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(54) **Titre : COMPOSITIONS PURIFIEES DE PROTEINES IVIG ET KH POUR LA MODULATION DES LYMPHOCYTES ET LE TRAITEMENT CONTRE LE VIRUS DE L'HEPATITE B**  
(54) **Title: PURIFIED COMPOSITIONS OF IVIG AND KH PROTEINS FOR MODULATING LYMPHOCYTES AND TREATING HEPATITIS B VIRUS**

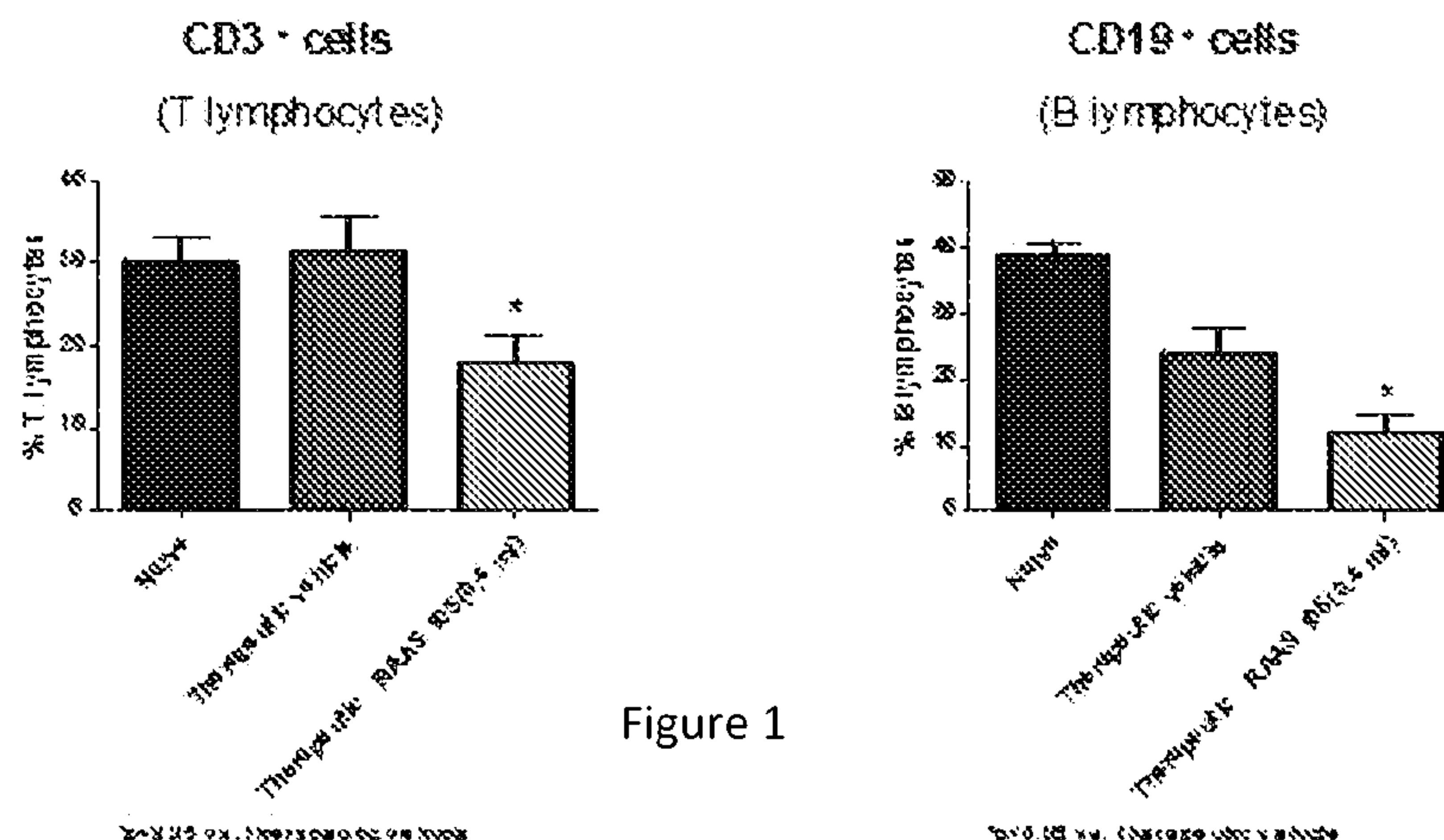


Figure 1

(57) **Abrégé/Abstract:**

The present invention provides purified blood plasma products from fraction II+III containing proteins at concentrations useful for the treatment of various diseases and infections including hepatitis B virus. Methods of manufacture and treatment are also provided. The purified blood plasma products regulate levels of immune cells and their proteins in the organs and peripheral blood of treated subjects. Examples of immune cells and associated proteins regulated by the purified blood plasma products include CD62L levels on T cells, CD4+, CD8+, CD28+, and Foxp3+ T cells, B cells, as well as granulocytes and macrophages.



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KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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(54) Title: PURIFIED COMPOSITIONS OF IVIG AND KH PROTEINS FOR MODULATING LYMPHOCYTES AND TREATING HEPATITIS B VIRUS

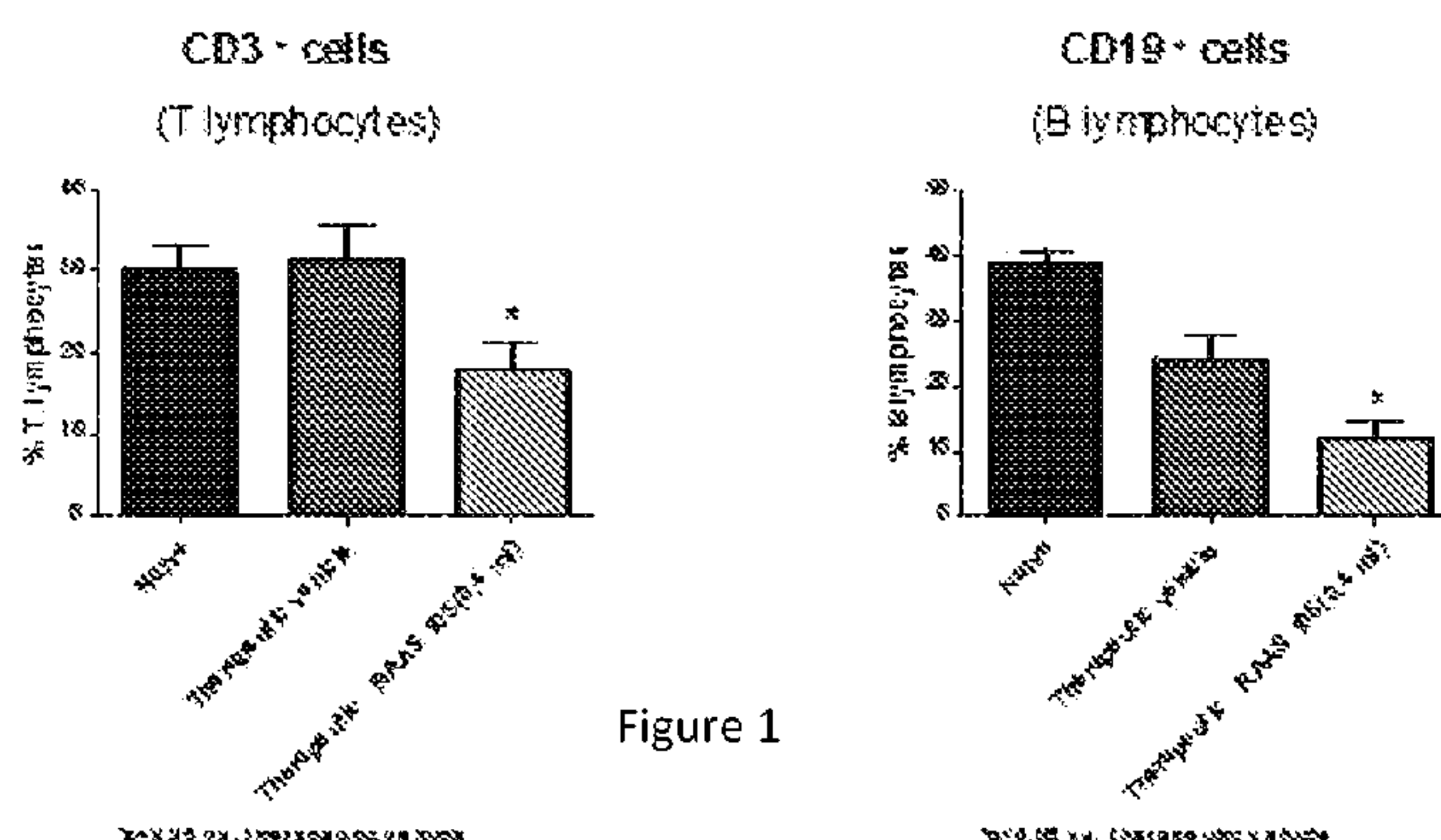


Figure 1

(57) Abstract: The present invention provides purified blood plasma products from fraction II+III containing proteins at concentrations useful for the treatment of various diseases and infections including hepatitis B virus. Methods of manufacture and treatment are also provided. The purified blood plasma products regulate levels of immune cells and their proteins in the organs and peripheral blood of treated subjects. Examples of immune cells and associated proteins regulated by the purified blood plasma products include CD62L levels on T cells, CD4+, CD8+, CD28+, and Foxp3+ T cells, B cells, as well as granulocytes and macrophages.

Purified compositions of IVIG and KH proteins for modulating lymphocytes and treating hepatitis B virus

### **CROSS REFERENCE TO RELATED APPLICATIONS**

This application claims priority under 35 USC 119(e) to provisional application No. 62/003,664, filed May 28, 2014, which is incorporated by reference in its entirety. This application is also a continuation in part of non-provisional application No. 13/756,034, filed on January 31, 2013, which claims priority to provisional application No. 61/593,183, filed on January 31, 2012, provisional patent application No. 61/593,196, filed on January 31, 2012, provisional application No. 61/648,281, filed on May 17, 2012, provisional application No. 61/692,273, filed on August 23, 2012 and provisional application No. 61/710,930, filed on October 8, 2012. This application is also a continuation in part of non-provisional application No. 13/756,478, filed on January 31, 2013, which claims priority to provisional application No. 61/593,164, filed on January 31, 2012, provisional application No. 61/593,183, filed on January 31, 2012, provisional application No. 61/593,196, filed on January 31, 2012, provisional application No. 61/648,281, filed on May 17, 2012, provisional application No. 61/692,273, filed on August 23, 2012 and provisional application No. 61/710,930, filed on October 8, 2012, all of which are hereby incorporated herein by reference in their entireties. This application is also a continuation in part of non-provisional application No. 14/151,147, filed on January 9, 2014, which is a continuation in part of non-provisional application No. 13/108,970, filed May 6, 2011, which is a continuation in part of non-provisional patent application No. 13/064,070, filed March 4, 2011.

**Field of the Invention:**

The invention relates to the isolation and purification of blood plasma, products derived therefrom, and methods of modifying levels of immune cells and related proteins in peripheral blood and organs of a treated individual.

**Background of the Invention:**

The practice of administering antibodies or antitoxins acquired from exposed or vaccinated individuals or animals to a patient susceptible to the disease in question has been the underlying medical practice involved in passive immunotherapy since the late 1800s. Since the 1940s human albumin and other therapeutic proteins have been extracted from plasma to address specific clinical needs.

In comparison to most antibiotics, antibody-based therapies that use human antibodies have low toxicity and high specificity. The high specificity means that the antibody targets only the disease-causing microorganism that causes disease without affecting the host's endogenous organisms, therefore minimizing adverse reactions and the chance of the development of resistant organisms. This also means, however, that more than one antibody preparation may be required to target micro-organisms with high antigenic variation. Combination plasma products containing antibodies specific for a variety of diseases and afflictions, as well as therapies for administering the same, are therefore desired for addressing a range of diseases while minimizing damage to healthy cells.

The identification of various fractions of human plasma as well as the proteins residing therein and the unique characteristics of those proteins, has resulted in new life saving treatments for a variety of chronic and acute, hereditary and acquired diseases. Improvements in the manufacturing processes that ensure product safety and efficacy, and the identification of specific clinical applications require new advances in the technology.

Various techniques to remove protein aggregates, such as chromatography, have made some products more tolerable when administered intravenously and the addition of virus

removal/inactivation steps has made the products essentially free of lipid and nonlipid enveloped viruses.

Intravenous immunoglobulin (IVIG) is a blood product generally administered intravenously. IVIG is administered to patients with immunodeficiencies and its benefits for secondary ailments related to immunodeficiencies has made it an increasingly appealing first or second line treatment.

IVIG is manufactured from pooled human plasma and contains white blood cells called lymphocytes. A lymphocyte is any of three types of immune cells including: (1) natural killer cells (NK cells, which function in cell-mediated, cytotoxic innate immunity), (2) T cells (for cell-mediated, cytotoxic adaptive immunity), and (3) B cells (for humoral, antibody-driven adaptive immunity).

Antibodies are produced by the B-cells and plasma cells after exposure to antigens. They can be either immunoglobulin G (IgG), IgA, IgM, IgE, or IgD, but in the case of hyper-immunes, IgG are the antibodies of interest. IgG consists of four polypeptide chains, two pairs of polypeptide chains, two pairs of heavy and light chains in a Y-shaped arrangement. The top ends of the IgG molecule, Fab or antibody binding region, are created from one heavy and one light chain, forming the antigen binding site. This fragment variable (Fv) region contains various amino acid combinations, which makes each antibody unique. Importantly, purified IVIG intravenous hyperimmune products contain human IgG protein, of which at least 96% is IgG containing specific antibodies against the specific antigen. Significantly, since the mid to late 2000s the need for more efficient manufacture of isolated purified IVIG has increased dramatically. Products regulating the percentages of B and T cells to target specific ailments and disease are also desirable.

### **Summary of the Invention:**

The invention relates to isolated purified human immunoglobulin plasma products, methods of their manufacture and their use in treating diseases and infections such as hepatitis B virus. The purified human immunoglobulin plasma products are useful in treating a variety of chronic and

acute, hereditary and acquired diseases by regulating the levels of immune cells and their related proteins in the treated subject.

In embodiments of the invention various purified blood plasma products are used to treat viral infections such as HBV by modifying lymphocyte proliferation in an individual.

Certain embodiments of the invention include the regulation of B and T cell levels in the peripheral blood and organs of a treated individual through prophylactic or therapeutic administration of purified blood plasma products.

Other embodiments include the regulation of granulocyte and macrophage levels in the peripheral blood and organs of a treated individual through prophylactic or therapeutic administration of purified blood plasma products.

In one embodiment of the invention a purified protein complex is obtained by purifying intravenous immunoglobulin G (IVIG) from human plasma fraction II+III paste. **FIG. 73.** In addition to the main component of immunoglobulin, analysis of the protein complex has shown the product to contain the following proteins: 120/E19 IGHV4-31, IGHG1 44kDa, 191/H18 IGHV4 31, IGHG1 32kDa, IGHG1 putative uncharacterized protein, DKFZp686G11190, and KH proteins 33-37. **FIG 75.** The combination of KH proteins 33-37 with a concentration of 30% has been found to very effective against viruses such as H1N1, H5N1, foot and mouth disease, and to stop hepatitis B viral DNA replication.

In another embodiment of the invention a purified protein complex is obtained by purifying hepatitis B immune globulin (HBIG) from human plasma fraction II+III of donors having high antibody levels of the hepatitis B surface antigen. **FIG. 74.** In addition to immunoglobulin proteins, HBIG contains the protein TF serotransferrin (sequence no. 197/H24). This complex contains KH proteins 22-37 and has been found to be effective in stopping hepatitis B viral DNA replication.

In yet another embodiment a purified protein complex is formulated to combat the scarcity of the hepatitis B antibody. **FIGs 77-78**. This purified protein complex is a combination of 80% purified normal immunoglobulin and 20% purified hepatitis B immune globulin containing high levels of hepatitis B antibodies. In this embodiment both of the products have a concentration by ultra filtration of at least 30%. The purified protein complex of this embodiment contains proteins designated as KH22-37 and KH51. Additional information regarding KH designated proteins is included herein.

In a related embodiment a method of manufacture for a purified protein complex comprises: following manufacturing protocol to separately manufacture normal immunoglobulin and hepatitis B antibody up to the step of obtaining non-sterile final bulk for both products, taking 80% normal immunoglobulin non-sterile final bulk and mixing with 20% hepatitis B antibody non-sterile final bulk, and performing sterile filtration for filling the final product. **FIG 77**.

In another embodiment the method of manufacture for a purified protein complex comprises: taking 80% of normal immunoglobulin fraction II+III and 20% hepatitis B antibody fraction II+III, and dissolving the fractions together in a process tank for production of the normal immunoglobulin until the final product is filled. **FIG 78**.

Embodiments of the invention include purified protein complexes containing various proteins having unique characteristics useful in treating infection and disease. A “KH” designation has been assigned to certain proteins contained in the purified protein complexes. Those designations, as well as additional information corresponding to those proteins is found in the figures below.

538 functions have been identified for the 55 KH proteins, which provide them with unique characteristics for treating a wide range of disease, infection, and other cellular disturbances as expressed in some embodiments of the invention as described.

| Number       | GI code                                                                          | Fraction – P<br>(process), C<br>(component),<br>F (function) | Sequence<br>name | Sequence desc.                                                                   |
|--------------|----------------------------------------------------------------------------------|--------------------------------------------------------------|------------------|----------------------------------------------------------------------------------|
| KH 1         | 21749960                                                                         | cryopaste                                                    | gi 21749960      | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | F                                                            | GO:0005102       | receptor binding                                                                 |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | P                                                            | GO:0043547       | positive regulation of GTPase activity                                           |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | P                                                            | GO:0016477       | cell migration                                                                   |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | P                                                            | GO:0007165       | signal transduction                                                              |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | P                                                            | GO:0006935       | chemotaxis                                                                       |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | C                                                            | GO:0005737       | cytoplasm                                                                        |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | F                                                            | GO:0005083       | small GTPase regulator activity                                                  |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | F                                                            | GO:0019904       | protein domain specific binding                                                  |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | P                                                            | GO:0048583       | regulation of response to stimulus                                               |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | F                                                            | GO:0005096       | GTPase activator activity                                                        |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | F                                                            | GO:0051020       | GTPase binding                                                                   |
| gi 21749960  | dock4_humandedicator of cytokinesis protein 4 os=homo sapiens gn=dock4 pe=1 sv=3 | C                                                            | GO:0016020       | membrane                                                                         |
| KH 2         | 215415640                                                                        | cryopaste                                                    | gi 215415640     | apoa1_humanapolipoprotein a-i os=homo sapiens gn=apoa1 pe=1 sv=1                 |
| gi 215415640 | apoa1_humanapolipoprotein a-i os=homo sapiens gn=apoa1 pe=1 sv=1                 | P                                                            | GO:0070508       | cholesterol import                                                               |
| gi 215415640 | apoa1_humanapolipoprotein a-i os=homo sapiens gn=apoa1 pe=1 sv=1                 | C                                                            | GO:0030139       | endocytic vesicle                                                                |

|              |                                                                        |   |            |                                                                             |
|--------------|------------------------------------------------------------------------|---|------------|-----------------------------------------------------------------------------|
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0050728 | negative regulation of<br>inflammatory response                             |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0033344 | cholesterol efflux                                                          |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0034115 | negative regulation of<br>heterotypic cell-cell adhesion                    |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0018206 | peptidyl-methionine<br>modification                                         |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0042157 | lipoprotein metabolic process                                               |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0043691 | reverse cholesterol transport                                               |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0005543 | phospholipid binding                                                        |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0002740 | negative regulation of cytokine<br>secretion involved in immune<br>response |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0008203 | cholesterol metabolic process                                               |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0050713 | negative regulation of<br>interleukin-1 beta secretion                      |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0018158 | protein oxidation                                                           |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0006656 | phosphatidylcholine biosynthetic<br>process                                 |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0001540 | beta-amyloid binding                                                        |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0060228 | phosphatidylcholine-sterol O-<br>acyltransferase activator activity         |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0042632 | cholesterol homeostasis                                                     |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0015485 | cholesterol binding                                                         |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0042060 | wound healing                                                               |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0034191 | apolipoprotein A-I receptor<br>binding                                      |

|              |                                                                        |   |            |                                                                         |
|--------------|------------------------------------------------------------------------|---|------------|-------------------------------------------------------------------------|
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0042802 | identical protein binding                                               |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010903 | negative regulation of very-low-density lipoprotein particle remodeling |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010804 | negative regulation of tumor necrosis factor-mediated signaling pathway |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0034380 | high-density lipoprotein particle assembly                              |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0007186 | G-protein coupled receptor signaling pathway                            |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0050821 | protein stabilization                                                   |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:0034361 | very-low-density lipoprotein particle                                   |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0032488 | Cdc42 protein signal transduction                                       |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0060354 | negative regulation of cell adhesion molecule production                |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0055091 | phospholipid homeostasis                                                |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010873 | positive regulation of cholesterol esterification                       |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0017127 | cholesterol transporter activity                                        |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0019899 | enzyme binding                                                          |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0070653 | high-density lipoprotein particle receptor binding                      |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0070328 | triglyceride homeostasis                                                |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:0034366 | spherical high-density lipoprotein particle                             |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0033700 | phospholipid efflux                                                     |
| gi 215415640 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0051345 | positive regulation of hydrolase activity                               |

|              |                                                                      |        |              |                                                                             |
|--------------|----------------------------------------------------------------------|--------|--------------|-----------------------------------------------------------------------------|
| KH 3         | 215415638                                                            | Fr III | gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1        |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0070508   | cholesterol import                                                          |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | C      | GO:0030139   | endocytic vesicle                                                           |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0050728   | negative regulation of<br>inflammatory response                             |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0033344   | cholesterol efflux                                                          |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0034115   | negative regulation of<br>heterotypic cell-cell adhesion                    |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0018206   | peptidyl-methionine<br>modification                                         |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0042157   | lipoprotein metabolic process                                               |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0043691   | reverse cholesterol transport                                               |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | F      | GO:0005543   | phospholipid binding                                                        |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0002740   | negative regulation of cytokine<br>secretion involved in immune<br>response |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0008203   | cholesterol metabolic process                                               |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0050713   | negative regulation of<br>interleukin-1 beta secretion                      |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0018158   | protein oxidation                                                           |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0006656   | phosphatidylcholine biosynthetic<br>process                                 |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | F      | GO:0001540   | beta-amyloid binding                                                        |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | F      | GO:0060228   | phosphatidylcholine-sterol O-<br>acyltransferase activator activity         |
| gi 215415638 | apo1_humanapolipoprotein a-i<br>os=homo sapiens gn=apo1 pe=1<br>sv=1 | P      | GO:0042632   | cholesterol homeostasis                                                     |

|              |                                                                        |   |            |                                                                         |
|--------------|------------------------------------------------------------------------|---|------------|-------------------------------------------------------------------------|
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0015485 | cholesterol binding                                                     |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0042060 | wound healing                                                           |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0034191 | apolipoprotein A-I receptor binding                                     |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0042802 | identical protein binding                                               |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010903 | negative regulation of very-low-density lipoprotein particle remodeling |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010804 | negative regulation of tumor necrosis factor-mediated signaling pathway |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0034380 | high-density lipoprotein particle assembly                              |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0007186 | G-protein coupled receptor signaling pathway                            |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0050821 | protein stabilization                                                   |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:0034361 | very-low-density lipoprotein particle                                   |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0032488 | Cdc42 protein signal transduction                                       |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0060354 | negative regulation of cell adhesion molecule production                |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0055091 | phospholipid homeostasis                                                |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0010873 | positive regulation of cholesterol esterification                       |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0017127 | cholesterol transporter activity                                        |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0019899 | enzyme binding                                                          |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:0070653 | high-density lipoprotein particle receptor binding                      |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:0070328 | triglyceride homeostasis                                                |

|              |                                                                        |        |              |                                                             |
|--------------|------------------------------------------------------------------------|--------|--------------|-------------------------------------------------------------|
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C      | GO:0034366   | spherical high-density<br>lipoprotein particle              |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P      | GO:0033700   | phospholipid efflux                                         |
| gi 215415638 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P      | GO:0051345   | positive regulation of hydrolase activity                   |
| KH 4         | 40044478                                                               | Fr III |              |                                                             |
| KH 5         | 194383496                                                              | Fr III | gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0032879   | regulation of localization                                  |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0048468   | cell development                                            |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:2000026   | regulation of multicellular organismal development          |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0010557   | positive regulation of macromolecule biosynthetic process   |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0030194   | positive regulation of blood coagulation                    |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | F      | GO:0005102   | receptor binding                                            |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0009967   | positive regulation of signal transduction                  |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | C      | GO:0005615   | extracellular space                                         |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0030168   | platelet activation                                         |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | F      | GO:0008236   | serine-type peptidase activity                              |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0016477   | cell migration                                              |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0006508   | proteolysis                                                 |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0001934   | positive regulation of protein phosphorylation              |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0007166   | cell surface receptor signaling pathway                     |

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|--------------|------------------------------------------------------------------------|--------|--------------|------------------------------------------------------------------------|
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0048523   | negative regulation of cellular process                                |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0006810   | transport                                                              |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0042730   | fibrinolysis                                                           |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | C      | GO:0005622   | intracellular                                                          |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0048731   | system development                                                     |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | C      | GO:0016020   | membrane                                                               |
| gi 194383496 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2            | P      | GO:0051480   | cytosolic calcium ion homeostasis                                      |
| KH 6         | 28071026                                                               | Fr III | gi 28071026  | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 |
| gi 28071026  | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | F      | GO:0005488   | binding                                                                |
| gi 28071026  | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | C      | GO:0044464   | cell part                                                              |
| gi 28071026  | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | C      | GO:0016020   | membrane                                                               |
| gi 28071026  | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | P      | GO:0006955   | immune response                                                        |
| KH 7         | 300621695                                                              | Fr III | gi 300621695 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 |
| gi 300621695 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | P      | GO:0006955   | immune response                                                        |
| KH 8         | 1335098                                                                | Fr III | gi 1335098   | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2             |
| gi 1335098   | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2             | P      | GO:0008152   | metabolic process                                                      |
| gi 1335098   | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2             | P      | GO:0051179   | localization                                                           |
| gi 1335098   | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2             | C      | GO:0005615   | extracellular space                                                    |

|                  |                                                                                                                       |        |                  |                                                                                                                       |
|------------------|-----------------------------------------------------------------------------------------------------------------------|--------|------------------|-----------------------------------------------------------------------------------------------------------------------|
| gi 1335098       | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | F      | GO:00055<br>15   | protein binding                                                                                                       |
| gi 1335098       | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | P      | GO:00485<br>22   | positive regulation of cellular<br>process                                                                            |
| gi 1335098       | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | P      | GO:00508<br>96   | response to stimulus                                                                                                  |
| KH 9             | 10434804                                                                                                              | Fr III | gi 1043480<br>4  | mthsd_humanmethenyltetrahydr<br>ofolate synthase domain-<br>containing protein os=homo<br>sapiens gn=mthfsd pe=1 sv=2 |
| gi 10434804      | mthsd_humanmethenyltetrahydr<br>ofolate synthase domain-<br>containing protein os=homo<br>sapiens gn=mthfsd pe=1 sv=2 | F      | GO:00055<br>24   | ATP binding                                                                                                           |
| gi 10434804      | mthsd_humanmethenyltetrahydr<br>ofolate synthase domain-<br>containing protein os=homo<br>sapiens gn=mthfsd pe=1 sv=2 | P      | GO:00093<br>96   | folic acid-containing compound<br>biosynthetic process                                                                |
| gi 10434804      | mthsd_humanmethenyltetrahydr<br>ofolate synthase domain-<br>containing protein os=homo<br>sapiens gn=mthfsd pe=1 sv=2 | F      | GO:00302<br>72   | 5-formyltetrahydrofolate cyclo-<br>ligase activity                                                                    |
| KH 10            | 221044726                                                                                                             | Fr III | gi 2210447<br>26 | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            |
| gi 22104472<br>6 | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | F      | GO:00055<br>15   | protein binding                                                                                                       |
| gi 22104472<br>6 | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | C      | GO:00056<br>15   | extracellular space                                                                                                   |
| gi 22104472<br>6 | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | P      | GO:00099<br>87   | cellular process                                                                                                      |
| gi 22104472<br>6 | hemo_humanhemopexin<br>os=homo sapiens gn=hpx pe=1<br>sv=2                                                            | P      | GO:00650<br>07   | biological regulation                                                                                                 |
| KH 11            | 215415638                                                                                                             | PCC    | same as<br>KH 3  |                                                                                                                       |
| KH 12            | 189066554                                                                                                             | PCC    | gi 1890665<br>54 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2                                                           |
| gi 18906655<br>4 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2                                                           | C      | GO:00444<br>46   | intracellular organelle part                                                                                          |
| gi 18906655<br>4 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2                                                           | P      | GO:00487<br>12   | negative regulation of astrocyte<br>differentiation                                                                   |
| gi 18906655<br>4 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2                                                           | C      | GO:00432<br>33   | organelle lumen                                                                                                       |

|              |                                                             |     |              |                                                                                                |
|--------------|-------------------------------------------------------------|-----|--------------|------------------------------------------------------------------------------------------------|
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0030194   | positive regulation of blood coagulation                                                       |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | F   | GO:0005102   | receptor binding                                                                               |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:2000379   | positive regulation of reactive oxygen species metabolic process                               |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0045861   | negative regulation of proteolysis                                                             |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C   | GO:0005615   | extracellular space                                                                            |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0030168   | platelet activation                                                                            |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:1900738   | positive regulation of phospholipase C-activating G-protein coupled receptor signaling pathway |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0016477   | cell migration                                                                                 |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C   | GO:0043231   | intracellular membrane-bounded organelle                                                       |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0001934   | positive regulation of protein phosphorylation                                                 |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C   | GO:0005886   | plasma membrane                                                                                |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | F   | GO:0070053   | thrombospondin receptor activity                                                               |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0051281   | positive regulation of release of sequestered calcium ion into cytosol                         |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | F   | GO:0004252   | serine-type endopeptidase activity                                                             |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0042730   | fibrinolysis                                                                                   |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C   | GO:0044444   | cytoplasmic part                                                                               |
| gi 189066554 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P   | GO:0032967   | positive regulation of collagen biosynthetic process                                           |
| KH 13        | 194391084                                                   | PCC | gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2                                  |

|              |                                                               |     |              |                                                               |
|--------------|---------------------------------------------------------------|-----|--------------|---------------------------------------------------------------|
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | F   | GO:0005515   | protein binding                                               |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0055065   | metal ion homeostasis                                         |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0051241   | negative regulation of multicellular organismal process       |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0007596   | blood coagulation                                             |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | C   | GO:0043229   | intracellular organelle                                       |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0048523   | negative regulation of cellular process                       |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0008152   | metabolic process                                             |
| gi 194391084 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0003008   | system process                                                |
| KH 14        | 158255114                                                     | PCC | gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | F   | GO:0005515   | protein binding                                               |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0055065   | metal ion homeostasis                                         |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0051241   | negative regulation of multicellular organismal process       |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0007596   | blood coagulation                                             |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | C   | GO:0043229   | intracellular organelle                                       |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0048523   | negative regulation of cellular process                       |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0008152   | metabolic process                                             |
| gi 158255114 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0003008   | system process                                                |
| KH 15        | 213506121                                                     | PCC | gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 |

|              |                                                               |     |              |                                                               |
|--------------|---------------------------------------------------------------|-----|--------------|---------------------------------------------------------------|
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | F   | GO:0005515   | protein binding                                               |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0055065   | metal ion homeostasis                                         |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0051241   | negative regulation of multicellular organismal process       |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0007596   | blood coagulation                                             |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | C   | GO:0043229   | intracellular organelle                                       |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0048523   | negative regulation of cellular process                       |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0008152   | metabolic process                                             |
| gi 213506121 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0003008   | system process                                                |
| KH 16        | 213506103                                                     | PCC | gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | F   | GO:0005515   | protein binding                                               |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0055065   | metal ion homeostasis                                         |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0051241   | negative regulation of multicellular organismal process       |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0007596   | blood coagulation                                             |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | C   | GO:0043229   | intracellular organelle                                       |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0048523   | negative regulation of cellular process                       |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0008152   | metabolic process                                             |
| gi 213506103 | kng1_humankininogen-1<br>os=homo sapiens gn=kng1 pe=1<br>sv=2 | P   | GO:0003008   | system process                                                |
| KH 17        | 194376310                                                     | PCC | gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1            |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1            | P   | GO:0009888   | tissue development                                            |

|              |                                                     |     |              |                                                     |
|--------------|-----------------------------------------------------|-----|--------------|-----------------------------------------------------|
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0030048   | actin filament-based movement                       |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0003012   | muscle system process                               |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | C   | GO:0030017   | sarcomere                                           |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0030239   | myofibril assembly                                  |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0044238   | primary metabolic process                           |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | C   | GO:0005884   | actin filament                                      |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0072358   | cardiovascular system development                   |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0044237   | cellular metabolic process                          |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0048513   | organ development                                   |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | F   | GO:0005515   | protein binding                                     |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0042221   | response to chemical stimulus                       |
| gi 194376310 | cytoplasmic 1 os=homo sapiens<br>gn=actb pe=1 sv=1  | P   | GO:0008015   | blood circulation                                   |
| KH 18        | 194388064                                           | PCC | gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0009888   | tissue development                                  |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0030048   | actin filament-based movement                       |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0003012   | muscle system process                               |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | C   | GO:0030017   | sarcomere                                           |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0030239   | myofibril assembly                                  |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0044238   | primary metabolic process                           |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | C   | GO:0005884   | actin filament                                      |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0072358   | cardiovascular system development                   |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0044237   | cellular metabolic process                          |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0048513   | organ development                                   |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0042221   | response to chemical stimulus                       |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | F   | GO:0008092   | cytoskeletal protein binding                        |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | P   | GO:0065008   | regulation of biological quality                    |
| gi 194388064 | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1 | C   | GO:0044451   | nucleoplasm part                                    |

|              |                                                                                                |      |             |                                                                                                |
|--------------|------------------------------------------------------------------------------------------------|------|-------------|------------------------------------------------------------------------------------------------|
| gi 194388064 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1                                               | P    | GO:0008015  | blood circulation                                                                              |
| gi 194388064 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1                                               | F    | GO:0019899  | enzyme binding                                                                                 |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | F    | GO:0005515  | protein binding                                                                                |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0055065  | metal ion homeostasis                                                                          |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0051241  | negative regulation of multicellular organismal process                                        |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0007596  | blood coagulation                                                                              |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | C    | GO:0043229  | intracellular organelle                                                                        |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0048523  | negative regulation of cellular process                                                        |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0008152  | metabolic process                                                                              |
| gi 194391084 | kng1_humankininogen-1 os=homo sapiens gn=kng1 pe=1 sv=2                                        | P    | GO:0003008  | system process                                                                                 |
| KH 19        | IPI00964149                                                                                    | PCC  | IPI00964149 | pacrl_humanpacrg-like protein os=homo sapiens gn=pacrgl pe=1 sv=2                              |
| KH 20        | IPI00966721                                                                                    | PCC  | IPI00966721 | ce028_humantransmembrane protein c5orf28 os=homo sapiens gn=c5orf28 pe=2 sv=1                  |
| IPI00966721  | ce028_humantransmembrane protein c5orf28 os=homo sapiens gn=c5orf28 pe=2 sv=1                  | C    | GO:0016021  | integral to membrane                                                                           |
| KH 21        | IPI00966826                                                                                    | FrIV | IPI00966826 | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 |
| IPI00966826  | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 | P    | GO:0008156  | negative regulation of DNA replication                                                         |
| IPI00966826  | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 | C    | GO:0005730  | nucleolus                                                                                      |
| IPI00966826  | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 | C    | GO:0000785  | chromatin                                                                                      |
| IPI00966826  | pds5a_humansister chromatid cohesion protein pds5 homolog a                                    | F    | GO:0005515  | protein binding                                                                                |

|             |                                                                                                |                        |               |                                                                       |
|-------------|------------------------------------------------------------------------------------------------|------------------------|---------------|-----------------------------------------------------------------------|
|             | os=homo sapiens gn=pds5a pe=1 sv=1                                                             |                        |               |                                                                       |
| IPI00966826 | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 | P                      | GO:0008283    | cell proliferation                                                    |
| IPI00966826 | pds5a_humansister chromatid cohesion protein pds5 homolog a os=homo sapiens gn=pds5a pe=1 sv=1 | C                      | GO:0005886    | plasma membrane                                                       |
| KH 22       | IPI00760788                                                                                    | FrIV                   | IPI00760788   | klh22_humankelch-like protein 22 os=homo sapiens gn=klhl22 pe=1 sv=2  |
| IPI00760788 | klh22_humankelch-like protein 22 os=homo sapiens gn=klhl22 pe=1 sv=2                           | P                      | GO:0051301    | cell division                                                         |
| IPI00760788 | klh22_humankelch-like protein 22 os=homo sapiens gn=klhl22 pe=1 sv=2                           | C                      | GO:0031463    | Cul3-RING ubiquitin ligase complex                                    |
| KH 23       | IPI00917278                                                                                    | FrIV                   |               |                                                                       |
| KH 24       | IPI00966721                                                                                    | Apolipoprotein complex | same as KH 20 |                                                                       |
| KH 25       | IPI01012037                                                                                    | Apolipoprotein complex | IPI01012037   | mcm8_humandna helicase mcm8 os=homo sapiens gn=mcm8 pe=1 sv=2         |
| IPI01012037 | mcm8_humandna helicase mcm8 os=homo sapiens gn=mcm8 pe=1 sv=2                                  | P                      | GO:0051329    | interphase of mitotic cell cycle                                      |
| IPI01012037 | mcm8_humandna helicase mcm8 os=homo sapiens gn=mcm8 pe=1 sv=2                                  | P                      | GO:0034645    | cellular macromolecule biosynthetic process                           |
| IPI01012037 | mcm8_humandna helicase mcm8 os=homo sapiens gn=mcm8 pe=1 sv=2                                  | P                      | GO:0090304    | nucleic acid metabolic process                                        |
| KH 26       | IPI00940730                                                                                    | Apolipoprotein complex | IPI00940730   | enoph_humanenolase-phosphatase e1 os=homo sapiens gn=enoph1 pe=1 sv=1 |
| IPI00940730 | enoph_humanenolase-phosphatase e1 os=homo sapiens gn=enoph1 pe=1 sv=1                          | P                      | GO:0019509    | L-methionine salvage from methylthioadenosine                         |
| IPI00940730 | enoph_humanenolase-phosphatase e1 os=homo sapiens gn=enoph1 pe=1 sv=1                          | F                      | GO:0043874    | acireductone synthase activity                                        |
| KH 27       | IPI00977191                                                                                    | Apolipoprotein complex |               |                                                                       |
| KH 28       | IPI00022434                                                                                    | HemoRAAS               | IPI00022434   | albu_humanserum albumin os=homo sapiens gn=alb pe=1 sv=2              |
| IPI00022434 | albu_humanserum albumin os=homo sapiens gn=alb pe=1 sv=2                                       | P                      | GO:0008202    | steroid metabolic process                                             |
| IPI00022434 | albu_humanserum albumin os=homo sapiens gn=alb pe=1 sv=2                                       | P                      | GO:0051704    | multi-organism process                                                |

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|-------------|----------------------------------------------------------------|---|----------------|-------------------------------------------------|
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | C | GO:00444<br>46 | intracellular organelle part                    |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00516<br>41 | cellular localization                           |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00517<br>16 | cellular response to stimulus                   |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | F | GO:00082<br>89 | lipid binding                                   |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00430<br>69 | negative regulation of<br>programmed cell death |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00442<br>60 | cellular macromolecule<br>metabolic process     |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00316<br>67 | response to nutrient levels                     |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | C | GO:00432<br>31 | intracellular membrane-bounded<br>organelle     |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00442<br>81 | small molecule metabolic<br>process             |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | F | GO:00055<br>15 | protein binding                                 |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00068<br>10 | transport                                       |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00650<br>08 | regulation of biological quality                |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00071<br>54 | cell communication                              |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | F | GO:00198<br>42 | vitamin binding                                 |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00069<br>50 | response to stress                              |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | C | GO:00444<br>44 | cytoplasmic part                                |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | P | GO:00325<br>01 | multicellular organismal process                |
| IPI00022434 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2 | C | GO:00444<br>21 | extracellular region part                       |

|             |                                                                   |           |               |                                                                   |
|-------------|-------------------------------------------------------------------|-----------|---------------|-------------------------------------------------------------------|
| KH 29       | IPI00022434                                                       | HemoRAAS  | same as KH 28 |                                                                   |
| KH 30       | IPI00219713                                                       | FibroRAAS | IPI00219713   | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | P         | GO:0009987    | cellular process                                                  |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | C         | GO:0009897    | external side of plasma membrane                                  |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | F         | GO:0043499    | eukaryotic cell surface binding                                   |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | C         | GO:0005615    | extracellular space                                               |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | C         | GO:0031091    | platelet alpha granule                                            |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | P         | GO:0032501    | multicellular organismal process                                  |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | P         | GO:0065007    | biological regulation                                             |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3 | P         | GO:0051592    | response to calcium ion                                           |
| KH 31       | IPI00219713                                                       | FibroRAAS | same as KH 30 |                                                                   |
| KH 32       | IPI00220327                                                       | FibroRAAS | IPI00220327   | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | P         | GO:0009987    | cellular process                                                  |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | P         | GO:0048731    | system development                                                |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | P         | GO:0009888    | tissue development                                                |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | C         | GO:0005856    | cytoskeleton                                                      |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | F         | GO:0005515    | protein binding                                                   |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | P         | GO:0001867    | complement activation, lectin pathway                             |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | F         | GO:0030246    | carbohydrate binding                                              |
| IPI00220327 | type ii cytoskeletal 1 os=homo sapiens gn=krt1 pe=1 sv=6          | C         | GO:0016020    | membrane                                                          |
| KH 33       | IPI00029739                                                       | GammaRAAS | IPI00029739   | cfah_humancomplement factor h os=homo sapiens gn=cfh pe=1 sv=4    |
| IPI00029739 | cfah_humancomplement factor h os=homo sapiens gn=cfh pe=1 sv=4    | P         | GO:0030449    | regulation of complement activation                               |

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| IPI00029739 | cfah_humancomplement factor h<br>os=homo sapiens gn=cfh pe=1<br>sv=4   | P         | GO:00450<br>87  | innate immune response                                                 |
| KH 34       | IPI00384853                                                            | GammaRAAS |                 |                                                                        |
| KH 35       | IPI00479708                                                            | GammaRAAS | IPI004797<br>08 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 |
| IPI00479708 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | F         | GO:00054<br>88  | binding                                                                |
| IPI00479708 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | C         | GO:00444<br>64  | cell part                                                              |
| IPI00479708 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | C         | GO:00160<br>20  | membrane                                                               |
| IPI00479708 | ighm_humanig mu chain c region<br>os=homo sapiens gn=ighm pe=1<br>sv=3 | P         | GO:00069<br>55  | immune response                                                        |
| KH 36       | IPI00298497                                                            | GammaRAAS | IPI002984<br>97 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | F         | GO:00510<br>87  | chaperone binding                                                      |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | P         | GO:00515<br>92  | response to calcium ion                                                |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | C         | GO:00056<br>15  | extracellular space                                                    |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | P         | GO:00511<br>79  | localization                                                           |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | C         | GO:00310<br>91  | platelet alpha granule                                                 |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | C         | GO:00098<br>97  | external side of plasma<br>membrane                                    |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | P         | GO:00507<br>94  | regulation of cellular process                                         |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | P         | GO:00069<br>50  | response to stress                                                     |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | F         | GO:00434<br>99  | eukaryotic cell surface binding                                        |
| IPI00298497 | fibb_humanfibrinogen beta chain<br>os=homo sapiens gn=fgb pe=1<br>sv=2 | P         | GO:00325<br>01  | multicellular organismal process                                       |
| KH 37       | IPI00021841                                                            | GammaRAAS | IPI000218<br>41 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 |

|             |                                                                        |   |                |                                                                             |
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| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00705<br>08 | cholesterol import                                                          |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:00301<br>39 | endocytic vesicle                                                           |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00507<br>28 | negative regulation of<br>inflammatory response                             |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00333<br>44 | cholesterol efflux                                                          |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00341<br>15 | negative regulation of<br>heterotypic cell-cell adhesion                    |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00182<br>06 | peptidyl-methionine<br>modification                                         |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00421<br>57 | lipoprotein metabolic process                                               |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00436<br>91 | reverse cholesterol transport                                               |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00055<br>43 | phospholipid binding                                                        |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00027<br>40 | negative regulation of cytokine<br>secretion involved in immune<br>response |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00082<br>03 | cholesterol metabolic process                                               |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00507<br>13 | negative regulation of<br>interleukin-1 beta secretion                      |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00181<br>58 | protein oxidation                                                           |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00066<br>56 | phosphatidylcholine biosynthetic<br>process                                 |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00015<br>40 | beta-amyloid binding                                                        |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00602<br>28 | phosphatidylcholine-sterol O-<br>acyltransferase activator activity         |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00426<br>32 | cholesterol homeostasis                                                     |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00154<br>85 | cholesterol binding                                                         |

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| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00420<br>60 | wound healing                                                                  |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00341<br>91 | apolipoprotein A-I receptor<br>binding                                         |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00428<br>02 | identical protein binding                                                      |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00109<br>03 | negative regulation of very-low-<br>density lipoprotein particle<br>remodeling |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00108<br>04 | negative regulation of tumor<br>necrosis factor-mediated<br>signaling pathway  |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00343<br>80 | high-density lipoprotein particle<br>assembly                                  |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00071<br>86 | G-protein coupled receptor<br>signaling pathway                                |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00508<br>21 | protein stabilization                                                          |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:00343<br>61 | very-low-density lipoprotein<br>particle                                       |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00324<br>88 | Cdc42 protein signal<br>transduction                                           |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00603<br>54 | negative regulation of cell<br>adhesion molecule production                    |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00550<br>91 | phospholipid homeostasis                                                       |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00108<br>73 | positive regulation of cholesterol<br>esterification                           |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00171<br>27 | cholesterol transporter activity                                               |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00198<br>99 | enzyme binding                                                                 |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | F | GO:00706<br>53 | high-density lipoprotein particle<br>receptor binding                          |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | P | GO:00703<br>28 | triglyceride homeostasis                                                       |
| IPI00021841 | apoal_humanapolipoprotein a-i<br>os=homo sapiens gn=apoal pe=1<br>sv=1 | C | GO:00343<br>66 | spherical high-density<br>lipoprotein particle                                 |

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|-------------|------------------------------------------------------------------------|------|-----------------|-------------------------------------------------------------------------|
| IPI00021841 | apoA1_humanapolipoprotein a-i<br>os=homo sapiens gn=apoA1 pe=1<br>sv=1 | P    | GO:00337<br>00  | phospholipid efflux                                                     |
| IPI00021841 | apoA1_humanapolipoprotein a-i<br>os=homo sapiens gn=apoA1 pe=1<br>sv=1 | P    | GO:00513<br>45  | positive regulation of hydrolase<br>activity                            |
| KH 38       | IPI00783987                                                            | AFCC | IPI007839<br>87 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2            |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | C    | GO:00444<br>64  | cell part                                                               |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | P    | GO:00105<br>75  | positive regulation vascular<br>endothelial growth factor<br>production |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | P    | GO:00304<br>49  | regulation of complement<br>activation                                  |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | P    | GO:00071<br>65  | signal transduction                                                     |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | P    | GO:00450<br>87  | innate immune response                                                  |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | F    | GO:00055<br>15  | protein binding                                                         |
| IPI00783987 | co3_humancomplement c3<br>os=homo sapiens gn=c3 pe=1<br>sv=2           | C    | GO:00160<br>20  | membrane                                                                |
| KH 39       | IPI00878282                                                            | AFCC | IPI008782<br>82 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2          |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | P    | GO:00082<br>02  | steroid metabolic process                                               |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | F    | GO:00510<br>87  | chaperone binding                                                       |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | C    | GO:00444<br>46  | intracellular organelle part                                            |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | F    | GO:00156<br>43  | toxin binding                                                           |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | P    | GO:00442<br>60  | cellular macromolecule<br>metabolic process                             |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | C    | GO:00056<br>15  | extracellular space                                                     |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2         | P    | GO:00516<br>59  | maintenance of mitochondrion<br>location                                |

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| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | F | GO:00081<br>44 | drug binding                                  |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | C | GO:00432<br>31 | intracellular membrane-bounded<br>organelle   |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00442<br>81 | small molecule metabolic<br>process           |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | F | GO:00055<br>04 | fatty acid binding                            |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00422<br>21 | response to chemical stimulus                 |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | F | GO:00036<br>77 | DNA binding                                   |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00092<br>67 | cellular response to starvation               |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | F | GO:00301<br>70 | pyridoxal phosphate binding                   |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00068<br>10 | transport                                     |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | F | GO:00198<br>25 | oxygen binding                                |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00508<br>78 | regulation of body fluid levels               |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00430<br>66 | negative regulation of apoptotic<br>process   |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | C | GO:00444<br>44 | cytoplasmic part                              |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00096<br>11 | response to wounding                          |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00198<br>36 | hemolysis by symbiont of host<br>erythrocytes |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | P | GO:00069<br>55 | immune response                               |
| IPI00878282 | albu_humanserum albumin<br>os=homo sapiens gn=alb pe=1<br>sv=2                | C | GO:00198<br>14 | immunoglobulin complex                        |
| IPI00784842 | ighg1_humanig gamma-1 chain c<br>region os=homo sapiens<br>gn=ighg1 pe=1 sv=1 | P | GO:00507<br>76 | regulation of immune response                 |

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| IPI00784842 | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 | F                              | GO:0005515    | protein binding                                                         |
| KH 40       | IPI00784842                                                             | AFCC                           | IPI00784842   | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 |
| IPI00784842 | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 | P                              | GO:0050776    | regulation of immune response                                           |
| IPI00784842 | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 | F                              | GO:0005515    | protein binding                                                         |
| KH 41       | IPI00022434                                                             | Fraction III-II                | same as KH 28 |                                                                         |
| KH 42       | IPI00298497                                                             | Fraction III                   | same as KH 36 |                                                                         |
| KH 43       | IPI00965713                                                             | Fraction III                   | IPI00965713   | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | P                              | GO:0042221    | response to chemical stimulus                                           |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | F                              | GO:0005515    | protein binding                                                         |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | C                              | GO:0005615    | extracellular space                                                     |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | P                              | GO:0051179    | localization                                                            |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | C                              | GO:0031091    | platelet alpha granule                                                  |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | C                              | GO:0044425    | membrane part                                                           |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | P                              | GO:0050794    | regulation of cellular process                                          |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | P                              | GO:0006950    | response to stress                                                      |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | C                              | GO:0005886    | plasma membrane                                                         |
| IPI00965713 | fibb_humanfibrinogen beta chain os=homo sapiens gn=fgb pe=1 sv=2        | P                              | GO:0032501    | multicellular organismal process                                        |
| KH 44       | IPI00645363                                                             | FibringluRAA S® Human Thrombin | IPI00645363   | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 |
| IPI00645363 | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 | P                              | GO:0050776    | regulation of immune response                                           |

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| IPI00645363 | ighg1_humanig gamma-1 chain c region os=homo sapiens gn=ighg1 pe=1 sv=1 | F                              | GO:0005515    | protein binding                                                       |
| KH 45       | IPI00219713                                                             | FibringluRAA S® Human Thrombin | same as KH 30 |                                                                       |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | P                              | GO:0009987    | cellular process                                                      |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | C                              | GO:0009897    | external side of plasma membrane                                      |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | F                              | GO:0043499    | eukaryotic cell surface binding                                       |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | C                              | GO:0005615    | extracellular space                                                   |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | C                              | GO:0031091    | platelet alpha granule                                                |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | P                              | GO:0032501    | multicellular organismal process                                      |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | P                              | GO:0065007    | biological regulation                                                 |
| IPI00219713 | fibg_humanfibrinogen gamma chain os=homo sapiens gn=fgg pe=1 sv=3       | P                              | GO:0051592    | response to calcium ion                                               |
| KH 46       | IPI00022371                                                             | FibringluRAA S® Human Thrombin | IPI00022371   | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0043065    | positive regulation of apoptotic process                              |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0010468    | regulation of gene expression                                         |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0032956    | regulation of actin cytoskeleton organization                         |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0016525    | negative regulation of angiogenesis                                   |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:2000504    | positive regulation of blood vessel remodeling                        |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0043254    | regulation of protein complex assembly                                |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1   | P                              | GO:0002839    | positive regulation of immune response to tumor cell                  |

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| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0008201 | heparin binding                                                             |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0010593 | negative regulation of lamellipodium assembly                               |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0050832 | defense response to fungus                                                  |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0020037 | heme binding                                                                |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0019865 | immunoglobulin binding                                                      |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0030168 | platelet activation                                                         |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0043395 | heparan sulfate proteoglycan binding                                        |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:1900747 | negative regulation of vascular endothelial growth factor signaling pathway |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0008270 | zinc ion binding                                                            |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | F | GO:0043498 | cell surface binding                                                        |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:2001027 | negative regulation of endothelial cell chemotaxis                          |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0008285 | negative regulation of cell proliferation                                   |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0051894 | positive regulation of focal adhesion assembly                              |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0030193 | regulation of blood coagulation                                             |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0050730 | regulation of peptidyl-tyrosine phosphorylation                             |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0033629 | negative regulation of cell adhesion mediated by integrin                   |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | P | GO:0030308 | negative regulation of cell growth                                          |
| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | C | GO:0005576 | extracellular region                                                        |

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| IPI00022371 | hrg_humanhistidine-rich glycoprotein os=homo sapiens gn=hrg pe=1 sv=1 | C                           | GO:0019814    | immunoglobulin complex                                    |
| KH 47       | IPI00022371                                                           | Fibrinolytic Human Thrombin | same as KH 46 |                                                           |
| KH 48       | IPI00022463                                                           | AFOD                        | IPI00022463   | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3 |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | P                           | GO:0009987    | cellular process                                          |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | P                           | GO:0065008    | regulation of biological quality                          |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | P                           | GO:0006810    | transport                                                 |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0009925    | basal plasma membrane                                     |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0005739    | mitochondrion                                             |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0030139    | endocytic vesicle                                         |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0005905    | coated pit                                                |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0005770    | late endosome                                             |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0005769    | early endosome                                            |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0055037    | recycling endosome                                        |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | F                           | GO:0005515    | protein binding                                           |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0048471    | perinuclear region of cytoplasm                           |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | C                           | GO:0016324    | apical plasma membrane                                    |
| IPI00022463 | trfe_humanserotransferrin os=homo sapiens gn=tf pe=1 sv=3             | P                           | GO:0006950    | response to stress                                        |
| KH 49       | IPI00023006                                                           | AFOD                        | IPI00023006   | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1             | C                           | GO:0005865    | striated muscle thin filament                             |

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| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | F                                                 | GO:0017022    | myosin binding                                   |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0030240    | skeletal muscle thin filament assembly           |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0006200    | ATP catabolic process                            |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0072144    | glomerular mesangial cell development            |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0006936    | muscle contraction                               |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0033275    | actin-myosin filament sliding                    |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | C                                                 | GO:0042643    | actomyosin, actin part                           |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0042221    | response to chemical stimulus                    |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | F                                                 | GO:0005524    | ATP binding                                      |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | C                                                 | GO:0001725    | stress fiber                                     |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | F                                                 | GO:0016887    | ATPase activity                                  |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0065008    | regulation of biological quality                 |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | C                                                 | GO:0044451    | nucleoplasm part                                 |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0009615    | response to virus                                |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | P                                                 | GO:0060047    | heart contraction                                |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | F                                                 | GO:0019899    | enzyme binding                                   |
| IPI00023006 | alpha cardiac muscle 1 os=homo sapiens gn=actc1 pe=1 sv=1 | C                                                 | GO:0016459    | myosin complex                                   |
| KH 50       | IPI00021841                                               | AFOD                                              | same as KH 37 |                                                  |
| KH 51       | IPI00023006                                               | AlbuRAAS                                          | same as KH 49 |                                                  |
| KH 52       | IPI00930226                                               | FibringluRAA S® High Concentrate Human Fibrinogen | IPI00930226   | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1 |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | P                                                 | GO:0009888    | tissue development                               |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | P                                                 | GO:0030048    | actin filament-based movement                    |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | P                                                 | GO:0003012    | muscle system process                            |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | C                                                 | GO:0030017    | sarcomere                                        |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | P                                                 | GO:0030239    | myofibril assembly                               |
| IPI00930226 | cytoplasmic 2 os=homo sapiens gn=actg1 pe=1 sv=1          | P                                                 | GO:0044238    | primary metabolic process                        |

|                  |                                                             |                       |                  |                                                                                                          |
|------------------|-------------------------------------------------------------|-----------------------|------------------|----------------------------------------------------------------------------------------------------------|
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | C                     | GO:00058<br>84   | actin filament                                                                                           |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00723<br>58   | cardiovascular system<br>development                                                                     |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00442<br>37   | cellular metabolic process                                                                               |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00485<br>13   | organ development                                                                                        |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00422<br>21   | response to chemical stimulus                                                                            |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | F                     | GO:00080<br>92   | cytoskeletal protein binding                                                                             |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00650<br>08   | regulation of biological quality                                                                         |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | C                     | GO:00444<br>51   | nucleoplasm part                                                                                         |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | P                     | GO:00080<br>15   | blood circulation                                                                                        |
| IPI00930226      | cytoplasmic 2 os=homo sapiens<br>gn=actg1 pe=1 sv=1         | F                     | GO:00198<br>99   | enzyme binding                                                                                           |
| KH 53            | 194373497                                                   | AFCC<br>(Fraction IV) | gi 1943734<br>97 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2                                              |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C                     | GO:00444<br>46   | intracellular organelle part                                                                             |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:00487<br>12   | negative regulation of astrocyte<br>differentiation                                                      |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C                     | GO:00432<br>33   | organelle lumen                                                                                          |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:00301<br>94   | positive regulation of blood<br>coagulation                                                              |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | F                     | GO:00051<br>02   | receptor binding                                                                                         |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:20003<br>79   | positive regulation of reactive<br>oxygen species metabolic<br>process                                   |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:00458<br>61   | negative regulation of proteolysis                                                                       |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | C                     | GO:00056<br>15   | extracellular space                                                                                      |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:00301<br>68   | platelet activation                                                                                      |
| gi 19437349<br>7 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2 | P                     | GO:19007<br>38   | positive regulation of<br>phospholipase C-activating G-<br>protein coupled receptor<br>signaling pathway |

|              |                                                                 |             |              |                                                                        |
|--------------|-----------------------------------------------------------------|-------------|--------------|------------------------------------------------------------------------|
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | P           | GO:0016477   | cell migration                                                         |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | C           | GO:0043231   | intracellular membrane-bounded organelle                               |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | P           | GO:0001934   | positive regulation of protein phosphorylation                         |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | C           | GO:0005886   | plasma membrane                                                        |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | F           | GO:0070053   | thrombospondin receptor activity                                       |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | P           | GO:0051281   | positive regulation of release of sequestered calcium ion into cytosol |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | F           | GO:0004252   | serine-type endopeptidase activity                                     |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | P           | GO:0042730   | fibrinolysis                                                           |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | C           | GO:0044444   | cytoplasmic part                                                       |
| gi 194373497 | thrb_humanprothrombin<br>os=homo sapiens gn=f2 pe=1<br>sv=2     | P           | GO:0032967   | positive regulation of collagen biosynthetic process                   |
| KH 54        | 194380034                                                       | Transferrin | gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3        |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | P           | GO:0009987   | cellular process                                                       |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | P           | GO:0065008   | regulation of biological quality                                       |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | P           | GO:0006810   | transport                                                              |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0009925   | basal plasma membrane                                                  |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0005739   | mitochondrion                                                          |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0030139   | endocytic vesicle                                                      |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0005905   | coated pit                                                             |

|              |                                                                 |             |                  |                                 |
|--------------|-----------------------------------------------------------------|-------------|------------------|---------------------------------|
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0005770       | late endosome                   |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0005769       | early endosome                  |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0055037       | recycling endosome              |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | F           | GO:0005515       | protein binding                 |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0048471       | perinuclear region of cytoplasm |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | C           | GO:0016324       | apical plasma membrane          |
| gi 194380034 | trfe_humanserotransferrin<br>os=homo sapiens gn=tf pe=1<br>sv=3 | P           | GO:0006950       | response to stress              |
| KH 55        | 194380034                                                       | Transferrin | same as<br>KH 54 |                                 |

Additional protein sequence information as well as sequence identifiers and accession numbers for KH proteins 1-55 are found in the table below.

| KH Protein/SEQ ID NO | Sequence Identifier(s)     | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----------------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1                    | gi:21749960<br>BAC03696.1  | MDTYIESHFA GALAYRDLIK VLKWYVDRIE EAERQEHIQE VLKAQEYIFK YIVQSRRLFS 60<br>LATGGQNEEE FRCCIQELLM SVRFFLSQES KGSGALSQSQ AVFLSSFPAY YSELLKLFDV 120<br>REVANLVQDT LGSLEPTILHV DDSLQAIKLQ CIGKTVESQL YTNPDSTRYIL LPVVLHHLHI 180<br>HLQEQKDLIM CARILSNVFC LIKKNSSEKS VLEEIDVIVA SLLDILLRTI LEITSRPQPS 240<br>SSAMRFQFQD VTGEFVACLL SLLRQMTDRH YQQLLDSFNT KEELRDFLLQ IFTVFRILIR 300<br>PEMFPKDWTM MRLVANNVIL TTVLYLSDAL RKNFLNENFD YKIWDSEYFYL AVIFINQLCL 360<br>QLEMFTPSKK KKVLEKYGDM RVTMGCEIFS MWQNLGEHKL HFIPALIGPF LEVTLIPQPD 420<br>LRNVMIPFIH DMMDWEQRRS GNFKQVEAKL IDKLDSLMS EGEDETYREL FNSIIPLFGP 480<br>YPSLLKKIER ETWRESGVSL IATVTRLMER LLDYRDCMKM GEVDGKKIGC TVSLLNFYKT 540<br>ELNKEEMYIR YIHKLYDLHL KAQNFTEAAY TLLLYDELLE WSDRPLREFL TYPMQTEWQR 600<br>KEHLHLTIIQ NFDRGKCWEN GIILCRKIAE QYESYYDYRN LSKMRMMEAS LYDKIMDQQR 660<br>LEPEFFRVGF YGKKFPFFLR NKEFVCRGHD YERLEAFQQR MLNEFPFAIA MQHANQPDET 720<br>IFQAEAQYLQ IYAVTPIPES QEVLRQREGVP DNIKSFYKVN HIWKFRYDRP FHKGT 775 |
| 2                    | gi:215415640<br>CAT02162.1 | DEPPQSPWDR VKDLATVYVD VLKDSGRDYV SQFEQSALGK QLNKLLDNW DSVTSTFSKL 60<br>REQLGPVTQE FWDNLEKETE GLRQEMSKDL EEVKAKVQPY LDDFQKKWQE EMELYRQKVE 120<br>PLRAELQEGA RQKLHELQEK LSPLGEEMRD CARAHVDALR THLAPYDEL RQRLAARLEA 180<br>LKENG GARLA EYHAKATEHL STLSEKAKPA LEDLRQGLLP VLESFKVSFL SALEEYTKKL 240<br>N 241                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 3                    | gi:215415638<br>CAT02161.1 | DEPPQSPWDR VKDLATVYVD VLKDSGRDYV SQFEQSALGK QLNKLLDNW DSVTSTFSKL 60<br>REQLGPVTQE FWDNLEKETE GLCQEMSKDL EEVKAKVQPY LDDFQKKWQE EMELYRQKVE 120<br>PLRAELQEGA RQKLHELQEK LSPLGEEMRD RARAHVDALR THLAPYDEL RQRLAARLEA 180<br>LKENG GARLA EYHAKATEHL STLSEKAKPA LEDLRQGLLP VLESFKVSFL SALEEYTKKL 240<br>NTQ 243                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 4                    | gi: 40044478<br>CAF01015.1 | MGCKRASEVC GXAVEGLRDP LKPSEPSQGA AGKRKGTEYL MKQKLEFGGR GEELLLGVHL 60<br>RGAQKTGGGW RR 72                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 5                    | gi:194383496<br>BAG64719.1 | TATDVFWAKY TACETARTPR DKLAACLEGN CAEGLGTNYR GHVNITRSGI ECQLWRSRYP 120<br>HKPEINSTTH PGADLQENFC RNPDSSTTGP WCYTDTPTVR RQECSTPVCV QDQVTVAMTP 180<br>RSEGSSVNLS PPLEQCVPDR GQQYQGR LAV TTHGLPCLAW ASAQAKALSK HQDFNSAVQL 240<br>VENFCRNPDG DEEGVWCYVA GKPGDFGYCD LNYCEEAVEE ETGDGLDEDS DRAIEGRTAT 300<br>SEYQTTFFNR TFGSGEADCG LRPLFEKKSL EDKTERELLE SYIDGRIVEG SDAEIGMSPW 360<br>QVMLFRKSPQ ELLCGASLIS DRWVLTAAHC LLYPPWDKNF TENDLLVRIG KHSRTRYERN 420<br>IEKISMLEKI YIHPRYNWRE NLDRDIALMK LKPKVAFSDY IHPVCLPDRE TAASLLQAGY 480<br>KGRVTGWGNL KETWTANVGK GQPSVLQVVN LPIVERPVCK DSTRIRITDN MFCAGYKPDE 540<br>GKRGDACEGD SGGPFVMKSP FNNRWYQMG I VSWGEGCDRD GKYGFYTHVF RLKKWIQKVI 600<br>DQFGE 605                                                                                                                                                                                                                                                                                   |
| 6                    | gi:28071026<br>CAD61894.1  | MQGTDEHVVC KVQHPNGNKE KNVPLPVIAE LPPKVSFVFP PRDGFFGNPR KSKLICQATG 60<br>FSPRQIQVSW LREGKQVGSG VTTDQVQAEA KESGPTTYKV TSTLTIKESD WLSQSMFTCR 120<br>VDHRGLTFQQ NASSMCGPDQ DTAIRVFAIP PSFASIFLTK STKLTCLVTD LTTYDSVTIS 180<br>WTRQNGEAVK THTNISESHP NATFSAVGEA SICEDDWNSG ERFTCTVTHT DLPSPLKQTI 240<br>SRPKGVALHR PDVYLLPPAR EQLNLRESAT ITCLVTGFSP ADVFVQWMQR GQPLSPEKYV 300<br>TSAPMPEPQA PGRYFAHSIL TVSEEEWNTG ETYTCVVAHE ALPNRV TERT VDKSTGKPTL 360<br>YNVSLVMSDT AGTCY 375                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 7                    | gi:300621695<br>CBU30464.1 | MEFGLSWLFL VAILKGVQCE VQLLESGGGL VQPGGSLRLS CAASGFTFSS YAMSWVRQAP 60<br>GKGLEWVSAI SSGYTTYTA DSVKGRFTIS RDNSKNTLYL QMNSLRAEDT AVYYCAKKPG 120<br>DYSGSGSYLD YWQGQTLTVT SSGSASAPTL FPLVSCENSP SDTSSVAVGC LAQDFLPDSI 180<br>TFSWKYKNN DISSTRGFPS VLRGGKYAAT SQVLLPSKDV MQGTDEHVVC KVQHPNGNKE 240<br>KNVPLPVIAE LPPKVSFVFP PRDGFFGNPR KSKLICQATG FSPRQIQVSW LREGKQVGSG 300<br>VTTDQVQAEA KESGPTTYKV TSTLTIKESD WLSQSMFTCR VDHRGLTFQQ NASSMCGPDQ 360<br>DTAIRVFAIP PSFASIFLTK STKLTCLVTD LTTYDSVTIS WTRQNGEAVK THTNISESHP 420<br>NATFSAVGEA SICEDDWNSG ERFTCTVTHT DLPSPLKQTI SRPKGVALHR PDVYLLPPAR 480<br>EQLNLRESAT ITCLVTGFSP ADVFVQWMQR GQPLSPEKYV TSAPMPEPQA PGRYFAHSIL 540<br>TVSEEEWNTG ETYTCVVAHE ALPNRV TERT VDKSTGKPTL YNVSLVMSDT AGTCY 595                                                                                                                                                                                                                                |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)  | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|----------------------------|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 8                          | gi:1335098<br>CAA26382.1   | TPLPPTSAHG NVAEGETKPD PDVTERCSDG WSFDATTLDD NGTMLFFKGE FVWKSHKWDR 60<br>ELISERWKNF PSPVDAAFRQ GHNSVFLIKG DKVWVYPPEK KEKGYPKLLQ DEFPGIPSP 120<br>DAAVECHRGE CQAEGLVFFQ GDREWFWDLA TGTMKERSWP AVGNCSSALR WLGRYYCFQG 180<br>NQFLRFDPVR GEVPPRYPRD VRDYFMPCPG RGHGHRNGTG HGNSTHHGPE YMRCSPHLVL 240<br>SALTSDNHGA TYAFSGTHYW RLDTSRDGWH SWPIAHQWPQ GPSAVDAAFS WEEKLYLVQG 300<br>TQVYVFLTKG GYTLVSGYPK RLEKEVGTPH GIILDSVDAA FICPGSSRLH IMAGRRLWWL 360<br>DLKSGAQATW TELPWPHEKV DGALCMEKSL GPNSCSANGP GLYLIHGPNL YCYSDVEKLN 420<br>AAKALPQPQN VTSLLGCTH 439                                                                                                                                                                                                                                 |
| 9                          | gi:10434804<br>BAB14383.1  | MEPRAVGVSQ QDIREQIWGY MESQNLADFP RRVHHRIPNF KGSYLACQNI KDLDVFARAQ 60<br>EVKVDPAKPL EGVRLVLVQS KKTLLVPTPR LRTGLFNKIT PPPGATKDIL RKCATSQGVR 120<br>NYSVPIGLDS RVLVDLVVVG SVAASEKGWR IGKGEYADL EYAMMVSMGA VSKETPVVTI 180<br>VHDCQVVDIP EELVEEHDIT VDYILTPTRV IATGCKRPPK MGITWFKISL EMMEKIPILR 240<br>SLRAREQQAG KDVTLQGEHQ HLPEPGCQQT VPLSVGRRPP DTPGPETNSM EAAPGSPPGE 300<br>GAPLAADVIV GNLPRDARVS DLKRALRELG SVPLRLTWQG PRRRAFLHYP DSAAASRPSP 360<br>ACRACAWAPT P 371                                                                                                                                                                                                                                                                                                                  |
| 10                         | gi:221044726<br>BAH14040.1 | MARVLGAPVA LGLWSLCWSL AIATPLPPTS AHGNVAEGET KPDPDVTERC SDGWSFDATT 60<br>LDDNGTMLFF KGEFVWKSHK WDRELISERL KNFPSPVDAA FRQGHNSVFL IKVLLGQNQG 120<br>QAGKGWNRHW GPFPMALAW SP 142                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 11                         | gi:215415638<br>CAT02161.1 | Same as KH3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 12                         | gi:189066554<br>BAG35804.1 | MAHVRGLQLP GCLALAALCS LVHSQHVFLA PQQARSLQVR VRRANTFLEE VRKGNLEREC 60<br>VEETCSYEAA FEALESSTAT DVFWAKYTAC ETARTPRDKL AACLEGNCAE GLGTNYRGHV 120<br>NITRSGIECQ LWRSPYHPKP EINSTTHPGA DLQENFCRNP DSSTMGPWCY TTDPTVRRQE 180<br>CSIPVCGQDQ VTVAMTPRSE GSSVNLSPPL EQCVPDRGQQ YQGR LAVTTH GLPCLAWASA 240<br>QAKALSKHQD FNSAVQLVEN FCRNPDGDEE GVWCYVAGKP GDFGYCDLNY CEEAVEEETG 300<br>DGLDESDRA IEGRTATSEY QTFFNPRTFG SGEADCGLRP LFEKKSLEDK TERELLESYI 360<br>DGRIVEGSDA EIGMSPWQVM LFRKSPQELL CGASLISDRW VLTAAHCLLY PPWDKNFTEN 420<br>DLLVRIGKHS RTRYERNIEK ISMLEKIYIH PRYNWRENLD RDIALMKLKK PVAFSDYIHP 480<br>VCLPDRETAA SLLQAGYKGR VTGWGNLKET WTANVGKGQP SVLQVVNLPI VERPVCKDST 540<br>RIRITDNMFC AGYKPDEGKR GDACEGDSGG PFVMKSPFNN RWYQMGIVSW GEGCDRDGKY 600<br>GFYTHVFLRK KWIQKVIDQF GE 622 |
| 13                         | gi:194391084<br>BAG60660.1 | MKLSLTQESQ SEEIDCNDKD LFKAVDAALK KYNSQNQSNQ QFVLYRITEA TKTVGS DTFY 60<br>SFKYEIKEGD CPVQSGKTWQ DCEYKDAAKA ATGECTATVG KRSSTKFSVA TQTCQITPAE 120<br>GPVVTAQYDC LGCVHPISQ SPDLEPILRH GIQYFNNNTQ HSSLFMLNEV KRAQRQVVAG 180<br>LNFRITYSIV QTNC SKENFL FLTPDCKSLW NGDTGECTDN AYIDIQLRIA SFSQNC DIYP 240<br>GKDFVQPPK ICVGCPRDIP TNSPELEETL THTITKLNAE NNATFYFKID NVKKARVQVV 300<br>AGKKYFIDFV ARETTCSKES NEELTESCET KKLQSLDCN AEVYVVPWEK KIYPTVNCQP 360<br>LGMISLMKRP PGFSPFRSSR IGEIKEETTS HLRSC EYKGR PPKAGAEPAS EREVS 415                                                                                                                                                                                                                                                                |
| 14                         | gi:158255114<br>BAF83528.1 | MKLITILFLC SRRLLSLTQE SQSEEIDCND KDFFKAVDAA LKKYNSQNQS NNQFVLYRIT 60<br>EATKTVGSDT FYSFKYEIKE GDCEYKDAA WQDCEYKDAA KAATGECTAT VGKRSSTKFS 120<br>VATQTCQITP AEGPVVTAQY DCLGCVHPIS TQSPDLEPIL RHGIQYFNNN TQHSSLFMLN 180<br>EVKRAQRQVV AGLNFRITYS IVQTNC SKEN FLFLTPDCKS LWNGDTGECT DNAYIDIQLR 240<br>IASFSQNC DI YPGKDFVQPP TKICVGCPRD IPTNSPELEE TLTHTITKLN AENNATFYFK 300<br>IDNVKKARVQ AVAGKKYFID FVARETTCSK ESNEELTESC ETKKLQSLD CNAEVYVVPW 360<br>EKKIYPTVNC QPLGMISLMK RPPGFSPFRS SRIGEIKEET TSHLRSC EYK GRPPKAGAEP 420<br>ASEREVS 427                                                                                                                                                                                                                                            |
| 15                         | gi:213506121<br>CAS91511.1 | MKLITILFLC SRRLLSLTQE SQSEEIDCND KDLFKAVDAA LKKYNSQNQS NNQFVLYRIT 60<br>EATKTVGSDT FYSFKYEIKE GDCEYKDAA WQDCEYKDAA KAATGECTAT VGKRSSTKFS 120<br>VATQTCQITP AEGPVVTAQY DCLGCVHPIS TQSPDLEPIL RHGIQYFNNN TQHSSLFMLN 180<br>EVKRAQRQVV AGLNFRMTYS IVQTNC SKEN FLFLTPDCKS LWNGDTGECT DNAYIDIQLR 240<br>IASFSQNC DI YPGKDFVQPP TKICVGCPRD IPTNSPELEE TLTHTITKLN AENNATFYFK 300<br>IDNVKKARVQ VVAGKKYFID FVARETTCSK ESNEELTESC ETKKLQSLD CNAEVYVVPW 360<br>EKKIYPTVNC QPLGMISLMK RPPGFSPFRS SRIGEIKEET TSHLRSC EYK GRPPKAGAEP 420<br>ASEREVS 427                                                                                                                                                                                                                                            |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)               | Protein Sequence |            |             |             |             |             |      |  |
|----------------------------|-----------------------------------------|------------------|------------|-------------|-------------|-------------|-------------|------|--|
| 16                         | gi:213506103<br>CAS91502.1              | MKLITILFLC       | SRLLLSLTQE | SQSEEIDCND  | KDLFKAVDAA  | LKKYNSQNQS  | NNQFVLYRIT  | 60   |  |
|                            |                                         | EATKTVGSDT       | FYSFKYEIKE | GDCPVQSGKT  | WQDCEYKDAA  | KAATGECTAT  | VGKRSSTKFS  | 120  |  |
|                            |                                         | VATQTCQITP       | AEGPVVTAQY | DCLGCVHPIS  | TQSPDLEPIL  | RHGIQYFNNN  | TQHSSLFMLN  | 180  |  |
|                            |                                         | EVKRAQRQVV       | AGLNFRTYS  | IVQTNCSEN   | FLFLTPDCKS  | LWNGDTGECT  | DNAYIDIQLR  | 240  |  |
|                            |                                         | IASFSQNCDI       | YPGKDFVQPP | TKICVGCPRD  | IPTNPELEE   | TLTHTITKLN  | AENNATFYFK  | 300  |  |
|                            |                                         | IDNVKKARVQ       | VVAGKKYFID | FVARETTCSE  | ESNEELTESC  | ETKKLGQSLD  | CNAEVYVVPW  | 360  |  |
|                            |                                         | EKKIYPTVNC       | QPLGMISLMK | RPPGFSPPRS  | SRIGEIKEET  | TSHLRSCEYK  | GRPPKAGAEP  | 420  |  |
|                            |                                         | ASEREVS          |            |             |             |             |             | 427  |  |
| 17                         | gi:194376310<br>BAG62914.1              | MDDDIAALVV       | DNGSGMCKAG | FAGDDAPRAV  | FPSIVGRPRH  | QGVVMGIVTN  | WDDMEKIWHH  | 60   |  |
|                            |                                         | TFYNELRVAP       | EEHPVLLTEA | PLNPKANREK  | MTQIMFETFN  | TPAMYVAIQA  | VLSLYASGRT  | 120  |  |
|                            |                                         | TGIVMDSGDG       | VTHTVPIYEG | YALPHAILRL  | DLAGRDLTDY  | LMKILTERGY  | SFTTTAEREI  | 180  |  |
|                            |                                         | VRDIKEKLCY       | VALDFEQEMA | TAASSSSLEK  | SYELPDGQVI  | TIGNERFRCP  | EALFQPSFLG  | 240  |  |
|                            |                                         | MESCGIHETT       | FNSIMKCDVD | IRKDLYANTV  | LSGGTTMYPG  | IADRMQKEIT  | ALAPSTMKIK  | 300  |  |
|                            |                                         | IIAPPERKYS       | VWIGGSILAS | LSTFQQMWIS  | KQEYDESGPS  | IVHRKCF     |             | 347  |  |
| 18                         | gi:194388064<br>BAG65416.1              | MEEEIAALVI       | DNGSGMCKAG | FAGDDAPRAV  | FPSIVGRPRH  | QGVVMGMGQK  | DSYVGDEAQS  | 60   |  |
|                            |                                         | KRGILTTLKYP      | IEHGIVTNWD | DMEKIWHHTF  | YNELRVAPPE  | HPVLLTEAPL  | NPKANREKMT  | 120  |  |
|                            |                                         | QIMFETFNNT       | GIVMDSGDGV | THTVPIYEGY  | ALPHAILRLD  | LAGRDLTDYL  | MKILTERGYS  | 180  |  |
|                            |                                         | FTTTAEREIV       | VDIKEKLCYV | ALDFEQEMAT  | AASSSSLEKS  | YELPDGQVIT  | IGNERFRCPPE | 240  |  |
|                            |                                         | ALFQPSFLGM       | ESCGIHETTF | NSIMKCDVDI  | RKDLYANTVL  | SGGTTMYPGI  | ADRMQKEITA  | 300  |  |
|                            |                                         | LAPSTMKIKI       | IAPPERKYSV | WIGGSILASL  | STFQQMWISK  | QEYDESGPSI  | VHRKCF      | 356  |  |
| 19                         | IPI00964149<br>gi:126215685<br>Q8N7B6.2 | MQKSESGSGT       | QLKNRATGNY | DQRTSSSTQL  | KHRNAVQGSK  | SSLSTSSPES  | ARKLHPRPSD  | 60   |  |
|                            |                                         | KLNPKTINPF       | GEQSRVPSAF | AAIYSKGGIP  | CRLVHGSKVH  | RLQWECPPES  | LSFDPLLITL  | 120  |  |
|                            |                                         | AEGLRETKHP       | YTFVSKEGFR | ELLLVKGAPPE | KAIPLLPRLI  | PVLKAALVHS  | DDEVFERGLN  | 180  |  |
|                            |                                         | ALVQLSVVVG       | PSLNDHLKHL | LTSLSKRLMD  | KKFKEPITSA  | LQKLEQHGGG  | GSLSLIKSKI  | 240  |  |
|                            |                                         | PTYCSICC         |            |             |             |             |             | 248  |  |
| 20                         | IPI00966721<br>gi:121940485<br>Q0VDI3.1 | MASETEKTHA       | LLQTCSTESL | ISSLGLGAFD  | LVADRLLQFS  | TIQQNDWLRA  | LSDNAVHCVI  | 60   |  |
|                            |                                         | GMWSWAVVTG       | IKKKTDGFEI | ILAGFLASVI  | DVDHFFLAGS  | MSLKAALTLP  | RRPFLHCSTV  | 120  |  |
|                            |                                         | IPVVVLTCLK       | TMHLFKLKDS | WCFLPWMLFI  | SWTSHHIRDG  | IRHGLWICPF  | GKTSPLPFWL  | 180  |  |
|                            |                                         | YVIITSSSLPH      | ICSFVMYLTG | TRQMMSSKHG  | VRIDV       |             |             | 215  |  |
| 21                         | IPI00966826<br>gi:121947590<br>Q29RF7.1 | MDFTAQPKPA       | TALCGVVSAD | GKIAYPGPKV  | EITDKITDTE  | MIKRLKMOVK  | TFMDMDQDSE  | 60   |  |
|                            |                                         | DEKQQYLPLA       | LHLASEFFLR | NPNKDVRLLV  | ACCLADIFRI  | YAPEAPYTSH  | DKLKDIFLFI  | 120  |  |
|                            |                                         | TRQLKGLDTE       | KSPQFNRYFY | LLENLAWVKS  | YNICFELEDC  | NEIFIQLFRT  | LFSVINNSHN  | 180  |  |
|                            |                                         | KKVQMHMLDL       | MSSIIMEGDG | VTQELLDLIL  | INLIPAHKNL  | NKQSFDLAKV  | LLKRTVQTIE  | 240  |  |
|                            |                                         | ACIANFFNQV       | LVLGRSSVSD | LSEHVFDLIQ  | ELFAIDPHLL  | LSVMPQLEFK  | LKSNDEGERL  | 300  |  |
|                            |                                         | AVVRLAKLFE       | GSKDSDLATQ | NRPLWQCFLG  | RFNDIHVPVR  | LESVKFASHC  | LMNHPDLAKD  | 360  |  |
|                            |                                         | LTEYLKVRSH       | DPEEAIKRDV | IVTIIITAAKR | DLALVNDQLL  | GFVRERTLDK  | RWRVRKEAMM  | 420  |  |
|                            |                                         | GLAQLYKKYC       | LHGEAGKEAA | EKVSNIKDKL  | LHIYYQNSID  | DKLLVEKIFA  | QYLVPHNLET  | 480  |  |
|                            |                                         | EERMKCLYYL       | YASLDPNAVK | ALNEMWKCQN  | MLRSHVRELL  | DLHKQPTSEA  | NCSAMFGKLM  | 540  |  |
|                            |                                         | TIAKNLDPDG       | KAQDFVKKFN | QVLGDDEKLR  | SQLELLISPT  | CSCQADICV   | REIARKLANP  | 600  |  |
|                            |                                         | KQPTNPFLFM       | VKFLLEIRAP | VHIDSEAISS  | LVKLMNKSIE  | GTADDEEEGV  | SPDTAIRSGL  | 660  |  |
|                            |                                         | ELLKVLSTFH       | PTSFHSAETY | ESLLQCLRME  | DDKVAEAAIQ  | IFRNTGHKIE  | TDLPQIRSTL  | 720  |  |
|                            |                                         | IPILHQKAKR       | GTPHQAKQAV | HCIHAIFTNK  | EVQLAQIFEP  | LSRSLNADVP  | EQLITPLVSL  | 780  |  |
|                            |                                         | GHISMLAPDQ       | FASPMKSVVA | NFIVKDLLMN  | DRSTGEKNGK  | LWSPDEEVSP  | EVLAKVQAIK  | 840  |  |
|                            |                                         | LLVRWLLGMK       | NNQSKSANST | LRLLSAMLVS  | EGDLTEQKRI  | SKSDMSRLRL  | AAGSAIMKLA  | 900  |  |
|                            |                                         | QEPCYHEIIT       | PEQFQLCALV | INDECYQVRQ  | IFAQKLHKAL  | VKLLLPLEYM  | AIFALCAKDP  | 960  |  |
|                            |                                         | VKERRAHARQ       | CLLKNISIRR | EYIKQNPMTA  | EKLLSLLPEY  | VVPYMIHLLA  | HDPDFTRSQD  | 1020 |  |
|                            |                                         | VDQLRDIKEC       | LWFMLEVLMT | KNENNSHAFM  | KKMAENIKLT  | RDAQSPDESK  | TNEKLYTVCD  | 1080 |  |
|                            |                                         | VALCVINSKS       | ALCNADSPKD | PVLPMKFFTQ  | PEKDFCNDKS  | YISEETRVLL  | LTGKPKPAGV  | 1140 |  |
|                            |                                         | LGAVNKPLSA       | TGRKPYVRST | GTETGSNINV  | NSELNPSTGN  | RSREQSSEAA  | ETGVSENEEN  | 1200 |  |
|                            |                                         | PVRIISVTPV       | KNIDPVKNKE | INSDQATQGN  | ISSDRGKKRT  | VTAAGAENIQ  | QKTDEKVDSE  | 1260 |  |
|                            |                                         | GPPAPSKPRR       | GRRPKSESQG | NATKNDDLNK  | PINKGRKRAA  | VGQESPGGLE  | AGNAKAPKLQ  | 1320 |  |
|                            |                                         | DLAKKAAPAE       | RQIDLQR    |             |             |             |             | 1337 |  |
| 22                         | IPI00760788<br>gi:109892504<br>Q53GT1.2 | MAEEQEFTQL       | CKLPAQPSHP | HCVNNTYRSA  | QHSQALLRGL  | LALRDSGILF  | DVVLVVEGRH  | 60   |  |
|                            |                                         | IEAHRILLAA       | SCDYFRGMFA | GGLKEMEQUE  | VLIHGVSINA  | MCQILHFIYT  | SELELSLSNV  | 120  |  |
|                            |                                         | QETLVAACQL       | QIPEIIHFCC | DFLMSWVDEE  | NILDVYRLAE  | LFDLSRLTEQ  | LDTYILKNFV  | 180  |  |
|                            |                                         | AFSRTDKYRQ       | LPLEKVYSLL | SSNRLEVSCD  | TEVYEGALLY  | HYSLEQVQAD  | QISLHEPPKL  | 240  |  |
|                            |                                         | LETVRFPPLME      | AEVLQRLHDK | LDPSPLRDTV  | ASALMYHRNE  | SLQPSLQSPQ  | TELRSDFQCV  | 300  |  |
|                            |                                         | VGFGGIHSTP       | STVLSDAQAY | LNPLLGEWKH  | FTASLAPRMS  | NQGI AVLNNF | VYLIGGDNNV  | 360  |  |
|                            |                                         | QGFRAESRCW       | RYDPRHNRWF | QIQSLQQEHA  | DL SVCVVGRY | IYAVAGRDIH  | NDLNAVERYD  | 420  |  |
|                            |                                         | PATNSWAYVA       | PLKREVIYAH | GATLEGKMYI  | TCGRRGEDYL  | KETHCYDPGS  | NTWHTLADGP  | 480  |  |
|                            |                                         | VRRAWHGMAT       | LLNKLYVIGG | SNNDAGYRRD  | VHQQVACYSCT | SGQWSSVCPL  | PAGHGEPGIA  | 540  |  |
|                            |                                         | VLDNRIYVLG       | GRSHNRGSRT | GYVHIYDVEK  | DCWEEGPQLD  | NSISGLAACV  | LTLPRSLLE   | 600  |  |
|                            |                                         | PPRGTPDRSQ       | ADPDFASEVM | SVSDWEEFDN  | SSD         |             |             | 634  |  |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)               | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| 23                         | IPI00917278<br>gi:                      | MKQLQPQPPP KMGDFYDPEH PTPEEEENEAE KIENVQKTGF IKGPMFKGVA SSRFLPKGTK 60<br>TKVNLEEQGR QKVSFSFSLT KKTLQNRFLT ALGNEKQSDT PNPPAVPLQV DSTPKMKMEI 120<br>GDTLSTAEES SPPKSRVELG KIHFKKHLH VTSRPLLATT TAVASPPHA APLPAVIAES 180<br>TTVDSPSSP PPPPPAQAT TLSSPAPVTE PVALPHTPIT VLMAAPVPLP VDVAVRSLKE 240<br>PPIIIVPESL EADTKQDTIS NSLEEHVTQI LNEQADISSK KEDSHIGKDE EIPDSSKISL 300<br>SCKKTGSKKK SSQSEGIFLG SESDEDSVRT SSSQRSHDLK FSASIEKERD FKKSSAPLKS 360<br>EDLGKPSRSK TDRDDKYFSY SKLERDTRYV SSRCSRERER RRSRSHSRSE RGSRTNLSYS 420<br>RSERSHYIDS DRRYHRSSPY RERTRYSRPY TDNRARESSD SEEEYKKTYS RRTSSHSSSY 480<br>RDLRTSSYSK SDRDCKTETS YLEMERRGKY SSKLERESKR TSENEAIKRC CSPPNELGFR 540<br>RGSSYSKHDS SASRYKSTLS KPIPKSDKFK NSFCCTELNE EIKQSHSFSL QTPCSKGSEL 600<br>RMINKNPERE KAGSPAPSNR LNDSPTLKKL DELPIFKSEF ITHDSHDSIK ELDSLKSVKN 660<br>DQLRSFCPIE LNINGSPEGAE SDLATFCTSK TDAVLMTSDD SVTGSSELSPL VKACMLSSNG 720<br>FQNISRCKEK DLDDTCMLHK KSESPFRETE PLVSPHQDKL MSMPVMTVDY SKTVVKEPVD 780<br>TRVSCCKTKD SDIYCTLNDS NPSLCNSEAE NIEPSVMKIS SNSFMNVHLE SKPVICDSRN 840<br>LTDHSKFACE EYKQSIGSTS SASVNHFDL YQPIGSSGIA SSLQSLPPGI KVDSLTLKLC 900<br>GENTSPVLDA VLKSKKSSEF LKHAGKETIV EVGSDLPDSDG KGFASRENRR NNGLSGKCLQ 960<br>EAQEEGNSIL PERRGRPEIS LDERGEGGHV HTSDDSEVVF SSCDLNLTME DSDGVTYALK 1020<br>CDSSGHAPEI VSTVHEDYSG SSESSNDESD SEDTDSDDSS IPRNRLQSVV VVPKNSTLPM 1080<br>EETSPCSSRS SQSYRHYS DH WEDERLESRR HLYEEKFESI ASKACPQTDK FFLHKGTEKN 1140<br>PEISFTQSSR KQIDNRLPEL SHPQSDGVDS TSHTDVKSDP LGHPNSEETV KAKIPSRQQE 1200<br>ELPIYSSDFE DVPNKSWQQT TFQNRPD SRL GKTELSFSSS CEIPHVDGLH SSEELRNLGW 1260<br>DFSQEKPSTT YQQPDSSYGA CGGHKYQQNA EQYGGTRDYW QGNGYWDPRS GRPPGTGVVY 1320<br>DRTQGQVPDS LTDDREEEEN WDQDQDGS HFS DQSDKFLLSL QKDKGSVQAP EISSNSIKDT 1380<br>LAVNEKKDFS KNLEKNDIKD RGPLKKRRQE IESDSESDGE LQDRKKVRVE VEQGETSVPP 1440<br>GSALVGPCSV MDDFRDPQRW KEC AQGKMP CYFDLIEENV YLTERKKNKS HRDIKRMQCE 1500<br>CTPLSKDERA QGEIACGEDC LNRLLMIECS SRCPNGDYCS NRRFQRKQHA DVEVILTEKK 1560<br>GWGLRAAKDL PSNTFVLEYC GEVLDHKEFK ARVKEYARNK NIHYFMALE NDEIIDATQK 1620<br>GNCSR FMNHS CEPNCETQKW TVNGQLRVGF FTTKLVPSSG ELTFDYQFQR YGKEAQKCF 1680<br>GSANCRGYLG GENRV SIRAA GGKMKKERSR KKDSVDGELE ALMENGEGLS DKNQVLSLSR 1740<br>LMVRIETLEQ KLTCLLELIQN THSQSCLKSF LERHGLSLW IWMAELGDGR ESNQKLQEEI 1800<br>IKTLEHLPIP TKNMLEESKV LP IIQRWSQT KTAVPPLSEG DGYSSENTSR AHTPLNTPDP 1860<br>STKLSTEADT DTPKKLMFRR LKIISENSMD SAISDATSEL EGKDGEDLD QLENVPVEEE 1920<br>EELQSQQLLP QQLPECKVDS ETNIEASKLP TSEPEADAEI EPKESNGTKL EEPINEETPS 1980<br>QDEEEGVSDV ESERSQEQPD KTVDISDLAT KLLDSWKDLK EVYRIPKKSQ TEKENTTTER 2040<br>GRDAVGFRDQ TPAPKTPNRS RERDPDKQTQ NKEKRKRSS LSPSSAYER GTKRPDDRYD 2100<br>TPTSKKKVRI KDRNKLSTEE RRKLFEQEVA QRE AQQQQ MQNLGMTSPL PYDSLGYNAP 2160<br>HHPFAGYPPG YPMQAYVDPS NPNAGKVLLP TSPMDPVCSP APYDHAQPLV GHSTEPLSAP 2220<br>PPVPVVPHVA APVEVSSSQY VAQSDGVVHQ DSSVAVLPVP APGPVQQG 2268 |
| 24                         | IPI00966721<br>gi:121940485<br>Q0VDI3.1 | Same as KH 20                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 25                         | IPI01012037<br>gi:74735024<br>Q9UHY7.1  | MNGEYRGRGF GRGRFQSWKR GRGGGNFSGK WREREHRPDL SKTTGKRTSE QTPQFLLSTK 60<br>TPQSMQSTLD RFIPYKGWKL YFSEVYSDSS PLIEKIQAFE KFFTRHIDLY DKDEIERKGS 120<br>ILVDFKELTE GGEVTNLIPD IATELRDAPE KTLACMGLAI HQVLT KDLER HAAELQAQEG 180<br>LSNDGETMVN VPHIHARVYN YEPLTQLKNV RANYYGKYIA LRGTVVRVSN IKPLCTKMAF 240<br>LCAACGEIQS FPLPDGKYSL PTKCPVPVCR GRSFTALRSS PLTVTMDWQS IKIQELMSDD 300<br>QREAGRIprt IECeLVHDLV DSCVP GDVT ITGIVKVSNA EEGSRNKNDK CMFLLYIEAN 360<br>SISNSKGQKT KSSEDGCKHG MLMEFSLKDL YAIQEIQAEE NLFKLIVNSL CPVIFGHELV 420<br>KAGLALALFG GSQKYAD DKN RIPIRGDPHI LVVGD PGLGK SQMLQAACNV APRGVYVCGN 480<br>TTTTSGLTVT LSKDSSSGDF ALEAGALVLG DQGICGIDEF DKMGNQH QAL LEAMEQQSIS 540<br>LAKAGVVC SL PARTSIIAAA NPVG GHYNKA KTVSEN LKMG SALLSRFDLV FILLDTPNEH 600<br>HDHLLSEHVI AIRAGKQRTI SSATVARMNS QDSNTSVLEV VSEKPLSERL KVVPGETIDP 660<br>IPHQLLRKYI GYARQYVYPR LSTEAARVLQ DFYLELRKQS QRLNSSPITT RQLES LIRLT 720<br>EARARLELRE EATKEDAEDI VEIMKYSMLG TYSDEFGNLD FERSQHSGSM SNRSTAKRFI 780<br>SALNNVAERT YNNIFQFHQL RQIAKELNIQ VADFENFIGS LNDQGYLLKK GPKVYQLQTM 840                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 26                         | IPI00940730<br>gi:                      | MVVLSPAEV TVILLDIEGT TTPIAFVKDI LFPYIEENVK EYLQTHWEEE ECQQDVSLLR 60<br>KQAEEDAHL D GAVPIPAASG NGVDDLQQMI QAVVDNVCWQ MSLDRKTTAL KQLQGHMWRA 120<br>AFTAGRMKAE FFADV VPAVR KWREAGMKVY IYSSGSVEAQ KLLFGHSTEG DILELVDGHF 180<br>DTKIGHKVES ESYRKIADSI GCSTNNILFL TDVTREASAA EEADVHVAVV VRPGNAGLTD 240<br>DEKTYYSLIT SFSELYLPSS T 261                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)               | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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| 27                         | IPI00977191<br>gi:23503077<br>P49321.2  | MAMESTATAA VAAELVSADK IEDVPAPSTS ADKVESLDVD SEAKKLLGLG QKHLVMGDIP 60<br>AAVNAFQEAA SLLGKKYGET ANECGEAFFF YGKSLLLELAR MENGVLGNAL EGVHVEEEEG 120<br>EKTEDESLVE NNDNIDEEAR EELREQVYDA MGEKEEA KKT EDKSLAKPET DKEQDSEMEK 180<br>GGREDMDISK SAEEPQEKVD LTLDWLTETS EEAKGGAAP E GPNEAEVTSG KPEQEV PDAE 240<br>EEKSVSGTDV QEECREKGGQ EKQGEVIVSI EEKPKEVSEE QPVVTLEKQG TAVEVEAESL 300<br>DPTVKPVDVG GDEPEEKVVT SENEAGKAVL EQLVGQEVPP AEESPEVTTE AAEASAVEAG 360<br>SEVSEKPGQE APVLPKDGAV NGPSVVGDQT PIEPQTSIER LTETKDGSGL EEKVRAKLVP 420<br>SQEETKLSVE ESEAAGDGVD TKVAQGATEK SPEDKVQIAA NEETQEREEQ MKEGEETEGS 480<br>EEDDKENDKT EEMPND SVLE NKSLQENEEE EIGNLELAWD MLDLAKIIFK RQETKEAQLY 540<br>AAQAHCLKLGE VSVESENYVQ AVEEFQSCLN LQEQYLEAHD RLLAETHYQL GLAYGYNSQY 600<br>DEAVAQFSKS IEVIENRMAV LNEQVKEAEG SSAEYKKEIE ELKELLPEIR EKIEDAKESQ 660<br>RSGNVAELAL KATLVESSTS GFTPGGGGSS VSMIASRKPT DGASSSNCVT DISHLVRKKR 720<br>KPEEESPRKD DAKKAKQEPE VNGGSGDAVP SGNEVSENME EEAENQAESR AAVEGTVEAG 780<br>ATVESTAC 788 |
| 28                         | IPI00022434<br>gi: 113576<br>P02768.2   | MKWVTFISLL FLFSSAYSRG VFRRDAH KSE VAHRFKDLGE ENFKALVLIA FAQYLQQCPF 60<br>EDHVKLVNEV TEFAKTCVAD ESAENC DKSL HTLFGDKLCT VATLRETYGE MADCCAKQEP 120<br>ERNECFLQHK DDNP NLRLV RPEVDVMCTA FHDNEETFLK KYLYEIARRH PYFYAPEL LF 180<br>FAKRYKAAFT ECCQAADKAA CLLPKLDEL R DEGKASSAQ RLKCASLQKF GERA FKA WAV 240<br>ARLSQRFPKA EFAEVSKLVT DLT KVHTECC HGD LLE CADD RADLAKYICE NQDSISSKLK 300<br>ECCEKPLLEK SHCIAEVEND EMPADLP SLA ADFVESKDVC KNYAEAKDVF LGMFLYEYAR 360<br>RHPDYSVLL LRLAKTYETT LEKCCAAADP HECYAKVFDE FKPLVEEPQN LIKQNC ELFE 420<br>QLGEYKFQNA LLVRYTKKVP QVSTPTLVEV SRNLGKVGSK CCKHPEAKRM PCAEDYLSV V 480<br>LNQLCVLHEK TPVSDRVTKC CTESLVNRRP CFSALEVDET YVPKEFNAET FTFHADICTL 540<br>SEKERQIKKQ TALVELVKHK PKATKEQLKA VMDDFAAFVE KCCKADDKET CFAEEGKKLV 600<br>AASQAALGL 609                                                                                                                                                                                                                       |
| 29                         | IPI00022434<br>gi:113576<br>P02768.2    | Same as KH 28                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 30                         | IPI00219713<br>gi:20178280<br>P02679    | MSWSLHPRNL ILYFYALLFL SSTCVAYVAT RDNCCILDER FGSYCPTTCG IADFLSTYQT 60<br>KVDKDLQSLE DILHQVENKT SEVKQLIKAI QLTYNPDESS KPNMIDAATL KSRKMLEEIM 120<br>KYEASILTHD SSIRYLQEIY NSNNQKIVNL KEKVAQLEAQ CQEPCKDTVQ IHDITGKDCQ 180<br>DIANKGAKQS GLYFIKPLKA NQQFLVYCEI DGSGNGWTVF QKRLDGSVDF KKNWIQYKEG 240<br>FGHLSPTGTT EFWLGNEKIH LISTQSAIPY ALRVELEDWN GRTSTADYAM FKVGP EADKY 300<br>RLTYAYFAGG DAGDAFDGFD FGDDPSDKFF TSHNGMQFST WDNDNDKFEG NCAEQD GSGW 360<br>WMNKCHAGHL NGVYYQGGTY SKASTPNGYD NGIIWATWKT RWYSMKKTTM KIIPFNRLTI 420<br>GEGQQHHLGG AKQVRPEHPA ETEYDSLYPE DDL 453                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 31                         | IPI00219713<br>gi:20178280<br>P02679    | Same as KH 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 32                         | IPI00220327<br>gi:238054406<br>P04264.6 | MSRQFSSRSG YRSGGGFSSG SAGIINYQRR TTSSSTRRSG GGGGRFSSCG GGGGSFGAGG 60<br>GFGSRSLVNL GGSKSISISV ARGGGRGSGF GGGYGGGGFG GGGFGGGGFG GGGIGGGGFG 120<br>GFGSGGGGFG GGGFGGGGYG GGYGPVCP PG GIQEV TINQS LLQPLNVEID PEIQKVKSRE 180<br>REQIKSLNNQ FASFIDKVR F LEQQNQVLQT KWELLQQVDT STRTHNLEPY FESFINNLRR 240<br>RVDQLKSDQS RLDSELKNMQ DMVEDYRNKY EDEINKRTNA ENEFVTIKKD VDGAYMTKVD 300<br>LQAKLDNLQQ EIDFLTALYQ AELSQMOTQI SETNVILSMD NNRS LDLD SI IAEVKAQYED 360<br>IAQKSKAEAE SLYQSKYEEL QITAGR HGDS VRNSKIEISE LNRVIQRLRS EIDNVKKQIS 420<br>NLQQSISDAE QRGENALKDA KNKLNDLEDA LQQAKEDLAR LLRDYQELMN TKLALDLEIA 480<br>TYRTLLEGEE SRMSGECAPN VSVSVSTSHT TISGGGSRGG GGGGYGSGGS SYGSGGGSYG 540<br>SGGGGGGGRG SYGSGGSSYG SGGGSYGSGG GGGGHGSYGS GSSSGGYRGG SGGGGGGSSG 600<br>GRGSGGGSSG GSIGGRGSSS GGVKSSGGSS SVK FVSTTYS GVTR 644                                                                                                                                                                                   |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)               | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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| 33                         | IPI00029739<br>gi:158517847<br>P08603.4 | MRLLAKIICL MLWAICVAED CNELPPRRNT EILTGSWSDQ TYPEGTQAIY KCRPGYRSLG 60<br>NVIMVCRKGE WVALNPLRKC QKRPCGHPGD TPFGTFTLTG GNVFEYGVKA VYTCNEGYQL 120<br>LGEINYRECD TDGWTNDIPI CEVVKCLPVT APENGKIVSS AMEPDREYHF GQAVRFVCNS 180<br>GYKIEGDEEM HCSDDGFWSK EKPKCVEISC KSPDVINGSP ISQKIIYKEN ERFQYKCNMG 240<br>YEYSERGDAV CTESGWRPLP SCEEKSCDNP YIPNGDYSPL RIKHRTGDEI TYQCRNGFYP 300<br>ATRGNTAKCT STGWIPAPRC TLKPCDYPDI KHGGLYHENM RRPYFPVAVG KYYSYVCDEH 360<br>FETPSGSYWD HIHCTQDGWS PAVPCLRKCY FPYLENGYNQ NYGRKFVQ GK SIDVACHPGY 420<br>ALPKAQTTVT CMENGWSPTP RCIRVKTC SK SSIDIENGFI SESQYTYALK EKAKYQCKLG 480<br>YVTADGETSG SITCGKDGWS AQPTCIKSCD IPVFMNARTK NDFTWFKLND TLDYEC HDGY 540<br>ESNTGSTTGS IVCGYNGWSD LPICYERECE LPKIDVHLVP DRKKDQYKVG EVLKFSC KPG 600<br>FTIVGPNSVQ CYHFGLSPDL PICKEQVQSC GPPPELLNGN VKEKTKEEYG HSEVVEYYCN 660<br>PRFLMKGP NK IQCVDGEWTT LPVCIVEEST CGDIPELEHG WAQLSSPPYY YGDSVEFNCS 720<br>ESFTMIGHRS ITCIHGVWTQ LPQCVAIDKL KKCKSSNLII LEEHLKNKKE FDHNSNIRYR 780<br>CRGKEGWIHT VCINGRWDPE VNCSMAQIQL CPPPPQIPNS HNMTTTLN YR DGEKVS VLCQ 840<br>ENYLIQEGEE ITCKDGRWQS IPLCVEKIPC SQPPQIEHGT INSSRSSQES YAHG TKLSYT 900<br>CEGGFRIS EE NETTCYMGKW SSPPQCEGLP CKSPPEISHG VVAHMSDSYQ YGEEV TYKCF 960<br>EGFGIDGPAI AKCLGEKWSH PPSCIKT DCL SLPSFENAIP MGEKKDVYKA GEQV TYTCAT 1020<br>YYKMDGASN V TCINSRWTGR PTCRDTSCVN PPTVQNAYIV SRQMSKYP SG ERVRYQCRSP 1080<br>YEMFGDEE VM CLNGNWTEPP QCKDSTGKCG PPPIDNGDI TSFPLSVYAP ASSVEYQCQN 1140<br>LYQLEGNKRI TCRNGQWSEP PKCLHPCVIS REIMENYNIA LRWTAKQKLY SRTGESVEFV 1200<br>CKRGYRLSSR SHTLR TTCWD GKLEYPTCAK R 1231 |
| 34                         | IPI00384853<br>gi:                      | QAHGRCSAGA QFVFCRRSAGAACTQQALSR (Sequence 59-88)<br>CLVGAQCVLSR (Sequence 100-110)<br>CTVCTQQALSR (Sequence 125-135)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 35                         | IPI00479708<br>gi:193806374<br>P01871.3 | GSASAPTLFP LVSCENSPSD TSSVAVGCLA QDFLPDSITL SWKYKNNSDI SSTRGFPSVL 60<br>RGGKYAATSQ VLLPSKDVMQ GTDEHV VCKV QHPNGNKEKN VPLPVIAELP PKVS VFVPPR 120<br>DGFFGNPRKS KLICQATGFS PRQIQVSWLR EGKQVGSGVT TDQVQAEAKE SGPTTYKVTS 180<br>TLTIKESDWL GQSMFTCRVD HRGLTFQQNA SSMCVPDQDT AIRVFAIPPS FASIFLTKST 240<br>KLTCLVTDLT TYDSVTISWT RQNGEAVKTH TNISESHPNA TFSAVGEASI CEDDWN SGER 300<br>FTCTVTH TDL PSPLKQTISR PKGVALHRPD VYLLPPAREQ LNLRESATIT CLVTGFSPAD 360<br>VFVQWMQRGQ PLSPEKYVTS APMPEPQAPG RYFAHSILTV SEEWNTGET YTCVAHEALP 420<br>NRVTERTVDK STGKPTLYNV SLVMSD TAGT CY 452                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 36                         | IPI00298497<br>gi:399492<br>P02675.2    | MKRMVSWSFH KLKTMK HLLL LLLCVFLVKS QGVNDNEEGF FSARGHRPLD KKREEAPSLR 60<br>PAPPPISGGG YRARPAKAAA TQKKVERKAP DAGGCLHADP DLGVLCPTGC QLQEALLQQE 120<br>RPIRNSVDEL NNNVEAVSQT SSSSFQMYL LKDLWQKRQK QVKDNENVVN EYSSELEKHQ 180<br>LYIDETVNSN IPTNLRVLRS ILENLRSKI Q KLES DVSAQM EYCRTPCTVS CNIPV VSGKE 240<br>CEEIIRKGGE TSEMYLIQPD SSVKPYRVYC DMNTENG GWT VIQNRQDGSV DFGRKWDPYK 300<br>QGFGNVATNT DGKNYCGLPG EYWLGN DKIS QLTRMGPT EL LIEMEDWKGD KVKAHYGGFT 360<br>VQNEANKYQI SVNKYRG TAG NALMDGASQL MGENRTMTIH NGMFFSTYDR DNDGWL TSDP 420<br>RKQCSKEDGG GWWYNRCHAA NPNGRY YWGG QYTWDMAKHG TDDGVVWMNW KGSWYSMRKM 480<br>SMKIRPFFPQ Q 491                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 37                         | IPI00021841<br>gi:113992<br>P02647.1    | MKAAVLT LAV LFLTGSQARH FWQQDEPPQS PWDRVKDLAT VYVDVLKDSG RDYVSQFEGS 60<br>ALGKQLNLKL LDNWD SVTST FSKLREQ LGP VTQEFWDNLE KETEG LRQEM SKDLEE VKAK 120<br>VQPYLDDFQK KWQEEMEL YR QKVEPLRAEL QEGARQKLHE LQEKLSPLGE EMRDRARAHV 180<br>DALRTHLAPY SDEL RQRLAA RLEALKENG G ARLAEYHAKA TEHLSTLSEK AKPALEDLRQ 240<br>GLLPVLESFK VSFLSALEEY TKKLNTQ 267                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)               | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
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| 38                         | IPI00783987<br>gi:119370332<br>P01024.2 | MGPTSGPSLL LLLLTHLPLA LGSPMYSIIT PNILRLESEE TMVLEAHDAQ GDVPVTVTVH 60<br>DFPGKKLVLS SEKTVLTPAT NHMGNVTFIT PANREFKSEK GRNKFVTVQA TFGTQVVEKV 120<br>VLVSLQSGYL FIQTDKTIYT PGSTVLYRIF TVNHKLLPVG RTVMVNIENP EGIPVKQDSL 180<br>SSQNQLGVLP LSWDIPELVN MGQWKIRAYY ENSPQQVFST EFEVKEYVLP SFEVIVEPTE 240<br>KFYYIYNEKG LEVTITARFL YGKKVEGTAF VIFGIQDGEQ RISLPESLKR IPIEDGSGEV 300<br>VLSRKVLLDG VQNPRaedLV GKSLYVSATV ILHSGSDMVQ AERSGIPiVT SPYQIHFTKT 360<br>PKYFKPGMPF DLMVFVTNPD GSPAYRVPVA VQGEDTVQSL TQGDGVAKLS INTHPSQKPL 420<br>SITVRTKKQE LSEAEQATRT MQALPYSTVG NSNNYLHLSV LRTELRPGET LNVNfLLRMD 480<br>RAHEAKIRYY TYLIMNKGRL LKAGRQVREP GQDLVVLP LS ITTDFIPSFR LVAYYTLIGA 540<br>SGQREVVADS VWVDVKDSCV GSLVVKSGQS EDRQPVPGQQ MTLKIEGDHG ARVVLVAVDK 600<br>GVFVLNKKNK LTQSKIWDVV EKADIGCTPG SGKDYAGVFS DAGLTFTSSS GQQTAAQRAEL 660<br>QCPQPAARRR RSVQLTEKRM DKVGKYPKEL RKCCEDGMRE NPMRFSCQRR TRFISLGEAC 720<br>KKVFLDCCNY ITELRRQHAR ASHLGLARSN LDEDIIAEEN IVSRSEFPES WLWNVEDLKE 780<br>PPKNGISTKL MNIFLKDSIT TWEILAVSMS DKGICVADP FEVTVMQDFF IDLRLPYSVV 840<br>RNEQVEIRAV LYNyRQNQEL KVRVELLHNP AFCSLATTKR RHQQTVTIPP KSSLSPYVI 900<br>VPLKTGLQEV EVKAAVYHHF ISDGVRKSLK VVPEGIRMNK TVAVRTLDP E RLGREGVQKE 960<br>DIPPADLSDQ VPDTESETRI LLQGTpVAQM TEDAVDAERL KHLIVTPSGC GEQNMIGMTp 1020<br>TVIAVHYLDE TEQWEKFGLE KRQGALELIK KGYTQQLAFR QPSSAFAAFV KRAPSTWLTA 1080<br>YVVKVfSLAV NLIAIDSQVL CGAVKWLiLE KQKPDGVFQE DAPVIHQEMI GGLRNNNEKD 1140<br>MALTAfVLIS LQEAKDICEE QVNSLPGSiT KAGDFLEANY MNLQRSYTVA IAGYALAQMG 1200<br>RLKGpLLNKf LTTAKDKNRW EDPGKQLYNV EATSYALLAL LQLKDFDFVP PVVRWLNEQR 1260<br>YYGGGYGSTQ ATFMVFQALA QYQKDAPDHQ ELNLDVSLQL PSRSSKiTHR IHWESASLLR 1320<br>SEETKENEGF TVTAEGKGQG TlSVVTMyHA KAKDQLTCNK FDLKVTIKPA PETEKRPQDA 1380<br>KNTMiLEICT RYRGDQDATM SiLDISMMTG FAPDTDDLKQ LANGVDRIYIS KYELDKAFSD 1440<br>RNTLiIYLDK VSHSEDDCLA FKvHQYFNVE LiQPGAVKVY AAYNLEESCT RFYHPEKEDG 1500<br>KLNKLcRDEL CRCAEENCfi QKSDDKVtLE ERLDKACEPG VDyVYKTRLV KVQLSNDfDE 1560<br>YIMAIEQTIK SGSDEVQVGQ QRTFiSPiKc REALKLEEK HYLmWGLSSD FWGEKPNLSY 1620<br>IIGKDTWVEH WPeeDECQDE ENQKQCQDLG AfTESMvVFG CPN 1663 |
| 39                         | IPI00878282<br>gi:113576<br>P02768.2    | MKwVTFISLL FLfSSAYSrG VFRRDAHKSE VAHRFKDLGE ENFKALVLIA FAQYLQQCPf 60<br>EDHVKLvNEV TEfAKTCVAD ESaENCdKSL HTLFGDKLCT VATLRETYGE MADCCAKQEP 120<br>ERNECfLQHK DDNPnLpRLV RPEVDVMCTA FHDNEETFLK KYLYEIARRH PYFYAPELLf 180<br>fAKRYKAAfT ECCQAADKAA CLLPKLDELr DEGKASSAKQ RLKcASLQKF GERAFKAWAV 240<br>ARLSQRfPKA EfAEVSKLVt DLTKVHTECC HGDLLcCADD RADLAKYICE NQDSiSSKLK 300<br>ECCEKPLLEK SHCIAEVEND EMPADLPSLA ADFVESKDVC KNYAEAKDVf LGMFLYEyAR 360<br>RHPDYSVVLl LRLAKTYETT LEKCCAAADP HECYAKVFDE FKPLVEEPQN LiKQNCeLFE 420<br>QLGEYKfQNA LLVRYTKKVP QVSTPTLVEV SRNLGKVGSK CCKHPEAKRM PCaEDYLSVv 480<br>LNQLCvLHEK TPVSDRVTKC CTESLVNRRP CFSALEVDET YVPKEfNAET FTFHADiCTL 540<br>SEKERQIKKQ TALVELVKHK PKATKEQLKA VMDDFAAFVE KCCKADDKET CFaEEGKKLV 600<br>AASQAALGL 609                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 40                         | IPI00784842<br>gi:                      | GRFTISGDISTNTLYLQMHS LR (Sequence 85-106)<br>TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK (Sequence 284-316)<br>ALPAPIEK (Sequence 355-362)<br>GQPREPQVYTLPPSRDELTKGFYPSDIAVEWESNGQPENNYK (Sequence 369-420)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 41                         | IPI00022434<br>gi: 113576<br>P02768.2   | Same as KH28                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 42                         | IPI00298497<br>gi:399492<br>P02675.2    | Same as KH36                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 43                         | IPI00965713<br>gi:399492<br>P02675.2    | MKRmVSWSFH KLKTmKHLlL LLLCVFLVKS QGVNDNEEGF FSARGHRPLD KKREEAPSLR 60<br>PAPPPISGGG YRARPAKAAA TQKKVERKAP DAGGCLHADP DLGVLCPTGC QLQEAALLQQE 120<br>RPIRNSVDEL NNNVEAVSQT SSSSFQYMYL LKDLWQKRQK QVKDNENVVN EYSSELEKHQ 180<br>LYIDETVNSN IPTNLRVLRS ILENLRSKiQ KLESdVSAQM EYCRTPCTVS CNIPVVSGKE 240<br>CEEIIRKGGE TSEMYLIQPD SSVKPYRVYC DMNTENGgWT ViQNRQDGSV DfGRKWDPYK 300<br>QGFGNVATNT DGKNYCGLPg EyWLGNDKiS QLTRMGPTeL LiEMEDWKGD KVKAHYGGFT 360<br>VQNEANKYQi SVNKYRGtAG NaLMDGASQL MGENRTMTiH NGMFFSTYDR DNDGWLtSDP 420<br>RKQCSKEDGG GWWYNRCHAA NPNGRYyWGG QYTWDMAKHG TDDGVVWMNW KGSWYSMRKM 480<br>SMKIRPFFPQ Q 491                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

| KH Protein/SEQ ID NO | Sequence Identifier(s)                  | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| 44                   | IPI00645363<br>gi:                      | NSLYLQMNSLRAEDTALYYCAK (Sequence 96-117)<br>GPSVFPLAPSSK (Sequence 147-158)<br>TPEVTCVVVDVSHEDPEVK (Sequence 281-299)<br>FNWYVDGVEVHNAK (Sequence 300-313)<br>ALPAPIEK (Sequence 352-359)<br>GQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK (Sequence 366-417)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 45                   | IPI00219713<br>gi:20178280<br>P02679    | Same as KH30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 46                   | IPI00022371<br>gi:123523<br>P04196.1    | MKALIAALLL ITLQYSCAVS PTDCSAVEPE AEKALDLINK RRRDGYLFQL LRIADAHLDR 60<br>VENTTVYYLV LDVQESDCSV LSRKYWNDCE PPDSRRPSEI VIGQCKVIAT RHSHESQDLR 120<br>VIDFNCTTSS VSSALANTKD SPVLIDFFED TERYRKQANK ALEKYKEEND DFASFRVDRI 180<br>ERVARVRGGE GTGYFVDFSV RNCPRHHFPR HPNVFGFCRA DLFYDVEALD LESPKNLVIN 240<br>CEVFDPQEHE NINGVPPHLG HPFHWGGHER SSTTKPPFKP HGSRDHHHPH KPHEHGPPPP 300<br>PDERDHSHGP PLPQGPPPLL PMSCSSCQHA TFGTNGAQRH SHNNNSSDLH PHKHHSHEQH 360<br>PHGHHPHAAH PHEHDTHRQH PHGHHPHGHH PHGHHPHGHH PHGHHPHCHD FQDYGPCDPP 420<br>PHNQGHCCHG HGPPPGHLRR RGPKGKPRPF HCRQIGSVYR LPPLRKGEVL PLPEANFPSPF 480<br>PLPHHKHPLK PDNQPFQSV SESCOGKFKS GFPQVSMFFT HTFPK 525                                                                                                                                                                                                                |
| 47                   | IPI00022371<br>gi:123523<br>P04196.1    | Same as KH46                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 48                   | IPI00022463<br>gi:313104271<br>P02787.3 | MRLAVGALLV CAVLGLCLAV PDKTVRWCAV SEHEATKCQS FRDHMKSVIP SDGPSVACVK 60<br>KASYLDCIRA IAANEADAVT LDAGLVYDAY LAPNNLKPVV AEFYGSKEDP QTFYYAVAVV 120<br>KKDSGFQMNQ LRGKKSCHTG LGRSAGWNIP IGLLYCDLPE PRKPLEKAVA NFFSGSCAPC 180<br>ADGTDFPQLC QLCPGCGCST LNQYFGYSGA FKCLKDGAGD VAFVKHSTIF ENLANKADRD 240<br>QYELLCLDNT RKPVDEYKDC HLAQVPSHTV VARSMGGKED LIWELLNQAQ EHFGKDKSKE 300<br>FQLFSSPHGK DLLFKDSAHG FLKVPPRMDA KMYLGYEYVT AIRNLREGTC PEAPTDECKP 360<br>VKWCALSHHE RLKCEWSVN SVGKIECVSA ETTEDCIAKI MNGEADAMSL DGGFVYIAGK 420<br>CGLVPVLAEN YNKSDNCEDT PEAGYFAIAV VKKSASDLTW DNLKGKKSCH TAVGRTAGWN 480<br>IPMGLLYNKI NHCRFDEFFS EGCAPGSKKD SSLCKLCMGS GLNLCEPNNK EGYGYTGAF 540<br>RCLVEKGDVA FVKHQTVPQN TGGKNPDPA KNLNEKDYEL LCLDGTRKPV EEYANCHLAR 600<br>APNHAVVTRK DKEACVHKIL RQQQHLEFSN VTDCSGNFCL FRSETKDLLF RDDTVCLAKL 660<br>HDRNTYEKYL GEEYKAVGN LRKCSTSSLL EACTFRRP 698 |
| 49                   | IPI00023006<br>gi:54036697<br>P68032.1  | MCDDEETTAL VCDNGSGLVK AGFAGDDAPR AVFPSIVGRP RHQGVVMGMG QKDSYVGDEA 60<br>QSKRGILTLK YPIEHGIITN WDDMEKIWHH TFYNELRVAP EEHPTLLTEA PLNPKANREK 120<br>MTQIMFETFN VPAMYVAIQ A VLSLYASGRT TGIVLDSGDG VTHNVPIYEG YALPHAIMRL 180<br>DLAGRDLTDY LMKILTERGY SFVTTAEREI VRDIKEKLCY VALDFENEMA TAASSSSLEK 240<br>SYELPDGQVI TIGNERFRCP ETLFQPSFIG MESAGIHETT YNSIMKCDID IRKDLYANNV 300<br>LSGGTTMYPG IADRMQKEIT ALAPSTMKIK IIAPPERKYS VWIGGSILAS LSTFQQMWIS 360<br>KQEYDEAGPS IVHRKCF 377                                                                                                                                                                                                                                                                                                                                                                                                |
| 50                   | IPI00021841<br>gi:113992<br>P02647.1    | Same as KH 37                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 51                   | IPI00023006<br>gi:54036697<br>P68032.1  | Same as KH49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 52                   | IPI00930226<br>gi:54036678<br>P63261.1  | MEEEEIALVI DNGSGMCKAG FAGDDAPRAV FPSIVGRPRH QGVMVGMGQK DSYVGDEAQS 60<br>KRGILTLKYP IEHGIVTNWD DMEKIWHHTF YNELRVAP EEHPVLLTEAPL NPKANREKMT 120<br>QIMFETFNTP AMYVAIQAVL SLYASGRTTG IVMDSGDGVT HTVPIYEGYA LPHAILRLDL 180<br>AGRDLTDYLM KILTERGYSF TTTAEREIVR DIKEKLCYVA LDFEQEMATA ASSSSLEKSY 240<br>ELPDGQVITI GNERFRCP EA LFQPSFLGME SCGIHETTFN SIMKCDVDIR KDLYANTVLS 300<br>GGTTMYPGIA DRMQKEITAL APSTMKIKII APPERKYSVW IGGSILASLS TFQQMWISKQ 360<br>EYDESGPSIV HRKCF 375                                                                                                                                                                                                                                                                                                                                                                                                  |

| KH<br>Protein/SEQ<br>ID NO | Sequence<br>Identifier(s)  | Protein Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----------------------------|----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 53                         | gi:194373497<br>BAG56844.1 | MEESLPTNPD SSTMGPWCYT TDPTVRRQEC SIPVCGQDQV TVAMTPRSEG SSVNLSPPLE 60<br>QCVPD RGQQY QGRLAVTTHG LPCLAWASAQ AKALSKHQDF NSAVQLVENF CRNPDGDEEG 120<br>VWCYVAGKPG DFGYCDLNYC EEAVEEETGD GLDESDRAI EGRTATSEYQ TFFNPRTFGS 180<br>GEADCGLRPL FEKKSLEDKT ERELLESYID GRIVEGSDAE IGMSPWQVML FRKSPQELLC 240<br>GASLISDRWV LTAAHCLLYP PWDKNFTEND LLVRIGKHSR TRYERNIEKI SMLEKIYIHP 300<br>RYNWRENLDR DIALMKLKKP VAFSDYIHPV CLPDRETAAS LLQAGYKGRV TGWGNLKETW 360<br>TANVGKGQPS VLQVVNLPIV ERPVCKDSTR IRITDNMFCA GYKPDEGKRG DACEGDSGGP 420<br>FVMKSPFNNR WYQMGIVSWG EGCDRDGKYG FYTHVFRLKK WIQKVIDQFG E 471                                                                                                                              |
| 54                         | gi:194380034<br>BAG58369.1 | MNQLRGKKSC HTGLGRSAGW NIPIGLLYCD LPEPRKPLEK AVANFFSGSC APCADGTDFP 60<br>QLCQLCPGCG CSTLNQYFGY SGAFKCLKDG AGDVAFVKHS TIFENLANKA DRDQYELLCL 120<br>DNTRKPVDEY KDCHLAQVPS HTVVARSMGS KEDLIWELLN QAQEHFGKDK SKEFQLFSSP 180<br>HGKDLLFKDS AHGFLKVPPR MDAKMYLGYE YVTAIRNLRE GTCPEAPTDE CKPVKWCALS 240<br>HHERLKCDEW SVNSVGKIEC VSAETTEDCI AKIMNGEADA MSLDGGFVYI AGKCGLVPVL 300<br>AENYNKSDNC EDTPEAGYFA VAVVKKSASD LTWDNLKGKK SCHTAVGRTA GWNIPMGLLY 360<br>NKINHCRFDE FFSEGCAPGS KKDSSLCKLC MGSGNLNCEP NNKEGYGYT GAFRCLVEKG 420<br>DVAFVKHQTV PQNTGGKNPD PWAKNLNEKD YELLCLDGTR KPVEEYANCH LARAPNHAVV 480<br>TRKDKEACVH KILRQQQHLLF GSNVTDCSGN FCLFRSETKD LLFRDDTVCL AKLHDRNTYE 540<br>KYLGE EYVKA VGNLRKCSTS SLLEACTFRR P 571 |
| 55                         | gi:194380034<br>BAG58369.1 | Same as 54                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

The details of one or more embodiments of the present invention are set forth in the accompanying figures and the description below. Further areas of applicability will become apparent from the description provided herein. It should be understood that the description and specific examples are intended for purposes of illustration only and are not intended to limit the scope of the present disclosure.

**Brief Description of the Drawings:**

Figure 1 is a graph depicting percentages of T and B lymphocytes in peripheral blood, with and without therapeutic RAAS 105 treatment.

Figure 2 is a graph depicting percentages of T and B lymphocytes in peripheral blood, with further analysis done on CD4 and CD8 T cell lineages, with and without therapeutic RAAS 105 treatment.

Figure 3 is a graph depicting percentages of CD4 and CD8 T cells in peripheral blood, with and without therapeutic RAAS 105 treatment.

Figure 4 is a graph depicting percentages of CD4 and CD8 T cells in peripheral blood, with further analysis done on the percentages of CD11c<sup>+</sup> dendritic cells (DC) and Gr-1<sup>+</sup> granulocytes.

Figure 5 is graphs depicting percentages of dendritic cells and granulocytes in peripheral blood, with and without therapeutic RAAS 105 treatment.

Figure 6 is graph showing another representation of Gr-1 vs. CD 11c cells, with and without therapeutic RAAS 105 treatment.

Figure 7 is a graph depicting the percentage of monocytes in peripheral blood, with and without therapeutic RAAS 105 treatment.

Figure 8 is a graph showing another representation of monocytes in peripheral blood, with and without therapeutic RAAS 105 treatment.

Figure 9 is graphs depicting percentages of T and B lymphocytes in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 10 is a graph showing another representation of T and B lymphocytes in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 11 is graphs depicting percentages of CD4 and CD8 T cells in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 12 is a graph showing another representation of CD4 and CD8 T cells in the spleen, with CD3 T cells being gated, with and without therapeutic RAAS 105 treatment.

Figure 13 is graphs depicting T cell subset percentages in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 14 is a graph of CD4 T cell subset percentages in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 15 is graphs depicting T cell subset percentages in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 16 is a graph of CD8 T cell subset percentages in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 17 is a graph depicting percentages of regulatory T cells in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 18 is another graphical representation of percentages of regulatory T cells in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 19 is graphs depicting percentages of mDc and pDcs in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 20 is another graphical representation of mDC and pDcs in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 21 is graphs depicting percentages of macrophages and granulocytes in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 22 is another graphical representation of percentages of macrophages and granulocytes in the spleen, with and without therapeutic RAAS 105 treatment.

Figure 23 is a graph depicting percentages of T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 24 is graphs showing percentages of CD3 T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 25 is graphs depicting percentages of CD4 and CD8 T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 26 is another graphical representation of CD4 and CD8 T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 27 is graphs depicting CD4 T cell subset percentages in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 28 is another graphical representation of CD4 T cell subset percentages in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 29 is graphs depicting CD8 T cell subset percentages in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 30 is another graphical representation of CD8 T cell subset percentages in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 31 is a graph depicting percentages of Foxp3 regulatory T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 32 is another graphical representation of Foxp3 regulatory T cells in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 33 is a graph depicting percentages of DCs in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 34 is another graphical representation of percentages of DCs in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 35 is graphs depicting percentages of macrophages and granulocytes in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 36 is another graphical representation of percentages of macrophages and granulocytes in the lymph nodes, with and without therapeutic RAAS 105 treatment.

Figure 37 is graphs depicting T and B lymphocytes in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 38 is another graphical representation of T and B cells in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 39 is graphs depicting percentages of CD4 and CD 8 T cells in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 40 is another graphical representation of CD4 and CD 8 T cells in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 41 is graphs depicting percentages of dendritic cells and granulocytes in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 42 is another graphical representation of dendritic cells and granulocytes in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 43 is a graph depicting percentages of monocytes in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 44 is another graphical representation of percentages of monocytes in peripheral blood, with and without prophylactic RAAS 105 treatment.

Figure 45 is graphs depicting percentages of T and B lymphocytes in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 46 is another graphical representation of percentages of T and B lymphocytes in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 47 is graphs depicting percentages of CD4 and CD8 T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 48 is another graphical representation of percentages of CD4 and CD8 T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 49 is graphs depicting subset percentages of T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 50 is another graphical representation of subset percentages of T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 51 is graphs depicting subset percentages of T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 52 is another graphical representation of subset percentages of T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 53 is a graph depicting Foxp3 regulator T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 54 is another graphical representation of Foxp3 regulator T cells in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 55 is graphs depicting percentages of pDCs and mDCs in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 56 is another graphical representation of percentages of pDCs and mDCs in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 57 is graphs depicting percentages of macrophages and granulocytes in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 58 is another graphical representation of percentages of macrophages and granulocytes in the spleen, with and without prophylactic RAAS 105 treatment.

Figure 59 is a graph depicting percentages of T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 60 is another graphical representation of percentages of CD3 T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment..

Figure 61 is graphs depicting percentages of CD4 and CD8 T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 62 is another graphical representation of percentages of CD4 and CD8 T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 63 is graphs depicting T cell subset percentages in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 64 is another graphical representation of T cell subset percentages in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 65 is graphs depicting T cell subset percentages in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 66 is another graphical representation of T cell subset percentages in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 67 is a graph depicting percentages of Foxp3 regulatory T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 68 is another graphical representation of Foxp3 regulatory T cells in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 69 is a graph depicting percentages of DCs in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 70 is another graphical representation of percentages of DCs in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 71 is graphs depicting percentages of macrophages and granulocytes in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 72 is another graphical representation of percentages of macrophages and granulocytes in the lymph nodes, with and without prophylactic RAAS 105 treatment.

Figure 73 is a process flowchart of the manufacturing of AFOD RAAS 102 from fraction II+III paste.

Figure 74 is a process flowchart of the manufacturing of AFOD RAAS 104 HBIG purification process from Fraction II+III paste.

Figure 75 is a protein analysis of HBIG beside the immunoglobulin proteins containing the protein TF serotransferrin.

Figure 76 is a protein analysis comparison of immunoglobulin from fraction II+III paste, immunoglobulin produced from fraction III paste, and hepatitis B immunoglobulin produced from fraction II+III paste, including a depiction of the different proteins in each of the products alongside the main immunoglobulin protein analysis.

Figure 77 is a process flowchart for AFOD RAAS 105.

Figure 78 is a process flowchart for AFOD RAAS 105.

**Detailed Description of the Invention:****Characterization of lymphoid tissues and peripheral blood in HBV infected BALB/c mice treated with RAAS 105****Executive Summary**

Investigation was made into the effects of RAAS 105 on multiple cell lineages in lymphoid tissues and peripheral blood in HBV infected BALB/c mice. HBV infection and RAAS 105 treatment were performed by ID unit at Wuxi. At the termination, blood samples and lymphoid tissues were provided to us for analysis of various cell lineages by FACS.

Two independent experiments were performed. One experiment was to test therapeutic effects of RAAS 105 and the other experiment was to test prophylactic effects of RAAS 105.

Compared with the vehicle group, the differences observed in the animals treated with RAAS 105 therapeutically include: 1) percentages of T cells and B cells in peripheral blood, spleen and lymph nodes were decreased significantly; 2) CD62L was greatly downregulated on both CD4<sup>+</sup> and CD8<sup>+</sup>T cells in the spleen and lymph nodes; 3) granulocytes and monocytes/macrophages in peripheral blood and lymph nodes increased significantly; 4) the percentages of regulatory T cells (CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup>) in the spleen and lymph nodes were increased significantly.

However, prophylactic treatment with RAAS 105 led to somewhat different results. In the group treated with RAAS 105, T- and B-lymphocytes were also decreased. The percentages of monocytes and macrophages were increased albeit to a less degree.

These results suggested that administration of RAAS 105 had significant effects on the frequencies of immune cell lineages.

## List of Abbreviations

|      |                             |
|------|-----------------------------|
| FACS | Flow Cytometry              |
| mDC  | Myeloid dendritic cell      |
| pDC  | Plasmacytoid dendritic cell |

## Materials and Methods

### Materials

#### Reagents

FITC, Rat Anti-Mouse CD4, BD, Cat: 557307

PerCP-Cy5.5, Rat Anti-Mouse CD4, BD, Cat: 550954

FITC, Rat Anti-MouseCD3 molecular complex, BD, Cat: 561798

PerCP-Cy5.5, Rat Anti-Mouse CD3, BD, Cat:560527

PerCP-Cy5.5, Rat Anti-Mouse CD8a, BD, Cat: 551162

PE, Rat Anti-MouseCD8a, BD, Cat:553032

PE, Rat Anti-Mouse B220/CD45R, BD, Cat: 553089

APC, Rat Anti-Mouse CD11b, BD, Cat: 553312

APC, Ar Ham Anti-Mouse CD11c, BD, Cat: 550261

PE, Rat Anti-Mouse CD62L, BD, Cat: 553151

APC, Rat Anti-Mouse CD44, BD, Cat: 559250

PE,Rat Anti-Mouse Gr-1(Ly-6G and Ly-6C), BD, Cat: 553128

Alexa Fluor® 647, Rat Anti-Mouse Foxp3, BD, Cat: 560401

PerCP-Cy5.5, Rat Anti-Mouse CD19, BD, Cat: 551001

PE, Rat Anti-Mouse CD25, BD, Cat: 553075

ACK Lysing buffer, Invitrogen, Cat: A10492-01

RPMI 1640 medium, Invitrogen Gibco, Cat: 22400105

Dulbecco's Phosphate Buffered Saline, Thermo. Cat: SH30028.01B.

Fetal bovine serum, Invitrogen Gibco, Cat: 10099141

## Equipment

Vi-CELL Cell Viability Analyzer, Beckman Coulter, Cat: 731050

FACS Caliburflow cytometer, BD, Cat: 342975

Cell strainer (70µm), BD, Cat: 352350

BD Falcon tubes (12x75 mm, 5 ml), BD, Cat: 352054

## Methods

Peripheral blood was collected through cardiac puncture. After removing red blood cells with lysis buffer followed by two rounds of washing using 1×PBS, mononuclear cells (monocytes, macrophages, dendritic cells, and lymphocytes) and granulocytes were obtained. Spleen and lymph nodes cell suspension were obtained after filtering through 70µm cell strainer. Cell viability and number were analyzed by Vi-CELL Cell Viability Analyzer followed by cell surface staining. Cells were centrifuged and resuspended in staining buffer (0.08% NaN<sub>3</sub>/PBS+ 1% FBS) containing appropriate fluorescent-conjugated antibodies. After 30 min incubation at 4 °C in the dark, cells were washed twice with 0.08% NaN<sub>3</sub>/PBS (200 µl per sample), and resuspended with 400 µl 0.08% NaN<sub>3</sub>/PBS in BD Falcon tubes (12x75 mm, 5 ml) followed by FACS analysis.

## **Data analysis**

FACS data were analyzed by flowjo software.

## **Study Summary**

### **S t u d y   i n i t i a t i o n   d a t e   a n d   c o m p l e t i o n   d a t e**

To investigate the therapeutic and prophylactic effect of RAAS 105 on the immune system in mice infected with HBV, the study had divided into two parts.

### **S t u d y   p u r p o s e**

The purpose of this study was to investigate the effect of RAAS 105 on cellular composition in lymphoid tissues and peripheral blood of HBV infected mice treated with RAAS 105.

### **S t u d y   r e s u l t s**

## **Effect of therapeutic treatment with RAAS 105**

### **Mice information**

Total 10 female BALB/c mice including 2 naïve mice at the same age were transferred from Infectious Disease (ID) Group of WuxiApptec. The group and the regimen information were shown by Table 1.

**Table 1. The experimental group and dosing regimen of the 1<sup>st</sup> part of the study**

|             | <b>Groups</b> | <b>N</b> | <b>Group ID</b>      | <b>Dose</b>  | <b>1<sup>st</sup> or last dosing</b> | <b>Analysis</b> |
|-------------|---------------|----------|----------------------|--------------|--------------------------------------|-----------------|
| <b>Cell</b> | 1             | 4        | Therapeutic vehicle  | --           | 1 <sup>st</sup> , 4 hrs post-HDI     | Day 5           |
|             | 3             | 4        | Therapeutic RAAS 105 | 0.4 ml/mouse | 1 <sup>st</sup> , 4 hrs post-HDI     | Day 5           |
|             | 11            | 2        | Naive                | -            | -                                    | -               |

**populations in peripheral blood**

After removing red blood cells, T cell lineages, B cells, DCs, granulocytes, and monocytes/macrophages in peripheral blood were analyzed by FACS analysis.

Total T cells and B cells were characterized by CD3 and CD19, respectively. HBV infection did not change the percentages of CD3<sup>+</sup> T cells compared with naïve mice. Therapeutic treatment of RAAS 105 reduced the percentages of both CD3<sup>+</sup> T cells and CD19<sup>+</sup> B cells significantly (Figure 1). The representative FACS profiles from each group were illustrated in Figure 2.

**Figure 1.** Percentages of T and B lymphocytes in peripheral blood. Total lymphocytes were gated. After therapeutic treated by RAAS 105, percentages of T/B cells significantly decreased in peripheral blood. (by test)

**Figure 2.** Percent of T cells and B cells in peripheral blood. Total lymphocytes were gated.

Further analysis of the percentages of CD4<sup>+</sup> and CD8<sup>+</sup> (non-CD4<sup>+</sup>) T cell lineages were performed gating on total CD3<sup>+</sup> T cells. The results showed there were no differences in the percentages of CD4<sup>+</sup> and CD8<sup>+</sup> T cells among all the groups (Figures 3). The representative FACS profiles from each group were illustrated in Figure 4.

**Figure 3.** Percentages of CD4 and CD8 T cells in peripheral blood. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages.

**Figure 4.** Percentages of CD4 and CD8 T cells in peripheral blood. Total CD3 T cells were gated.

Percentages of total CD11c<sup>+</sup> dendritic cells (DC) and Gr-1<sup>+</sup> granulocytes in peripheral blood were investigated. HBV infection reduced the percentages of CD11c<sup>+</sup>DCs, a phenomenon which also be observed in human patients, whereas the percentages of Gr-1<sup>+</sup> granulocytes were not affected. Therapeutic treatment of RAAS 105 did not show any effect on CD11c<sup>+</sup>DCs, but increased the percentages of Gr-1<sup>+</sup> granulocytes significantly (Figure 5). The representative FACS profiles from each group were illustrated in Figure 6.

**Figure 5.** Percents of Dendritic cells and Granulocytes in peripheral blood. Total live cells were gated. After therapeutic treatment, percents of granulocytes increased in peripheral blood (by T test)

**Figure 6.** Percents of Granulocytes / Dendritic cells in peripheral blood. Total live cells were gated.

Percentages of Monocytes were examined using surface marker CD11b. It increased significantly as same as Gr1<sup>+</sup> granulocytes compared with the vehicle group (Figure 7). The representative FACS profiles from each group were illustrated in Figure 8.

**Figure 7.** Percentages of Monocytes in peripheral blood. Total live cells were gated. After treatment, percentages of monocytes in peripheral blood significantly increased (t test)

**Figure 8.** Percentages of monocytes in peripheral blood. Total live cells were gated.

### Cell populations in spleen

Cell lineages in spleen including T cell lineages (CD4<sup>+</sup>/CD8<sup>+</sup> T cells, naïve T cells, memory T cells and regulatory T cells), B cells, mDCs, pDCs, granulocytes and macrophages were characterized by cell surface and intracellular markers.

Percentages of total T cells and B cells in spleen were investigated. Therapeutic treatment of RAAS 105 reduced the percentages of both CD3<sup>+</sup> T cells and CD19<sup>+</sup>B cells significantly (Figure 9). The representative FACS profiles from each group were illustrated in Figure 10.

**Figure 9.** Percentages of T and B lymphocytes in spleen. Total lymphocytes were gated. After therapeutic treatment by RAAS 105, percents of T cells and B cells significantly decreased in spleen.

**Figure 10.** Percents of T cells and B cells in spleen. Total lymphocytes were gated.

Further analysis of the percentages of CD4<sup>+</sup>(non-CD8<sup>+</sup>) and CD8<sup>+</sup>T cell lineages were performed gating on total CD3<sup>+</sup> T cells. There were no differences in the percentages of CD4<sup>+</sup> and CD8<sup>+</sup>T cells among all the groups (Figure 11).The representative FACS profiles from each group were illustrated in Figure 12.

**Figure 11.** Percentages of CD4 and CD8 T cells in spleen. Total CD3 T cells were gated and further analyzed for CD4 /CD8 percentages.

**Figure 12.** Percentages of CD4 and CD8 T cells in spleen. Total CD3 T cells were gated.

Three T cell lineages, naïve T cells (CD44<sup>low</sup>CD62L<sup>high</sup>), central memory T cells (T<sub>CMS</sub>, CD44<sup>high</sup>CD62L<sup>high</sup>) and Effector memory T cells (T<sub>EMS</sub>, CD44<sup>high</sup>CD62L<sup>low</sup>), were characterized by surface markers CD44 and CD62L. Percentages of these T cell lineages in CD4<sup>+</sup> or CD8<sup>+</sup> T cells were analyzed respectively. Both in CD4<sup>+</sup> and CD8<sup>+</sup> T cells, percentages of naïve T cells and T<sub>CMS</sub> decreased and T<sub>EMS</sub> increased after the therapeutic treatment of RAAS 105, suggesting the compound may have effect to promote the transformation of T cells from naïve T cells to memory T cells in spleen (Figure 13 and 15). The representative FACS profiles from each group were illustrated in Figure 14 and 16.

**Figure 13.** T cell subsets percentages in spleen. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 14.** CD4 T cell subsets percentages in spleen. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 15.** T cell subsets percentages in spleen. Total CD8 T cells were gated and T cell subsets were determined.

**Figure 16.** CD8 T cell subsets percentages in spleen. Total CD8 T cells were gated and T cell subsets were determined.

Regulatory T cells (Tregs) were analyzed by cell surface staining of anti-CD4 and anti-CD25 antibodies followed by intracellular staining of anti-Foxp3 antibody. Percents of Tregs in spleen increased compared with the vehicle group (Figure 17). The representative FACS profiles from each group were illustrated in Figure 18.

**Figure 17.** Percentages of Foxp3 regulatory T cells in spleen. Foxp3 regulatory T cells were analyzed by intracellular staining. After treatment, the percentage of T regulate cells is increased.

**Figure 18.** Percentages of regulatory T cells in spleen. Total CD4 T cells were gated.

Dendritic cells, including myeloid dendritic cells (mDC, B220<sup>-</sup>CD11c<sup>+</sup>) and plasmacytoid dendritic cells (pDC, B220<sup>+</sup>CD11c<sup>+</sup>) in spleen were analyzed. No significant differences of mDCs and pDCs were observed among all groups (Figure 19). The representative FACS profiles from each group were illustrated in Figure 20.

**Figure 19.** Percentages of pDcs and mDcs in spleen. Total live cells were gated. There were no significant differences after compound treatment. (by t test)

**Figure 20.** Percentages of mDc and pDcs in spleen. Total live cells were gated.

CD11b<sup>+</sup> macrophages and Gr-1<sup>+</sup> granulocytes in spleen were analyzed. There were no significant alterations among all groups in the percentages of these cell lineages in spleen, as shown in Figure 21. The representative FACS profiles from each group were illustrated in Figure 22.

**Figure 21.** Percentages of Macrophages and Granulocytes in Spleen. Total live cells were gated. There were no significant differences after compound treatment. (by t test)

**Figure 22.** Percentages of macrophages/Granulocytes in spleen. Total live cells were gated.

### **Cell populations in draining lymph nodes**

Cell lineages in draining lymph nodes including T cell lineages (CD4<sup>+</sup>/CD8<sup>+</sup> T cells, naïve T cells, memory T cells and regulatory T cells), DCs, granulocytes and macrophages were characterized by cell surface and intracellular markers.

Percentages of total T cells in lymph nodes were analyzed. HBV infection did not affect the percentages of CD3<sup>+</sup> T cells but therapeutic treatment of RAAS 105 reduced it significantly compared with vehicle group (Figure 23). The representative FACS profiles from each group were illustrated in Figure 24.

**Figure 23.** Percentages of T cells in lymph nodes. Total lymphocytes were gated. After the treatment, the percentage of T cells in the lymph nodes were significantly decreased (t test)

**Figure 24.** Percentages of CD3 T cells in lymph nodes. Total lymphocytes were gated.

Further analysis of the percentages of CD4<sup>+</sup> and CD8<sup>+</sup> T cell lineages were performed gating on total CD3<sup>+</sup> T cells. Percentages of CD4<sup>+</sup> T cells tended to decrease while CD8<sup>+</sup> T cells tended to increase, suggesting that therapeutic treatment of RAAS 105 may have effect on the ratio of CD4<sup>+</sup>/CD8<sup>+</sup> T cells in lymph nodes (Figure 25). The representative FACS profiles from each group were illustrated in Figure 26.

**Figure 25.** Percentages of CD4 and CD8 T cells in lymph nodes. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages. After therapeutic treatment, the percentage of CD4 T cells decreased. (by t test)

**Figure 26.** Percentages of CD4 and CD8 T cells in lymph nodes. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages.

Three T cell lineages, naïve T cells, T<sub>CMS</sub> and T<sub>EMS</sub> were characterized by surface markers CD44 and CD62L. Percentages of these T cell lineages in CD4<sup>+</sup> or CD8<sup>+</sup> T cells were analyzed respectively. The results in lymph nodes were comparable to those in spleen. Both in CD4<sup>+</sup> and CD8<sup>+</sup> T cells, percentages of naïve T cells and T<sub>CMS</sub> decreased and T<sub>EMS</sub> increased after the therapeutic treatment of RAAS 105, suggesting the compound also have effect to promote the transformation of T cells from naïve T cells to memory T cells in lymph nodes (Figure 27 and 29). The representative FACS profiles from each group were illustrated in Figure 28 and 30.

**Figure 27.** CD4 T cell subsets percentages in lymph nodes. Total CD4 T cells were gated and T cell subsets were determined. No significant differences were found in all the groups compared to vehicle group.

**Figure 28.** CD4 T cell subset percentages in lymph nodes. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 29.** CD8 T cell subsets percentages in lymph nodes. Total CD8 T cells were gated and T cell subsets were determined.

**Figure 30.** CD8 T cell subsets percentages in lymph nodes. Total CD8 T cells were gated and T cell subsets were determined.

Regulatory T cells (Tregs) were analyzed. Percentages of Tregs in lymph node slightly increased without significant differences (Figure 31). The representative FACS profiles from each group were illustrated in Figure 32.

**Figure 31.** Percentages of Foxp3 regulatory T cells in lymph nodes. There were no significant alterations after compound treatment

**Figure 32.** Percentages of regulatory T cells in lymph nodes. Total CD4 T cells were gated. One representative profile from each group is shown.

Total dendritic cells in lymph nodes were analyzed. Therapeutic treatment of RAAS 105 may reverse the reduction of DCs induced by HBV infection (Figure 33). The representative FACS profiles from each group were illustrated in Figure 34.

**Figure 33.** Percentages of DCs in lymph nodes. Total live cells were gated. After treatment, percents of DCs increased significantly (by t test)

**Figure 34.** Percentages of DCs in lymph nodes. Total live cells were gated.

CD11b<sup>+</sup> macrophages and Gr-1<sup>+</sup> granulocytes in lymph nodes were analyzed. Both percentages of CD11b<sup>+</sup> macrophages and Gr-1<sup>+</sup> granulocytes increased significantly (Figure 35). The representative FACS profiles from each group were illustrated in Figure 36.

**Figure 35.** Percentages of Macrophages and Granulocytes in lymph nodes. Total live cells were gated. Percentages of macrophages and granulocytes significantly increased in lymph node. (by t test)

**Figure 36.** Percentages of Macrophages/Granulocytes in lymph nodes. Total live cells were gated.

### Effect of prophylactic treatment with RAAS 105

#### Mice information

Total 14 female BALB/c mice including 2 naïve mice at the same age were transferred from Infectious Disease (ID) Group of Wuxi Apptec. The group and the regimen information were shown by Table 2.

**Table 2. The experimental group and dosing regimen of the 2<sup>nd</sup> part of the study**

| Groups | N | Group ID                          | Dose         | 1 <sup>st</sup> or last dosing     | Analysis |
|--------|---|-----------------------------------|--------------|------------------------------------|----------|
| 5      | 4 | Prophylactic vehicle <sup>#</sup> | --           | last, 4 hrs<br>pre-HDI             | Day 5    |
| 7      | 4 | Prophylactic RAAS 105             | 0.4 ml/mouse | last, 4 hrs<br>pre-HDI             | Day 5    |
| 10     | 4 | ETV                               | 0.1 mg/kg    | 1 <sup>st</sup> , 4 hrs<br>pre-HDI | Day 5    |
| 11     | 2 | Naive                             | -            | -                                  | -        |

#### Cell populations in peripheral blood

After removing red blood cells, T cell lineages, B cells, DCs, granulocytes, and monocytes/macrophages in peripheral blood were analyzed by FACS analysis.

Total T cells and B cells were characterized. Unlike therapeutic treatment, prophylactic treatment of RAAS 105 had no effect on percentages of CD3<sup>+</sup> T cells but reduced the percentages of CD19<sup>+</sup>B cells although the statistical significance was not found (Figure 37). The representative FACS profiles from each group were illustrated in Figure 38.

**Figure 37.** Percents of T and B lymphocytes in peripheral blood. Total lymphocytes were gated.

**Figure 38.** Percents of T cells and B cells in peripheral blood. Total lymphocytes were gated.

Further analysis of the percentages of CD4<sup>+</sup> and CD8<sup>+</sup>(non-CD4<sup>+</sup>) T cell lineages were performed gating on total CD3<sup>+</sup> T cells. Unlike therapeutic treatment, prophylactic treatment reduced percentages of CD4<sup>+</sup> T cells and increased percentage of CD8<sup>+</sup> T cells, suggesting the potential effect of RAAS 105 to reduce the ratio of CD4<sup>+</sup>/CD8<sup>+</sup> T cells in peripheral blood (Figure 39). The representative FACS profiles from each group were illustrated in Figure 40.

**Figure 39.** Percentages of CD4 and CD8 T cells in peripheral blood. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages. After prophylactic treated by RAAS 105, percentages of CD4 T cells decreased while CD8 T cells increased (by t test)

**Figure 40.** Percentages of CD4 and CD8 T cells in peripheral blood. Total CD3 T cells were gated.

Results of total CD11c<sup>+</sup> dendritic cells (DC) and Gr-1<sup>+</sup> granulocytes in peripheral blood were also different from those in therapeutic treatment. Prophylactic treatment of RAAS 105 reversed the reduction of DCs induced by HBV infection, but had no significant effect on granulocytes in peripheral blood (Figure 41). The representative FACS profiles from each group were illustrated in Figure 42.

**Figure 41.** Percentages of Dendritic cells and Granulocytes in peripheral blood. Total live cells were gated. After prophylactic treated, percents of dendritic cells increased in peripheral blood.

**Figure 42.** Percentages of Granulocytes/Dendritic cells in peripheral blood. Total live cells were gated.

Percentages of Monocytes were examined. There were no significant differences among all groups (Figure 43). The representative FACS profiles from each group were illustrated in Figure 44.

**Figure 43.** Percentages of Monocytes in peripheral blood. Total live cells were gated.

**Figure 44.** Percentages of monocytes in peripheral blood. Total live cells were gated.

### Cell populations in spleen

Cell lineages in spleen including T cell lineages ( $CD4^+/CD8^+$  T cells, naïve T cells, memory T cells and regulatory T cells), B cells, mDCs, pDCs, granulocytes and macrophages were characterized by cell surface and intracellular markers.

Percentages of total T cells and B cells in spleen were investigated. Unlike therapeutic treatment, prophylactic treatment did not show effects on percentages of  $CD3^+$  T cells and  $CD19^+$  B cells (Figure 45). The representative FACS profiles from each group were illustrated in Figure 46.

**Figure 45.** Percentages of T and B lymphocytes in spleen. Total lymphocytes were gated.

**Figure 46.** Percentages of T and B cells in spleen. Total lymphocytes were gated.

Further analysis of the percentages of  $CD4^+$ (non- $CD8^+$ ) and  $CD8^+$  T cell lineages were performed gating on total  $CD3^+$  T cells. Percentages of  $CD4^+$  T cells slightly decreased and  $CD8^+$  T cells slightly increased in spleen (Figure 47). The representative FACS profiles from each group were illustrated in Figure 48.

**Figure 47.** Percentages of CD4 and CD8 T cells in spleen. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages. After prophylactic treated by RAAS 105, the percentage of CD4 T cells slightly decreased while CD8 T cells slightly increased (by t test)

**Figure 48.** Percentages of CD4 and CD8 T cells in spleen. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages.

Naïve T cells, central memory T cells and Effector memory T cells were investigated. Percentages of these T cell lineages in CD4<sup>+</sup> or CD8<sup>+</sup> T cells in spleen were analyzed respectively. Both in CD4<sup>+</sup> and CD8<sup>+</sup> T cells, percentages of naïve T cells decreased and T<sub>EMS</sub> increased significantly after the prophylactic treatment of RAAS 105 (Figure 49 and 51). The representative FACS profiles from each group were illustrated in Figure 50 and 52.

**Figure 49.** T cell subset percentages in spleen. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 50.** T Cell subsets percentages in spleen. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 51.** T cell subsets percentages in spleen. Total CD8 T cells were gated and T cell subsets were determined.

**Figure 52.** T cell subsets percentages in spleen. Total CD8 T cells were gated and T cell subsets were determined.

Results of regulatory T cells (Tregs) were comparable with those in therapeutic treatment. Percentages of Tregs in spleen increased compared with the vehicle group by prophylactic treatment of RAAS 105 (Figure 53). The representative FACS profiles from each group were illustrated in Figure 54.

**Figure 53.** Percentages of Foxp3 regulatory T cells in spleen. Foxp3 regulatory T cells were analyzed by intracellular staining.

**Figure 54.** Percentages of regulatory T cells in spleen. Total CD4 T cells were gated.

Dendritic cells, including mDCs and pDCs in spleen were analyzed. No significant differences of mDCs and pDCs were observed among all groups after prophylactic treatment (Figure 55). The representative FACS profiles from each group were illustrated in Figure 56.

**Figure 55.** Percentages of pDCs and mDC in spleen. Total live cells were gated. There were no significant differences after compound treatment (by t test)

**Figure 56.** Percentages of mDCs and pDCs in spleen. Total live cells were gated.

CD11b<sup>+</sup> macrophages and Gr-1<sup>+</sup> granulocytes in spleen were analyzed. Percentages of macrophages and granulocytes increased, but no statistical differences were observed, as shown in Figure 57. The representative FACS profiles from each group were illustrated in Figure 58.

**Figure 57.** Percentages of Macrophages and Granulocytes in spleen. Total live cells were gated. There were no significant differences after compound treatment. (by t test)

**Figure 58.** Percentages of macrophages/granulocytes in spleen. Total live cells were gated.

### Cell populations in draining lymph nodes

Cell lineages in draining lymph nodes including T cell lineages (CD4<sup>+</sup>/CD8<sup>+</sup> T cells, naïve T cells, memory T cells and regulatory T cells), DCs, granulocytes and macrophages were characterized by cell surface and intracellular markers.

Percentages of total T cells in lymph nodes were analyzed. Similar with therapeutic treatment, HBV infection did not affect the percentages of CD3<sup>+</sup> T cells but prophylactic treatment of RAAS 105 reduced it significantly compared with vehicle group (Figure 59). The representative FACS profiles from each group were illustrated in Figure 60.

**Figure 59.** Percentages of T cells in lymph nodes. Total lymphocytes were gated. After the treatment, percents of T cells in the lymph nodes were significantly decreased. (t test)

**Figure 60.** Percentages of CD3 T cells in lymph nodes. Total lymphocytes were gated.

Further analysis of the percentages of CD4<sup>+</sup> and CD8<sup>+</sup> T cell lineages were performed gating on total CD3<sup>+</sup> T cells. Percentages of CD4<sup>+</sup> T cells tended to decrease while CD8<sup>+</sup> T cells tended to increase after prophylactic treatment, as was seen in therapeutic treatment (Figure 61). The representative FACS profiles from each group were illustrated in Figure 62.

**Figure 61.** Percentages of CD4 and CD8 T cells in lymph nodes. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages. After prophylactic treatment, percents of CD4 T cells decreased (by t test)

**Figure 62.** Percentages of CD4 and CD8 T cells in lymph nodes. Total CD3 T cells were gated and further analyzed for CD4/CD8 percentages.

Results of naïve T cells, central memory T cells and Effector memory T cells were totally difference with those in therapeutic treatment. Prophylactic treatment did not show significant effects on naïve T cells and T<sub>CMS</sub>, but increased percentages of T<sub>EMS</sub> (Figure 63 and 65). The representative FACS profiles from each group were illustrated in Figure 64 and 66.

**Figure 63.** T cell subsets percentages in lymph nodes. Total CD4 cells were gated and T cell subsets were determined. No significant differences were found except effector memory T cells compared to vehicle group.

**Figure 64.** T cell subsets percentages in lymph nodes. Total CD4 T cells were gated and T cell subsets were determined.

**Figure 65.** T cell subsets percentages in lymph nodes. Total CD8 T cells were gated and T cell subsets were determined. No significant differences were found in all the groups compared to vehicle group.

**Figure 66.** T cell subsets percentages in lymph nodes. Total CD8 T cells were gated and T cell subsets were determined.

Regulatory T cells were analyzed. There were no significant differences among all groups (Figure 67). The representative FACS profiles from each group were illustrated in Figure 68.

**Figure 67.** Percentages of Foxp3 regulatory T cells in lymph nodes. Foxp3 regulatory T cells were analyzed by intracellular staining. There were no significant alterations after compound treatment. (by t test)

**Figure 68.** Percentages of regulatory T cells in lymph nodes. Total CD4 T cells were gated.

Results of total dendritic cells in lymph nodes were similar with those in therapeutic treatment. Prophylactic treatment of RAAS 105 also increased the percentages of DCs significantly compared with vehicle group (Figure 69). The representative FACS profiles from each group were illustrated in Figure 70.

**Figure 69.** Percentages of DCs in lymph nodes. Total live cells were gated. After the treatment, percentages of the DCs increased significantly (by t test)

**Figure 70.** Percentages of DCs in lymph nodes. Total live cells were gated.

CD11b<sup>+</sup> macrophages and Gr-1<sup>+</sup> granulocytes in lymph nodes were analyzed. Both macrophages and granulocytes increased significantly (Figure 71). The representative FACS profiles from each group were illustrated in Figure 72.

**Figure 71.** Percentages of Macrophages and Granulocytes in lymph nodes. Total live cells were gated. After therapeutic treated by RAAS 105, percents of macrophages and granulocytes significantly increased. (by t test)

**Figure 72.** Percentages of Macrophages/Granulocytes in lymph nodes. Total live cells were gated.

## Conclusions

The effects of RAAS 105 on different cell lineages in lymphoid tissues and peripheral blood in HBV infected mice were investigated by FACS analysis. T cell lineages (including CD4<sup>+</sup>/CD8<sup>+</sup> T cells, naïve T cells, memory T cells and regulatory T cells), B cells, dendritic cells (including mDCs, pDCs), granulocytes and monocytes/macrophages were analyzed. RAAS 105 was administered in two different time schedules for therapeutic and prophylactic treatment.

Therapeutic treatment revealed some interesting findings. The animals treated with RAAS 105 exhibited alterations in multiple immune cells and various lineages compared with that in the vehicle group, including reduction of lymphocytes and increase of granulocytes and monocytes. Prophylactic treatment led to less dramatic alterations in the immune cells.

## CLAIMS

1. An isolated purified IVIG plasma product comprising an isolated purified protein complex containing proteins defined by amino acid sequences SEQ ID NOs 33-37.
2. The isolated purified protein complex of claim 1 further comprising proteins defined by amino acid sequences SEQ ID NOs 22-31.
3. The isolated purified protein complex of claim 1 further comprising a protein defined by amino acid sequence SEQ ID NO: 51.
4. An isolated purified IVIG plasma product comprising an isolated purified protein complex containing:
  - a first substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 22;
  - a second substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 23;
  - a third substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 24;
  - a fourth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 25;
  - a fifth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 26;
  - a sixth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 27;
  - a seventh substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 28;

an eighth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 29;

a ninth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 30;

a tenth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 31;

an eleventh substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 32;

a twelfth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 33;

a thirteenth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 34;

a fourteenth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 35;

a fifteenth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 36; and

a sixteenth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 37.

5. An isolated purified IVIG plasma product comprising an isolated purified protein complex containing:

a first substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 33;

a second substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 34;

a third substantially pure protein having at least 90% homology to amino acid SEQ ID NO: 35;

a fourth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 36; and

a fifth substantially pure protein having at least 90% homology to amino acid sequence SEQ ID NO: 37.

6. An isolated purified IVIG plasma product comprising an isolated purified protein complex containing:

a first substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 22, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 22;

a second substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 23, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 23;

a third substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 24, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 24;

a fourth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 25, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 25;

a fifth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 26, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 26;

a sixth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 27, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 27;

a seventh substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 28, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 28;

an eighth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 29, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 29;

a ninth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 30, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 30;

a tenth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 31, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 31;

an eleventh substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 32, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 32;

a twelfth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 33, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 33;

a thirteenth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 34, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 34;

a fourteenth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 35, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 35;

a fifteenth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 36, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 36; and

a sixteenth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 37, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 37.

7. An isolated purified IVIG plasma product comprising an isolated purified protein complex containing:

a first substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 33, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 33;

a second substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 34, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 34;

a third substantially pure protein having at least 80% homology to amino acid SEQ ID NO: 35, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 35;

a fourth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 36, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 36; and

a fifth substantially pure protein having at least 80% homology to amino acid sequence SEQ ID NO: 37, wherein said substantially pure protein has the same activity as the protein defined by amino acid sequence SEQ ID NO: 37.

8. The isolated purified IVIG plasma product of claim 1 wherein the proteins defined by amino acid sequences SEQ ID NOs 33-37 have a concentration of at least 30%.

9. The isolated purified IVIG plasma product of claim 2 wherein the proteins defined by amino acid sequences SEQ ID NOs 22-37 have a concentration of at least 30%.

10. The isolated purified IVIG plasma product of claim 3 wherein the proteins defined by amino acid sequences SEQ ID NOs 22-37, and 51 have a concentration of at least 30%.

11. A method of treating hepatitis B in a patient comprising:

administering to said patient an effective dose of an isolated purified IVIG plasma product, wherein the isolated purified IVIG plasma product comprises:

a first protein defined by amino acid sequence SEQ ID NO: 33;

a second protein defined by amino acid sequence SEQ ID NO: 34;

a third protein defined by amino acid sequence SEQ ID NO 35;

a fourth protein defined by amino acid sequence SEQ ID NO 36; and

a fifth protein defined by amino acid sequence SEQ ID NO 37.

12. The method according to claim 11 wherein the isolated purified IVIG plasma product further comprises:

a sixth protein defined by amino acid sequence SEQ ID NO: 22;

a seventh protein defined by amino acid sequence SEQ ID NO: 23;

an eighth protein defined by amino acid sequence SEQ ID NO: 24;

a ninth protein defined by amino acid sequence SEQ ID NO: 25;

a tenth protein defined by amino acid sequence SEQ ID NO: 26;

an eleventh protein defined by amino acid sequence SEQ ID NO: 27;

a twelfth protein defined by amino acid sequence SEQ ID NO: 28;

a thirteenth protein defined by amino acid sequence SEQ ID NO: 29;

a fourteenth protein defined by amino acid sequence SEQ ID NO: 30;

a fifteenth protein defined by amino acid sequence SEQ ID NO: 31; and

a sixteenth protein defined by amino acid sequence SEQ ID NO: 32.

13. The method according to claim 12 wherein the isolated IVIG plasma product further comprises a sixteenth protein defined by amino acid sequence SEQ ID NO: 51.
14. The method according to claim 13 wherein CD62L is regulated to an effective range on CD4+ T cells in peripheral blood of a hepatitis B patient for treating HBV.
15. The method according to claim 13 wherein CD62L is regulated to an effective range on CD4+ T cells in the spleen of a hepatitis B patient for treating HBV.
16. The method according to claim 13 wherein CD62L is regulated to an effective range on CD8+ T cells in peripheral blood of a hepatitis B patient for treating HBV.
17. The method according to claim 13 wherein CD62L is regulated to an effective range on CD8+ T cells in the spleen of a hepatitis B patient for treating HBV.
18. The method according to claim 13 wherein levels of CD4+ T cells are regulated to an effective range in peripheral blood of a hepatitis B patient for treating HBV.
19. The method according to claim 13 wherein levels of CD4+ T cells are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.
20. The method according to claim 13 wherein levels of CD28+ T cells are regulated to an effective range in peripheral blood of a hepatitis B patient for treating HBV.
21. The method according to claim 13 wherein levels of CD28+ T cells are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.
22. The method according to claim 13 wherein levels of Foxp3+ T cells are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.
23. The method according to claim 13 wherein levels of Foxp3+ T cells are regulated to an effective range on T cells in peripheral blood of a hepatitis B patient for treating HBV.
24. The method according to claim 13 wherein levels of CD28+ T cells are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.

25. The method according to claim 13 wherein B cell levels are regulated to an effective range in the peripheral blood of a hepatitis B patient for treating HBV.
26. The method according to claim 13 wherein B cell levels are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.
27. The method according to claim 13 wherein granulocyte levels are regulated to an effective range in the peripheral blood of a hepatitis B patient for treating HBV.
28. The method according to claim 13 wherein granulocyte levels are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.
29. The method according to claim 13 wherein macrophage levels are regulated to an effective range in the peripheral blood of a hepatitis B patient for treating HBV.
30. The method according to claim 13 wherein macrophage levels are regulated to an effective range in the spleen of a hepatitis B patient for treating HBV.

31. A method of manufacturing an isolated purified IVIG plasma product containing proteins defined by amino acid sequences SEQ ID NOs 33-37 comprising:

- a) obtaining a fraction II+III paste from human blood plasma;
- b) suspending and diluting the fraction II+III paste at a ratio of 1:17;
- c) adjusting the pH of the diluted fraction II+III paste to a pH of 5.2 to produce an adjusted fraction II+III paste;
- d) adding ethanol to the adjusted fraction II+III paste to produce a 17% ethanol fraction II+III product;
- e) press filtering the 17% ethanol fraction II+III product and collecting a filtrate comprising fraction III;
- f) concentrating the filtrate by ultrafiltration to form a 100k ultrafiltrate;
- g) adjusting the pH of the 100k ultrafiltrate to a pH of 4.0;
- h) filtering the pH adjusted ultrafiltrate using a .45 um filter and collecting a filtered product; and
- i) nanofiltrating the filtered product with a 50 nm filter to obtain a final product.

32. A method of manufacturing an isolated purified IVIG plasma product containing proteins defined by amino acid sequences SEQ ID NOs 22-37 comprising:

- a) obtaining a fraction II+III paste from human hepatitis B immune globulin having high levels of hepatitis B surface antigen;
- b) suspending and diluting the fraction II+III paste at a ratio of 1:17;
- c) adjusting the pH of the diluted fraction II+III paste to a pH of 5.2 to produce an adjusted fraction II+III paste;
- d) adding ethanol to the adjusted fraction II+III paste to produce a 17% ethanol fraction II+III product;
- e) press filtering the 17% ethanol fraction II+III product and collecting a filtrate comprising fraction III;
- f) concentrating the filtrate by ultrafiltration to form a 100k ultrafiltrate;
- g) adjusting the pH of the 100k ultrafiltrate to a pH of 4.0;
- h) filtering the pH adjusted ultrafiltrate using a .45 um filter and collecting a filtered product; and
- i) nanofiltrating the filtered product with a 50 nm filter to obtain a final product.

33. A method of producing an isolated purified IVIG plasma product containing proteins defined by amino acid sequences SEQ ID NOs 22-37, and 51 comprising:

- a) manufacturing a non-sterile final bulk of normal immunoglobulin;
- b) manufacturing a non-sterile final bulk of hepatitis B immune globulin;
- c) creating a immunoglobulin mixture comprising 80% of the non-sterile final bulk of normal immunoglobulin and 20% of the non-sterile final bulk of hepatitis B immune globulin;
- d) performing sterile filtration on the immunoglobulin mixture and collecting a final product.

Figure 1

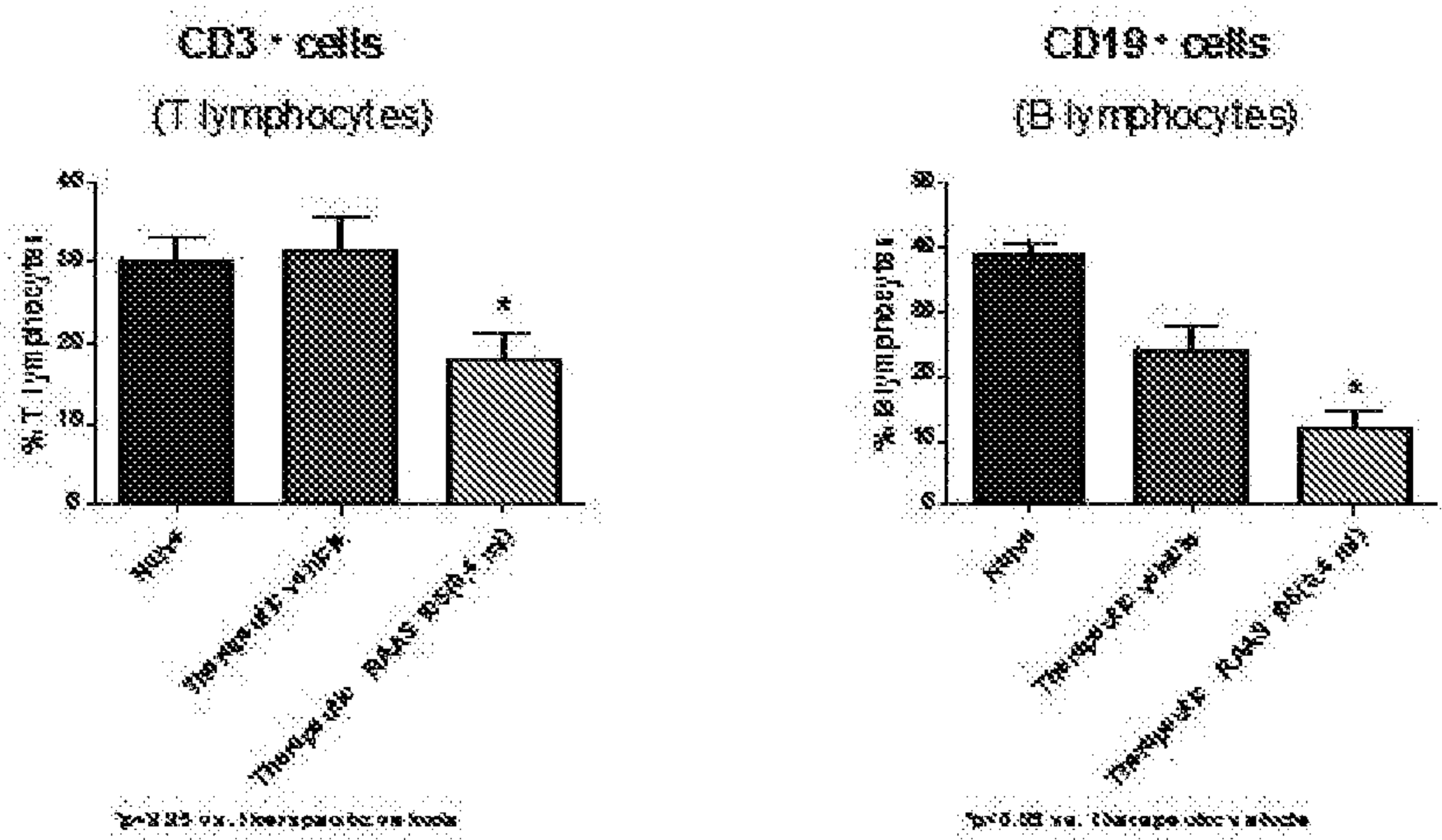


Figure 2

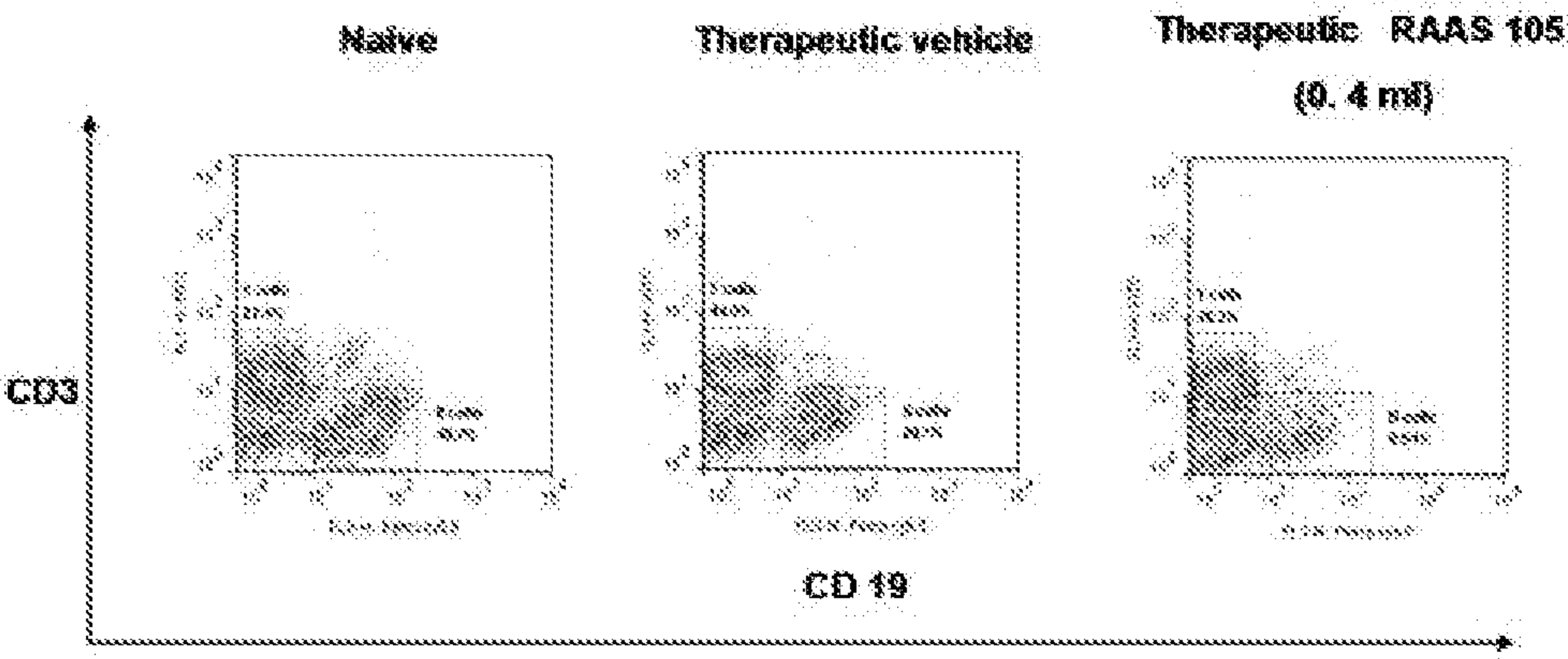


Figure 3

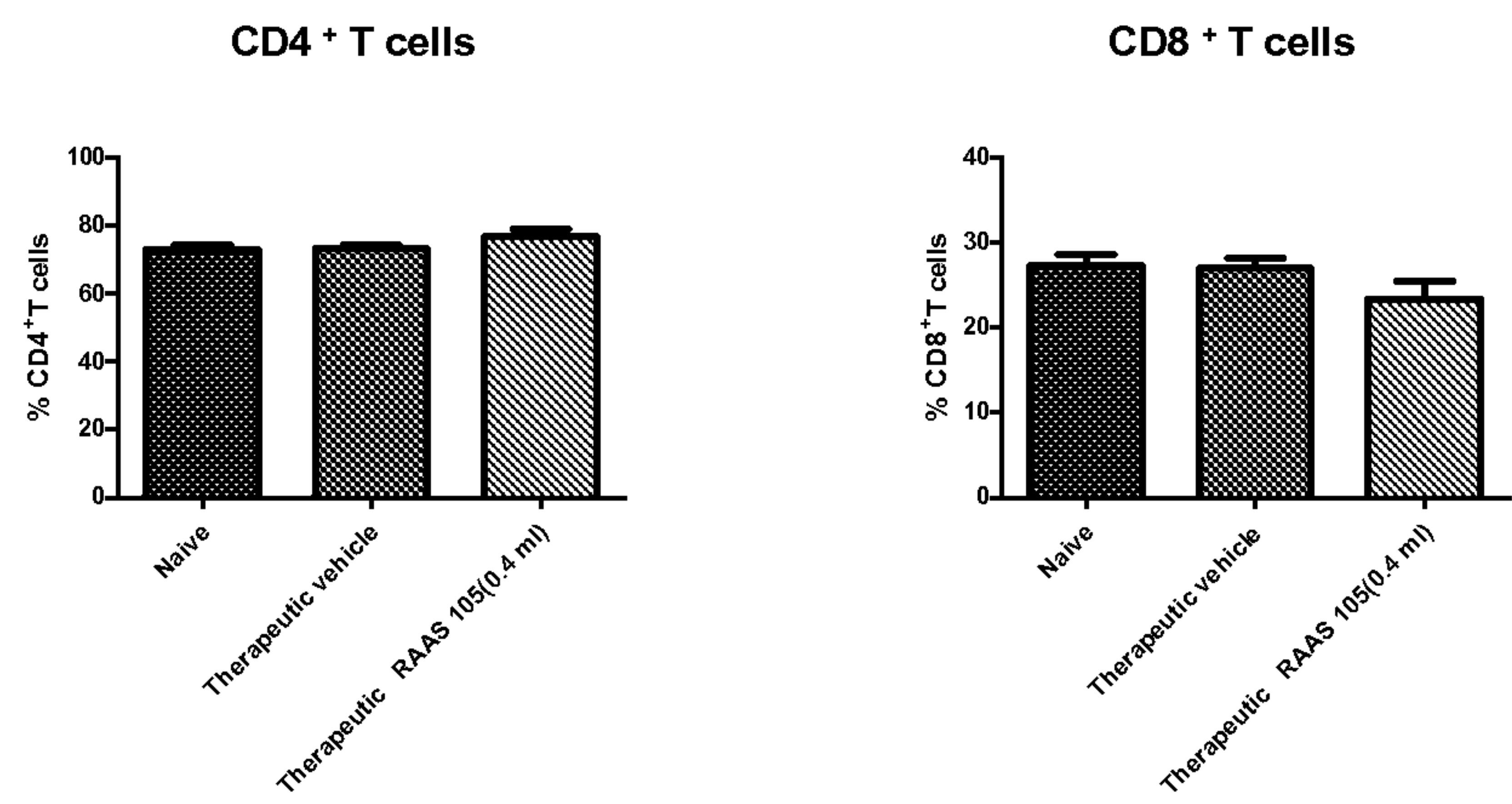


Figure 4

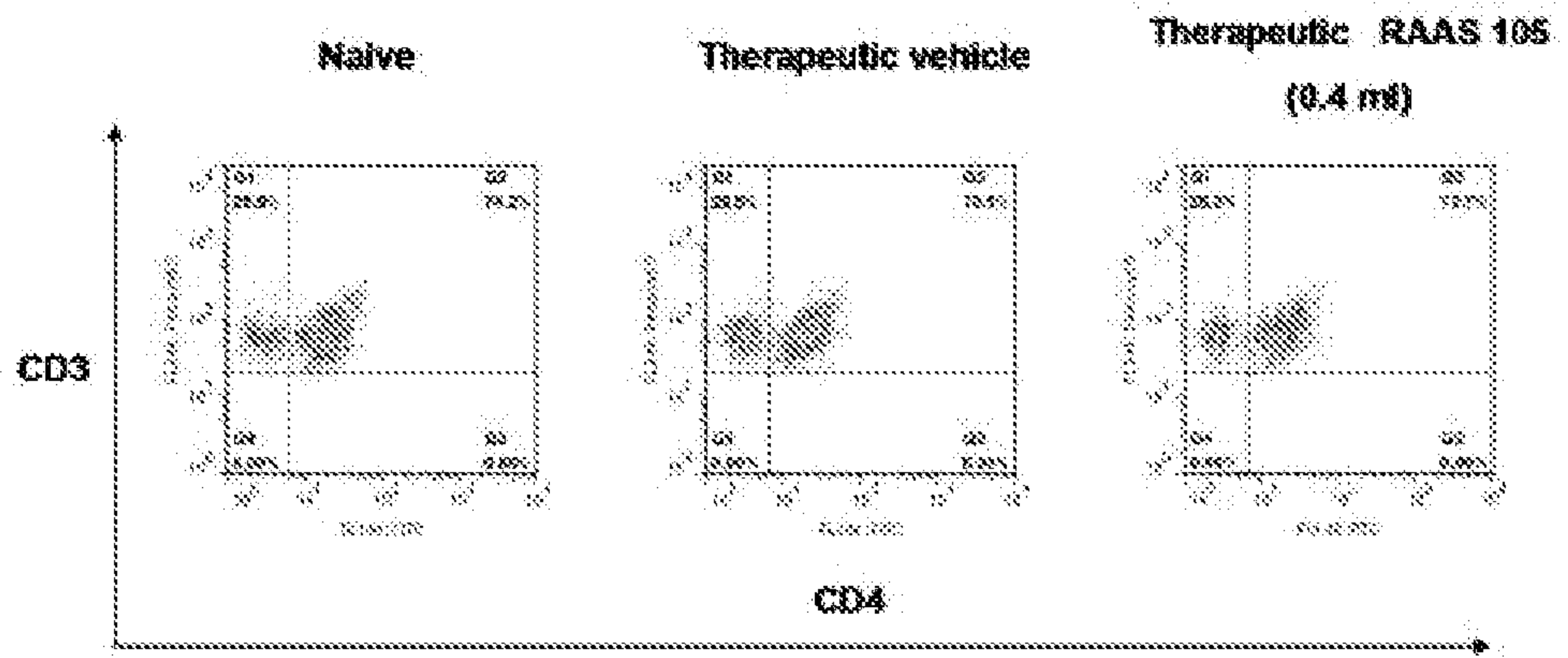


Figure 5

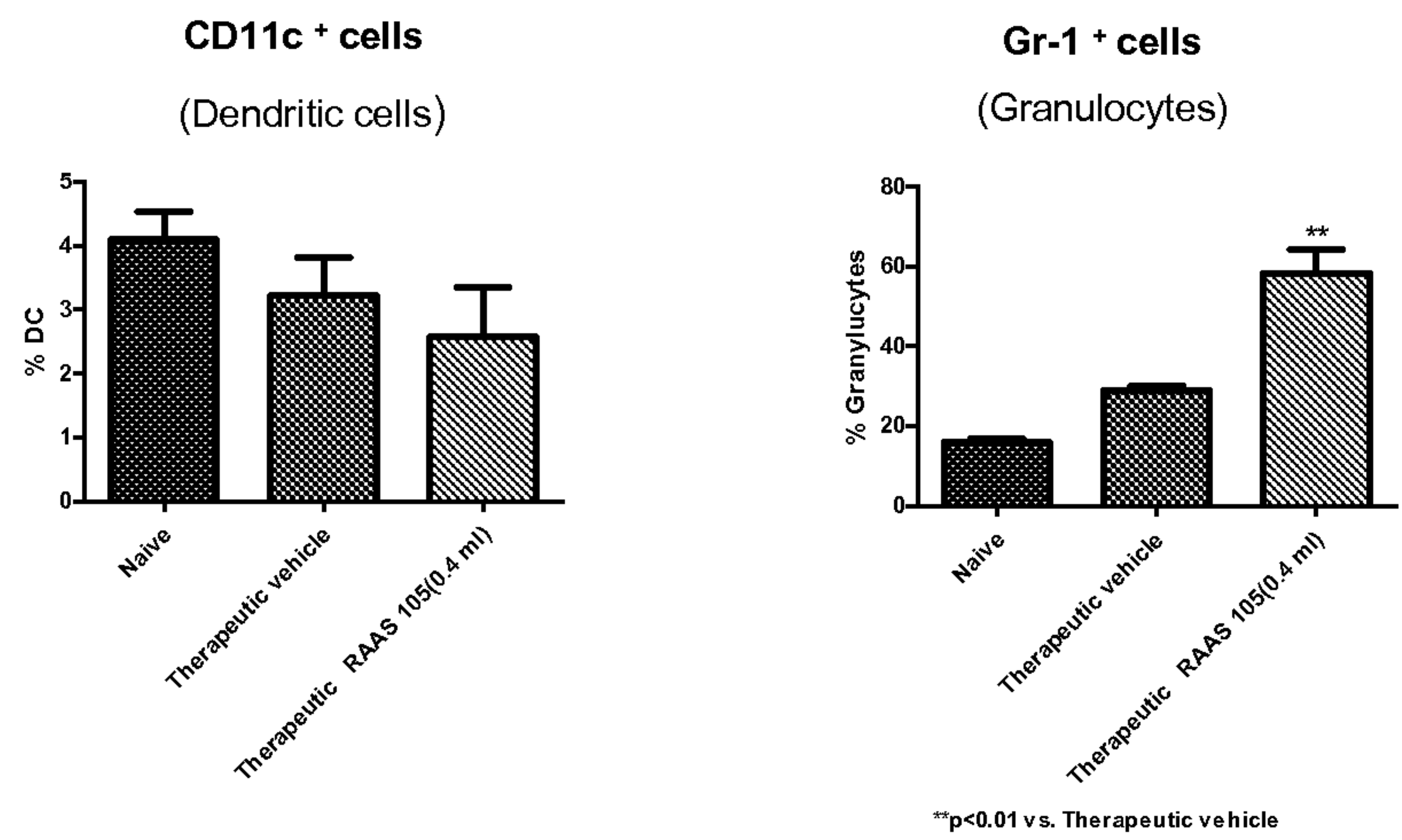


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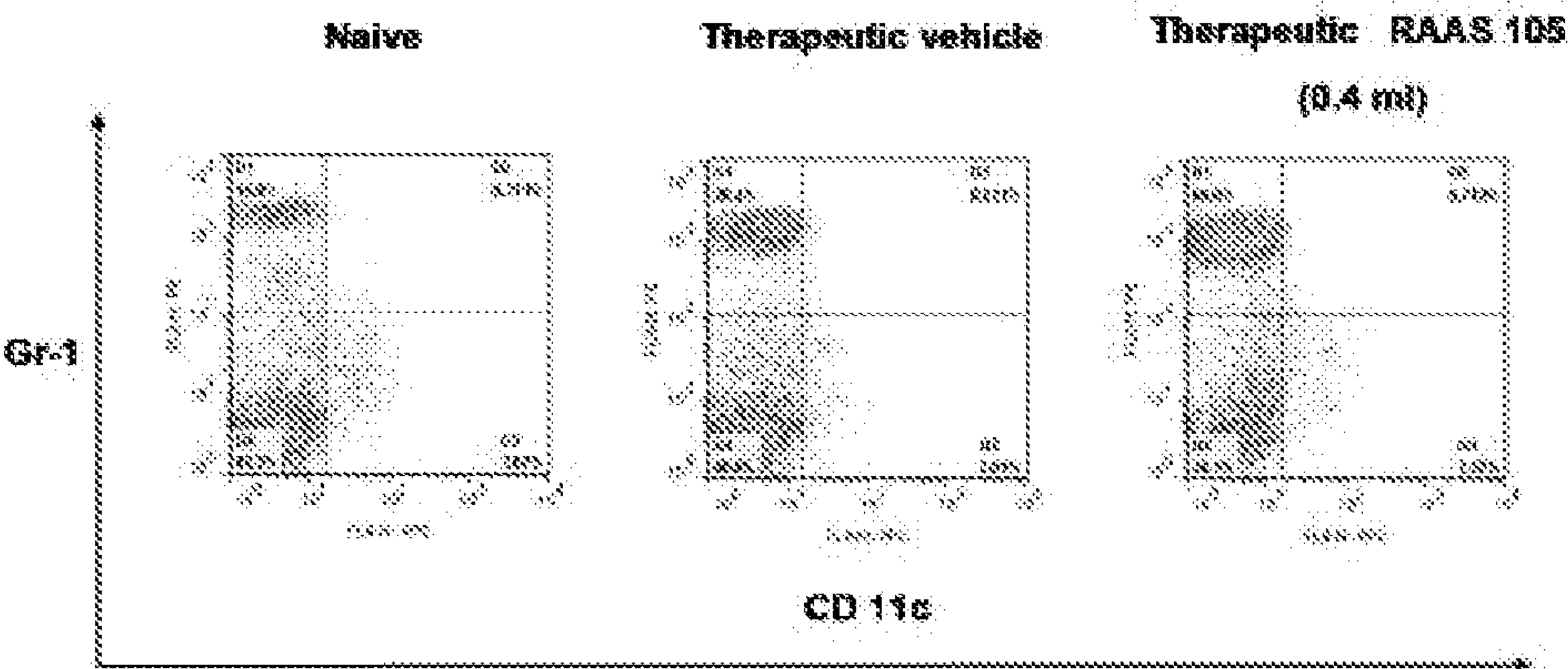


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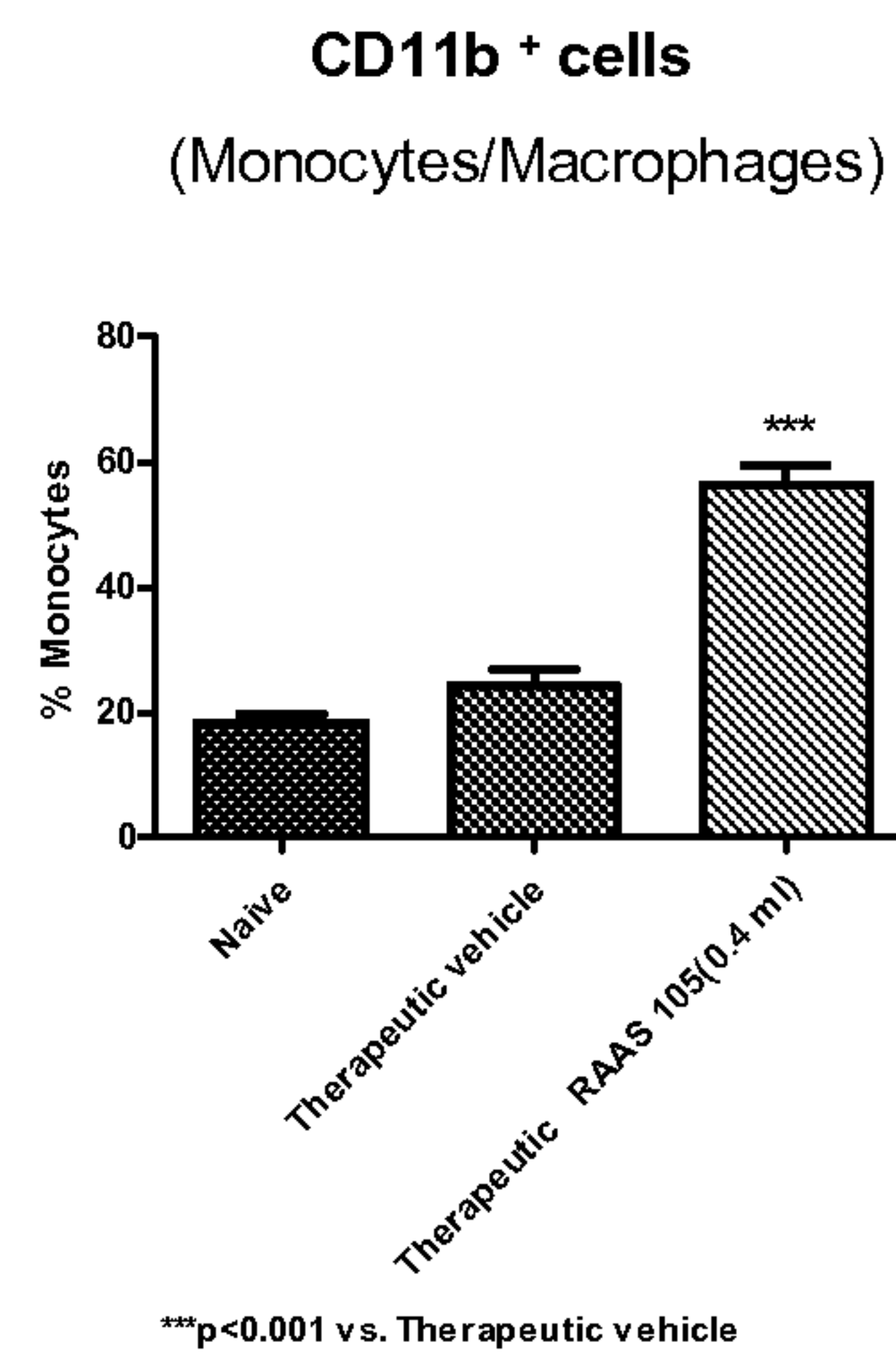


Figure 8

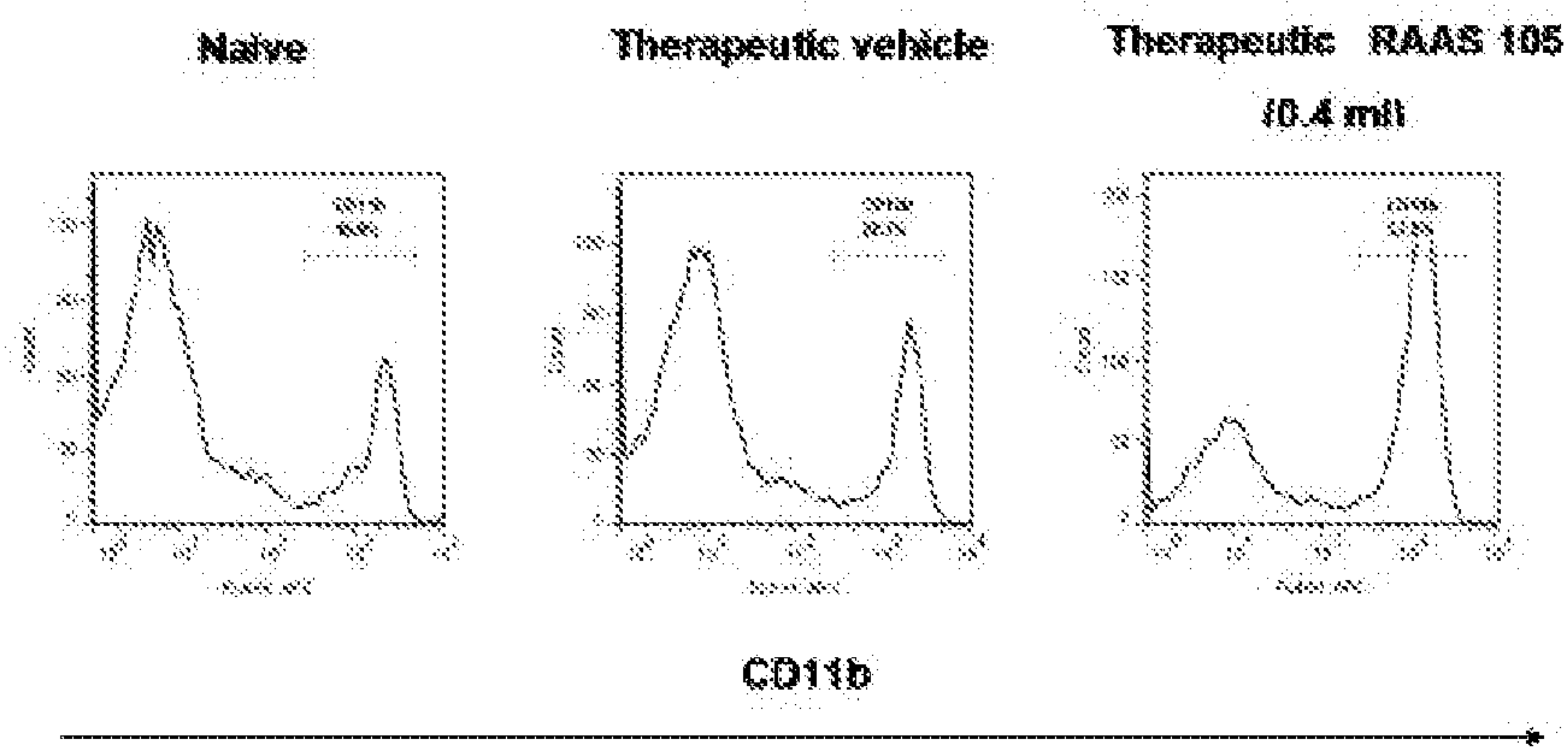


Figure 9

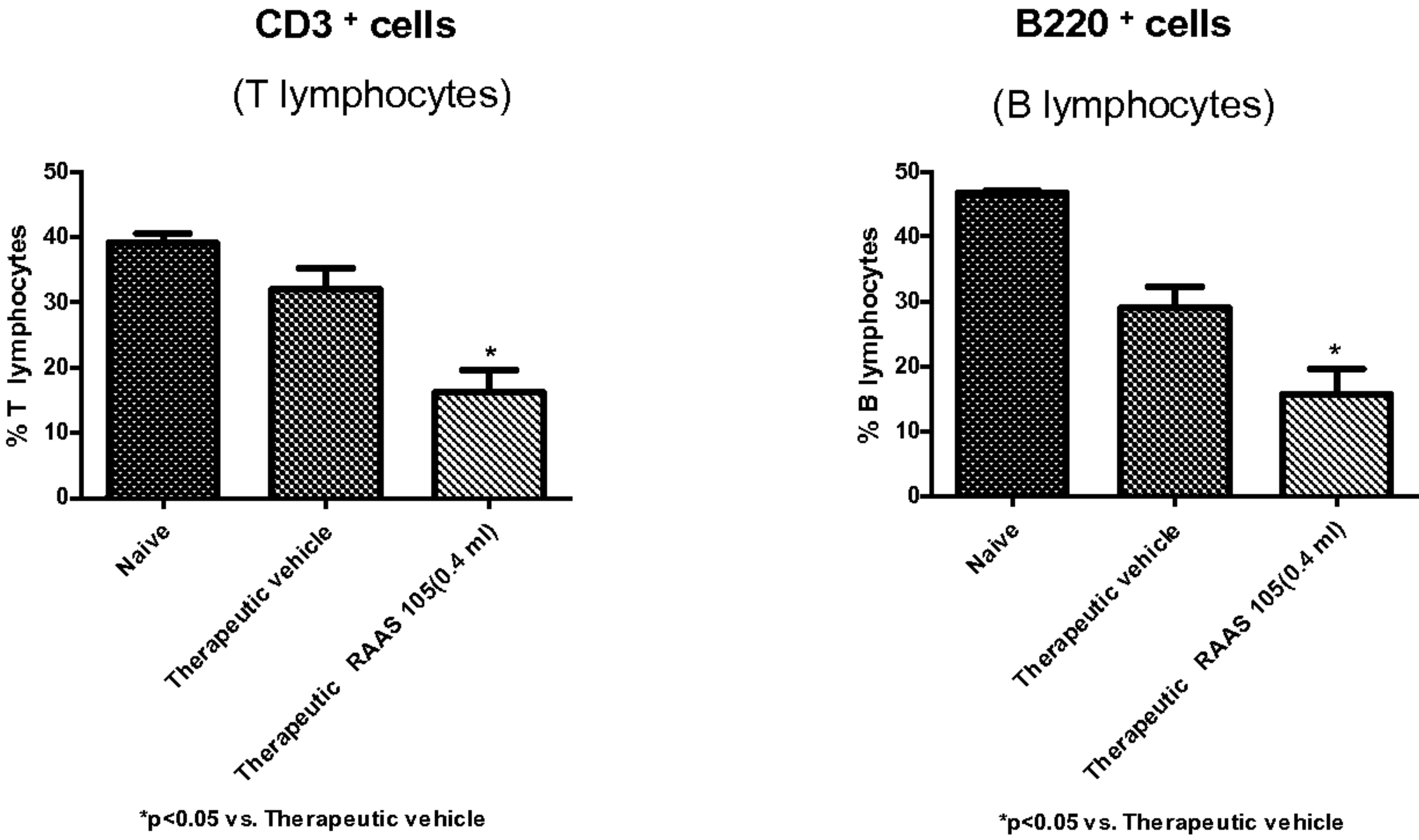


Figure 10

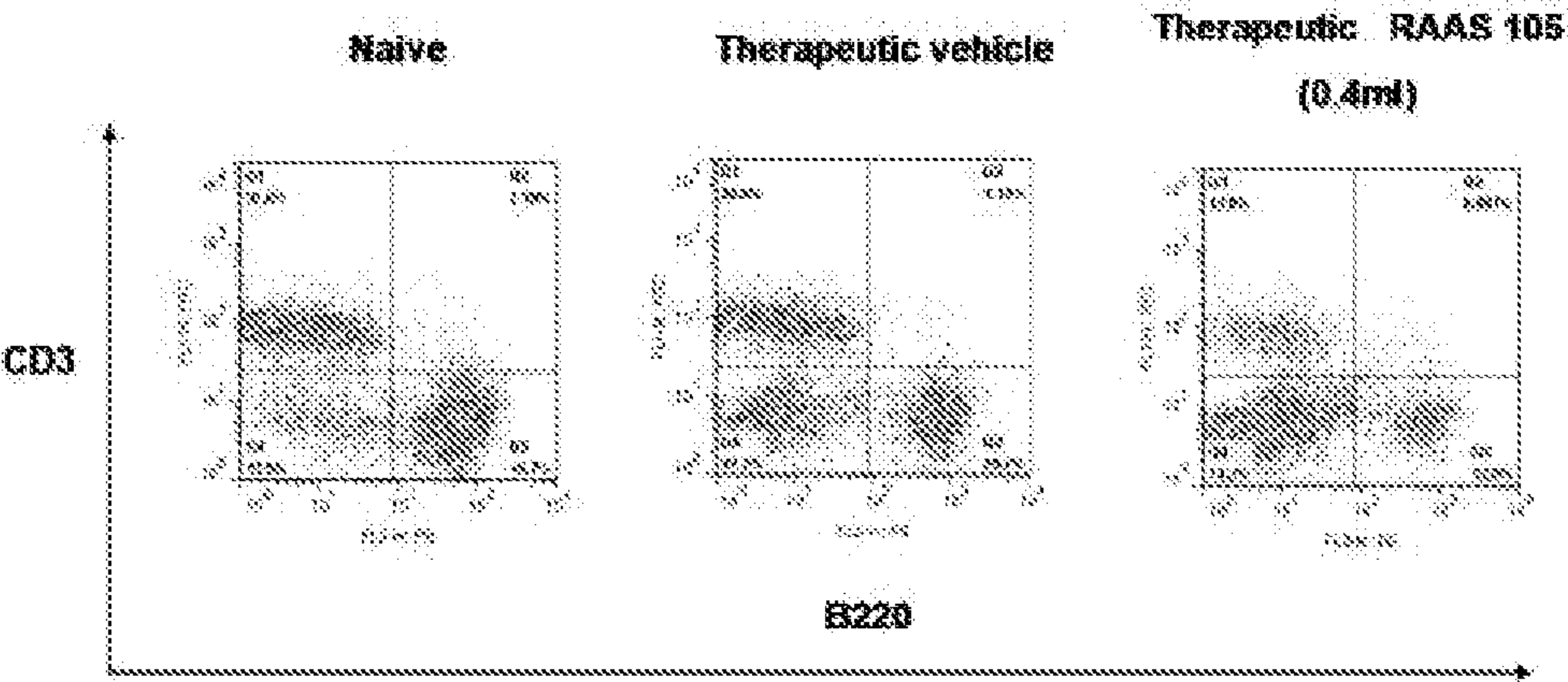


Figure 11

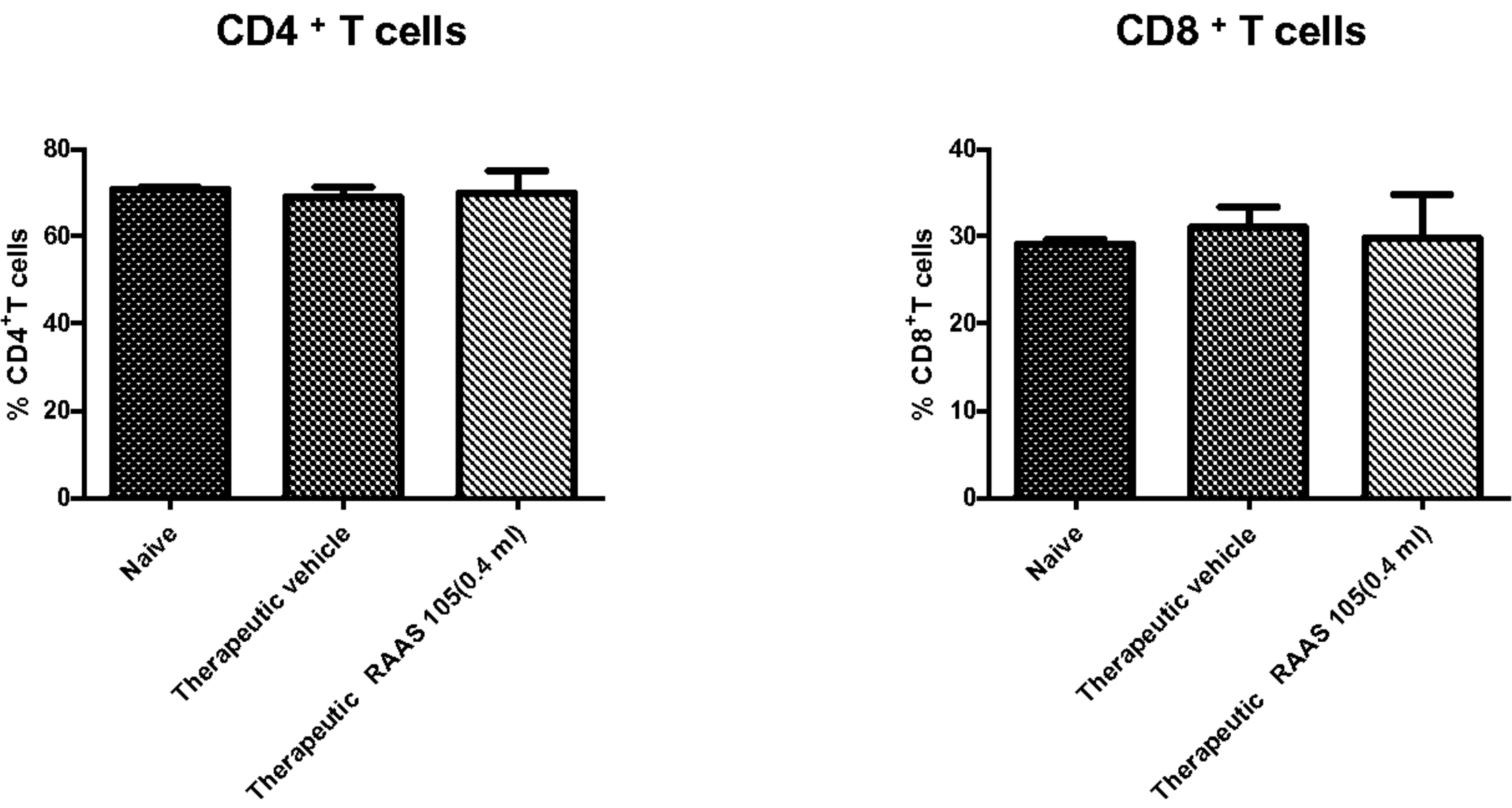


Figure 12

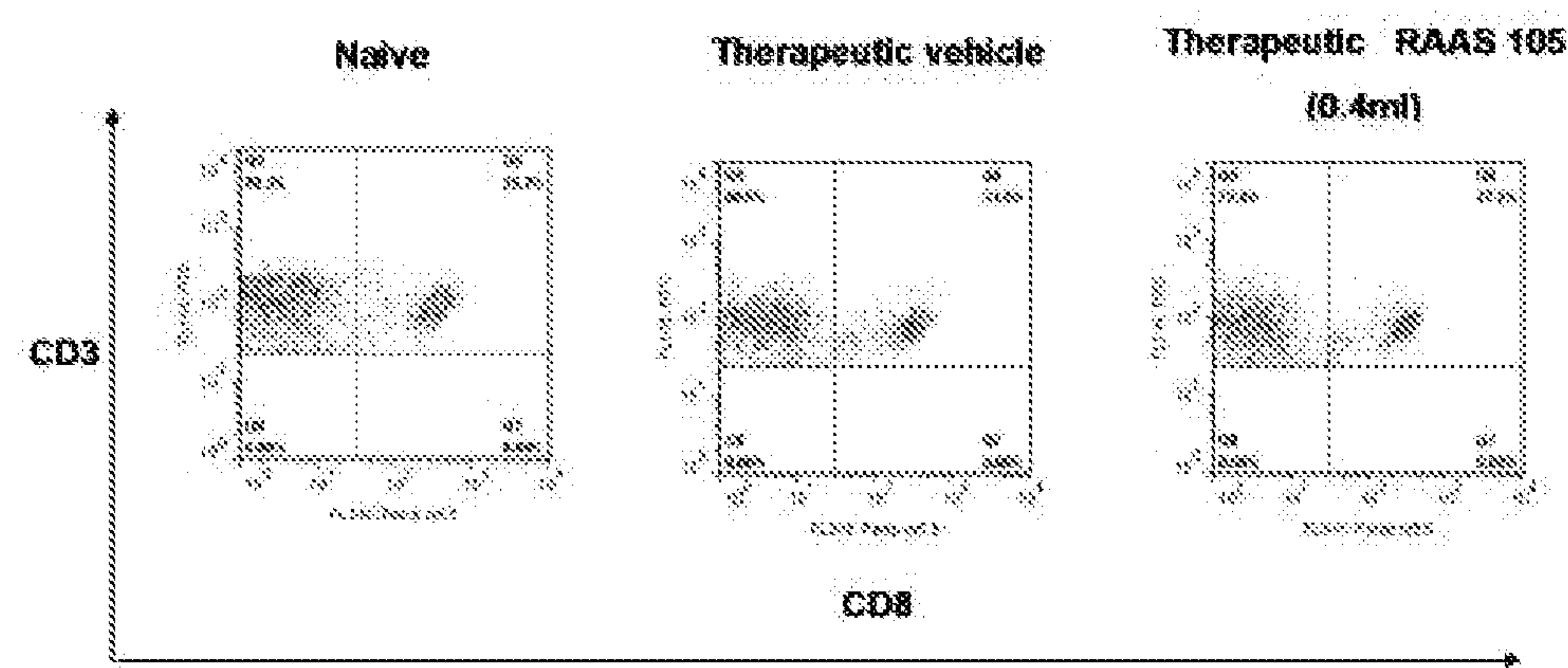


Figure 13

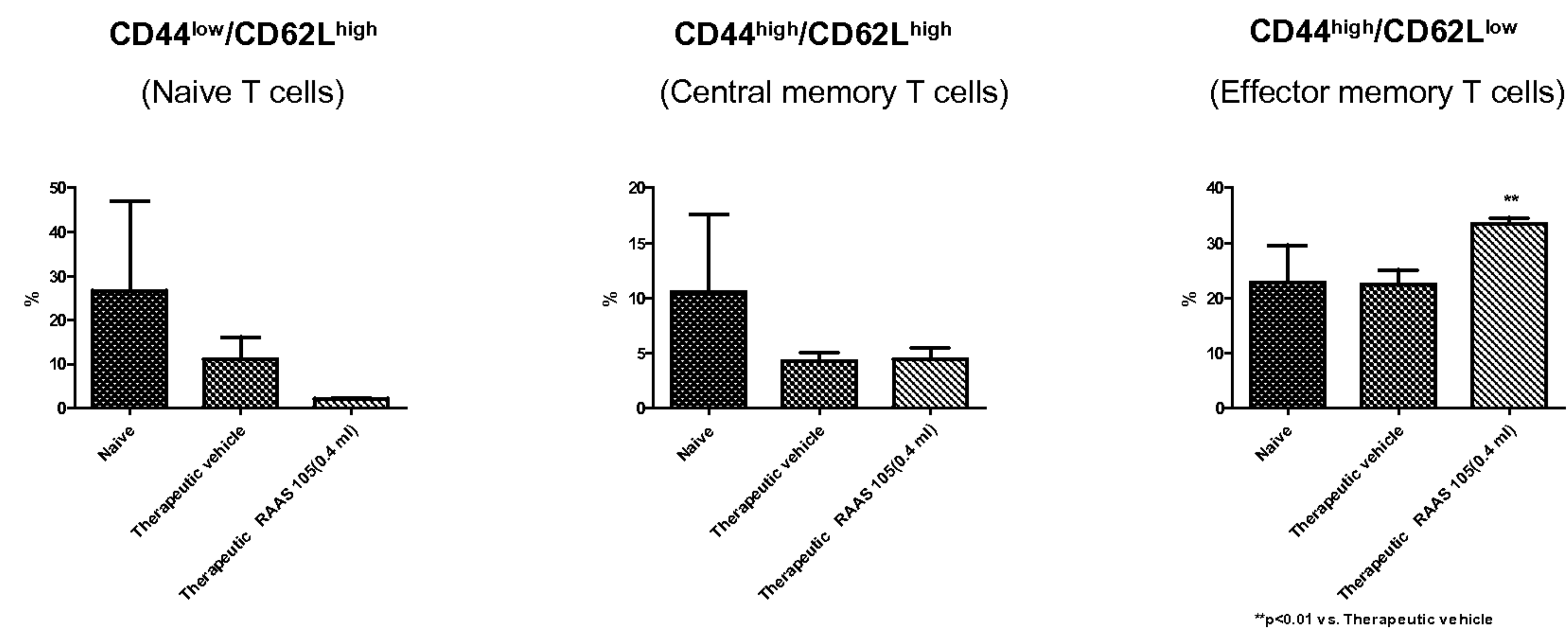


Figure 14

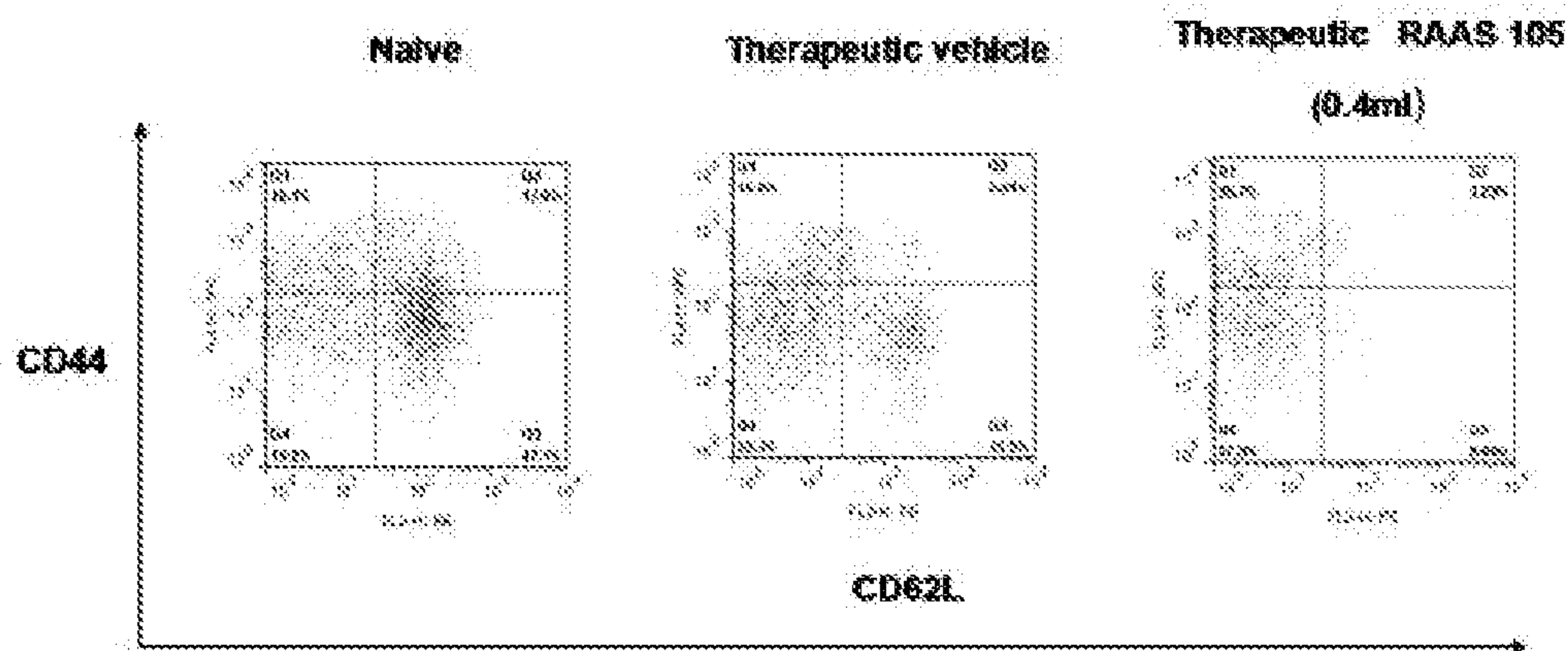


Figure 15

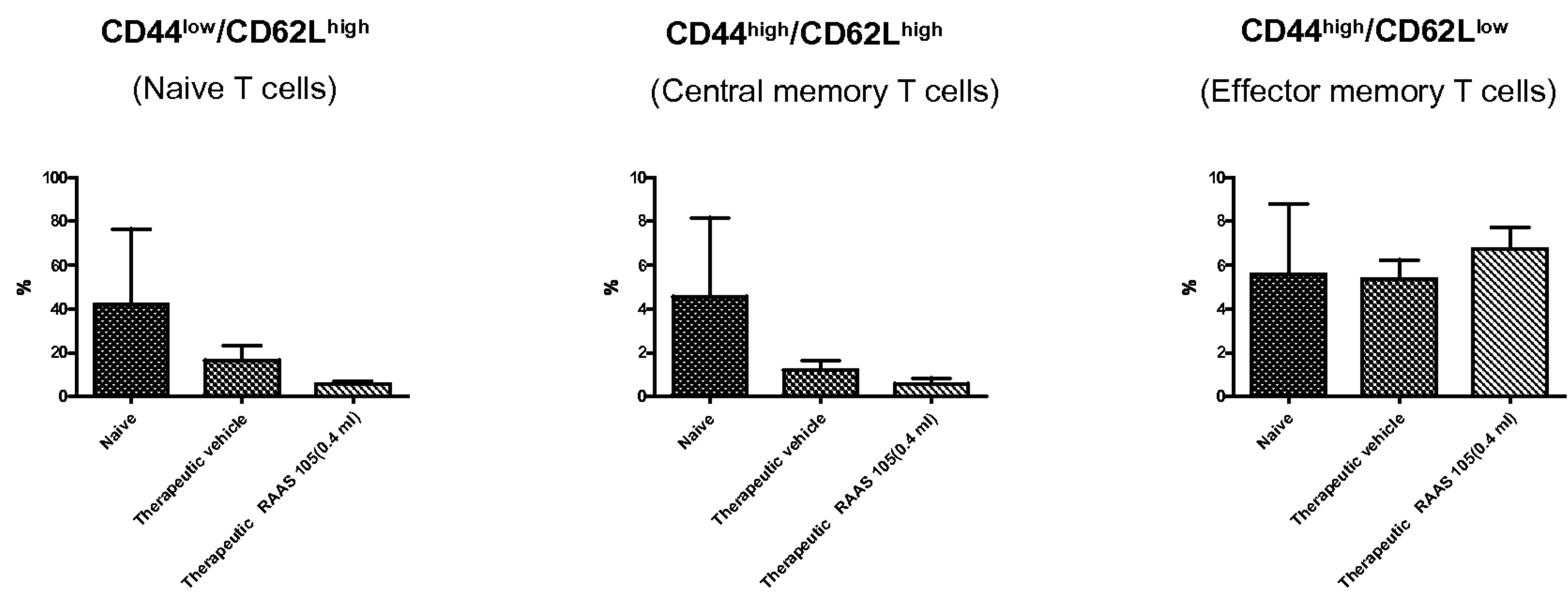


Figure 16

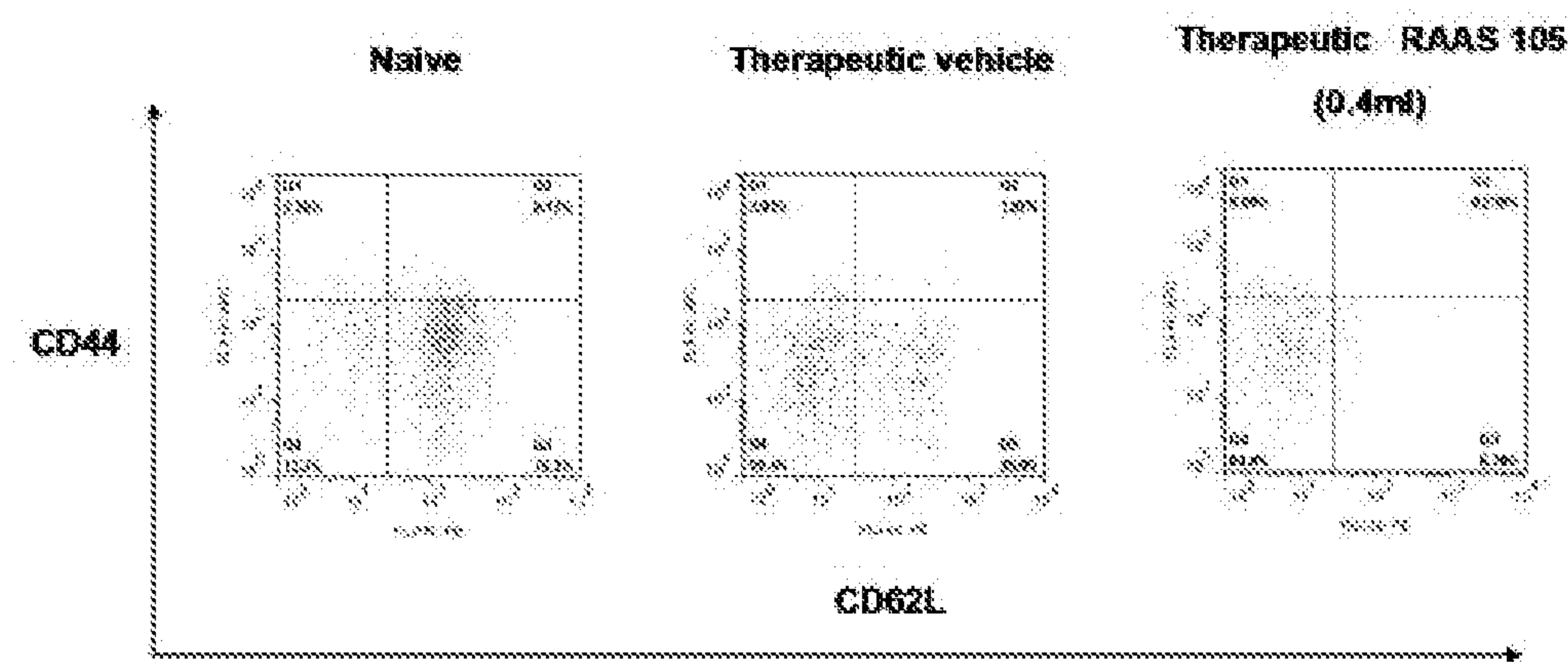


Figure 17

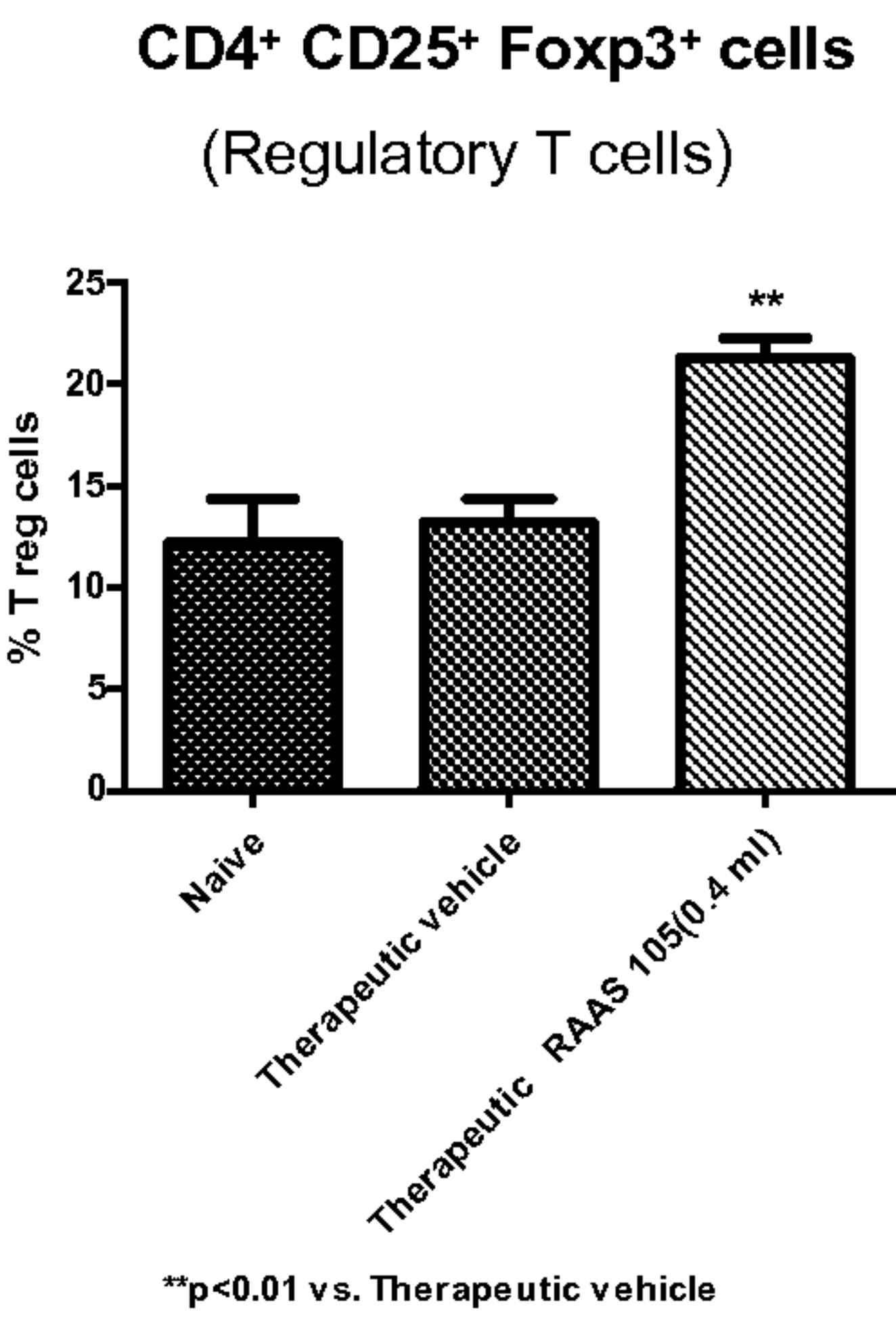


Figure 18

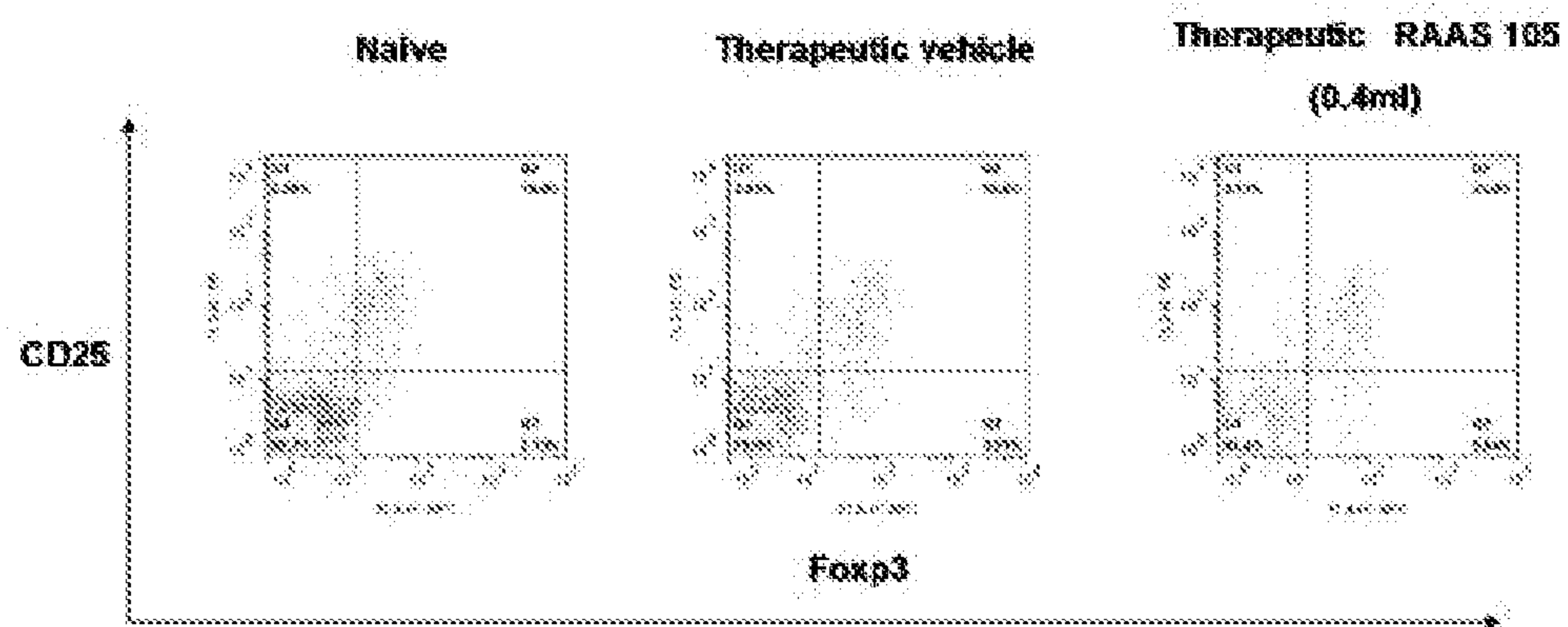


Figure 19

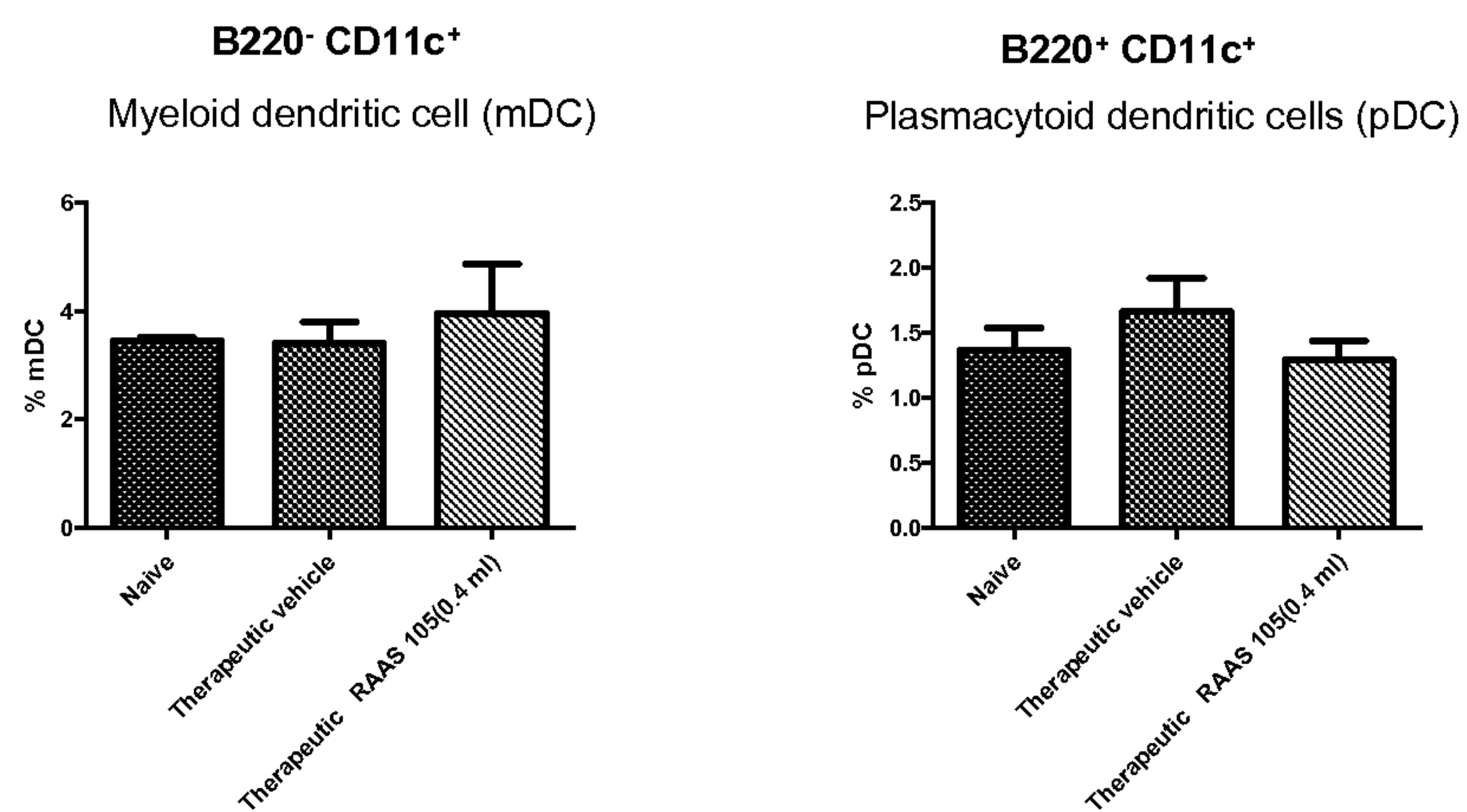


Figure 20

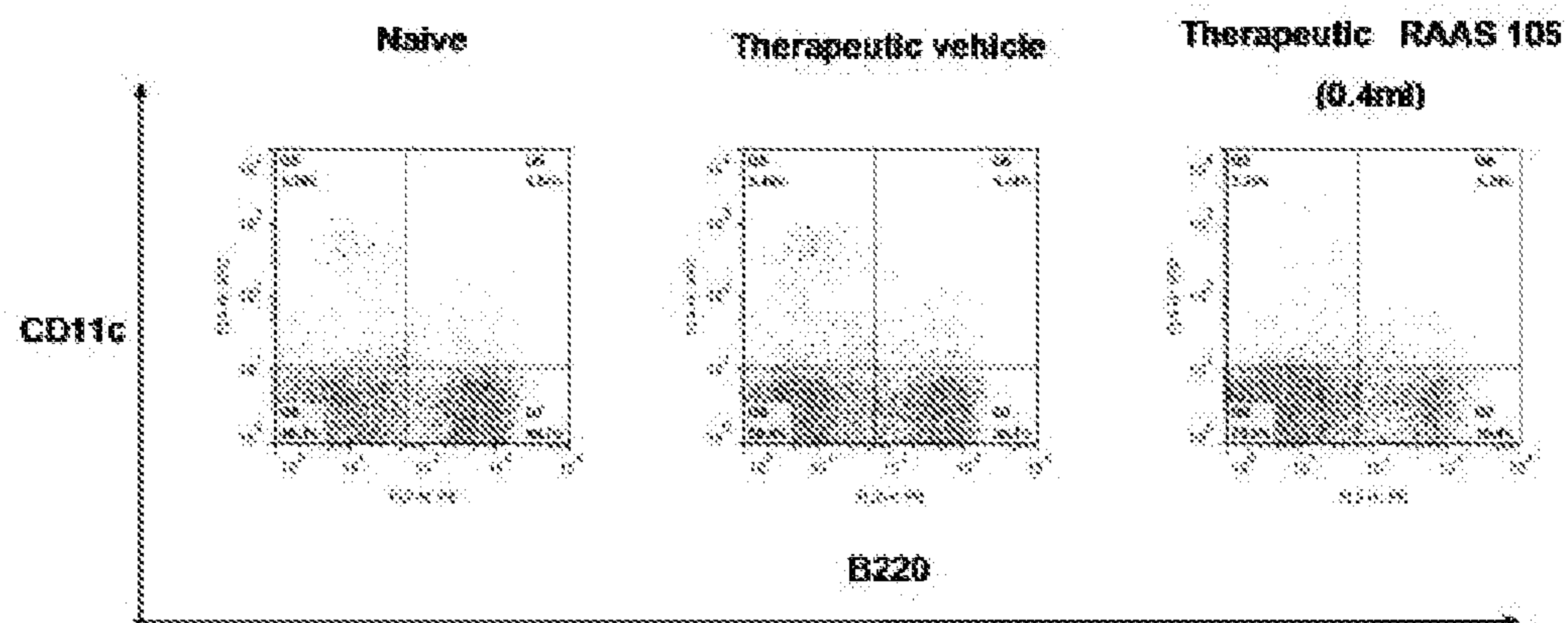


Figure 21

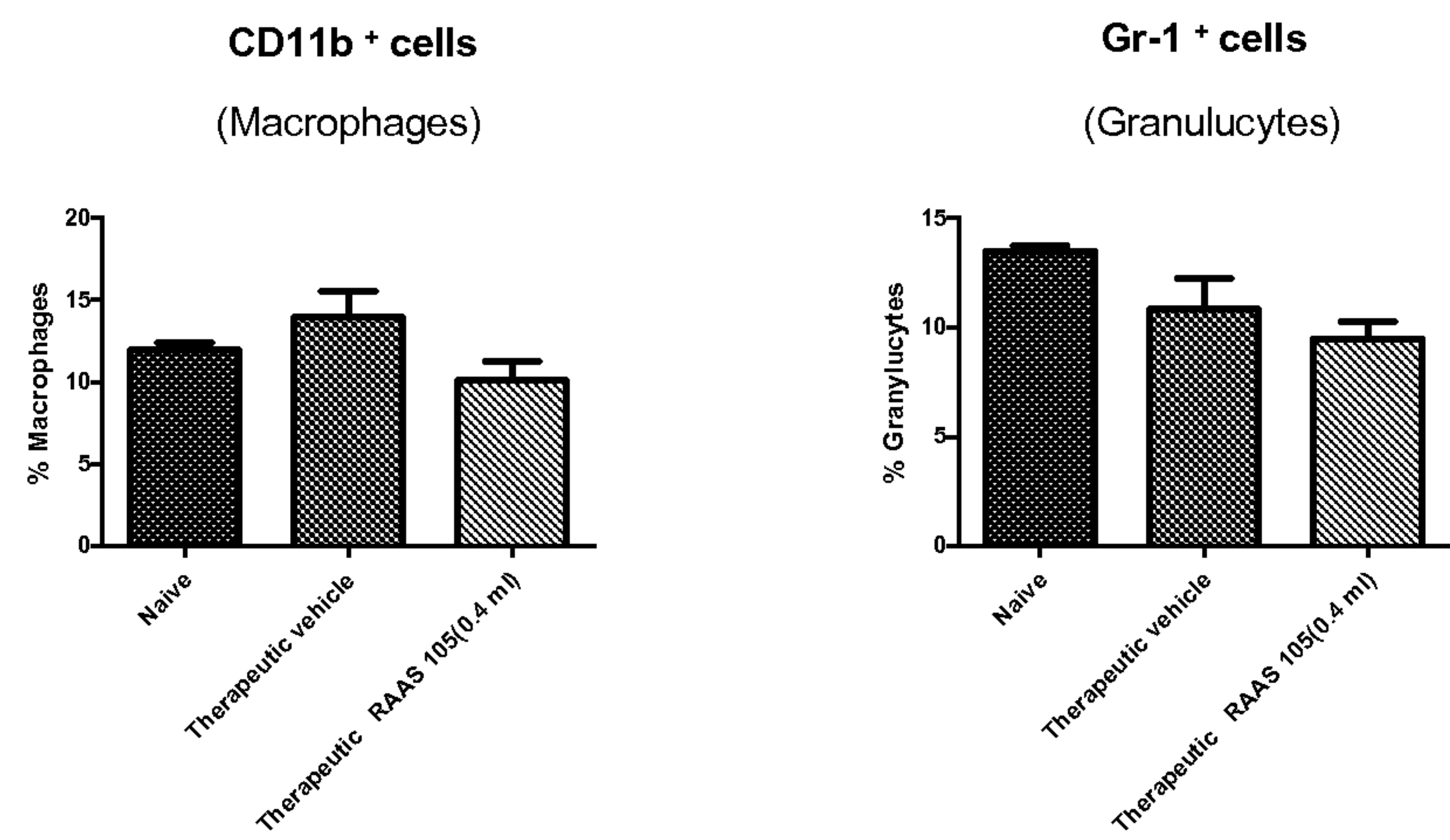


Figure 22

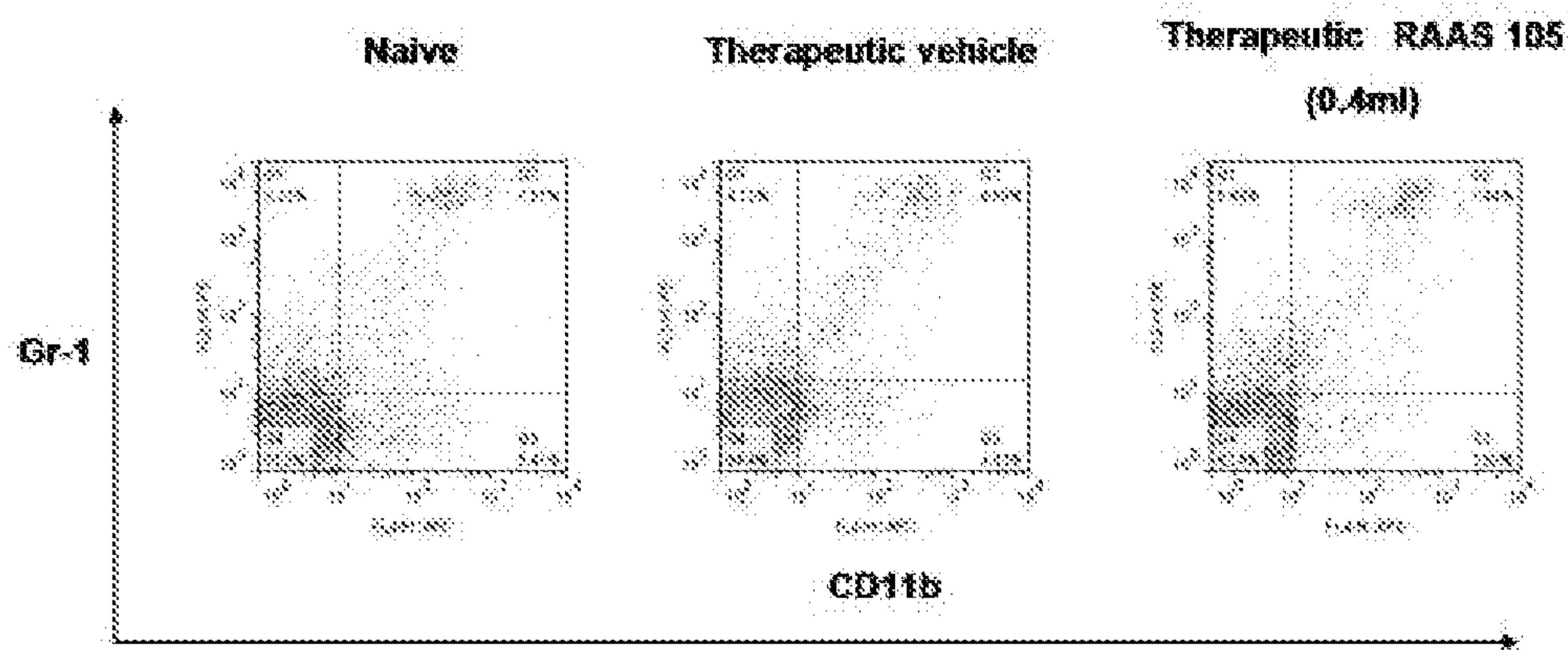


Figure 23

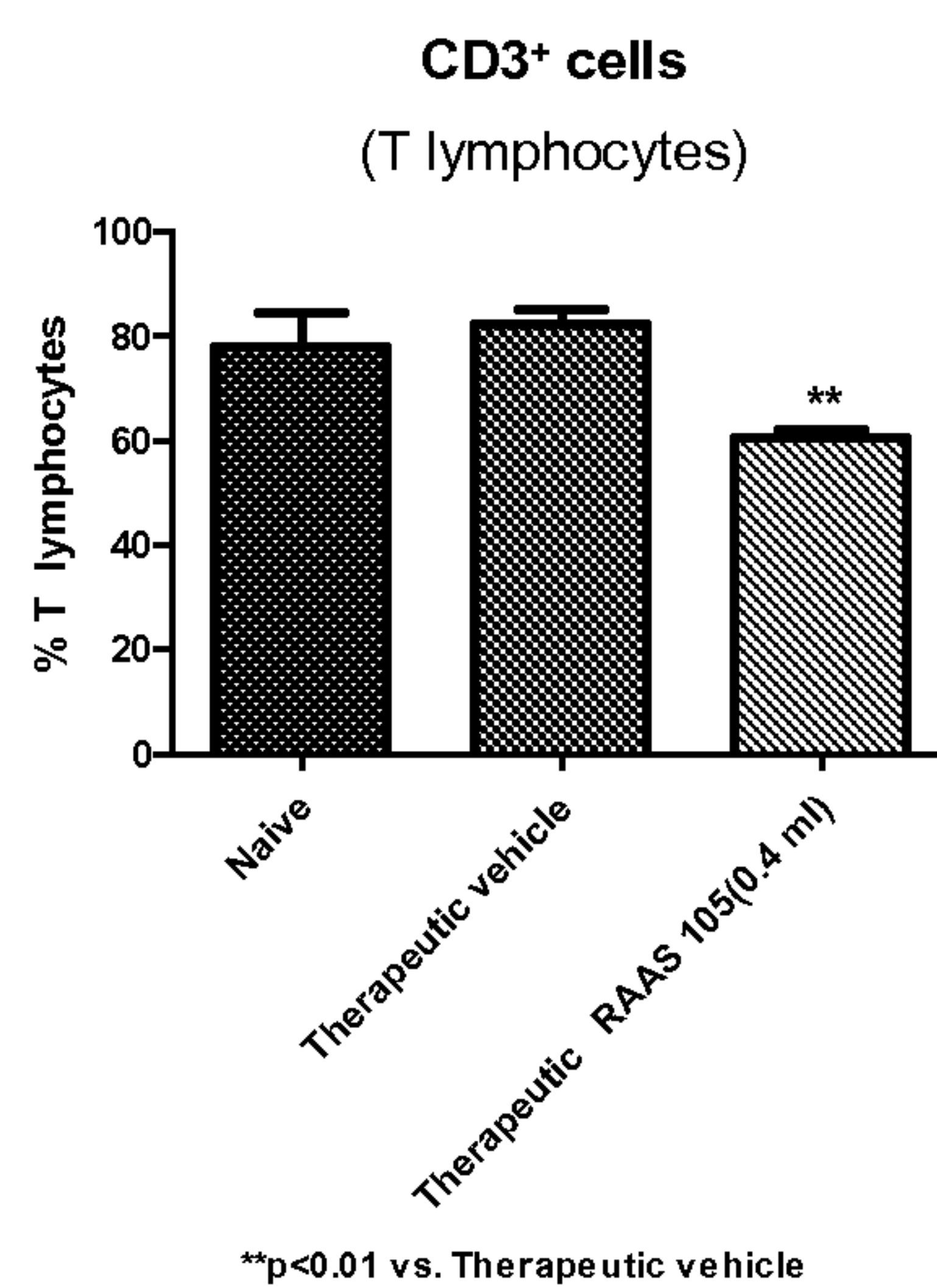


Figure 24

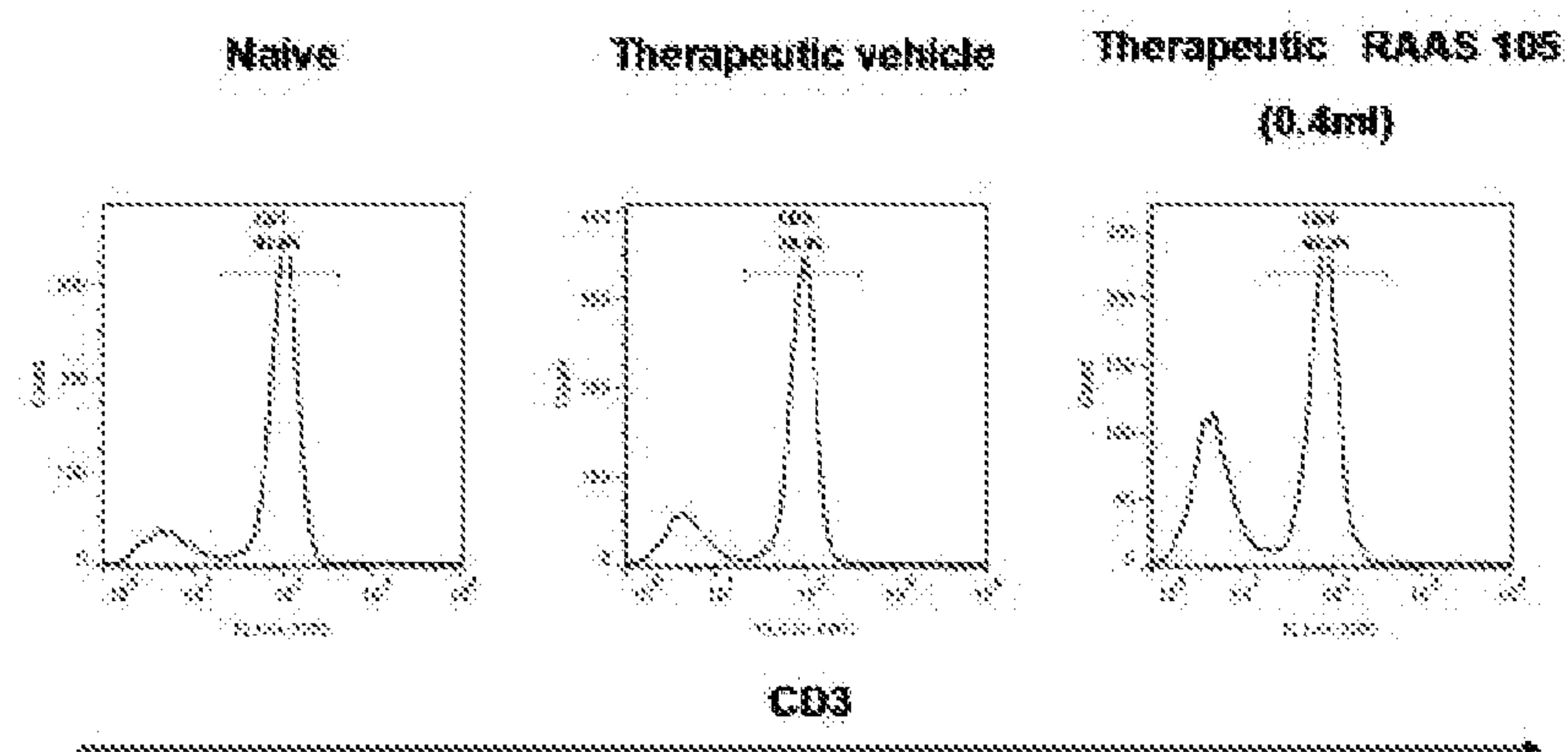


Figure 25

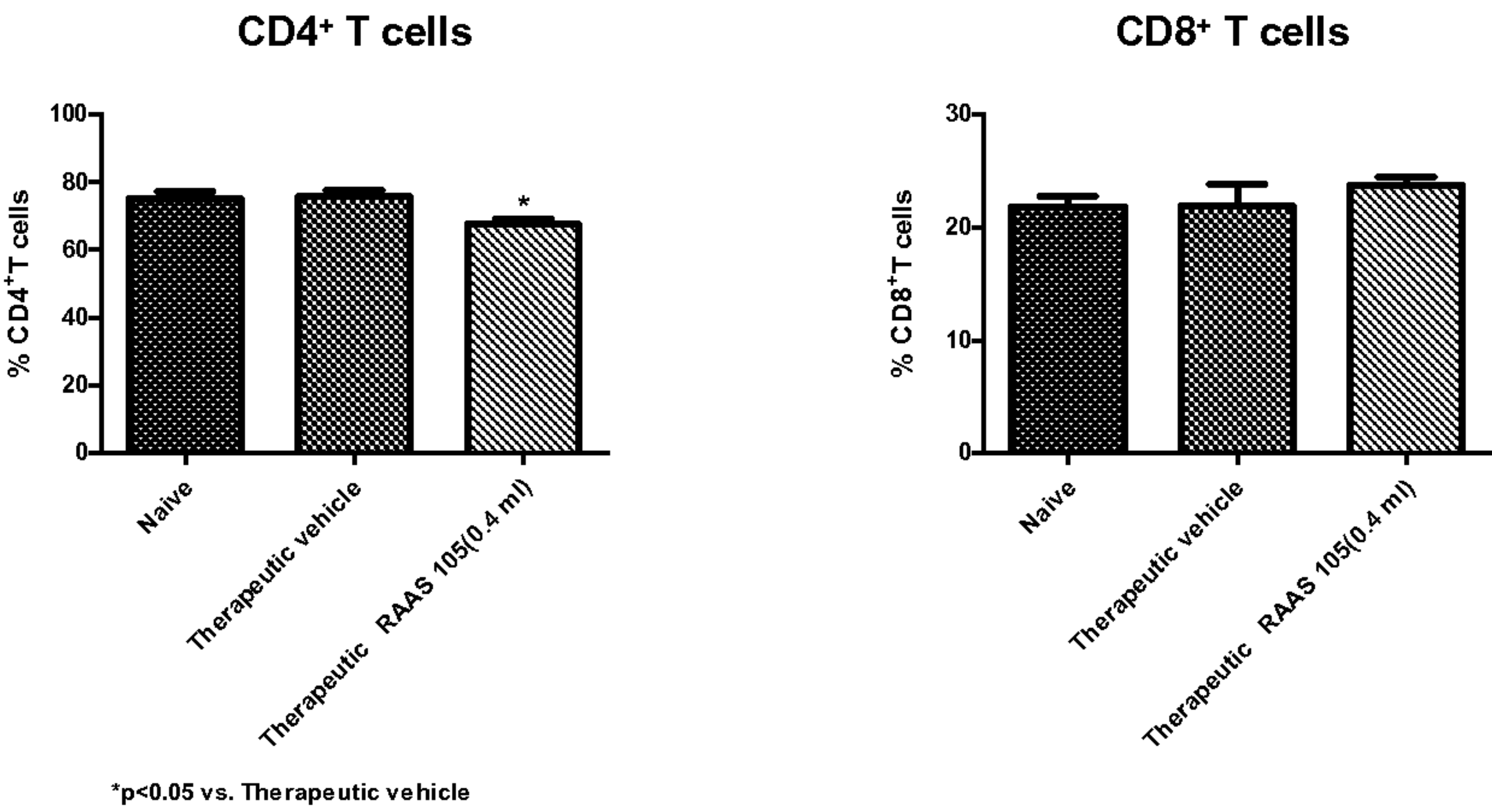


Figure 26

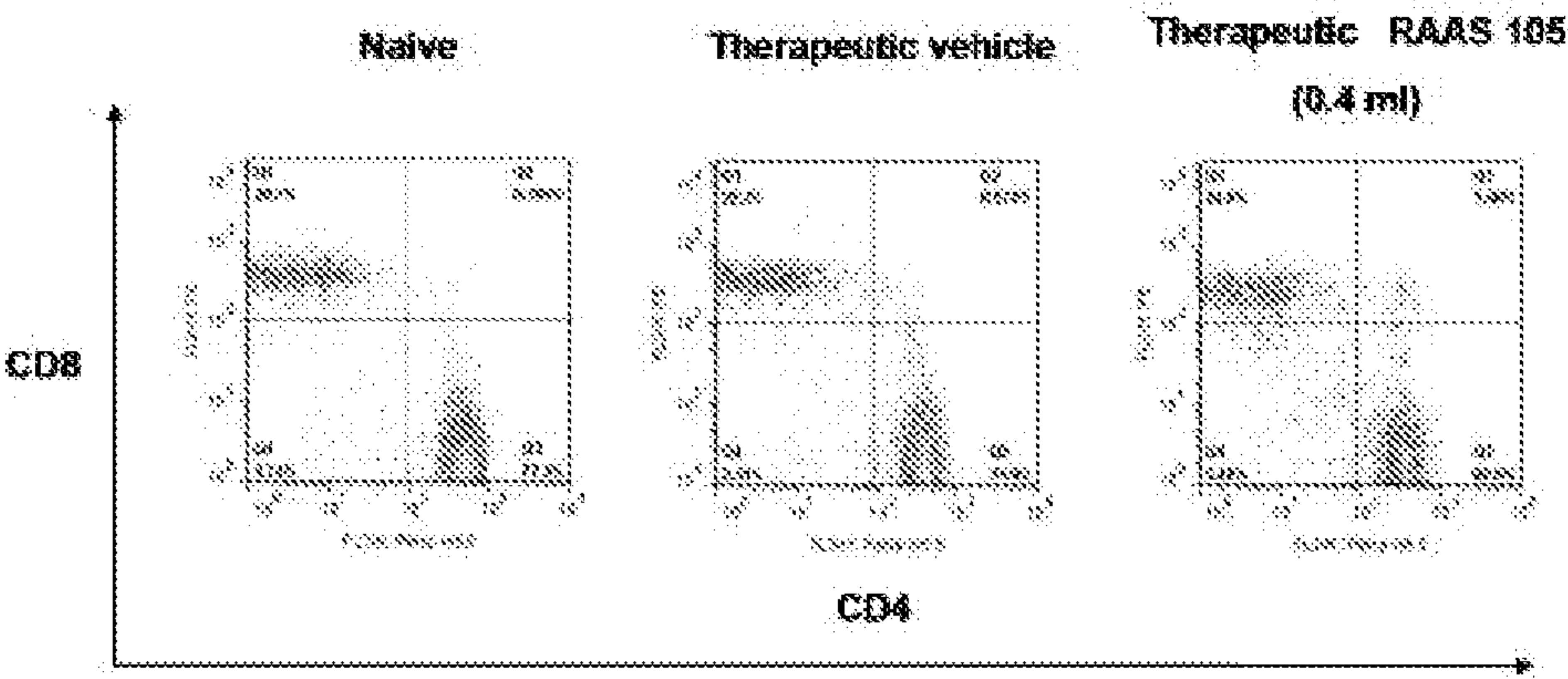


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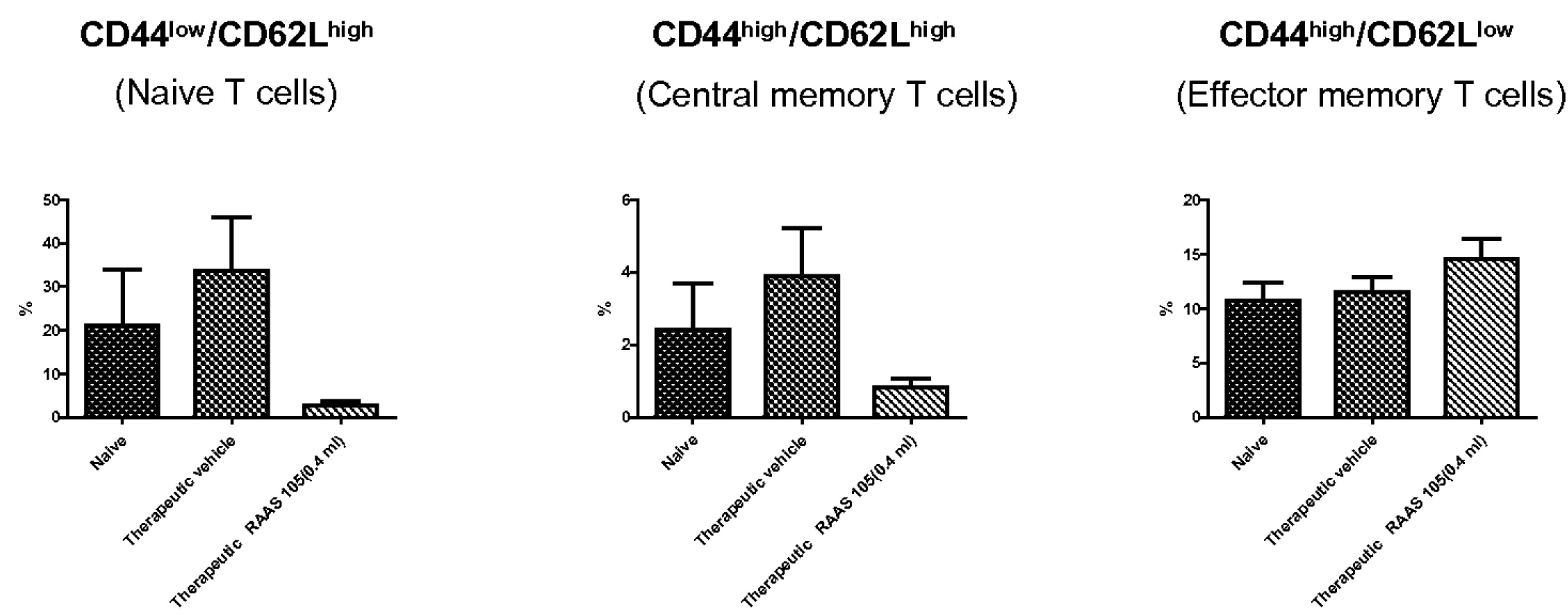


Figure 28

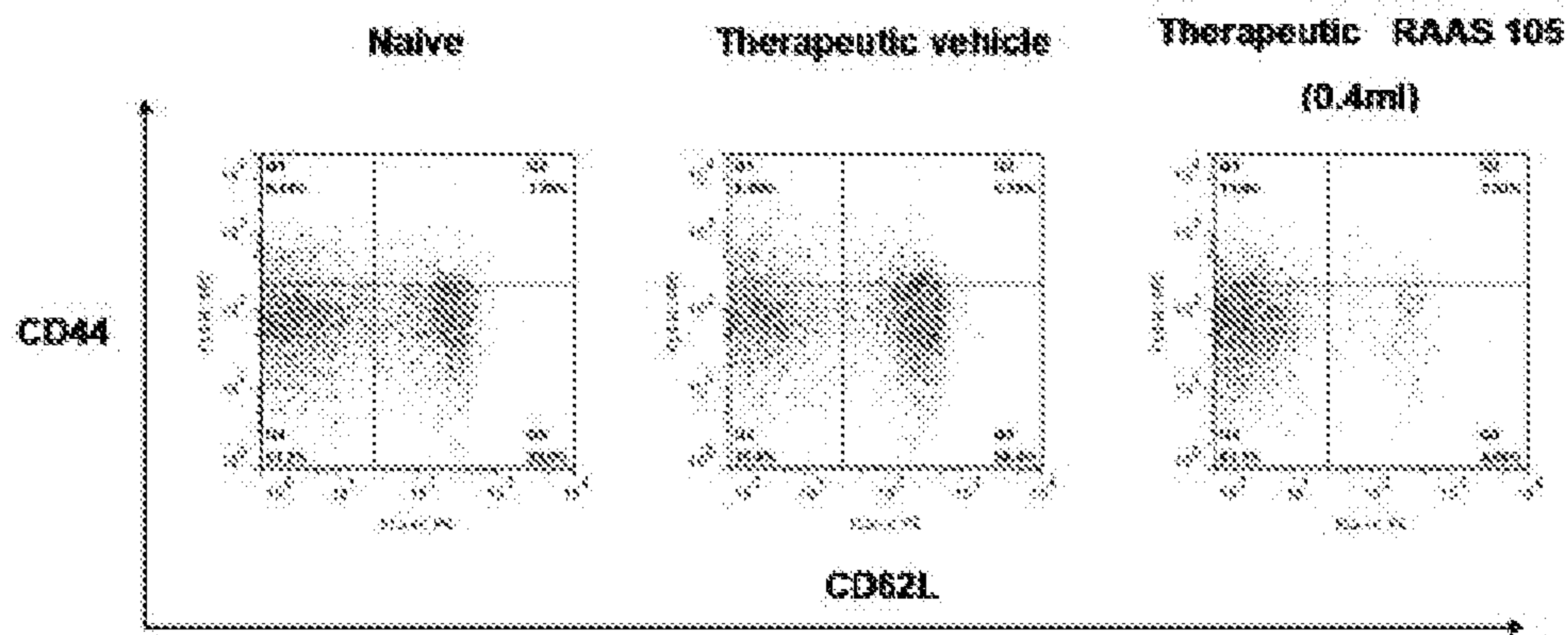


Figure 29

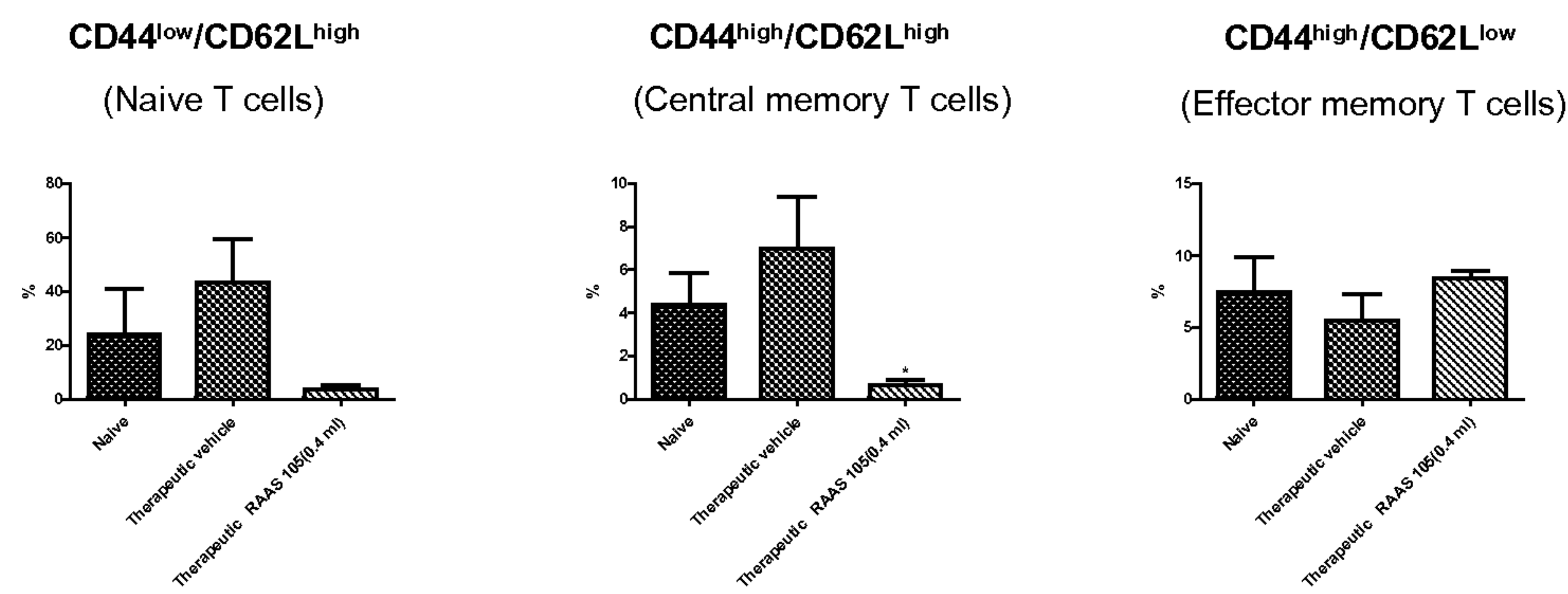


Figure 30

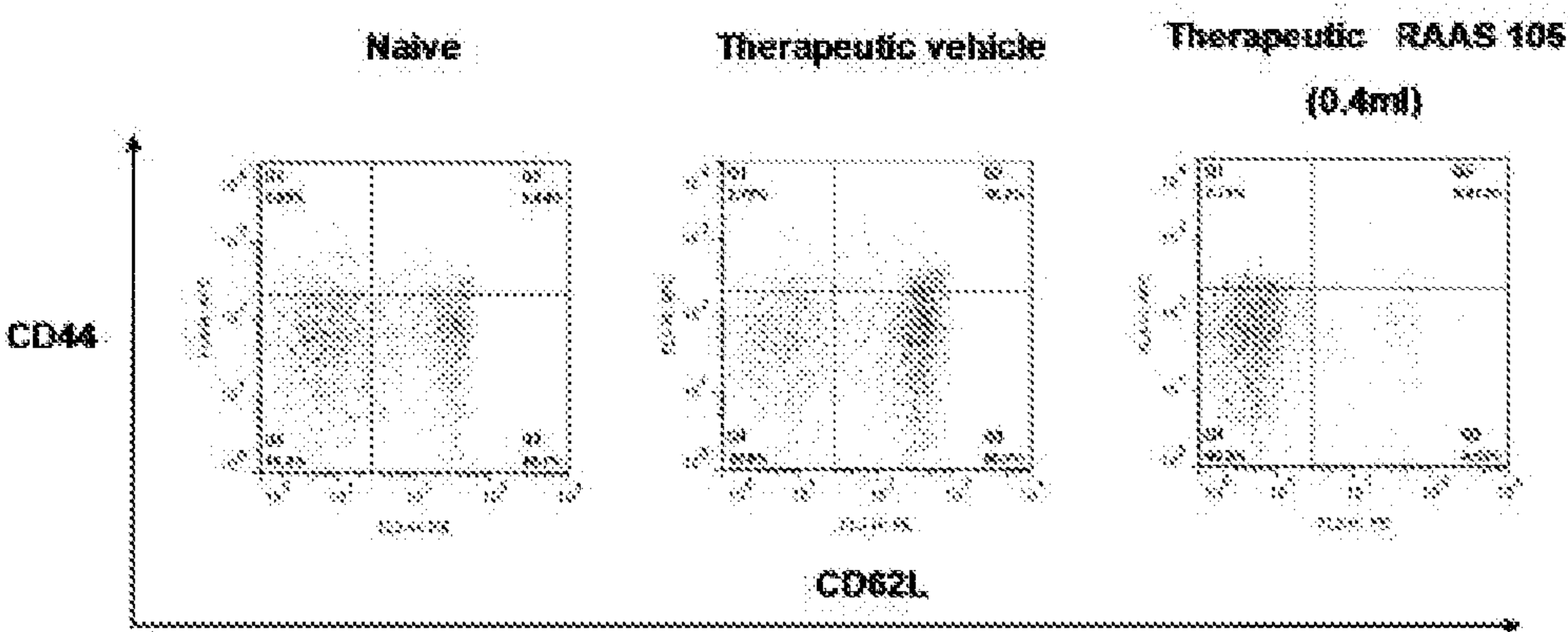


Figure 31

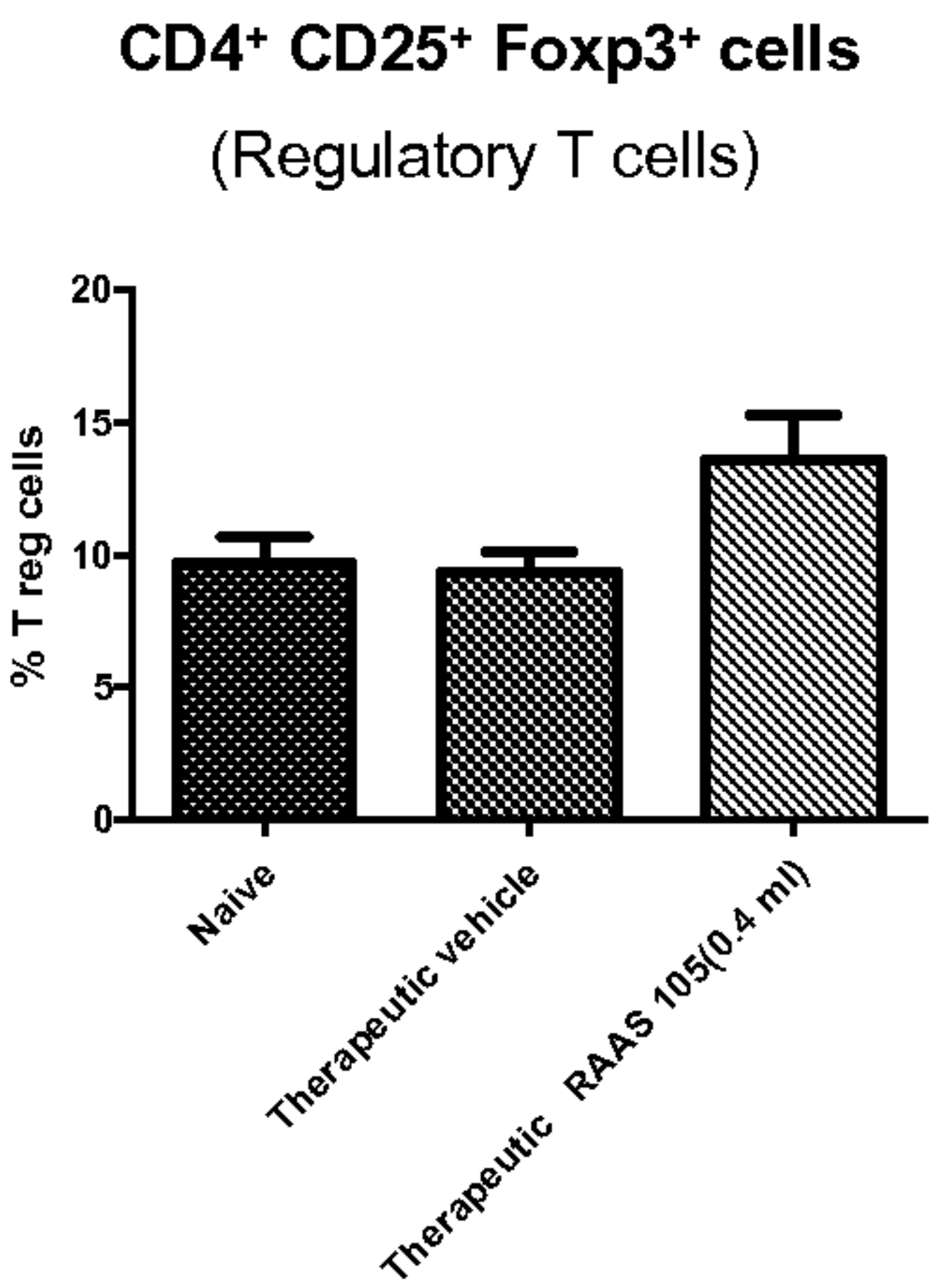


Figure 32

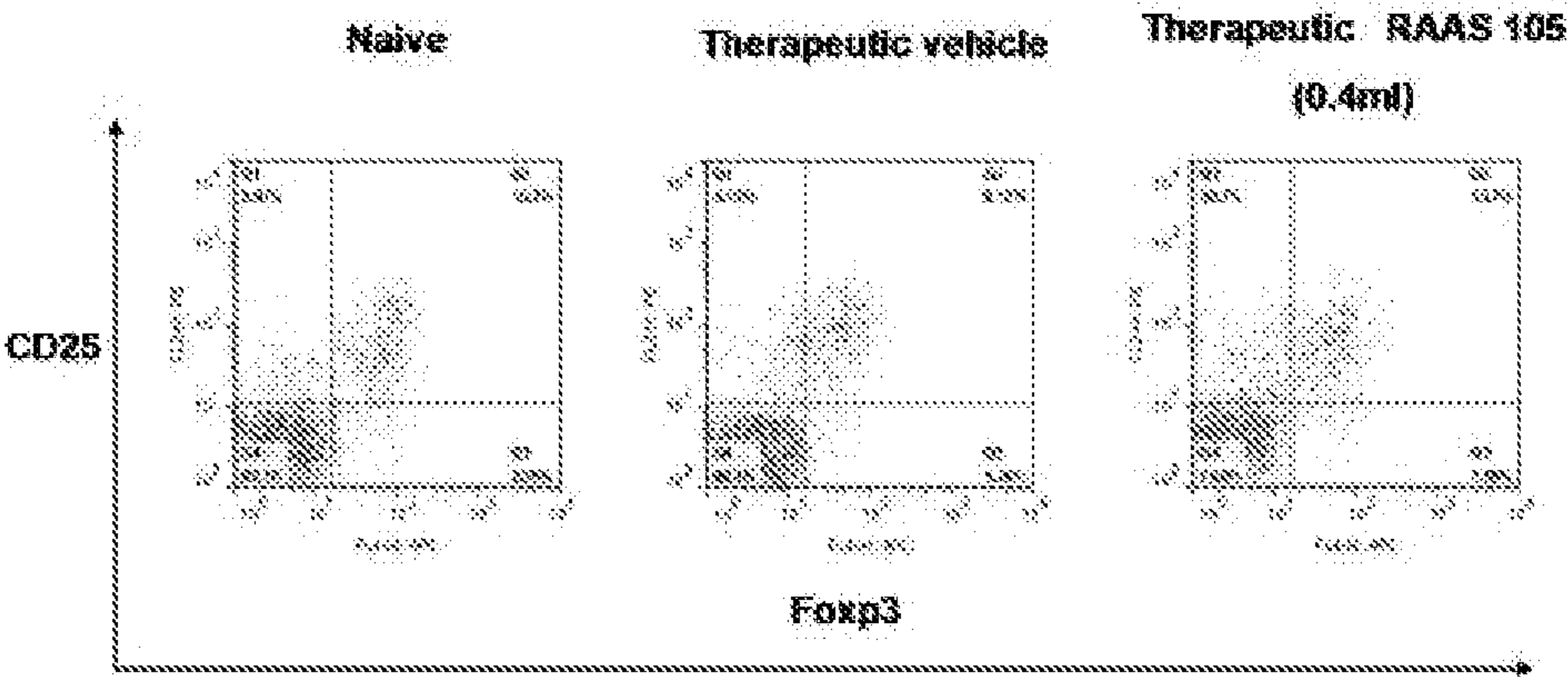


Figure 33

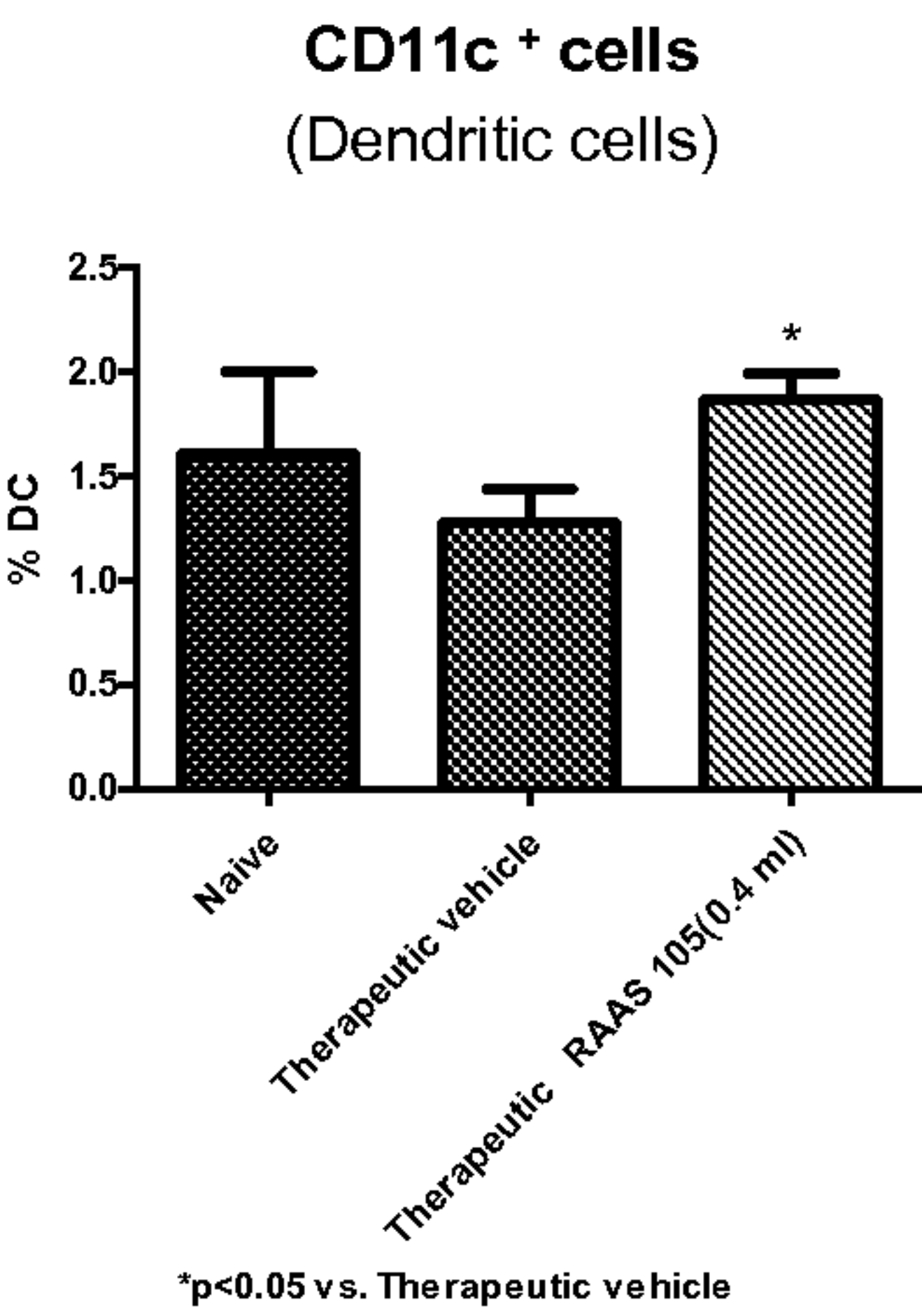


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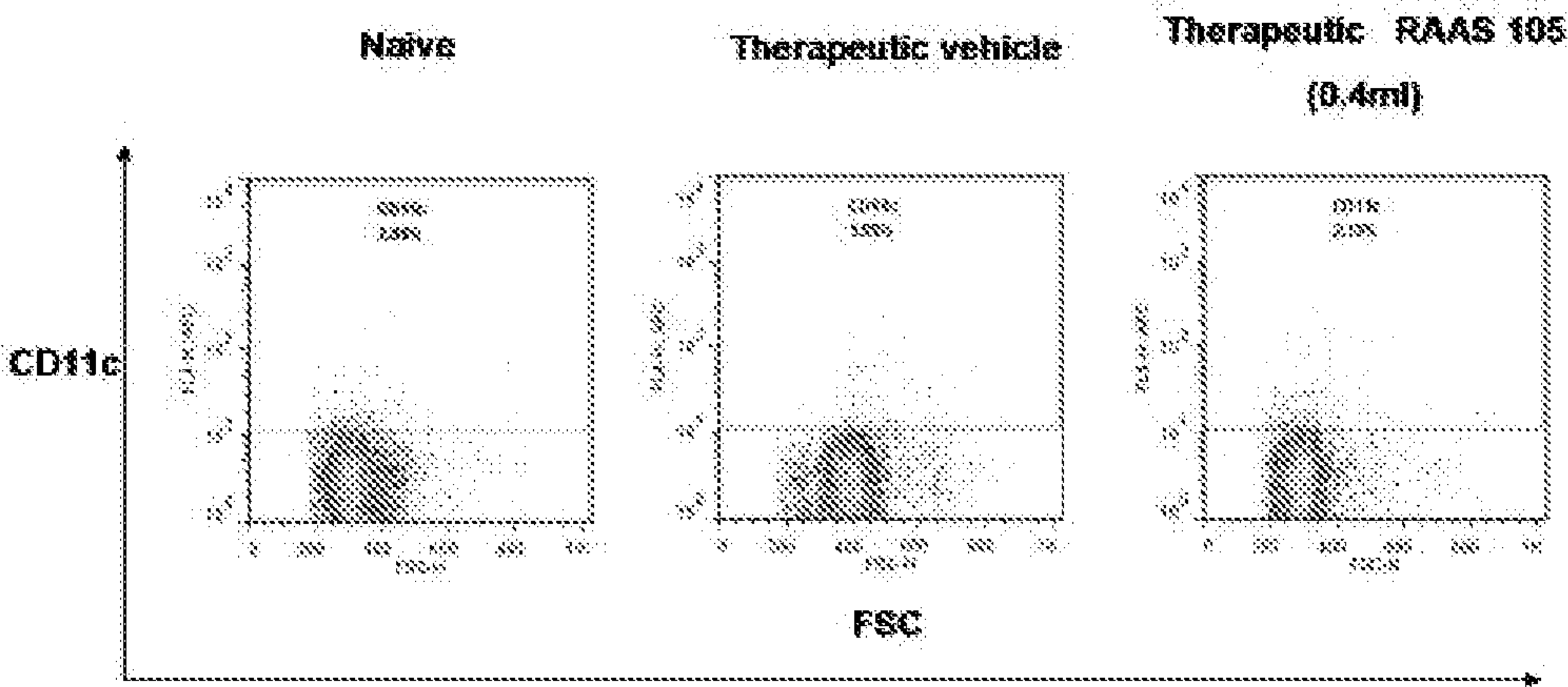


Figure 35

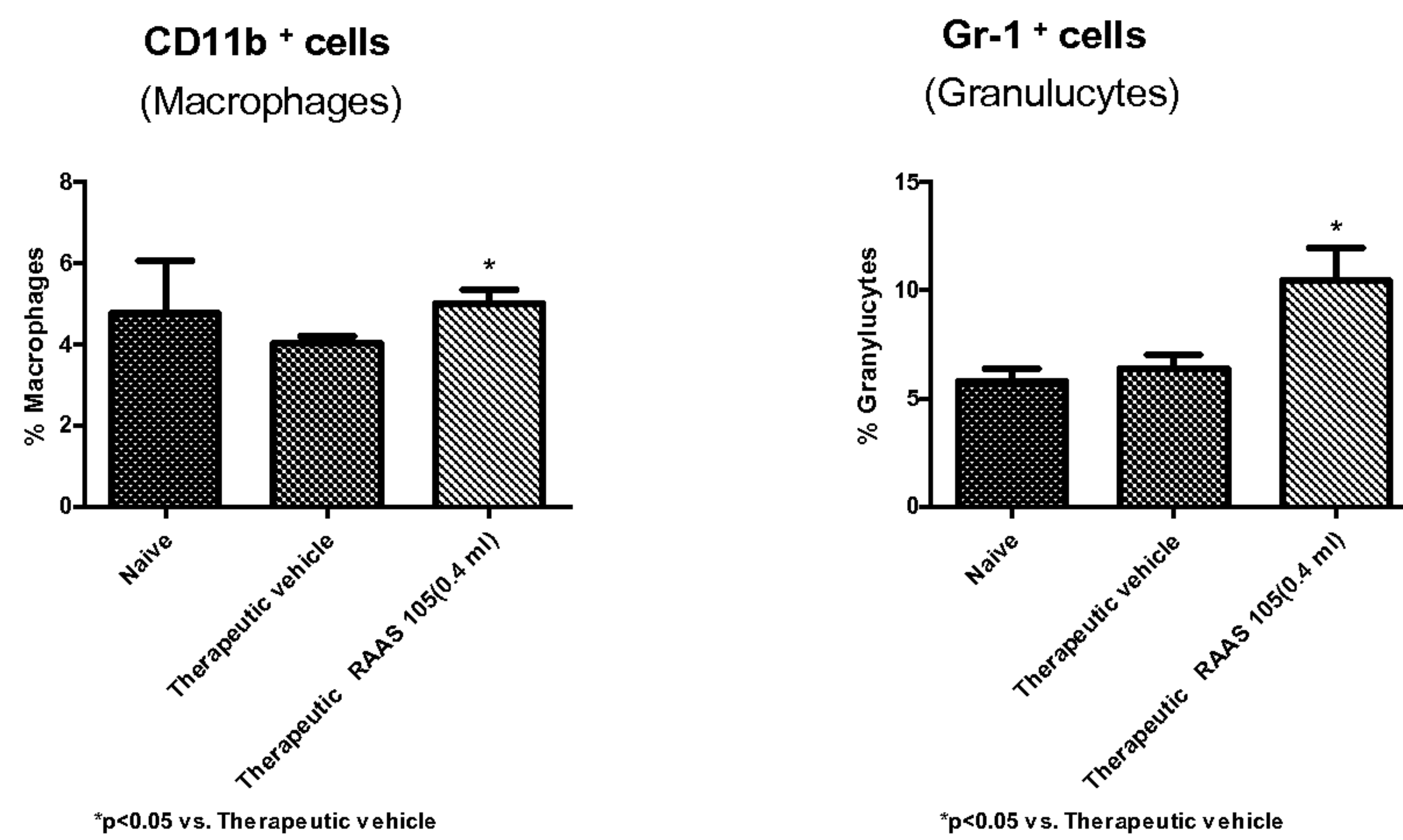


Figure 36

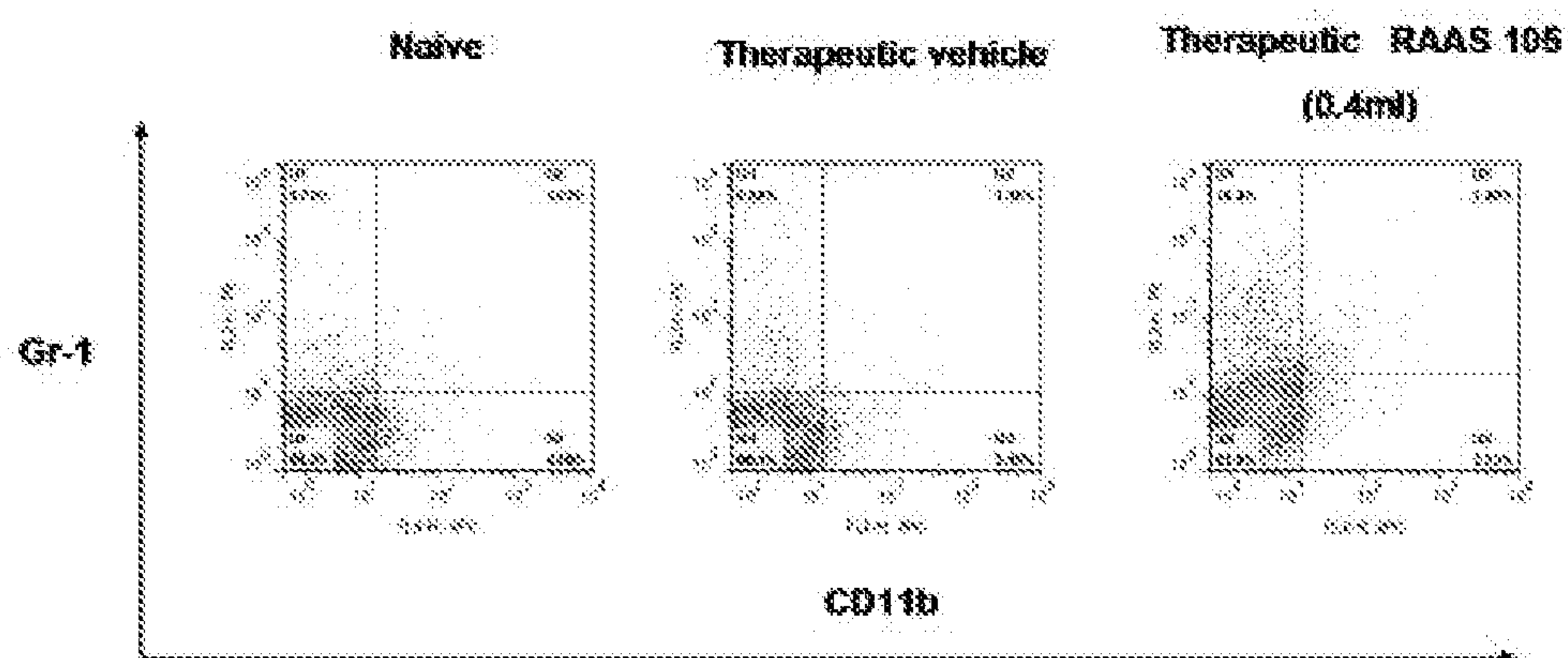


Figure 37

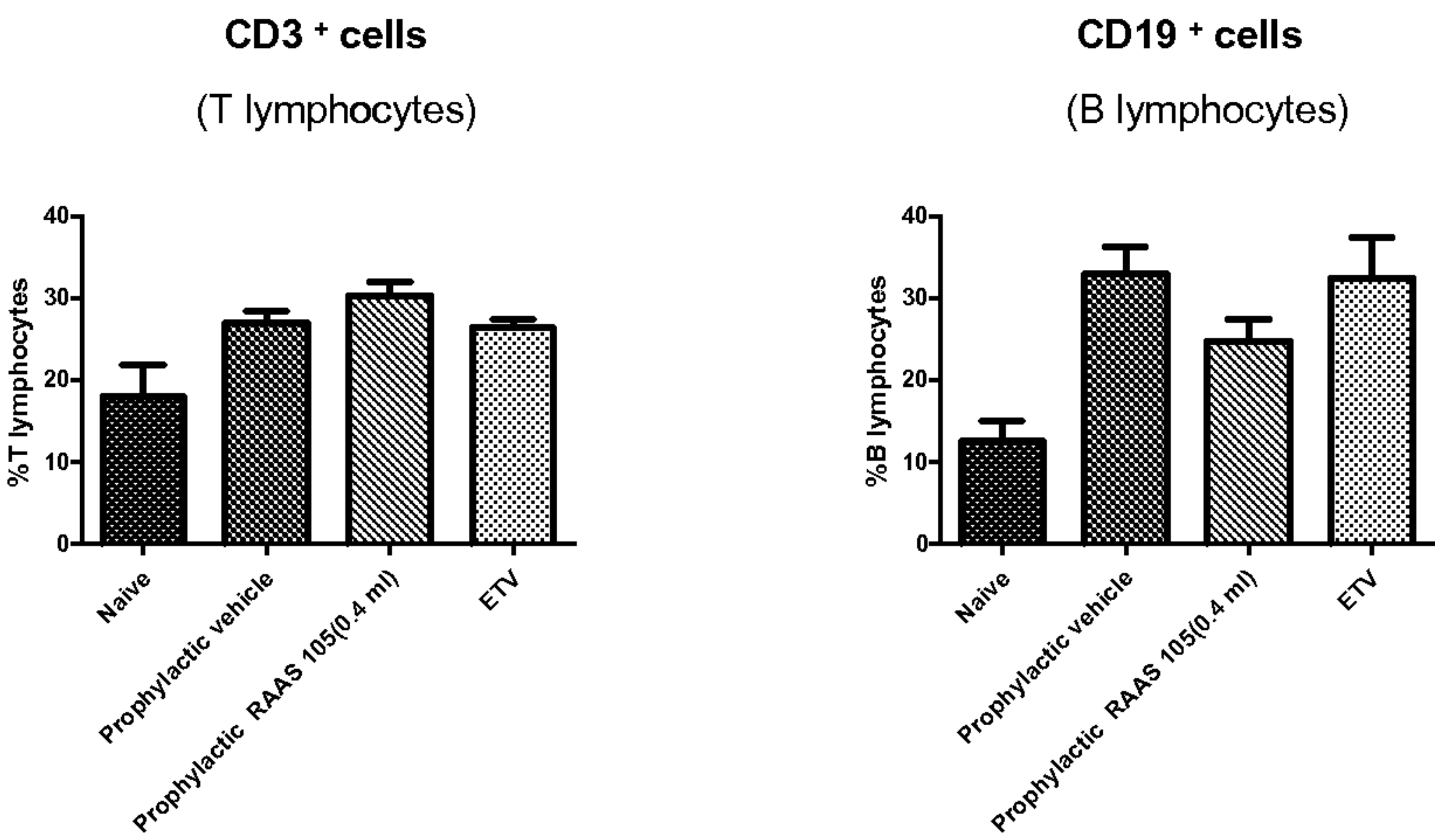


Figure 38

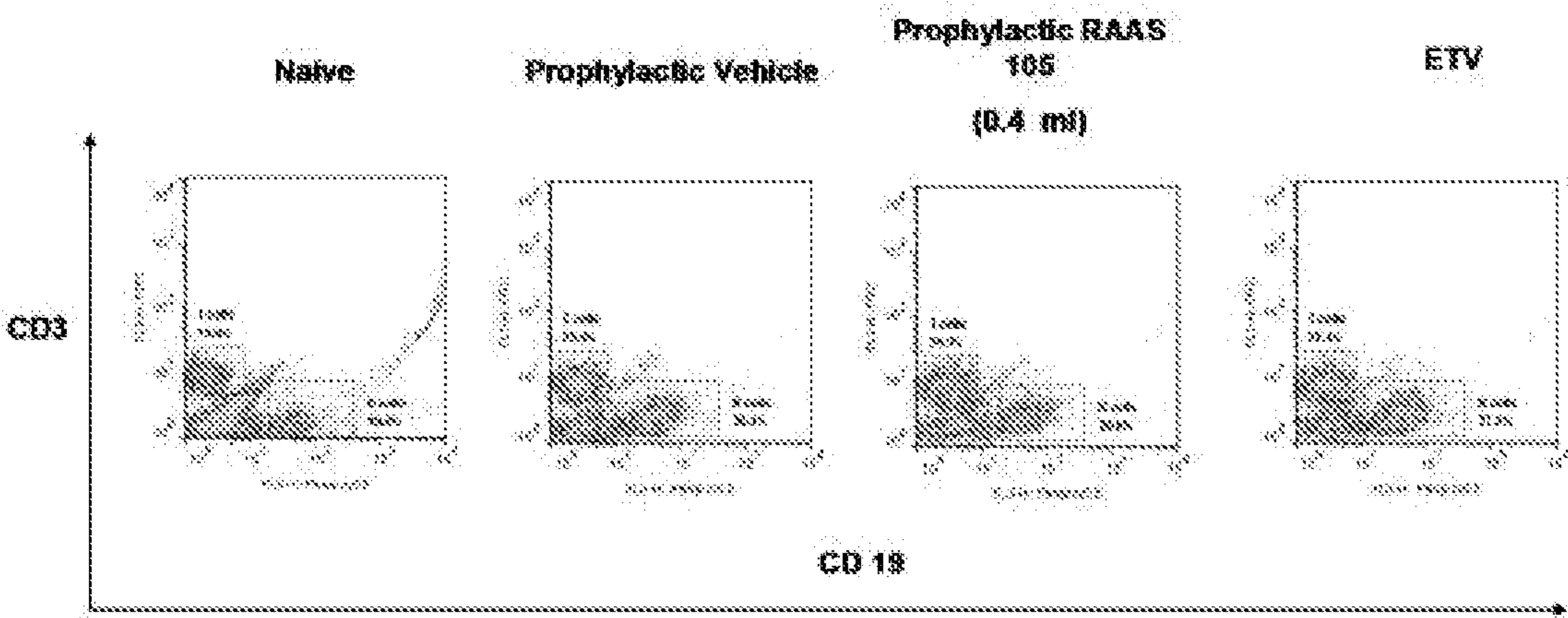


Figure 39

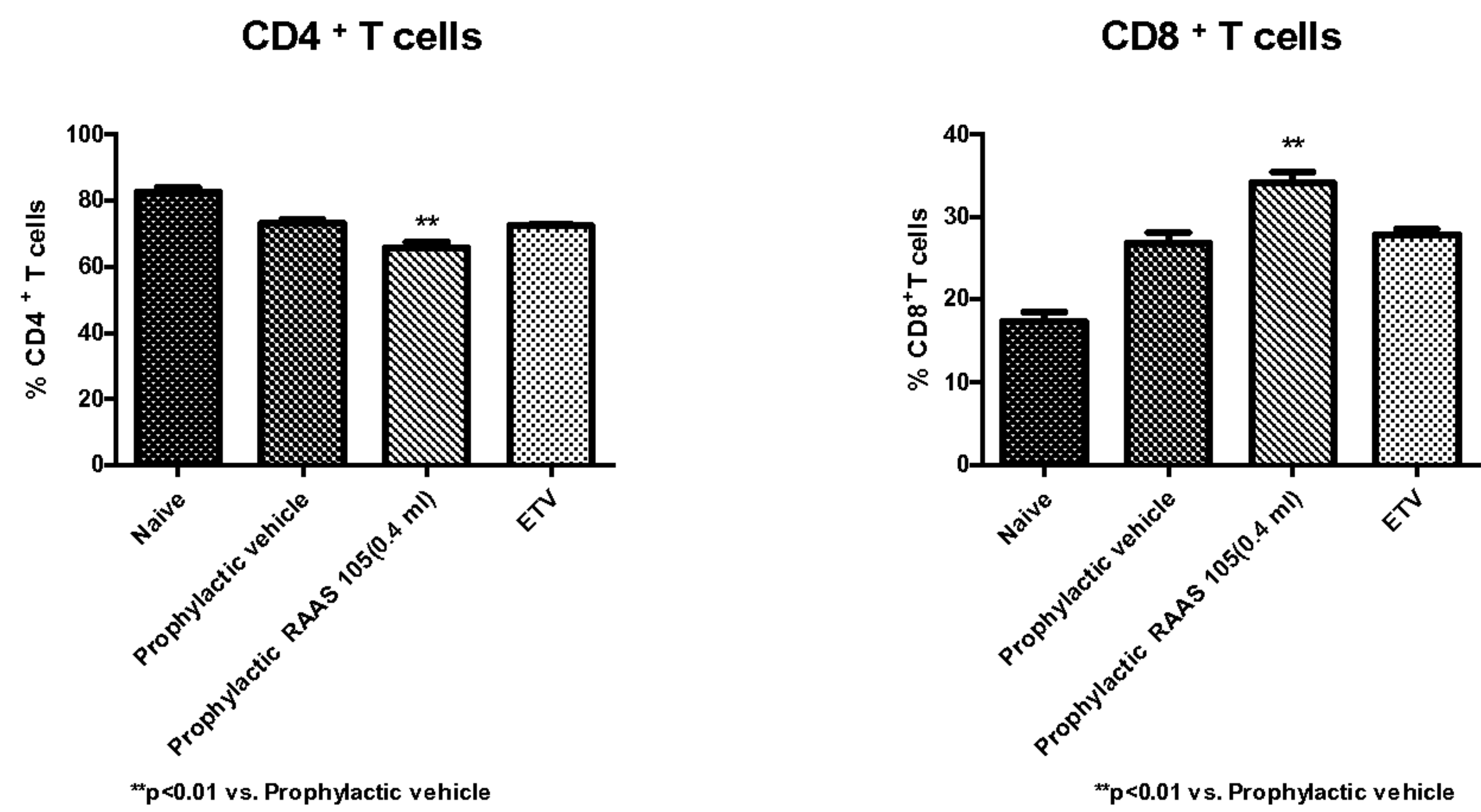


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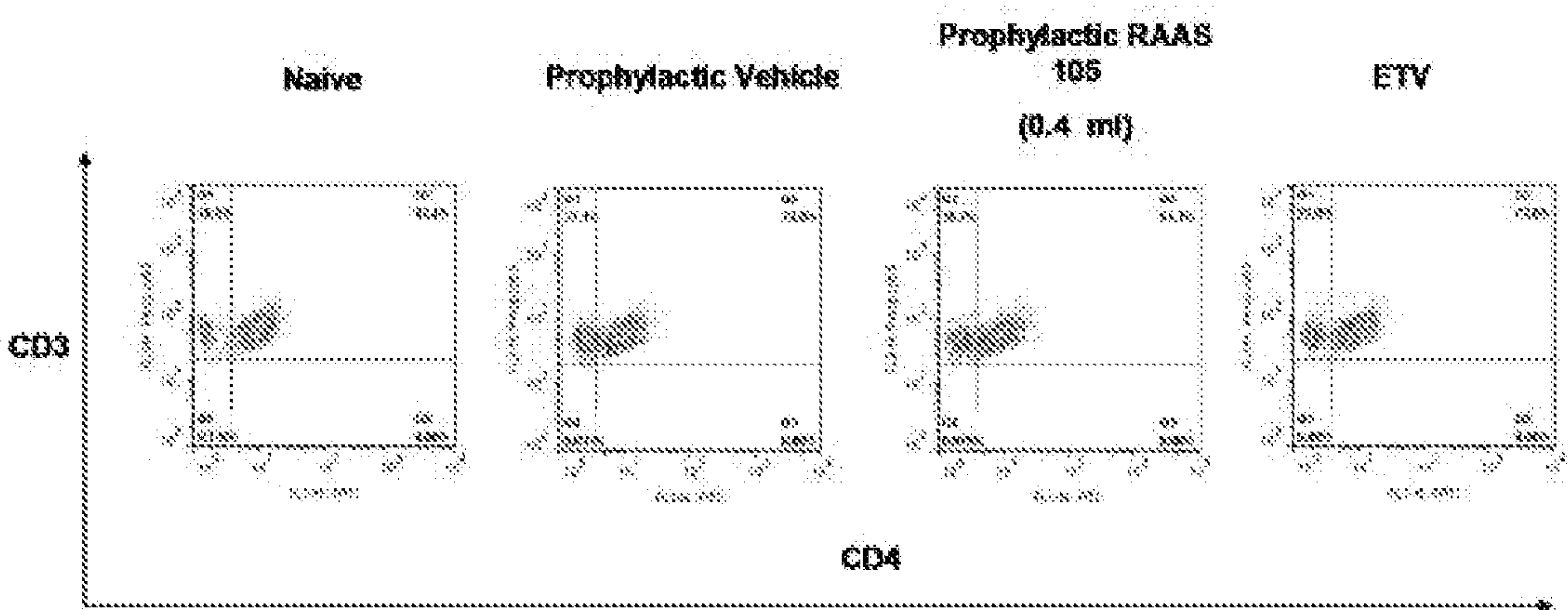


Figure 41

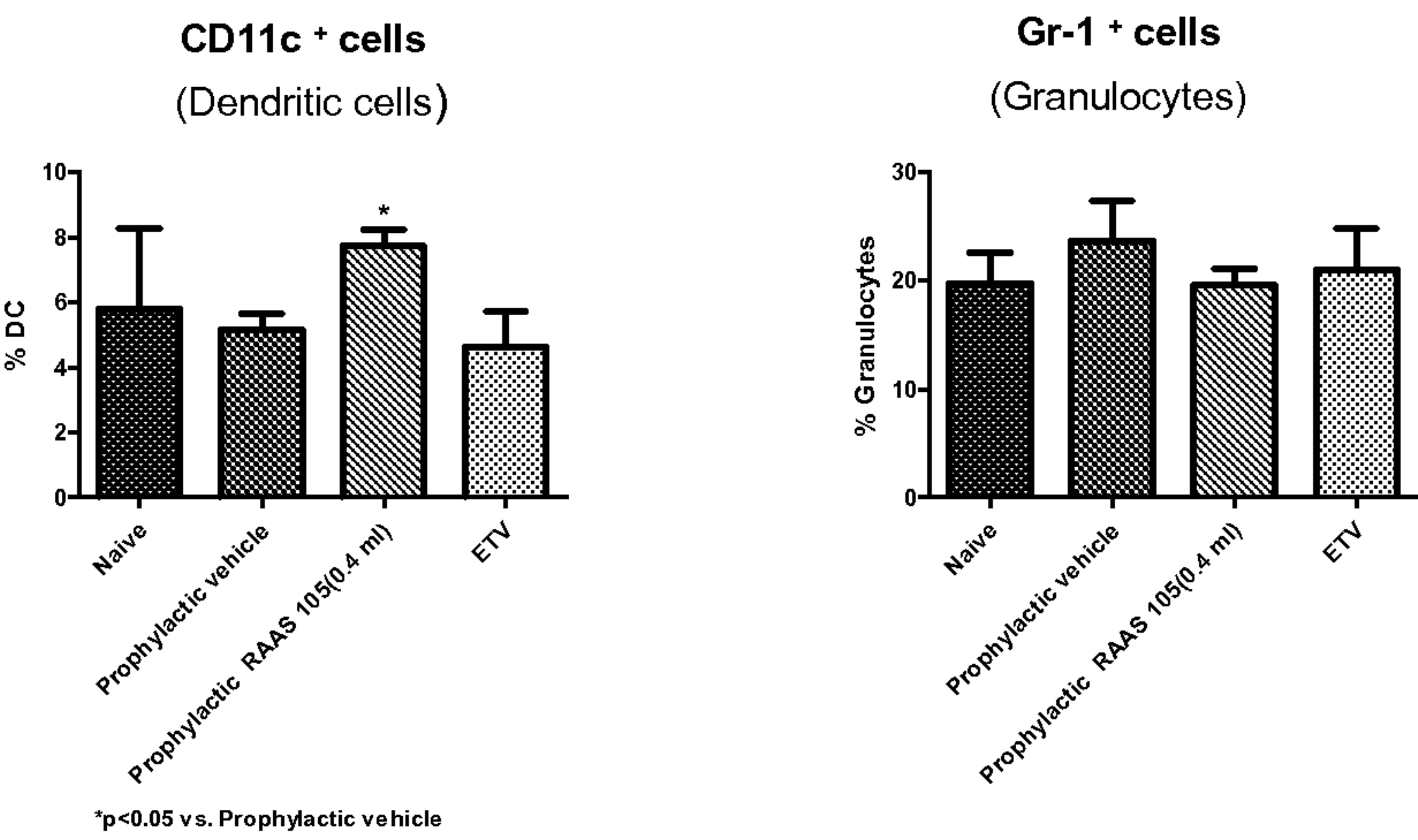


Figure 42

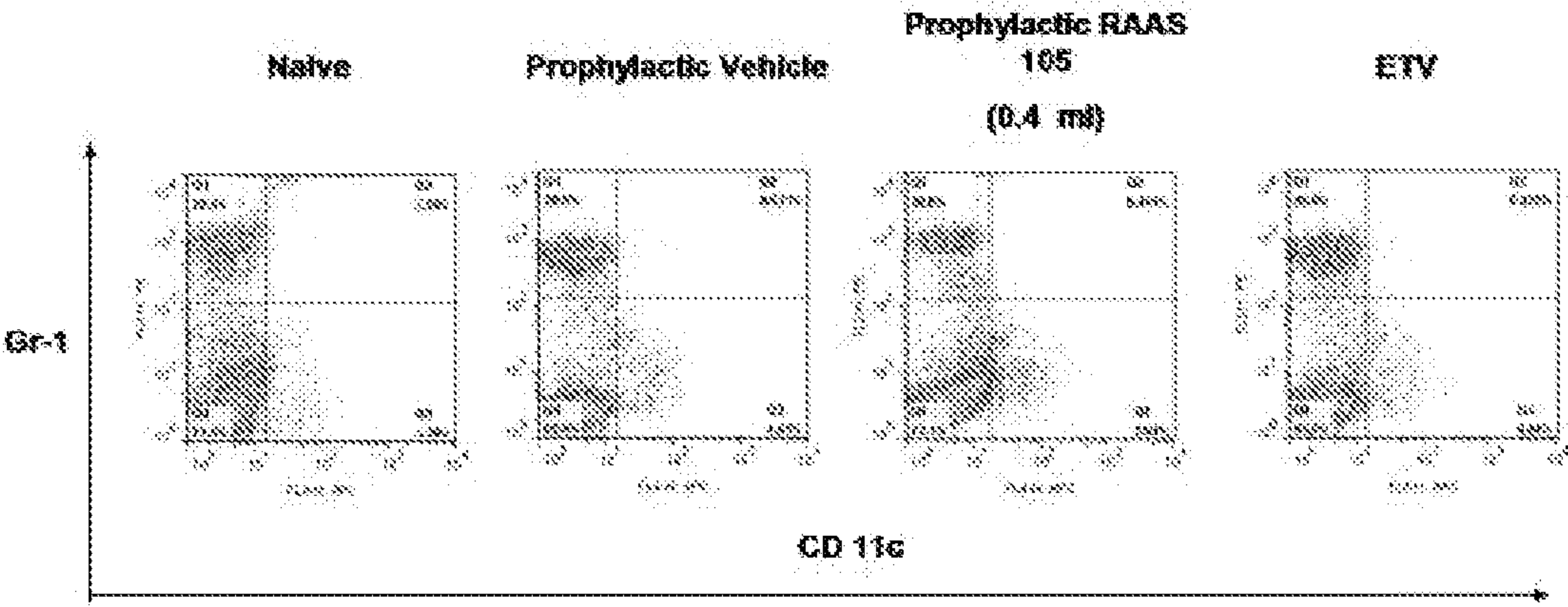


Figure 43

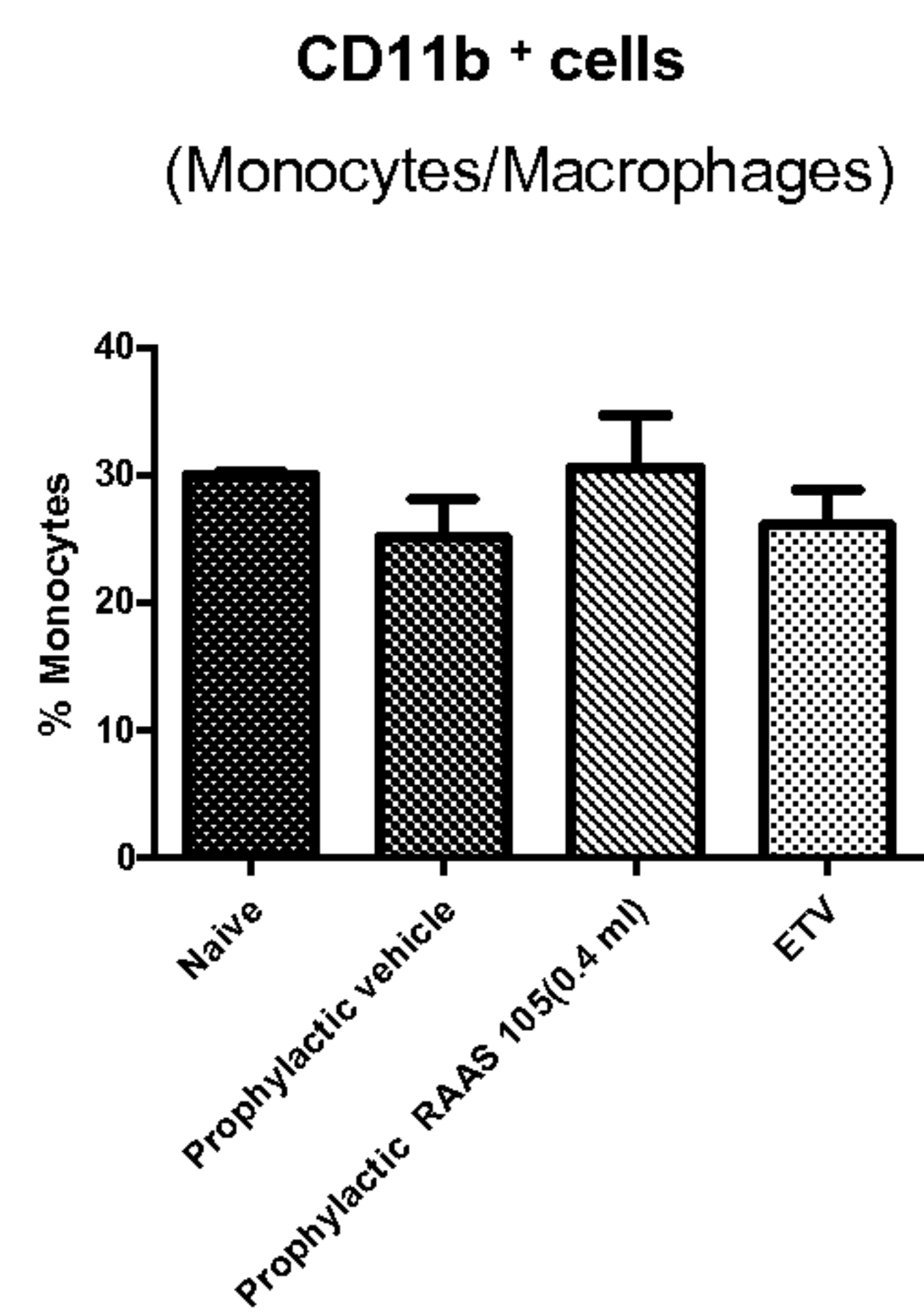


Figure 44

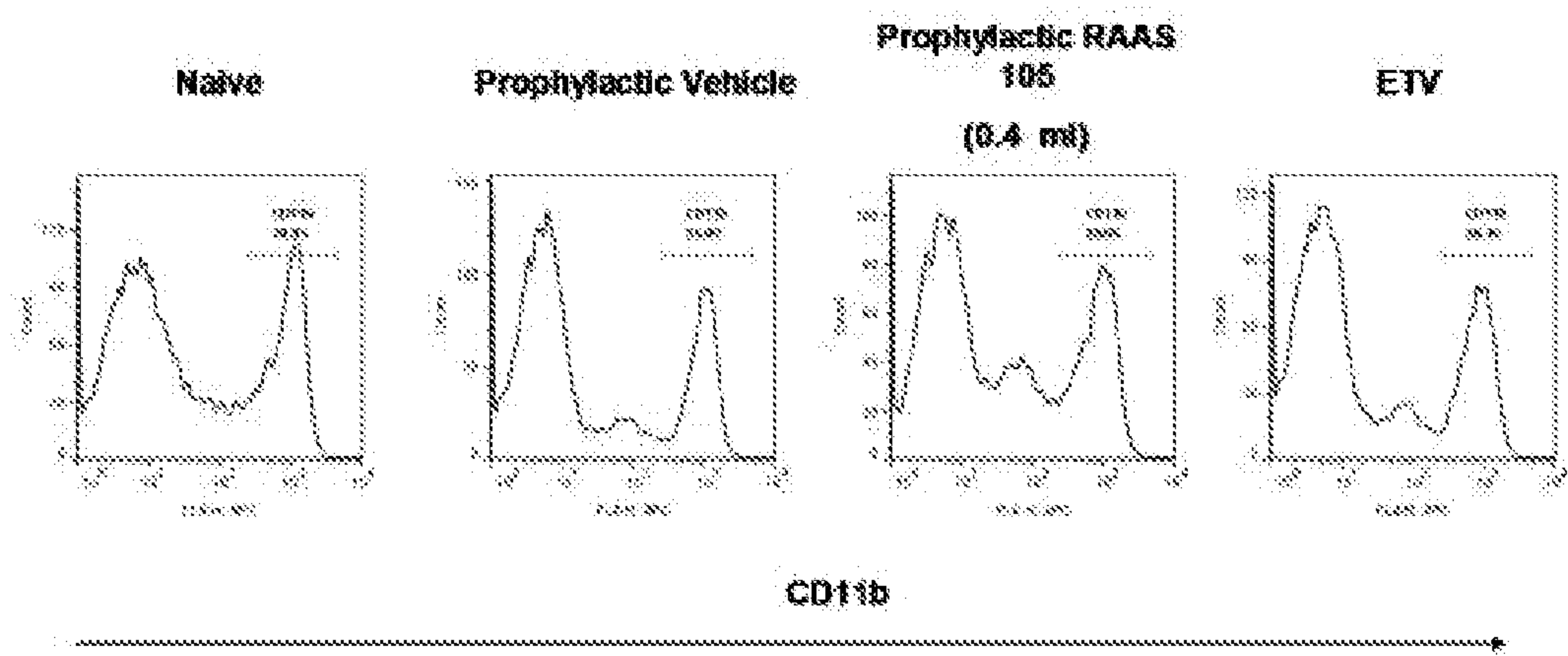


Figure 45

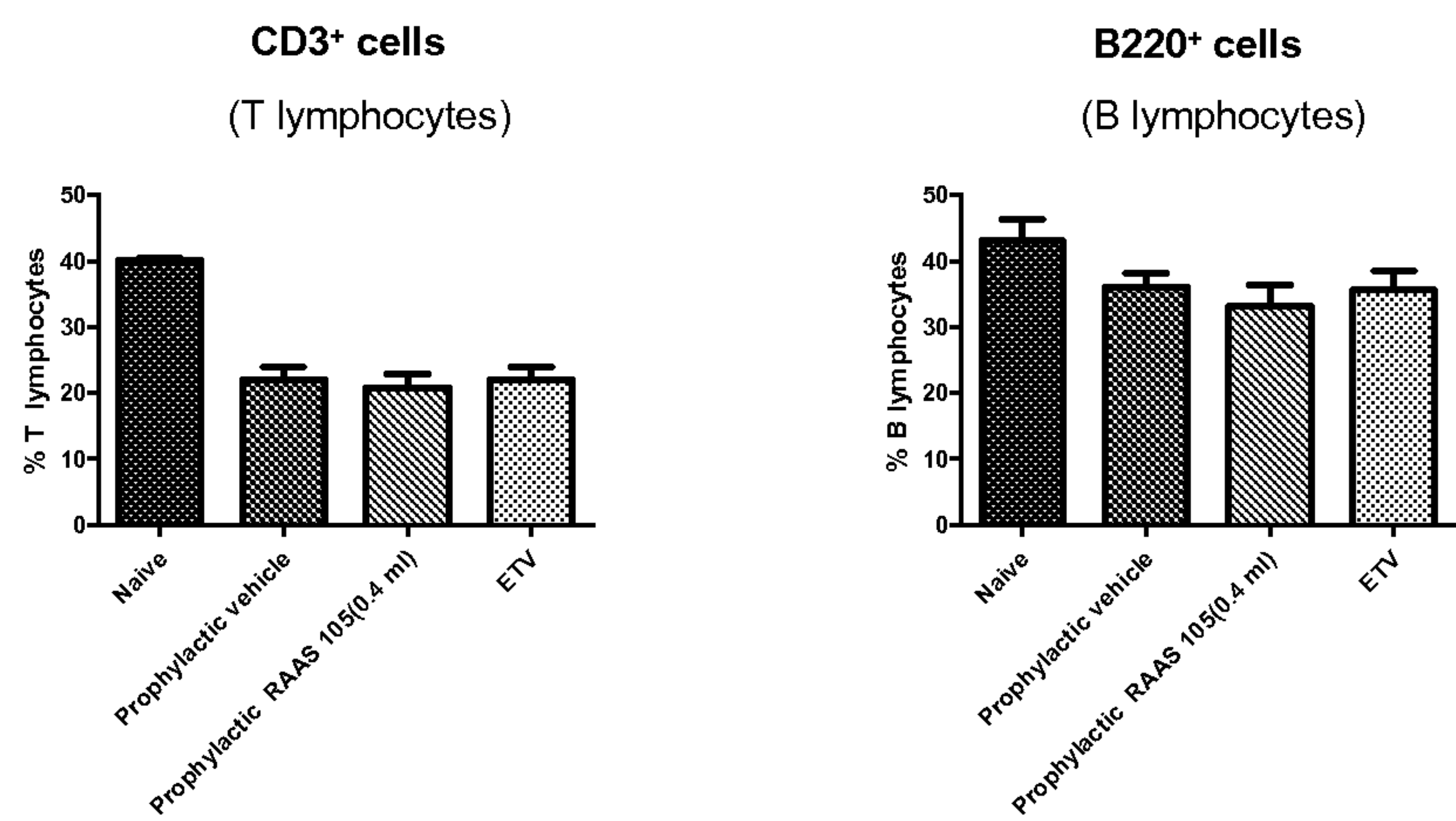


Figure 46

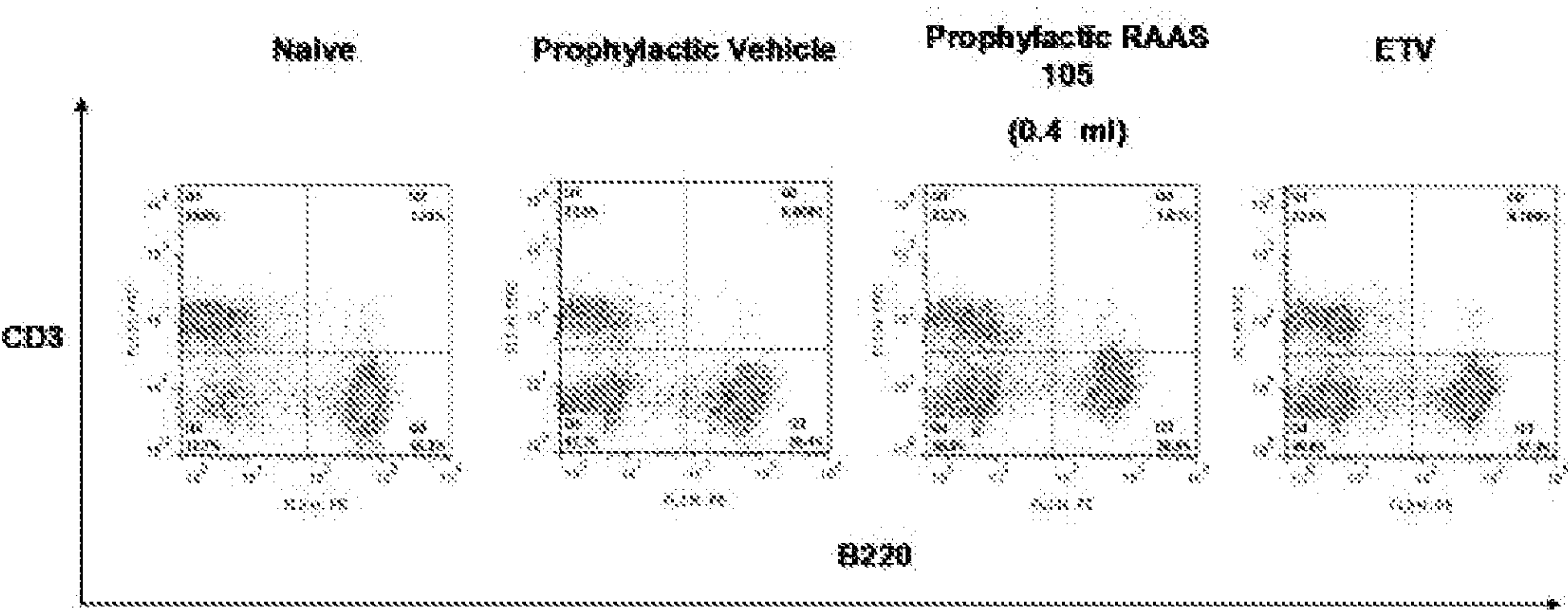


Figure 47

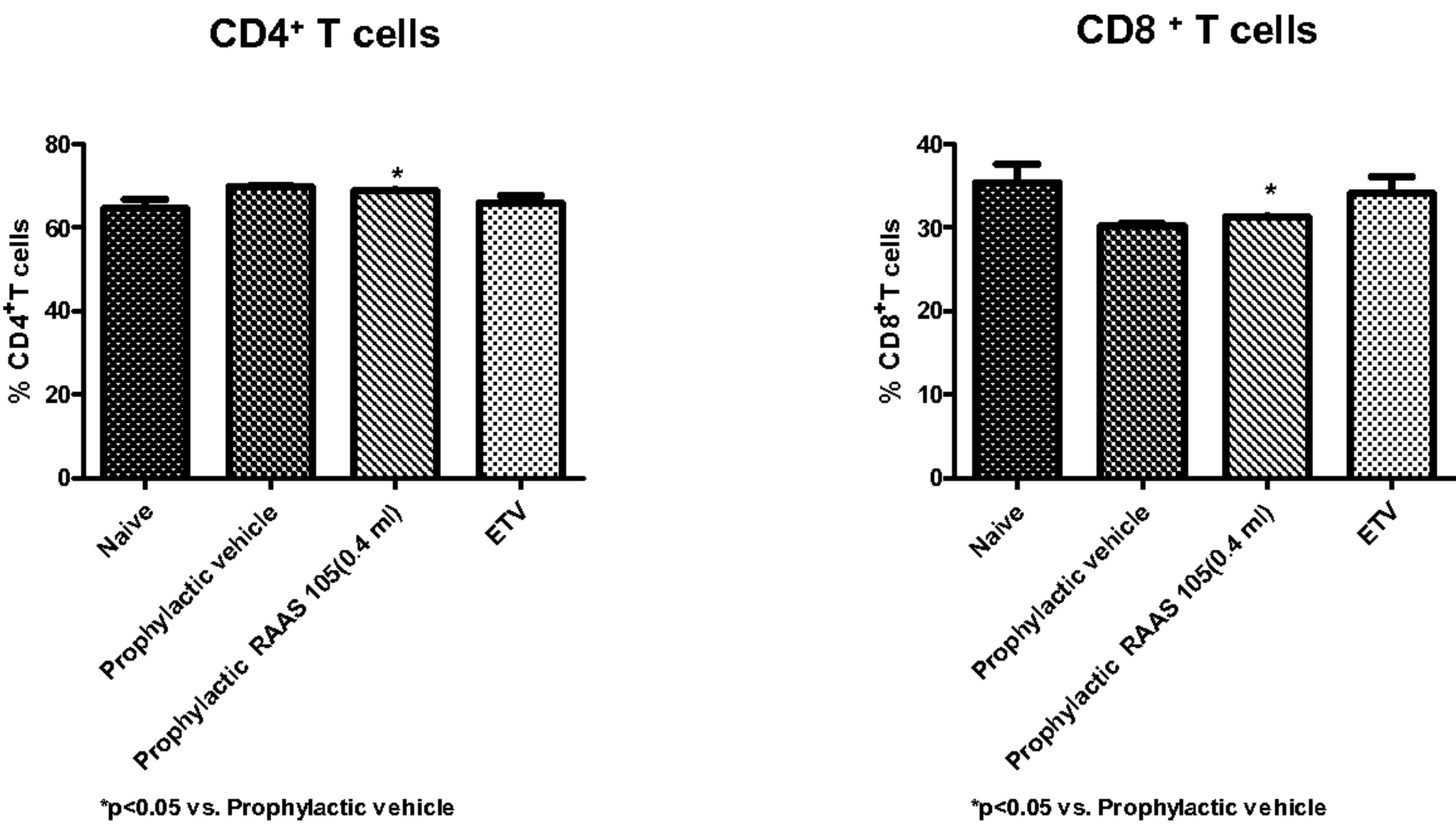


**Figure 47. Percents of CD4<sup>+</sup> and CD8<sup>+</sup> T cells in spleen.** Total CD3<sup>+</sup> T cells were gated and further analyzed for CD4<sup>+</sup>/CD8<sup>+</sup> percentages. After prophylactic treated by RAAS 105, the percentage of CD4 T cells slightly decreased while CD8 T cells slightly increased (by *t* test).

Figure 48

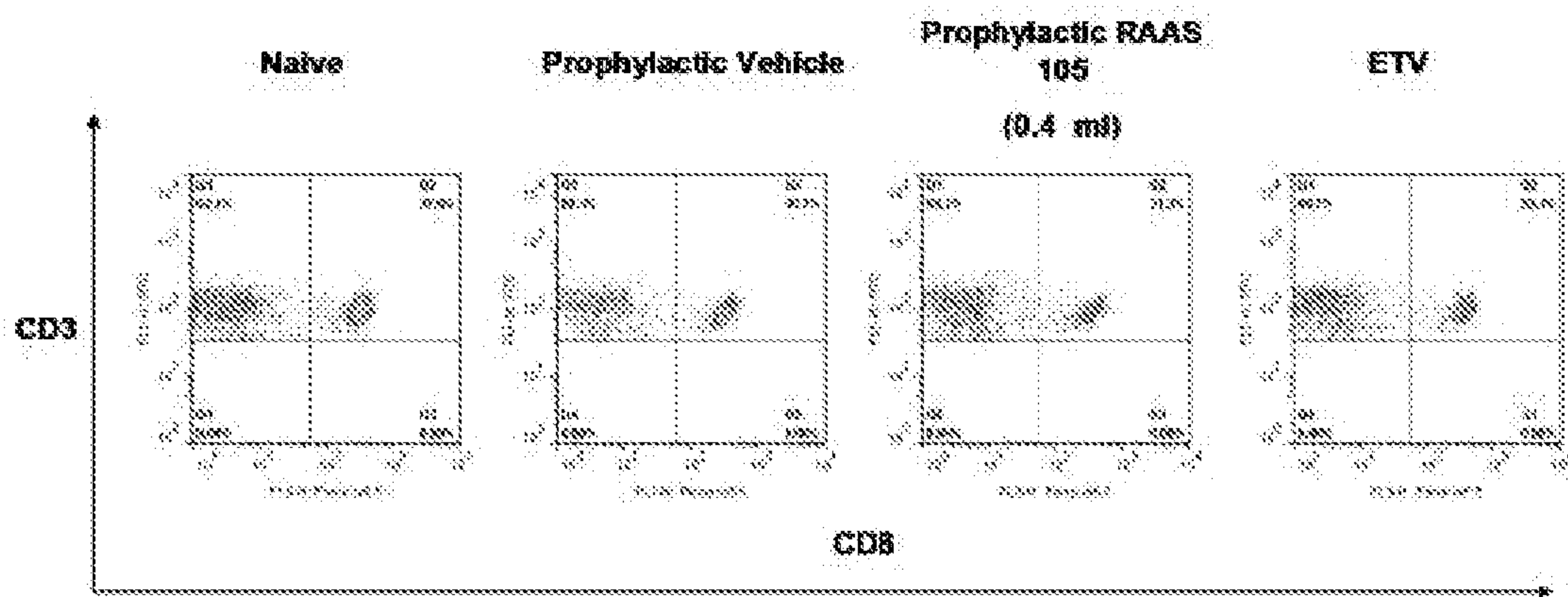


**Figure 48. Percents of CD4<sup>+</sup> and CD8<sup>+</sup> T cells in spleen.** Total CD3<sup>+</sup> T cells were gated and further analyzed for CD4<sup>+</sup>/CD8<sup>+</sup> percentages.

Figure 49

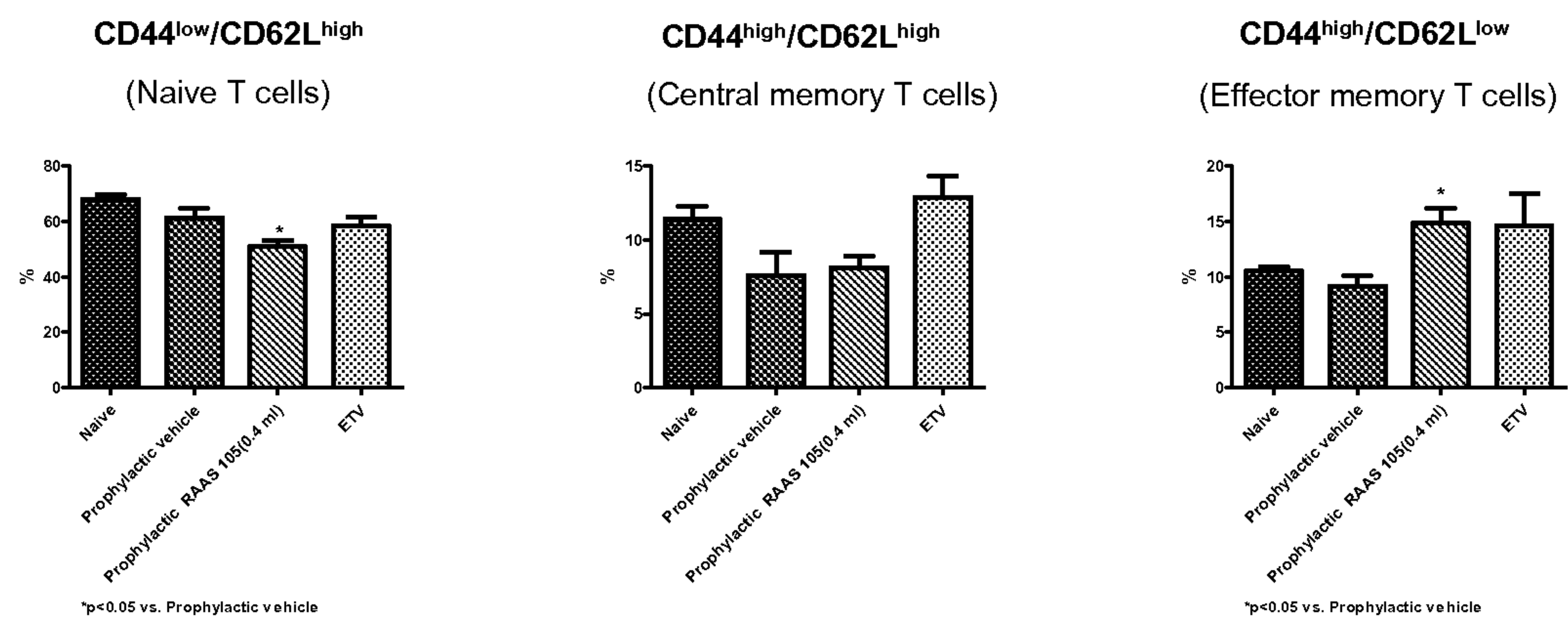


Figure 49. T cell subset percents in spleen. Total CD4<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 50

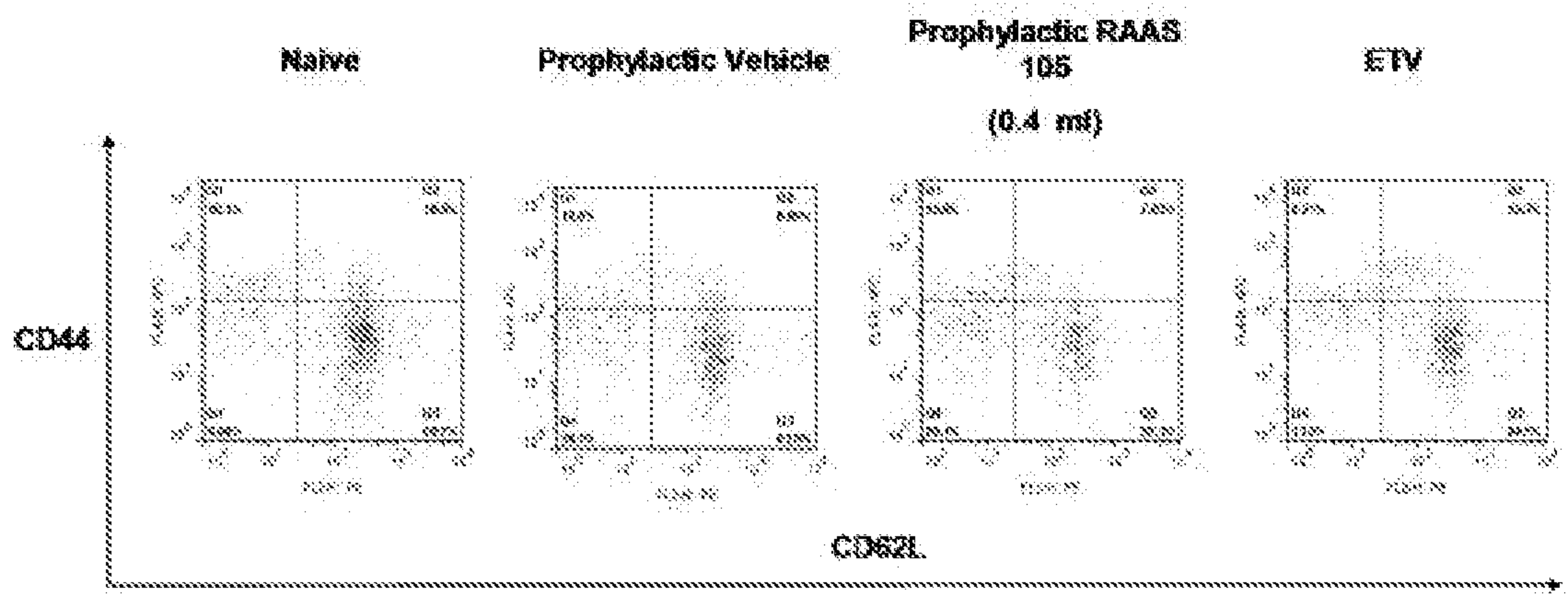


Figure 50. T cell subsets percents in spleen. Total CD4<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 51

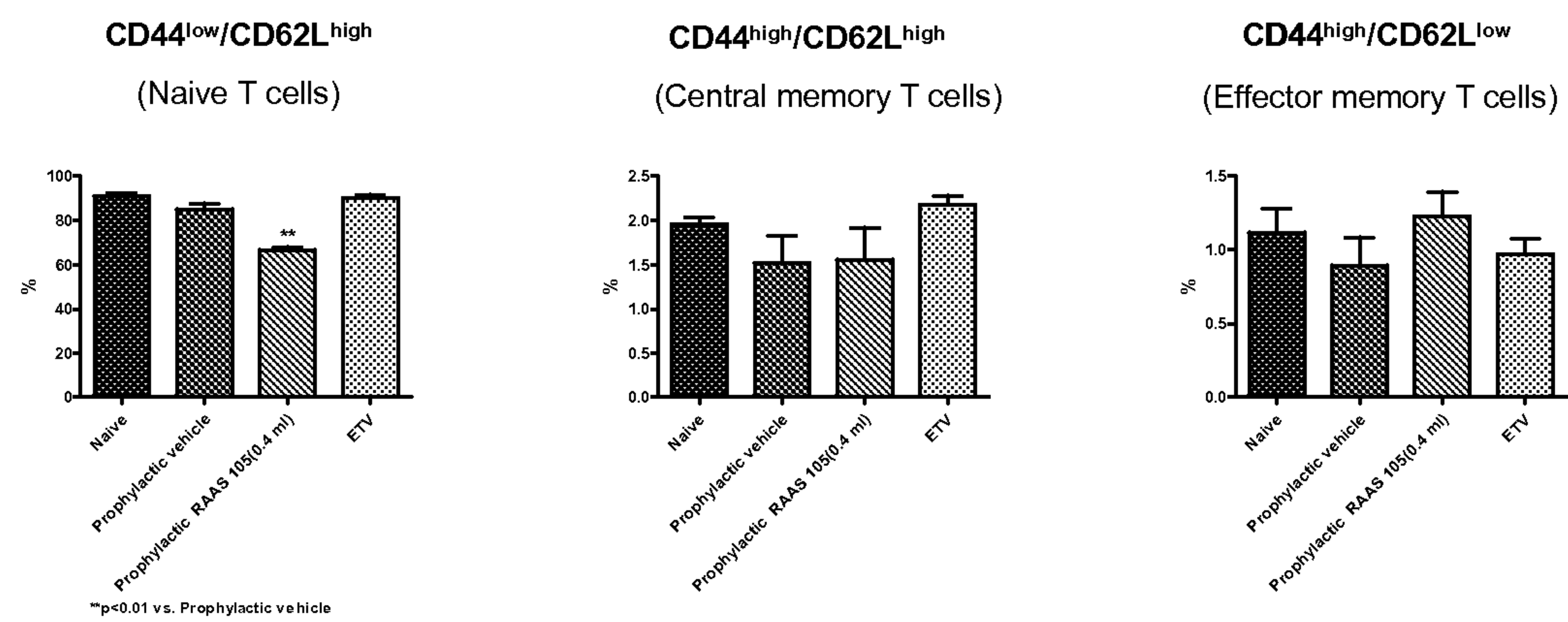


Figure 51. T cell subsets percents in spleen. Total CD8<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 52

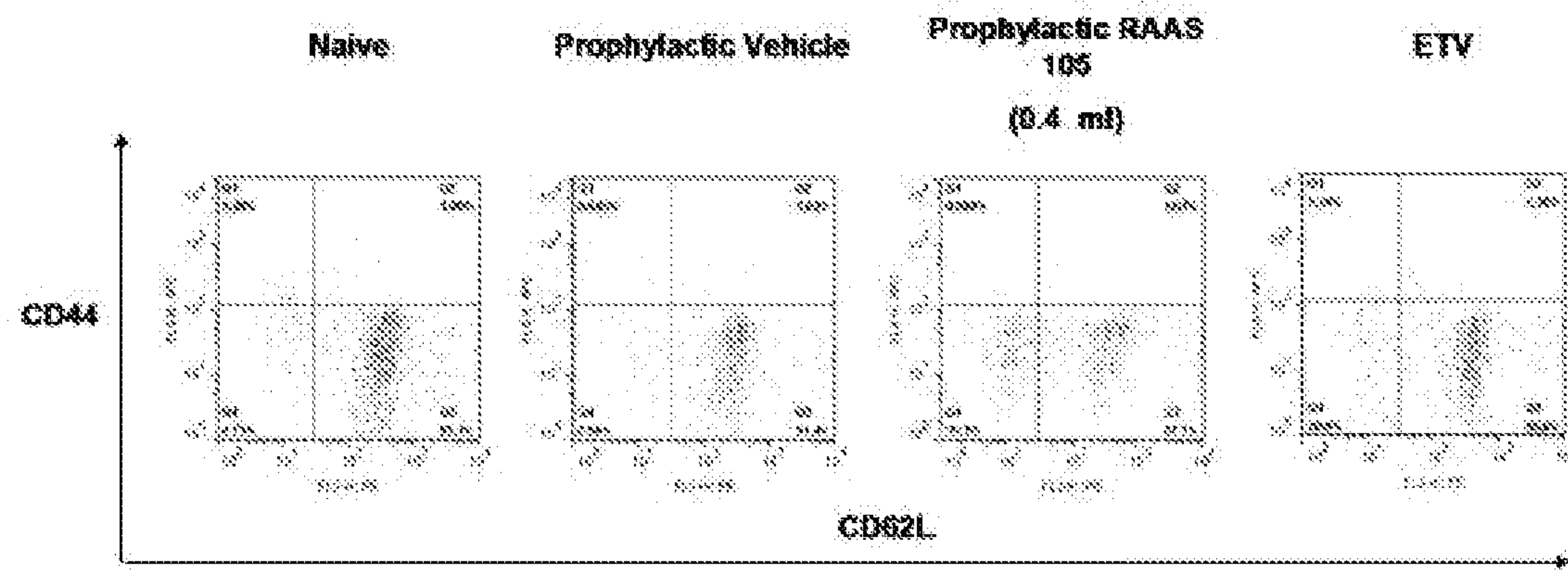


Figure 52. T cell subsets percents in spleen. Total CD8<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 53

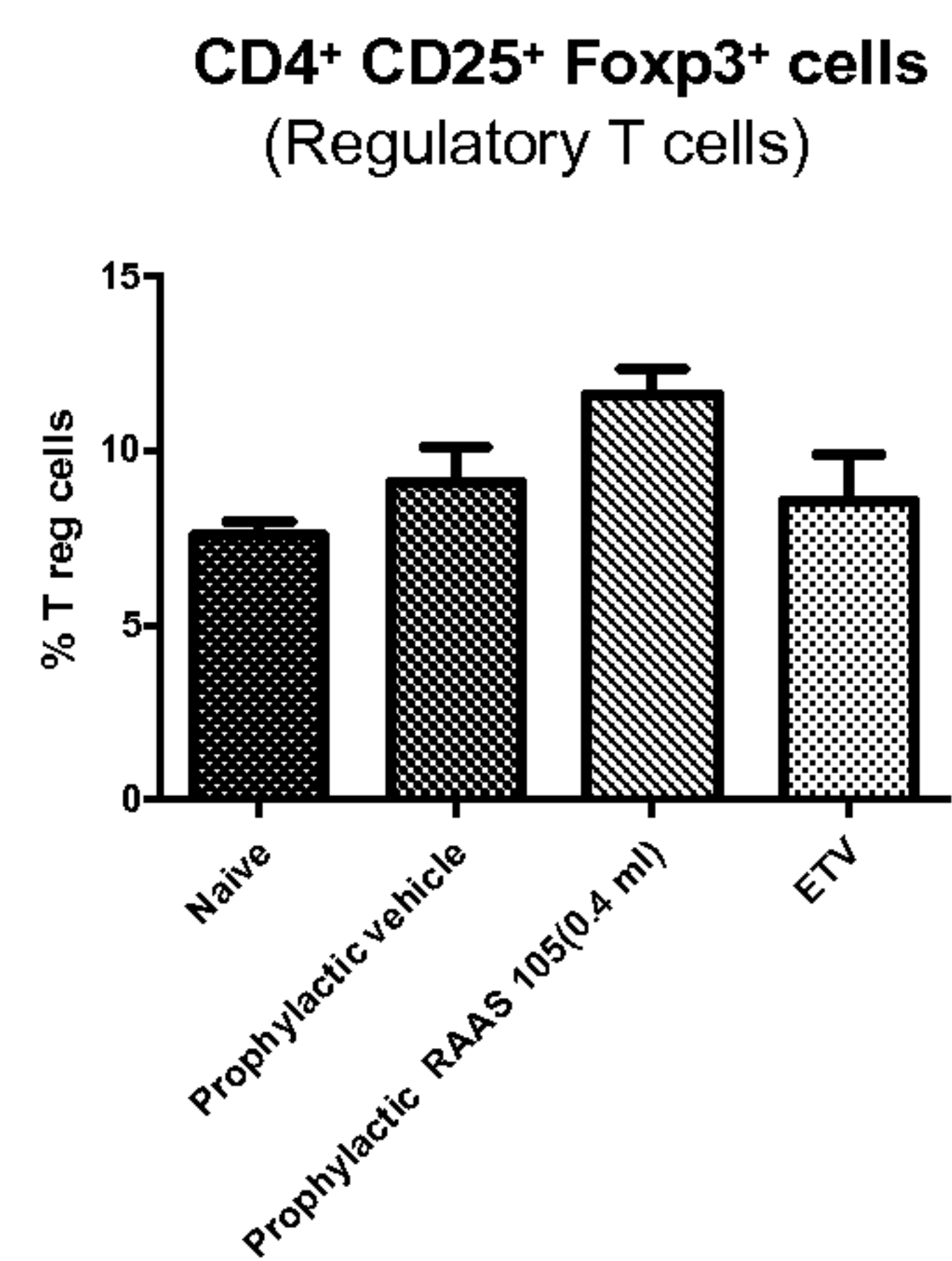


**Figure 53. Percents of Foxp3<sup>+</sup> regulatory T cells in spleen.** Foxp3<sup>+</sup> regulatory T cells were analyzed by intracellular staining.

Figure 54

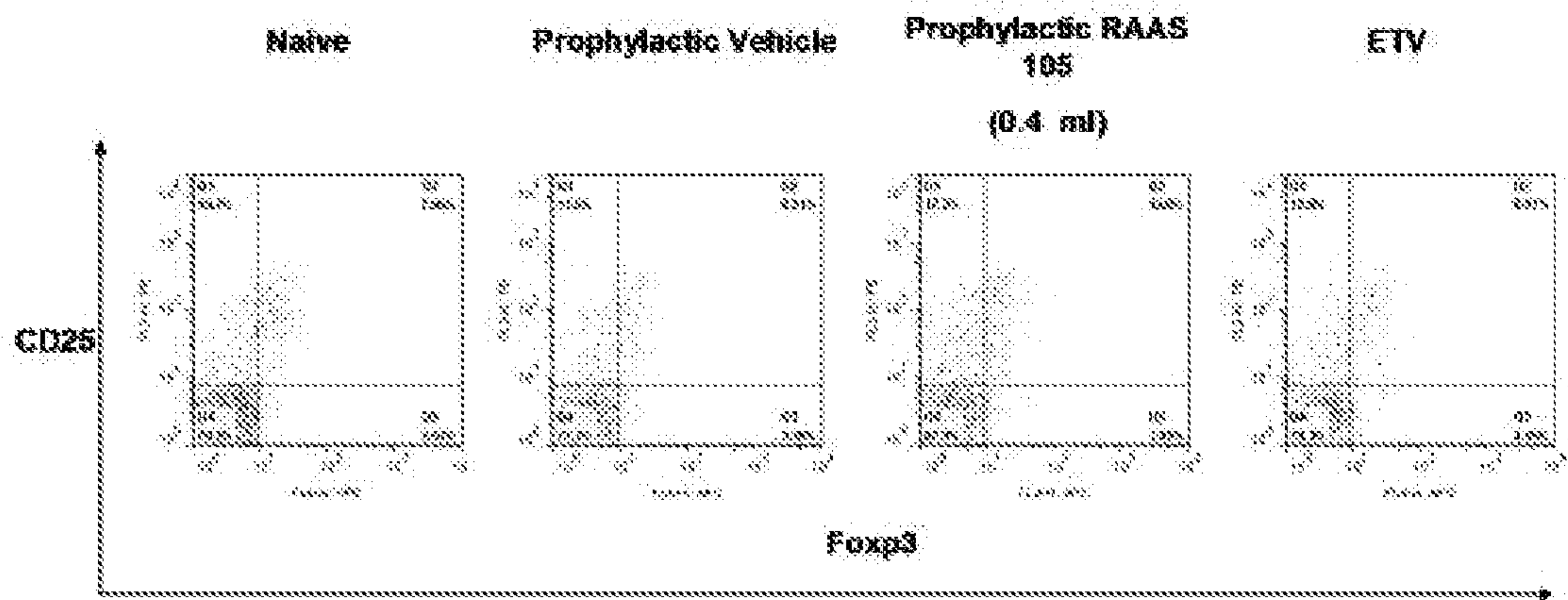


**Figure 54. Percents of regulatory T cells in spleen.** Total CD4<sup>+</sup> T cells were gated.

Figure 55

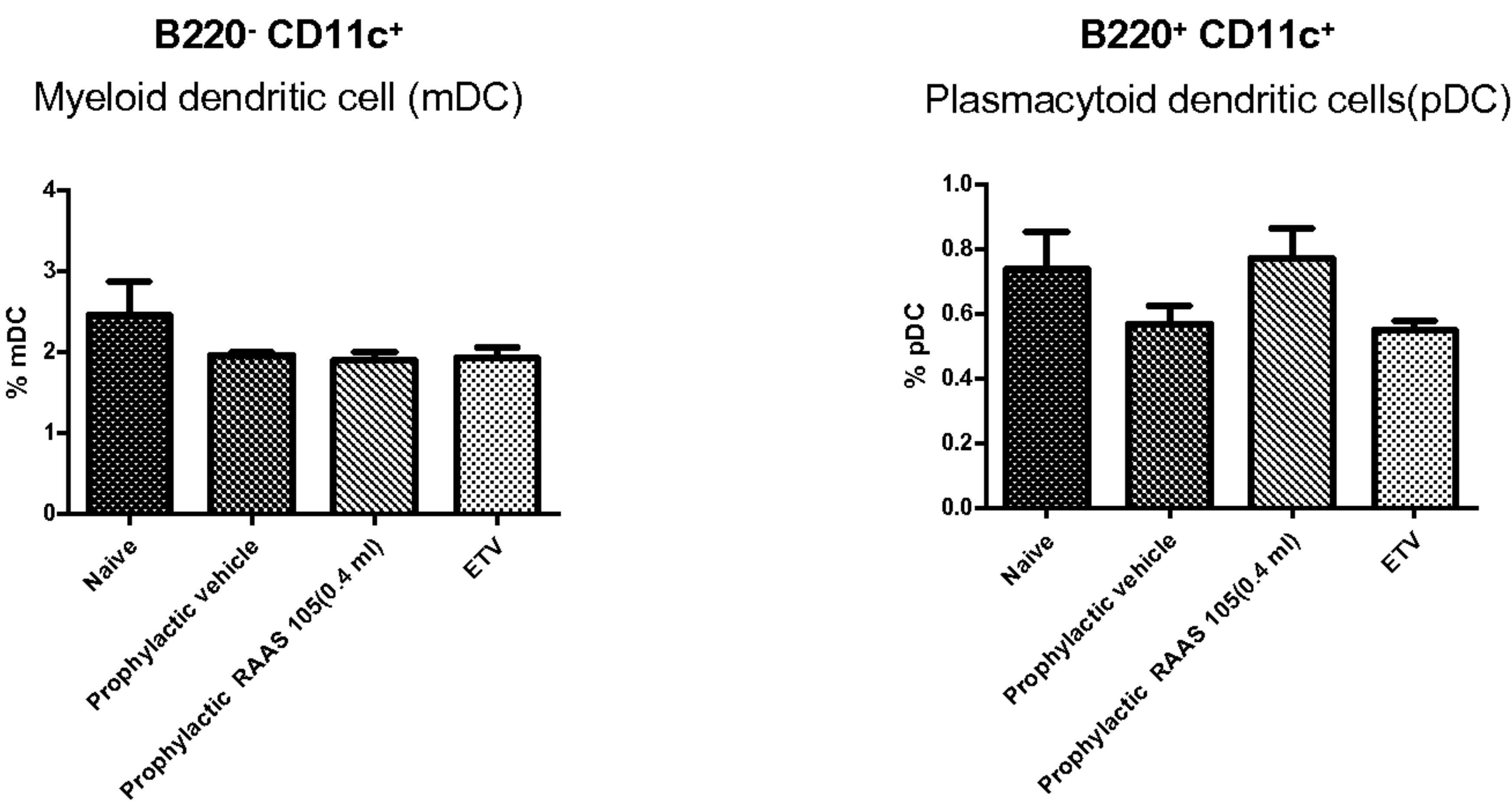


**Figure 55. Percents of pDCs and mDCs in spleen.** Total live cells were gated. There were no significant differences after compound treatment. (by *t* test)

Figure 56

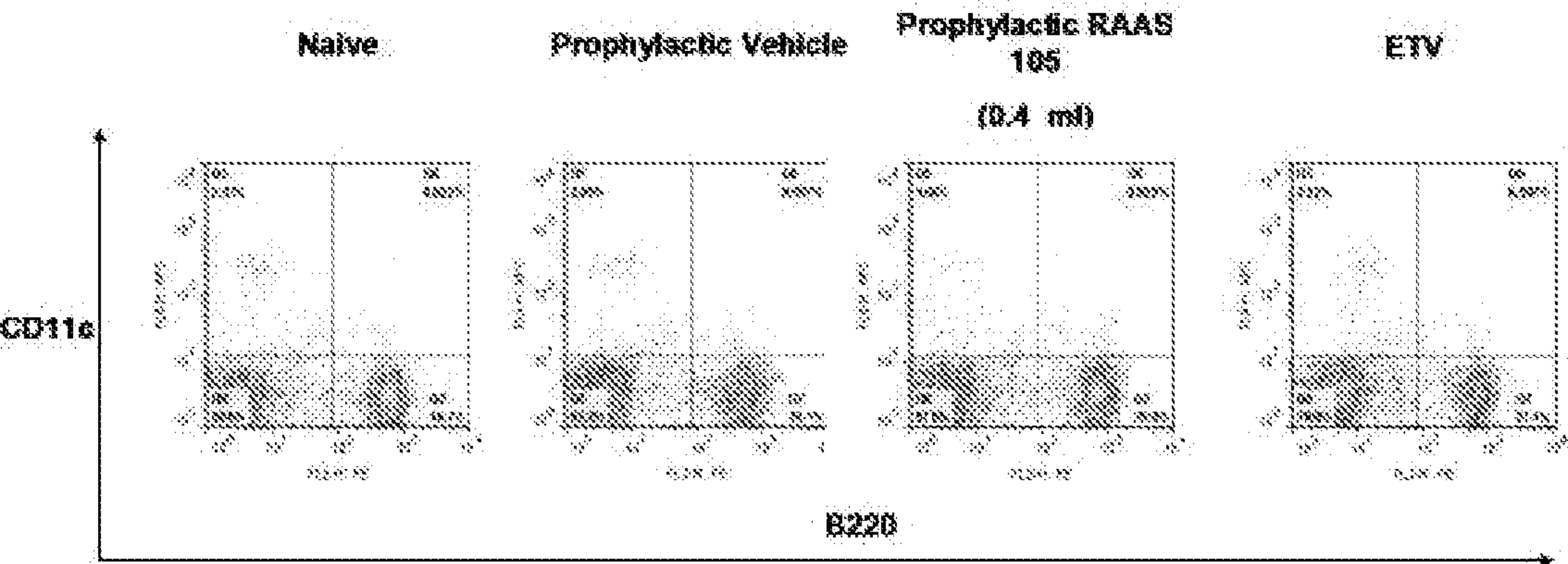


**Figure 56. Percents of mDCs and pDCs in spleen.** Total live cells were gated.

Figure 57

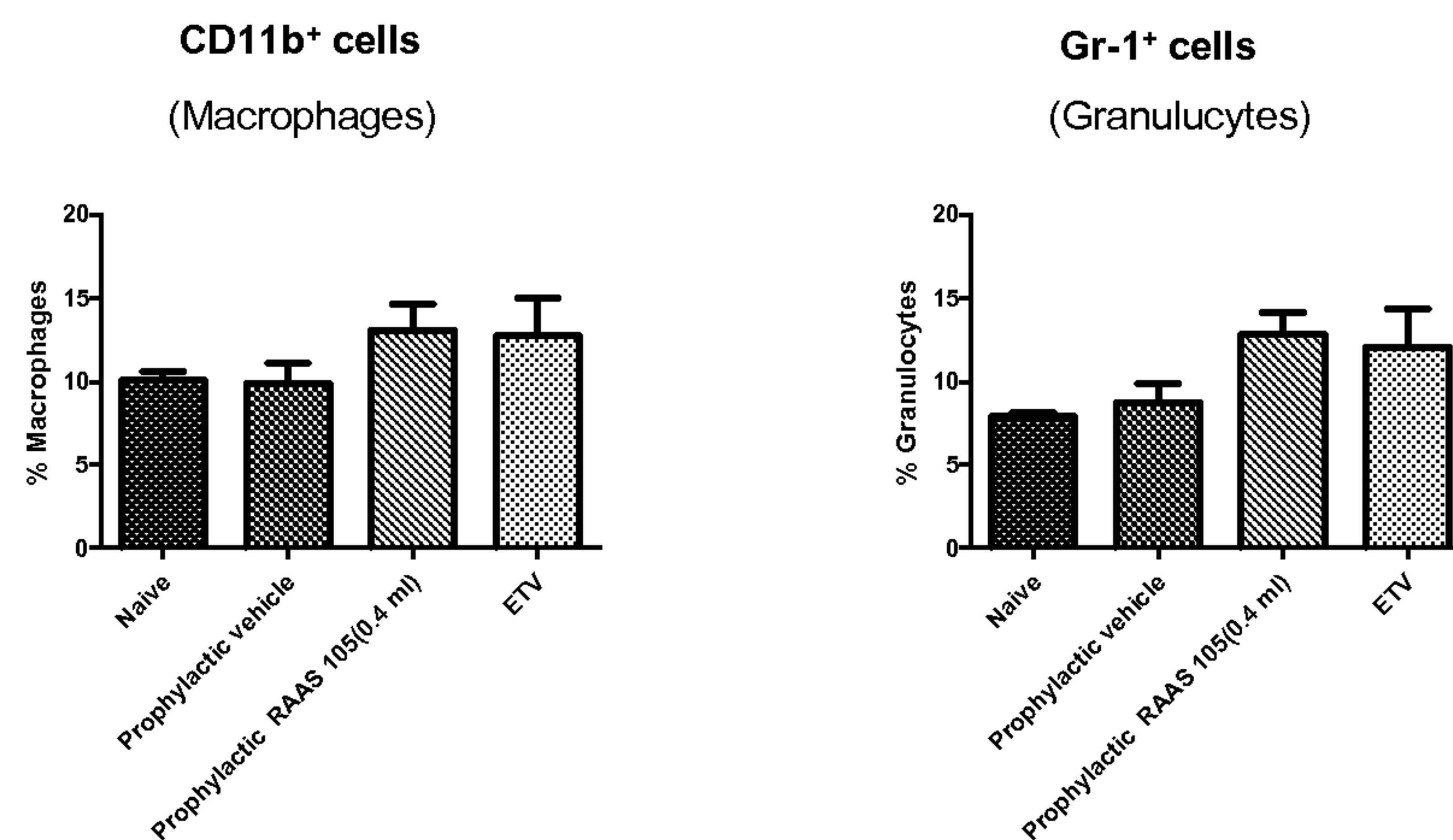


**Figure 57. Percents of Macrophages and Granulocytes in spleen.** Total live cells were gated. There were no significant differences after compound treatment. (by *t* test).

Figure 58

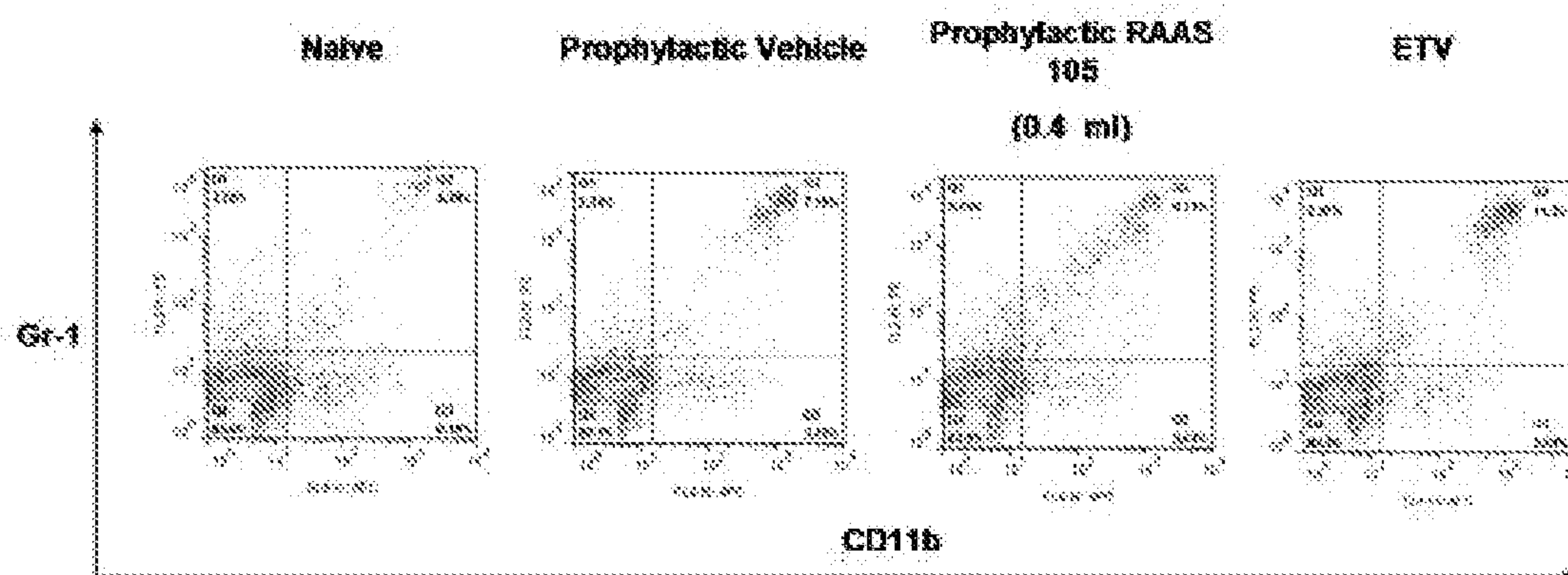


**Figure 58. Percents of macrophages/granulocytes in spleen.** Total live cells were gated.

Figure 59

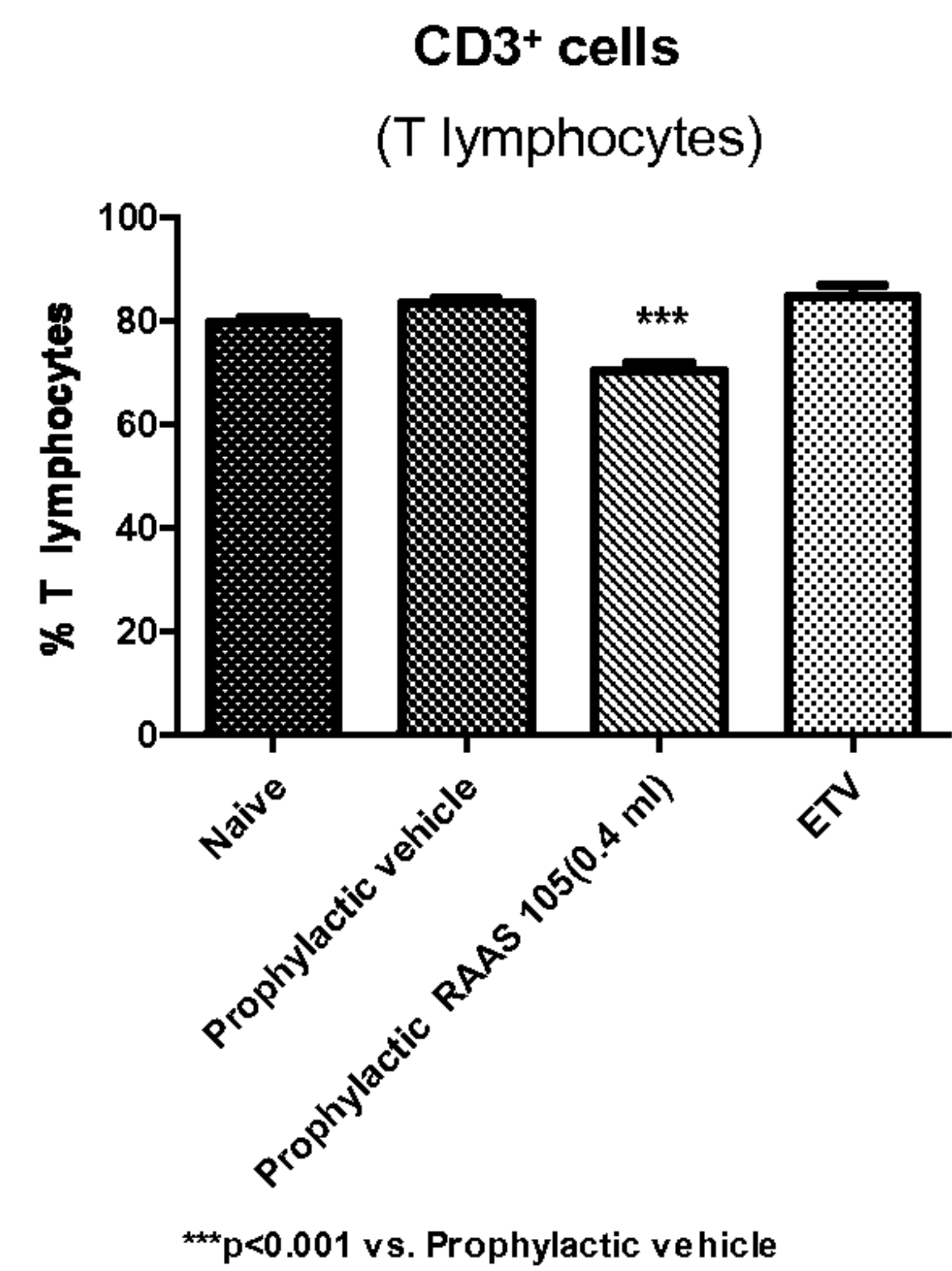


**Figure 59. Percents of T cells in lymph nodes.** Total lymphocytes were gated. After the treatment, percents of T cells in the lymph nodes were significantly decreased (*t* test).

Figure 60

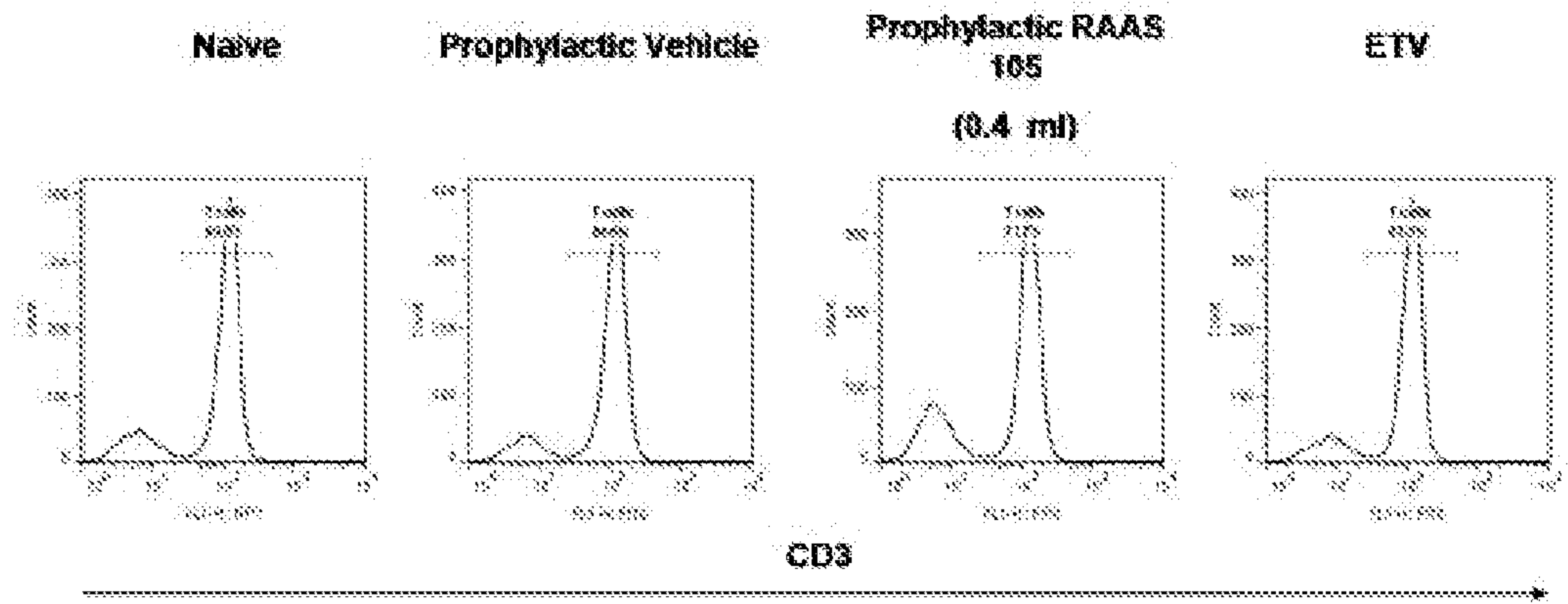


**Figure 60. Percents of CD3<sup>+</sup> T cells in lymph nodes.** Total lymphocytes were gated.

Figure 61

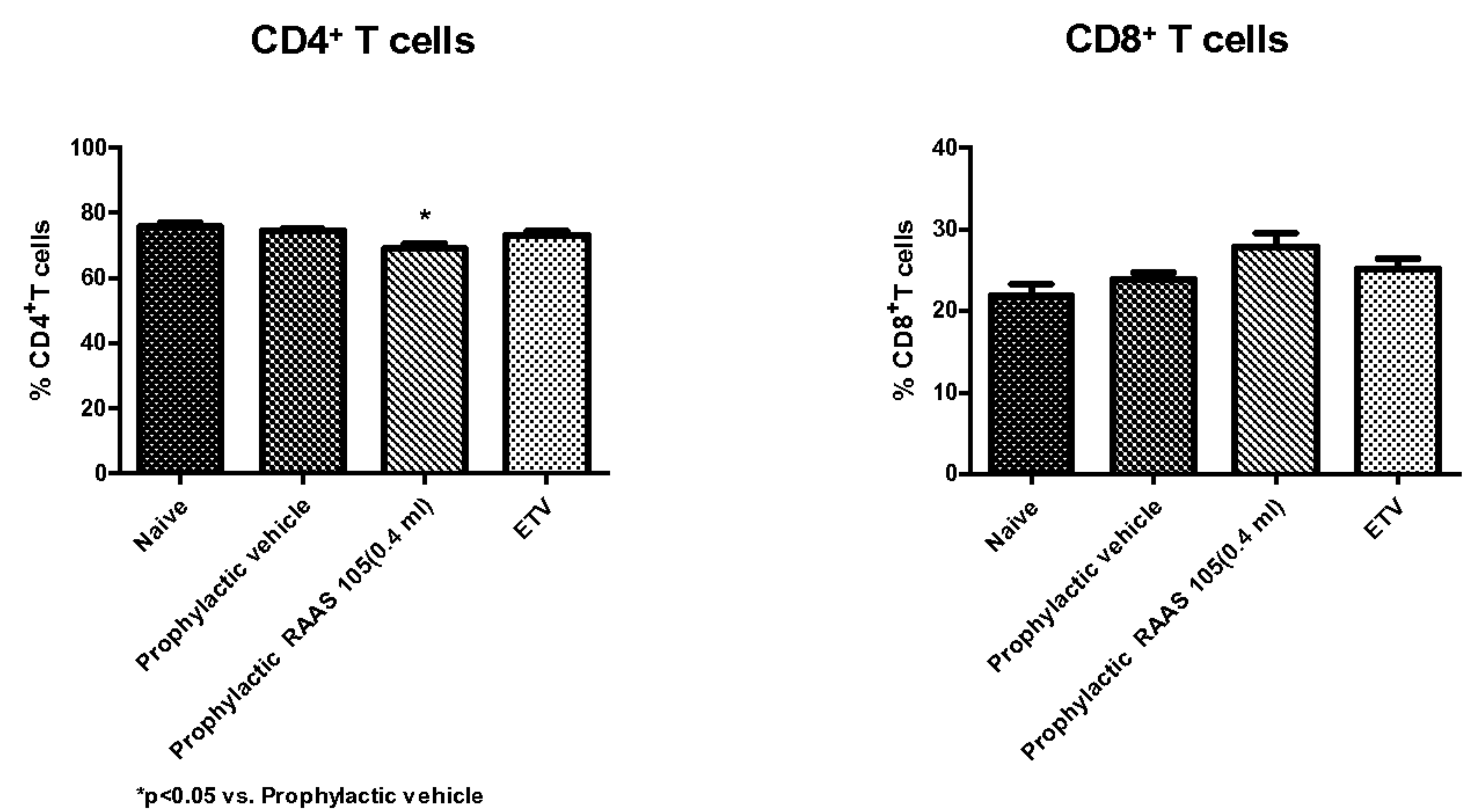


**Figure 61. Percents of CD4<sup>+</sup> and CD8<sup>+</sup> T cells in lymph nodes.** Total CD3<sup>+</sup> T cells were gated and further analyzed for CD4<sup>+</sup>/CD8<sup>+</sup> percentages. After prophylactic treatment, percents of CD4<sup>+</sup> T cells decreased. (by *t* test)

Figure 62

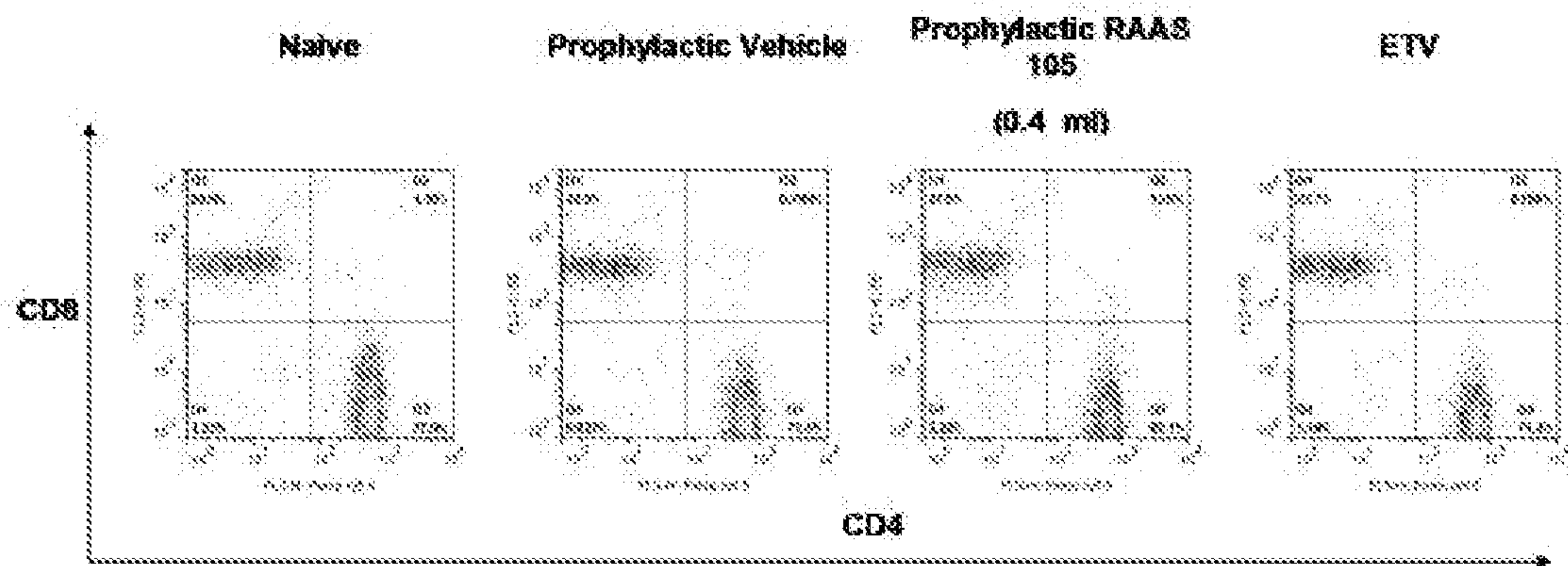


**Figure 62. Percents of CD4<sup>+</sup> and CD8<sup>+</sup> T cells in lymph nodes.** Total CD3<sup>+</sup> T cells were gated and further analyzed for CD4<sup>+</sup>/CD8<sup>+</sup> percentages.

Figure 63

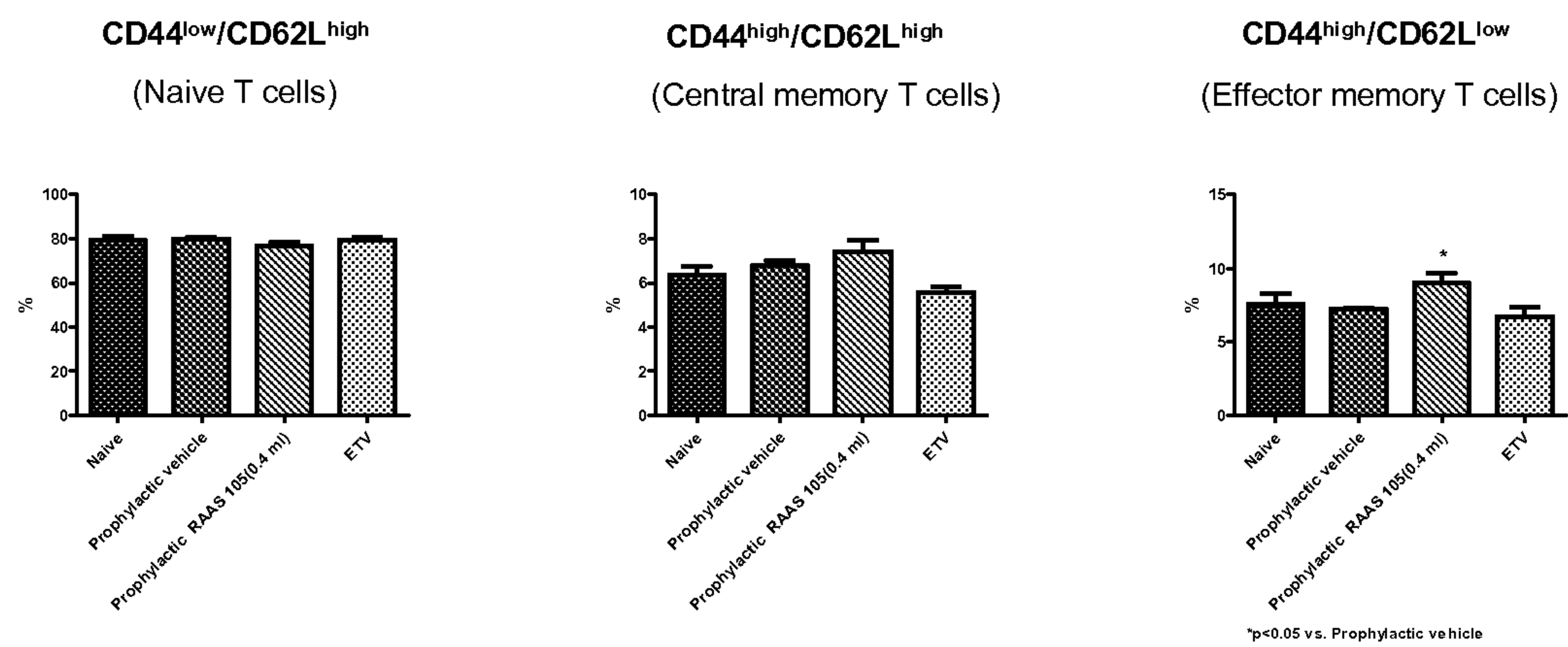


**Figure 63. T cell subsets percents in lymph nodes.** Total CD4<sup>+</sup> T cells were gated and T cell subsets were determined. No significant differences were found except effector memory T cells compared to vehicle group.

Figure 64

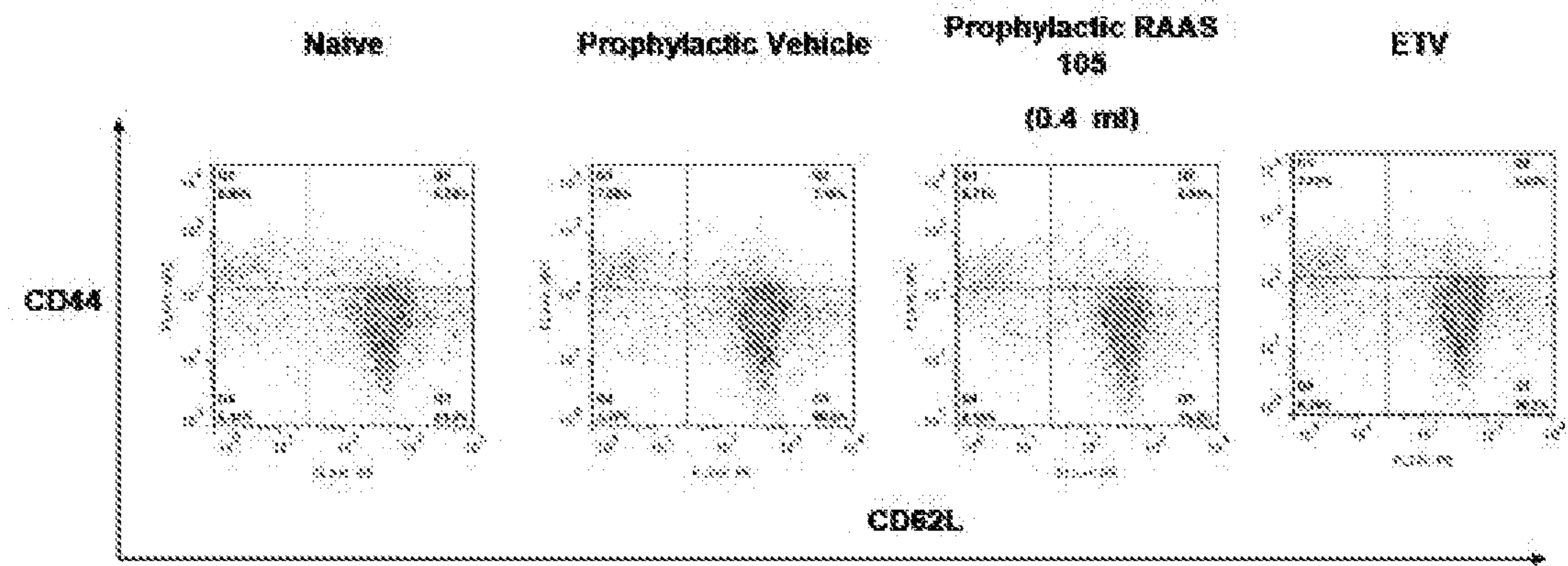


**Figure 64. T cell subsets percents in lymph nodes.** Total CD4<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 65

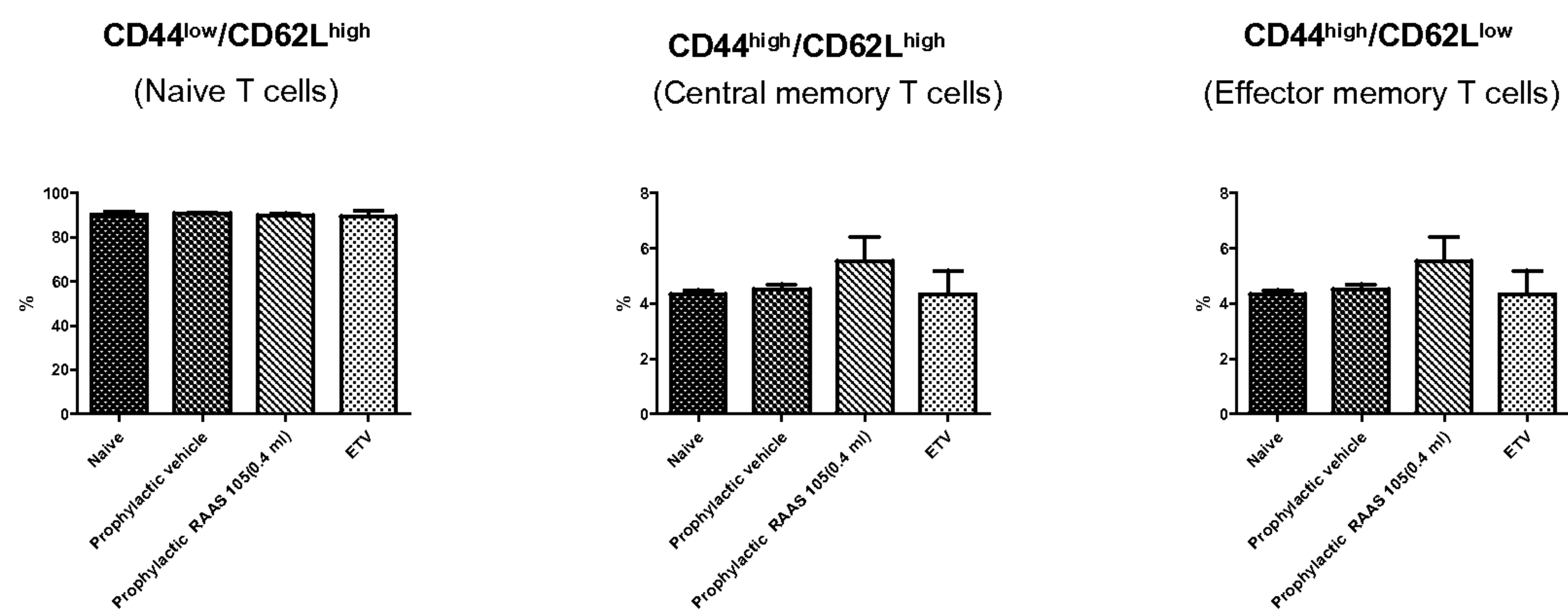


**Figure 65. T cell subsets percents in lymph nodes.** Total CD8<sup>+</sup> T cells were gated and T cell subsets were determined. No significant differences were found in all the groups compared to vehicle group.

Figure 66

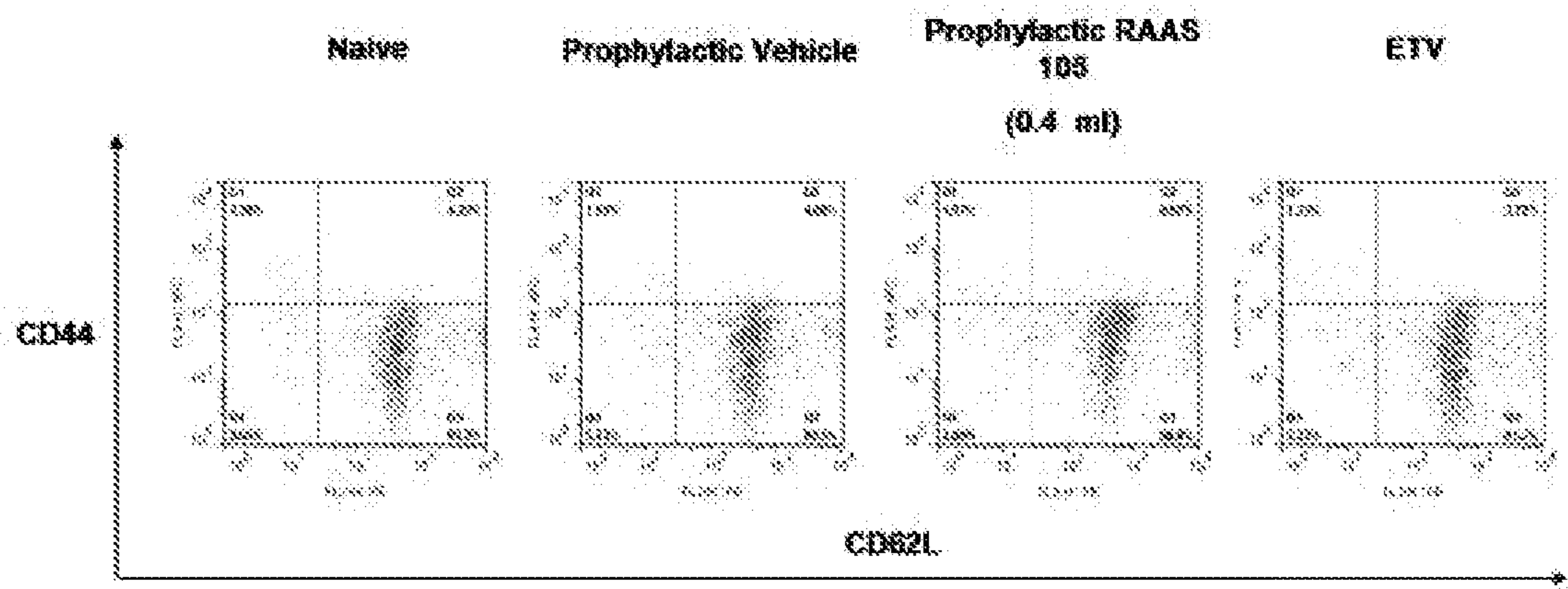


**Figure 66. T cell subsets percents in lymph nodes.** Total CD8<sup>+</sup> T cells were gated and T cell subsets were determined.

Figure 67

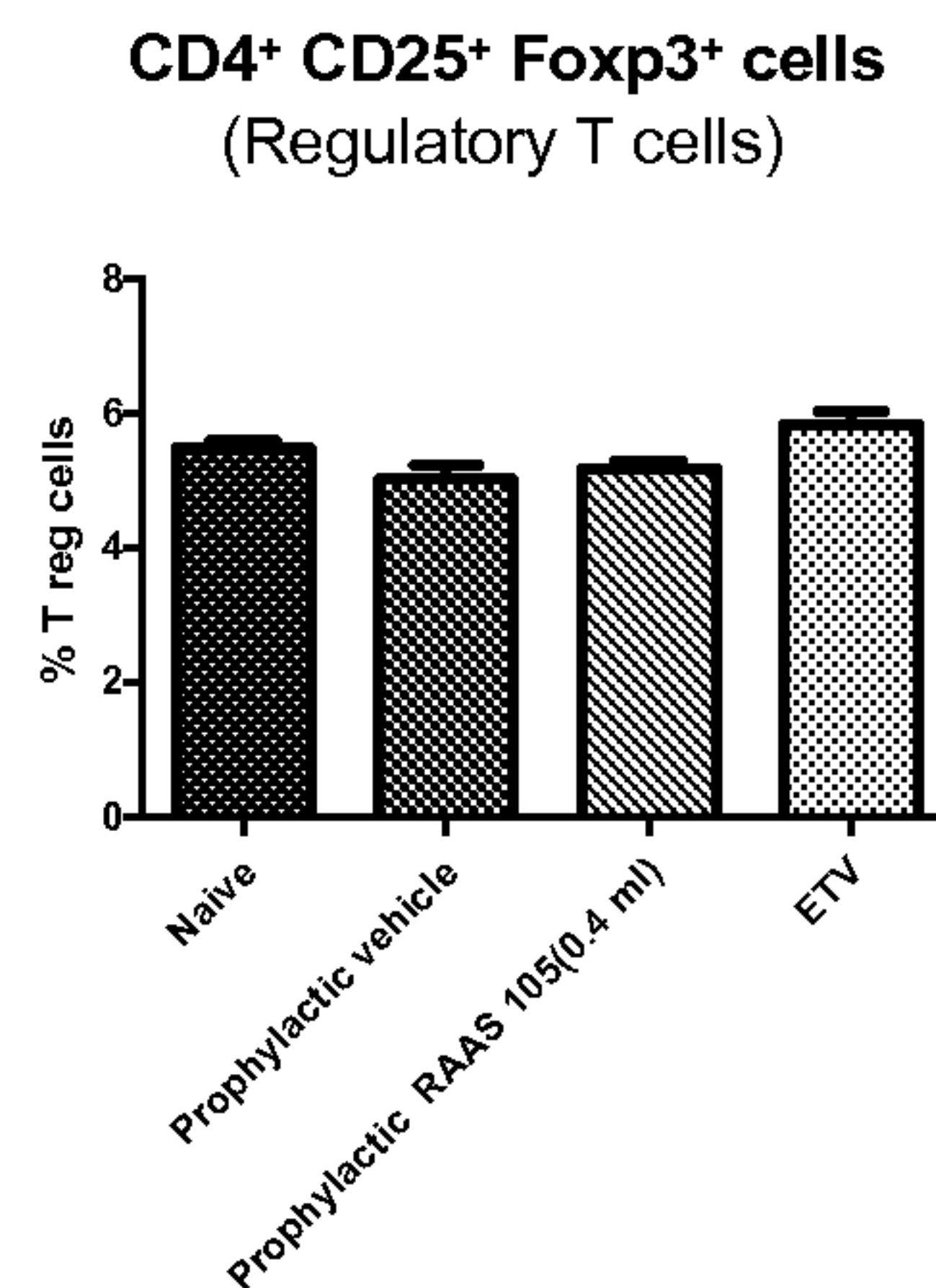


**Figure 67. Percents of Foxp3<sup>+</sup> regulatory T cells in lymph nodes.** Foxp3<sup>+</sup> regulatory T cells were analyzed by intracellular staining. There were no significant alterations after compound treatment. (by *t* test)

Figure 68

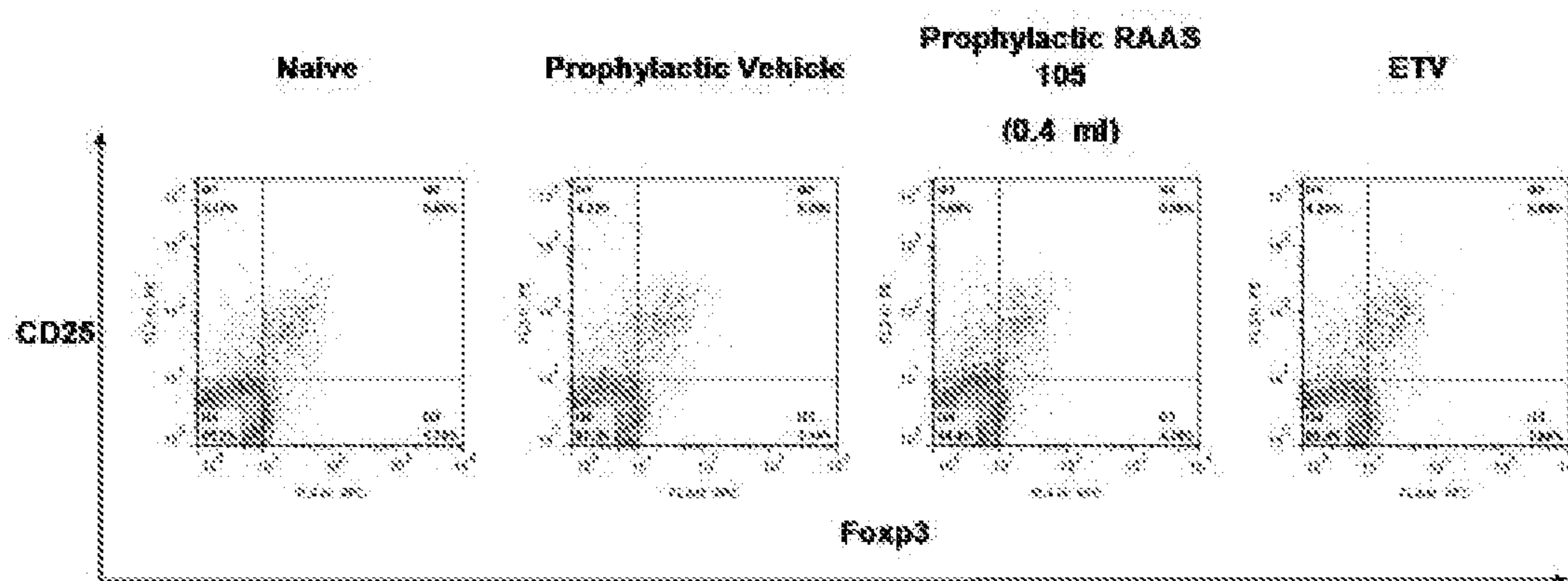


**Figure 68. Percents of regulatory T cells in lymph nodes.** Total CD4<sup>+</sup> T cells were gated.

Figure 69

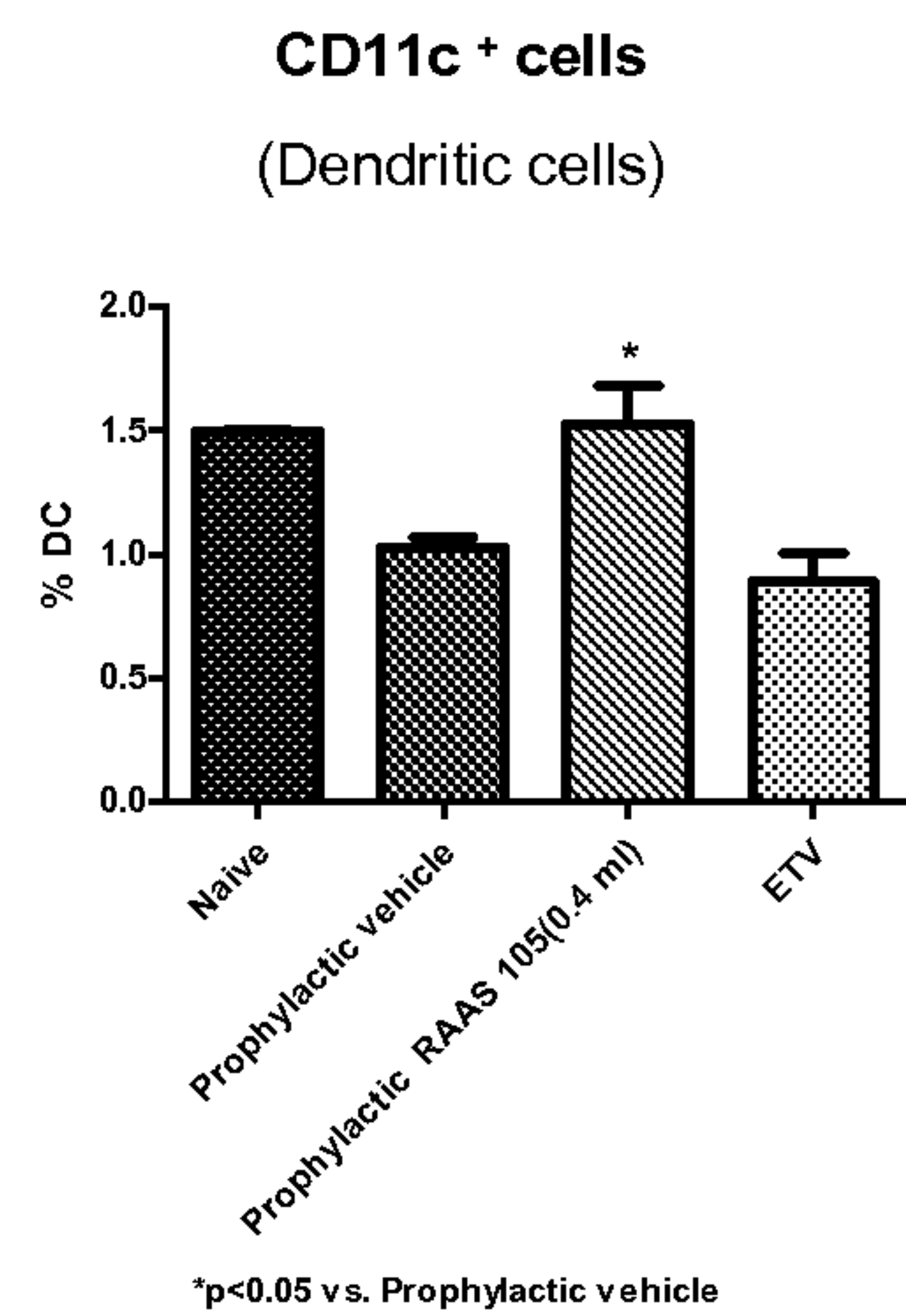


**Figure 69. Percents of DCs in lymph nodes.** Total live cells were gated. After the treatment, percents of DCs increased significantly (by t test).

Figure 70

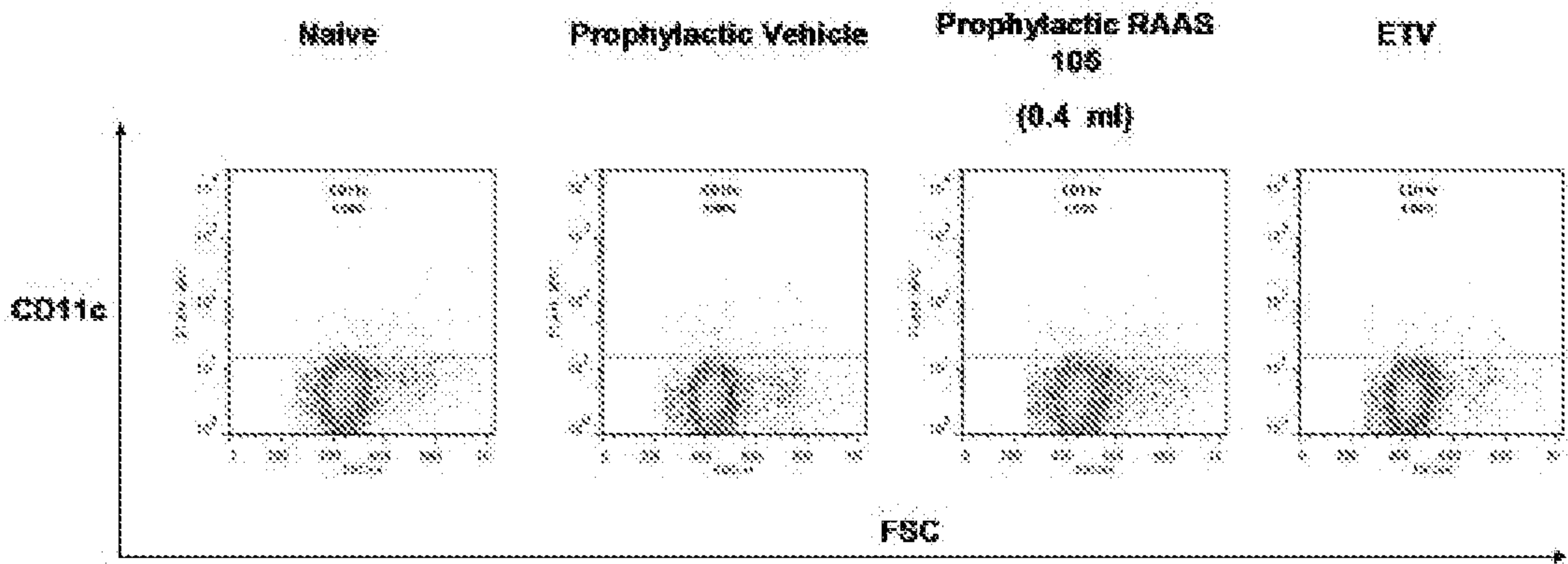


**Figure 70. Percents of DCs in lymph nodes.** Total live cells were gated.

Figure 71

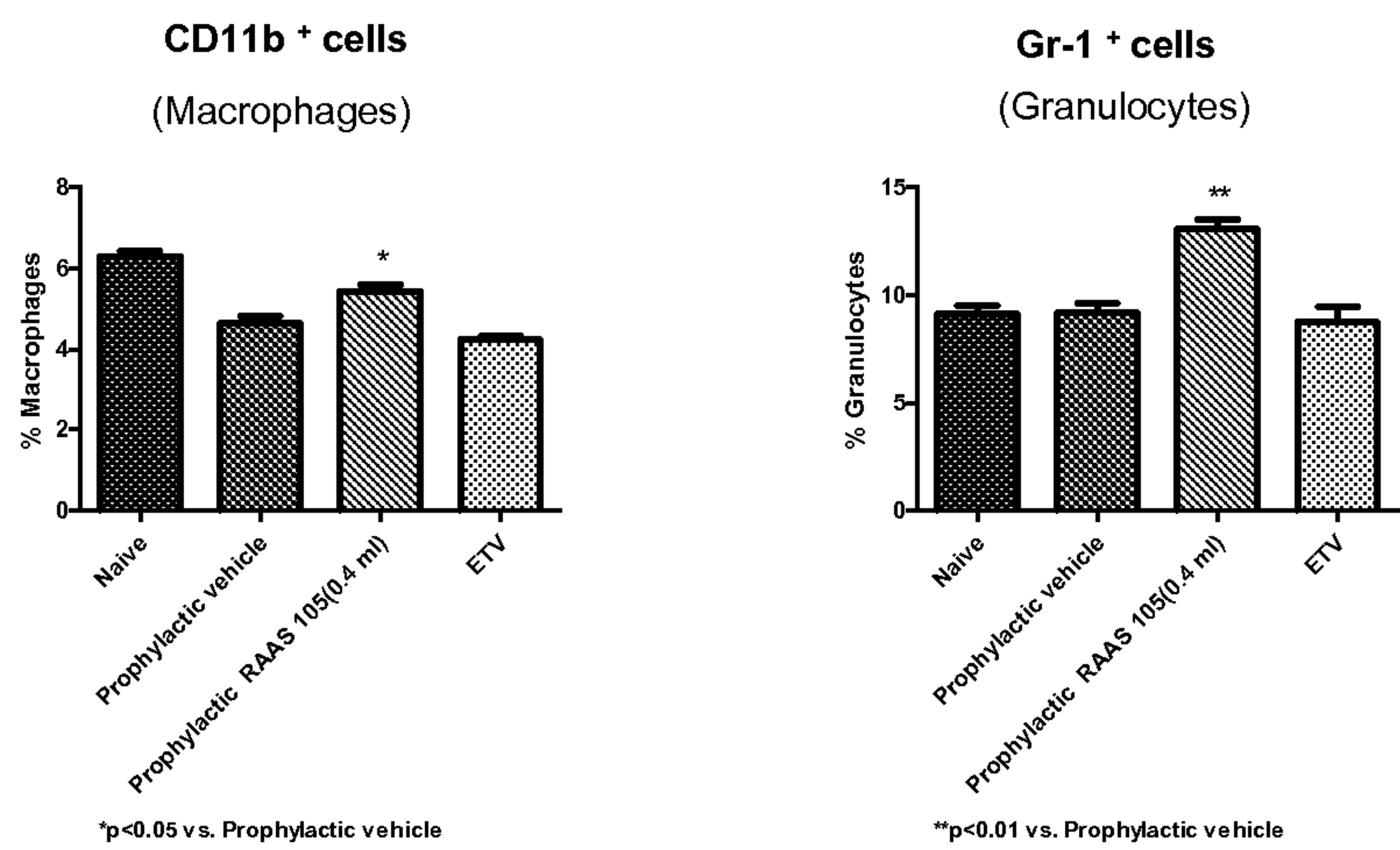


**Figure 71. Percents of Macrophages and Granulocytes in lymph nodes.** Total live cells were gated. After therapeutic treated by RAAS 105, percents of macrophages and granulocytes significantly increased (by *t* test).

Figure 72

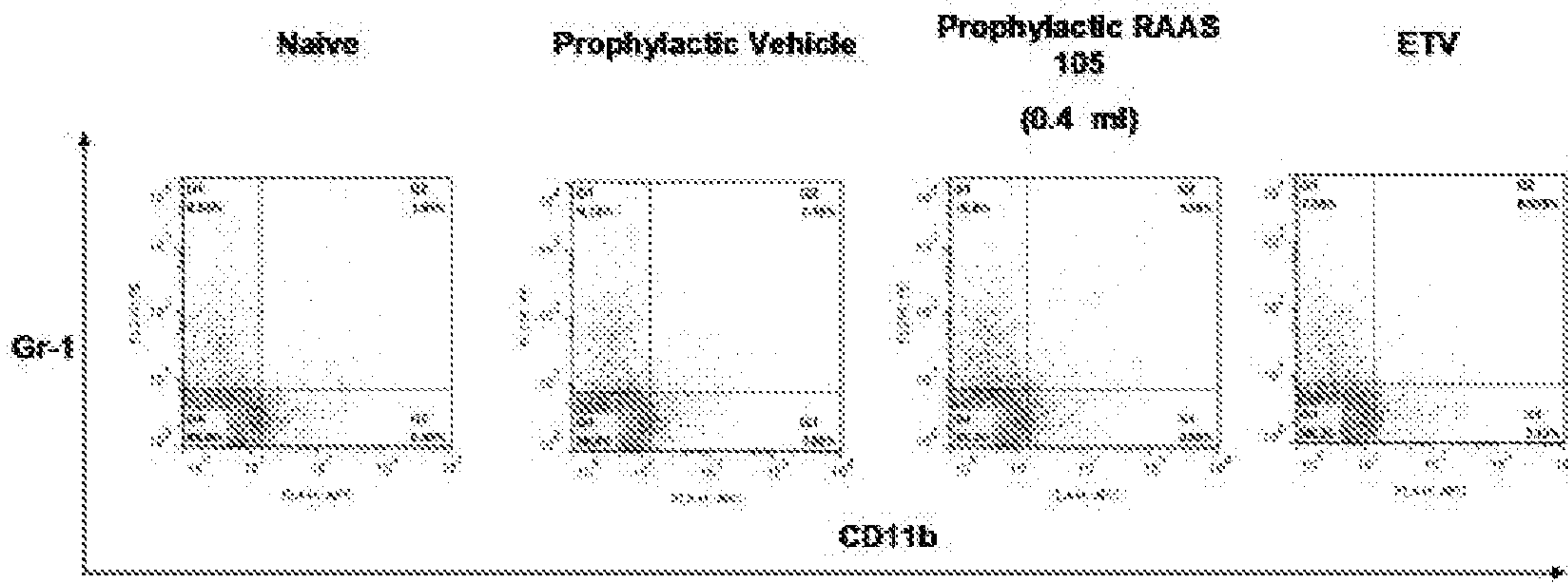


**Figure 72. Percents of Macrophages/Granulocytes in lymph nodes.** Total live cells were gated.

Figure 73

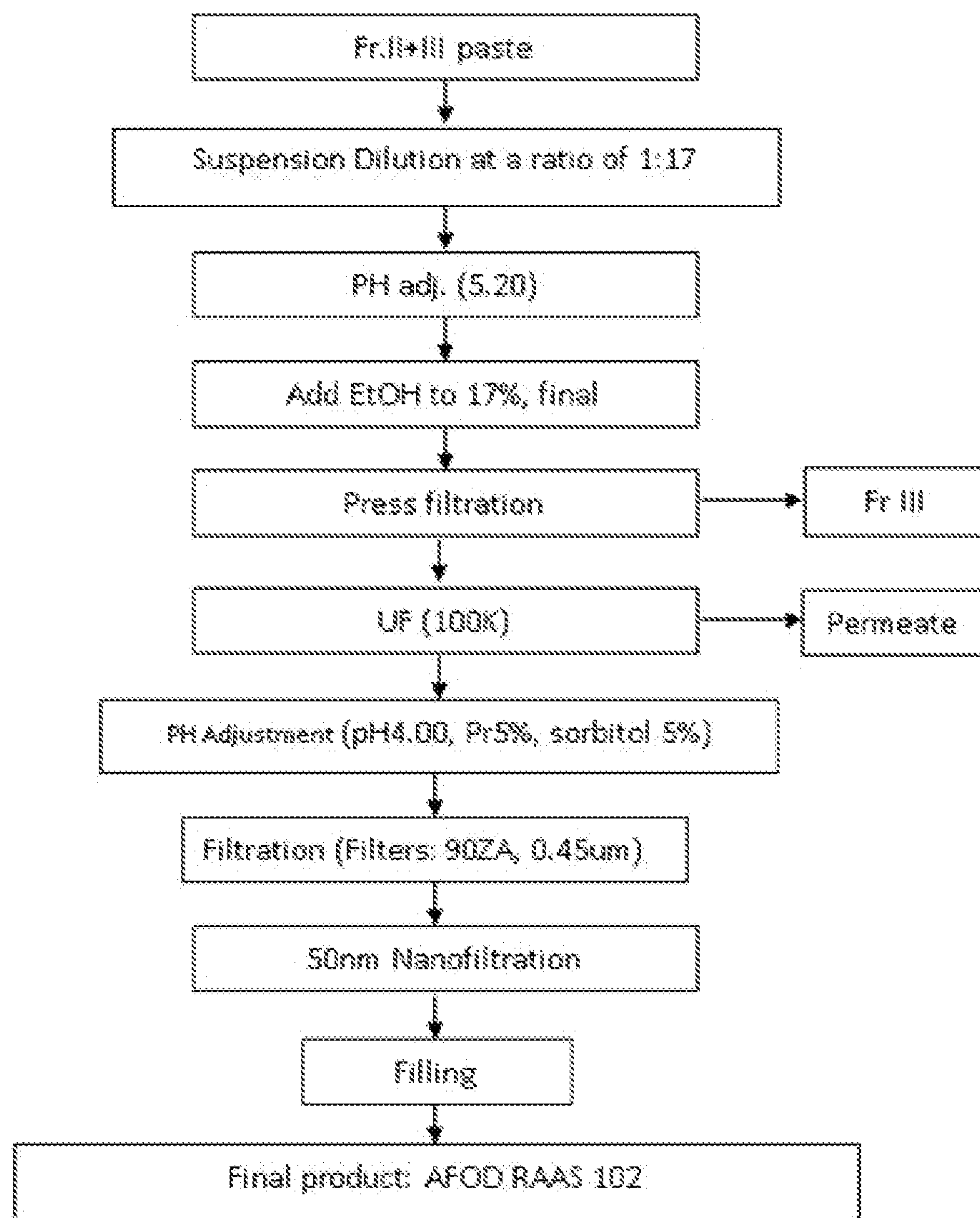


Figure 74

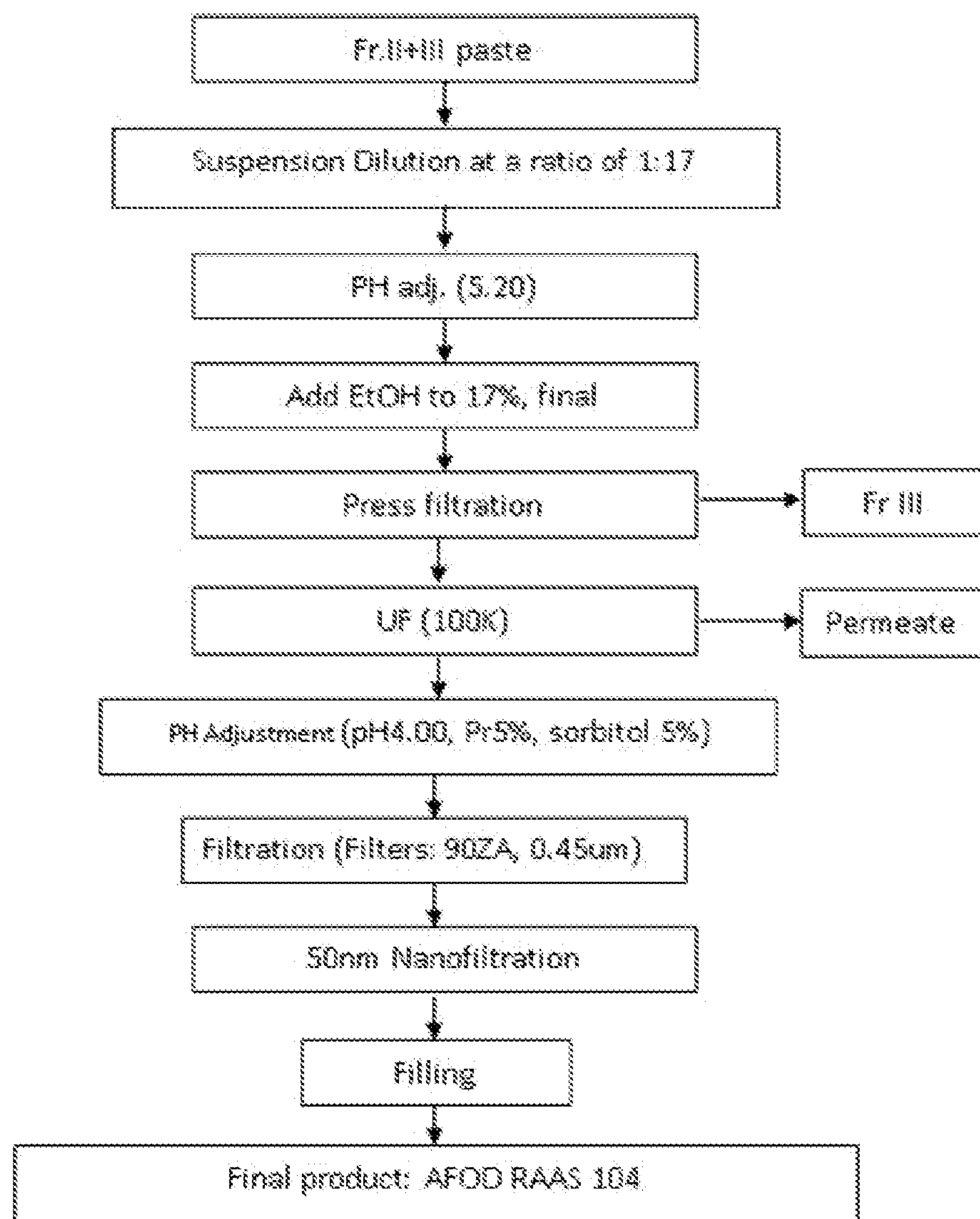


Figure 75

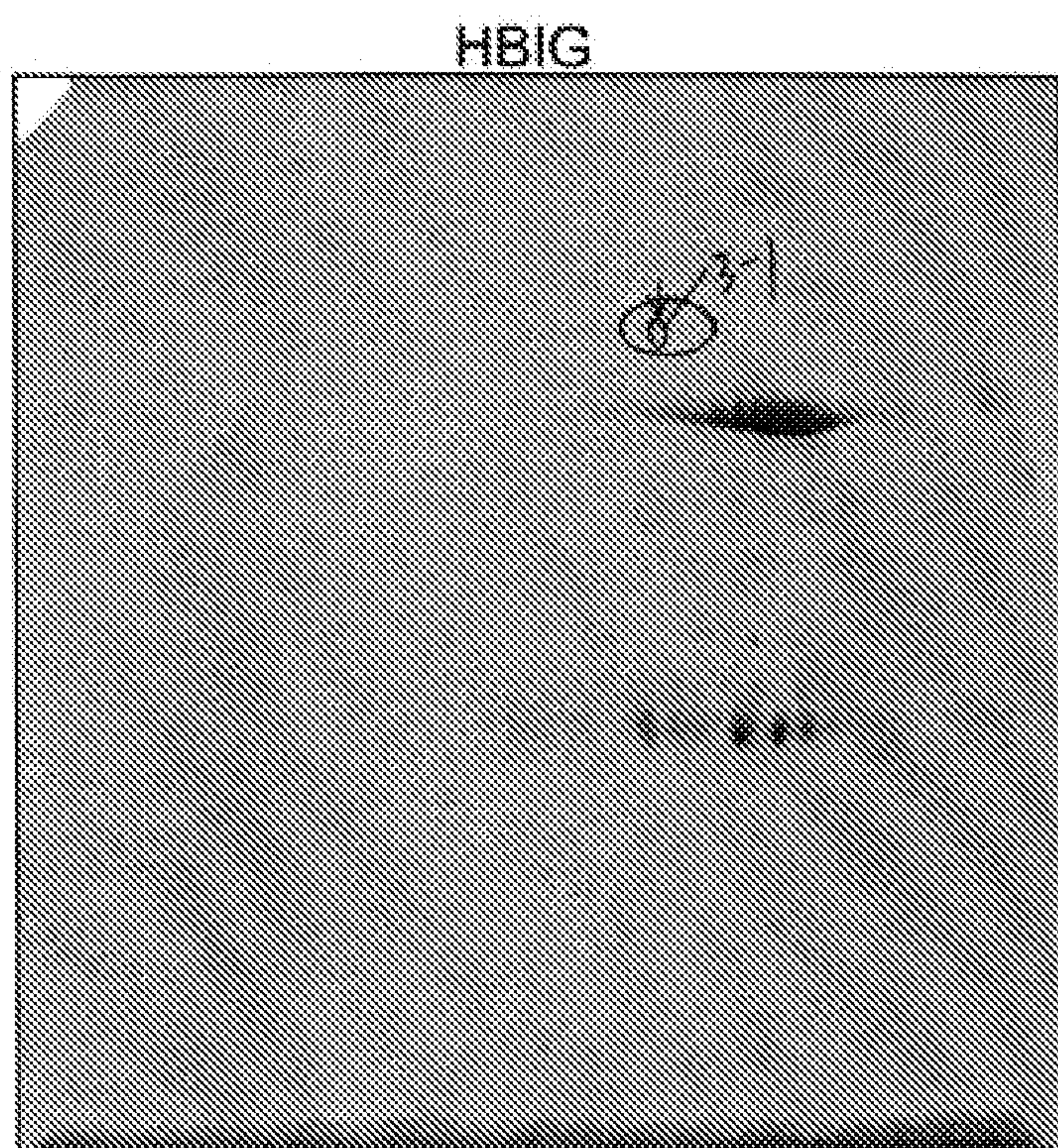


Figure 76

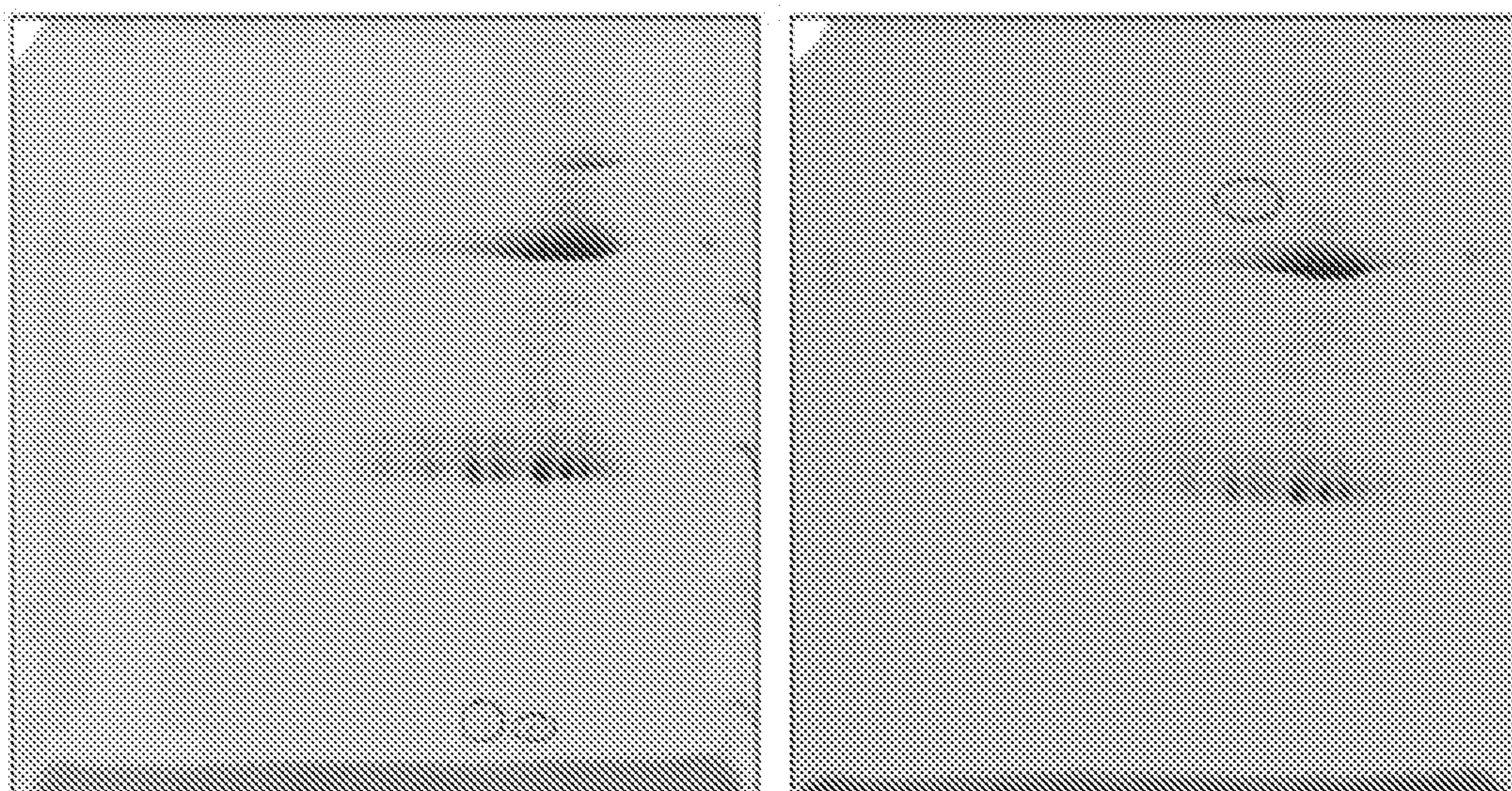


Figure 77

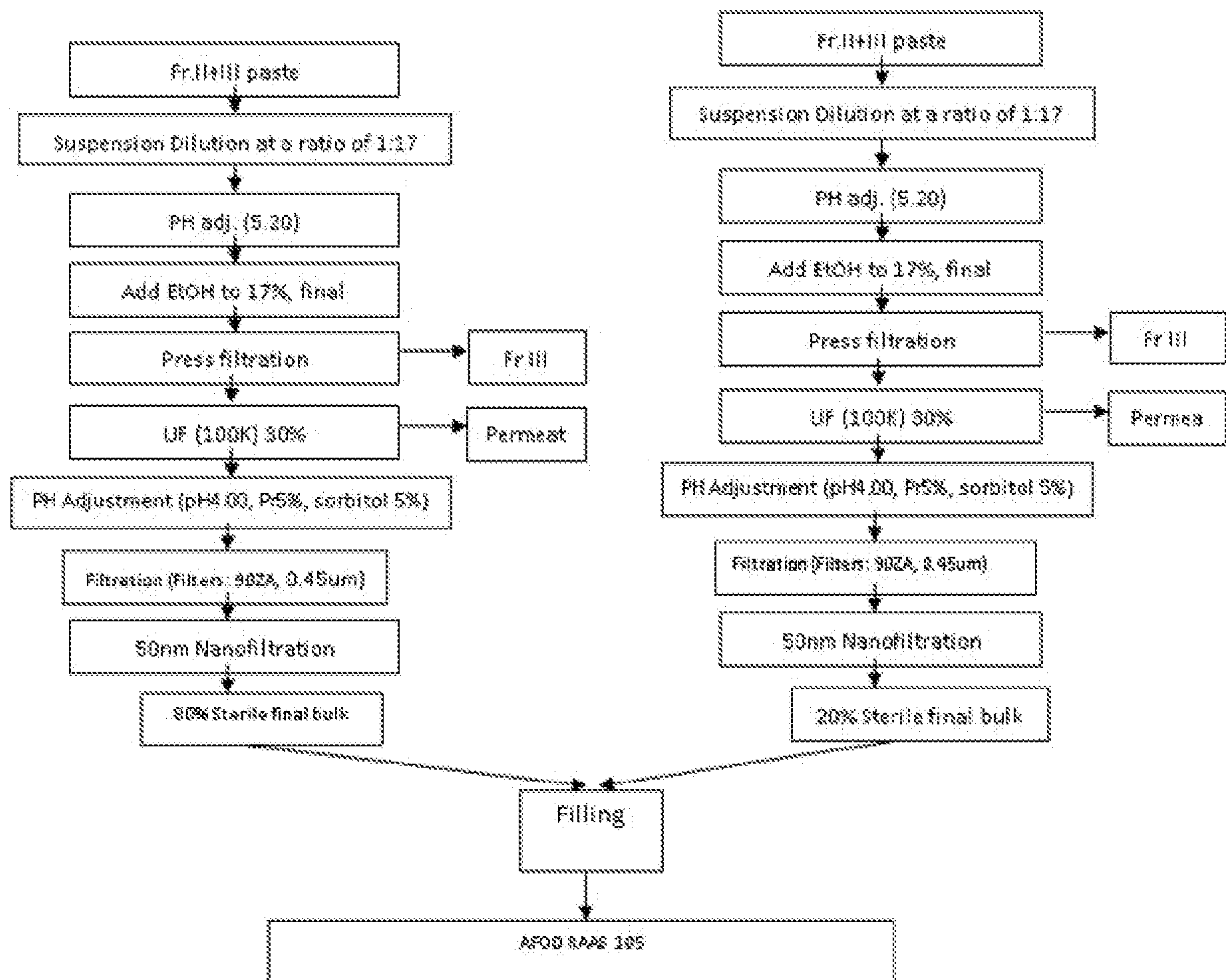
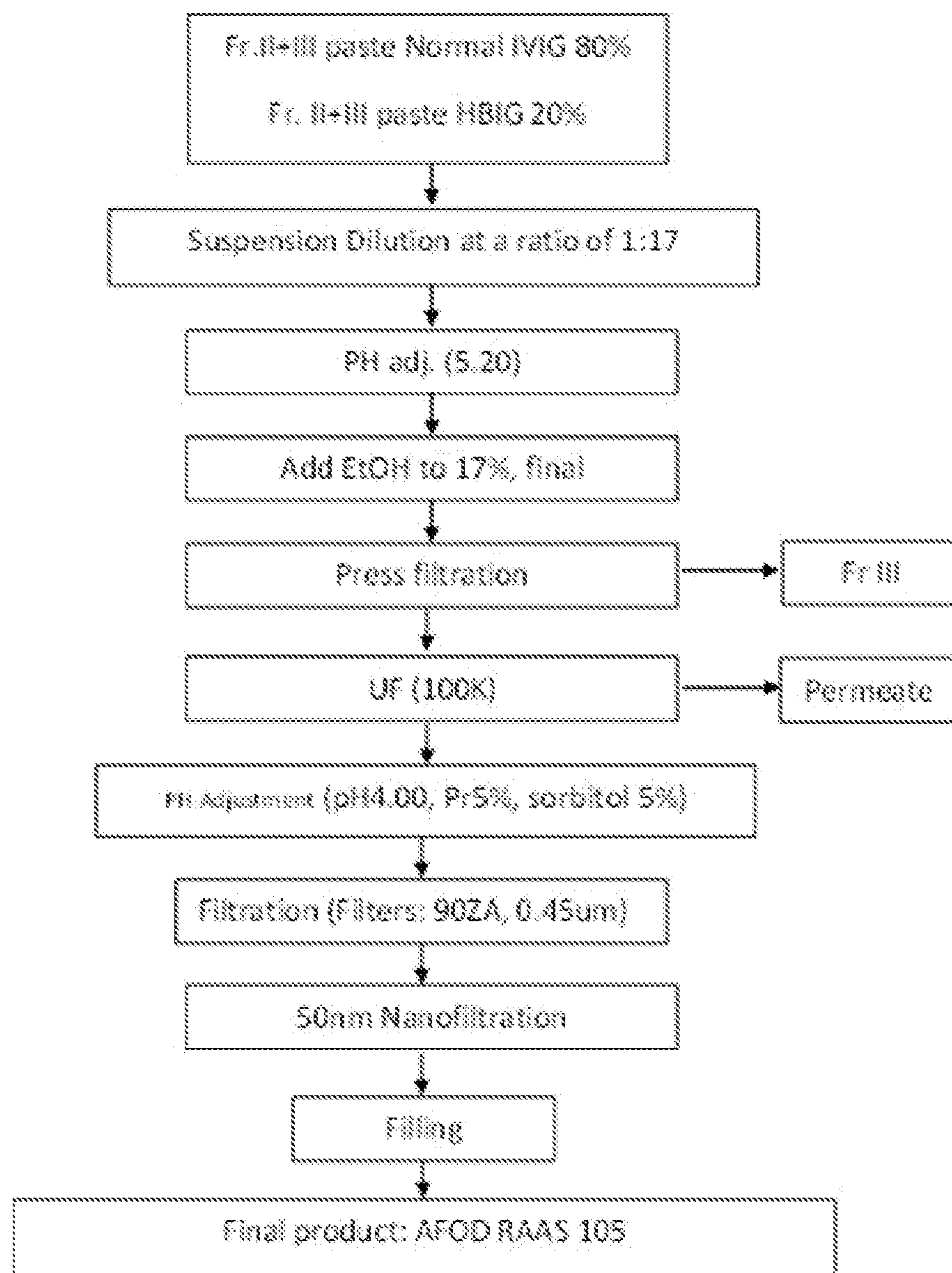


Figure 78



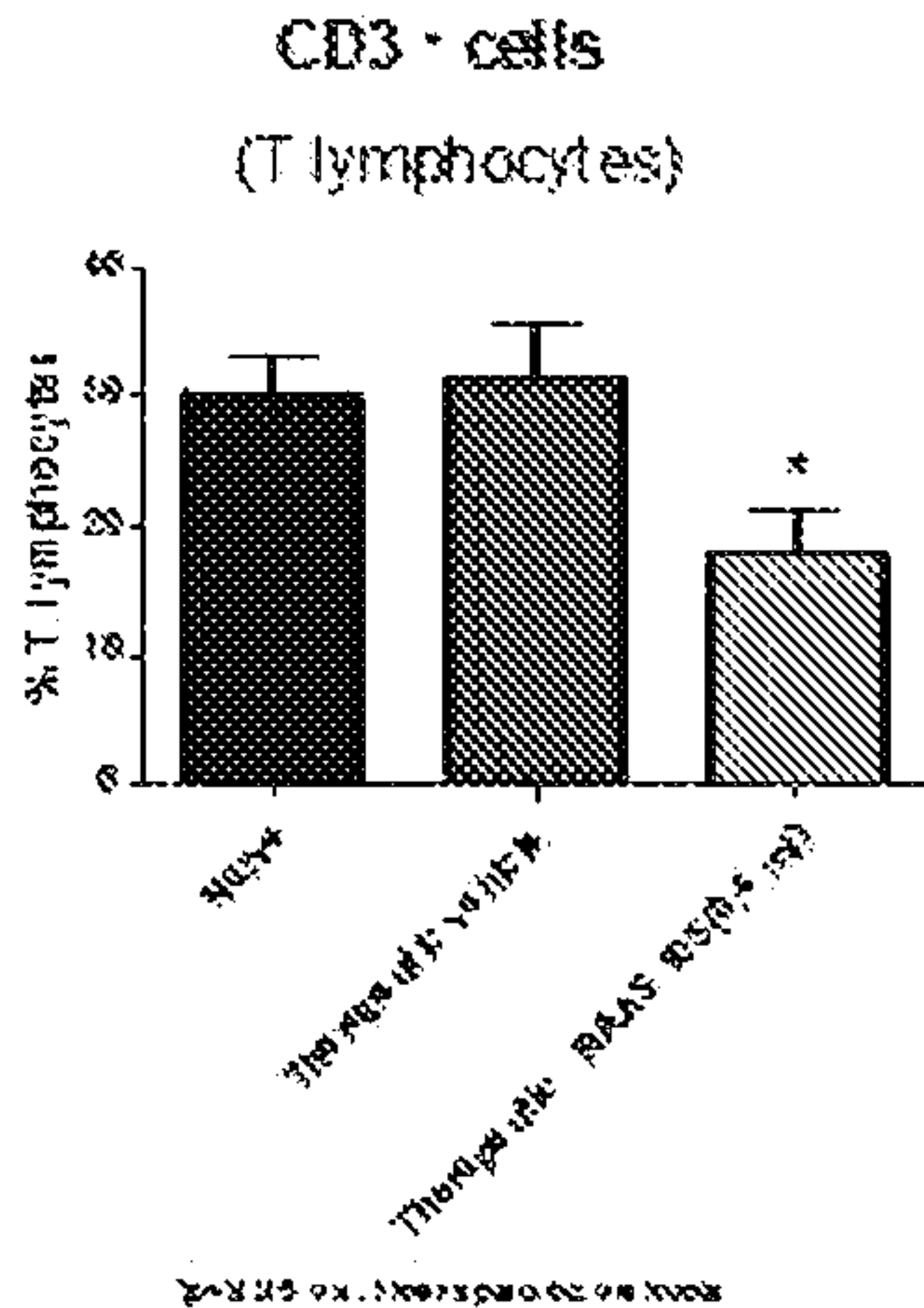


Figure 1

