTLMISRTPEV
 TCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
 PENNYKTTTPVLDSDFSFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASD
 20 TTEPATPTTPVTTDQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKKHNGKLCDLDGVKPLILR
DCSVAGWLLGNPMCDEFINPEWSYIVEKANPVNDLCYPGDFNDYEELKHLLSRINHFEKIQIIP
KSSWSSHEASLGVSSACPYQGKSSFFRNVWLIKKNSTYPTIKRSYNNTNQEDLLVLWGIHPN
DAAEQTKLYQNPTTYISVGTSTLNQRLVPRIATRSKVNGQSGRMEFFWTILKPNDAINFESNGNFI
APEYAYKIVKKGDSTIMKSELEYGNCNTKCQTPMGAINSSMPFHNIHPLTIGECPKYVKSNRLVL
 25 AHHHHHH (SEQ ID NO. 62)

C804 rAB-cetHS-puro [mAnti-Langerin2G3H-LV-hIgGK-C-Flex-hPSA] The coding region for this H chain-PSA fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGC restriction site.

30 **ATG**ACATTGAACATGCTGTTGGGGCTGAAGTGGGTTTTCTTTGTTGTTTTTTATCAAGGTGTG
 CATTGTGAGGTGCAGCTTGTTGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAA
 ACTCTCATGTGCAGCCTCTGGATTAACTTCAATATCTACGCCATGAACTGGGTCCGCCAGG
 CTCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAGAAATAAAAGTAATAATTATGCAAC
 ATATTATGCCGATTCAGTGAAAGACAGGTTCAACCATCTCCAGAGATGATTCACAAAGCTTGC
 35 TCTATCTGCAAATGAACAACCTTGAAAACCTGAGGACACAGCCATGTATTACTGTGTGGGACG
 GGACTGGTTTGATTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGAAG
 GGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCT
 GGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAAGTCAAGGCGCC
 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 40 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCCCTAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 45 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAAGGTCTCCAACAAAGGCCTCC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 CGTCCTCCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTCAAGCTGACCTGCCTGGTGC
 AAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 50 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAGCTAGCGATAC

AACAGAACCTGCAACACCTACAACACCTGTAACAACACCGACAACAACACTTCTAGCGCCC
 CTCATCCTGTCTCGGATTGTGGGAGGCTGGGAGTGCGAGAAGCATTCCCAACCCTGGCAGGT
 GCTTGTGGCCTCTCGTGGCAGGGCAGTCTGCGGCGGTGTTCTGGGTGCACCCCCAGTGGGTCC
 TCACAGCTGCCCCACTGCATCAGGAACAAAAGCGTGATCTTGCTGGGTGCGGCACAGCCTGTTT
 5 CATCCTGAAGACACAGGCCAGGTATTTTCAGGTCAGCCACAGCTTCCCACACCCGCTCTACGA
 TATGAGCCTCCTGAAGAATCGATTCTCAGGCCAGGTGATGACTCCAGCCACGACCTCATGC
 TGCTCCGCCTGTCAGAGCCTGCCGAGCTCACGGATGCTGTGAAGGTCATGGACCTGCCACC
 CAGGAGCCAGCACTGGGGACCACCTGCTACGCCTCAGGCTGGGGCAGCATTGAACCAGAGG
 AGTTCTTGACCCCAAAGAACTTCAGTGTGTGGACCTCCATGTTATTTCCAATGACGTGTGT
 10 GCGCAAGTTCACCCTCAGAAGGTGACCAAGTTCATGCTGTGTGCTGGACGCTGGACAGGGG
 GCAAAAGCACCTGCTCGGGTGATTCTGGGGGCCCCACTTGTCTGTAATGGTGTGCTTCAAGGT
 ATCACGTCATGGGGCAGTGAACCATGTGCCCTGCCCCGAAAGGCCTTCCCTGTACACCAAGGT
 GGTGCATTACCGGAAGTGGATCAAGGACACCATCGTGGCCAACCCCTGA (SEQ ID NO. 63)

The mature H chain sequence for C804 heavy chain is shown below. Joining sequence AS is bold and
 15 PSA is underlined. A flexible linker joining sequence is italicized.

EVQLVESGGGLVQPKGSLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYY
 ADSVKDRFTISRDDSQSLLYLQMNNLKTEDTAMYYCVGRDWFYWGQGLVTVSAAKTKGPS
 VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
 SSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCAPEFEGGPSVFLFPPKPKDTLMISRTPEV
 20 TCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
 KVSNNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
 PENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASD
TTEPATPTTPVTPTTTLL APLILSRIVGGWECEKHSOPWQVLVASRGRAVCGGVLVHPQWVLTA
AHCIRNKSVILLGRHSLFHPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHDLMLLRLSE
 25 PAELTDAVKVMDLPTQEPALGTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKV
TKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKD
TIVANP (SEQ ID NO. 64)

C87 rAB-pIRES2 [mAnti-Langerin15B10H-SLAMF-V-hIgG4H-Flex-FluHA5-1-6xHis] The coding
 region for this H chain-Flu HA5-1 fusion protein is shown below. Start and stop codons are in bold, as is
 30 the joining GCTAGC restriction site.

ATGGACCCCAAAGGCTCCCTTTCTGAGAGAATACTTCTGTTTCTCTCCCTGGCTTTTGAGTTG
 TCGTACGGACAGGTTTCAGCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGT
 GAAGATGTCCTGCAAGGCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGC
 AGAGAACTGGACAGGGCCTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTC
 35 TACAATGAGAACTTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCT
 ACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTAT
 AACTACCCTTTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAAC
 GGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCC
 TGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAAGTCAAGGCGCC
 40 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCCCTAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCC
 45 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 CGTCCTCCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCAGGAGGAGATGACCAAGAACCAGGTGACCTGACCTGCCTGGTC
 50 AAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGACA
 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG

CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**GCTAGCG**GATAC
AACAGAACCTGCAACACCTACAACACCTGTAACAACAGATCAGATTTGCATTGGTTACCATG
CAAACAACCTCGACAGAGCAGGTTGACACAATAATGGAAAAGAACGTTACTGTTACACATGC
CCAAGACATACTGGAAAAGAAACACAACGGGAAGCTCTGCGATCTAGATGGAGTGAAGCCT
 5 CTAATTTTGAGAGATTGTAGCGTAGCTGGATGGCTCCTCGGAAACCCAATGTGTGACGAATT
CATCAATGTGCCGGAATGGTCTTACATAGTGGAGAAGGCCAATCCAGTCAATGACCTCTGTT
ACCCAGGGGATTTCAATGACTATGAAGAATTGAAACACCTATTGAGCAGAATAAACCATTTT
GAGAAAATTCAGATCATCCCCAAAAGTTCTTGGTCCAGTCATGAAGCCTCATTAGGGGTGAG
CTCAGCATGTCCATACCAGGGAAAGTCCTCCTTTTTTCAGAAATGTGGTATGGCTTATCAAAA
 10 AGAACAGTACATACCCAACAATAAAGAGGAGCTACAATAATACCAACCAAGAAGATCTTTT
GGTACTGTGGGGGATTACCATCCTAATGATGCGGCAGAGCAGACAAAGCTCTATCAAAAC
CCAACCACCTATATTTCCGTTGGGACATCAACACTAAACCAGAGATTGGTACCAAGAATAGC
TACTAGATCCAAAGTAAACGGGCAAAGTGGAAGGATGGAGTTCTTCTGGACAATTTTAAAG
CCGAATGATGCAATCAACTTCGAGAGTAATGGAAATTTTCATTGCTCCAGAATATGCATACAA
 15 AATTGTCAAGAAAGGGGACTCAACAATTATGAAAAGTGAATTGGAATATGGTAACTGCAAC
ACCAAGTGTCAAACCTCAATGGGGGCGATAAACTCTAGCATGCCATTCCACAATATACACCC
TCTCACCATTGGGGGAATGCCCCAAATATGTGAAATCAAACAGATTAGTCCTTGCGCACCATC
ACCATCACCATTGA (SEQ ID NO. 65)

The mature H chain sequence for C87 heavy chain is shown below. Joining sequence AS is bold and Flu
 20 HA5-1 is underlined.

QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYNPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDPHKPSNTKVDKRVESKYGPCCPAPPEFEGGPSVFLFPPKPKDTLMISRTPEVTC
 25 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASDT
TEPATPTTPVTTDQICIGYHANNSTEQVDTIMEKNVTVTTHAQDILEKKHNGKLCDLGDKPLILRD
CSVAGWLLGNPMCDEFINVPESYIVEKANPVDNLCPYPGDFNDYEELKHLISRINHFEEKIQIIPKS
 30 SWSSHEASLGVSACPYQGKSSFFERNVWLIKKNSTYPTIKRSYNNTNQEDLLVLWGIHHPNDA
AEQTKLYQNPTTYISVGTSTLNQRLVPRIATRSKVNGQSGRMEFFWTILKPNDAINFESNGNFIAP
EYAYKIVKKGDSTIMKSELEYGNCNTKQCQTPMGAINSSMPFHNIHPLTIGECPKYVKS NRLVLAH
 HHHHH (SEQ ID NO. 66)

C88 rAB-pIRES2 [mAnti-Langerin15B10H-SLAML-V-hIgG4H-C-Dockerin] The coding region for this
 35 H chain-dockerin fusion protein is shown below. Start and stop codons are in bold, as is the joining
 GCTAGC restriction site.

ATGGACCCCAAAGGCTCCCTTTCCTGGAGAATACTTCTGTTTCTCTCCCTGGCTTTTGAGTTG
 TCGTACGGACAGGTTTCAGCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGT
 GAAGATGTCCTGCAAGGCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGC
 40 AGAGAACTGGACAGGGCCTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTC
 TACAATGAGAACTTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCT
 ACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTAT
 AACTACCCTTTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAAC
 GGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCC
 45 TGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACCTCAGGCGCC
 CTGACCAGCGGCGTGACACCTTCCCGGCTGTCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 CACCCTGCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCC AAAACCC
 50 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC

CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTC
 AAAGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 5 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAGCTAGCAATTCT
 CCTCAAAATGAAGTACTGTACGGAGATGTGAATGATGACGGAAAAGTAAACTCCACTGACT
 TGACTTTGTAAAGATATGTTCTTAAAGCCGTCTCAACTCTCCCTTCTTCCAAAGCTGAAA
 10 AGAACGCAGATGTAAATCGTGACGGAAGAGTTAATTCCAGTGATGTCACAATACTTTCAAG
 ATATTTGATAAGGGTAATCGAGAAATTACCAATA**TAA** (SEQ ID NO. 67)

The mature H chain sequence for C88 heavy chain is shown below. Joining sequence AS is bold and
 dockerin is shaded grey. A flexible linker joining sequence is underlined.

QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 15 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDPKPSNTKVDKRVERSKYGPCCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTC
 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
 VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
 20 ENNYKTTTPVLDSGDSFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGKAS**NS**
 PQNEVLYGDVNDDGKVNSTDLTLLKRYVLKAVSTLPSSKA**AEKN**ADVNRDGRVNSSDV**TILSR**
LIRVIEKLPI (SEQ ID NO. 68)

C89 rAB-pIRES2[mAnti-Langerin15B10H-SLAMF-V-hIgG4H-Flex-FluHA1-1-6xHis] The coding
 region for this H chain-Flu HA1-1 fusion protein is shown below. Start and stop codons are in bold, as is
 25 the joining GCTAGC restriction site.

ATGGACCCCAAAGGCTCCCTTTCCTGGAGAATACTTCTGTTTCTCTCCCTGGCTTTTGAGTTG
 TCGTACGGACAGGTTTCAGCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGT
 GAAGATGTCCTGCAAGGCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGC
 AGAGAACTGGACAGGGCCTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTC
 30 TACAATGAGAACTTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCT
 ACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTAT
 AACTACCCTTTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAAC
 GGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCC
 TGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAAGTCAAGGCGCC
 35 CTGACCAGCGGCGTGACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 CACCCTGCCCAGCACCTGAGTTCTGAAGGGGGACCATCAGTCTTCCTGTTCCCCCCTAAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACGCTGCGTGGTGGTGGACGTGAGCC
 40 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCCAGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTC
 45 AAAGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACA
 ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAGCTAGCGATAC
 AACAGAACCTGCAACACCTACAACACCTGTAACAACAGACACAATATGTATAGGCTACCAT
 50 GCGAACAATTCAACCGACACTGTTGACACAGTACTCGAGAAGAATGTGACAGTGACACACT
 CTGTAAACCTGCTCGAAGACAGCCACAACGGAAAACCTATGTAGATTAAAAGGAATAGCCCC
 ACTACAATTGGGGAAATGTAACATCGCCGGATGGCTCTTGGGAAACCCAGAATGCGACCCA

CTGCTTCCAGTGAGATCATGGTCCTACATTGTAGAAACACCAAACCTCTGAGAATGGAATATG
 TTATCCAGGAGATTTTCATCGACTATGAGGAGCTGAGGGAGCAATTGAGCTCAGTGTCATCAT
 TCGAAAGATTTCGAAATATTTCCCAAAGAAAGCTCATGGCCCAACCACAACACAAACGGAGT
 AACGGCAGCATGCTCCCATGAGGGGAAAAGCAGTTTTTTACAGAAATTTGCTATGGCTGACG
 5 GAGAAGGAGGGCTCATACCCAAAGCTGAAAAATTCTTATGTGAACAAAAAAGGGAAAGAA
GTCCTTGTACTGTGGGGTATTCATCACCCGCCTAACAGTAAGGAACAACAGAATCTCTATCA
GAATGAAAATGCTTATGTCTCTGTAGTGACTTCAAATTATAACAGGAGATTTACCCCGGAAA
TAGCAGAAAGACCCAAAGTAAGAGATCAAGCTGGGAGGATGAACTATTACTGGACCTTGCT
AAAACCCGGAGACACAATAATATTTGAGGCAAATGGAAATCTAATAGCACCAATGTATGCT
 10 TTCGCACTGAGTAGAGGCTTTGGGTCCGGCATCATCACCTCAAACGCATCAATGCATGAGTG
TAACACGAAGTGTCAAACACCCCTGGGAGCTATAAACAGCAGTCTCCCTTACCAGAATATA
CACCCAGTCACAATAGGAGAGTGCCCAAAATACGTCAGGAGTGCCAAATTGAGGATGGTTC
ACCATCACCATCACCAT**TGA** (SEQ ID NO. 69)

The mature H chain sequence for C89 heavy chain is shown below. Joining sequence AS is bold and Flu
 15 HA1-1 is underlined. A flexible linker joining sequence is italicized.

QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDPKPSNTKVDKRVESKYGPPCPPPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTC
 20 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASDT
TEPATPTTPVTTDTICIGYHANNSTDVDTVLEKNVTVTHSVNLLED SHNGKLCRLKGIAPLQLGK
CNIAGWLLGNPECDPLLPVRSWSYIVETPNSENGICYPGDFIDYEELREQLSSVSSFERFEIFPKESS
 25 WPNHNTNGVTAACSHEGKSSFYRNLLWLTEKEGSYPKLKNSYVNKKGKEVLVLWGIHHPNSK
EQONLYQNENAYVSVVTSNYNRRFTPEIAERPVRDQAGRMNYYWTLLKPGDTIIFEANGNLIA
PMYAFALSRGFGSGIITSNASMHECNTKCQTPLGAINSSLPYQNIHPVTIGECPKYVRS AKLRMV
HHHHHH (SEQ ID NO. 70)

30 C246 rAB-pIRES2[mAnti-Langerin15B10H-SLAMF-V-hIgG4H-Viralgag] The coding region for this H
 chain-gag fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGC
 restriction site.

ATGGACCCCAAAGGCTCCCTTTCCTGGAGAATACTTCTGTTTCTCTCCCTGGCTTTTGAGTTG
 TCGTACGGACAGGTTCAGCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGT
 35 GAAGATGTCCTGCAAGGCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGC
 AGAGAACTGGACAGGGCCTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTC
 TACAATGAGAACTTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCT
 ACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTAT
 AACTACCCTTTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAAC
 40 GGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCC
 TGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAAGTCAAGGCGCC
 CTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG
 CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGAT
 CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCC
 45 CACCCTGCCCAGCACCTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCC AAAACCC
 AAGGACACTCTCATGATCTCCCGGACCCCTGAGGTACAGTGCGTGGTGGTGGACGTGAGCC
 AGGAAGACCCCGAGGTCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAA
 GACAAAGCCGCGGGAGGAGCAGTTCAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
 CTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCC
 50 CGTCCTCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTA
 CACCCTGCCCCCATCCAGGAGGAGATGACCAAGAACCAGGTACGCTGACCTGCCTGGTC
 AAAGGCTTCTACCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGACA

ACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAGGCTA
 ACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGG
 CTCTGCACAACCACTACACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**GCTAGCGACAT**
 GGCCAAGAAGGAGACAGTCTGGAGGCTCGAGGAGTTCGGTAGGCCTATAGTGCAGAACATC
 5 CAGGGGCAAATGGTACATCAGGCCATATCACCTAGAACTTTAAATGCATGGGTAAAAGTAG
TAGAAGAGAAGGCTTTCAGCCCAGAAGTAATACCCATGTTTTTCAGCATTATCAGAAGGAGC
CACCCCACAAGATTTAAACACCATGCTAAACACAGTGGGGGGACATCAAGCAGCCATGCAA
ATGTTAAAAGAGACCATCAATGAGGAAGCTGCAGAATGGGATAGAGTACATCCAGTGCATG
CAGGGCCTATTGCACCAGGCCAGATGAGAGAACCAAGGGGAAGTGACATAGCAGGAACTA
 10 CTAGTACCCTTCAGGAACAAATAGGATGGATGACAAATAATCCACCTATCCCAGTAGGAGA
AATTTATAAAAGATGGATAATCCTGGGATTAAATAAAATAGTAAGAATGTATAGCCCTACC
AGCATTCTGGACATAAGACAAGGACCAAAAGAACCTTTTAGAGACTATGTAGACCGGTTCT
ATAAACTCTAAGAGCCGAGCAAGCTTCACAGGAGGTAAAAAATTGGATGACAGAAACCTT
GTTGGTCCAAAATGCGAACCAGATTGTAAGACTATTTTAAAAGCATTGGGACCAGCGGCT
 15 ACACTAGAAGAAATGATGACAGCATGTCAGGGAGTAGGAGGACCCGGCCATAAGGCAAGA
GTTTTGTGA (SEQ ID NO. 71)

The mature H chain sequence for C89 heavy chain is shown below. Joining sequence AS is bold and Gag p24 is underlined. A flexible linker joining sequence is italicized.

QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 20 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDPHKPSNTKVDKRVESKYGPCCPPCAPEFEGGPSVFLFPPKPKDTLMISRTPEVTC
 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
 VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
 25 ENNYKTTTPVLDSGDFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGKASD
MAKKETVWRLEEFGRPIVQNIQGQMVHQAISPRTLNAWVKVVEEKAFSPEVIPMFSA
DLNTMLNTVGGHQAMQMLKETINEEAAEWDRVHPVHAGPIAPGOMREPRGSDIAGTTSTLQE
QIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPSILDIRQGPKEPFRDYVDRFYKTLRAEQASQ
EVKNWMTETLLVQNPDPCKTILKALGPAATLEEMMTACQGVGGPGHKARVL (SEQ ID NO.
 30 72)

C742 rAB-cetHS-puro[mAnti-Langerin15B10H-LV-hIgG4H-C-Flex-hPSA] The coding region for this H chain-PSA fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGC restriction site.

ATGGAATGGAGGATCTTTCTCTTCATCCTGTCAGGAACTGCAGGTGTCCACTCCCAGGTTCA
 35 GCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAG
 GCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGCAGAGAACTGGACAGGG
 CCTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTCTACAATGAGAACTTCA
 AGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCTACATGCAGCTCAGCAG
 CCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTATAACTACCTTTTGCTTA
 40 CTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACGGGGCCCATCCGTCTTCC
 CCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAA
 GGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG
 CACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT
 GCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAAC
 45 ACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCCCACCCTGCCCAGCAC
 CTGAGTTCGAAGGGGGACCATCAGTCTTCCTGTTCCCCCAAAACCCAAGGACACTCTCATG
 ATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGG
 TCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGA
 GGAGCAGTTCAACAGCACGTACCGTGTGGTGCAGCGTCCTACCGTCCTGCACCAGGACTGGC
 50 TGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCCTCCATCGAGAA
 AACCATCTCCAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCC
 CAGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTACCCCA

GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGC
 CTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAGGCTAACCGTGGACAAGAGC
 AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA
 CACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAG**CTAGCG**GATACAACAGAACCTGCAACA
 5 CCTACAACACCTGTAACAACACCGACAACAACACTTCTAGCGCCCCTCATCCTGTCTCGGAT
TGTGGGAGGCTGGGAGTGCGAGAAGCATTCCCAACCCTGGCAGGTGCTTGTGGCCTCTCGTG
GCAGGGCAGTCTGCGGCGGTGTTCTGGTGCACCCCCAGTGGGTCCTCACAGCTGCCCCACTGC
ATCAGGAACAAAAGCGTGATCTTGCTGGGTGCGCACAGCCTGTTTCATCCTGAAGACACAG
GCCAGGTATTTAGGTCAGCCACAGCTTCCACACCCGCTCTACGATATGAGCCTCCTGAAG
 10 AATCGATTCTCAGGCCAGGTGATGACTCCAGCCACGACCTCATGCTGCTCCGCCTGTCAGA
GCCTGCCGAGCTCACGGATGCTGTGAAGGTCATGGACCTGCCCACCCAGGAGCCAGCACTG
GGGACCACCTGCTACGCCTCAGGCTGGGGCAGCATTGAACCAGAGGAGTTCTTGACCCCAA
AGAACTTCAGTGTGTGGACCTCCATGTTATTTCCAATGACGTGTGTGCGCAAGTTCACCT
CAGAAGGTGACCAAGTTCATGCTGTGTGCTGGACGCTGGACAGGGGGGCAAAAGCACCTGCT
 15 CGGGTGATTCTGGGGGCCCCACTTGTCTGTAATGGTGTGCTTCAAGGTATCACGTCATGGGGC
AGTGAACCATGTGCCCTGCCCGAAAGGCCTTCCCTGTACACCAAGGTGGTGCATTACCGGAA
GTGGATCAAGGACACCATCGTGGCCAACCCCTGA (SEQ ID NO. 73)

The mature H chain sequence for C742 heavy chain is shown below. Joining sequence AS is bold and
 20 PSA is underlined. A flexible linker joining sequence is italicized.

QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDPKPSNTKVDKRVESKYGPCCPAPAFEGGPSVFLFPPKPKDTLMISRTPEVTC
 25 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASDT
TEPATPTTPVTTPTTTLLAPLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWVLTA
HCIRNKSIVLLGRHSLFHPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHDLMLRLSEP
 30 AELTDAVKVMDLPTQEPALGTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKVT
KFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKDTI
VANP (SEQ ID NO. 74)

C1011 rAB-cetHS-puro [mAnti-Langerin15B10H-LV-hIgG4H-C-Flex-v1-Pep-gag17-f1-gag253-f2-
 nef116-f3-nef66-f4-pol158] a.k.a. Anti-Langerin15B10H-HIPO5. The coding region for this H chain-
 35 HIV peptides fusion protein is shown below. Start and stop codons are in bold, as is the joining GCTAGT
 restriction site.

ATGGAAATGGAGGATCTTTCTCTTCATCCTGTCAGGAACTGCAGGTGTCCACTCCCAGGTTCA
 GCTGCGGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAG
 GCTTCTGGATACACATTTACTGACTATGTTATAAGTTGGGTGAAGCAGAGAACTGGACAGGG
 40 CTTGAGTGGATTGGAGATATTTATCCTGGAAGTGGTTATTCTTTCTACAATGAGAACTTCA
 AGGGCAAGGCCACACTGACTGCAGACAAATCCTCCACCACAGCCTACATGCAGCTCAGCAG
 CCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAACCTACTATAACTACCTTTTGTCTTA
 CTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACGGGGCCCATCCGTCTTCC
 CCCTGGCGCCCTGCTCCAGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTGCCTGGTCAA
 45 GGACTACTTCCCCGAACCGGTGACGGTGTGCTGGAAGTCAAGGCGCCCTGACCAGCGGCGTG
 CACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGT
 GCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCAAC
 ACCAAGGTGGACAAGAGAGTTGAGTCCAAATATGGTCCCCCATGCCACCCTGCCCAGCAC
 CTGAGTTCGAAGGGGGACCATCAGTCTTCCCTGTTCCCCCAAAACCCAAGGACACTCTCATG
 50 ATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGG
 TCCAGTTCAACTGGTACGTGGATGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGA
 GGAGCAGTTCAACAGCACGTACCGTGTGGTCAAGCGTCCTCACCGTCCTGCACCAGGACTGGC

TGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCCTCCATCGAGAA
 AACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAGCCACAGGTGTACACCCTGCCCCCATCC
 CAGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTACCCCA
 GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGC
 5 CTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC
 AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA
 CACACAGAAGAGCCTCTCCCTGTCTCTGGGTAAAGCTAGTCAGACCCCCACCAACACCATC
AGCGTGACCCCCACCAACAACAGCACCCCCACCAACAACAGCAACCCCAAGCCCAACCCCG
CTAGTGAGAAGATCCGGCTGCGGCCCGGCGGCAAGAAGAAGTACAAGCTGAAGCACATCGT
 10 GGCTAGTAGCAGCGTGAGCCCCACCACCAGCGTGACCCCCACCCCAACCAGCGTGCCCCC
ACCCCAACCAAGAGCAGCCCCGCTAGTAACCCCCCATCCCCGTGGGCGAGATCTACAAGC
GGTGGATCATCCTGGGCCTGAACAAGATCGTGCGGATGTACAGCCCCACCAGCATCCTGGA
CGCTAGTCCCACCAGCACCCCCGCGGACAGCAGCACCATCACCCCCACCGCCACCCCCACCG
CCACCCCCACCATCAAGGGCGCTAGTCACACCCAGGGCTACTTCCCCGACTGGCAGAACTAC
 15 ACCCCCGGCCCCGGCGTGCGGTACCCCCTGACCTTCGGCTGGCTGTACAAGCTGGCTAGTAC
CGTGACCCCCACCGCCACCGCCACCCCCAGCGCCATCGTGACCACCATCACCCCCACCGCCA
CCACCAAGCCCGCTAGTGTGGGCTTCCCCGTGACCCCCCAGGTGCCCTGCGGGCCCATGACC
TACAAGGCCGCGCTGGACCTGAGCCACTTCCTGAAGGAGAAGGGCGGCCTGGCTAGTACCA
ACGGCAGCATCACCGTGGCCGCCACCGCCCCCACCCTGACCCCCACCGTGAACGCCACCCC
 20 CAGCGCCGCGCTAGTGCCATCTTCCAGAGCAGCATGACCAAGATCCTGGAGCCCTTCCGGA
AGCAGAACCCCGACATCGTGATCTACCAGTACATGGACGACCTGTACGCTAGCTGA (SEQ ID
 NO. 75)

The mature H chain sequence for C1011 heavy chain is shown below. Joining sequences AS are bold and HIV peptides are underlined. A flexible linker joining sequence is italicized.

25 QVQLRQSGPELVKPGASVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENF
 KGKATLTADKSSTTAYMQLSSLTSEDSAVYFCATYYNYPFAYWGQGLVTVSAAKTTGPSVFP
 LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL
 GTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMISRTPEVTC
 VVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK
 30 VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
 ENNYKTTTPVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKASQT
PTNTISVTPTNNTPTNNSNPKNPASEKIRLRPGGKKKYKLKHIVASSSVSPTTSVHPTPTSPPTPTK
SSPASNPPIPVGEIYKRWIILGLNKIVRMYSPTSILDASPTSTPADSSTITPTATPTATPTIKGASHTQG
YFPDWQNYTPGPGVRYPLTFGWLYKLASTVTPTATATPSAIVTTITPTATTKPASVGFVTPQVPLR
 35 PMTYKAAVDLSHFLKEKGGLASTNGSITVAATAPTVTPTVNATPSAAASAIFQSSMTKILEPFRKQN
PDIVIYQYMDDLYAS (SEQ ID NO. 76)

Figure 8 shows the binding of recombinant anti-Langerin antibodies fused to antigens retain their ability to bind to beads decorated with human and non-human primate (NHP) Langerin ectodomain proteins. Lumindex beads of different colors were covalently linked to cellulose binding protein fused to dockerin.

40 The beads were then mixed with either human Langerin ectodomain fused to cohesin, or with NHP (Rhesus macaque) Langerin ectodomain fused to cohesin. The beads were washed and mixed, then incubated with serial dilutions of various pure recombinant anti-Langerin 2G3 or 15B10 mouse V region-human IgG4 chimeric antibodies or the same antibodies with C-terminal fusions to human prostate specific antigen (PSA), or control pure recombinant anti-CD40 12E12 mouse V region-human IgG4

45 chimeric antibody. After washing, the beads were incubated with an anti-human Fc-PE reagent, washed again, and then read on a BioPlex instrument to detect fluorescence bound to the different colored beads (expressed as % MFI relative to the maximal signal seen on each bead type).

Figure 9 shows the ability of recombinant anti-Langerin 15B10 antibody fused to Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain to evoke potent antigen-specific antibody production in NHP. NHP were injected intramuscularly (im) with 10E6 pr8 Flu virus and subcutaneously (sc) HIV gag p24 protein (First boost); ~2 months later the NHP were again injected with HIV gag p24 protein (Second boost); about 6 weeks and 4 months later, the NHP were injected intradermal (id) with 100 µg anti-Langerin 15B10 HA1-1 fusion protein with poly IC as adjuvant, or with anti-DCIR HA1-1 fusion protein with poly IC, or with a standard dose of commercial Vaccigrip Flu vaccine and 10E6 pr8 Flu virus. At the indicated dates, serum samples were taken and pooled (4 NHP per group) and serial dilutions were tested for HA1-1 specific IgG antibodies by a baed-based assay. The data shows that the anti-Langerin-HA1-1 vaccine raises potent high titer anti-HA1-1 antibody responses in NHP – the titers observed were 1-2 logs higher than observed with the Vaccigrip control group.

These data show that both anti-Langerin 15B10 and 2G3 recombinant antibodies or such antibodies linked to a cancer antigen retain significant binding to NHP Langerin – a very desirable property for commercial development of these antibodies as antigen-targeting vaccines [this enables mechanism-based preclinical testing of safety and efficacy in NHP models].

Figure 10 shows that recombinant fusion proteins of anti-human DC receptors and antigens induce antigen-specific immune responses in NHP: Rhesus macaques (4 animals in each group) immunized i.m. with live influenza virus (A/PR8, H1N1) and HIVgag-derived p24-PLA on day 0. On day 28, animals were boosted with p24-PLA alone. On day 77 and day 119, each group of animals was immunized as described in Figure 18 (below). Anti-Langerin-HA1 response in Rhesus macaque - IFN-γ response measured by ELISPOT after ex vivo stimulation with HA peptides. Red arrows indicate priming injections with live influenza virus (A/PR8, H1N1). Blue arrows indicate boost injections. Control group (4 animals) were immunized i.m. with live influenza virus and commercial flu vaccine, VACCIGRIP, with 100 ug poly I:C per animal. Experimental group (4 animals) were boosted i.d. with anti-DCIR-HA1 (100 µg/animals) with 100 µg of poly I:C per animal. The data above show that anti-Langerin-HA1 elicited potent HA1-specific T cells responses as measured by IFNγ ELISPOT.

Figure 11 shows that the Anti-Langerin G3 antibody specifically stains NHP Langerhans cells. Rhesus macaque skin sections were prepared and stained with anti-Langerin 2G3 and then Texas Red-labeled goat ant-mouse reagent. Cell nuclei were stained with DAPI [blue]. This shows specific staining of NHP LC demonstrating the specific cross-reactivity of this anti-human Langerin antibody with NHP Langerin.

The 15B10.3 hydridoma has been deposited under the Budapest Treaty with the U.S. American Type Culture Collection and received Deposit No. PTA-9852; and the 2G3.6 hybridoma received Deposit No. PTA-9853.

Figure 12 shows the antibody titers for anti-HIV-gag antibodies in NHP vaccination with a gag-microparticle, an anti-hlGG4-gag antibody, an anti-DCIR-gag vaccine and an anti-Langerin-gag-p24 vaccine, all with or without poly I:C as an adjuvant. Briefly, non-human primates (NHP) were

immunized and anti-Langerin-gag24 antibody responses were determined. It was found that more potent were possible with the anti-Langerin-gagp24 constructs than with gag p24 on a microcarrier or control antibody-p24. Unlike anti-DCIR targeting, it was found that anti-Langerin-Ag vaccination is relatively independent of poly I:C adjuvant. Each curve is an individual monkey, the assay is serum dilutions tested for antibodies against p24. Cynomolgus macaques were injected i.d. with 250 ug of each antibody-HIV gag p24 vaccine or gag p24 attached to a microcarrier (p24 amount was normalized to correspond to the actual amount of p24 mass injected). The animals were then injected twice more at 6 week intervals. The Figure 12 graph shows represents ELISA assay for antigen-specific anti-gag p24 titers of serum samples taken 2 weeks after the third injection. Figure 12 shows serial dilutions of the sera graphed for each individual monkey [graph lines shown in blue]. A parallel group of monkeys were co-injected with the p24 proteins and poly I:C adjuvant [graph lines shown in red].

Figure 13 – FACS analysis on Langerin clones: 293F cells were transiently transfected with vectors directing the expression of full-length (cell surface) langerin from human, Rhesus macaque, and mouse. Cells were stained with a dilution series of the pure monoclonal antibodies, washed, then counterstained with an anti-mouse IgG-PE conjugate, then washed again. Cells were analyzed by flow cytometry. The data are expressed as % cells giving a positive cell surface staining signal relative to the control untransfected cells.

Figure 14 – ELISA analysis in two formats – direct (antigen bound to plate directly and bound antibody detected with an anti-mouse IgG-HRP conjugate) and capture (antibody bound to plate, capturing a fixed concentration of biotinylated Langerin ectodomain protein, detected with a neutravidin-HRP reagent). ELISA data for human, Rhesus macaque, and mouse Langerin ectodomain proteins are shown.

Table 1. Immunogenicity in cynomolgus macaques of anti-Langerin-Gag and anti-DCIR-Gag fusion protein, for Figure 12.

Group 1 (n=6) 0.25mg anti-Langerin-Gag
 Group 2 (n=6) 0.25mg anti-Langerin-Gag + 0.25mg PolyIC
 Group 3 (n=6) 0.25mg anti-DCIR-Gag
 Group 4 (n=6) 0.25mg anti-DCIR-Gag + 0.25mg PolyIC
 Group 5 (n=3) 0.25mg IgG4-Gag
 Group 6 (n=3) 0.25mg IgG4-Gag + 0.25mg PolyIC
 Group 7 (n=3) 0.0635mg Gag
 Group 8 (n=3) 0.0635mg Gag + 0.25mg PolyIC

	Timepoints(weeks) post priming	Blood			Rectal Wash
		PBMC	Micorarray	Plasma	
	-3	X	X	X	
	-2	X		X	X
	-1	X		X	
Vaccination	0			X	X

	2	X		X	X
Vaccination	6	X		X	X
	8	X	X	X	X
	10			X	X
Vaccination	12			X	X
	13		X	X	X
	14		X	X	X
	15	X		X	X
	16		X	X	X
	18	X		X	X
	22	X	X	X	X

mAnti-Langerin 91E7K light chain sequence

ATGGATTTTCAGATGCAGATTATCAGCTTGCTGCTAATCAGTGTCACAGTCATAGTGTCTAA
TGGAGAAATTGTGCTCACCCAGTCTCCAACCACCATGGCTGCATCTCCCGGGGAGAAGATCA
5 CTATCACCTGCAGTGCCAGCTCAAGTATAAGTTCCCATTACTTACATTGGTATCAGCAGAAG
CCAGGATTCTCCCCTAAACTCTTGATTTATAGGACATCCAATCTGGCTTCTGGAGTCCCAGCT
CGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCTCACAATTGACACCATGGAGGCTGA
AGATGTTGCCACTTACTACTGCCAGCAGGGTAGTAGTATAACCATTACGTTTCGGCTCGGGGA
CAAAGTTGGAAATAAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCCAGT
10 GAGCAGTTAACATCTGGAGGTGCCTCAGTCGTGTGCTTCTTGAACAACCTTCTACCCCAAAGA
CATCAATGTCAAGTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGTTGG
ACTGATCAGGACAGCAAAGACAGCACCTACAGCATGAGCAGCACCTCACGTTGACCAAGG
ACGAGTATGAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTCACC
CATCGTCAAGAGCTTCAACAGGAATGAGTGTTAG (SEQ ID NO.: 51)

15 mAnti-Langerin 91E7K light chain sequence

EIVLTQSPTTMAASPGEKITITCSASSSISSHYLHWYQQKPGFSPKLLIYRTSNLASGVPARFSGSG
SGTSYSLTIDTMEAEDVATYYCQQGSSIPFTFGSGTKLEIKRADAAPTVSIFPPSSEQLTSGGASVV
CFLNMFYPKDINVKWKIDGSRQNGVLNSWTDQDSKDYSTYSMSSTLTTLTKDEYERHNSYTCEAT
HKTSTSPIVKSFNRENC (SEQ ID NO.: 52)

20 mAnti-Langerin 91E7H [mouse IgG2a] heavy chain

ATGAGATCACTGTTCTCTTTACAGTTACTGAGCACACAGGACCTCGCCATGGGATGGAGCTG
TATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACTCTCAGGTCCAACCTGCAGCAGC
CTGGGGCTGAACTTGTGAAGCCTGGGGCTTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTAC
ACCTTCACCAGTTACTGGATGCAGTGGGTAAAGCAGAGGCCTGGACAGGGCCTTGAGTGGA
25 TCGGAGAGATTGATCCTTCTGATAGCTATACTAACTACAATCAAAGGTTCAAGGGCAAGGCC
ACATTGACTGTGGACACATCCTCCAGCACAGCCTACATACAGCTCAGCAGCCTGACGTCTGA
GGACTCTGCGGTCTGTTTCTGTGCAAGACGCTACTATGGTAACTACGATGGGTTTGCTTACT

GGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACAGCCCCATCGGTCTATCCA
 CTGGCCCCTGTGTGTGGAGGTACAACCTGGCTCCTCGGTGACTCTAGGATGCCTGGTCAAGGG
 TTATTTCCCTGAGCCAGTGACCTTGACCTGGAACCTCTGGATCCCTGTCCAGTGGTGTGCACA
 CCTTCCCAGCTCTCCTGCAGTCTGGCCTCTACACCCTCAGCAGCTCAGTGACTGTAACCTCGA
 5 ACACCTGGCCCAGCCAGACCATCACCTGCAATGTGGCCCACCCGGCAAGCAGCACCAAAGT
 GGACAAGAAAATTGAGCCCAGAGTGCCCATAACACAGAACCCCTGTCCTCCACTCAAAGAG
 TGTCCCCCATGCGCAGCTCCAGACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAAG
 ATCAAGGATGTACTCATGATCTCCCCGAGCCCCATGGTCCACATGTGTGGTGGTGGATGTGAG
 CGAGGATGACCCAGACGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTACACACAGCT
 10 CAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTGCCCTCCCCA
 TCCAGCACCAAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAACAGAGCCCT
 CCCATCCCCCATCGAGAAAACCATCTCAAAACCCAGAGGGCCAGTAAGAGCTCCACAGGTA
 TATGTCTTGCCTCCACCAGCAGAAGAGATGACTAAGAAAGAGTTCAGTCTGACCTGCATGAT
 CACAGGCTTCTTACCTGCCGAAATTGCTGTGGACTGGACCAGCAATGGGCGTACAGAGCAA
 15 AACTACAAGAACACCGCAACAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAGCT
 CAGAGTACAAAAGAGCACTTGGGAAAGAGGAAGTCTTTTCGCCTGCTCAGTGGTCCACGAG
 GGTCTGCACAATCACCTTACGACTAAGACCATCTCCCGGTCTCTGGGTAAAG**GCTAGCTGA**
 [GCTAGC in bold is for the in-frame fusion of antigens at the H-chain C-terminus] (SEQ ID NO.: 53)

mAnti-Langerin 91E7H [mouse IgG2a] Mature H heavy chain sequence

20 QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLEWIGEIDPSDSYTNYNQ
 RFKGKATLTVDTSSSTAYIQLSSLTSEDSAVCFRCARRYYGNYDGFAYWGQGLVTVSAAKTTAP
 SVYPLAPVCGGTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPALLQSGLYTLSSSVTVT
 SNTWPSQTITCNVAHPASSTKVDKKIEPRVPITQNPCPPLKECPPCAAPDLLGGPSVFIFPPKIKDV
 LMISPSPMVTCVVVDVSEDDPDVQISWVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDW
 25 MSGKEFKCKVNNRALPSPIEKTISKPRGPRAPQVYVLPPPAAEEMTKKEFSLTCMITGFLPAEIAV
 DWTSNGRTEQNYKNTATVLDSGYSYFMYSKLRVQKSTWERGSLFACSVVHEGLHNHLTTKTIS
 RSLGKAS (SEQ ID NO.: 54)

mAnti-Langerin 37C1K light chain

ATGAGGGCCCCTGCTCAGTTTTTTGGGATCTTGTTGCTCTGGTTTCCAGGTATCAGATGTGAC
 30 ATCAAGATGACCCAGTCTCCATCCTCCATGTATGCATCGCTGGGAGAGAGAGTCACTATTAC
 TTGCAAGGCGAGTCAGGACATTAAAAGCTATTTAACTTGGTACCAGCAGAAACCATGGAAA
 TCTCCTAAGACCCTGATCAATTATGCAACAAGCTTGGCAGATGGGGTCCCATCAAGATTCAG
 TGGCAGTGGATCTGGACAAGATTATTCTCTAACCATCAGCAGCCTGGAGTCTGACGATACAG
 CAACTTATTACTGTCTACAGCATGGTCAGAGTCCGTTACGTTTCGGAGGGGGGACCAGGCTG
 35 GAGATAAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCCAGTGAGCAGTT
 AACATCTGGAGGTGCCTCGGTCTGTGCTTCTTGAACAACCTTCTACCCCAAAGACATCAATG
 TCAAGTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGTTGGACTGATCA

GGACAGCAAAGACAGCACCTACAGCATGAGCAGCACCTCACGTTGACCAAGGACGAGTAT
GAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTCACCCATCGTCA
AGAGCTTCAACAGGAATGAGTGTTAG (SEQ ID NO.: 55)

mAnti-Langerin 37C1K light chain

5 DIKMTQSPSSMYASLGERVTITCKASQDIKSYLTWYQQKPWKSPKTLINYATSLADGVPSRFSGS
GSGQDYSLTISSLESDDTATYYCLQHGGQSPFTFGGGTRLEIKRADAAPTVSIFPPSSEQLTSGGASV
VCFLNNFYPKDINVKWKIDGSRQNGVLNSWTDQDSKDYSTYSMSSTLTTLTKDEYERHNSYTCE
ATHKTSTSPIVKSFNRNEC (SEQ ID NO.: 56)

mAnti-Langerin 37C1H [mouse IgG2a] heavy chain

10 ATGAGATCACTGTTCTCTTTACAGTTACTGAGCACACAGGACCTCGCCATGGGATGGAGCTG
TATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACTCTCAGGTCCAACTGCAGCAGC
CTGGGGCTGAGCTTGTGAAGCCTGGGGCTTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTAC
ACCTTCACCAGTTACTGGATGCAGTGGGTAAAGCAGAGGCCTGGACAGGGCCTTGAGTGGA
CCGGAGAGATTGATCCTTCTGATAGCTATACTAACTACAATCAAAGGTTCAAGGGCAAGGC
15 CACATTGACTGTGGACACATCCTCCAGCACAGCCTACACACAGCTCAGCAGCCTGACGTCTG
AGGACTCTGCGGTCCATTTCTGTGCAAGACGCTACTATGGTAACTACGATGGGTTTGCTTAC
TGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACAACAGCCCCATCGGTCTATCC
ACTGGCCCCTGTGTGTGGAGGTACAACCTGGCTCCTCGGTGACTCTAGGATGCCTGGTCAAGG
GTTATTTCCCTGAGCCAGTGACCTTGACCTGGAACCTCTGGATCCCTGTCCAGTGGTGTGCAC
20 ACCTTCCCAGCTCTCCTGCAGTCTGGCCTCTACACCCTCAGCAGCTCAGTGACTGTAACCTCG
AACACCTGGCCCAGCCAGACCATCACCTGCAATGTGGCCCACCCGGCAAGCAGCACCAAAG
TGGACAAGAAAATTGAGCCCAGAGTGCCCATACACAGAACCCCTGTCCTCCACTCAAAGA
GTGTCCCCCATGCGCAGCTCCAGACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAA
GGTCAAGGATGTACTCATGATCTCCCTGAGCCCCATGGTCACATGTGTGGTGGTGGATGTGA
25 GCGAGGATGACCCAGACGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTACACACAGC
TCAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTGCCCTCCCC
ATCCAGCACCAAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAACAGAGCCC
TCCCATCCCCCATCGAGAAAACCATCTCAAAACCCAGAGGGCCAGTAAGAGCTCCACAGGT
ATATGTCTTGCCTCCACCAGCAGAAGAGATGACTAAGAAAGAGTTCAGTCTGACCTGCATG
30 ATCACAGGCTTCTTACCTGCCGAAATTGCTGTGGACTGGACCAGCAATGGGCGTACAGAGC
AAAACCTACAAGAACACCGCAACAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAG
CTCAGAGTACAAAAGAGCACTTGGGAAAGAGGAAGTCTTTTCGCCTGCTCAGTGGTCCACG
AGGGTCTGCACAATCACCTTACGACTAAGACCATCTCCCGGTCTCTGGGTAAAGCTAGCTG
A (SEQ ID NO.: 57)

35 mAnti-Langerin 37C1H [mouse IgG2a] heavy chain

QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLEWTGEIDPSDSYTNYNQ
RFK GKATLTVDTSSTAYTQLSSLTSEDSAVHFCARRYYGNYDGFAYWGQGTLLTVSAAKTTA
PSVYPLAPVCGGTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPALLQSGLYTLSSSVTV
TSNTWPSQTITCNVAHPASSTKVDKKIEPRVPITQNPCPPLKECPPCAAPDLLGGPSVFIFPPKVKD
5 VLMISLSPMVTCTVVVDVSEDDPDVQISWVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQD
WMSGKEFKCKVNNRALPSPIEKTISKPRGPVRAPQVYVLPPPAAEMTKKEFSLTCLMITGFLPAEIA
VDWTSNGRTEQNYKNTATVLDSGYSYFMYSKLRVQKSTWERSLFACSVVHEGLHNHLTTKTI
SRSLGKAS (SEQ ID NO.: 58)

mAnti-Langerin 4C7K (light chain)

10 ATGGATTTTCAAGTGCAGATTTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGA
GGACAAATTGTTCTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAAGGTCAC
AATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATGCACTGGTACCAGCGGAAGCCAGGA
TCCTCCCCCAAACCCTGGATTTATGCCACATCCAACCTGGCTTCTGGAGTCCCTGCTCGCTTC
AGTGGCAGTGGGTCTGGGACCTCTTATTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATGC
15 TGCCACTTATTACTGCCAGCAGTGGAGTAGTAACCCGCTCACGTTCCGGTGCTGGGACCAAGC
TGGAGCTGAAACGGGCTGATGCTGCACCAACTGTATCCATCTTCCCACCATCCAGTGAGCAG
TTAACATCTGGAGGTGCCTCAGTCGTGTGCTTCTTGAACAACCTTCTACCCCAAAGACATCAA
TGTC AAGTGGAAGATTGATGGCAGTGAACGACAAAATGGCGTCCTGAACAGTTGGACTGAT
CAGGACAGCAAAGACAGCACCTACAGCATGAGCAGCACCCCTCACGTTGACCAAGGACGAGT
20 ATGAACGACATAACAGCTATACCTGTGAGGCCACTCACAAGACATCAACTTCACCCATCGTC
AAGAGCTTCAACAGGAATGAGTGTTAG (SEQ ID NO.: 77)

QIVLSQSPAILSASPGEKVTMTCRASSSVSYMHWYQRKPGSSPKPWIYATSNLASGVPARFSGSG
SGTSYSLTISRVEAEDAATYYCQQWSSNPLTFGAGTKLELKRADAAPTVSIFPPSSEQLTSGGASV
VCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTTLTKDEYERHNSYTCE

25 ATHKTSTSPIVKSFNRNEC (SEQ ID NO.: 78)

mAnti-Langerin 4C7H [mouse IgG2a] Heavy Chain

ATGGAATGGAGCTGGGTCTTTCTCTTCCTCCTGTCAGTAATTGCAGGTGTCCAATCCCAGGTT
CAGCTGCAGCAGTCTGGGGCTGAGCTGGTGAGGCCTGGGGCTTCAGTGACGCTGTCCTGCA
AGGCTTCGGGCTACACATTTATTGACCATGATATGCACTGGGTGCAGCAGACACCTGTGTAT
30 GGCCTGGAATGGATCGGAGCTATTGATCCTGAAACTGGTGATACTGGCTACAATCAGAAGTT
CAAGGGCAAGGCCATACTGACTGCAGACAAATCCTCCAGGACAGCCTACATGGAACCTCCGC
AGCCTGACATCTGAGGACTCTGCCGTCTATTACTGTACAATCCCCTTCTACTATAGTAACTAC
AGCCCGTTTGCTTACTGGGGCCAAGGGGCTCTGGTCACTGTCTCTGCAGCCAAAACAACAGC
CCCATCGGTCTATCCACTGGCCCCTGTGTGTGGAGGTACAACCTGGCTCCTCGGTGACTCTAG
35 GATGCCTGGTCAAGGGTTATTTCCCTGAGCCAGTGACCTTGACCTGGAACCTCTGGATCCCTG
TCCAGTGGTGTGCACACCTTCCCAGCTCTCCTGCAGTCTGGCCTCTACACCCTCAGCAGCTCA

GTGACTGTAACTCGAACACCTGGCCCAGCCAGACCATCACCTGCAATGTGGCCCACCCGGC
 AAGCAGCACCAAAGTGGACAAGAAAATTGAGCCCAGAGTGCCCATAACACAGAACCCCTGT
 CCTCCACTCAAAGAGTGTCCCCCATGCGCAGACCTCTTGGGTGGACCATCCGTCTTCATCTTC
 CCTCCAAAGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATGGTCACATGTGTGGTGGT
 5 GGATGTGAGCGAGGATGACCCAGACGCCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTA
 CACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTG
 CCCTCCCCATCCAGCACCAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAA
 CAGAGCCCTCCCATCCCCCATCGAGAAAACCATCTCAAAACCCAGAGGGCCAGTAAGAGCT
 CCACAGGTATATGTCTTGCCTCCACCAGCAGAAGAGATGACTAAGAAAGAGTTCAGTCTGA
 10 CCTGCATGATCACAGGCTTCTTACCTGCCGAAATTGCTGTGGACTGGACCAGCAATGGGCGT
 ACAGAGCAAAACTACAAGAACACCGCAACAGTCCTGGACTCTGATGGTTCTTACTTCATGTA
 CAGCAAGCTCAGAGTACAAAAGAGCACTTGGGAAAGAGGAAGTCTTTTCGCCTGCTCAGTG
 GTCCACGAGGGTCTGCACAATCACCTTACGACTAAGACCATCTCCCGGTCTCTGGGTAAAGC
 TAGCTGA (SEQ ID NO.: 79)

15 mAnti-Langerin 4C7H [mouse IgG2a] Heavy Chain

QVQLQQSGAELVRPGASVTLCKASGYTFIDHDMHWVQQTPVYGLEWIGAIDPETGDTGYNQK
 FKGKAILTADKSSRTAYMELRSLTSEDSAVYYCTIPFYYSNYSPPFAYWGQALVTVSAAKTAP
 SVYPLAPVCGGTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPALLQSGLYTLSSSVTVT
 SNTWPSQTITCNVAHPASSTKVDKKIEPRVPITQNPCPPLKECPPCADLLGGPSVFIFPPKIKDVLM
 20 ISLSPMVTCTVVVDVSEDDPDAQISWFVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDWMS
 GKEFKCKVNNRALPSPIEKTISKPRGPRAPQVYVLPPPAEEMTKKEFSLTCMITGFLPAEIAVDW
 TSNGRTEQNYKNTATVLDSDGSYFMYSKLRVQKSTWERSLFACSVVHEGLHNHLTTKTISRSL
 GKAS (SEQ ID NO.: 80)

It is contemplated that any embodiment discussed in this specification can be implemented with respect
 25 to any method, kit, reagent, or composition of the invention, and vice versa. Furthermore, compositions
 of the invention can be used to achieve methods of the invention.

It will be understood that particular embodiments described herein are shown by way of illustration and
 not as limitations of the invention. The principal features of this invention can be employed in various
 embodiments without departing from the scope of the invention. Those skilled in the art will recognize,
 30 or be able to ascertain using no more than routine experimentation, numerous equivalents to the specific
 procedures described herein. Such equivalents are considered to be within the scope of this invention and
 are covered by the claims.

All publications and patent applications mentioned in the specification are indicative of the level of skill
 of those skilled in the art to which this invention pertains. All publications and patent applications are
 35 herein incorporated by reference to the same extent as if each individual publication or patent application
 was specifically and individually indicated to be incorporated by reference.

The use of the word “a” or “an” when used in conjunction with the term “comprising” in the claims and/or the specification may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.” The use of the term “or” in the claims is used to mean “and/or” unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although
5 the disclosure supports a definition that refers to only alternatives and “and/or.” Throughout this application, the term “about” is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

As used in this specification and claim(s), the words “comprising” (and any form of comprising, such as
10 “comprise” and “comprises”), “having” (and any form of having, such as “have” and “has”), “including” (and any form of including, such as “includes” and “include”) or “containing” (and any form of containing, such as “contains” and “contain”) are inclusive or open-ended and do not exclude additional, unrecited elements or method steps. As used herein, the phrase “consisting essentially of” limits the scope of a claim to the specified materials or steps and those that do not materially affect the basic and
15 novel characteristic(s) of the claimed invention. As used herein, the phrase “consisting of” excludes any element, step, or ingredient not specified in the claim except for, e.g., impurities ordinarily associated with the element or limitation.

The term “or combinations thereof” as used herein refers to all permutations and combinations of the listed items preceding the term. For example, “A, B, C, or combinations thereof” is intended to include at
20 least one of: A, B, C, AB, AC, BC, or ABC, and if order is important in a particular context, also BA, CA, CB, CBA, BCA, ACB, BAC, or CAB. Continuing with this example, expressly included are combinations that contain repeats of one or more item or term, such as BB, AAA, MB, BBC, AAABCCCC, CBBAAA, CABABB, and so forth. The skilled artisan will understand that typically there is no limit on the number of items or terms in any combination, unless otherwise apparent from the
25 context.

As used herein, words of approximation such as, without limitation, “about”, “substantial” or “substantially” refers to a condition that when so modified is understood to not necessarily be absolute or perfect but would be considered close enough to those of ordinary skill in the art to warrant designating the condition as being present. The extent to which the description may vary will depend on how great a
30 change can be instituted and still have one of ordinary skilled in the art recognize the modified feature as still having the required characteristics and capabilities of the unmodified feature. In general, but subject to the preceding discussion, a numerical value herein that is modified by a word of approximation such as “about” may vary from the stated value by at least $\pm 1, 2, 3, 4, 5, 6, 7, 10, 12$ or 15%.

All of the compositions and/or methods disclosed and claimed herein can be made and executed without
35 undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and in the steps or in the

sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

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5 SLE. *Curr Opin Rheumatol*. 2003;in press.
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downregulated by tumor necrosis factor α . *J Exp Med*. 1994;179:1109-1118.
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colony-stimulating factor differentiate peripheral blood monocytes into potent antigen-presenting cells. *J*
Leukoc Biol. 1998;64:358-367.
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30 by physiologic stimuli: prostaglandin E(2) regulates the migratory capacity of specific DC subsets.
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CLAIMS

1. A vaccine comprising an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides at the carboxy-terminus of the anti-Langerin antibody, wherein when two or more antigens are present, they are separated by one or more linker peptides that comprise at least one glycosylation site.
2. The vaccine of claim 1, wherein the antibody binding fragment is selected from an Fv, Fab, Fab', F(ab')₂, Fc, or a ScFv fragment.
3. The vaccine of claim 1, wherein the antibody comprises one or more complementarity determining regions selected from:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTNFTLKISRVE
AEDLGLYFCS (SEQ ID NO.: 45);

SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46);

VTLTCSRSTGAVTTSNYANWVQEKPDHLFTGLIGGTNNRVSGVPARFSGSLIGDKAALTITGAQT
EDEAIYFCA (SEQ ID NO.: 47);

SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYCY (SEQ ID NO.: 48); or a direct equivalent thereof.
4. The vaccine of claim 1, wherein the antigenic peptide is a cancer antigen selected from:

MWVPVVFLTLSVTWIGAAPLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWV
(SEQ ID NO.: 9);

LTAAH CIRNKS VILLGRHSLFHPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHD (SEQ
ID NO.: 10);

LMLRLSEPAELTDAVKVMDLPTQEPALGTTCYASGWGSIEPEEFLTPKKLQCVDLHVIS (SEQ
ID NO.: 11);

NDVCAQVHPQKVTKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERP
(SEQ ID NO.: 12);

SLYTKVVHYRKWIKDTIVANP (SEQ ID NO.: 13);

IMDQVPFSV (SEQ ID NO.: 14);

ITDQVPFSV (SEQ ID NO.: 15);

YLEPGPVTV (SEQ ID NO.: 16);

YLEPGPVTA (SEQ ID NO.: 17);

KTWGQYWQV (SEQ ID NO.: 18);

- APLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWVLTAAH CIRNKS VILLGRHSLF
HPEDTGQVFQVSHSFPHPLYDMSLLKNRFLRPGDDSSHDLMLLRLSEPAELTDAVKVMDLPTQE
PALGTTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKVTKFMLCAGRWTGGKST
CSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKDTIVANP (SEQ ID NO.:
5 19);
- DTTEPATPTTPVTTPTTTTKVPRNQDWLGVSRLRTKAWNRQLYPEWTEAQRLDCWRGGQVSL
KVSNDGPTLIGANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFP
DGGPCPSGSWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLGHTMEVTVYHRRGS
QSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQ (SEQ ID NO.: 20);
- 10 PLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRAXVVTHTYLEPGPVTAQVVLQAAIPLTSC
GSSPVPAS (SEQ ID NO.: 21);
- GTTDGHRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAEST
GMTPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAA (SEQ ID NO.: 22);
- QVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRYGS
15 FSVTLDIVQ (SEQ ID NO.: 23);
- GIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLPSPACQLVLHQI
LKGGSGTYCLNVSLADTNSLAVVSTQLIVPGILLTGQEAGLGQ (SEQ ID NO.: 24);
- MEMKILRALNFGLGRPLPLHFLRRASKIGEVDVEQHTLAKYLMELTMLDY (SEQ ID NO.: 25);
- DWLVQVQMKFRLLQETMYMTVSIIDRFMQNNCVPKK (SEQ ID NO.: 26);
- 20 MEHQLLCCEVETIRRAYPDANLLNDRVLRAMLKAEETCAPSVSYFKCV (SEQ ID NO.: 27);
- QKEVLPSMRKIVATWMLEVCEEQKCEEEVFPLAMNYLDRFLSLEPVKKSRLQLLGATCMFVAS
KMKETIPLTAEKLCIYTDNSIRPEELLQMELL (SEQ ID NO.: 28);
- LVNKLKWNLAAMTPHDFIEHFLSKMPEAEENKQIIRKHAQTFVALCATDVKFISNPPSMV (SEQ
ID NO.: 29); or
- 25 AAGSVVAAVQGLNLRSPNNFLSYRLTRFLSRVIKCDPDCLRACQEIEALLESSLRQAQQNMD
PKAAEEEEEEEEVDLACTPTDVRDVDI (SEQ ID NO.: 30), or binding fragments thereof.
5. The vaccine of claim 1, wherein the antigenic peptide is a viral antigen selected from:
- VGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGL (SEQ ID NO.: 31);
- HTQGYFPDWQNYTPGPGVRYPLTFGWLYKL (SEQ ID NO.: 32);
- 30 EKIRLRPGGKKKYKLKHIV (SEQ ID NO.: 33);
- NPPIPVGEIYKRWIILGLNKIVRMYSPTSILD (SEQ ID NO.: 34);
- AIFQSSMTKILEPFRKQNPDIVIYQYMDDLY (SEQ ID NO.: 35);

DTICIGYHANNSTDTVDTVLEKNVTVTHTSVNLLLED SHNGKLCRLKGIAPLQLGKCNIAGWLLGN
 PECDLLPVRSWSYIVETPNSENGICYPGDFIDYEELREQLSSVSSFERFEIFPKESSWPNHNTNGV
 TAACSHEGKSSFYRNLLWLTEKEGSYPKLKNSYVNKKGKEVLVLWGIHHPNSKEQQONLYQNE
 NAYVSVVTSNYNRRFTPEIAERP KVRDQAGRMNYYWTLLKPGDTIIFEANGNLIAPMYAFALSR
 5 GFGSGIITSNASMHECNTKCQTPLGAINSSLPYQNIHPVTIGECPKYVRS AKLRMV (SEQ ID NO.:
 36);

DQICIGYHANNSTEQVD TIMEKNVTVTHTAQDILEKKHNGKLCDL DGVKPLILRDCSVAGWLLGN
 PMCDEFINVPEWSYIVEKANPVNDLCYPGDFNDYEELKHLLSRINHFEKIQIIPKSSWSSHEASLG
 VSSACPYQGKSSFFRNVVWLIKKNSTYPTIKRSYNNTNQEDLLVLWGIHHPNDAAEQTKLYQNP
 10 TTYISVGTSTLNQRLVPRIATRSKVNGQSGRMEFFWTILKPNDAINFESNGNFI APEYAYKIVKKG
 DSTIMKSELEYGNCNTKCQTPMGAINSSMPFHNIHPLTIGECPKYVKS NRLVLA (SEQ ID NO.:
 37); or

PIVQNIQGQM VHQAI SPRTLNAWVKVVEEKAFSPEVIPMFSAL SEGATPQDLNTMLNTVGGHQA
 AMQMLKETINEEAAEWDRVHPVHAGPIAPGQMREPRGSDIAGTTSTLQE QIGWMTNNPPIPVGE
 15 IYKRWILGLNKIVRMYSPTSILDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQN
 ANPDCKTILKALGPAATLEEMMTACQGVGGPGHKARVL (SEQ ID NO.: 38).

6. The vaccine of claim 1, wherein the one or more peptide linkers are selected from:

SSVSPTTSVHPTPTSVPPTPTKSSP (SEQ ID NO.: 39);

PTSTPADSSTITPTATPTATPTIKG (SEQ ID NO.: 40);

20 TVTPTATATPSAIVTTITPTATTKP (SEQ ID NO.: 41); or

TNGSITVAATAPTPTPTVNATPSAA (SEQ ID NO.: 42).

7. The vaccine of claim 1, wherein the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof.

25 8. The vaccine of claim 1, wherein the anti-Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79.

9. The vaccine of claim 1, wherein the anti-Langerin antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853,
 30 91E7, 37C1, or 4C7 and humanized derivatives thereof.

10. The vaccine of claim 1, wherein the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein.

11. An isolated nucleic acid vector that expresses an anti-Langerin antibody or binding fragment thereof and two or more antigenic peptides at the carboxy-terminus of the light chain, the heavy chain or

both the light and heavy chains of the anti-Langerin antibody, wherein when two or more antigenic peptides are present, the antigenic peptides are separated by the one or more peptide linkers that comprise at least one glycosylation site.

12. The vector of claim 11, wherein the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC (Mucin) (e.g., MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, and Ki-67.

13. The vector of claim 11, wherein the antigenic peptides are cancer peptides are selected from tumor associated antigens comprising antigens from leukemias and lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia.

14. The vector of claim 11, wherein the antigenic peptides are selected from Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain, HLA-A201-FluMP (58-66) peptide (GILGFVFTL) tetramer, Avian Flu (HA5-1), dockerin domain from *C. thermocellum* (doc), HIV gag p24 (gag), or a string of HIV peptides (Lipo5), PSA (KLQCVDLHV)-tetramer, or an HIVgag-derived p24-PLA.

15. The vector of claim 11, wherein the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof.

16. The vector of claim 11, wherein the anti-Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79.

17. The vector of claim 11, wherein the anti-Langerin antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and humanized derivatives thereof.

18. The vector of claim 11, wherein the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein.

19. A method of enhancing T and B cell responses comprising:

immunizing a subject in need of vaccination with an effective amount of a vaccine comprising an isolated fusion protein comprising an anti-Langerin antibody or binding portion thereof and one or more antigenic peptides linked to the carboxy-terminus of the anti-Langerin antibody.

5 20. The method of claim 19, wherein the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC (Mucin) (e.g., MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate
10 serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, and Ki-67.

21. The method of claim 19, wherein the antigenic peptides are cancer peptides selected from tumor
15 associated antigens comprising antigens from leukemias, lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus,
20 rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia.

22. The method of claim 19, wherein the antigenic peptides are selected from Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain, HLA-A201-FluMP (58-66) peptide (GILGFVFTL) tetramer, Avian Flu (HA5-1), Influenza A Hemagglutinin HA-1 from a H1N1 Flu strain (HA1-1),
25 dockerin domain from *C. thermocellum* (doc), HIV gag p24 (gag), or a string of HIV peptides (Hipo5), PSA (KLQCVDLHV)-tetramer, or an HIVgag-derived p24-PLA.

23. A method of making an anti-Langerin-antigen fusion protein comprising:

expressing an isolated fusion protein comprising an anti-Langerin antibody or binding fragment thereof in a host cell, the fusion protein comprising one or more antigenic peptides at the carboxy-terminus of the
30 anti-Langerin antibody or binding fragment thereof, wherein when two or more cancer peptides are present, the cancer peptides are separated by one or more linkers, at least one linker comprising a glycosylation site; and
isolating the fusion protein.

24. The method of claim 23, wherein the fusion protein expressed in the host is further purified.

35 25. The method of claim 23, wherein the host is a eukaryotic cell.

26. The method of claim 23, wherein the antigenic peptides are cancer peptides selected from tumor associated antigens selected from CEA, prostate specific antigen (PSA), HER-2/neu, BAGE, GAGE, MAGE 1-4, 6 and 12, MUC-related protein (Mucin) (MUC-1, MUC-2, etc.), GM2 and GD2 gangliosides, ras, myc, tyrosinase, MART (melanoma antigen), MARCO-MART, cyclin B1, cyclin D, Pmel 17(gp100), GnT-V intron V sequence (N-acetylglucoaminyltransferase V intron V sequence), Prostate Ca psm, prostate serum antigen (PSA), PRAME (melanoma antigen), β -catenin, MUM-1-B (melanoma ubiquitous mutated gene product), GAGE (melanoma antigen) 1, BAGE (melanoma antigen) 2-10, c-ERB2 (Her2/neu), EBNA (Epstein-Barr Virus nuclear antigen) 1-6, gp75, human papilloma virus (HPV) E6 and E7, p53, lung resistance protein (LRP), Bcl-2, and Ki-67.
27. The method of claim 23, wherein the antigenic peptides are cancer peptides selected from tumor associated antigens comprising antigens from leukemias and lymphomas, neurological tumors such as astrocytomas or glioblastomas, melanoma, breast cancer, lung cancer, head and neck cancer, gastrointestinal tumors, gastric cancer, colon cancer, liver cancer, pancreatic cancer, genitourinary tumors such cervix, uterus, ovarian cancer, vaginal cancer, testicular cancer, prostate cancer or penile cancer, bone tumors, vascular tumors, or cancers of the lip, nasopharynx, pharynx and oral cavity, esophagus, rectum, gall bladder, biliary tree, larynx, lung and bronchus, bladder, kidney, brain and other parts of the nervous system, thyroid, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma and leukemia.
28. The method of claim 23, wherein the cancer peptides are selected from at least one of:
- MWVPVVFLTLSVTWIGAAPLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWV
(SEQ ID NO.: 9);
- LTAAH CIRN KSVILLGRHSLFHPEDTGQVFQVSHSFPHPPLYDMSLLKNRFLRPGDDSSHD (SEQ ID NO.: 10);
- LMLLRLSEPAELTDAVKVMDLPTQEPALGTTTCYASGWGSIEPEEFLTPKKLQCVDLHVIS (SEQ ID NO.: 11);
- NDVCAQVHPQKVTKFMLCAGRWTGGKSTCSGDSGGPLVCNGVLQGITSWGSEPCALPERP
(SEQ ID NO.: 12);
- SLYTKVVHYRKWIKDTIVANP (SEQ ID NO.: 13);
- IMDQVPFSV (SEQ ID NO.: 14);
- ITDQVPFSV (SEQ ID NO.: 15);
- YLEPGPVTV (SEQ ID NO.: 16);
- YLEPGPVTA (SEQ ID NO.: 17);
- KTWGQYWQV (SEQ ID NO.: 18);
- APLILSRIVGGWECEKHSQPWQVLVASRGRAVCGGVLVHPQWVLTAAHCIRN KSVILLGRHSLF
HPEDTGQVFQVSHSFPHPPLYDMSLLKNRFLRPGDDSSHD LMLLRLSEPAELTDAVKVMDLPTQE

PALGTTTCYASGWGSIEPEEFLTPKKLQCVDLHVISNDVCAQVHPQKVTKFMLCAGRWTGGKST
CSGDSGGPLVCNGVLQGITSWGSEPCALPERPSLYTKVVHYRKWIKDTIVANP (SEQ ID NO.:
19);

DTTEPATPTTPVTTPTTTTKVPRNQDWLGVSRLRTKAWNRQLYPEWTEAQRDCWRGGQVSL
5 KVSNDGPTLIGANASFSIALNFPQSQKVLPDGGQVIWVNNTIINGSQVWGGQPVPYQETDDACIFP
DGGPCPSGWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMLGHTMEVTVYHRRGS
QSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQ (SEQ ID NO.: 20);

PLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRAXVVTHTYLEPGPVTAQVVLQAAIPLTSC
GSSPVPAS (SEQ ID NO.: 21);

10 GTTDGHRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAEST
GMTPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAA (SEQ ID NO.: 22);

QVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCVLYRYGS
FSVTLDIVQ (SEQ ID NO.: 23);

GIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLPSACQLVLHQI
15 LKGGSGTYCLNVSLADTNSLAVVSTQLIVPGILLTGQEAGLGQ (SEQ ID NO.: 24);

MEMKILRALNFGLGRPLPLHFLRRASKIGEVDVEQHTLAKYLMELTMLDY (SEQ ID NO.: 25);

DWLVQVQMKFRLLQETMYMTVSIIDRFMQNNCVPPK (SEQ ID NO.: 26);

MEHQLLCCEVETIRRAYPDANLLNDRVLRAMLKAEETCAPSVSYFKCV (SEQ ID NO.: 27);

QKEVLPSMRKIVATWMLEVCEEQKCEEEVFPLAMNYLDRFLSLEPVKKSRLQLLGATCMFVAS
20 KMKETIPLTAEKLCIYTDNSIRPEELLQMELL (SEQ ID NO.: 28);

LVNKLKWNLAAMTPHDFIEHFLSKMPEAEENKQIRKHAQTFVALCATDVKFISNPPSMV (SEQ
ID NO.: 29); or

AAGSVVAAVQGLNLRSPNNFLSYRLTRFLSRVIKCDPDCLRACQEIEALLESSLRQAQQNMD
PKAAEEEEEEEEVLDLACTPTDVRDVDI (SEQ ID NO.: 30), or immunogenic fragments thereof.

25 29. A method of expanding antigen-specific T cells or B cells *in vitro* comprising:

isolating peripheral blood mononuclear cells (PBMCs) from a cancer patient;

incubating the isolated PBMCs with an immunogenic amount of an isolated anti-Langerin-(PL-Ag)_x or
anti-Langerin-(Ag-PL)_x vaccine, wherein Ag is a tumor associated antigen and *x* is an integer 1 to 20;

expanding the PBMCs in the presence of an effective amount of IL-2;

30 harvesting the cells; and

assessing the cytokine production by the cells to determine the presence of anti-cancer specific T cells or
B cells.

30. A tumor associated antigen-specific T cell or B cell made by the method comprising:
 isolating peripheral blood mononuclear cells (PBMCs) from a cancer patient;
 incubating the isolated PBMCs with an immunogenic amount of an anti-Langerin-(PL-Ag) x or anti-Langerin-(Ag-PL) x vaccine, wherein Ag is a tumor associated antigen and x is an integer 1 to 20;
 5 expanding the PBMCs in the presence of an effective amount of IL-2;
 harvesting the cells; and
 assessing the cytokine production by the cells to determine the presence of tumor associated antigen-specific T cells or B cells.
31. A therapeutic vaccine comprising an isolated fusion protein comprising the formula: Ab-(PL-Ag) x ; Ab-(Ag-PL) x ; Ab-(PL-Ag-PL) x ; Ab-(Ag-PL-Ag) x ; Ab-(PL-Ag) x -PL; or Ab-(Ag-PL) x -Ag;
 10 wherein Ab is an anti-Langerin monoclonal antibody or binding fragment thereof; PL is at least one peptide linker comprising at least one glycosylation site; Ag is at least one infectious disease antigen; and x is an integer from 1 to 20.
32. A method of expanding antigen-specific T cells or B cells *in vitro* comprising:
 15 isolating peripheral blood mononuclear cells (PBMCs) from a patient suspected of having an infection;
 incubating the isolated PBMCs with an immunogenic amount of an isolated anti-Langerin-(PL-Ag) x or α Langerin-(Ag-PL) x vaccine, wherein Ag is an antigen of the infectious agent and x is an integer 1 to 20;
 expanding the PBMCs in the presence of an effective amount of one or more cytokines;
 harvesting the cells; and
 20 assessing the cytokine production by the cells to determine the presence of anti-infections agent specific T cells or B cells.
33. A viral associated antigen-specific T cell or B cell made by the method comprising:
 isolating peripheral blood mononuclear cells (PBMCs) from a patient suspected of having a viral infection;
 25 incubating the isolated PBMCs with an immunogenic amount of an isolated anti-Langerin-(PL-Ag) x or anti-Langerin-(Ag-PL) x vaccine, wherein Ag is a viral associated antigen and x is an integer 1 to 20;
 expanding the PBMCs in the presence of an effective amount of one or more cytokines;
 harvesting the cells; and
 assessing the cytokine production by the cells to determine the presence of viral associated antigen-specific T cells or B cells.
 30
34. A therapeutic vaccine comprising an isolated fusion protein comprising the formula: Ab-(PL-Ag) x ; Ab-(Ag-PL) x ; Ab-(PL-Ag-PL) x ; Ab-(Ag-PL-Ag) x ; Ab-(PL-Ag) x -PL; or Ab-(Ag-PL) x -Ag;

wherein Ab is an anti-Langerin monoclonal antibody or binding fragment thereof; PL is at least one peptide linker comprising at least one glycosylation site; Ag is at least one viral antigen; and x is an integer from 1 to 20.

35. An isolated antibody comprising one or more of complementarity determining regions selected from:

ASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTNFTLKISRVE
AEDLGLYFCS (SEQ ID NO.: 45);

SVKMSCKASGYTFTDYVISWVKQRTGQGLEWIGDIYPGSGYSFYNNENFKGKATLTADKSSTTAY
MQLSSLTSEDSAVYFCA (SEQ ID NO.: 46);

VTLCRSSTGAVTTSNYANWVQEKPDLFTGLIGGTNNRVSGVPPARFSGSLIGDKAALTITGAQT
EDEAIYFCA (SEQ ID NO.: 47);

SLKLSCAASGLTFNIYAMNWVRQAPGKGLEWVARIRNKSNNYATYYADSVKDRFTISRDDSQS
LLYLQMNNLKTEDTAMYYC (SEQ ID NO.: 48); or a direct equivalent thereof.

36. The antibody of claim 27, wherein the antibody is humanized.

37. The antibody of claim 27, wherein the antibody is 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7, and humanized derivatives thereof.

38. An isolated nucleic acid that encodes a 15B10, 2G3, 91E7, 37C1, or 4C7 antibody, antibody binding fragment or a humanized derivative thereof.

39. The nucleic acid of claim 38, wherein the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80; or binding fragments thereof.

40. The nucleic acid of claim 38, wherein the anti-Langerin antibody is the expression product from the following pairs of nucleic acid sequences SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79; or binding fragments thereof.

41. A pharmaceutical composition comprising an isolated anti-Langerin antibody or binding fragment thereof and one or more antigenic peptides attached to the anti-Langerin antibody, wherein when two or more antigens are present, they are separated by one or more linker peptides that comprise at least one glycosylation site.

42. The composition of claim 41, wherein the antibody binding fragment is selected from an Fv, Fab, Fab', F(ab')₂, Fc, or a ScFv fragment.

43. The composition of claim 41, wherein the anti-Langerin antibody is selected from the following pairs of amino acid sequences SEQ ID NOS.: 2 and 4; 6 and 7; 52 and 54; 56 and 58; and 78 and 80 or binding fragments thereof.

44. The composition of claim 41, wherein the anti-Langerin antibody is the expression product of the following pairs of nucleic acid sequences SEQ ID NOS.: 1 and 3; 5 and 6; 51 and 53; 55 and 57; and 77 and 79.

5 45. The composition of claim 41, wherein the anti-Langerin antibody or binding fragment thereof is at least one of 15B10 having ATCC Accession No. PTA-9852, 2G3 having ATCC Accession No. PTA-9853, 91E7, 37C1, or 4C7 and humanized derivatives thereof.

46. The composition of claim 41, wherein the anti-Langerin antibody or binding fragment thereof and the antigenic peptide are a fusion protein.

47. The composition of claim 41, wherein the composition further comprises an adjuvant.

10 48. The composition of claim 41, wherein the composition further comprises one or more pharmaceutical excipients.

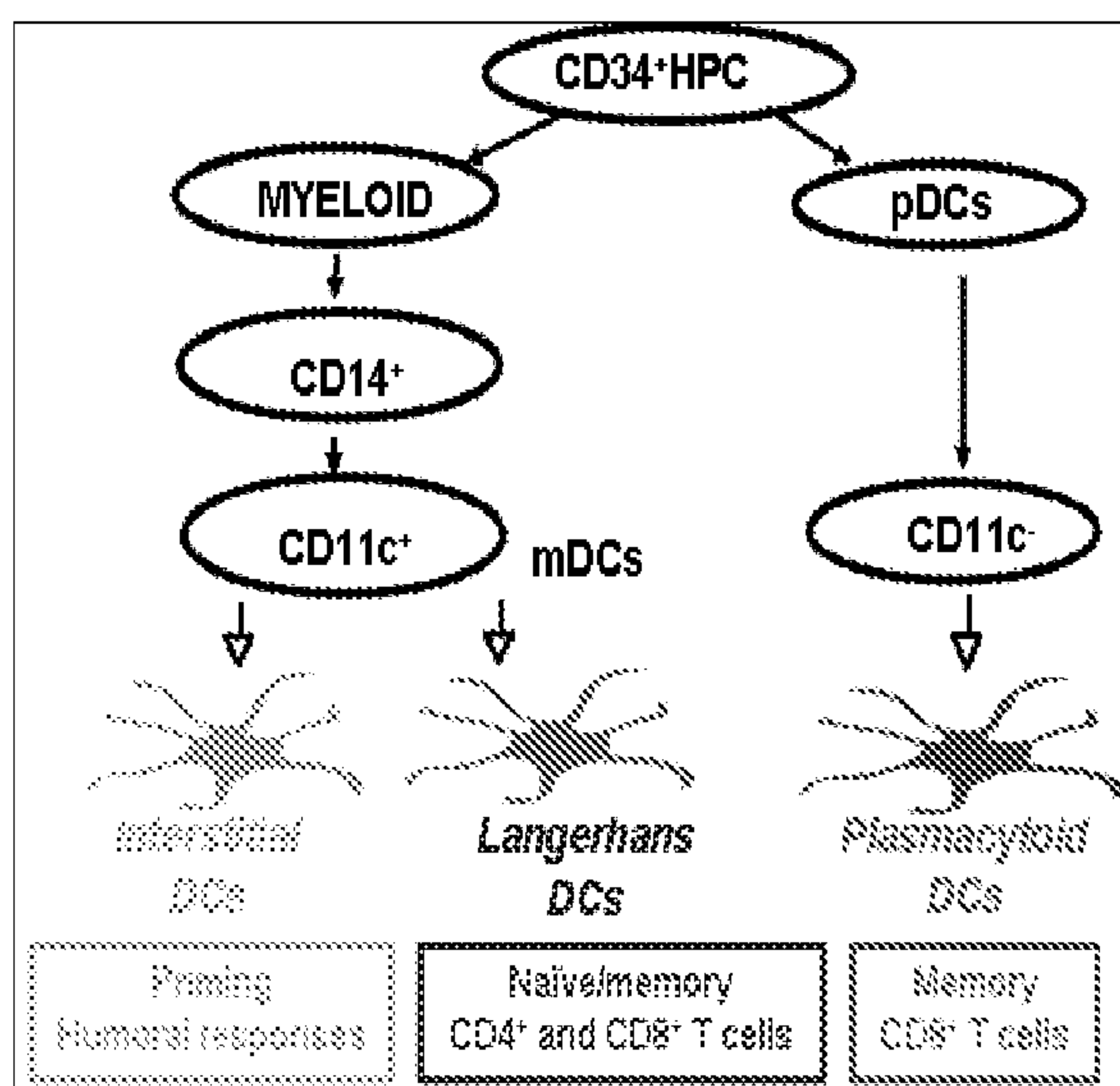
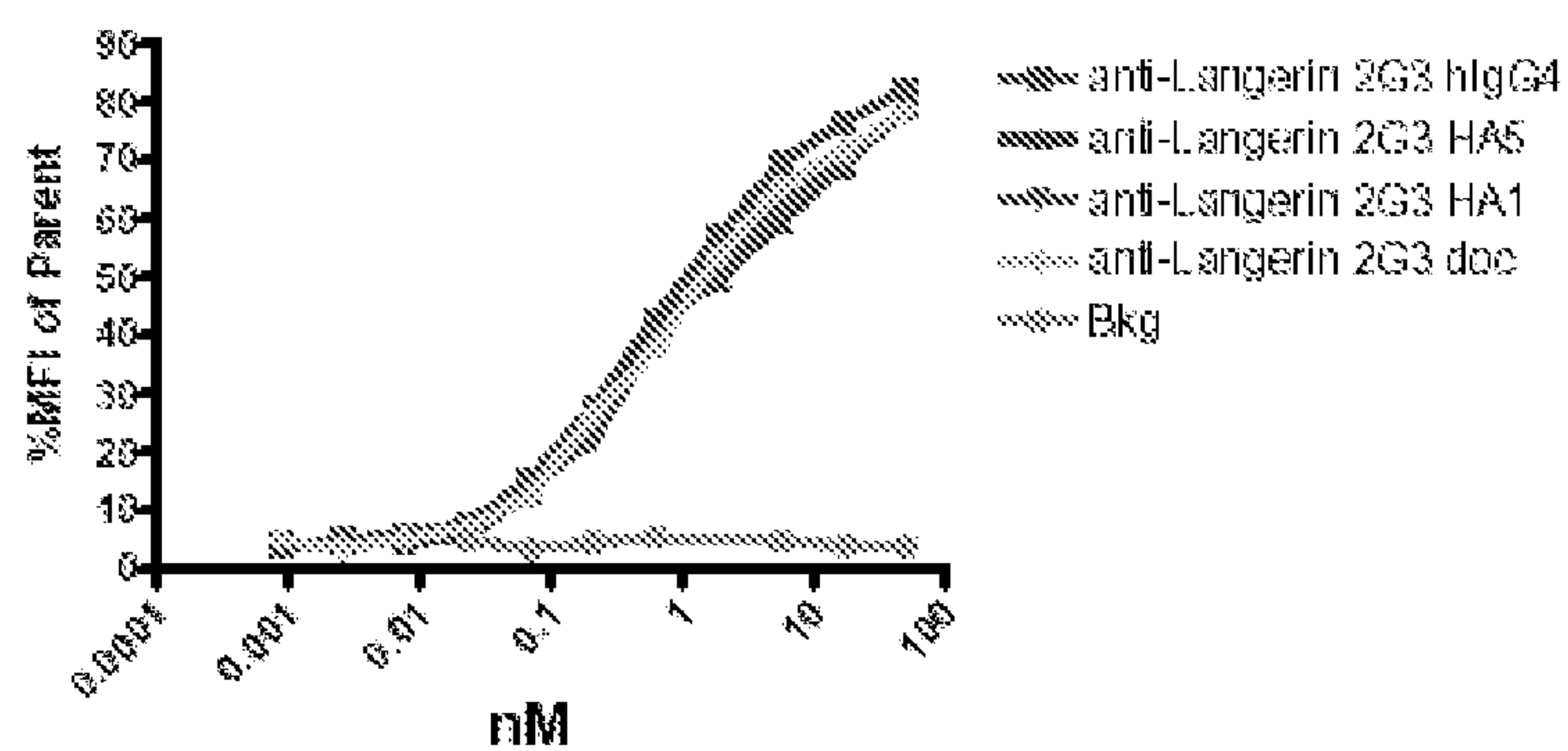


Figure 1

FACS on CHO stable Langerin Transfectants

Langerin 2G3 antibodies



Langerin 15B10 antibodies

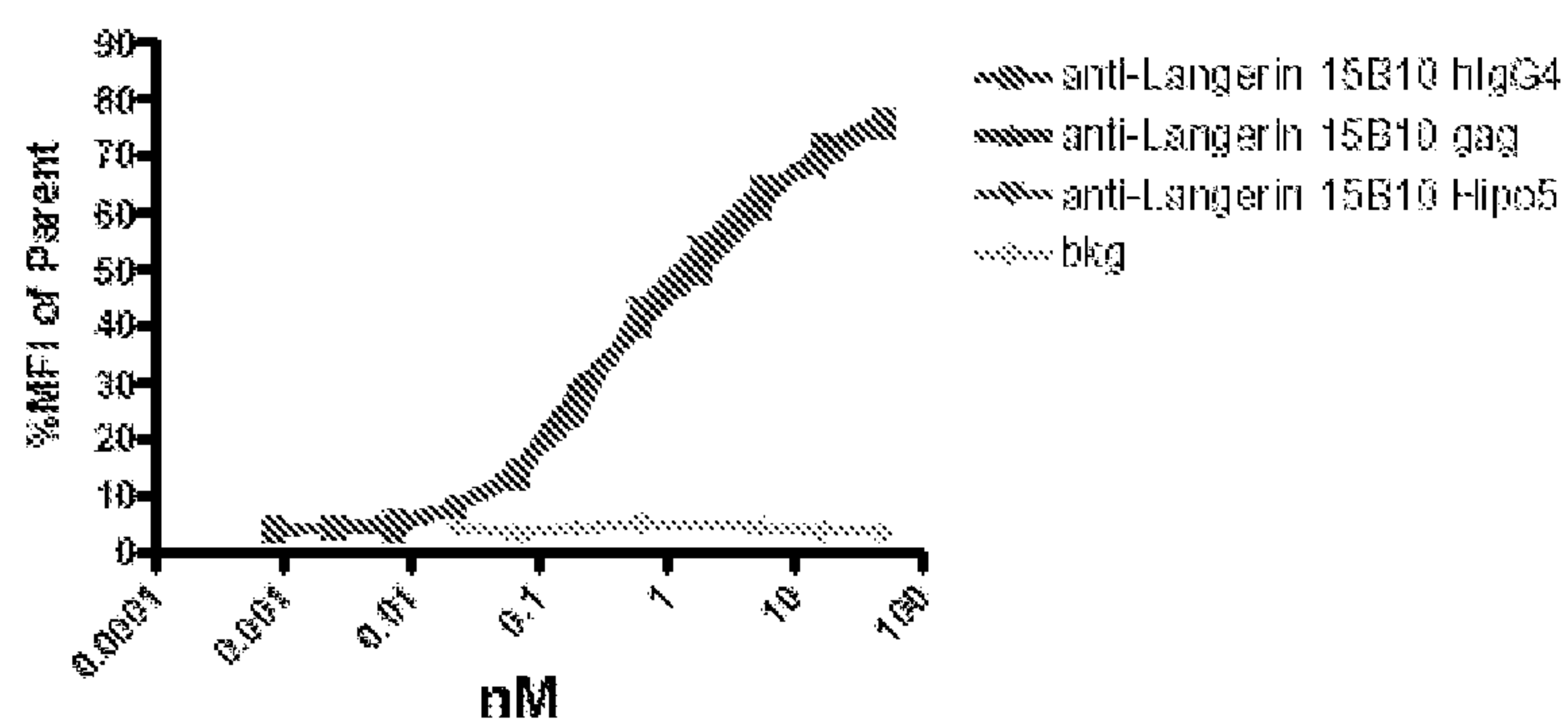


Figure 2

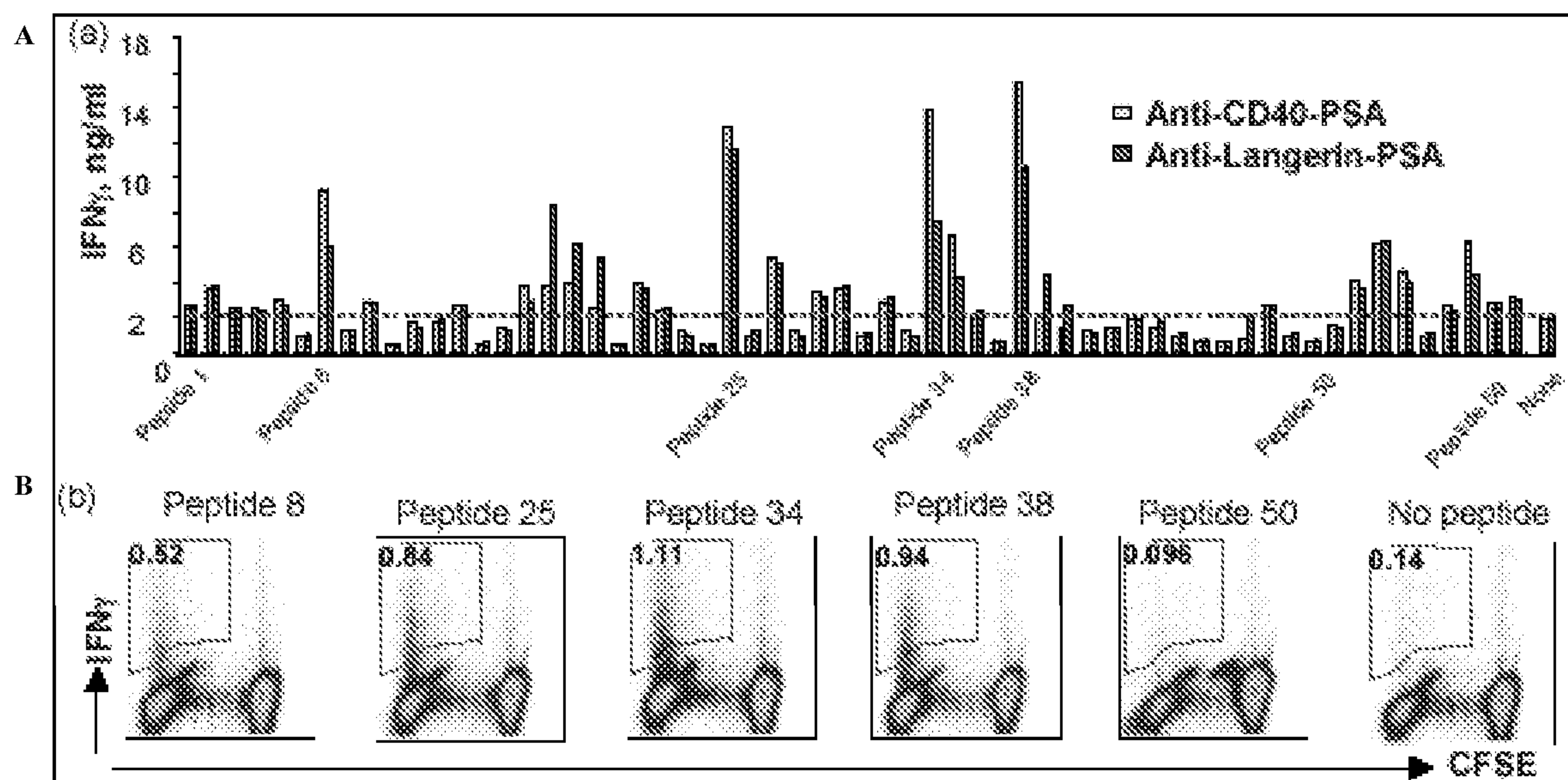


Figure 3

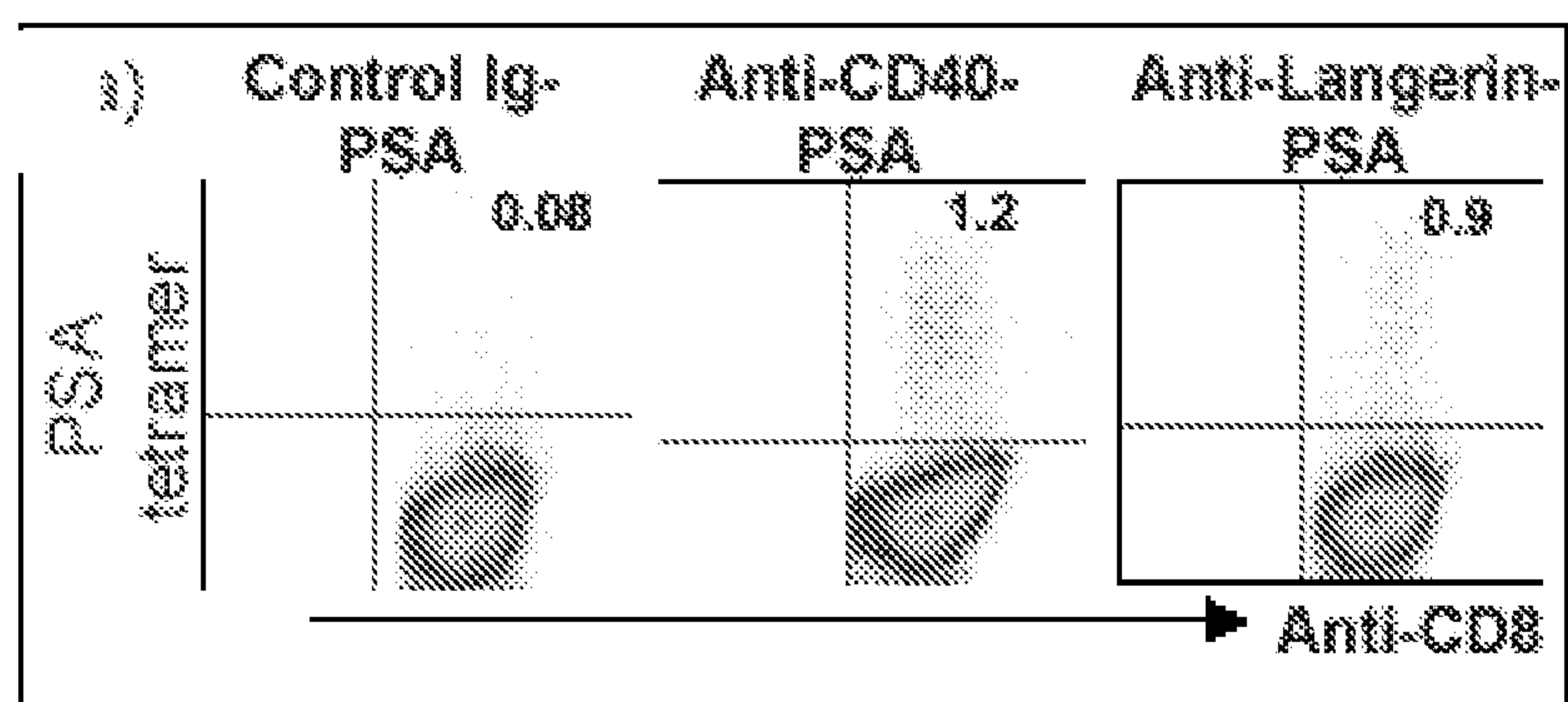


Figure 4

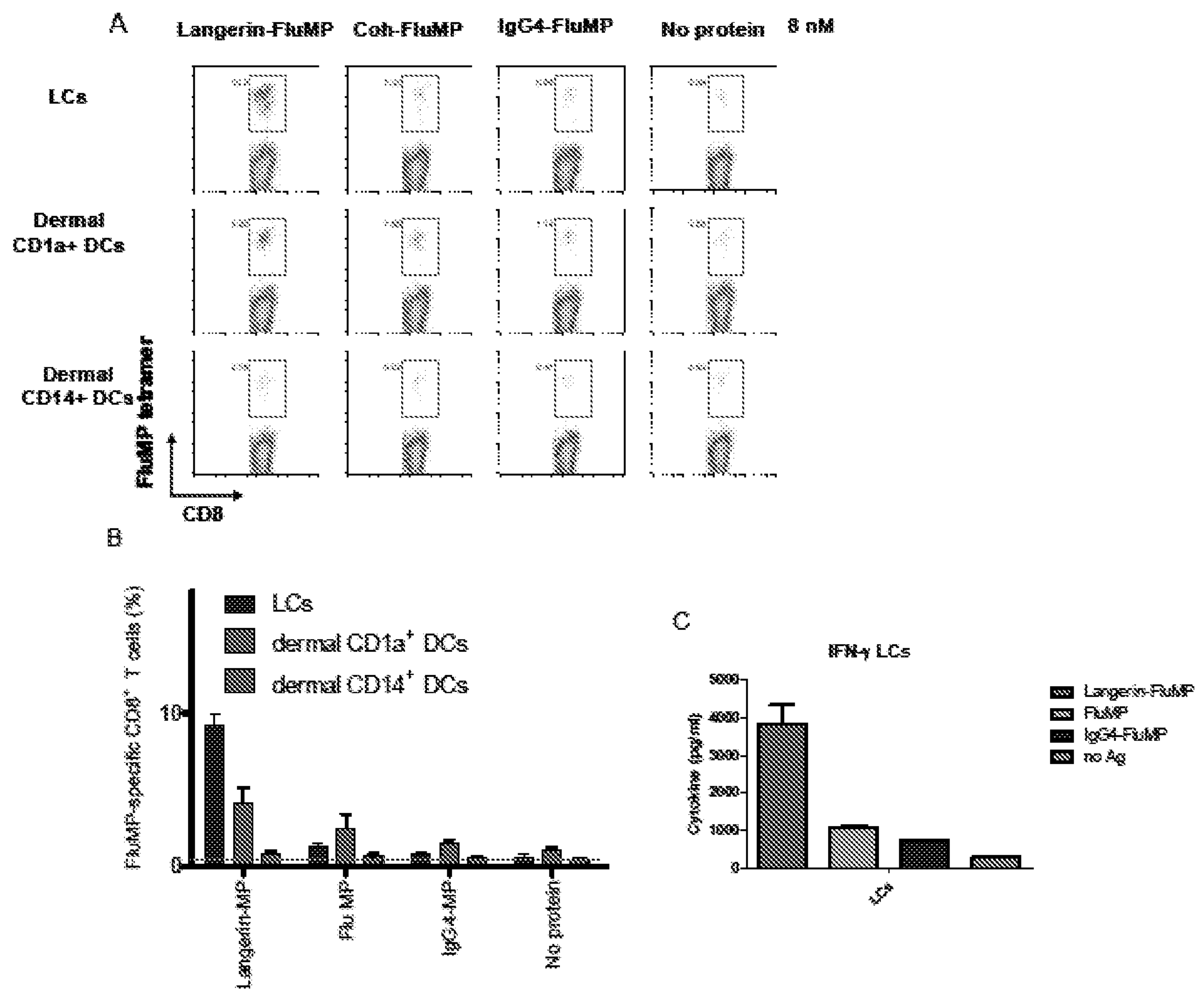


Figure 5

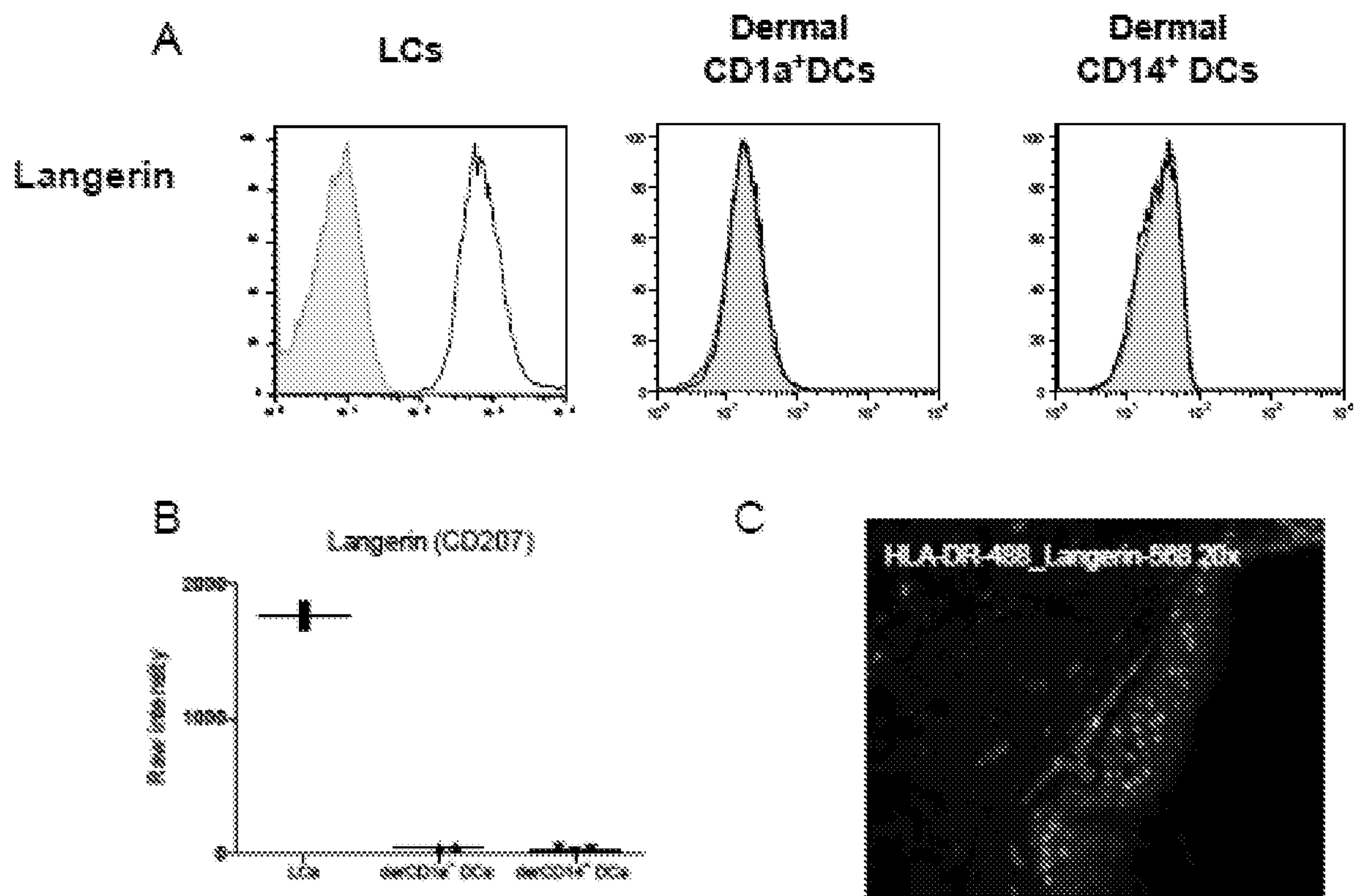


Figure 6

Human Epithelial Sheet

DR-FITC

Anti-Langerin 15b10-Alexa568

Confocal 63x objective

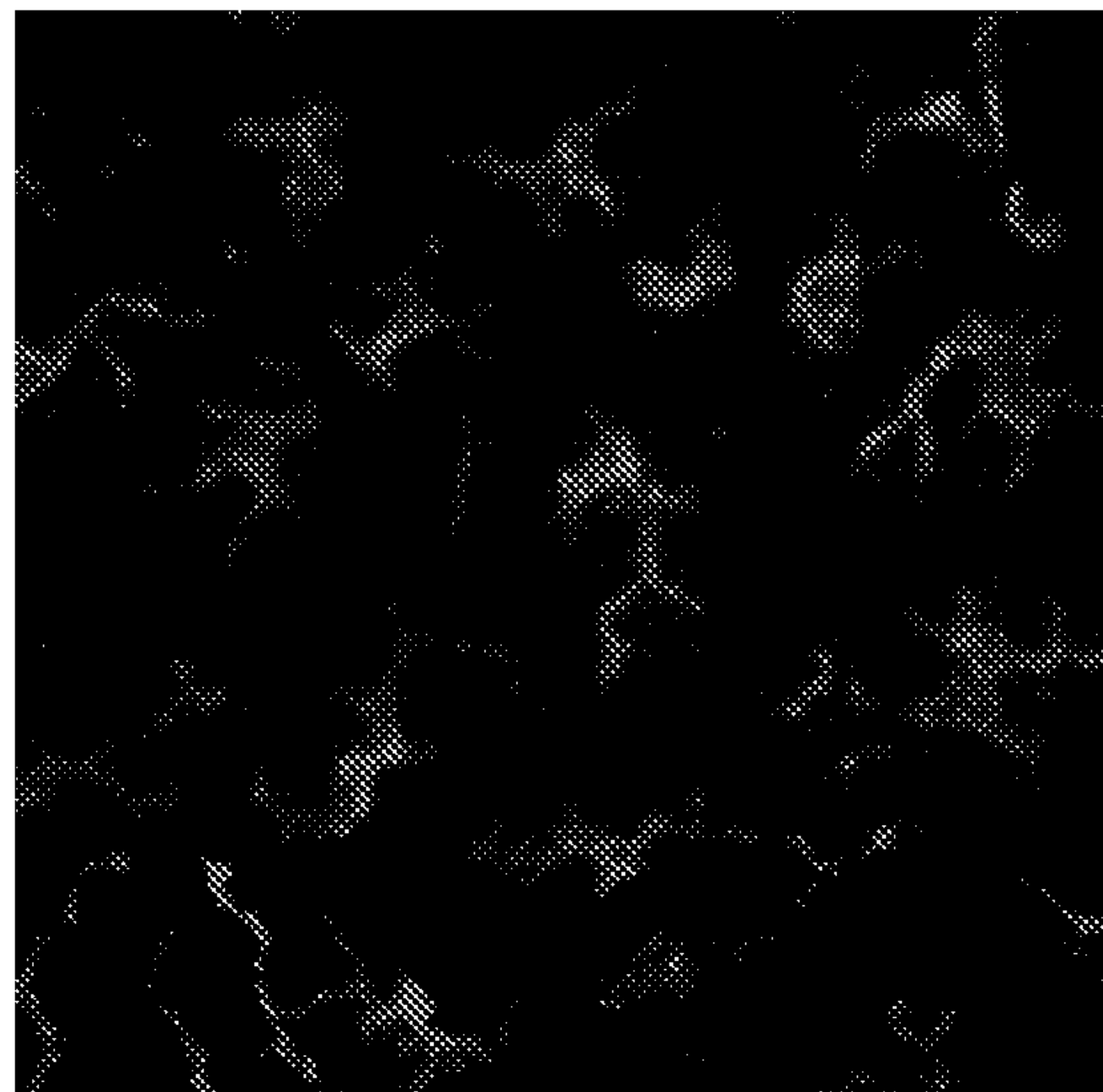
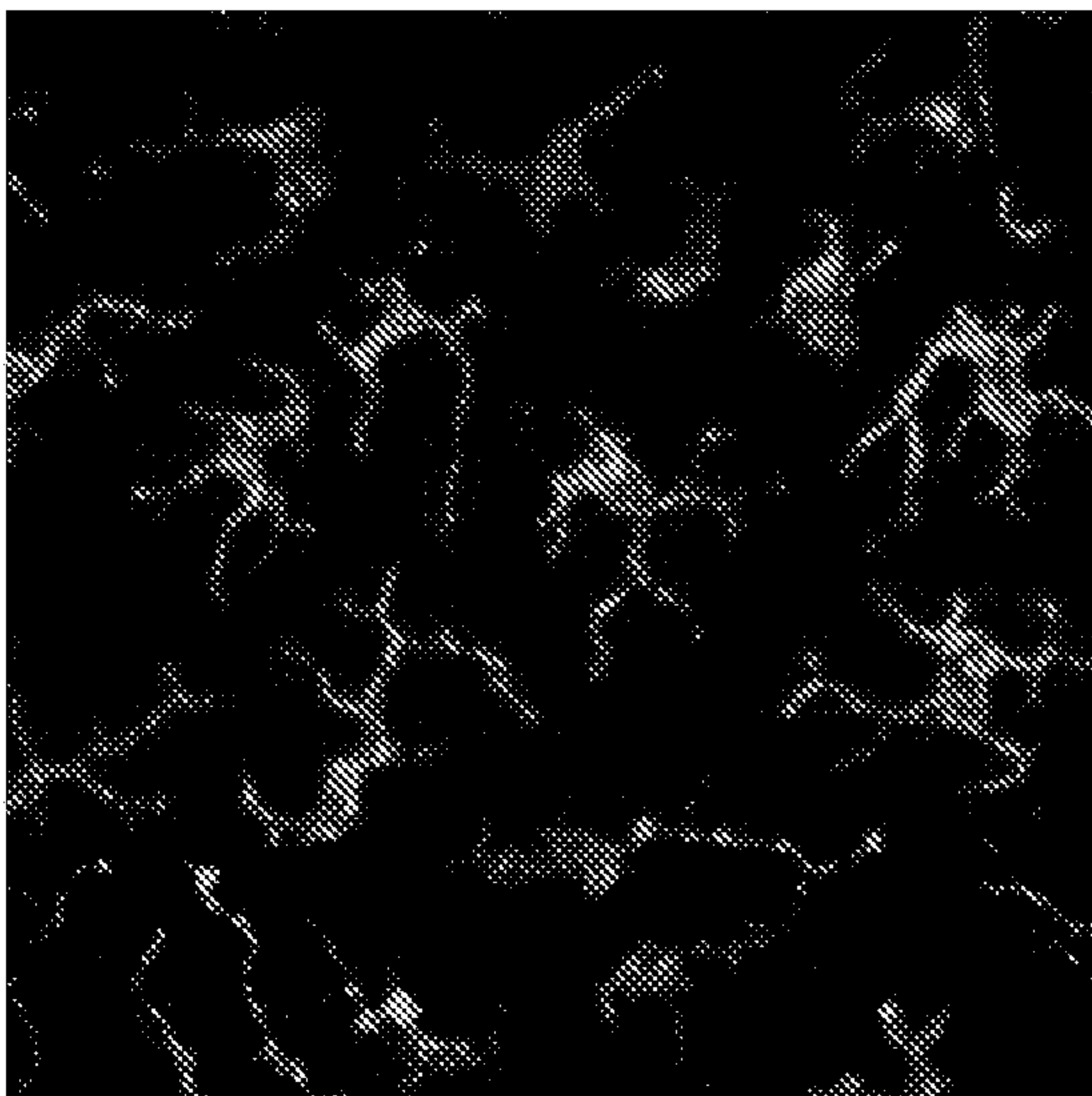
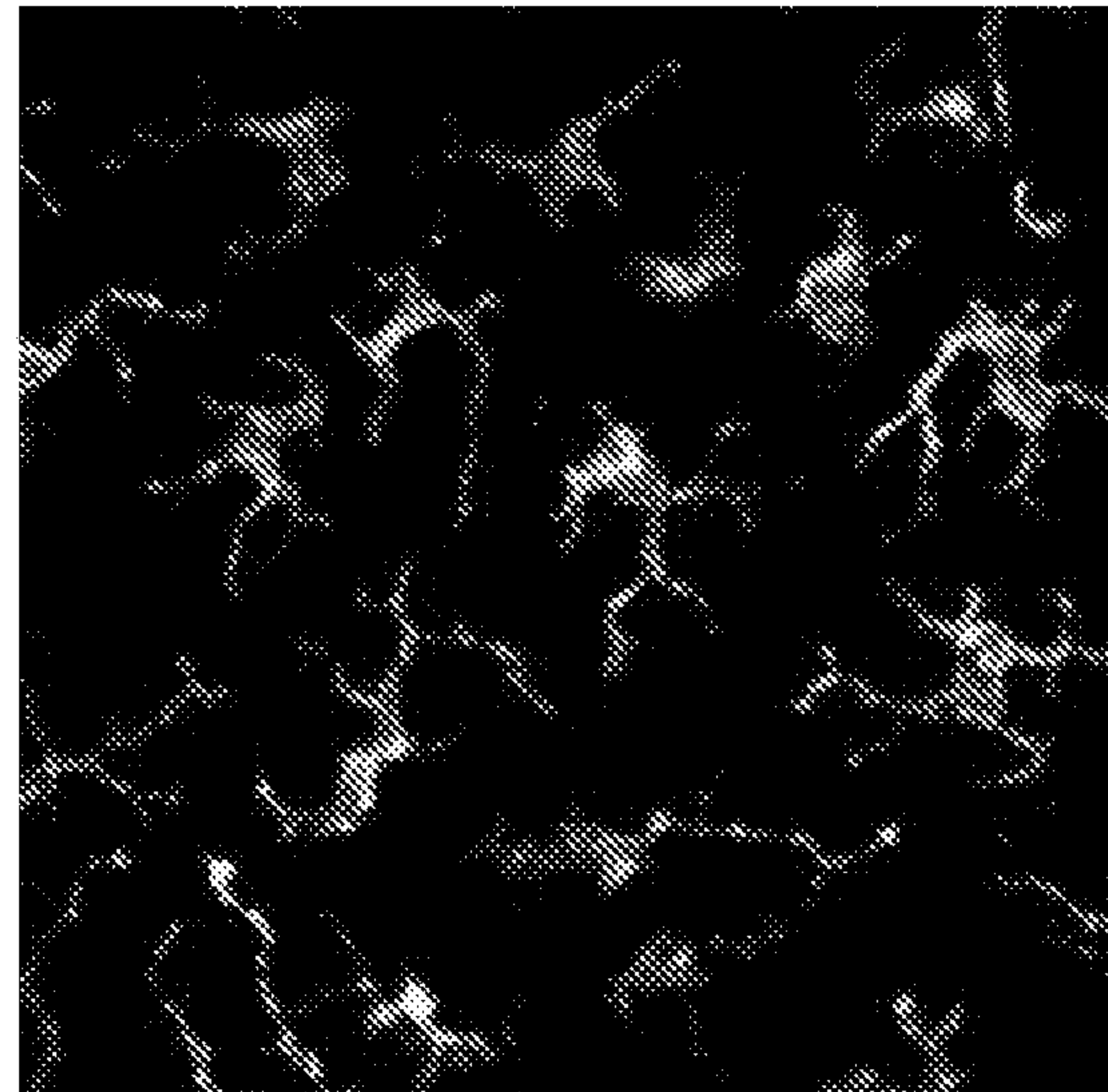


Figure 7

Multiplex Bead-Based ELISA: Human vs. NHP Langerin Ectodomain

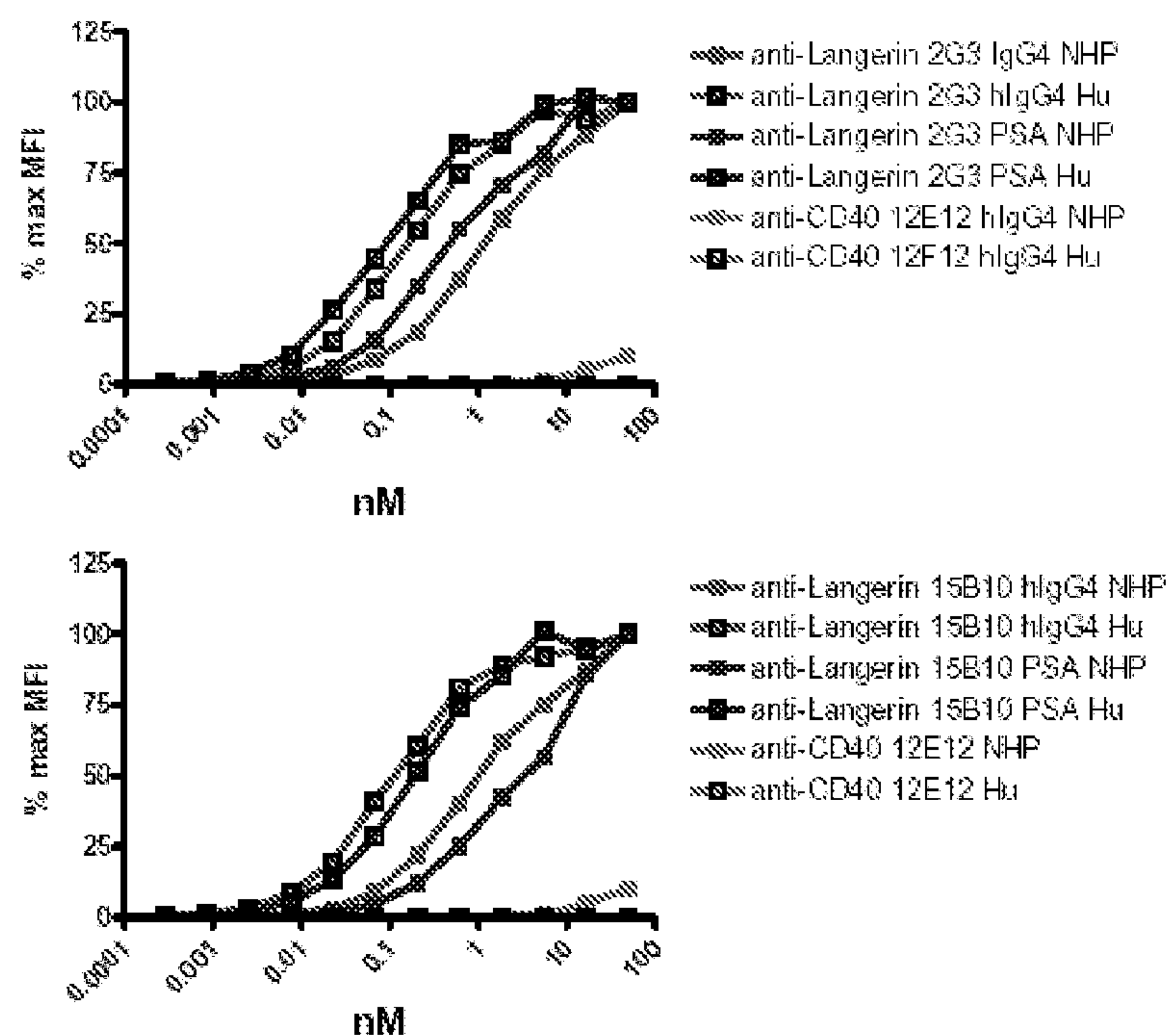


Figure 8

Antigen-specific IgG Bead-based assay

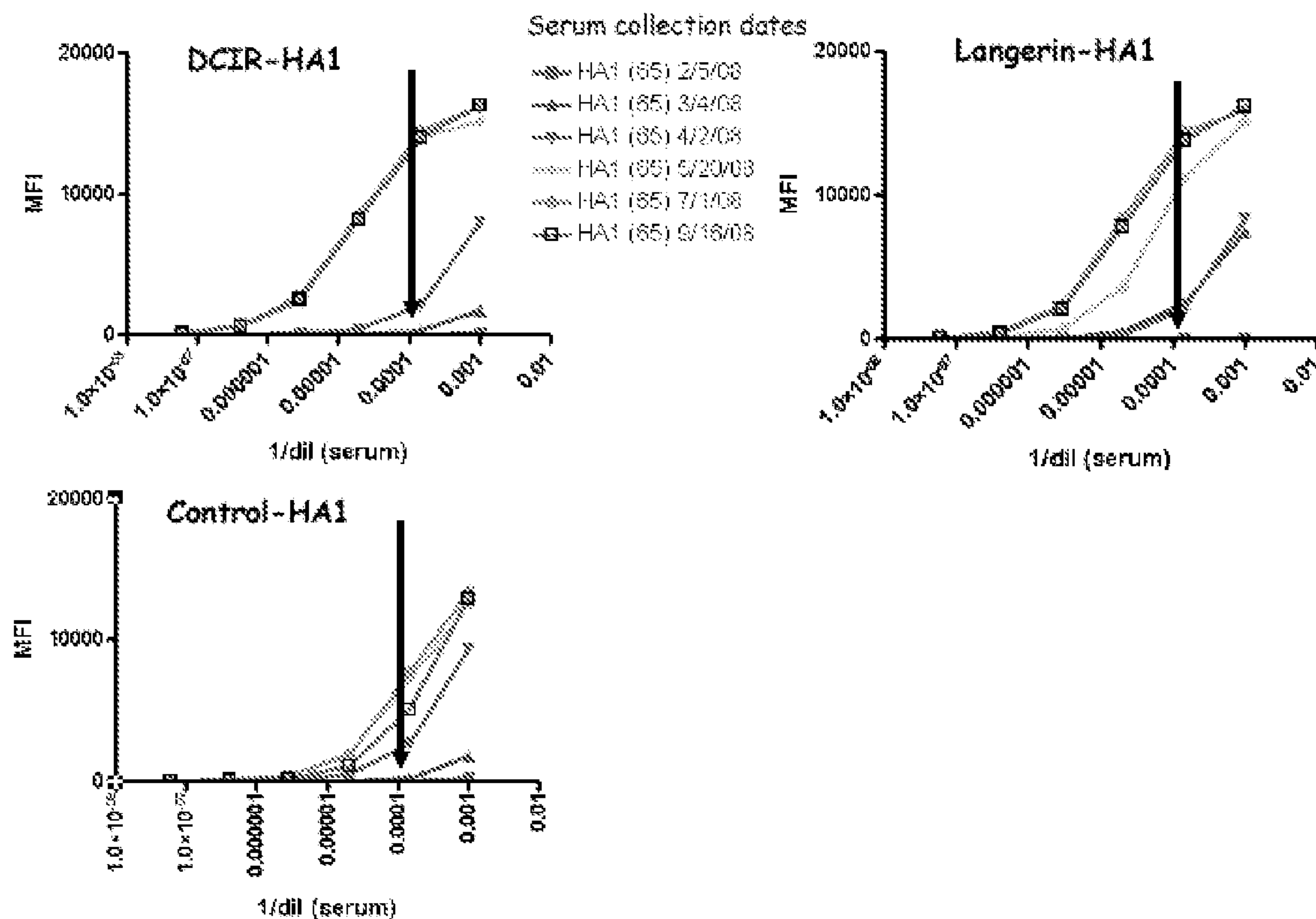


Figure 9

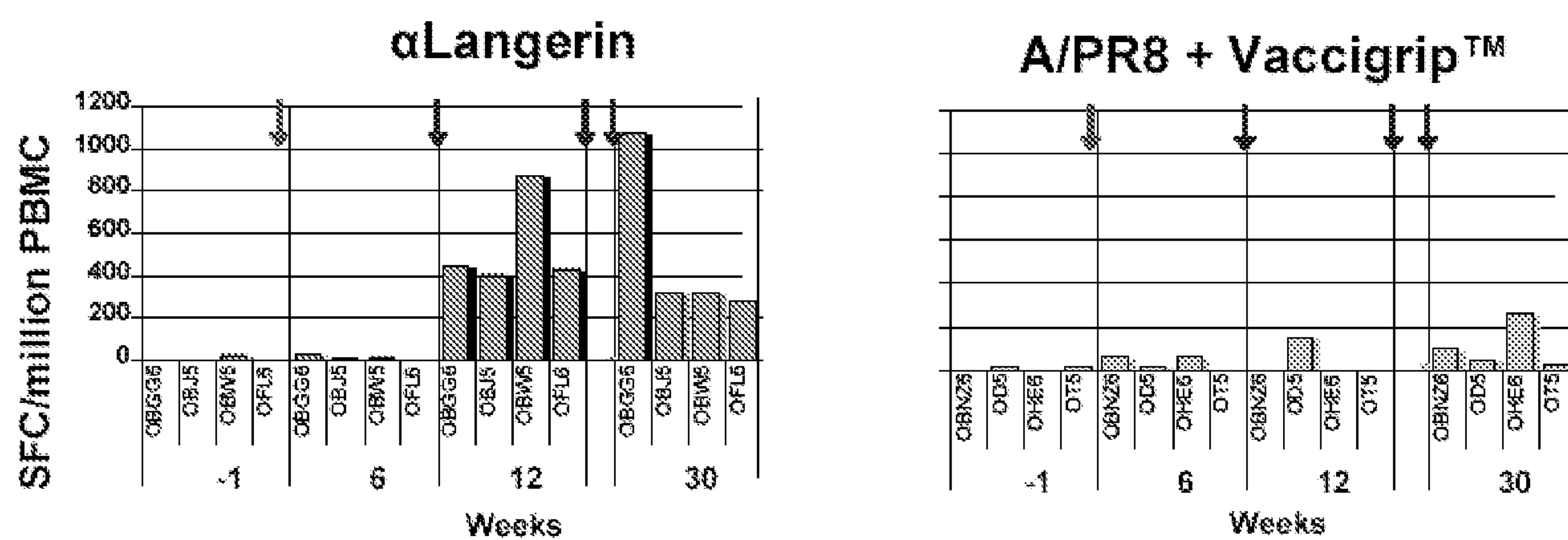


Figure10

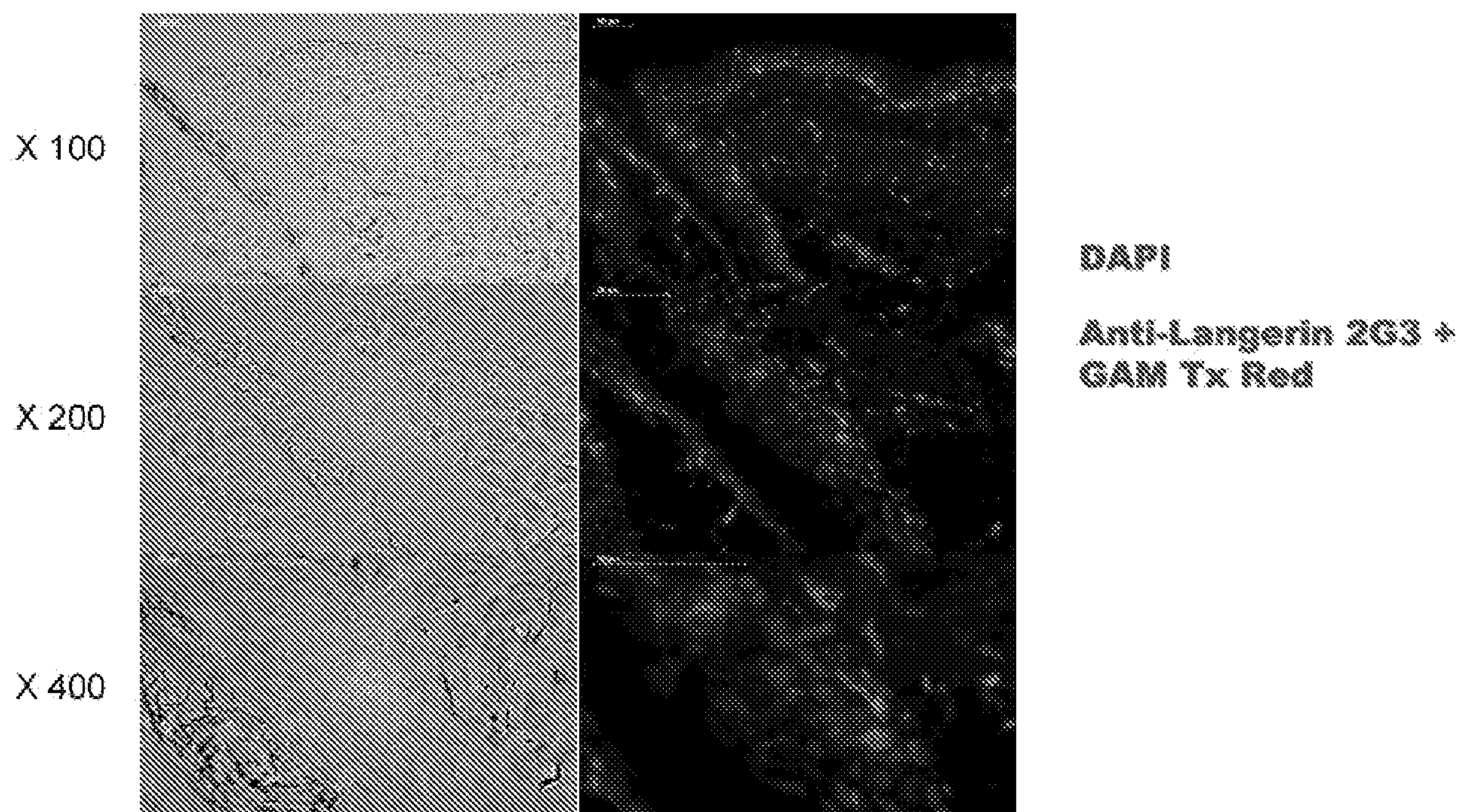


Figure 11

DC-targeting HIV Gag p24 vaccines in NHP

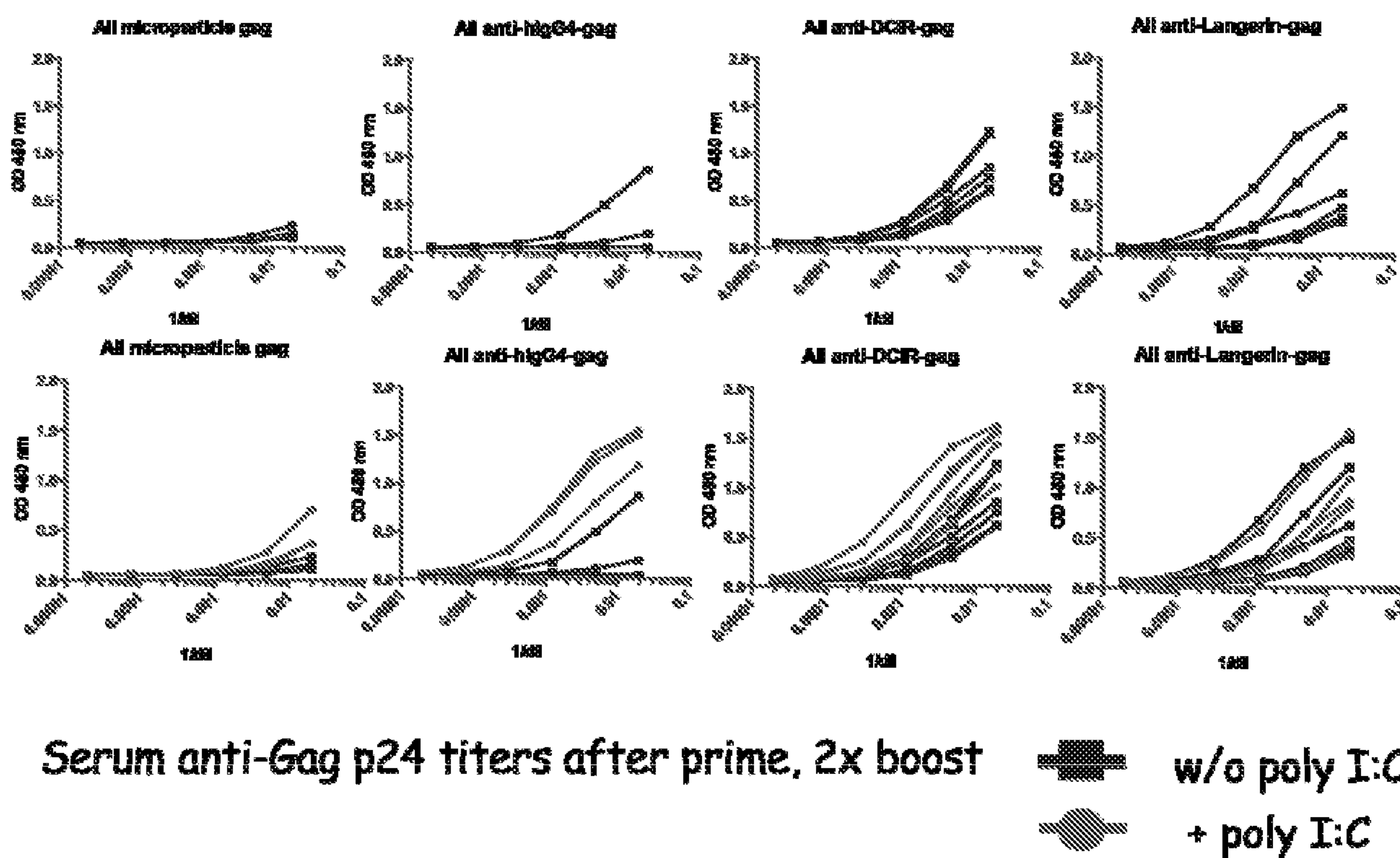
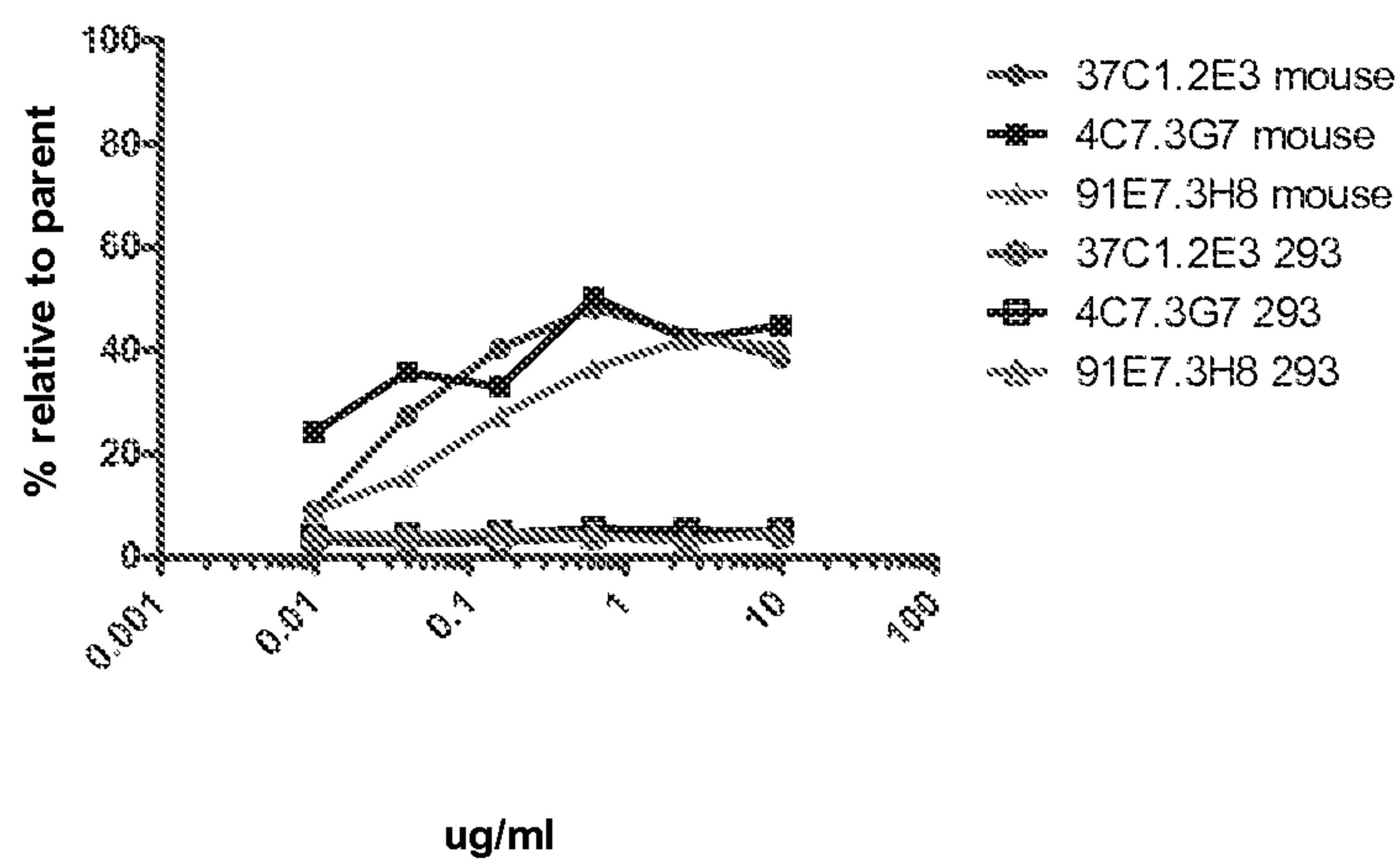


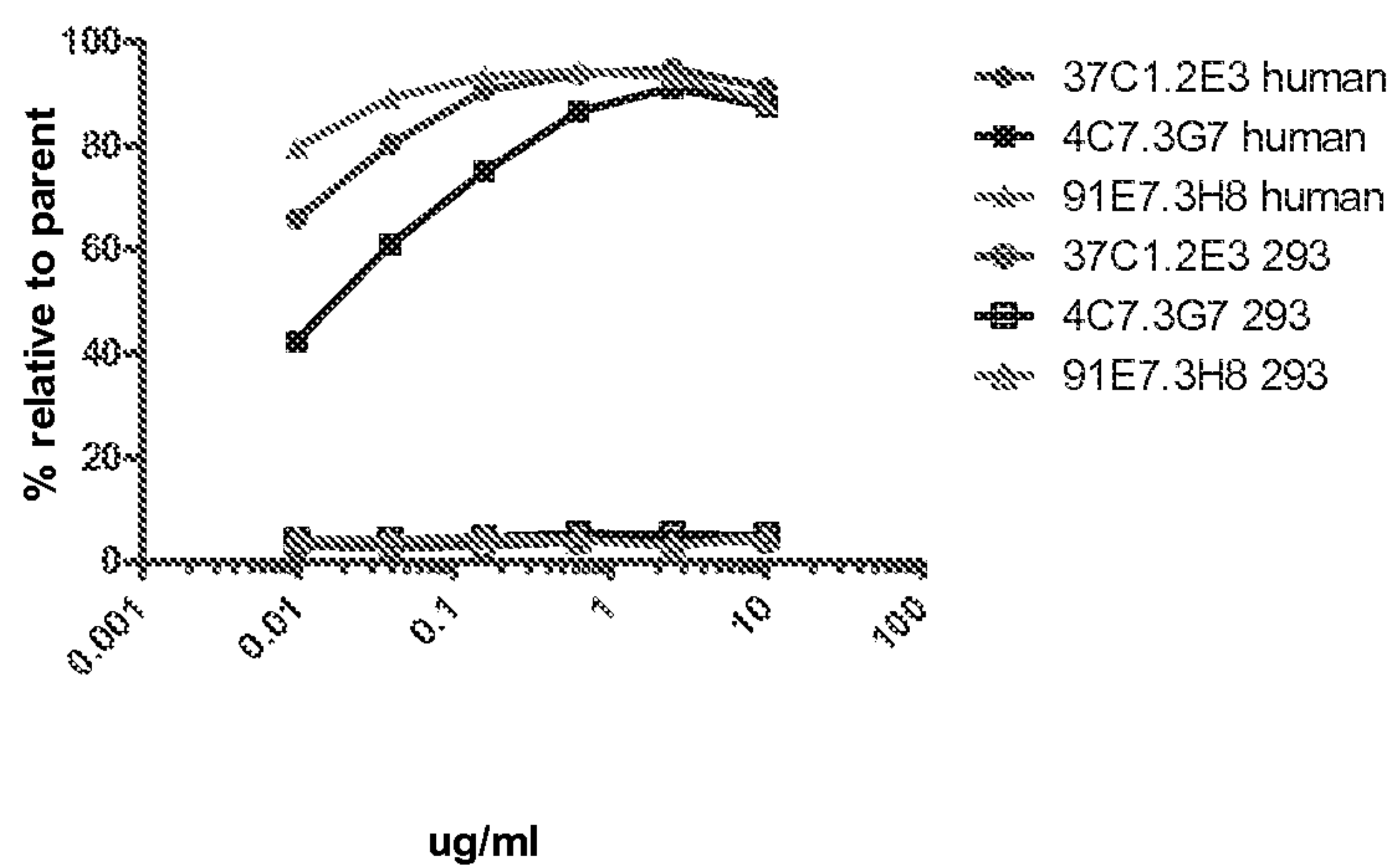
FIGURE 12

Langerin Clones

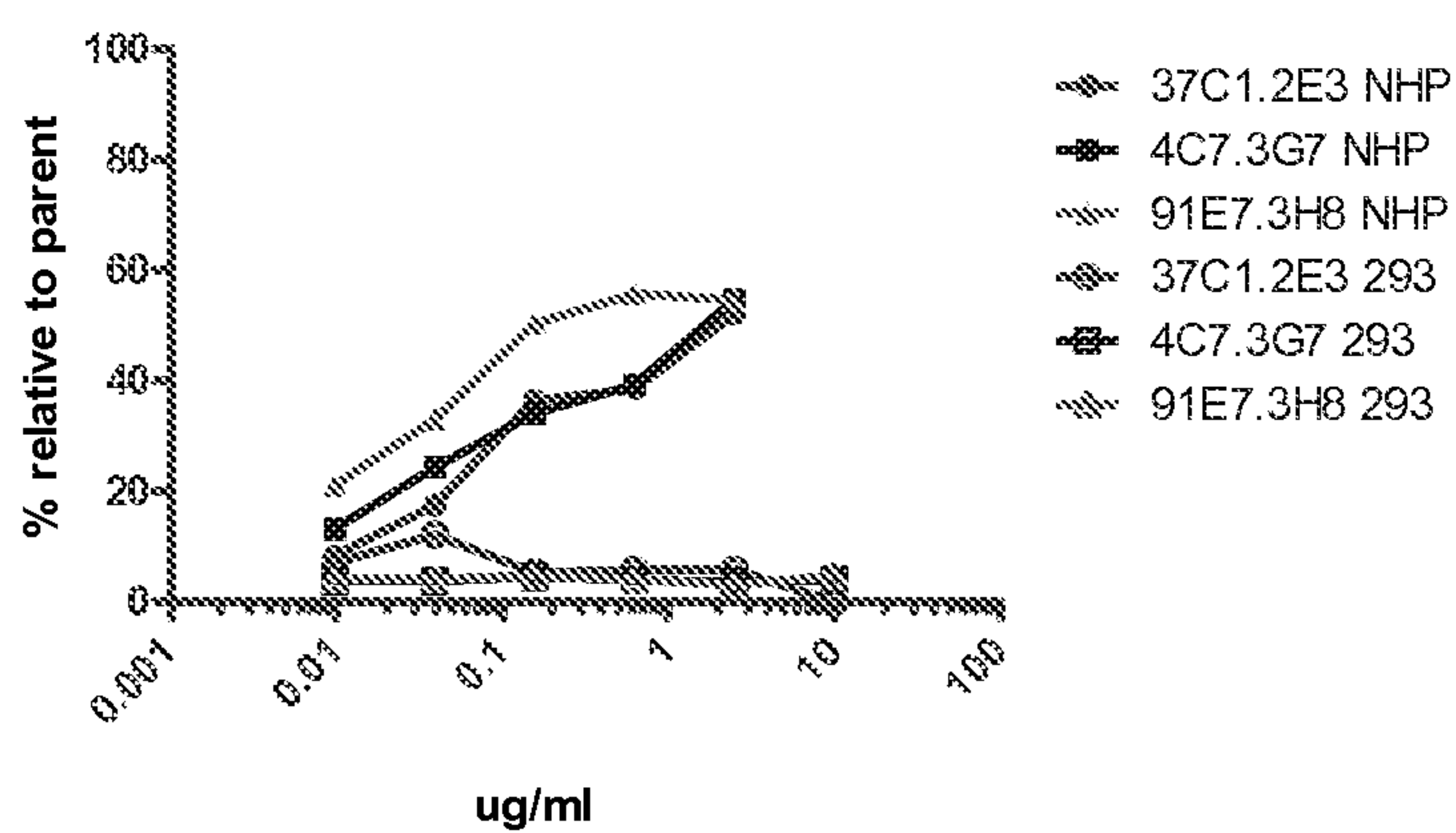
FACS Analysis on mouse 293 transfectant



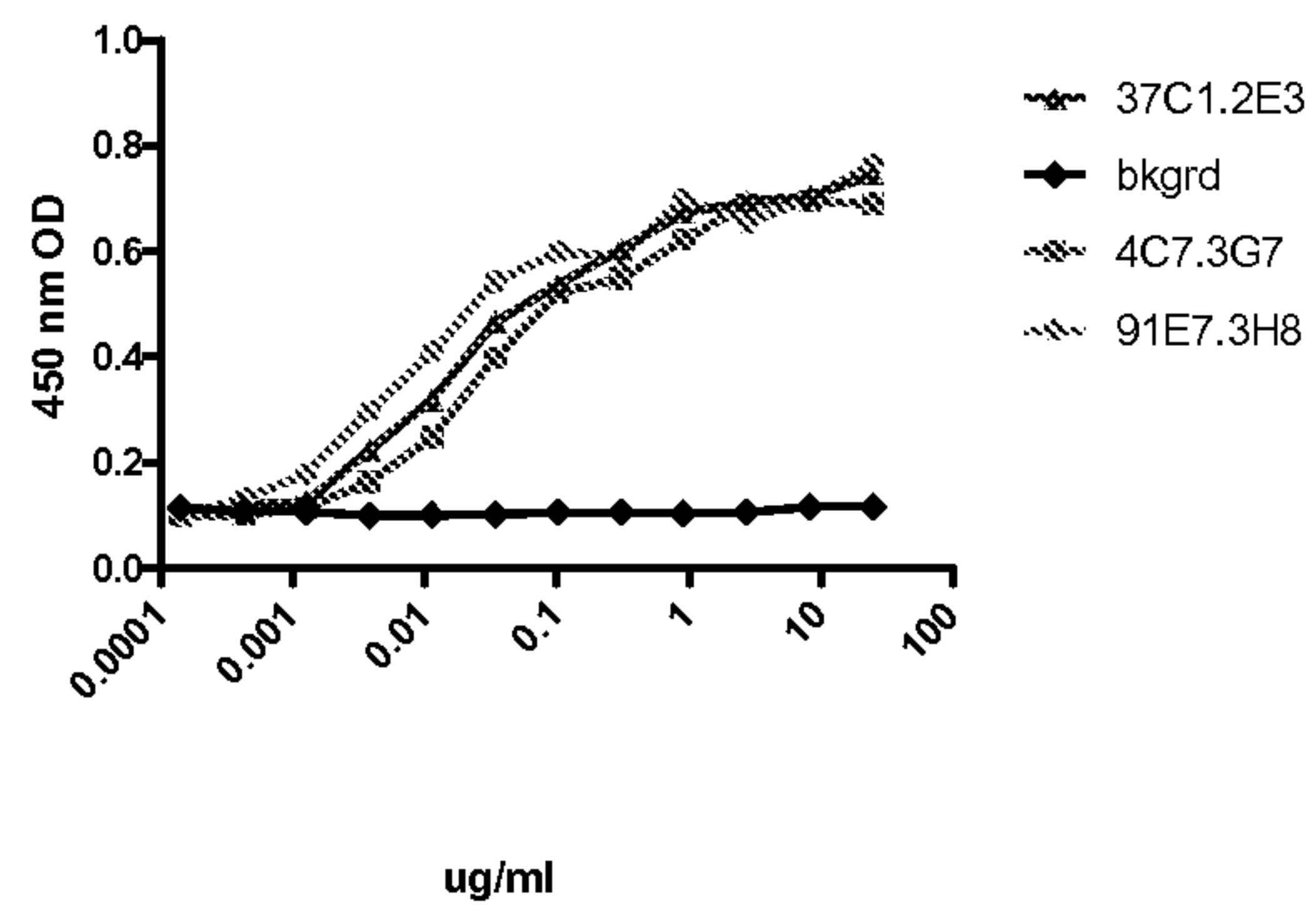
FACS Analysis on human 293 transfectant



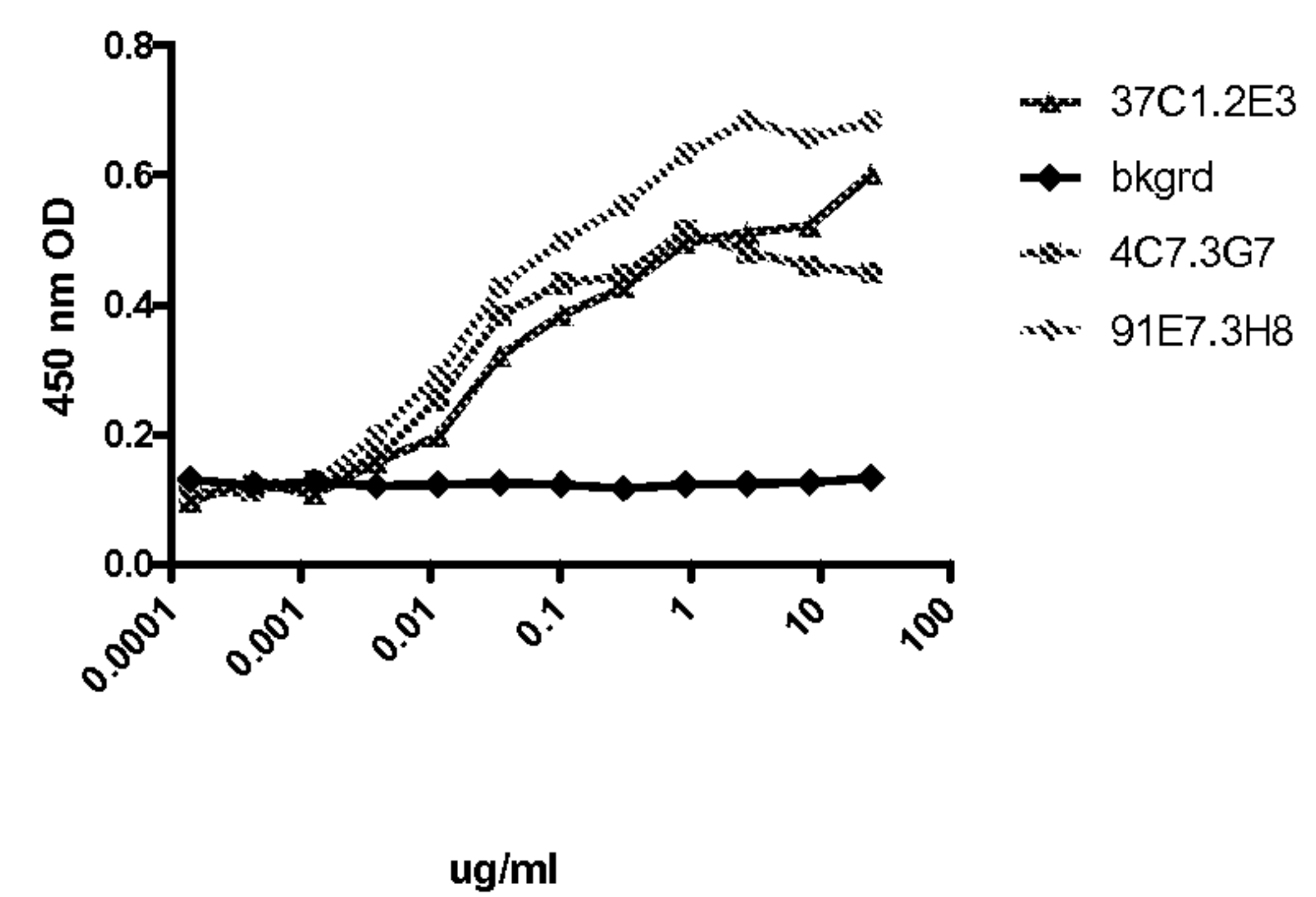
FACS Analysis on NHP 293 transfectant

**FIGURE 13**

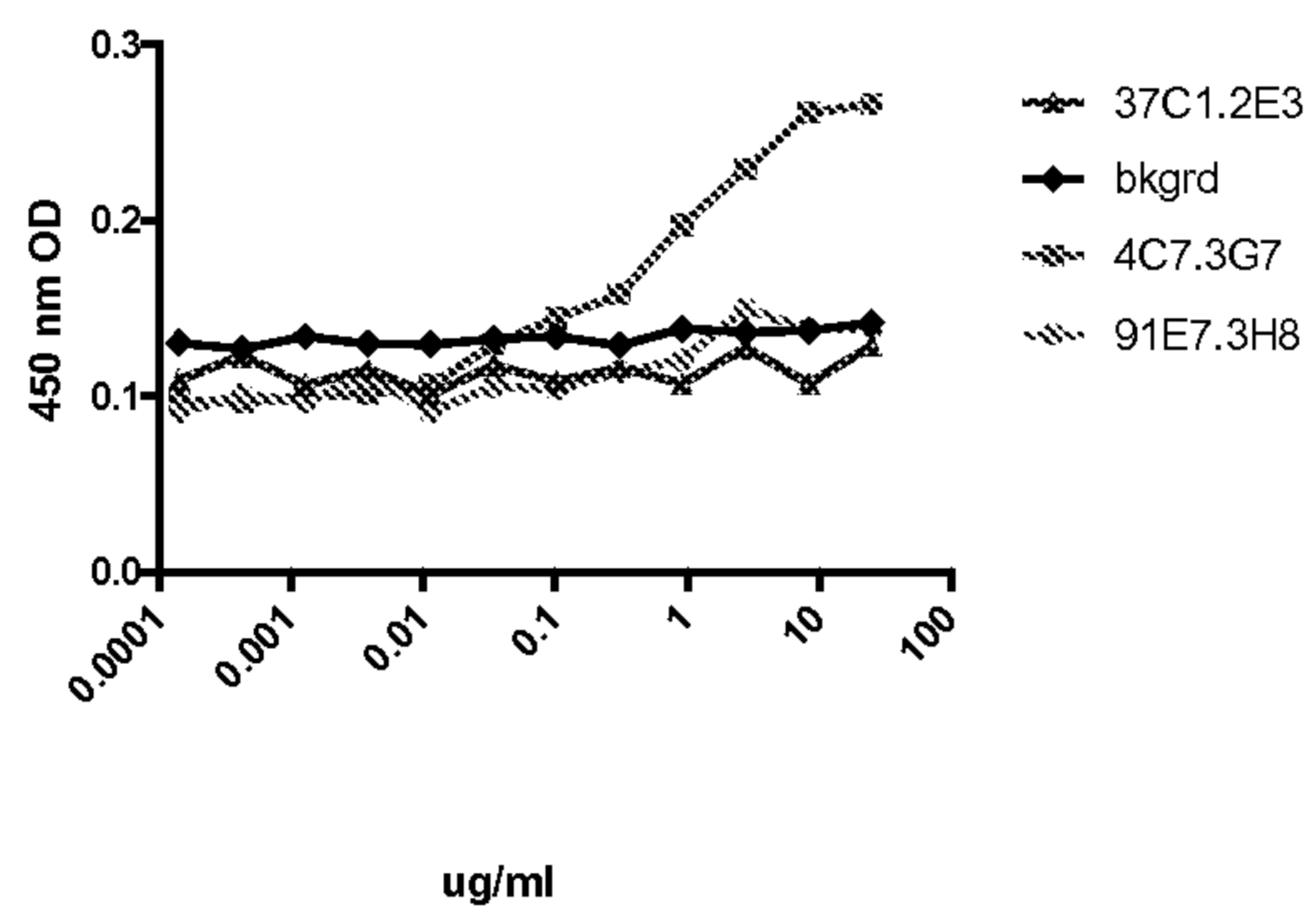
Langerin MAbs titration human Lang Direct ELISA



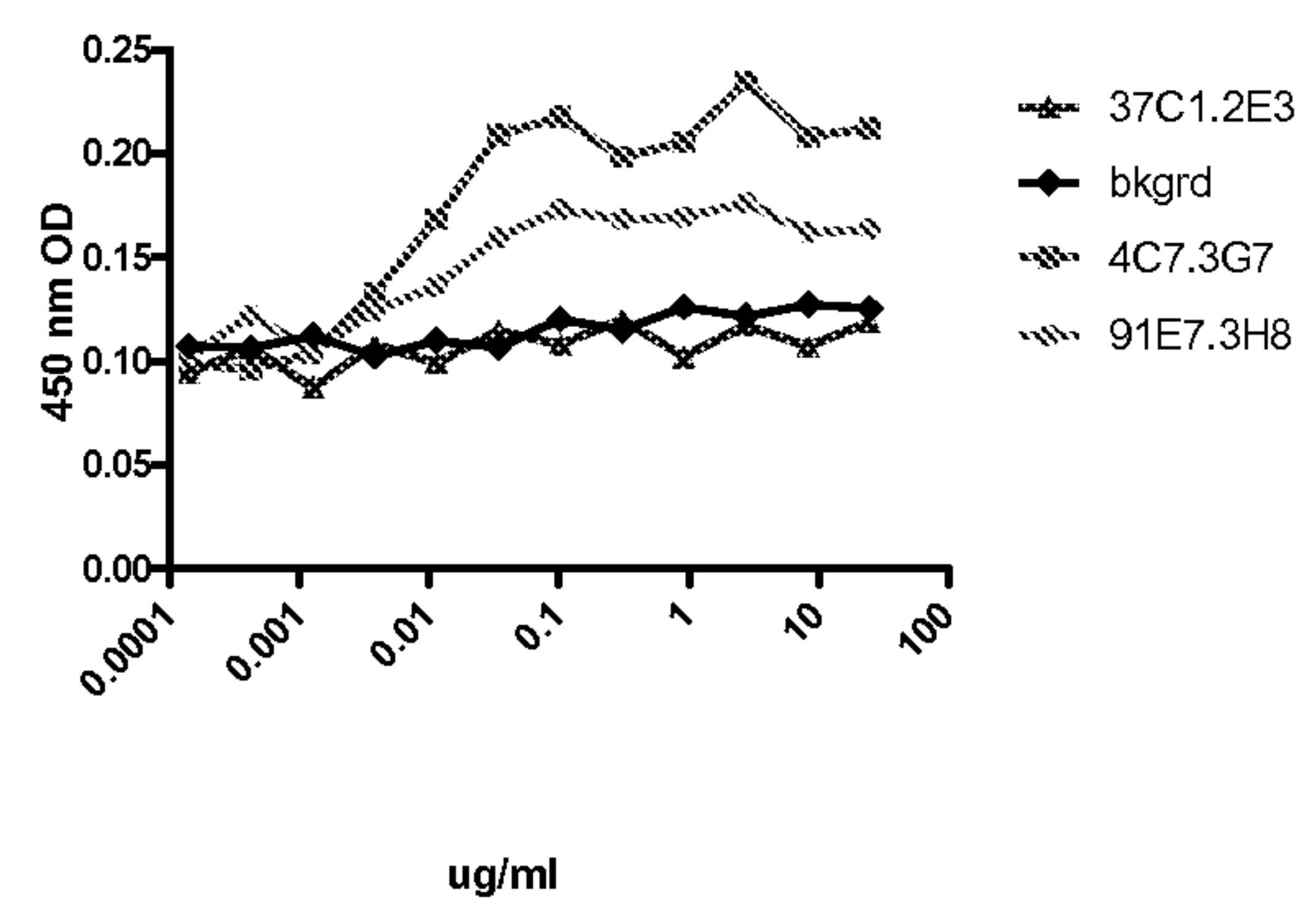
Langerin MAbs titration human Lang Capture ELISA



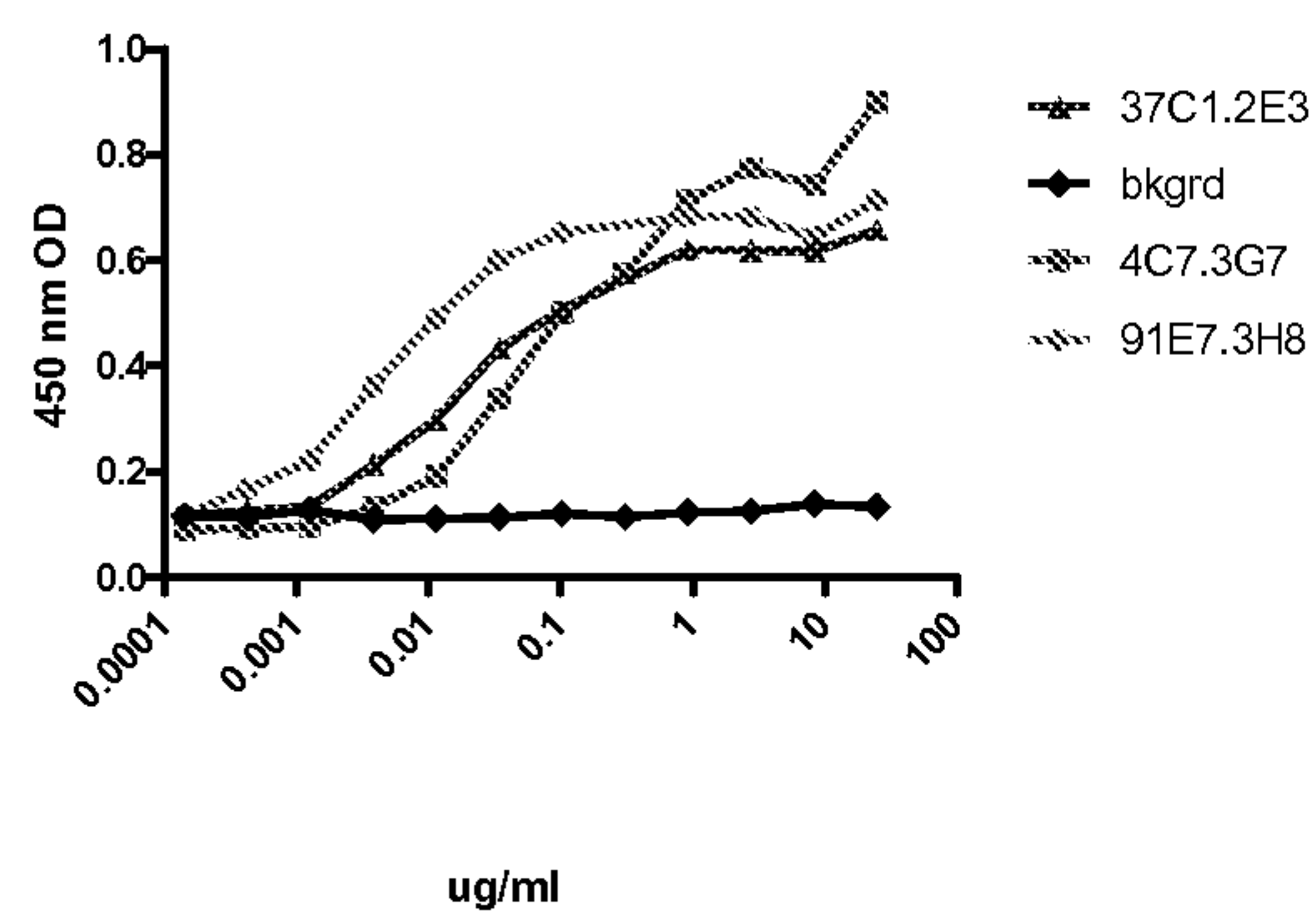
Langerin MAbs titration mouse Lang Direct ELISA



Langerin MAbs titration mouse Lang Capture ELISA



Langerin MAbs titration NHP Lang Direct ELISA



Langerin MAbs titration NHPLang Capture ELISA

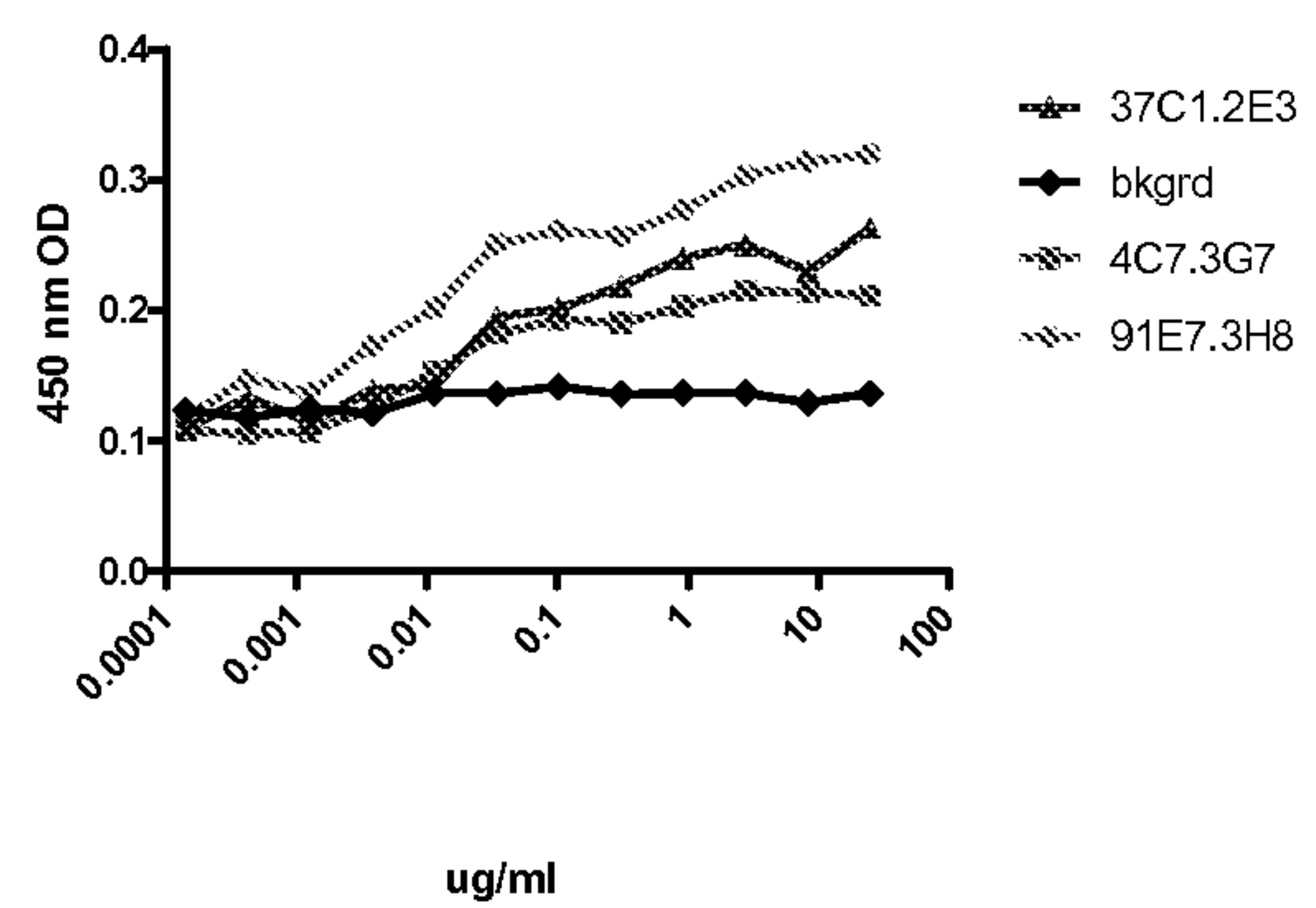


FIGURE 14

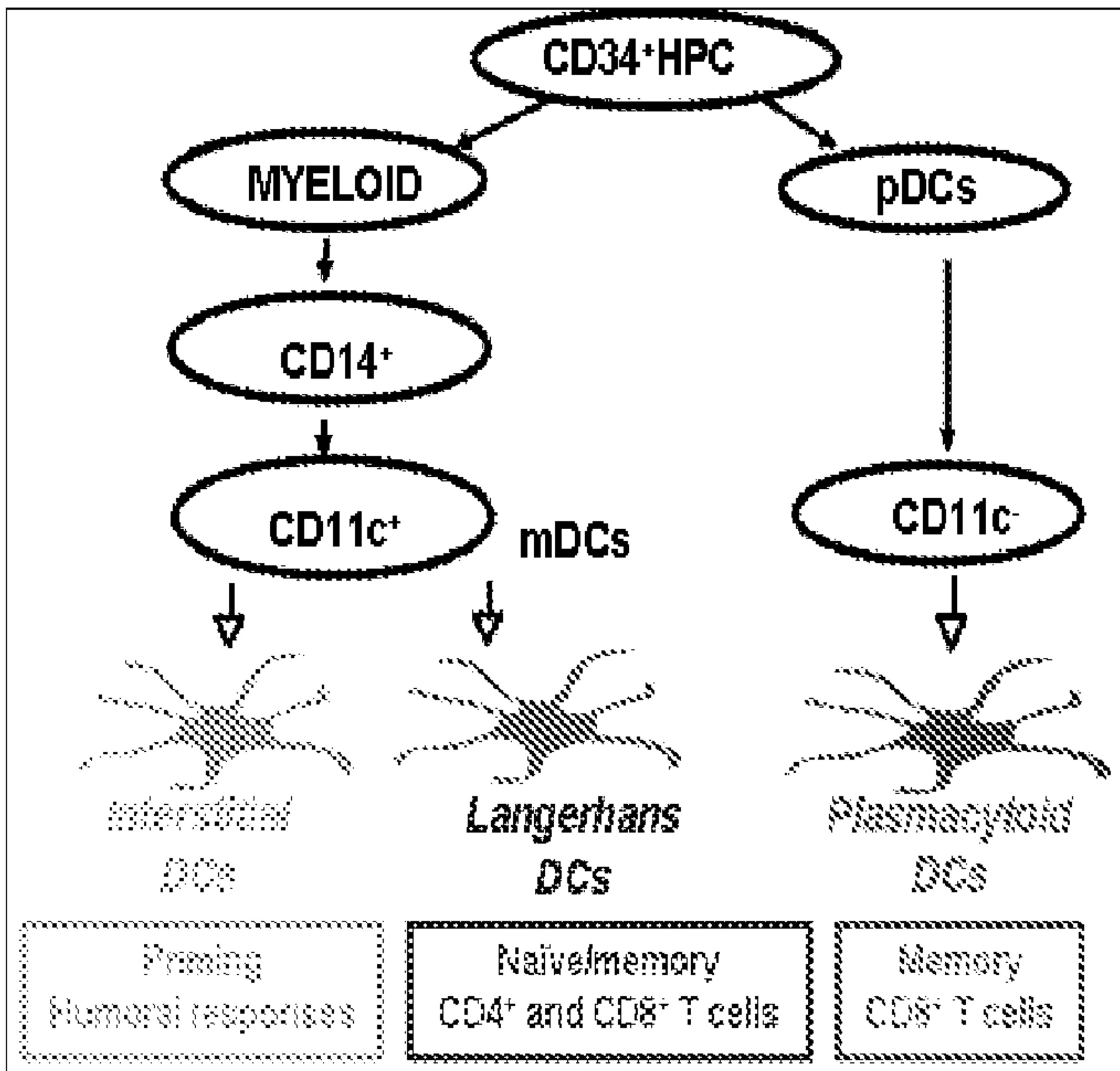


Figure 1