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(54) Titre : TRAITEMENT DE MALADIES INFLAMMATOIRES AVEC DES PEPTIDES ET COMPOSITIONS
PHARMACEUTIQUES
(54) Title: TREATMENT OF INFLAMMATORY DISEASES WITH PEPTIDES AND PHARMACEUTICAL COMPOSITIONS

(57) Abrégé/Abstract:

Disclosed are methods of treating inflammatory diseases with peptides and pharmaceutical compositions using peptides.

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Abstract:

Disclosed are methods of treating inflammatory diseases with peptides and pharmaceutical compositions using peptides.

PATENT APPLICATION

**Treatment of Inflammatory Diseases with Peptides and
Pharmaceutical Compositions****Cross-Reference to a Related Application**

5 This application claims the benefit of U.S. Provisional Application No. 62/985,603, filed on March 5, 2020, which application is hereby incorporated by reference in its entirety.

Technical Field

10 The present invention relates to treating inflammatory diseases with peptides and pharmaceutical compositions.

Background

15 Inflammation is a protective mechanism in mammals from invading pathogens. However uncontrolled inflammation can cause tissue damage and is the cause of many diseases. Inflammatory diseases, either chronic or acute in nature, afflict many patients every day and present an important problem in the health care industry. Diseases and disorders which have significant inflammatory components include skin disorders, bowel disorders, certain degenerative neurological disorders, arthritis, and autoimmune diseases. For some patients, dietary or environmental factors may trigger an autoimmune or inflammatory response. In other patients, 20 genetic factors can play a key part in disease. In many inflammatory conditions, pro-inflammatory cytokines, particularly IL-1 β , and IL-6, play an important role in the pathogenesis of various inflammation-related diseases.

25 Interleukin-6 (IL-6) is a major pro-inflammatory cytokine and consists of 212 amino acids with two N-linked glycosylation sites. The IL-6 glycoprotein has a molecular weight of about 26 kDa. IL-6 signaling is mediated by the binding of IL-6 to either soluble or surface bound IL-6 receptor chain (IL-6R), enabling interaction of the complex with the cell surface transmembrane gp130 subunit. The interaction mediates intracellular signaling and is responsible for the proliferation and differentiation of immune cells.

30 Interleukin-1 beta (IL-1 β) is a pro-inflammatory cytokine that is produced as a precursor by activated macrophages. The molecular weight of the proteolytically processed IL-1 β is 17.5 kDa. Upon proteolytic cleavage, signal transduction is

initiated by binding of active IL-1 β to IL-1 receptor type I (IL-1R1), which in turn associates with the transmembrane IL-1 receptor accessory protein (IL-1RAP). The formed complex triggers signal transduction. IL-1 β is key mediator in the inflammatory response and the cytokine affects a number of cellular activities such as cell proliferation, differentiation, and apoptosis.

New therapies for reducing inflammation are needed.

Summary of Invention

In one aspect, provided herein are methods of preventing or treating an IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine mediated disease or disorder in a subject, comprising administering to the subject a compound disclosed herein.

In a further aspect, provided are methods of reducing production of IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine in cells of a subject, comprising administering to the subject a compound disclosed herein.

In yet another aspect, provided are methods of reducing NF- κ B transcription activity in cells of a subject, comprising administering to the subject a compound disclosed herein.

In another aspect, provided are methods of preventing or treating Keratoconjunctivitis sicca (Dry Eye) in a subject, comprising administering to the subject a compound disclosed herein.

In yet another aspect, provided are methods of preventing or treating Dry Eye Disease (DED) in a subject, comprising administering to the subject a compound disclosed herein.

Brief Description of the Drawings

Figure 1A-1D are diagrams showing attenuation of IL-6 release of poly I:C stimulated primary human corneal epithelial cells by test compounds in a dose dependent manner; Compounds tested: YDE-093, YDE-096, YDE-100, YDE-101, YDE-102, YDE-103, YDE-104, YDE-105, YDE-106, and YDE-107.

Figure 2A – 2BF are diagrams showing an effect on cell proliferation of primary corneal epithelial cells after 48hrs and 72hrs with the following test

compounds: YDE-012, YDE-019, YDE-038, YDE-044, YDE-045, YDE-047, YDE-048, YDE-049, YDE-050, YDE-051, YDE-052, YDE-053, YDE-054, YDE-055, YDE-056, YDE-057, YDE-058, YDE-059, YDE-060, YDE-061, YDE-062, YDE-063, YDE-064, YDE-065, YDE-066, YDE-067, YDE-072, YDE-073, YDE-074, YDE-075, YDE-076, YDE-077, YDE-078, YDE-079, YDE-080, YDE-081, YDE-082, YDE-083, YDE-084, YDE-085, YDE-086, YDE-087, Diquas, and hEGF.

Figure 3 is a diagram showing the effect of YDE-053, YDE-060, or YDE-065 on the IL-1beta, IL-6, IL-8, MIP-1 alpha, MIP-1 beta, RANTES, and TNF-alpha release of poly I:C stimulated primary human corneal epithelial cells.

Figure 4 is a diagram showing the effect of YDE-053 on NF-κB (p65) transcription activity of poly I:C stimulated primary human corneal cells.

Figure 5 is a diagram representing the effect of test compounds on IL-6 release of poly I:C stimulated primary human corneal epithelial cells; Compounds tested: YDE-053, YDE-048, YDE-056, YDE-057, YDE-058, YDE-067, YDE-079, YDE-011, YDE-093, YDE-096, YDE-053, and YDE-043.

Figure 6 is a diagram showing the effect of various stimulants on the level of IL-6.

Figure 7 is a diagram showing the effect of Xiidra® on the level of IL-6 induced by various stimulants.

Figure 8 is a diagram showing the effect of YDE-011 on the level of IL-6 induced by various stimulants.

Figure 9 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-2 induced by LPS.

Figure 10 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-6 induced by LPS.

Figure 11 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-8 induced by LPS.

Figure 12 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-10 induced by LPS.

Figure 13 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of TNF- α induced by LPS.

Figure 14 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of MMP-3 induced by LPS.

Figure 15 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL2/MCP-1 induced by LPS.

Figure 16 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL3/MIP-1 α induced by LPS.

5 **Figure 17** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL4/MIP-1 β induced by LPS.

Figure 18 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-1 α /IL-1F1 induced by LPS.

10 **Figure 19** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-1 β /IL-1F2 induced by LPS.

Figure 20 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of TIMP-1 induced by LPS.

Figure 21 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of Leptin induced by LPS.

15 **Figure 22** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of MMP-9 induced by LPS.

Figure 23 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-10 induced by LPS.

20 **Figure 24** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-8 induced by LPS.

Figure 25 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-6 induced by LPS.

Figure 26 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of TNF- α induced by LPS.

25 **Figure 27** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL3/MIP-1 α induced by LPS.

Figure 28 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL4/MIP-1 β induced by LPS.

30 **Figure 29** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL5/RANTES induced by LPS.

Figure 30 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IFN- γ induced by LPS.

Figure 31 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL2/MCP-1 induced by LPS.

Figure 32 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of Fas Ligand induced by LPS.

5 **Figure 33** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of CCL20/MIP-3 α induced by LPS.

Figure 34 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-1 α induced by LPS.

10 **Figure 35** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-1 β /IL-1F2 induced by LPS.

Figure 36 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of TIMP-1 induced by LPS.

Figure 37 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of GM-CSF induced by LPS.

15 **Figure 38** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-2 induced by LPS.

Figure 39 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-17A induced by LPS.

20 **Figure 40** is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of IL-4 induced by LPS.

Figure 41 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of VEGF-A induced by LPS.

Figure 42 is a diagram showing the effect of YY-101, YDE-011, and YDE-043 on the level of MMP-9 induced by LPS.

25 **Figure 43** is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of Eotaxin & Gro- α _KC in rat tear.

Figure 44 is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of IL-17A & IL-1 β in rat tear.

30 **Figure 45** is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of IL-21 & IL-4 in rat tear.

Figure 46 is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of MCP-1 & MCP-3 in rat tear.

Figure 47 is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of sVCAM-1 & TNF- α in rat tear.

Figure 48 is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of IL-12p70 & VEGF-A in rat tear.

5 **Figure 49** is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of IL-1 α & IP-10 in rat tear.

Figure 50 is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of bNGF & Leptin in rat tear.

10 **Figure 51** is a diagram showing the effect of YY-101, YDE-011, YDE-043, YDE-048, and YDE-060 on the level of RANTES in rat tear.

Figure 52 is a diagram showing the effect of YDE-048 and YDE-043 on the level of Gro- α KC & IL-1 α in rat goblet cell.

Figure 53 is a diagram showing the effect of YDE-048 and YDE-043 on the level of IL-1 β & Leptin in rat goblet cell.

15 **Figure 54** is a diagram showing the effect of YDE-048 and YDE-043 on the level of IP-10 & VEGF-A in rat goblet cell.

Figure 55 is a diagram showing the effect of YDE-048 and YDE-043 on the level of Eotaxin & IL-17A in rat goblet cell.

20 **Figure 56** is a diagram showing the effect of YDE-048 and YDE-043 on the level of MCP-1 & MCP-3 in rat goblet cell.

Figure 57 is a diagram showing the effect of YDE-048 and YDE-043 on the level of RANTES & sVCAM-1 in rat goblet cell.

Figure 58 is a diagram showing the effect of YDE-048 and YDE-043 on the level of TGF- β & TNF- α in rat goblet cell.

25 **Figure 59** is a diagram showing the effect of YDE-048 and YDE-043 on the level of IL-12p70, IL-21, bNGF in rat goblet cell.

Figure 60 is a diagram showing the effect of YDE-048 and YDE-043 on the level of IL-4 in rat goblet cell.

30 **Figure 61** is a diagram showing the effect of YDE-048 and YDE-043 on the level of IL-6 in rat goblet cell.

Figure 62 shows an experimental schematic timeline of Mouse IBD Model in Example 12.

Figure 63 shows body weight & BW change over time, disease activity index.

a : found dead (G4; n=3); b : animals sacrificed moribund (G2; n=3, G3; n=1, G4; n=1, G5; n=1); a : found dead (G4; n=3); b : animals sacrificed moribund (G2; n=3, G3; n=1, G4; n=1, G5; n=1).

5 **Figure 64** shows clinical scores (individual scores of DAI). a: found dead (G4; n=3); b : animals sacrificed moribund (G2; n=3, G3; n=1, G4; n=1, G5; n=1); All values were presented as mean $\pm$ standard error (SEM); All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis; * : 0.05>p, ** : 0.01>p, *** : 0.001>p ; G2 vs G3, G4, G5.

10 **Figure 65** shows CRP Levels (C-Reactive Protein) from Plasma. G1; n=8, G2; n=8, G3; n=8, G4; n=5, G5; n=8. Statistical analysis. All values were presented as mean $\pm$ standard error (SEM). All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis. * : 0.05>p, ** : 0.01>p, *** : 0.001>p; G2 vs G3, G4, G5. # : 0.05>p, ## : 0.01>p, ### : 0.001>p; G1 vs G2, G3, G4, G5

15 **Figure 66** shows study design of Mouse CIA-induced Rheumatoid Arthritis Model.

Figure 67 shows Body weight & Hind Paw Thickness (Inflammation).

Figure 68 shows overall clinical symptom & score. Clinical score: 0 – no change; 1 – swelling and erythema of the digit; 2 – mild swelling and erythema of the limb; 3 – gross swelling and erythema of the digit; 4 – gross deformity and inability to use the limb.

Figure 69 shows a study scheme & group information of OVX induced Osteoporosis disease model in C57bL6 mouse.

25 **Figure 70** shows Body weight and Uterus Weight & Gross Observation. G1; n=7, G2; n=7, G3; n=7, G4; n=7. Statistical analysis: All values were presented as mean $\pm$ standard error (SEM). All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis. * : 0.05>p, ** : 0.01>p, *** : 0.001>p; G1 vs G2, G3, G4. # : 0.05>p, ## : 0.01>p, ### : 0.001>p; G2 vs G3, G4.

30 **Figure 71** shows results of Lumbar Vertebrae Bone Strength Test. 0.75kgf/1cm; 0.75 * 9.8 N * x cm = Force (N*cm). Top-right image shows device used for compress test. Middle-right image shows total weight. Bottom-right image shows sample before test.

Figure 72 shows Micro CT Parameters.

Figure 73 shows results of Micro CT: Trabecular Area Analysis. BMD : Bone Mineral Density; Tb.N : Trabecular Number; Tb.Th : Trabecular Thickness; Tb.Sp : Trabecular Separation; Conn.D : Connectivity density. TV : Total volume; BV : Trabecular Bone Volume; BS : Bone Separation; BV/TV : Bone Volume/Total Volume; BS/TV : Bone Separation/Total Volume; BS/BV : Bone Separation/Bone Volume. G1; n=7, G2; n=7, G3; n=7, G4; n=7. Statistical analysis: All values were presented as mean $\pm$ standard error (SEM). All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis. * : 0.05>p, ** : 0.01>p, *** : 0.001>p; G1 vs G2, G3, G4. # : 0.05>p, ## : 0.01>p, ### : 0.001>p; G2 vs G3, G4.

Figure 74 shows results of Micro CT: Cortical Area Analysis. BMD : Bone Mineral Density. BV : Cortical Bone Volume. Tt.Ar : Total cross-sectional area inside the periosteal envelope. Ct.Ar : Cortical bone area. Ma.Ar : Medullary (or marrow) area. Ct.Ar/Tt.Ar : Cortical area fraction. Ct.Th : Average cortical thickness. Ps.Pm : Periosteal perimeter. Ec.Pm : Endocortical perimeter. G1; n=7, G2; n=7, G3; n=7, G4; n=7. Statistical analysis. All values were presented as mean $\pm$ standard error (SEM). All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis. * : 0.05>p, ** : 0.01>p, *** : 0.001>p; G1 vs G2, G3, G4. # : 0.05>p, ## : 0.01>p, ### : 0.001>p; G2 vs G3, G4.

Figure 75 shows Micro CT: Femur 2D Images.

Figure 76 shows Micro CT: Trabecular 3D Images.

Figure 77 shows exemplary micrographs of inflammation and oxidative markers.

Figure 78 shows an exemplary graph of TNF- α measurement. Statistical analysis: All values were presented as mean $\pm$ standard error (SEM). All values were statistically analyzed by one-way ANOVA with LSD post-hoc analysis. * : 0.05>p, ** : 0.01>p, *** : 0.001>p ; G1 vs All group. # : 0.05>p, ## : 0.01>p, ### : 0.001>p ; G2 vs G3, G4, G5, G6.

Figure 79 shows exemplary nitrotyrosine histology stains.

Detailed Description of the Invention

Definitions

According to the convention used in the art, “ $\overset{\text{R}}{\text{---}}$ ” in the formulae herein is used to indicate that a moiety or substituent “R” is attached to a backbone structure.

“Alkyl” is a hydrocarbon having primary, secondary, tertiary, and/or quaternary carbon atoms, and encompasses straight, branched, and cyclic groups, or a combination thereof. For example, an alkyl group may have 1 to 20 carbon atoms (i.e., C₁-C₂₀ alkyl), 1 to 10 carbon atoms (i.e., C₁-C₁₀ alkyl), or 1 to 6 carbon atoms (i.e., C₁-C₆ alkyl). Examples of a suitable alkyl group include methyl (Me, -CH₃), ethyl (Et, -CH₂CH₃), 1-propyl (n-Pr, n-propyl, -CH₂CH₂CH₃), 2-propyl (i-Pr, i-propyl, -CH(CH₃)₂), 1-butyl (n-Bu, n-butyl, -CH₂CH₂CH₂CH₃), 2-methyl-1-propyl (i-Bu, i-butyl, -CH₂CH(CH₃)₂), 2-butyl (s-Bu, s-butyl, -CH(CH₃)CH₂CH₃), 2-methyl-2-propyl (t-Bu, t-butyl, -C(CH₃)₃), 1-pentyl (n-pentyl, -CH₂CH₂CH₂CH₂CH₃), 2-pentyl (-CH(CH₃)CH₂CH₂CH₃), 3-pentyl (-CH(CH₂CH₃)₂), 2-methyl-2-butyl (-C(CH₃)₂CH₂CH₃), 3-methyl-2-butyl (-CH(CH₃)CH(CH₃)₂), 3-methyl-1-butyl (-CH₂CH₂CH(CH₃)₂), 2-methyl-1-butyl (-CH₂CH(CH₃)CH₂CH₃), 1-hexyl (-CH₂CH₂CH₂CH₂CH₂CH₃), 2-hexyl (-CH(CH₃)CH₂CH₂CH₂CH₃), 3-hexyl (-CH(CH₂CH₃)(CH₂CH₂CH₃)), 2-methyl-2-pentyl (-C(CH₃)₂CH₂CH₂CH₃), 3-methyl-2-pentyl (-CH(CH₃)CH(CH₃)CH₂CH₃), 4-methyl-2-pentyl (-CH(CH₃)CH₂CH(CH₃)₂), 3-methyl-3-pentyl (-C(CH₃)(CH₂CH₃)₂), 2-methyl-3-pentyl (-CH(CH₂CH₃)CH(CH₃)₂), 2,3-dimethyl-2-butyl (-C(CH₃)₂CH(CH₃)₂), 3,3-dimethyl-2-butyl (-CH(CH₃)C(CH₃)₃), and octyl (-CH₂)₇CH₃), but it is not limited thereto.

“Alkoxy” refers to a group having the formula -O-alkyl, wherein the alkyl group as defined above is attached to the parent compound via an oxygen atom. The alkyl moiety of the alkoxy group may have, for example, 1 to 20 carbon atoms (i.e., C₁-C₂₀ alkoxy), 1 to 12 carbon atoms (i.e., C₁-C₁₂ alkoxy), 1 to 10 carbon atoms (i.e., C₁-C₁₀ alkoxy), or 1 to 6 carbon atoms (i.e., C₁-C₆ alkoxy). Examples of a suitable alkoxy group include methoxy (-O-CH₃ or -OMe), ethoxy (-OCH₂CH₃ or -OEt), and t-butoxy (-OC(CH₃)₃ or -O-tBu), but it is not limited thereto.

“Haloalkyl” is an alkyl group in which at least one of the hydrogen atoms of the alkyl group as defined above is replaced by a halogen atom. The alkyl moiety of the haloalkyl group may have 1 to 20 carbon atoms (i.e., C₁-C₂₀ haloalkyl), 1 to 12 carbon

atoms (i.e., C₁-C₁₂ haloalkyl), 1 to 10 carbon atoms (i.e., C₁-C₁₀ haloalkyl), or 1 to 6 carbon atoms (i.e., C₁-C₆ haloalkyl). Examples of a suitable haloalkyl group include -CF₃, -CHF₂, -CFH₂, and -CH₂CF₃, but it is not limited thereto.

“Alkenyl” is a hydrocarbon having primary, secondary, tertiary, and/or quaternary carbon atoms, and encompasses straight, branched, and cyclic groups, or a combination thereof, and having at least one unsaturated region, i.e., a carbon-carbon sp² double bond. For example, an alkenyl group may have 2 to 20 carbon atoms (i.e., C₂-C₂₀ alkenyl), 2 to 12 carbon atoms (i.e., C₂-C₁₂ alkenyl), 2 to 10 carbon atoms (i.e., C₂-C₁₀ alkenyl), or 2 to 6 carbon atoms (i.e., C₂-C₆ alkenyl). Examples of a suitable alkenyl group include vinyl (-CH=CH₂), allyl (-CH₂CH=CH₂), cyclopentenyl (-C₅H₇), and 5-hexenyl (-CH₂CH₂CH₂CH₂CH=CH₂), but it is not limited thereto.

“Alkynyl” is a hydrocarbon having primary, secondary, tertiary, and/or quaternary carbon atoms, and encompasses straight, branched, and cyclic groups, or a combination thereof, and having at least one carbon-carbon sp triple bond. For example, an alkynyl group may have 2 to 20 carbon atoms (i.e., C₂-C₂₀ alkynyl), 2 to 12 carbon atoms (i.e., C₂-C₁₂ alkynyl), 2 to 10 carbon atoms (i.e., C₂-C₁₀ alkynyl), or 2 to 6 carbon atoms (i.e., C₂-C₆ alkynyl). Examples of a suitable alkenyl group include acetylenic (-C≡CH) and propargyl (-CH₂C≡CH), but it is not limited thereto.

“Alkylene” refers to a saturated hydrocarbon group that may be branched, straight, or cyclic (or may have a combination of branched, straight, or cyclic moieties) and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkane. For example, an alkylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Examples of a typical alkylene group include 1,2-ethylene (-CH₂-CH₂-), but it is not limited thereto.

“Alkenylene” refers to an unsaturated hydrocarbon group that may be branched, straight, or cyclic (or may have a combination of branched, straight, or cyclic moieties) and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkene. For example, an alkenylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Examples of a typical alkenylene group include 1,2-ethenylene (-CH=CH-), but it is not limited thereto.

“Alkynylene” refers to an unsaturated hydrocarbon group that may be branched, straight, or cyclic (or may have a combination of branched, straight, or cyclic moieties) and has two valencies derived by a removal of two hydrogen atoms from the same carbon atom or two different carbon atoms of a parent alkyne. For example, an alkynylene group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 5 carbon atoms. Examples of a typical alkynylene radical include acetylenylene ($-\text{C}\equiv\text{C}-$), propargylene ($-\text{CH}_2\text{C}\equiv\text{C}-$), and 4-pentynylene ($-\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{C}-$), but it is not limited thereto.

“Aryl” refers to an aromatic hydrocarbon group. For example, an aryl group may have 6 to 20 carbon atoms, 6 to 14 carbon atoms, or 6 to 12 carbon atoms. Examples of a typical aryl group include a radical derived from benzene (e.g., phenyl), substituted benzene, substituted or unsubstituted naphthalene, substituted or unsubstituted anthracene, and the like, but it is not limited thereto.

“Arylalkyl” refers to an acyclic alkyl group in which one hydrogen atom bonded to a carbon atom, typically a terminal or other sp^3 carbon atom, is replaced by an aryl group. Examples of a typical arylalkyl group include benzyl, 2-phenylethan-1-yl, naphthylmethyl, 2-naphthylethan-1-yl, naphthobenzyl, 2-naphthophenylethan-1-yl, and the like (each of which may be substituted or unsubstituted), but it is not limited thereto. An arylalkyl group may have 7 to 20 carbon atoms. For example, the alkyl moiety thereof may have 1 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

“Arylalkenyl” refers to an acyclic alkenyl group in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or other sp^3 carbon atom, although an sp^2 carbon atom may also be used, is replaced by an aryl group. The aryl moiety of the arylalkenyl may be, for example, any aryl group described herein, and the alkenyl moiety of the arylalkenyl may comprise, for example, any of the alkenyl groups described herein. An arylalkenyl group may have 8 to 20 carbon atoms. For example, the alkenyl moiety thereof may have 2 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

“Arylalkynyl” refers to an acyclic alkynyl group in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or other sp^3 carbon atom, although an sp carbon atom may also be used, is replaced by an aryl group. The aryl moiety of the arylalkynyl may be, for example, any aryl group described herein, and

the alkynyl moiety of the arylalkynyl may comprise, for example, any of the alkynyl groups described herein. An arylalkynyl group may have 8 to 20 carbon atoms. For example, the alkynyl moiety thereof may have 2 to 6 carbon atoms, and the aryl moiety thereof may have 6 to 14 carbon atoms.

5 “Cycloalkyl” refers to a saturated monocycle or polycycle that comprises only carbon atoms in the ring. A cycloalkyl group may have 3 to 7 carbon atoms as a monocycle, 7 to 12 carbon atoms as a bicycle, and up to about 20 carbon atoms as a polycycle. A monocyclic cycloalkyl has 3 to 7 ring atoms, more typically 5 or 6 ring atoms. A bicyclic cycloalkyl may have 7 to 12 ring atoms and may be a fused ring
10 system, a spirocyclic ring system, or a bridged ring system. In exemplary cycloalkyl groups, the atoms may be arranged in a bicyclo[4,5], [5,5], [5,6], or [6,6] system. Non-limiting examples of a monocyclic cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl (each of which may be substituted or unsubstituted).

The term “substituted” with respect to alkyl, alkylene, aryl, arylalkyl,
15 heterocyclyl, and the like, for example, “substituted alkyl,” “substituted alkylene,” “substituted aryl,” “substituted arylalkyl,” “substituted heterocyclyl,” and “substituted carbocyclyl (e.g., substituted cycloalkyl),” means that at least one hydrogen atom of the alkyl, alkylene, aryl, arylalkyl, heterocyclyl, or carbocyclyl (e.g., cycloalkyl) is each independently replaced by a non-hydrogen substituent. Examples of the typical
20 substituent include halo, haloalkyl, oxo, -CN, -NO₂, =N-OH, -N₃, -R, -OR, -SR, -N(R)₂, -N(R)₃⁺, =NR, -NHC(=O)R, -C(=O)R, -C(=O)N(R)₂, -S(=O)₂R, -OS(=O)₂OR, -S(=O)₂OR, -S(=O)₂N(R)₂, -S(=O)R, -OP(=O)(OR)₂, -(alkylene)-C(=O)R, -C(=S)R, -C(=O)OR, -(alkylene)-C(=O)OR, -C(=S)OR, -C(=O)SR, -C(=S)SR, -(alkylene)-C(=O)N(R)₂, -C(=S)N(R)₂, and -C(-NR)N(R)₂, and R is independently H, alkyl, aryl,
25 arylalkyl, or heterocyclyl, but it is not limited thereto. The alkylene, alkenylene, and alkynylene groups may also be similarly substituted.

Those skilled in the art will understand that when a moiety such as “alkyl,” “aryl,” “heterocyclyl,” and the like is substituted with at least one substituent, they may optionally be referred to as a moiety of “alkylene,” “arylene,” “heterocyclylene,”
30 or the like (that is, at least one hydrogen atom of the parent “alkyl,” “aryl,” or “heterocyclyl” moiety is replaced by the substituent as described herein). If the moiety of “alkyl,” “aryl,” “heterocyclyl,” or the like is described herein as “substituted” or depicted in the drawings as substituted (or optionally substituted, for

example, the number of substituents is 0 or a positive number), the term “alkyl,” “aryl,” “heterocyclyl,” or the like should be understood to be interchangeable with “alkylene,” “arylene,” “heterocyclylene,” or the like.

Those skilled in the art will recognize that the substituents and other moieties of the compound of Formula I should be selected so as to provide a compound that is sufficiently stable as a pharmaceutically useful compound that can be formulated into an acceptably stable pharmaceutical composition. The compound of Formula I having such stability is to be understood to fall within the scope of the present invention.

“Heteroalkyl” refers to an alkyl group in which at least one carbon atom is replaced by a heteroatom such as O, N, or S. For example, if a carbon atom of the alkyl group attached to a parent molecule is replaced by a heteroatom (e.g., O, N, or S), the resulting heteroalkyl group may be an alkoxy group (e.g., -OCH₃), an amine group (e.g., -NHCH₃, -N(CH₃)₂, or the like), or a thioalkyl group (e.g., -SCH₃), respectively. If a non-terminal carbon atom of the alkyl group that is not attached to a parent molecule is replaced by a heteroatom (e.g., O, N, or S), the resulting heteroalkyl group may be an alkyl ether (e.g., -CH₂CH₂-O-CH₃ or the like), an alkylamine (e.g., -CH₂NHCH₃, -CH₂N(CH₃)₂, or the like), or a thioalkyl ether (e.g., -CH₂-S-CH₃), respectively. If the terminal carbon atom of the alkyl group is replaced by a heteroatom (for example, O, N, or S), the resulting heteroalkyl group may be a hydroxyalkyl group (e.g., -CH₂CH₂-OH), an aminoalkyl group (e.g., -CH₂NH₂), or an alkylthiol group (e.g., -CH₂CH₂-SH), respectively. For example, a heteroalkyl group may have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Preferably, a heteroalkyl group has from 2 to 20, 2 to 10, or 2 to 6 total atoms in the chain (i.e., carbon atoms plus heteroatoms combined). A C₁-C₆ heteroalkyl group refers to a heteroalkyl group having 1 to 6 carbon atoms.

The term “heterocycle” or “heterocyclyl” used herein includes those described in the documents such as Paquette, Leo A., Principles of Modern Heterocyclic Chemistry (W. A. Benjamin, New York, 1968), specifically Chapters 1, 3, 4, 6, 7, and 9; The Chemistry of Heterocyclic Compounds, A Series of Monographs (John Wiley & Sons, New York, from 1950 to the present), specifically Volumes 13, 14, 16, 19, and 28; and J. Am. Chem. Soc. (1960) 82:5566, but it is not limited thereto. In a specific embodiment of the present invention, “heterocycle” includes carbocycle as defined herein in which at least one (e.g., 1, 2, 3, or 4) carbon atom is replaced by a

heteroatom (e.g., O, N, or S). The term “heterocycle” or “heterocyclyl” includes saturated, partially unsaturated, and aromatic rings (i.e., a heteroaromatic ring). Substituted heterocycle, for example, includes a heterocyclic ring substituted with any of the substituents disclosed herein, inclusive of a carbonyl group.

5 Exemplary heterocycles include pyridyl, dihydropyridyl, tetrahydropyridyl(piperidyl), thiazolyl, tetrahydrothiophenyl, sulfur-oxidized tetrahydrothiophenyl, pyrimidinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, tetrazolyl, benzofuranyl, thianaphthenyl, indolyl, indolenyl, quinolinyl, isoquinolinyl, benzimidazolyl, piperidinyl, 4-piperidinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolinyl, 10 tetrahydrofuranlyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, octahydroisoquinolinyl, azocynyl, triazinyl, 6H-1,2,5-thiadiazinyl, 2H,6H-1,5,2-dithiazinyl, thianthrenyl, pyranyl, isobenzofuranyl, chromenyl, xanthenyl, phenoxatynyl, 2H-pyrrolyl, isothiazolyl, isoxazolyl, pyrazinyl, pyridazinyl, indolizynyl, isoindolyl, 3H-indolyl, 1H-indazolyl, purinyl, 4H- 15 quinolizinyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, phtheridinyl, 4aH-carbazolyl, carbazolyl, β -carbolinyl, phenanthridinyl, acridinyl, pyrimidinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, furazanyl, phenoxazinyl, isochromanyl, chromanyl, imidazolidinyl, imidazolynyl, pyrazolidinyl, pyrazolinyl, piperazinyl, indolynyl, isoindolynyl, quinuclidinyl, morpholynyl, oxazolidinyl, 20 benzotriazolyl, benzisoxazolyl, oxindolyl, and benzoxazolynyl (each of which may be substituted or unsubstituted), but it is not limited thereto.

As an example, a carbon-bonded heterocycle may be bonded at the 2, 3, 4, 5, or 6-position of pyrazine, at the 3, 4, 5, or 6-position of pyridazine, at the 2, 4, 5, or 6-position of pyrimidine, at the 2, 3, 5, or 6-position of pyrazine, at the 2, 3, 4, or 5- 25 position of furan, tetrahydrofuran, thiofuran, thiophene, pyrrole, or tetrahydropyrrole, at the 2, 4, or 5-position of oxazole, imidazole, or thiazole, at the 3, 4, or 5-position of isoxazole, pyrazole, or isothiazole, at the 2 or 3-position of aziridine, at the 2, 3, or 4-position of azetidine, at the 2, 3, 4, 5, 6, 7, or 8-position of quinoline, or at the 1, 3, 4, 5, 6, 7, or 8-position of isoquinoline, but it is not limited thereto. More typically, 30 examples of a carbon-bonded heterocycle include 2-pyridyl, 3-pyridyl, 4-pyridyl, 5-pyridyl, 6-pyridyl, 3-pyridazinyl, 4-pyridazinyl, 5-pyridazinyl, 6-pyridazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 2-pyrazinyl, 3-pyrazinyl, 5-

pyrazinyl, 6-pyrazinyl, 2-thiazolyl, 4-thiazolyl, and 5-thiazolyl (each of which may be substituted or unsubstituted).

As an example, a nitrogen-bonded heterocycle may be bonded at the 1-position of aziridine, azetidine, pyrrole, pyrrolidine, 2-pyrroline, 3-pyrroline, imidazole, 5 imidazolidine, 2-imidazoline, 3-imidazoline, pyrazole, pyrazoline, 2-pyrazoline, 3-pyrazoline, piperidine, piperazine, indole, indoline, or 1H-indazole, at the 2-position of isoindole or isoindoline, at the 4-position of morpholine, and at the 9-position of carbazole or β -carboline (each of which may be substituted or unsubstituted), but it is not limited thereto. More typically, examples of a nitrogen-bonded heterocycle 10 include 1-aziridinyl, 1-azetidyl, 1-pyrrolyl, 1-imidazolyl, 1-pyrazolyl, and 1-piperidinyl (each of which may be substituted or unsubstituted).

“Heterocyclalkyl” refers to an acyclic alkyl radical in which one hydrogen atom bonded to a carbon atom, typically a terminal or sp^3 carbon atom, is replaced by a heterocycl radical (i.e., a heterocycl-alkylene moiety). Examples of a typical 15 heterocyclalkyl group include heterocycl- CH_2 -, 2-(heterocycl)ethan-1-yl, and the like, but it is not limited thereto. The “heterocycl” moiety thereof used herein includes those described in the document such as “Principles of Modern Heterocyclic Chemistry” and any heterocycl group described above. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocycl group may 20 be attached to the alkyl moiety of the heterocyclalkyl through a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclalkyl group may have 2 to 20 carbon atoms. For example, the alkyl moiety of the heterocyclalkyl group may have 1 to 6 carbon atoms, and the heterocycl moiety thereof may have 2 to 14 carbon atoms. Examples of the heterocyclalkyl include a 5-membered heterocycle 25 containing sulfur, oxygen, and/or nitrogen such as thiazolymethyl, 2-thiazolyethan-1-yl, imidazolymethyl, oxazolymethyl, thiadiazolymethyl, and the like; and a 6-membered heterocycle containing sulfur, oxygen, and/or nitrogen such as piperidinylmethyl, piperazinylmethyl, morpholinylmethyl, pyridinylmethyl, pyridazylmethyl, pyrimidylmethyl, pyrazinylmethyl, and the like (each of which may 30 be substituted or unsubstituted), but it is not limited thereto.

“Heterocyclalkenyl” refers to an acyclic alkenyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or sp^3 carbon atom although an sp^2 carbon atom may also be used, is replaced by a heterocycl radical

(i.e., a heterocyclyl-alkenylene moiety). The heterocyclyl moiety of the heterocyclylalkenyl group includes those described in the document such as “Principles of Modern Heterocyclic Chemistry” and any heterocyclyl group described herein. The alkenyl moiety of the heterocyclylalkenyl group includes any alkenyl group described herein. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocyclyl group may be attached to the alkenyl moiety of the heterocyclylalkenyl via a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclylalkenyl group may have 3 to 20 carbon atoms. For example, the alkenyl moiety of the heterocyclylalkenyl group may have 2 to 6 carbon atoms, and the heterocyclyl moiety thereof may have 2 to 14 carbon atoms.

“Heterocyclalkynyl” refers to an acyclic alkynyl radical in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or sp^3 carbon atom although an sp carbon atom may also be used, is replaced by a heterocyclyl radical (i.e., a heterocyclyl-alkynylene moiety). The heterocyclyl moiety of the heterocyclalkynyl group includes those described in the document such as “Principles of Modern Heterocyclic Chemistry” and any heterocyclyl group described herein. The alkynyl moiety of the heterocyclalkynyl group includes any alkynyl group described herein. Those skilled in the art will understand that if the resulting group is chemically stable, the heterocyclyl group may be attached to the alkynyl moiety of the heterocyclalkynyl via a carbon-to-carbon bond or a carbon-to-heteroatom bond. A heterocyclalkynyl group may have 3 to 20 carbon atoms. For example, the alkynyl moiety of the heterocyclalkynyl group may have 2 to 6 carbon atoms, and the heterocyclyl moiety thereof may have 2 to 14 carbon atoms.

“Heteroaryl” refers to an aromatic heterocyclyl containing at least one heteroatom in the ring. Non-limiting examples of a suitable heteroatom that may be contained in the aromatic ring include oxygen, sulfur, and nitrogen. Non-limiting examples of a heteroaryl ring include all of those enumerated in the definition of “heterocyclyl” herein, inclusive of pyridinyl, pyrrolyl, oxazolyl, indolyl, isoindolyl, furanyl, thienyl, benzofuranyl, benzothiophenyl, carbazolyl, imidazolyl, thiazolyl, isoxazolyl, pyrazolyl, isothiazolyl, quinolyl, isoquinolyl, pyridazyl, pyrimidyl, pyrazyl, and the like (each of which may be substituted or unsubstituted).

“Carbocycle” or “carbocyclyl” refers to a saturated, partially unsaturated, or aromatic ring having 3 to 7 carbon atoms as a monocycle, 7 to 12 carbon atoms as a

bicycle, and up to about 20 carbon atoms as a polycycle. A monocyclic carbocycle has 3 to 7 ring atoms, more typically 5 or 6 ring atoms. A bicyclic cycloalkyl may have 7 to 12 ring atoms and may be a fused ring system, a spirocyclic ring system, or a bridged ring system. In exemplary cycloalkyl groups, the atoms are arranged in a bicyclo[4,5], [5,5], [5,6], or [6,6] system. Non-limiting examples of a monocyclic cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl (each of which may be substituted or unsubstituted).

“Acyl” refers to -C(=O)-alkyl, -C(=O)-carbocycle (which is substituted or unsubstituted), and -C(=O)-heterocycle (which is substituted or unsubstituted), wherein the alkyl, carbocycle, or heterocycle moiety is as defined herein. Non-limiting examples of “acyl” include -C(=O)CH₃, -C(=O)CH₂CH₃, -C(=O)CH(CH₃)₂, -C(=O)C(CH₃)₃, -C(=O)-phenyl (which is substituted or unsubstituted), -C(=O)-cyclopropyl (which is substituted or unsubstituted), -C(=O)-cyclobutyl (which is substituted or unsubstituted), -C(=O)-cyclopentyl (which is substituted or unsubstituted), -C(=O)-cyclohexyl (which is substituted or unsubstituted), and -C(=O)-pyridyl (which is substituted or unsubstituted).

“Arylheteroalkyl” refers to a heteroalkyl as defined herein, wherein a hydrogen atom (which may be attached to either a carbon atom or a heteroatom) is replaced by an aryl group as defined herein. If the resulting group is chemically stable, the aryl group may be attached to a carbon atom of the heteroalkyl group or the heteroatom of the heteroalkyl group. For example, an arylheteroalkyl group may have a formula of -alkylene-O-aryl, -alkylene-O-alkylene-aryl, -alkylene-NH-aryl, -alkylene-NH-alkylene-aryl, -alkylene-S-aryl, -alkylene-S-alkylene-aryl, or the like. In addition, any alkylene moiety in the above formulae may be further substituted with any of the substituents defined or exemplified herein.

“Heteroarylalkyl” refers to an alkyl group as defined herein, wherein a hydrogen atom is replaced by a heteroaryl group as defined herein. Non-limiting examples of heteroarylalkyl include -CH₂-pyridinyl, -CH₂-pyrrolyl, -CH₂-oxazolyl, -CH₂-indolyl, -CH₂-isoindolyl, -CH₂-furanyl, -CH₂-thienyl, -CH₂-benzofuranyl, -CH₂-benzothiophenyl, -CH₂-carbazolyl, -CH₂-imidazolyl, -CH₂-thiazolyl, -CH₂-isoxazolyl, -CH₂-pyrazolyl, -CH₂-isothiazolyl, -CH₂-quinolyl, -CH₂-isoquinolyl, -CH₂-pyridazyl, -CH₂-pyrimidyl, -CH₂-pyrazyl, -CH(CH₃)-pyridinyl, -CH(CH₃)-pyrrolyl, -CH(CH₃)-oxazolyl, -CH(CH₃)-indolyl, -CH(CH₃)-isoindolyl, -CH(CH₃)-furanyl, -CH(CH₃)-

thienyl, -CH(CH₃)-benzofuranyl, -CH(CH₃)-benzothiophenyl, -CH(CH₃)-carbazolyl, -CH(CH₃)-imidazolyl, -CH(CH₃)-thiazolyl, -CH(CH₃)-isoxazolyl, -CH(CH₃)-pyrazolyl, -CH(CH₃)-isothiazolyl, -CH(CH₃)-quinolyl, -CH(CH₃)-isoquinolyl, -CH(CH₃)-pyridazyl, -CH(CH₃)-pyrimidyl, -CH(CH₃)-pyrazyl, and the like.

5 “Silyloxy” refers to the group -O-SiR₃, wherein each R independently is alkyl, aryl (which is substituted or unsubstituted), or heteroaryl (which is substituted or unsubstituted). Non-limiting examples of silyloxy include -O-Si(CH₃)₃, -O-Si(CH₃)₂tBu, -O-Si(tBu)₂CH₃, -O-Si(tBu)₃, -O-Si(CH₃)₂Ph, -O-Si(Ph)₂CH₃, and -O-Si(Ph)₃.

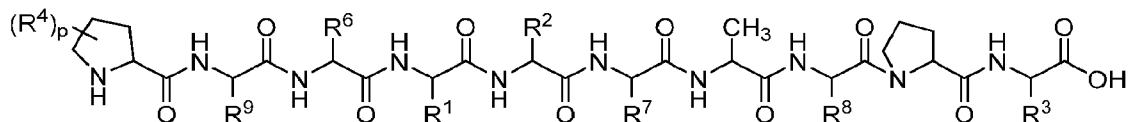
10 The term “optionally substituted” refers to a particular moiety (e.g., an optionally substituted aryl group) of the compound of Formula I that optionally has one, two, or more substituents.

The term “ester thereof” refers to any ester of a compound wherein any -COOH functional group of the molecule is modified to be a -COOR functional group or any -OH functional group of the molecule is modified to be a -OC(=O)R. Here, the R moiety of the ester may be any carbon-containing group that forms a stable ester moiety, which includes, but is not limited to, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, and substituted derivatives thereof. Examples of the ester may also include an ester such as those

20 described above of a “tautomeric enol” as described below.

Compounds

In certain embodiments, the invention provides a compound represented by Formula (I):



25 (I),
or a pharmaceutically acceptable salt thereof
wherein:

R¹, R², and R³ are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl,

30 heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

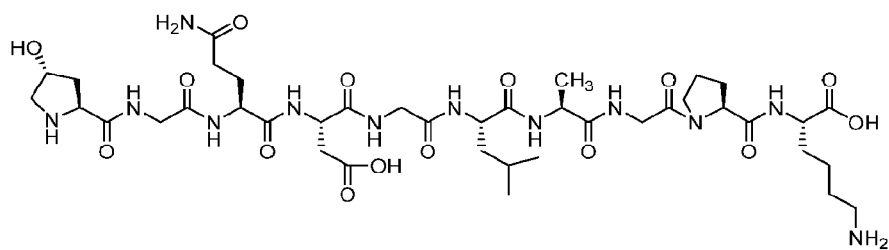
5 p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

preferably wherein the compound comprises at least one D-amino acid residue.

10 In certain embodiments, the invention provides a compound represented by Formula (I), or a pharmaceutically acceptable salt thereof, wherein the compound is not:



In certain embodiments, R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl;

15 R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, oxo, hydroxyl, $-OR^b$, hydroxyalkyl, $-CH_2OR^b$, and halo;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

20 In some embodiments, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-CN$, $-NO_2$, $=N-OH$, $-N_3$, $-R^a$, $-OR^a$, $-SR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $=NR^a$, $-NHC(=O)R^c$, $-C(=O)R^c$, $-C(=O)N(R^a)_2$, $-S(=O)_2R^c$, $-OS(=O)_2OR^a$, $-S(=O)_2OR^a$, $-S(=O)_2N(R^a)_2$, $-S(=O)R^c$, $-OP(=O)(OR^a)_2$, $-(alkylene)-C(=O)R^c$, $-C(=S)R^c$, $-C(=O)OR^a$, $-(alkylene)-C(=O)OR^a$, $-C(=S)OR^a$, $-C(=O)SR^a$, $-C(=S)SR^a$, $-(alkylene)-C(=O)N(R^a)_2$, $-C(=S)N(R^a)_2$, and $-C(-NR^a)N(R^a)_2$;

25

R^a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

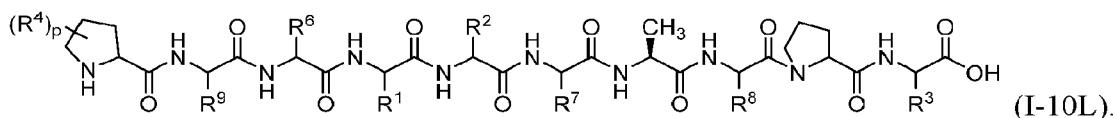
In more particular embodiments, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-R^a$, $-OR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $-NHC(=O)R^c$, $-C(=O)R^c$, $-C(=O)N(R^a)_2$, $-C(=O)OR^a$, $-(alkylene)-C(=O)OR^a$, and $-(alkylene)-C(=O)N(R^a)_2$;

R^a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

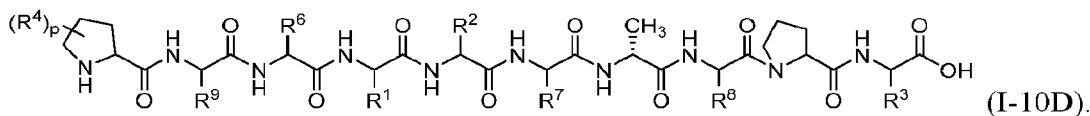
R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

In certain such embodiments, R^a , independently for each occurrence, is hydrogen, alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl; and R^c , independently for each occurrence, is alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl.

In certain embodiments, the compound has the structure of formula (I-10L):

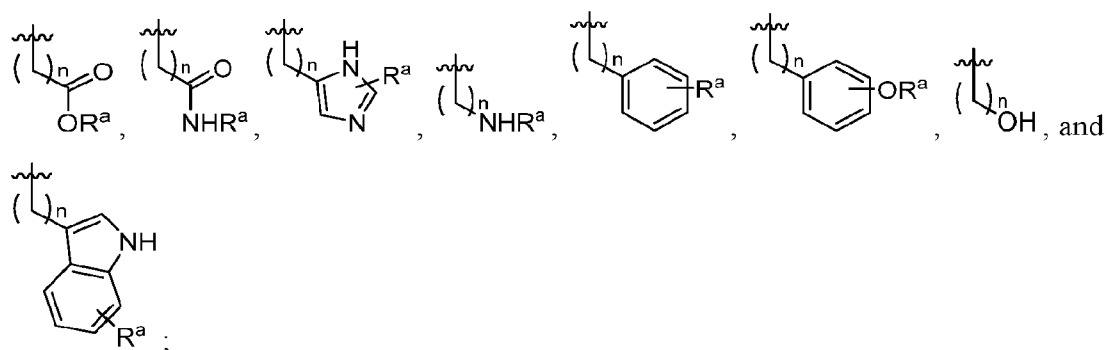


Alternatively, the compound may have the structure of formula (I-10D):



In certain embodiments, R^1 is substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

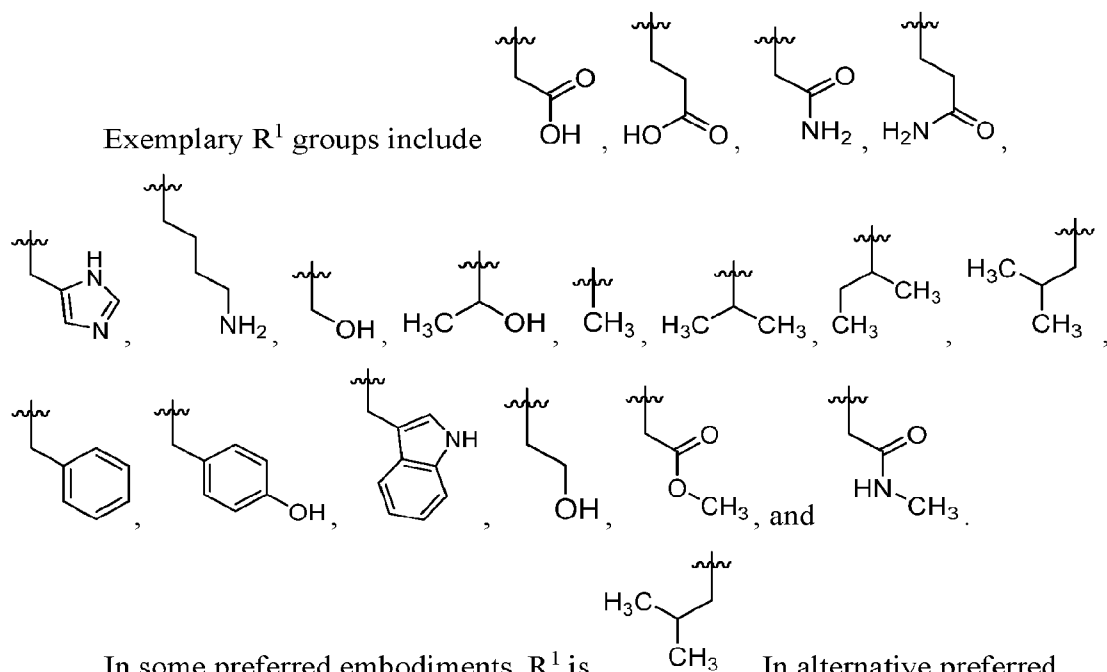
More specifically, R¹ may be selected from substituted or unsubstituted alkyl,



R^a is hydrogen or alkyl; and

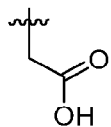
5 n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

Exemplary R^1 groups include

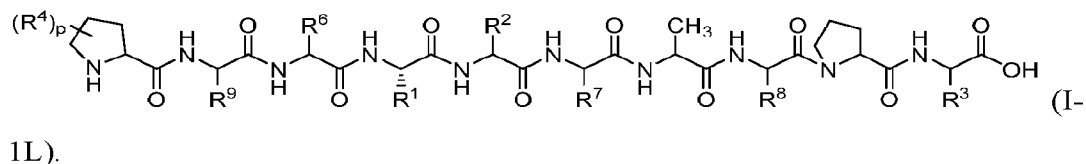


In some preferred embodiments, R¹ is CH₃. In alternative preferred

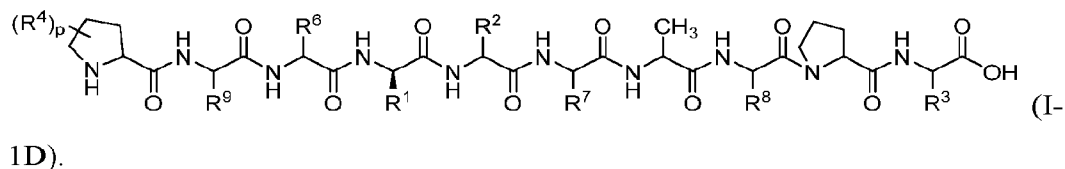
10 embodiments, $\mathbf{R}^1$ is



In certain embodiments, the compound has the structure of formula (I-1L):

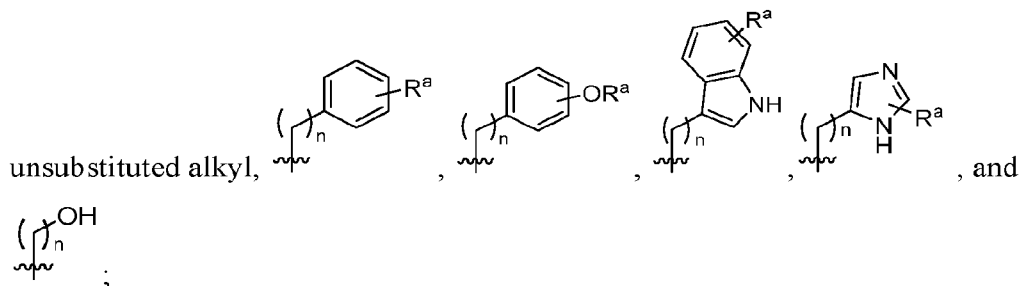


Alternatively, the compound may have the structure of formula (I-1D)



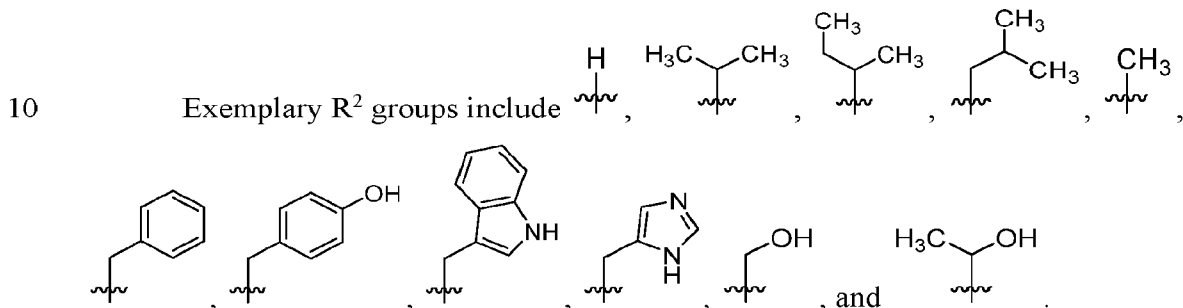
In certain embodiments, R^2 is H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

5 In some embodiments, R^2 is selected from hydrogen, substituted or



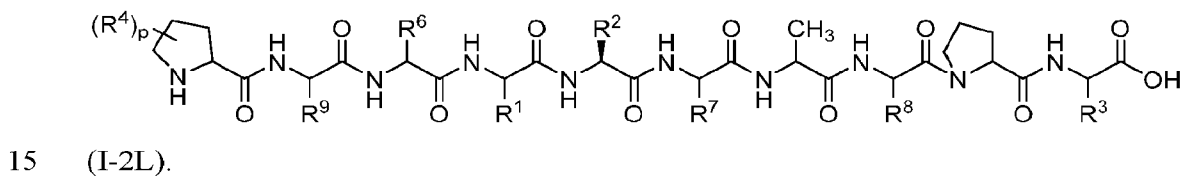
R^a is hydrogen or alkyl; and

n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

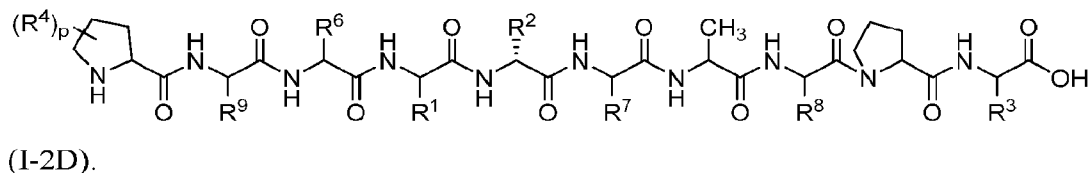


Preferably, R^2 is hydrogen.

In certain embodiments, the compound has the structure of formula (I-2L):

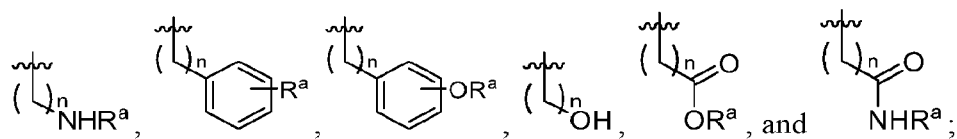


Alternatively, the compound may have the structure of formula (I-2D):



In certain embodiments, R^3 is substituted or unsubstituted alkyl or arylalkyl.

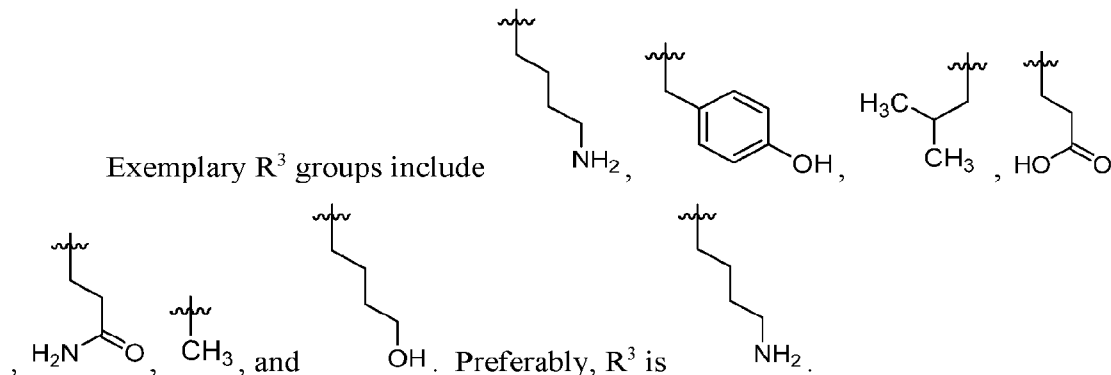
In some embodiments, R^3 is selected from substituted or unsubstituted alkyl,



R^a is hydrogen or alkyl; and

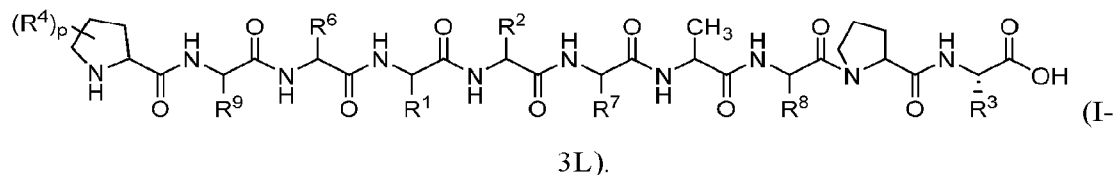
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

5 Exemplary R^3 groups include

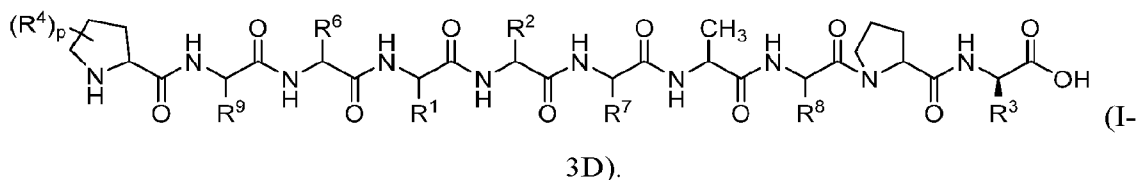


, $H_2N-C(=O)-CH_2-CH_2-$, $-CH_3$, and $-CH_2-CH_2-CH_2-OH$. Preferably, R^3 is

In certain embodiments, the compound has the structure of formula (I-3L):



10 Alternatively, the compound may have the structure of formula (I-3D):



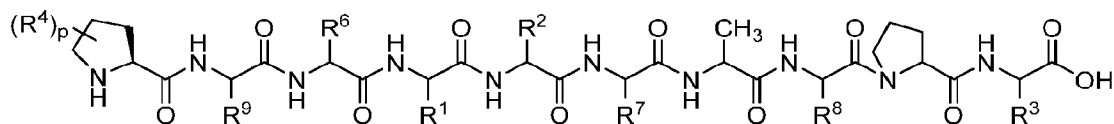
In certain embodiments, p is 1 or 2; and R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl.

In certain embodiments, p is 1 or 2; and R^4 , independently for each occurrence, is selected from $-CH_3$, halo, hydroxyl, and hydroxyalkyl.

In certain preferred embodiments, R^4 is hydroxyl. In alternative preferred embodiments, R^4 is $-CH_3$.

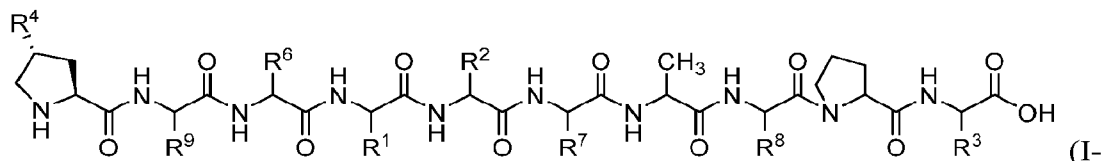
20 In any of the above embodiments, p may be 1.

In certain embodiments, the compound has the structure of formula (I-4Lg):



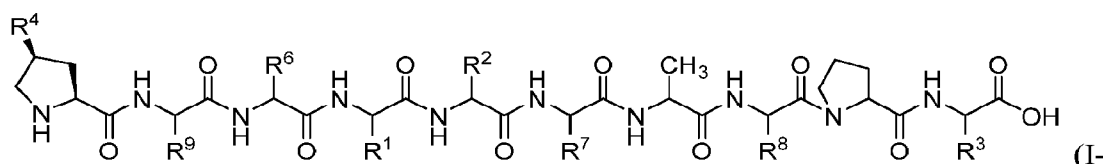
(I-4Lg).

In certain embodiments, the compound has the structure of formula (I-4La):



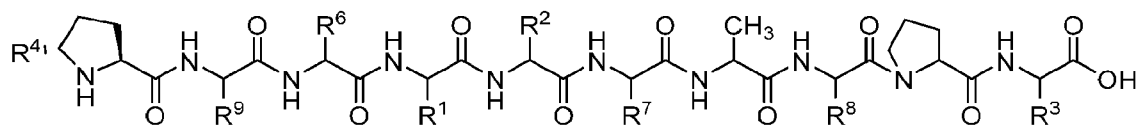
5 4La).

In certain embodiments, the compound has the structure of formula (I-4Lb):



4Lb).

In certain embodiments, the compound has the structure of formula (I-4Lc):

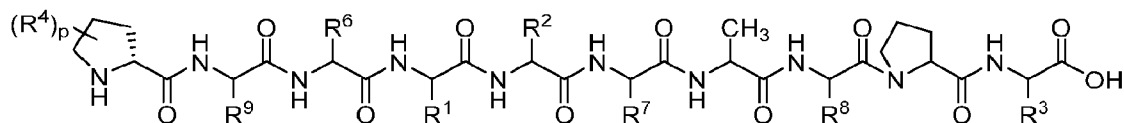


10

(I-4Lc).

In certain embodiments, the compound has the structure of formula (I-4Lc), provided that R⁴ is not hydroxyl.

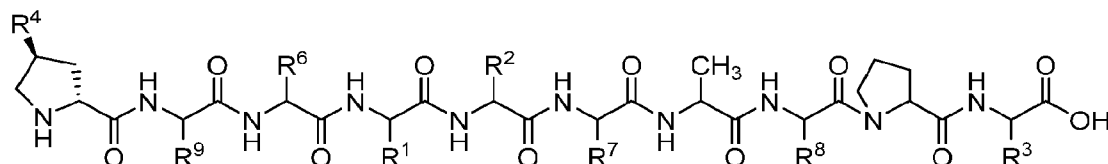
In certain embodiments, the compound has the structure of formula (I-4Dg):



15

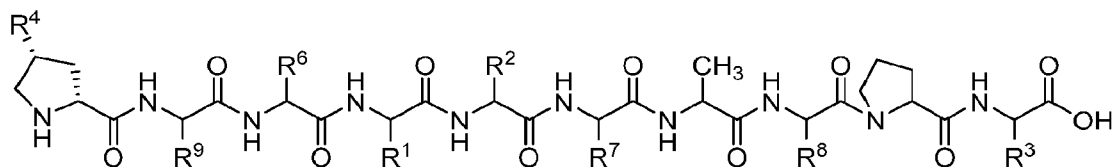
(I-4Dg).

In certain embodiments, the compound has the structure of formula (I-4Da):



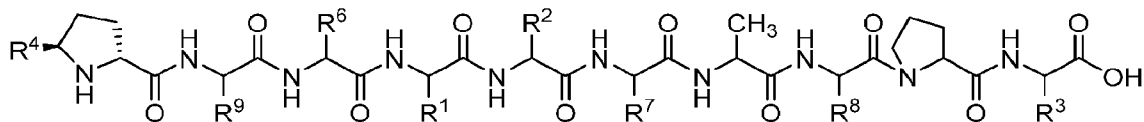
(I-4Da).

In certain embodiments, the compound has the structure of formula (I-4Db):



(I-4Db).

In certain embodiments, the compound has the structure of formula (I-4Dc):



5

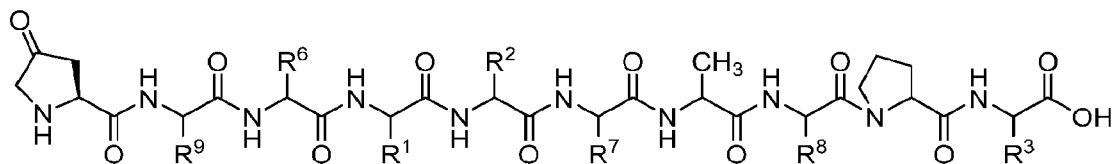
(I-4Dc).

In certain embodiments, the compound has the structure of formula (I-4Dc), provided that R^4 is not hydroxyl.

In certain embodiments, R^4 is oxo.

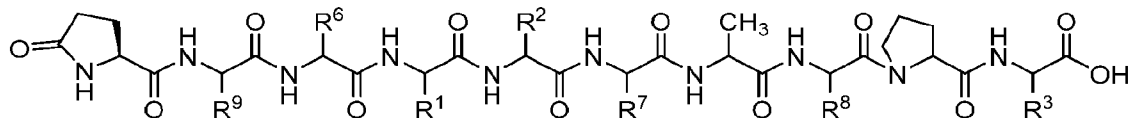
10

In certain embodiments, the compound has the structure of formula (I-4Ld):



(I-4Ld).

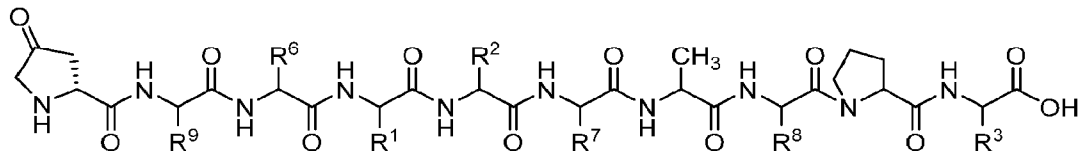
In certain embodiments, the compound has the structure of formula (I-4Le):



15

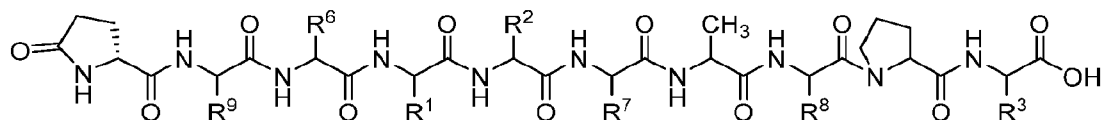
(I-4Le).

In certain embodiments, the compound has the structure of formula (I-4Dd):



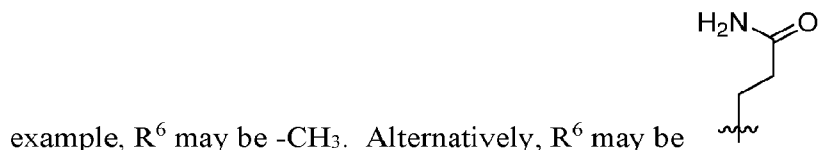
(I-4Dd).

In certain embodiments, the compound has the structure of formula (I-4De):

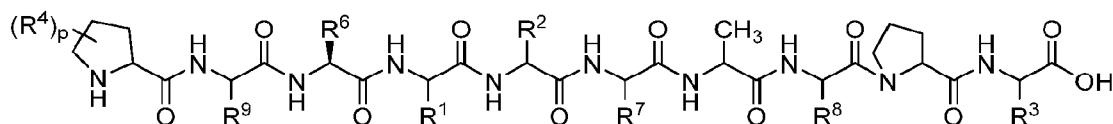


(I-4De).

In certain embodiments, R^6 is hydrogen or alkyl, wherein the alkyl is optionally substituted with one occurrence of $-C(=O)NH_2$. In certain embodiments, wherein R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$. For

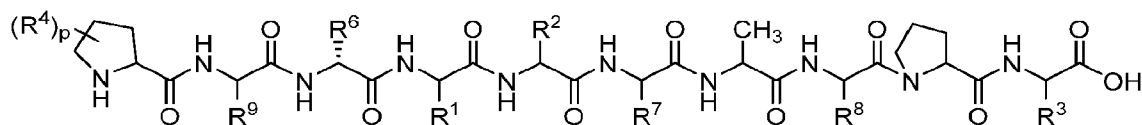


In certain embodiments, the compound has the structure of formula (I-6L):



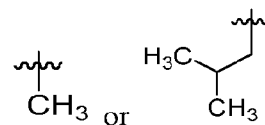
(I-6L).

Alternatively, the compound may have the structure of formula (I-6D):

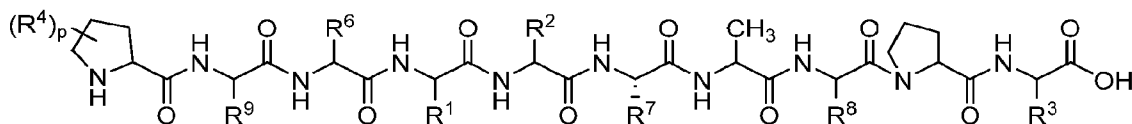


(I-6D).

In certain embodiments, R^7 is (C_1-C_{10}) alkyl, preferably

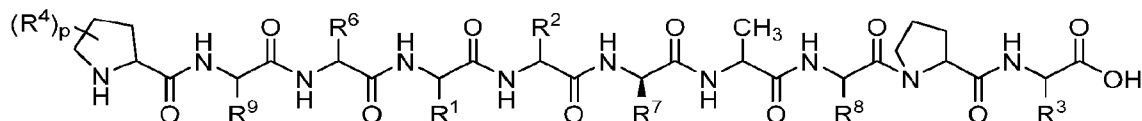


In certain embodiments, the compound has the structure of formula (I-7L):



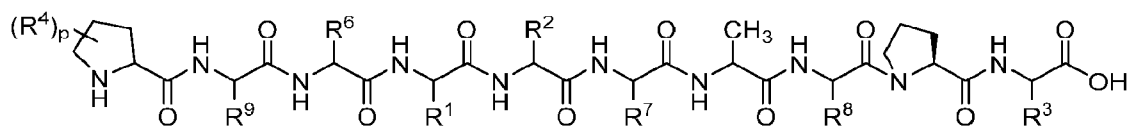
(I-7L).

Alternatively, the compound may have the structure of formula (I-7D):



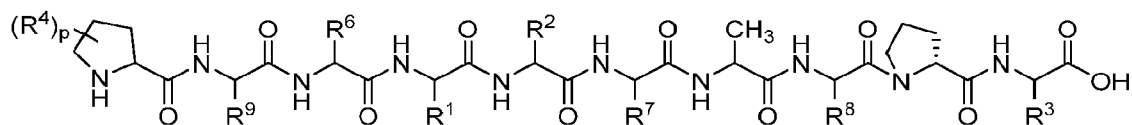
(I-7D).

In certain embodiments, the compound has the structure of formula (I-11L):



(I-11L).

Alternatively, the compound may have the structure of formula (I-11D):



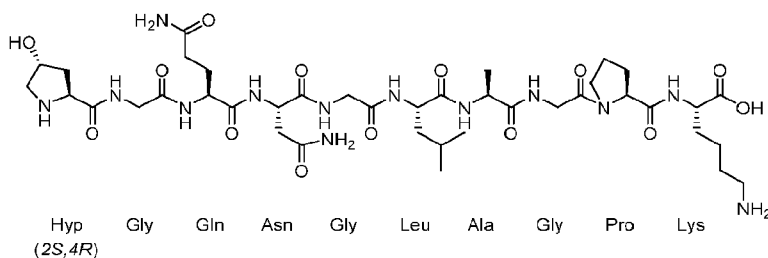
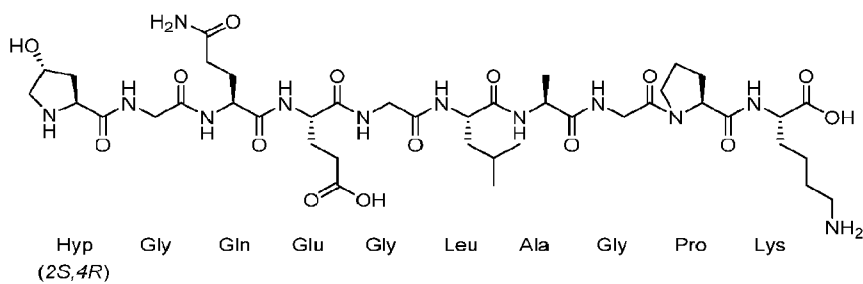
(I-11D).

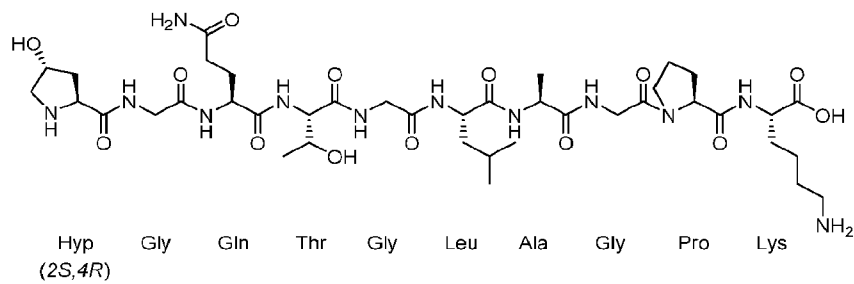
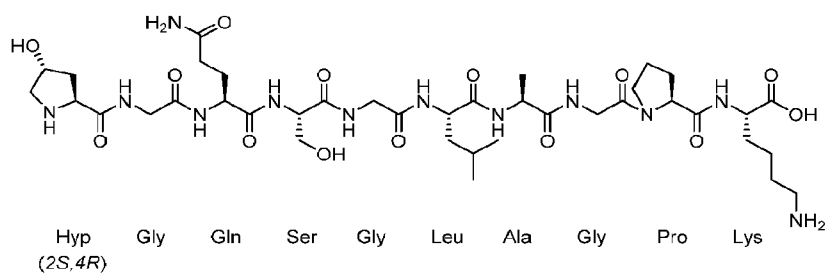
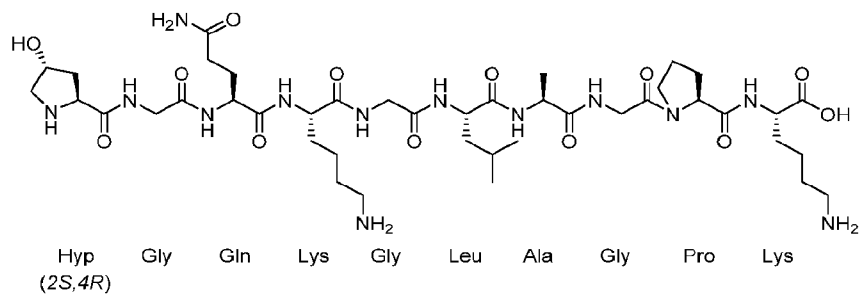
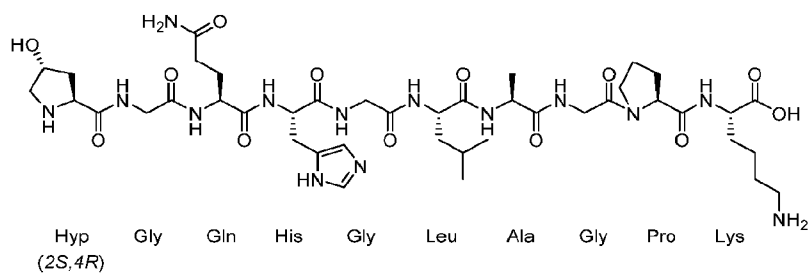
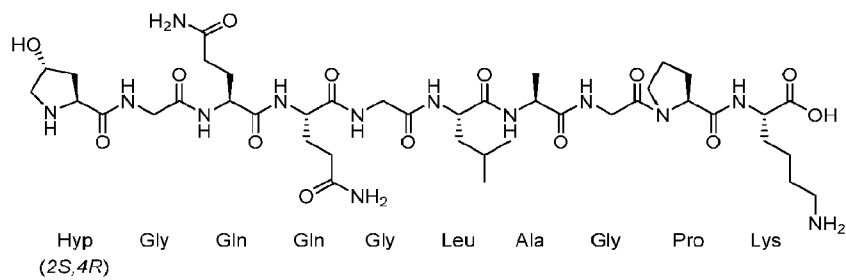
In certain embodiments, R^8 is $-\text{CH}_3$ or $-\text{H}$, preferably $-\text{H}$.

In certain embodiments, R^9 is $-\text{CH}_3$ or $-\text{H}$, preferably $-\text{H}$.

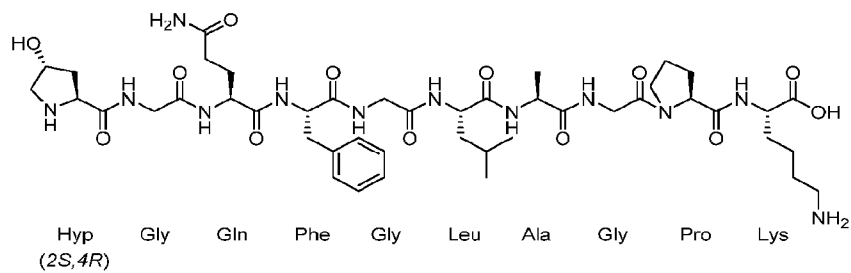
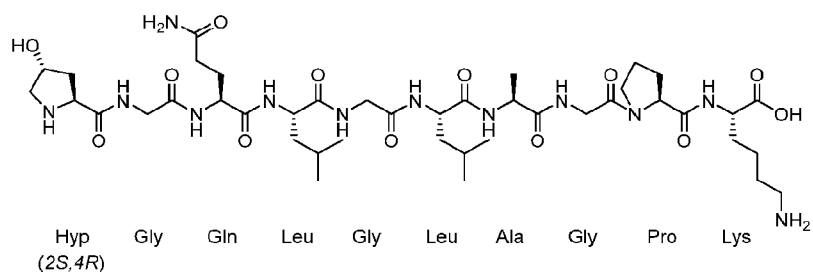
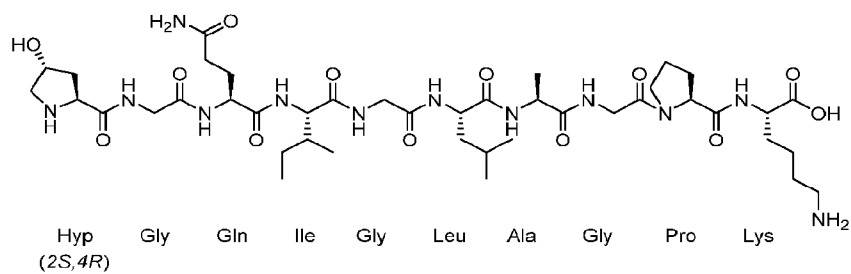
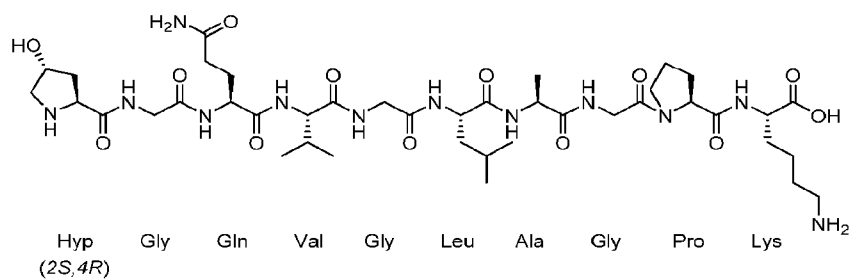
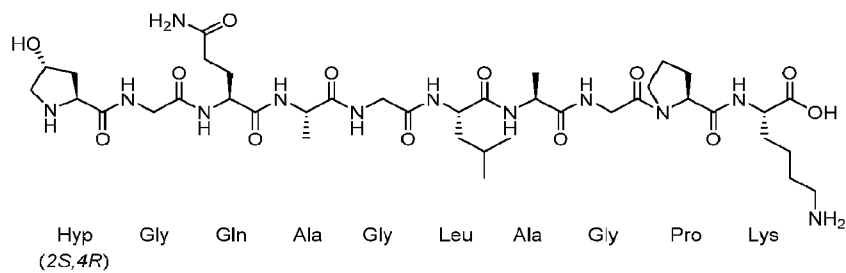
In certain embodiments, the compound comprises at least one, at least two, at least three, at least four, at least five, at least six, at least seven, or at least eight D-amino acid residues.

In certain embodiments, the invention provides a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following:

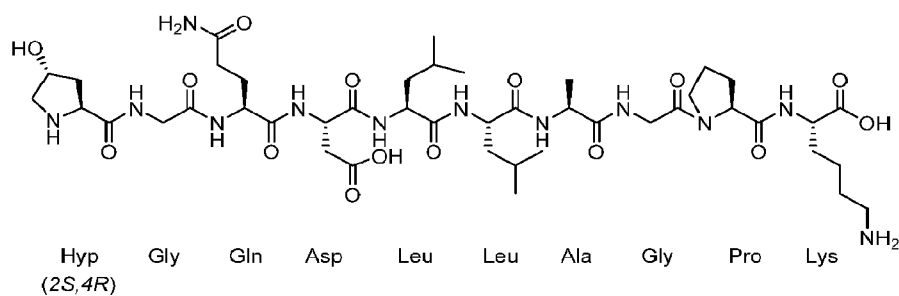
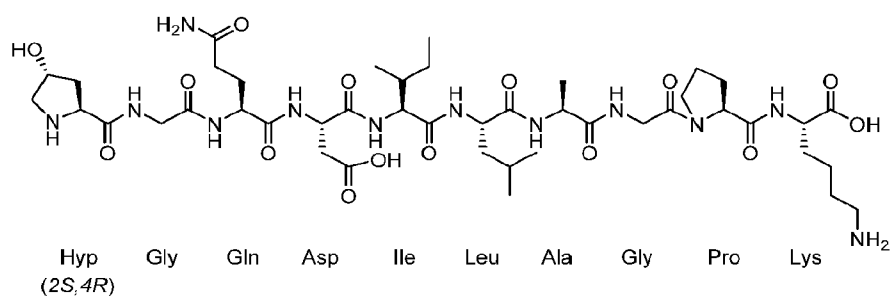
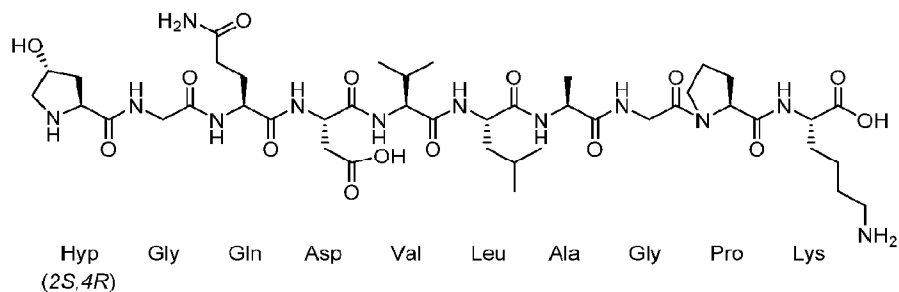
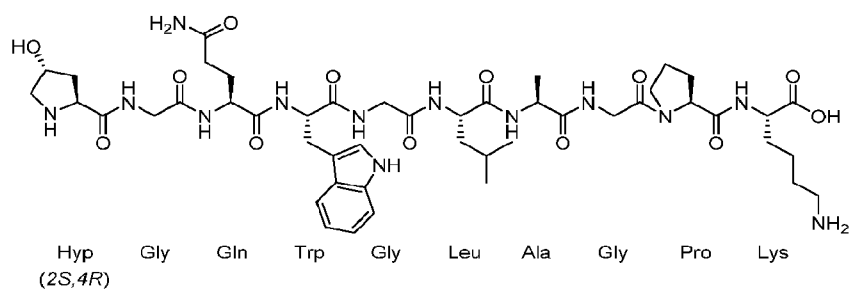
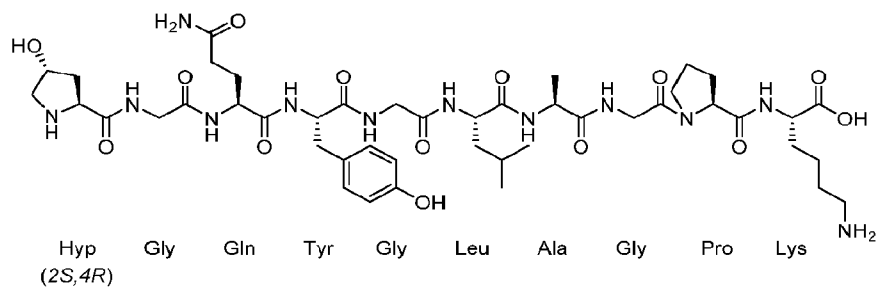




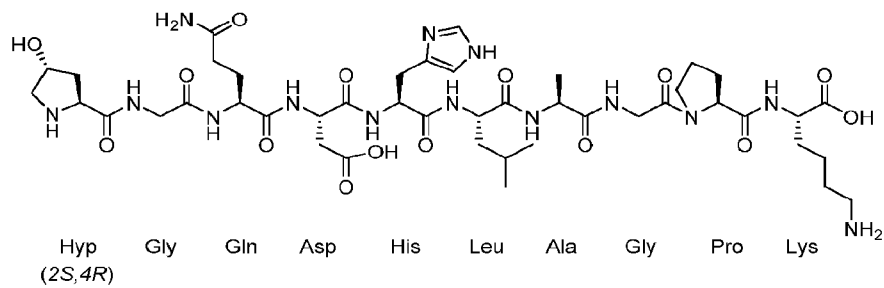
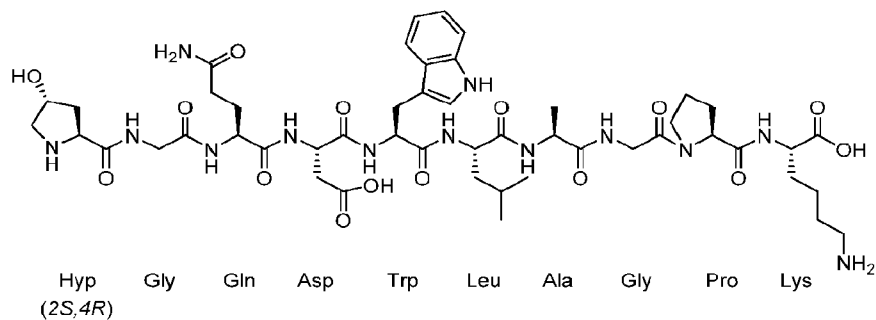
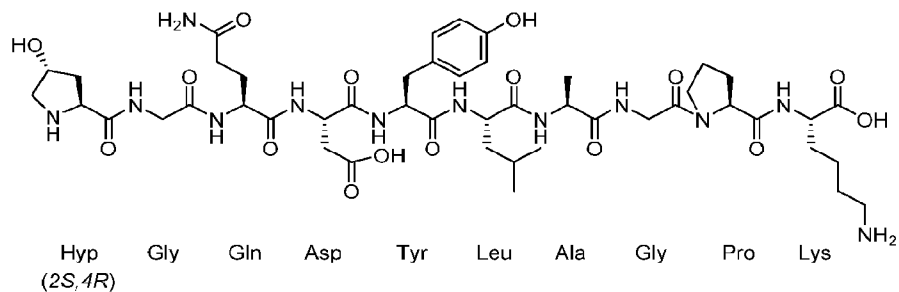
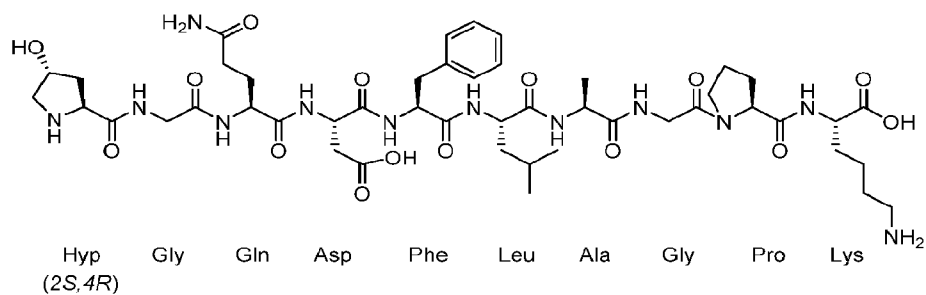
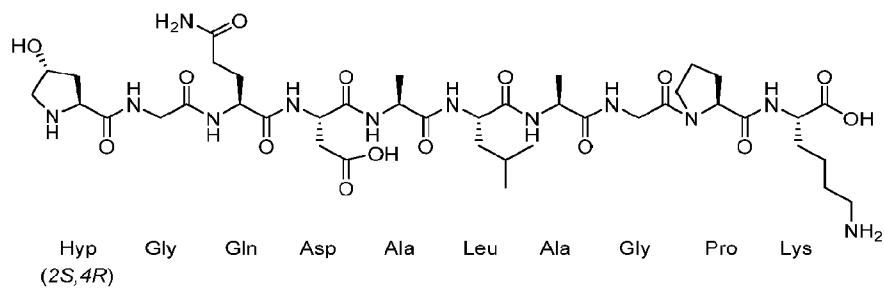
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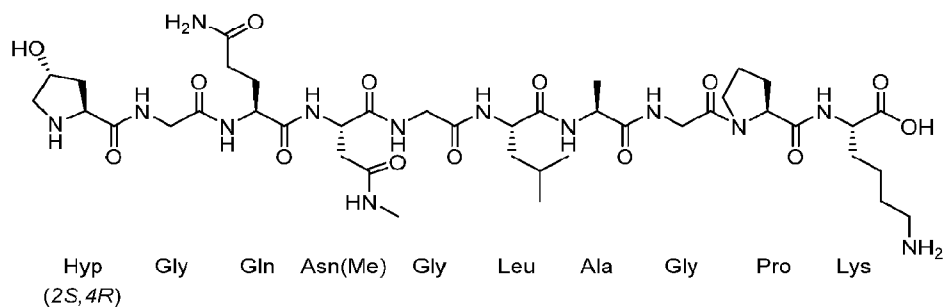
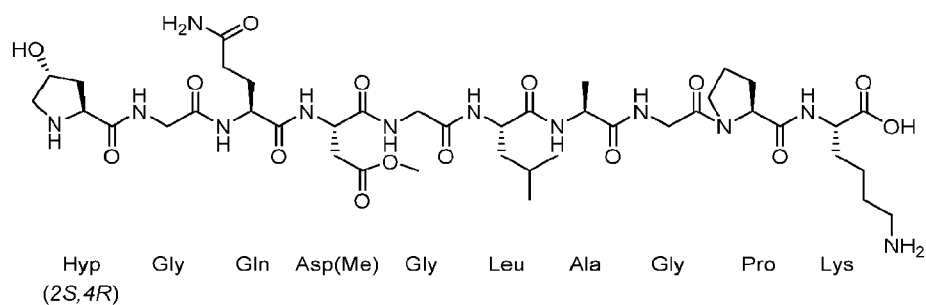
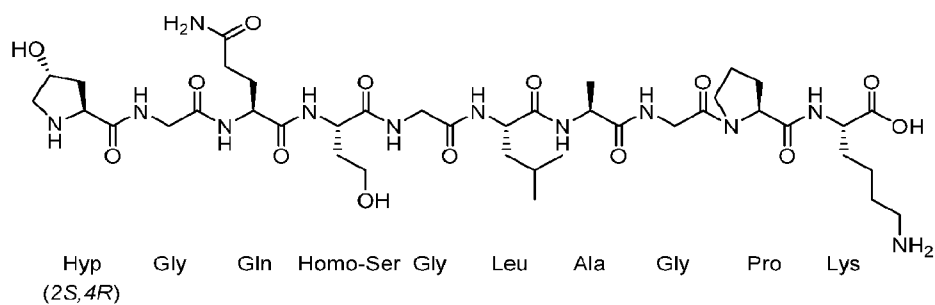
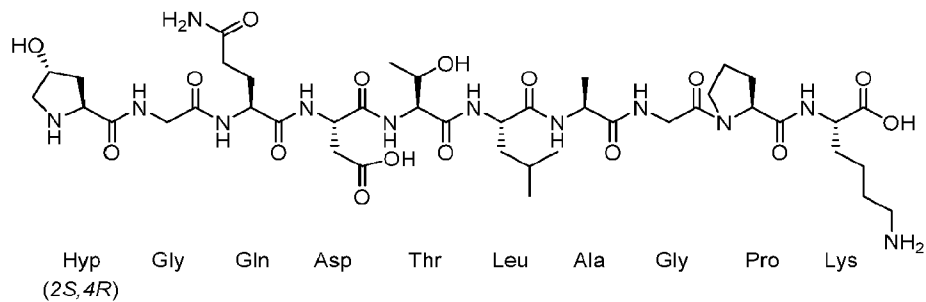
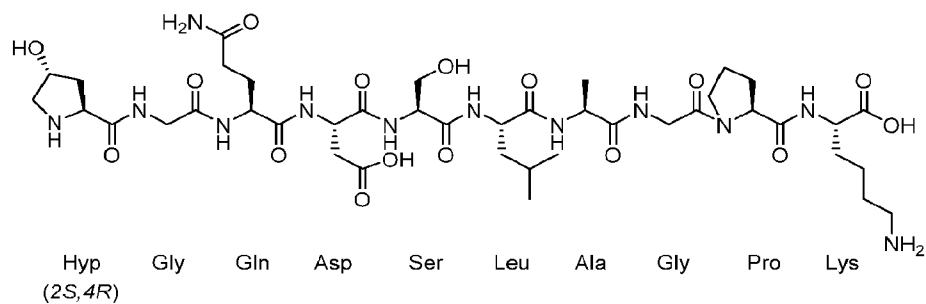
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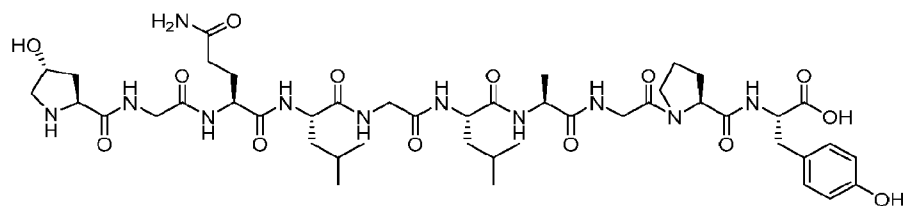


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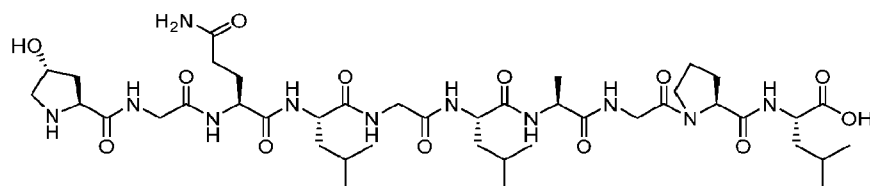


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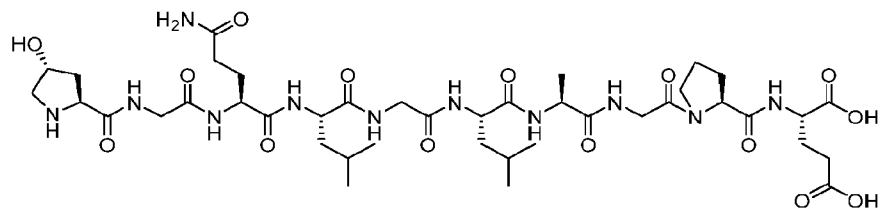




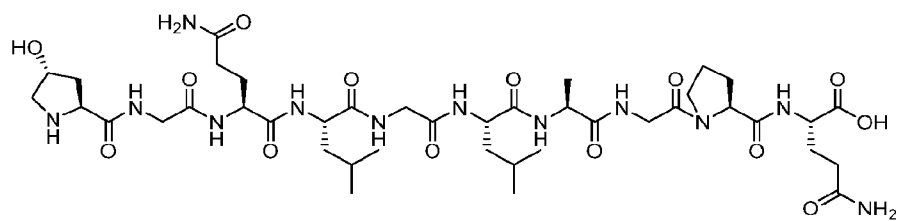
Hyp Gly Gln Leu Gly Leu Ala Gly Pro Tyr
(2S,4R)



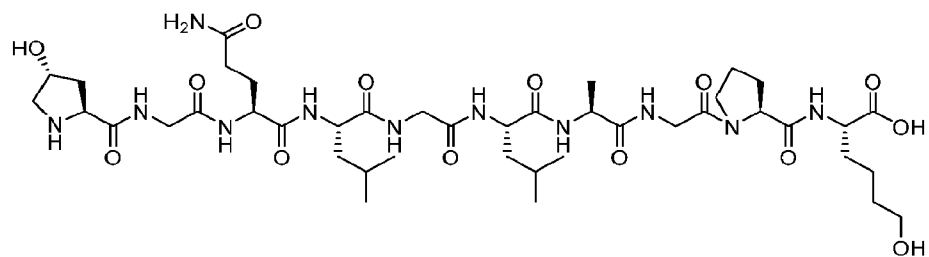
Hyp Gly Gln Leu Gly Leu Ala Gly Pro Leu
(2S,4R)



Hyp Gly Gln Leu Gly Leu Ala Gly Pro Glu
(2S,4R)

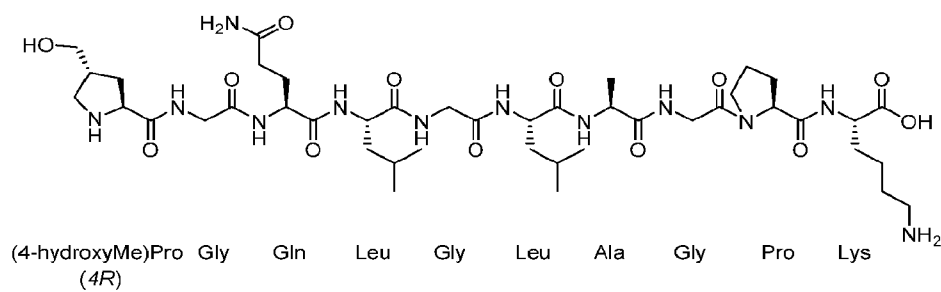
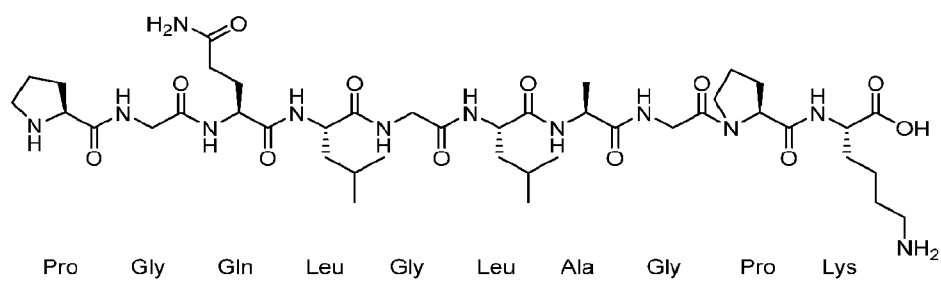
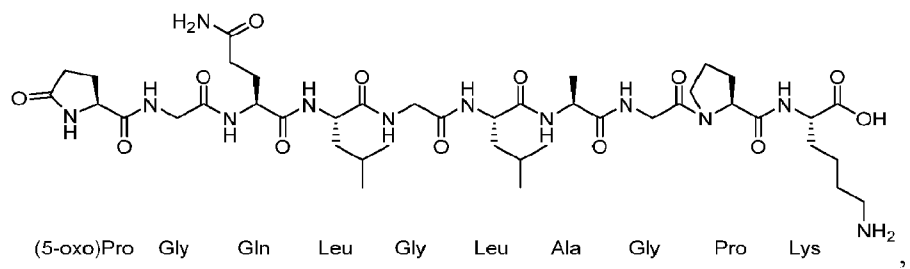
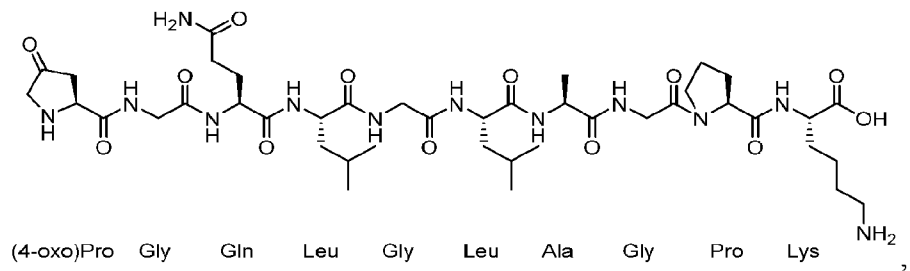
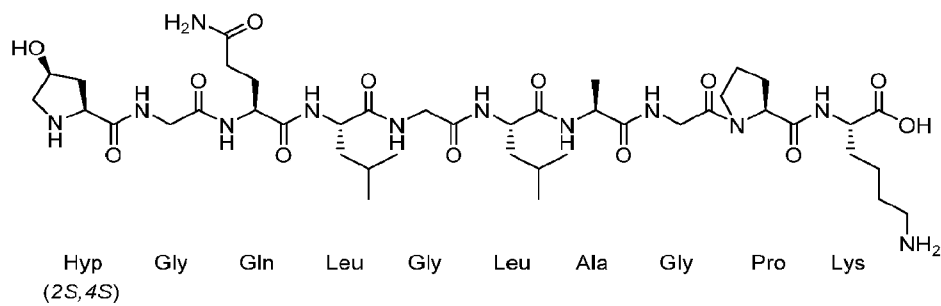


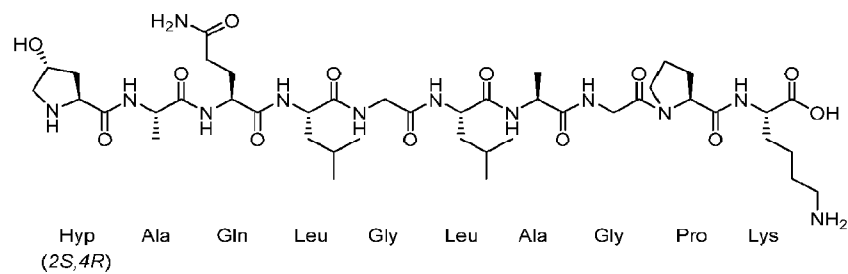
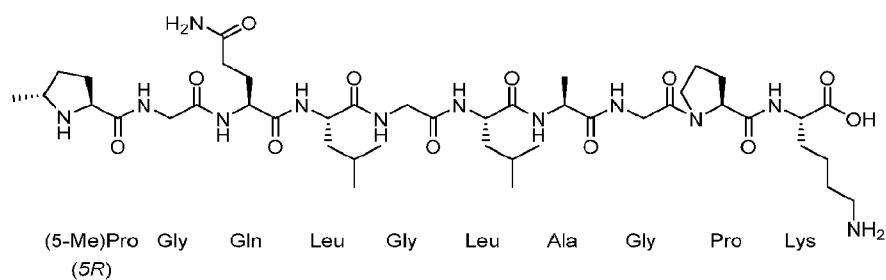
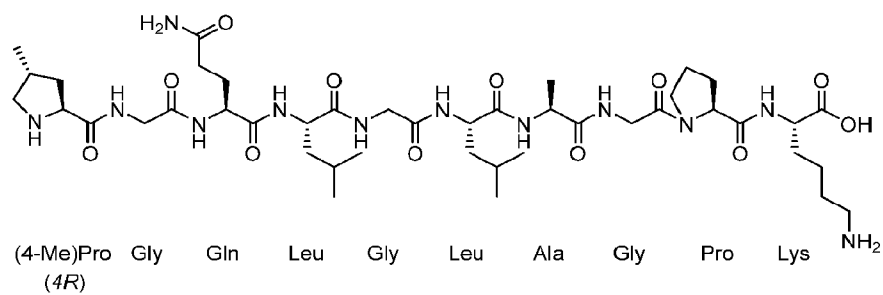
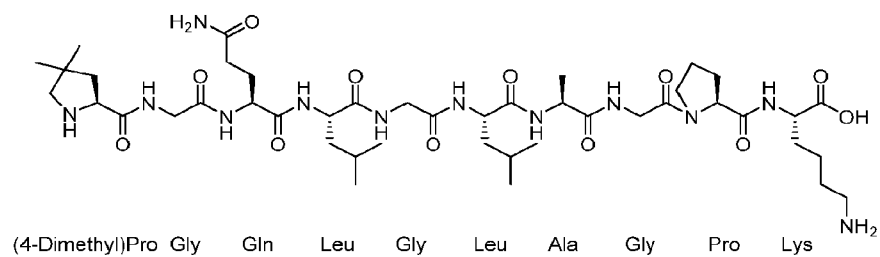
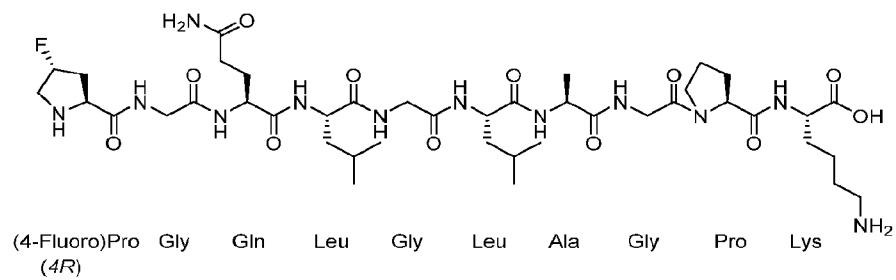
Hyp Gly Gln Leu Gly Leu Ala Gly Pro Gln
(2S,4R)

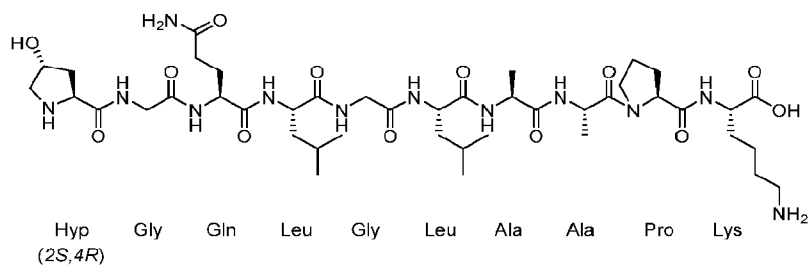
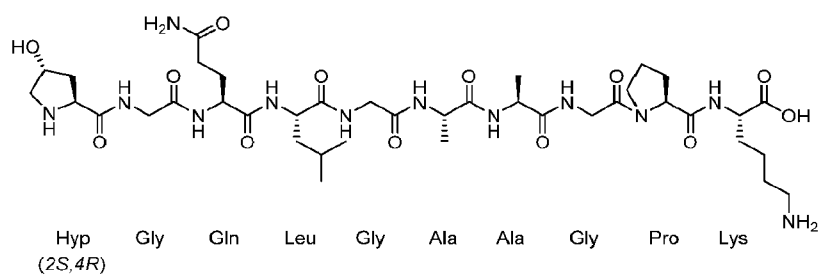
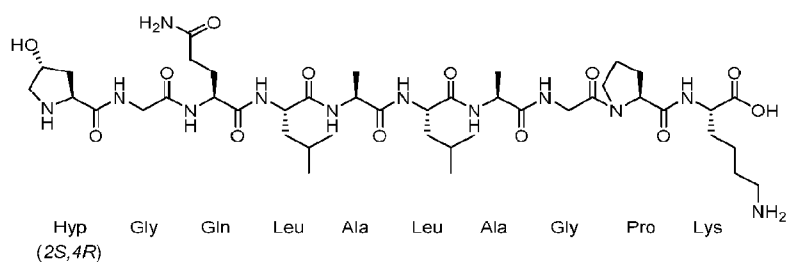
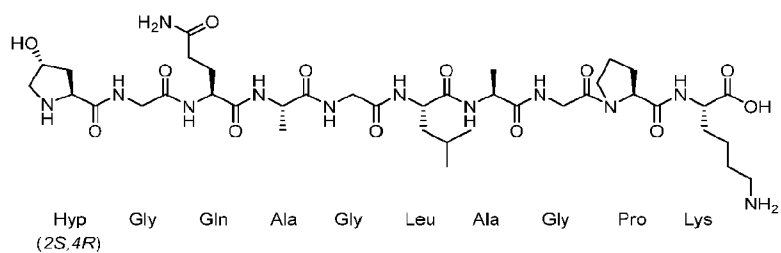
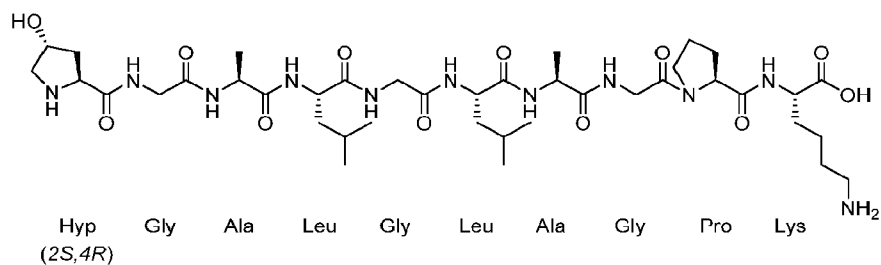


Hyp Gly Gln Leu Gly Leu Ala Gly Pro Nle(6-OH)
(2S,4R)

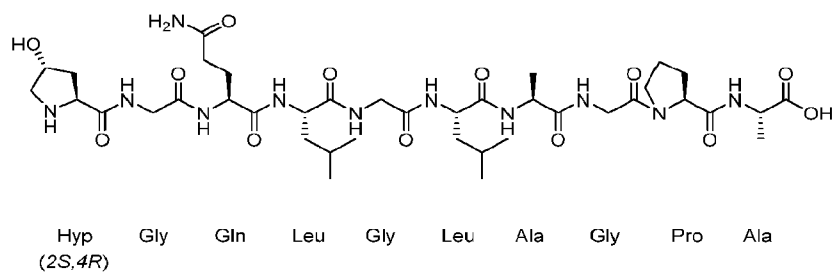
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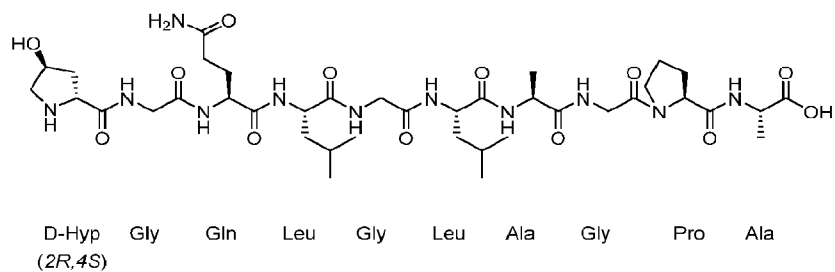
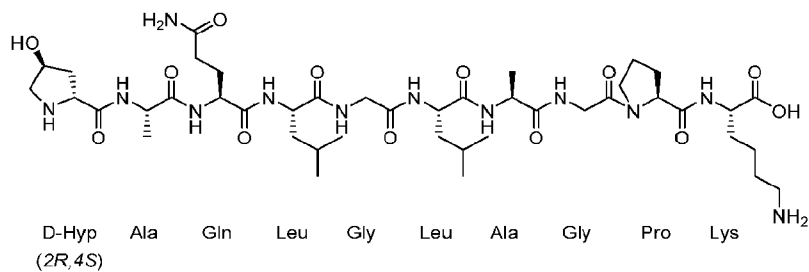
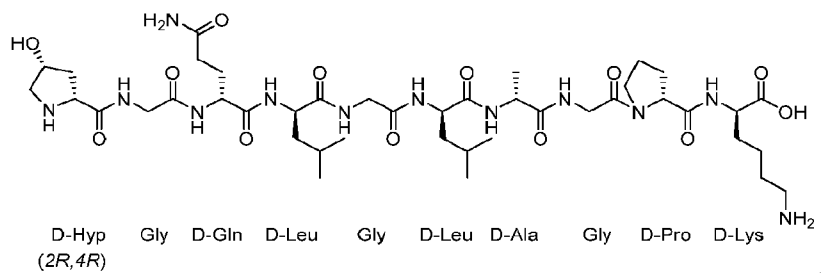
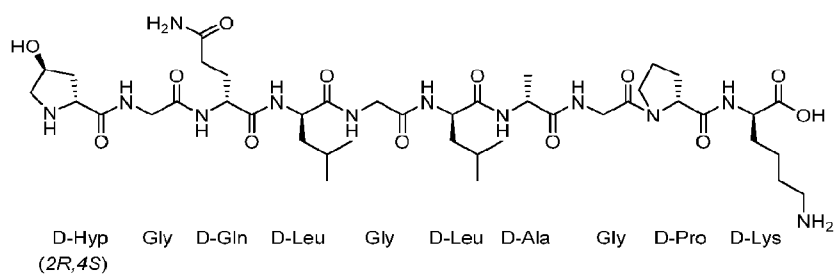
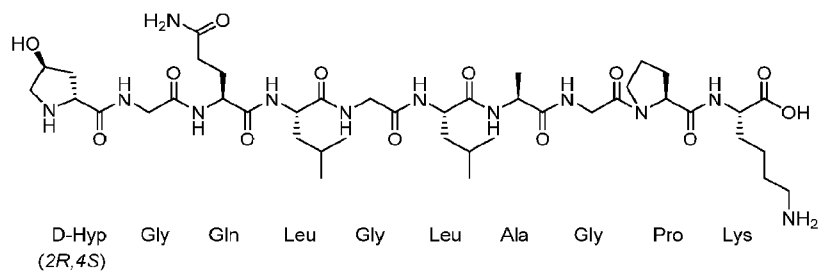




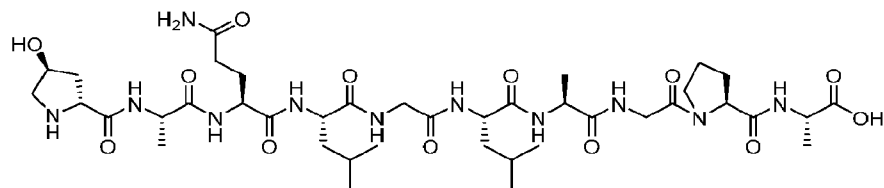


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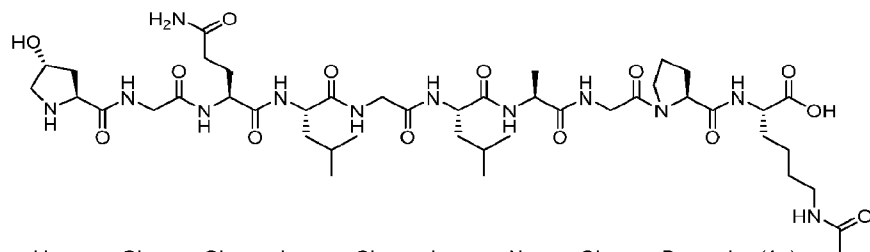




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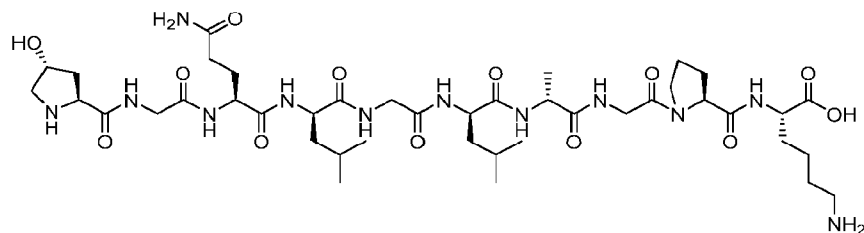


D-Hyp Ala Gln Leu Gly Leu Ala Gly Pro Ala
(2R,4S)



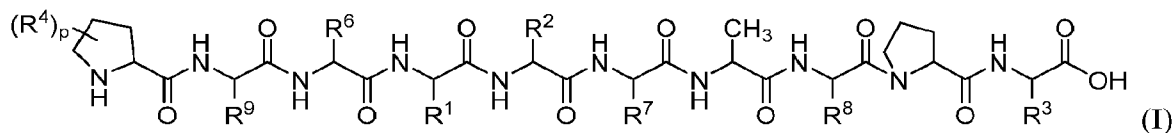
Hyp Gly Gln Leu Gly Leu Ala Gly Pro Lys(Ac)
(2S,4R)

; and



Hyp Gly Gln D-Leu Gly D-Leu D-Ala Gly Pro Lys
(2S,4R)

5 The present invention also provides a compound represented by Formula (I):



or a pharmaceutically acceptable salt thereof;

wherein:

10 R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

15 R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

p is 0, 1, or 2;

R⁶ is hydrogen or substituted or unsubstituted alkyl; and

R⁷, R⁸, and R⁹ are each independently hydrogen or alkyl;

wherein at least one of:

- 5 (a) at least one of R¹, R², and R³ is substituted or unsubstituted (C₂-C₁₀)haloalkyl;
- (b) at least one of alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl is substituted with one or more substituents selected from -R^a, -OR^a, -SR^a, -N(R^a)₂, -N(R^a)₃⁺, =NR^a, -NHC(=O)R^c, -C(=O)R^c, -C(=O)N(R^a)₂, -S(=O)₂R^c, -OS(=O)₂OR^a, -S(=O)₂OR^a, -S(=O)₂N(R^a)₂, -S(=O)R^c, -OP(=O)(OR^a)₂, -(alkylene)-C(=O)R^c, -C(=S)R^c, -C(=O)OR^a, -(alkylene)-C(=O)OR^a, -C(=S)OR^a, -C(=O)SR^a, -C(=S)SR^a, -(alkylene)-C(=O)N(R^a)₂, -C(=S)N(R^a)₂, and -C(-NR^a)N(R^a)₂; and
- 10 at least one occurrence of R^a or R^c is heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl;
- (c) the compound comprises at least one D-amino acid residue; or
- (d) at least two occurrences of R^a;
- at least two occurrences of R^c; or
- at least one occurrence of R^a and at least one occurrence of R^c; and
- 20 at least one occurrence of R^a and/or R^c differs from the other occurrences.

In certain embodiments, at least one of R¹, R², and R³ is substituted or unsubstituted (C₂-C₁₀)haloalkyl.

- 25 In certain embodiments, at least one of alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl is substituted with one or more substituents selected from -R^a, -OR^a, -SR^a, -N(R^a)₂, -N(R^a)₃⁺, =NR^a, -NHC(=O)R^c, -C(=O)R^c, -C(=O)N(R^a)₂, -S(=O)₂R^c, -OS(=O)₂OR^a, -S(=O)₂OR^a, -S(=O)₂N(R^a)₂, -S(=O)R^c, -OP(=O)(OR^a)₂, -(alkylene)-C(=O)R^c, -C(=S)R^c, -C(=O)OR^a, -(alkylene)-C(=O)OR^a, -C(=S)OR^a, -C(=O)SR^a, -C(=S)SR^a, -(alkylene)-C(=O)N(R^a)₂, -C(=S)N(R^a)₂, and -C(-NR^a)N(R^a)₂;
- 30 and at least one occurrence of R^a or R^c is heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

In certain embodiments, the compound comprises at least one D-amino acid residue.

In certain embodiments, the compound has:

at least two occurrences of R^a ;

5 at least two occurrences of R^c ; or

at least one occurrence of R^a and at least one occurrence of R^c ; and

at least one occurrence of R^a and/or R^c differs from the other occurrences.

In certain embodiments:

10 R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, oxo, hydroxyl, $-OR^b$, hydroxyalkyl, $-CH_2OR^b$, and halo;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycl;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

15 R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

In some embodiments, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkenyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-CN$, $-NO_2$, $=N-OH$, $-N_3$, $-R^a$, $-OR^a$, $-SR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $=NR^a$, $-NHC(=O)R^c$, $-C(=O)R^c$, $-C(=O)N(R^a)_2$, $-S(=O)_2R^c$, $-OS(=O)_2OR^a$, $-S(=O)_2OR^a$, $-S(=O)_2N(R^a)_2$, $-S(=O)R^c$, $-OP(=O)(OR^a)_2$, $-(alkylene)-C(=O)R^c$, $-C(=S)R^c$, $-C(=O)OR^a$, $-(alkylene)-C(=O)OR^a$, $-C(=S)OR^a$, $-C(=O)SR^a$, $-C(=S)SR^a$, $-(alkylene)-C(=O)N(R^a)_2$, $-C(=S)N(R^a)_2$, and $-C(-NR^a)N(R^a)_2$;

25 R^a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

In more particular embodiments, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkenyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-R^a$, $-OR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $-$

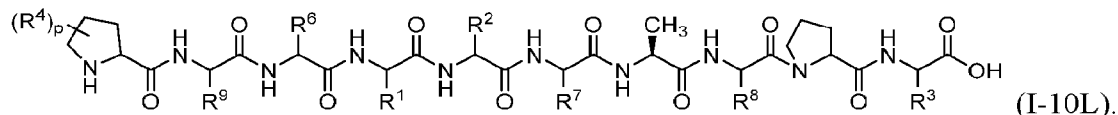
NHC(=O)R^c, -C(=O)R^c, -C(=O)N(R^a)₂, -C(=O)OR^a, -(alkylene)-C(=O)OR^a, and -(alkylene)-C(=O)N(R^a)₂;

R^a, independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

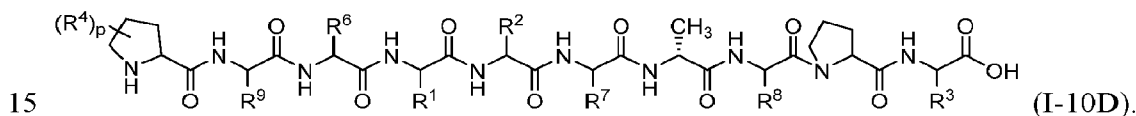
R^c, independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

In certain such embodiments, R^a, independently for each occurrence, is hydrogen, alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl; and R^c, independently for each occurrence, is alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl.

In certain embodiments, the compound has the structure of formula (I-10L):



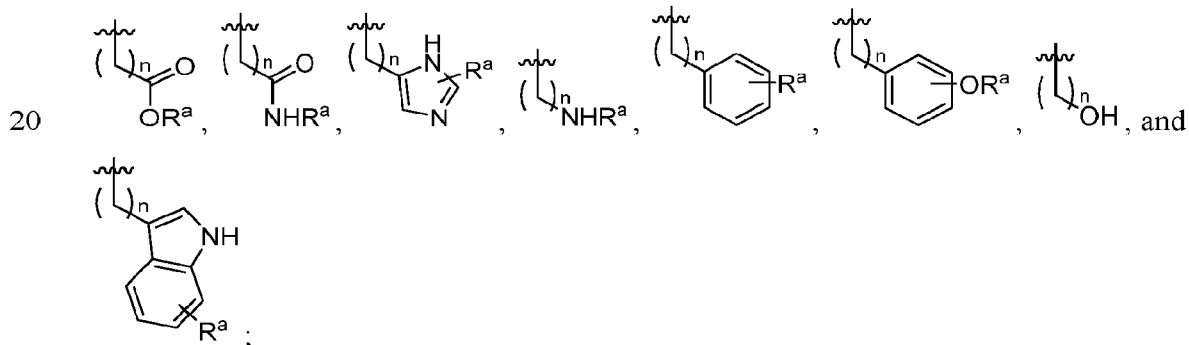
Alternatively, the compound may have the structure of formula (I-10D):



In certain embodiments, R¹ is substituted or unsubstituted (C₂-C₁₀)haloalkyl.

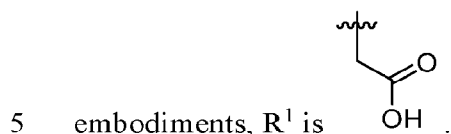
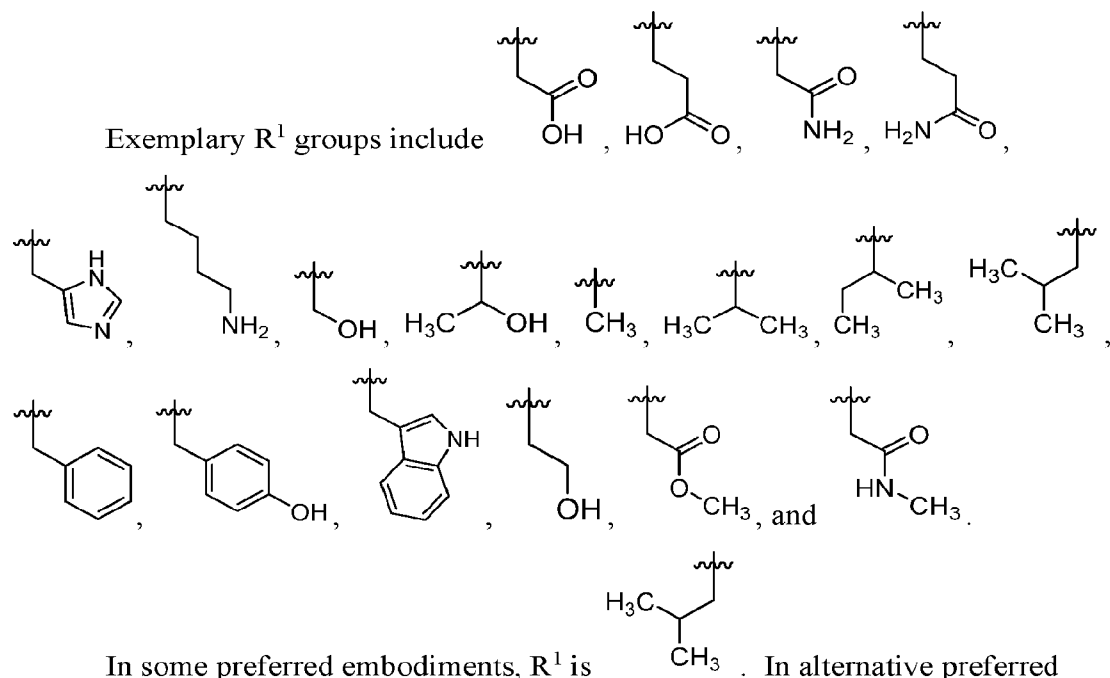
In certain embodiments, R¹ is substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

More specifically, R¹ may be selected from substituted or unsubstituted alkyl,

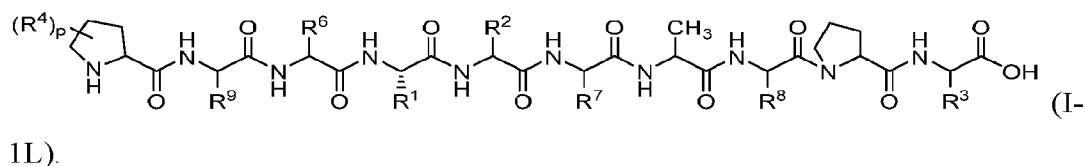


R^a is hydrogen or alkyl; and

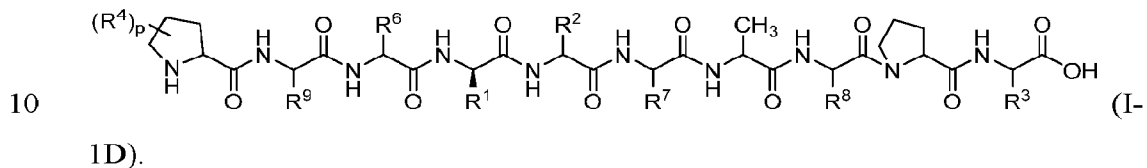
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.



In certain embodiments, the compound has the structure of formula (I-1L):



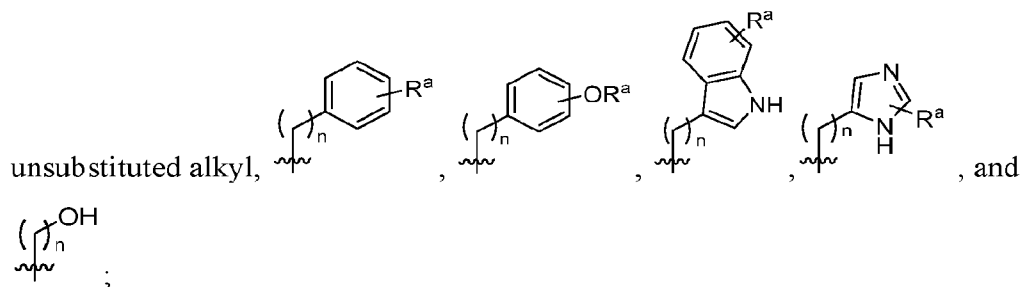
Alternatively, the compound may have the structure of formula (I-1D)



In certain embodiments, R^2 is substituted or unsubstituted (C₂-C₁₀)haloalkyl.

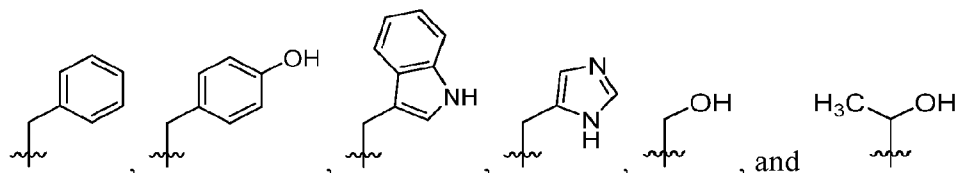
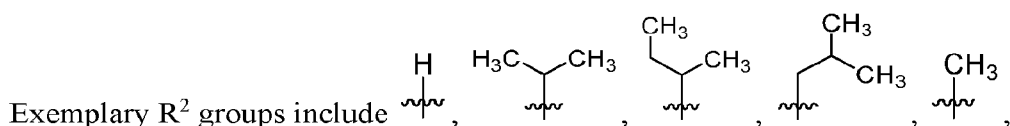
In certain embodiments, R^2 is H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

In some embodiments, R^2 is selected from hydrogen, substituted or



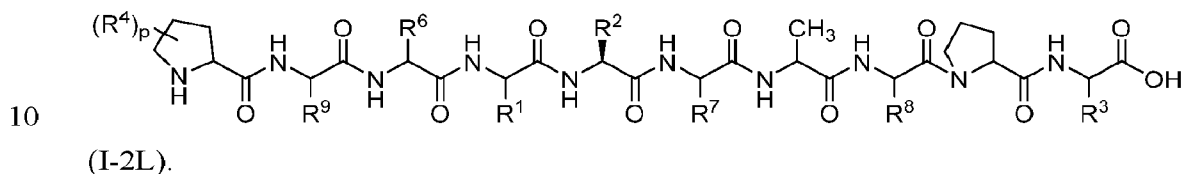
R^a is hydrogen or alkyl; and

5 n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

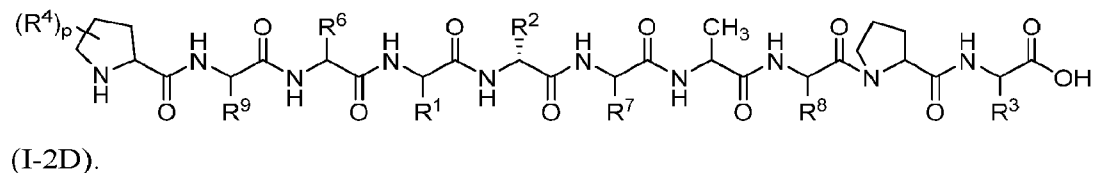


Preferably, R^2 is hydrogen.

In certain embodiments, the compound has the structure of formula (I-2L):



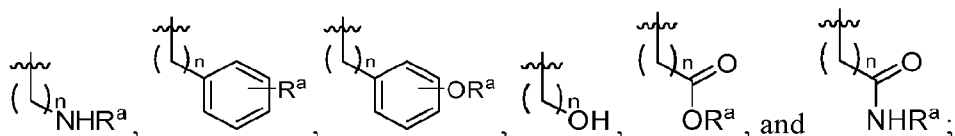
Alternatively, the compound may have the structure of formula (I-2D):



15 In certain embodiments, R^3 is substituted or unsubstituted (C_2 - C_{10})haloalkyl.

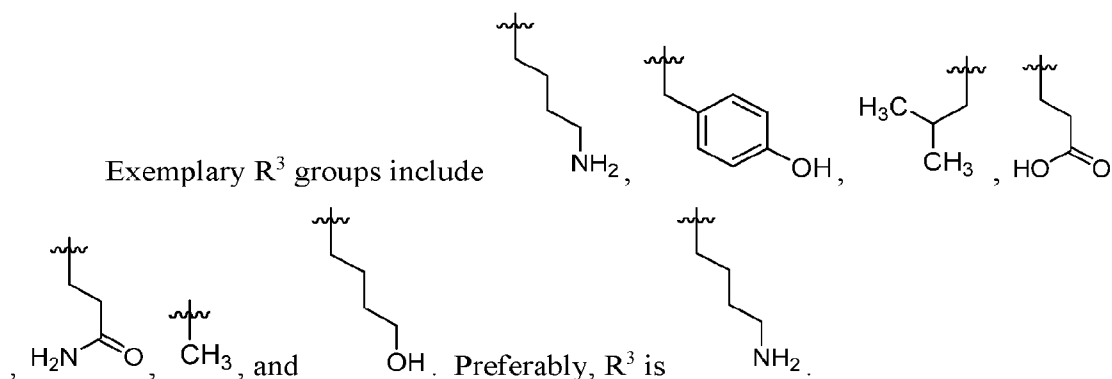
In certain embodiments, R^3 is substituted or unsubstituted alkyl or arylalkyl.

In some embodiments, R^3 is selected from substituted or unsubstituted alkyl,

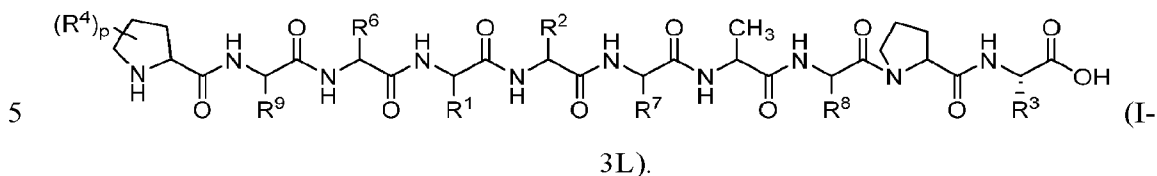


R^a is hydrogen or alkyl; and

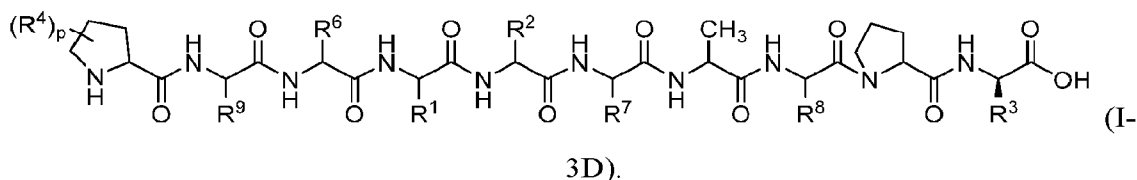
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.



In certain embodiments, the compound has the structure of formula (I-3L):



Alternatively, the compound may have the structure of formula (I-3D):



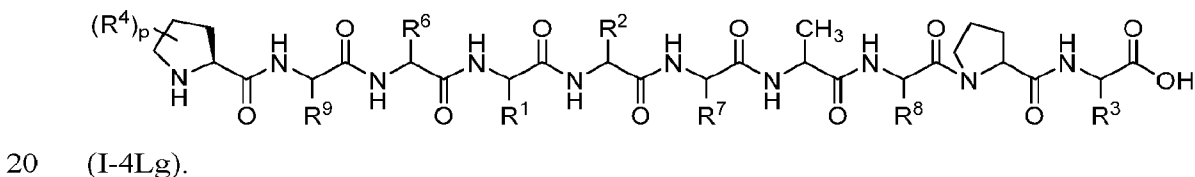
10 In certain embodiments, p is 1 or 2; and R⁴, independently for each occurrence, is selected from substituted or unsubstituted alkyl, -OR^b, -CH₂OR^b, halo, hydroxyl, and hydroxyalkyl.

In certain embodiments, p is 1 or 2; and R⁴, independently for each occurrence, is selected from -CH₃, halo, hydroxyl, and hydroxyalkyl.

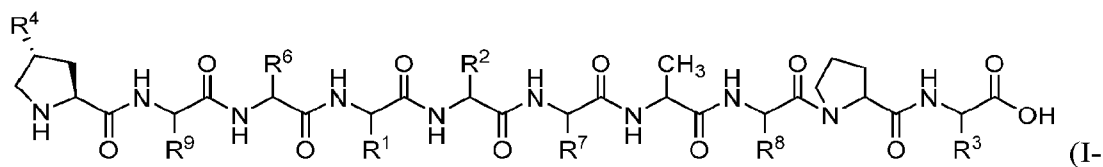
15 In certain preferred embodiments, R⁴ is hydroxyl. In alternative preferred embodiments, R⁴ is -CH₃.

In any of the above embodiments, p may be 1.

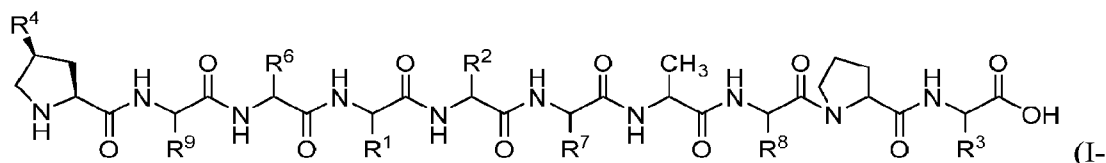
In certain embodiments, the compound has the structure of formula (I-4Lg):



In certain embodiments, the compound has the structure of formula (I-4La):

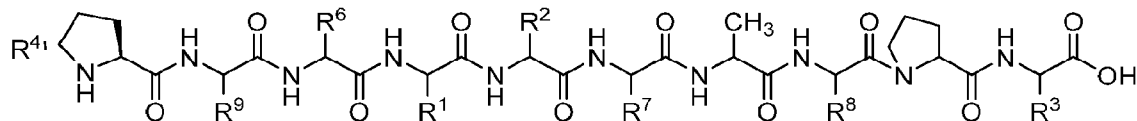


In certain embodiments, the compound has the structure of formula (I-4Lb):



5 4Lb).

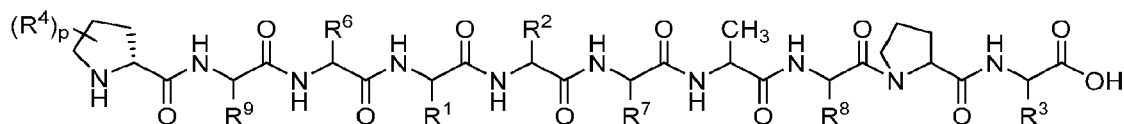
In certain embodiments, the compound has the structure of formula (I-4Lc):



(I-4Lc).

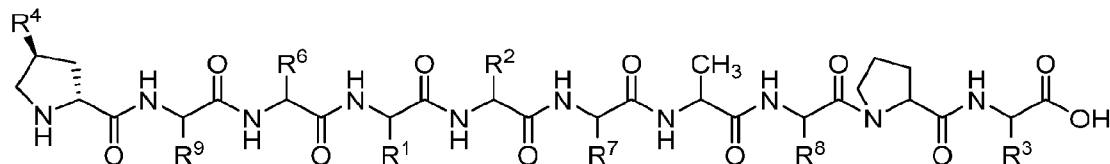
In certain embodiments, the compound has the structure of formula (I-4Lc),
10 provided that R^4 is not hydroxyl.

In certain embodiments, the compound has the structure of formula (I-4Dg):



(I-4Dg).

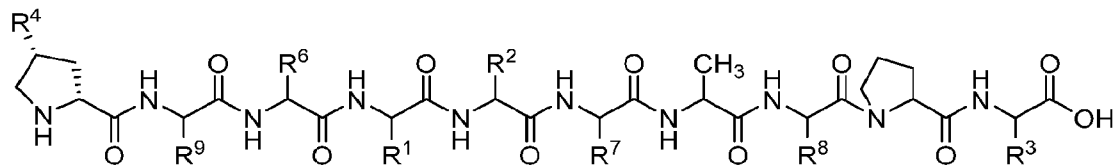
In certain embodiments, the compound has the structure of formula (I-4Da):



15

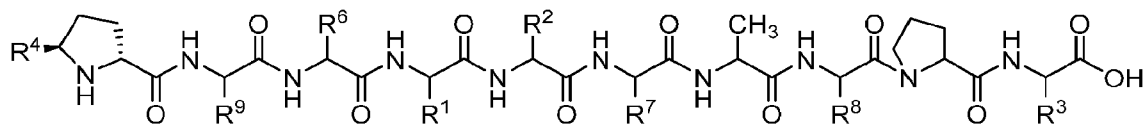
(I-4Da).

In certain embodiments, the compound has the structure of formula (I-4Db):



(I-4Db).

In certain embodiments, the compound has the structure of formula (I-4Dc):

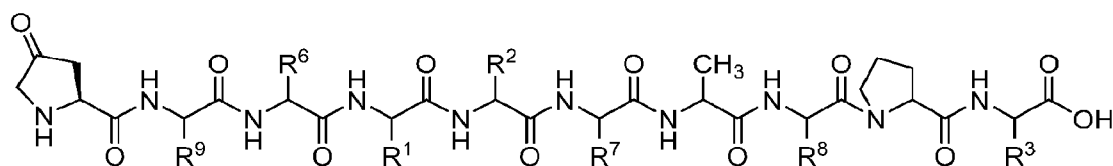


(I-4Dc).

In certain embodiments, the compound has the structure of formula (I-4Dc),
5 provided that R^4 is not hydroxyl.

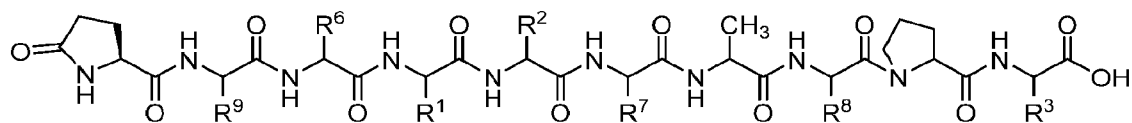
In certain embodiments, R^4 is oxo.

In certain embodiments, the compound has the structure of formula (I-4Ld):



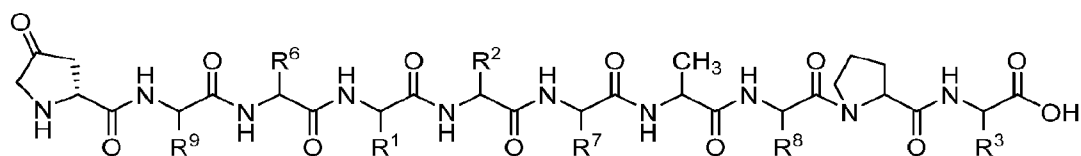
(I-4Ld).

10 In certain embodiments, the compound has the structure of formula (I-4Le):



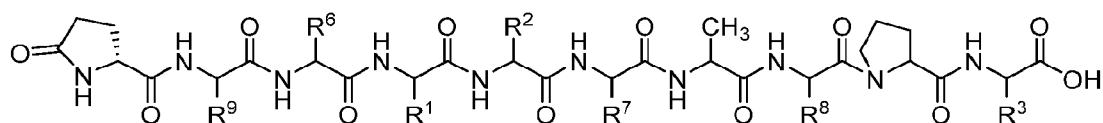
(I-4Le).

In certain embodiments, the compound has the structure of formula (I-4Dd):



15 (I-4Dd).

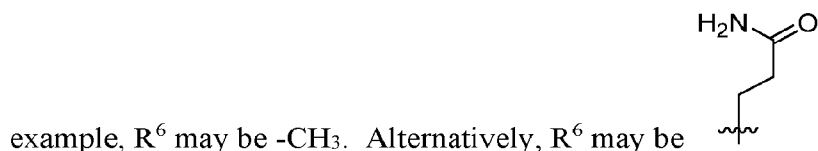
In certain embodiments, the compound has the structure of formula (I-4De):



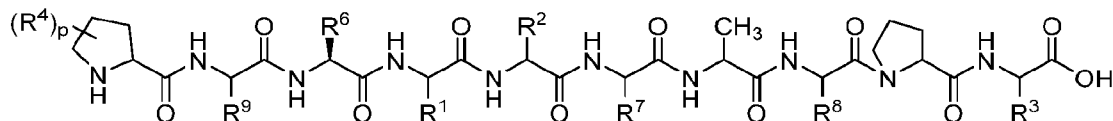
(I-4De).

In certain embodiments, R^6 is hydrogen or alkyl, wherein the alkyl is
20 optionally substituted with one occurrence of $-C(=O)NH_2$. In certain embodiments,

wherein R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$. For

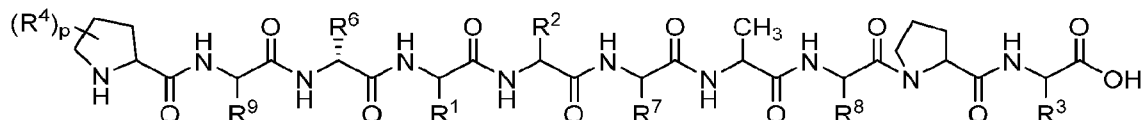


In certain embodiments, the compound has the structure of formula (I-6L):

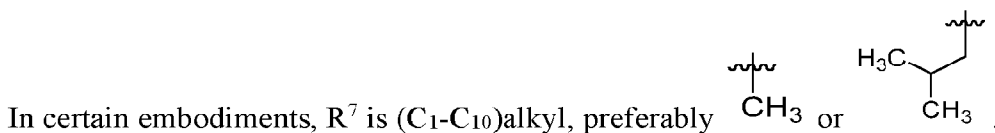


5 (I-6L).

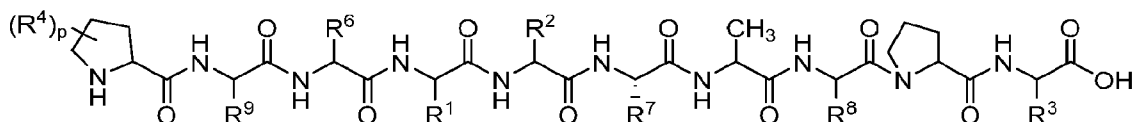
Alternatively, the compound may have the structure of formula (I-6D):



(I-6D).

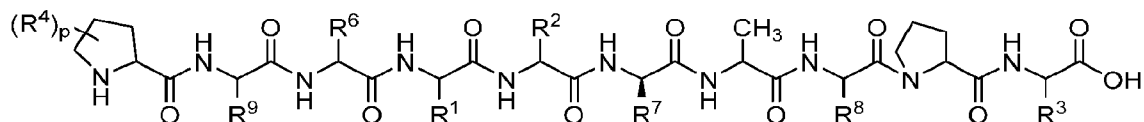


10 In certain embodiments, the compound has the structure of formula (I-7L):



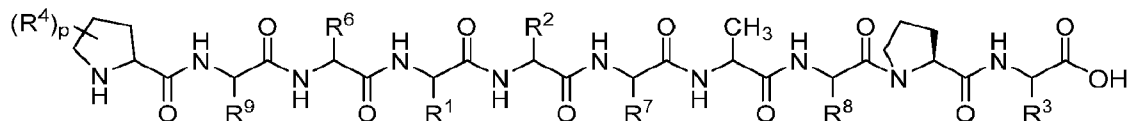
(I-7L).

Alternatively, the compound may have the structure of formula (I-7D):



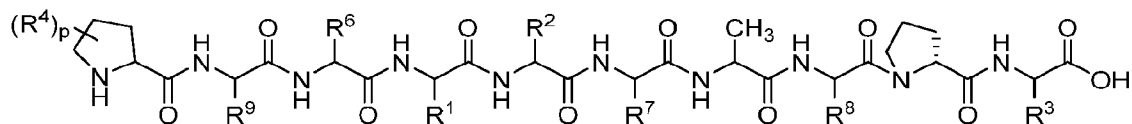
15 (I-7D).

In certain embodiments, the compound has the structure of formula (I-11L):



(I-11L).

Alternatively, the compound may have the structure of formula (I-11D):

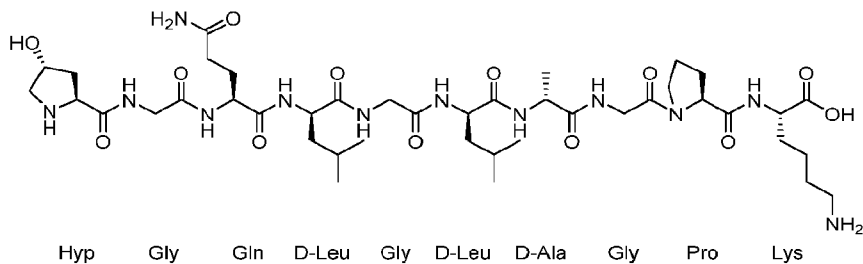


(I-11D).

In certain embodiments, R^8 is $-\text{CH}_3$ or $-\text{H}$, preferably $-\text{H}$.

In certain embodiments, R^9 is $-\text{CH}_3$ or $-\text{H}$, preferably $-\text{H}$.

5 In certain embodiments, the compound is



, or a pharmaceutically acceptable salt thereof.

In certain embodiments, the compound is a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys;

10 or a pharmaceutically acceptable salt and/or stereoisomer thereof; wherein Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me).

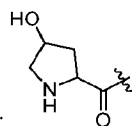
In certain such embodiments, at least one, at least two, at least three, at least four, at least five, at least six, or at least seven amino acid residues in the peptide are
15 D-amino acid residues.

The peptide may be a variant of a collagen type II $\alpha 1$ -derived peptide. The collagen type II $\alpha 1$ may be isolated from the extracellular matrix derived from animal chondrocytes.

The term “peptide” used in the present invention refers to a compound in
20 which two or more amino acids are linked by a peptide bond. Further, it is classified into dipeptide, tripeptide, tetrapeptide, and the like according to the number of constituent amino acids. An oligopeptide has about 10 or fewer peptide bonds, and a polypeptide has a plurality of peptide bonds. In addition, a peptide in the present invention includes a mutated peptide in which its amino acid residue is substituted.

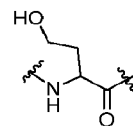
25 The term “HyP” used in the present invention refers to an amino acid called hydroxyproline, in which a hydroxyl group ($-\text{OH}$) is bonded to the carbon atom at the

4-position of proline. HyP has a structure of $C_5H_9NO_3$ and may be depicted as



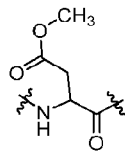
follows: . HyP may include all isomers. In addition, HyP may be an isomer represented by the stereochemistry of “2S,4R” unless otherwise specified.

The term “homo-Ser” used in the present invention is called homoserine and
5 refers to an α -amino acid having a hydroxyl group in the side chain. Homo-Ser is an intermediate present in the biosynthesis of threonine and methionine in



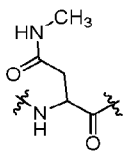
microorganisms and plants. Homo-Ser may be depicted as follows:

The term “Asp(Me)” used in the present invention indicates an amino acid in
10 which the hydrogen atom of the hydroxyl group (OH) bonded to the carbon atom at the 4-position of aspartic acid is substituted by a methyl group (CH_3). Asp(Me) may



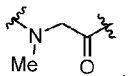
be depicted as follows:

The term “Asn(Me)” used in the present invention indicates an amino acid in
which the hydrogen atom of the amine group (NH_2) bonded to the carbon atom at the
4-position of asparagine is substituted by a methyl group (CH_3). Asn(Me) may be



15 depicted as follows:

The term “(N-Me)Gly” used in the present invention indicates an amino acid in
which the hydrogen atom of the amine group (NH_2) bonded to the carbon atom at the
2-position of glycine is replaced by a methyl group (CH_3). (N-Me)Gly may be



depicted as follows:

20 In certain embodiments, the compound is a peptide having an amino acid sequence represented by HyP-Gly-Gln-Asp-Xaa-Leu-Ala-Gly-Pro-Lys; or a pharmaceutically acceptable salt and/or stereoisomer thereof;

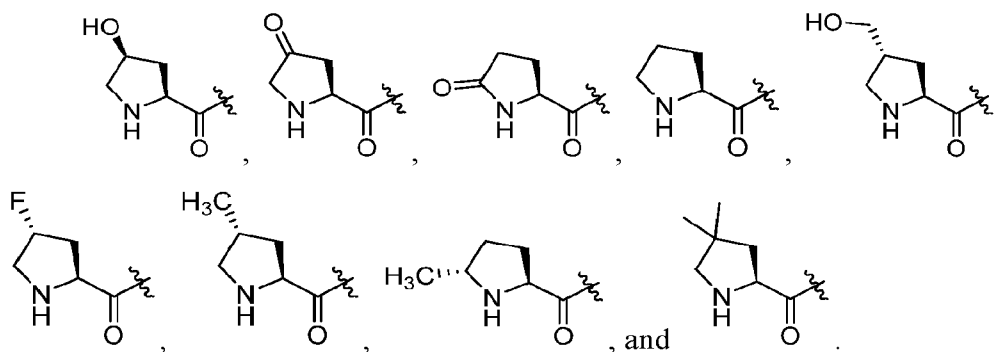
wherein Xaa is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly.

In certain such embodiments, at least one, at least two, at least three, at least four, at least five, at least six, or at least seven amino acid residues in the peptide are
 5 D-amino acid residues.

In certain embodiments, the compound is a peptide having an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xaa;
 or a pharmaceutically acceptable salt and/or stereoisomer thereof;
 wherein Xaa is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH).

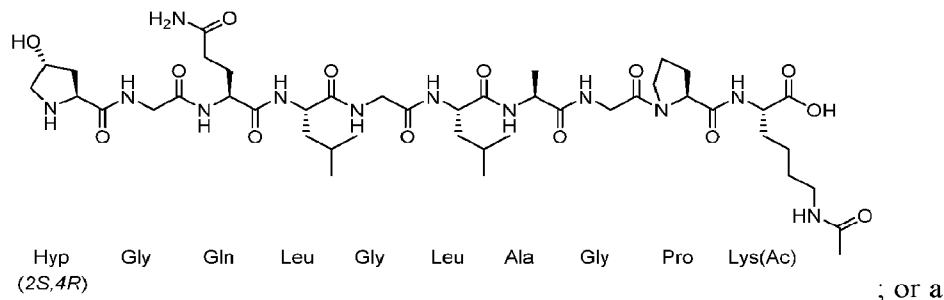
10 In certain such embodiments, at least one, at least two, at least three, at least four, at least five, at least six, or at least seven amino acid residues in the peptide are D-amino acid residues.

In certain embodiments, the compound is a peptide having an amino acid sequence represented by Xaa-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;
 15 or a pharmaceutically acceptable salt and/or stereoisomer thereof;
 wherein Xaa is selected from:



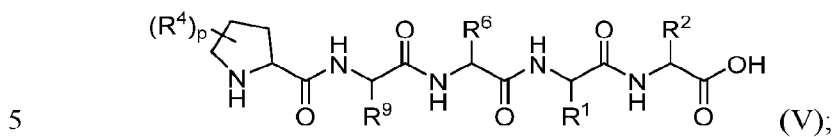
In certain such embodiments, at least one, at least two, at least three, at least four, at least five, at least six, or at least seven amino acid residues in the peptide are
 20 D-amino acid residues.

In certain embodiments, the invention provides a compound having the following structure:



pharmaceutically acceptable salt thereof.

In certain embodiments, the invention provides a compound represented by Formula (V):



or a pharmaceutically acceptable salt thereof;

wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^9 is hydrogen or alkyl.

In certain embodiments, R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

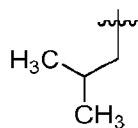
R^4 for each occurrence is hydroxyl;

p is 1;

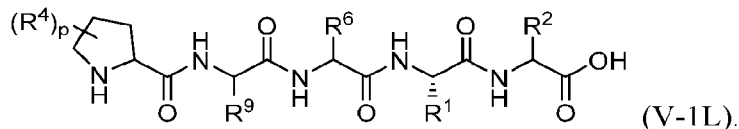
R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

R^9 is hydrogen.

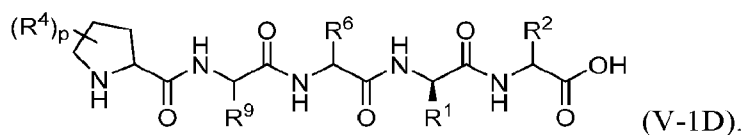
In certain embodiments, R^1 is substituted or unsubstituted alkyl, such as



In certain embodiments, the compound has the structure of formula (V-1L)



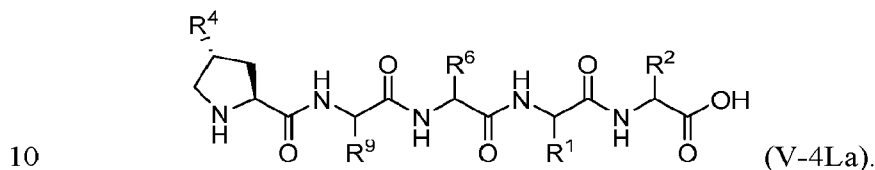
5 Alternatively, the compound may have the structure of formula (V-1D)



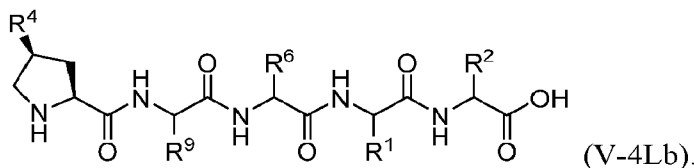
In certain embodiments, R^2 is H.

In certain embodiments, p is 1 and R^4 is hydroxyl.

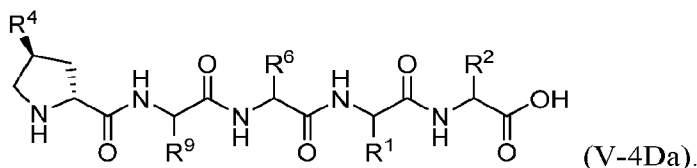
In certain embodiments, the compound has the structure of formula (V-4La):



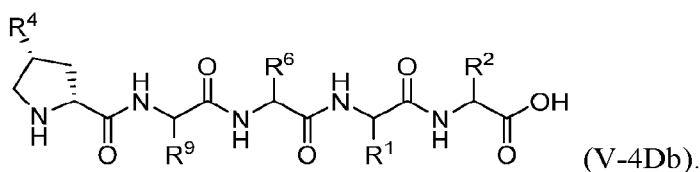
In certain embodiments, the compound has the structure of formula (V-4Lb):



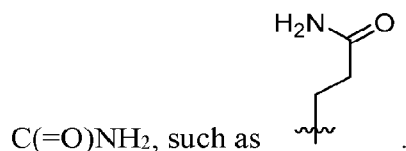
In certain embodiments, the compound has the structure of formula (V-4Da):



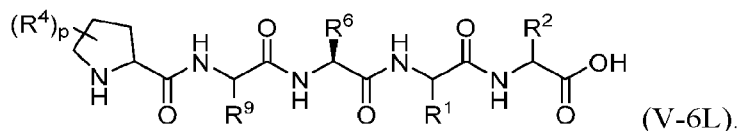
15 In certain embodiments, the compound has the structure of formula (V-4Db):



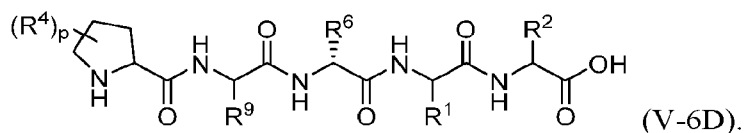
In certain embodiments, R⁶ is alkyl substituted with one occurrence of -



In certain embodiments, the compound has the structure of formula (V-6L):

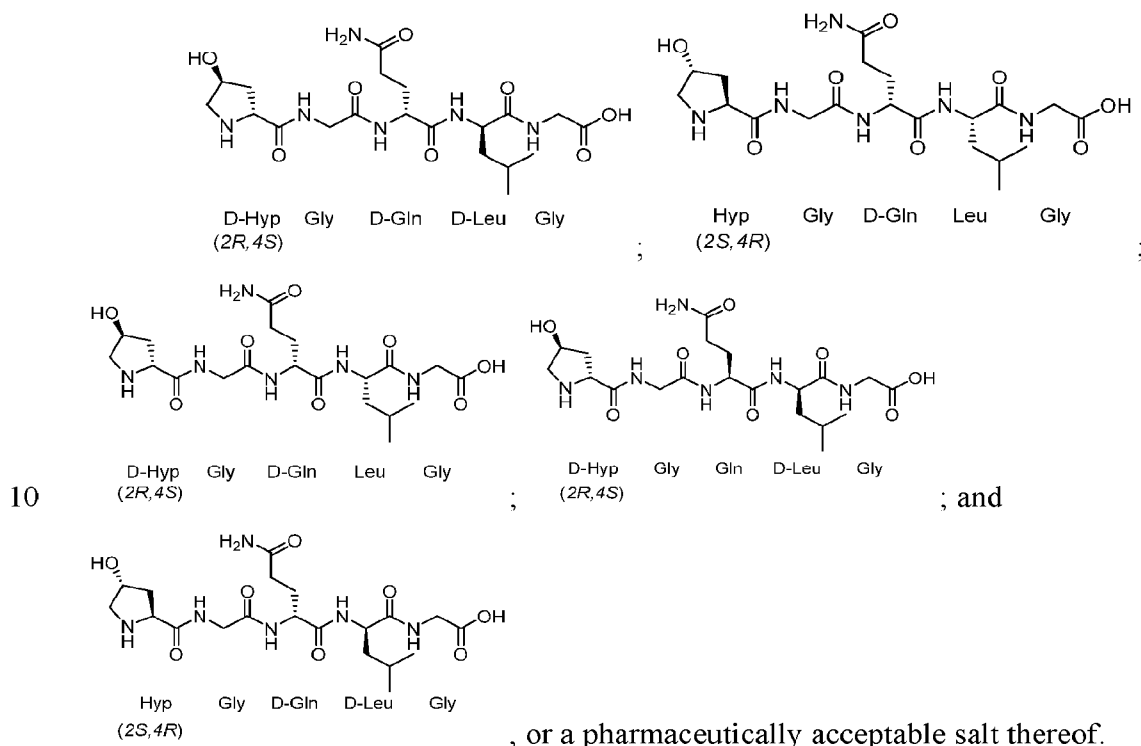


Alternatively, the compound may have the structure of formula (V-6D):

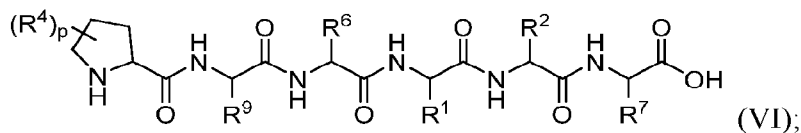


In certain embodiments, R⁹ is -H.

In certain embodiments, the compound is selected from the following:



In certain embodiments, the invention provides a compound represented by Formula (VI):



or a pharmaceutically acceptable salt thereof;

wherein:

- R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

- R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

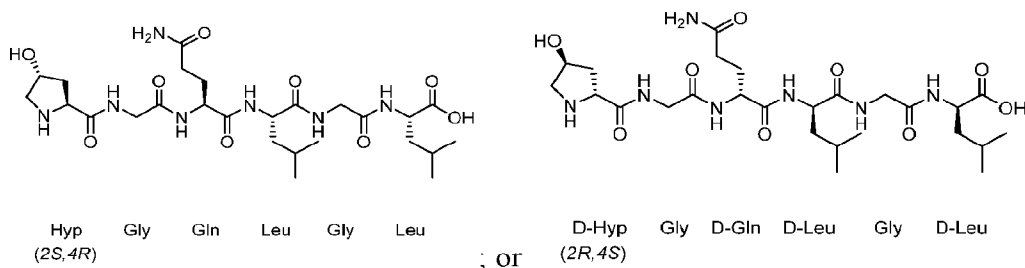
p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 is hydrogen or alkyl; and

R^9 is hydrogen or alkyl.

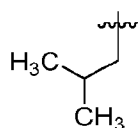
- In certain embodiments, the invention provides a compound represented by Formula (VI), wherein the compound is not:



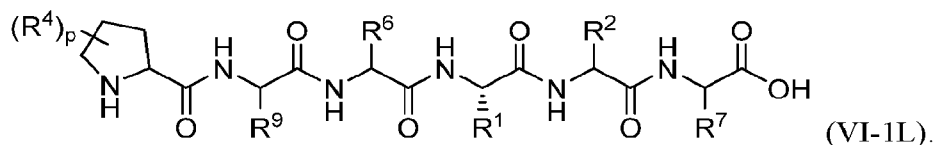
In certain embodiments:

- R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;
- R^4 for each occurrence is hydroxyl;
- p is 1;
- R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and
- R^9 is hydrogen.

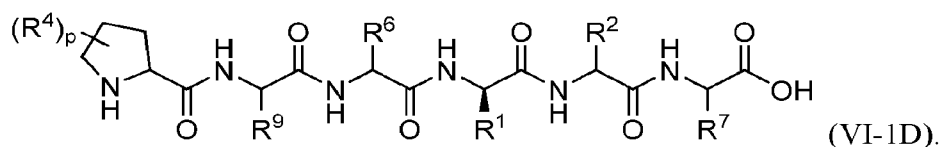
In certain embodiments, R^1 is substituted or unsubstituted alkyl, such as



In certain embodiments, the compound has the structure of formula (VI-1L)



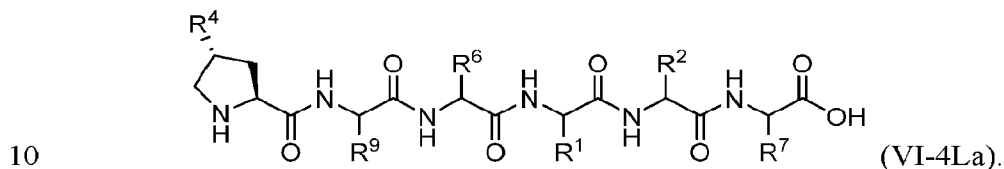
5 Alternatively, the compound may have the structure of formula (VI-1D)



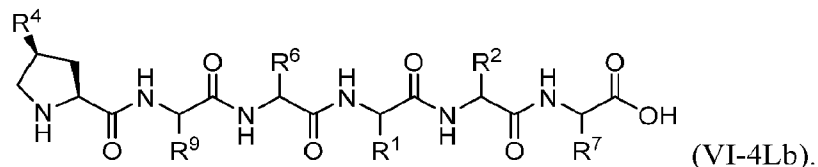
In certain embodiments, R^2 is H.

In certain embodiments, p is 1 and R^4 is hydroxyl.

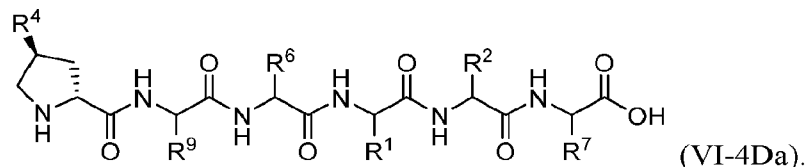
In certain embodiments, the compound has the structure of formula (VI-4La):



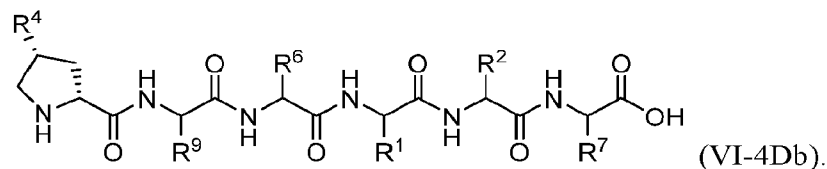
In certain embodiments, the compound has the structure of formula (VI-4Lb):



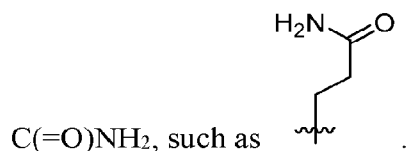
In certain embodiments, the compound has the structure of formula (VI-4Da):



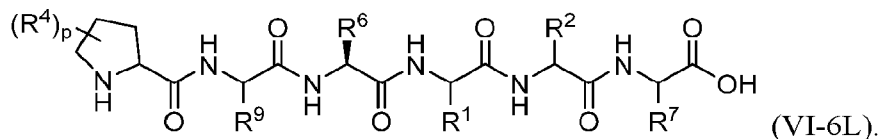
15 In certain embodiments, the compound has the structure of formula (VI-4Db):



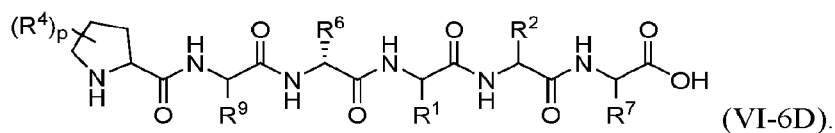
In certain embodiments, R⁶ is alkyl substituted with one occurrence of -



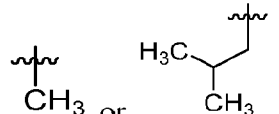
In certain embodiments, the compound has the structure of formula (VI-6L):



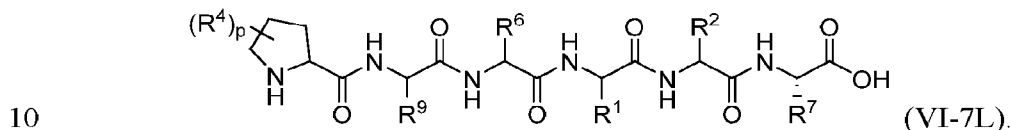
5 Alternatively, the compound may have the structure of formula (VI-6D):



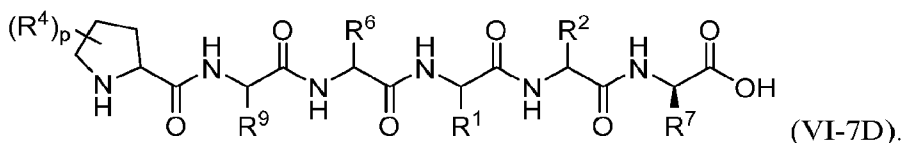
In certain embodiments, R⁹ is -H.

In certain embodiments, R⁷ is (C₁-C₁₀)alkyl, such as .

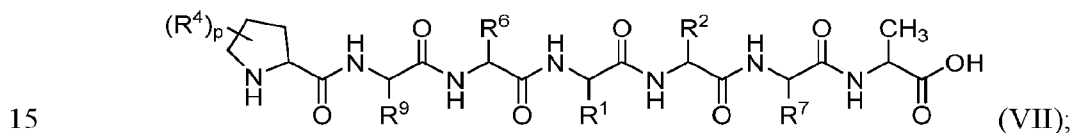
In certain embodiments, the compound has the structure of formula (VI-7L):



Alternatively, the compound may have the structure of formula (VI-7D):



In certain embodiments, the invention provides a compound represented by Formula (VII):



or a pharmaceutically acceptable salt thereof;

wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 is hydrogen or alkyl; and

R^9 is hydrogen or alkyl.

In certain embodiments:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

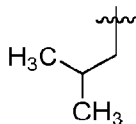
R^4 for each occurrence is hydroxyl;

p is 1;

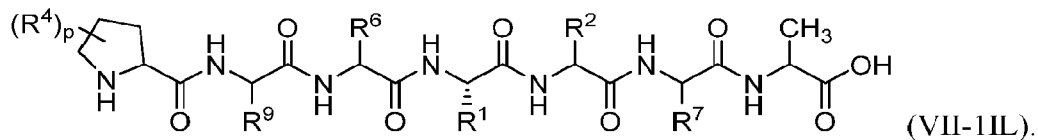
R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

R^9 is hydrogen.

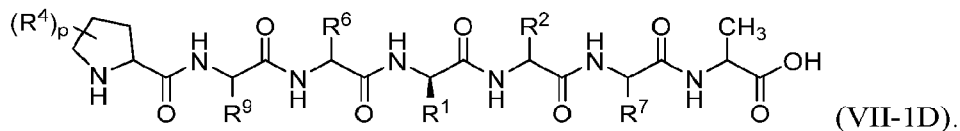
In certain embodiments, R^1 is substituted or unsubstituted alkyl, such as



In certain embodiments, the compound has the structure of formula (VII-1L)



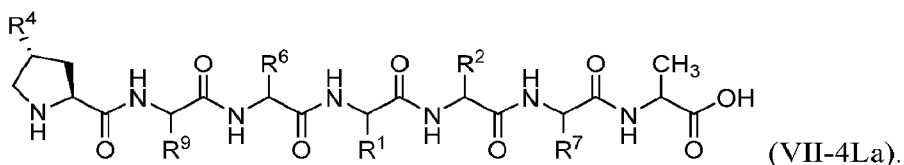
Alternatively, the compound may have the structure of formula (VII-1D)



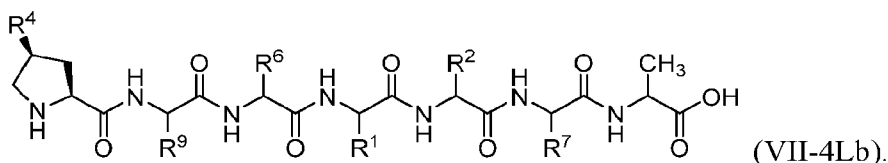
In certain embodiments, R^2 is H.

In certain embodiments, p is 1 and R^4 is hydroxyl.

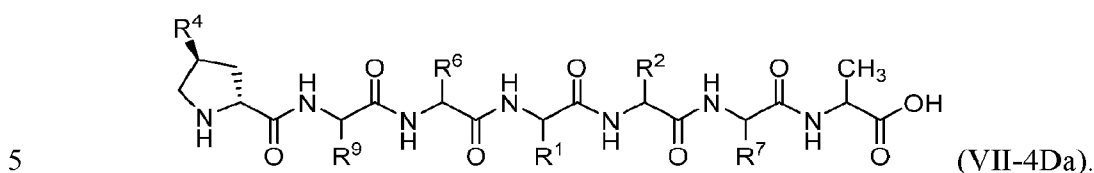
In certain embodiments, the compound has the structure of formula (VII-4La):



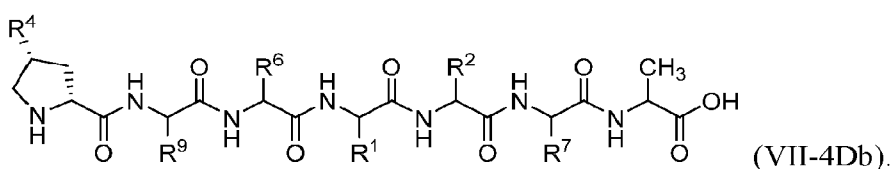
In certain embodiments, the compound has the structure of formula (VII-4Lb):



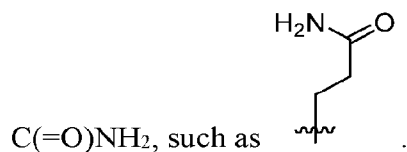
In certain embodiments, the compound has the structure of formula (VII-4Da):



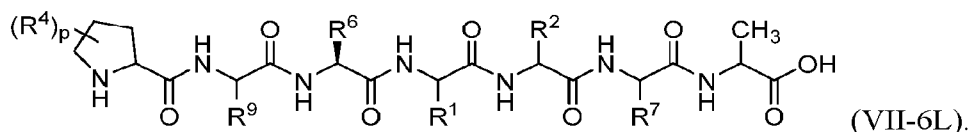
In certain embodiments, the compound has the structure of formula (VII-4Db):



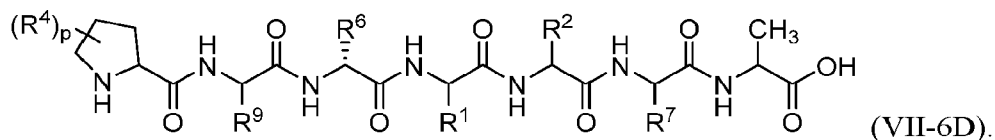
In certain embodiments, R⁶ is alkyl substituted with one occurrence of -



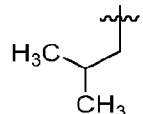
10 In certain embodiments, the compound has the structure of formula (VII-6L):



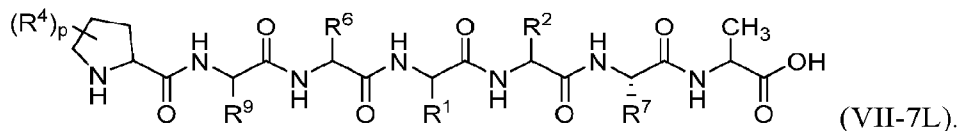
Alternatively, the compound may have the structure of formula (VII-6D):



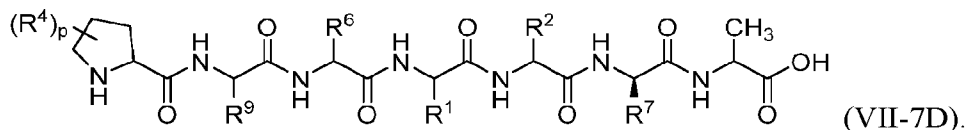
In certain embodiments, R⁹ is -H.

In certain embodiments, R^7 is (C₁-C₁₀)alkyl, such as  or .

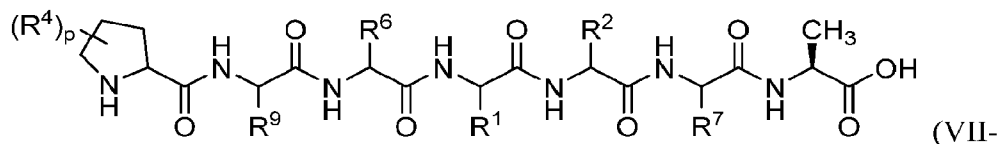
In certain embodiments, the compound has the structure of formula (VII-7L):



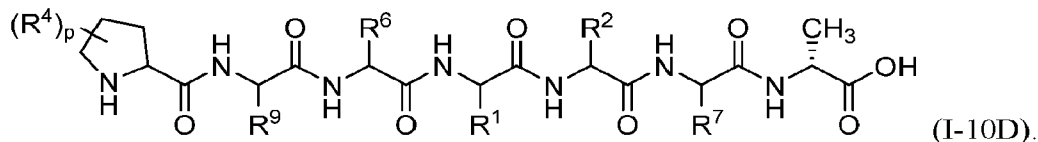
Alternatively, the compound may have the structure of formula (VII-7D):



In certain embodiments, the compound has the structure of formula (VII-10L):



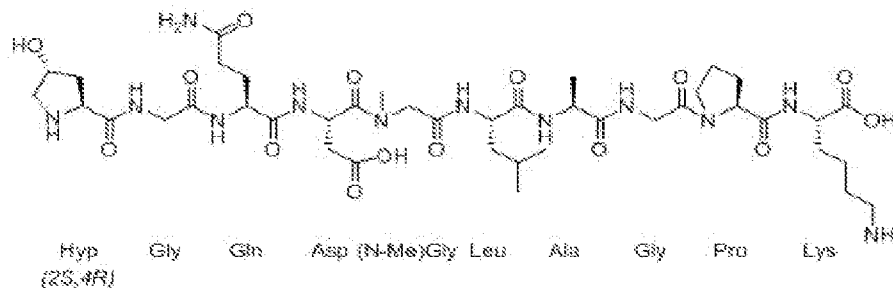
Alternatively, the compound may have the structure of formula VII-10D):



The invention also provides a salt of a compound represented by Formula 8:

[Formula 8]; and

a salt of a compound represented by Formula 10:



[Formula

15 10].

In certain embodiments, the compound may be a prodrug, e.g., wherein a hydroxyl in the parent compound is presented as an ester or a carbonate, a carboxylic

acid present in the parent compound is presented as an ester, or an amino group is presented as an amide. In certain such embodiments, the prodrug is metabolized to the active parent compound in vivo (e.g., the ester is hydrolyzed to the corresponding hydroxyl or carboxylic acid).

5 In certain embodiments, compounds of the invention may be racemic. In certain embodiments, compounds of the invention may be enriched in one enantiomer. For example, a compound of the invention may have greater than 30% ee, 40% ee, 50% ee, 60% ee, 70% ee, 80% ee, 90% ee, or even 95% or greater ee.

 The compounds of the invention have more than one stereocenter.

10 Accordingly, the compounds of the invention may be enriched in one or more diastereomers. For example, a compound of the invention may have greater than 30% de, 40% de, 50% de, 60% de, 70% de, 80% de, 90% de, or even 95% or greater de. In certain embodiments, the compounds of the invention have substantially one isomeric configuration at one or more stereogenic centers, and have multiple isomeric
15 configurations at the remaining stereogenic centers.

 In certain embodiments, the enantiomeric excess of a given stereocenter in the compound is at least 40% ee, 50% ee, 60% ee, 70% ee, 80% ee, 90% ee, 92% ee, 94% ee, 95% ee, 96% ee, 98% ee or greater ee.

 As used herein, single bonds drawn without stereochemistry do not indicate
20 the stereochemistry of the compound. The compound of formula (I) provides an example of a compound for which no stereochemistry is indicated.

 As used herein, hashed or bolded wedge bonds indicate absolute stereochemical configuration.

 In certain embodiments, a therapeutic preparation of the compound of the
25 invention may be enriched to provide predominantly one enantiomer of a compound. An enantiomerically enriched mixture may comprise, for example, at least 60 mol percent of one enantiomer, or more preferably at least 75, 90, 95, or even 99 mol percent. In certain embodiments, the compound enriched in one enantiomer is substantially free of the other enantiomer, wherein substantially free means that the
30 substance in question makes up less than 10%, or less than 5%, or less than 4%, or less than 3%, or less than 2%, or less than 1% as compared to the amount of the other enantiomer, *e.g.*, in the composition or compound mixture. For example, if a composition or compound mixture contains 98 grams of a first enantiomer and 2

grams of a second enantiomer, it would be said to contain 98 mol percent of the first enantiomer and only 2% of the second enantiomer.

In certain embodiments, a therapeutic preparation may be enriched to provide predominantly one diastereomer of the compound of the invention. A

5 diastereomerically enriched mixture may comprise, for example, at least 60 mol percent of one diastereomer, or more preferably at least 75, 90, 95, or even 99 mol percent.

Methods of Treatment

In certain aspect, provided herein are methods of preventing or treating an IL-
10 1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine mediated disease or disorder in a subject, comprising administering to the subject a compound disclosed herein.

In some embodiments, the subject has elevated levels of IL-1 α , IL-1 β , IL-2,
15 IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine.

In some embodiments, the IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine mediated disease is an autoimmune disease,
20 an inflammatory disease, or a cancer, such as Acute posterior multifocal placoid pigment epitheliopathy (APMPPE), Agammaglobulinemia, Alopecia Areata, Amyloidosis, Amyotrophic lateral sclerosis (ALS), Aniridia, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune hepatitis, Autoimmune inner ear disease, Autoimmune Lymphoproliferative Syndrome, Atopic
25 dermatitis, Asthma, Behçet's Disease, Best Disease, Birdshot Chorioretinopathy, Blepharitis, Bronchiolitis, Cancer (Chondrosarcoma, Cervical, Breast, Lung), Capillary Leak Syndrome, Castleman disease, Celiac disease, Chagas disease, Chalazia and Sty, Chandler's syndrome, Cholesteatoma of Middle Ear, Choroideremia, Chronic recurrent multifocal osteomyelitis, Cogan's syndrome,
30 Collagen Induced Arthritis (CIA), Cold agglutinin disease, Cone Rod Dystrophies, Conjunctivitis, Corneal Wound Healing, CREST syndrome, Crohn's disease, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dry Eye

Disease (DED), Dry macular degeneration (Dry AMD), Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Essential Iris Atrophy, Evan's syndrome, Farmer's Lung, Fibromyalgia, Giant cell arteritis, Giant cell myocarditis, Giant Papillary Conjunctivitis, Glomerulonephritis, Goodpasture's syndrome, Graft-Versus-Host Disease, Granulomatosis with polyangiitis, Graves' disease, Guillain-Barre syndrome, Gyrate Atrophy, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Hypogammaglobulinemia, Hypoproliferative anemia, IgA Nephropathy, Inclusion body myositis, Interstitial cystitis, Inflammatory Bowel Disease, Iritis, Irritant Dermatitis, Juvenile arthritis, Juvenile/Type 1 Diabetes, Juvenile macular degeneration, Juvenile myositis, Juvenile X-linked Retinoschisis, Kawasaki syndrome, Keratitis, Keratoconjunctivitis sicca (Dry Eye), Late-Onset Retinal Degeneration (L-ORD), Lichen planus, Lichen sclerosus, Lupus (SLE), Macular Edema, Meniere's disease, Multiple sclerosis, Myasthenia gravis, Microscopic polyangiitis, Neuropathic Corneal Pain, Neurotropic Keratitis, Ocular Allergy, Ocular Inflammation (uveitis), Ocular Pain, Ocular Neurodegeneration, Optic Nerve Atrophy, Optic neuritis, Oral Submucous Fibrosis, Osteoarthritis (OA), Osteoporosis, Parkinson's disease, Pars Planitis, Pemphigus, Photokeratitis, Polyarteritis nodosa, Polymyalgia rheumatica, Polymyositis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleritis, Sjogren's syndrome, Stargardt Disease, Stickler Syndrome, Temporal arteritis/Giant cell arteritis, Thyroid Eye Disease, Trachoma, Transverse myelitis, Trichiasis, Ulcerative colitis, Usher Syndrome, Uveitis, Vasculitis, Vitiligo, Viral myocarditis, or Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)), Wet macular degeneration, or Wound Healing.

25 In some preferred embodiments, the IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas and/or TIMP-1 mediated disease is an autoimmune disease, an inflammatory disease, or a cancer, such as Acute posterior multifocal placoid pigment epitheliopathy (APMPPE), Agammaglobulinemia, Alopecia Areata, Amyloidosis, Amyotrophic lateral sclerosis (ALS), Aniridia, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune hepatitis, Autoimmune inner ear disease, Autoimmune Lymphoproliferative Syndrome, Atopic dermatitis, Asthma, Behçet's Disease, Best Disease, Birdshot Chorioretinopathy, Blepharitis, Bronchiolitis, Cancer

(Chondrosarcoma, Cervical, Breast, Lung), Capillary Leak Syndrome, Castleman disease, Celiac disease, Chagas disease, Chalazia and Sty, Chandler's syndrome, Cholesteatoma of Middle Ear, Choroideremia, Chronic recurrent multifocal osteomyelitis, Cogan's syndrome, Collagen Induced Arthritis (CIA), Cold agglutinin disease, Cone Rod Dystrophies, Conjunctivitis, Corneal Wound Healing, CREST syndrome, Crohn's disease, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dry macular degeneration (Dry AMD), Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Essential Iris Atrophy, Evan's syndrome, Farmer's Lung, Fibromyalgia, Giant cell arteritis, Giant cell myocarditis, Giant Papillary Conjunctivitis, Glomerulonephritis, Goodpasture's syndrome, Graft-Versus-Host Disease, Granulomatosis with polyangiitis, Graves' disease, Guillain-Barre syndrome, Gyrate Atrophy, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Hypogammaglobulinemia, Hypoproliferative anemia, IgA Nephropathy, Inclusion body myositis, Interstitial cystitis, Inflammatory Bowel Disease, Iritis, Irritant Dermatitis, Juvenile arthritis, Juvenile/Type 1 Diabetes, Juvenile macular degeneration, Juvenile myositis, Juvenile X-linked Retinoschisis, Kawasaki syndrome, Keratitis, Late-Onset Retinal Degeneration (L-ORD), Lichen planus, Lichen sclerosus, Lupus (SLE), Macular Edema, Meniere's disease, Multiple sclerosis, Myasthenia gravis, Microscopic polyangiitis, Neuropathic Corneal Pain, Neurotropic Keratitis, Ocular Allergy, Ocular Inflammation (uveitis), Ocular Pain, Ocular Neurodegeneration, Optic Nerve Atrophy, Optic neuritis, Oral Submucous Fibrosis, Osteoarthritis (OA), Osteoporosis, Parkinson's disease, Pars Planitis, Pempigus, Photokeratitis, Polyarteritis nodosa, Polymyalgia rheumatica, Polymyositis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleritis, Sjogren's syndrome, Stargardt Disease, Stickler Syndrome, Temporal arteritis/Giant cell arteritis, Thyroid Eye Disease, Trachoma, Transverse myelitis, Trichiasis, Ulcerative colitis, Usher Syndrome, Uveitis, Vasculitis, Vitiligo, Viral myocarditis, or Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)), Wound Healing.

In some preferred embodiments, the disease or disorder is Dry Eye Disease (DED), Inflammatory Bowel Disease, Keratoconjunctivitis sicca (Dry Eye), Osteoporosis, or Rheumatoid arthritis.

In further preferred embodiments, the disease or disorder is Inflammatory Bowel Disease.

In further preferred embodiments, the disease or disorder is Keratoconjunctivitis sicca (Dry Eye).

5 In further preferred embodiments, the disease or disorder is Osteoporosis.

In further preferred embodiments, the disease or disorder is Rheumatoid arthritis.

In further preferred embodiments, the disease or disorder is Dry Eye Disease (DED)

10 In a further aspect, provided are methods of reducing production of IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine in cells of a subject, comprising administering to a subject a compound disclosed herein.

In some embodiments, administering the compound reduces the cytokine
15 and/or chemokine levels by at least 30%, at least 50%, or at least 70% compared to the untreated control.

In yet another aspect, provided are methods of reducing NF- κ B transcription activity in cells of a subject, comprising administering to a subject a compound disclosed herein.

20 In some embodiments, the subject is a mammal, such as a mouse or a human, preferably a human.

In another aspect, provided are methods of preventing or treating Keratoconjunctivitis sicca (Dry Eye) in a subject, comprising administering to the subject a compound disclosed herein.

25 In yet another aspect, provided are methods of preventing or treating Dry Eye Disease (DED) in a subject, comprising administering to the subject a compound disclosed herein.

Pharmaceutical Compositions

In certain embodiments, the invention provides a pharmaceutical composition
30 comprising a salt or compound of the invention, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

In certain embodiments, the pharmaceutical composition is formulated for topical administration to the eye, e.g., as eye drops.

In certain embodiments at least 50%, 60%, 70%, 80%, or 90% of the compound is present as a salt. Preferably, at least 95% of the compound is present as a salt.
5 a salt. Even more preferably, at least 99% of the compound is present as a salt.

In certain embodiments, the present invention provides a pharmaceutical preparation suitable for use in a human patient, comprising any salt or compound of the invention, and one or more pharmaceutically acceptable excipients. In certain embodiments, the pharmaceutical preparations may be for use in treating or
10 preventing a condition or disease as described herein. In certain embodiments, the pharmaceutical preparations have a low enough pyrogen activity to be suitable for use in a human patient.

One embodiment of the present invention provides a pharmaceutical kit comprising a salt or compound of the invention, or a pharmaceutically acceptable salt
15 thereof, and optionally directions on how to administer the compound.

The compositions and methods of the present invention may be utilized to treat an individual in need thereof. In certain embodiments, the individual is a mammal such as a human, or a non-human mammal. When administered to an animal, such as a human, the composition or the compound is preferably administered
20 as a pharmaceutical composition comprising, for example, a compound of the invention and a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers are well known in the art and include, for example, aqueous solutions such as water or physiologically buffered saline or other solvents or vehicles such as glycols, glycerol, oils such as olive oil, or injectable organic esters. In certain preferred
25 embodiments, when such pharmaceutical compositions are for human administration, particularly for invasive routes of administration (i.e., routes, such as injection or implantation, that circumvent transport or diffusion through an epithelial barrier), the aqueous solution is pyrogen-free, or substantially pyrogen-free. The excipients can be chosen, for example, to effect delayed release of an agent or to selectively target one
30 or more cells, tissues or organs. The pharmaceutical composition can be in dosage unit form such as tablet, capsule (including sprinkle capsule and gelatin capsule), granule, lyophile for reconstitution, powder, solution, syrup, suppository, injection or the like. The composition can also be present in a transdermal delivery system, e.g., a

skin patch. The composition can also be present in a solution suitable for topical administration, such as an eye drop.

A pharmaceutically acceptable carrier can contain physiologically acceptable agents that act, for example, to stabilize, increase solubility or to increase the
5 absorption of a compound such as a compound of the invention. Such physiologically acceptable agents include, for example, carbohydrates, such as glucose, sucrose or dextrans, antioxidants, such as ascorbic acid or glutathione, chelating agents, low molecular weight proteins or other stabilizers or excipients. The choice of a pharmaceutically acceptable carrier, including a physiologically acceptable agent,
10 depends, for example, on the route of administration of the composition. The preparation or pharmaceutical composition can be a selfemulsifying drug delivery system or a selfmicroemulsifying drug delivery system. The pharmaceutical composition (preparation) also can be a liposome or other polymer matrix, which can have incorporated therein, for example, a compound of the invention. Liposomes, for
15 example, which comprise phospholipids or other lipids, are nontoxic, physiologically acceptable and metabolizable carriers that are relatively simple to make and administer.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope
20 of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically acceptable carrier" as used herein means a pharmaceutically acceptable material, composition or vehicle, such as a liquid or solid
25 filler, diluent, excipient, solvent or encapsulating material. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically acceptable carriers include: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and
30 cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10)

glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) phosphate buffer solutions; and (21) other non-toxic compatible substances employed in pharmaceutical formulations.

A pharmaceutical composition (preparation) can be administered to a subject by any of a number of routes of administration including, for example, orally (for example, drenches as in aqueous or non-aqueous solutions or suspensions, tablets, capsules (including sprinkle capsules and gelatin capsules), boluses, powders, granules, pastes for application to the tongue); absorption through the oral mucosa (e.g., sublingually); anally, rectally or vaginally (for example, as a pessary, cream or foam); parenterally (including intramuscularly, intravenously, subcutaneously or intrathecally as, for example, a sterile solution or suspension); nasally; intraperitoneally; subcutaneously; transdermally (for example as a patch applied to the skin); and topically (for example, as a cream, ointment or spray applied to the skin, or as an eye drop). The compound may also be formulated for inhalation. In certain embodiments, a compound may be simply dissolved or suspended in sterile water. Details of appropriate routes of administration and compositions suitable for same can be found in, for example, U.S. Pat. Nos. 6,110,973, 5,763,493, 5,731,000, 5,541,231, 5,427,798, 5,358,970 and 4,172,896, as well as in patents cited therein.

The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the particular mode of administration. The amount of active ingredient that can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, out of one hundred percent, this amount will range from about 1 percent to about ninety-nine percent of active ingredient, preferably from about 5 percent to about 70 percent, most preferably from about 10 percent to about 30 percent.

Methods of preparing these formulations or compositions include the step of bringing into association an active compound, such as a compound of the invention,

with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association a compound of the present invention with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

5 Formulations of the invention suitable for oral administration may be in the form of capsules (including sprinkle capsules and gelatin capsules), cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), lyophile, powders, granules, or as a solution or a suspension in an aqueous or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or
10 syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouth washes and the like, each containing a predetermined amount of a compound of the present invention as an active ingredient. Compositions or compounds may also be administered as a bolus, electuary or paste

 To prepare solid dosage forms for oral administration (capsules (including
15 sprinkle capsules and gelatin capsules), tablets, pills, dragees, powders, granules and the like), the active ingredient is mixed with one or more pharmaceutically acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, alginates,
20 gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds; (7) wetting agents, such as, for example, cetyl alcohol and
25 glycerol monostearate; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; (10) complexing agents, such as, modified and unmodified cyclodextrins; and (11) coloring agents. In the case of capsules (including sprinkle capsules and gelatin capsules), tablets and pills, the
30 pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

The tablets, and other solid dosage forms of the pharmaceutical compositions, such as dragees, capsules (including sprinkle capsules and gelatin capsules), pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions that can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

Liquid dosage forms useful for oral administration include pharmaceutically acceptable emulsions, lyophiles for reconstitution, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents commonly used in the art, such as, for example, water or other solvents, cyclodextrins and derivatives thereof, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ (e.g., wheat germ), olive, castor and

sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring,
5 coloring, perfuming and preservative agents.

Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

10 Formulations of the pharmaceutical compositions for rectal, vaginal, or urethral administration may be presented as a suppository, which may be prepared by mixing one or more active compounds with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at
15 body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound.

Formulations of the pharmaceutical compositions for administration to the mouth may be presented as a mouthwash, or an oral spray, or an oral ointment.

Alternatively or additionally, compositions can be formulated for delivery via
20 a catheter, stent, wire, or other intraluminal device. Delivery via such devices may be especially useful for delivery to the bladder, urethra, ureter, rectum, or intestine.

Formulations which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such carriers as are known in the art to be appropriate.

25 Dosage forms for the topical or transdermal administration include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants that may be required.

30 The ointments, pastes, creams and gels may contain, in addition to an active compound, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

Powders and sprays can contain, in addition to an active compound, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

Transdermal patches have the added advantage of providing controlled delivery of a compound of the present invention to the body. Such dosage forms can be made by dissolving or dispersing the active compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the compound in a polymer matrix or gel.

Ophthalmic formulations, eye ointments, powders, solutions and the like, are also contemplated as being within the scope of this invention. Exemplary ophthalmic formulations are described in U.S. Publication Nos. 2005/0080056, 2005/0059744, 2005/0031697 and 2005/004074 and U.S. Patent No. 6,583,124, the contents of which are incorporated herein by reference. If desired, liquid ophthalmic formulations have properties similar to that of lacrimal fluids, aqueous humor or vitreous humor or are compatible with such fluids. A preferred route of administration is local administration (*e.g.*, topical administration, such as eye drops, or administration via an implant).

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

Pharmaceutical compositions suitable for parenteral administration comprise one or more active compounds in combination with one or more pharmaceutically acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

Examples of suitable aqueous and nonaqueous carriers that may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents that delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution, which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsulated matrices of the subject compounds in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer, and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions that are compatible with body tissue.

For use in the methods of this invention, active compounds can be given per se or as a pharmaceutical composition containing, for example, 0.1 to 99.5% (more preferably, 0.5 to 90%) of active ingredient in combination with a pharmaceutically acceptable carrier.

Methods of introduction may also be provided by rechargeable or biodegradable devices. Various slow release polymeric devices have been developed and tested *in vivo* in recent years for the controlled delivery of drugs, including proteinacious biopharmaceuticals. A variety of biocompatible polymers (including hydrogels), including both biodegradable and non-degradable polymers, can be used to form an implant for the sustained release of a compound at a particular target site.

Actual dosage levels of the active ingredients in the pharmaceutical compositions may be varied so as to obtain an amount of the active ingredient that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

The selected dosage level will depend upon a variety of factors including the activity of the particular compound or combination of compounds employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion of the particular compound(s) being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound(s) employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the therapeutically effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the pharmaceutical composition or compound at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved. By “therapeutically effective amount” is meant the concentration of a compound that is sufficient to elicit the desired therapeutic effect. It is generally understood that the effective amount of the compound will vary according to the weight, sex, age, and medical history of the subject. Other factors which influence the effective amount may include, but are not limited to, the severity of the patient's condition, the disorder being treated, the stability of the compound, and, if desired, another type of therapeutic agent being administered with the compound of the invention. A larger total dose can be delivered by multiple administrations of the agent. Methods to determine efficacy and dosage are known to

those skilled in the art (Isselbacher *et al.* (1996) Harrison's Principles of Internal Medicine 13 ed., 1814-1882, herein incorporated by reference).

In general, a suitable daily dose of an active compound used in the compositions and methods of the invention will be that amount of the compound that
5 is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above.

If desired, the effective daily dose of the active compound may be administered as one, two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage
10 forms. In certain embodiments of the present invention, the active compound may be administered two or three times daily. In preferred embodiments, the active compound will be administered once daily.

The patient receiving this treatment is any animal in need, including primates, in particular humans, and other mammals such as equines, cattle, swine and sheep;
15 and poultry and pets in general.

In certain embodiments, compounds of the invention may be used alone or conjointly administered with another type of therapeutic agent. As used herein, the phrase "conjoint administration" refers to any form of administration of two or more different therapeutic compounds such that the second compound is administered while
20 the previously administered therapeutic compound is still effective in the body (*e.g.*, the two compounds are simultaneously effective in the patient, which may include synergistic effects of the two compounds). For example, the different therapeutic compounds can be administered either in the same formulation or in a separate formulation, either concomitantly or sequentially. In certain embodiments, the
25 different therapeutic compounds can be administered within one hour, 12 hours, 24 hours, 36 hours, 48 hours, 72 hours, or a week of one another. Thus, an individual who receives such treatment can benefit from a combined effect of different therapeutic compounds.

In certain embodiments, conjoint administration of compounds of the
30 invention with one or more additional therapeutic agent(s) provides improved efficacy relative to each individual administration of the compound of the invention (*e.g.*, a compound of formula I, V, VI, or VII) or the one or more additional therapeutic agent(s). In certain such embodiments, the conjoint administration provides an

additive effect, wherein an additive effect refers to the sum of each of the effects of individual administration of the compound of the invention and the one or more additional therapeutic agent(s).

This invention includes the use of pharmaceutically acceptable salts of compounds of the invention in the compositions and methods of the present invention. The term “pharmaceutically acceptable salt” as used herein includes salts derived from inorganic or organic acids including, for example, hydrochloric, hydrobromic, sulfuric, nitric, perchloric, phosphoric, formic, acetic, lactic, maleic, fumaric, succinic, tartaric, glycolic, salicylic, citric, methanesulfonic, benzenesulfonic, benzoic, malonic, trifluoroacetic, trichloroacetic, naphthalene-2-sulfonic, oxalic, mandelic and other acids. Pharmaceutically acceptable salt forms can include forms wherein the ratio of molecules comprising the salt is not 1:1. For example, the salt may comprise more than one inorganic or organic acid molecule per molecule of base, such as two hydrochloric acid molecules per molecule of compound of Formula I, V, VI, or VII. As another example, the salt may comprise less than one inorganic or organic acid molecule per molecule of base, such as two molecules of compound of Formula I, V, VI, or VII per molecule of tartaric acid.

In further embodiments, contemplated salts of the invention include, but are not limited to, alkyl, dialkyl, trialkyl or tetra-alkyl ammonium salts. In certain embodiments, contemplated salts of the invention include, but are not limited to, L-arginine, benenthamine, benzathine, betaine, calcium hydroxide, choline, deanol, diethanolamine, diethylamine, 2-(diethylamino)ethanol, ethanolamine, ethylenediamine, N-methylglucamine, hydrabamine, 1H-imidazole, lithium, L-lysine, magnesium, 4-(2-hydroxyethyl)morpholine, piperazine, potassium, 1-(2-hydroxyethyl)pyrrolidine, sodium, triethanolamine, tromethamine, and zinc salts. In certain embodiments, contemplated salts of the invention include, but are not limited to, Na, Ca, K, Mg, Zn or other metal salts.

The pharmaceutically acceptable acid addition salts can also exist as various solvates, such as with water, methanol, ethanol, dimethylformamide, and the like. Mixtures of such solvates can also be prepared. The source of such solvate can be from the solvent of crystallization, inherent in the solvent of preparation or crystallization, or adventitious to such solvent.

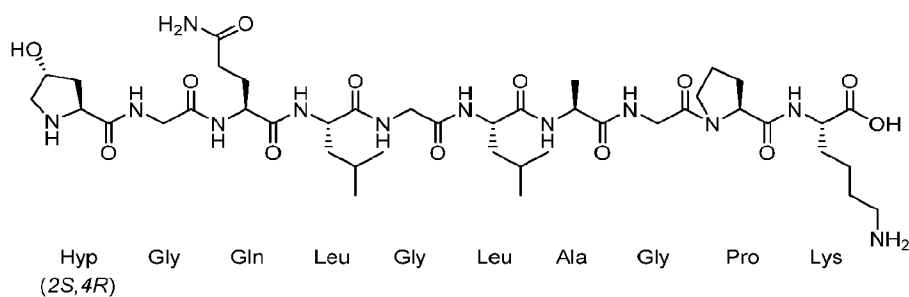
Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

- 5 Examples of pharmaceutically acceptable antioxidants include: (1) water-soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; (2) oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and (3) metal-chelating
- 10 agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

EXAMPLES

Example 1: Preparation of YDE-093 to YDE-107 peptides

YDE peptides (YDE-093 to YDE-107), derivatives of the amino acid sequence of the YDE-011 (WO2018/225961), were obtained through the C-terminal
5 modification or fragmentation of YDE-011.



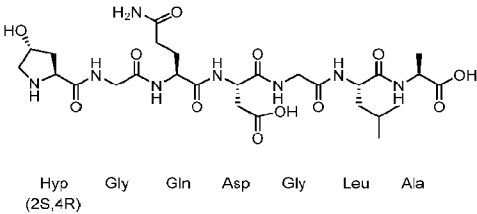
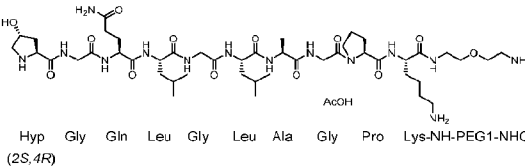
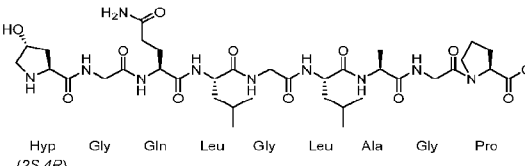
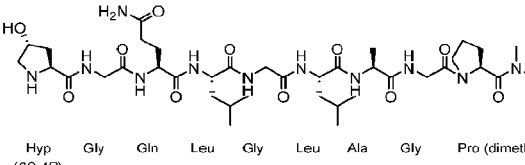
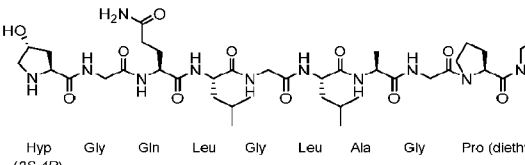
YDE-011 (WO2018/225961)

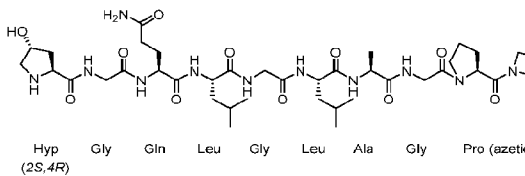
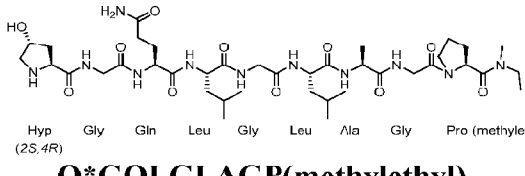
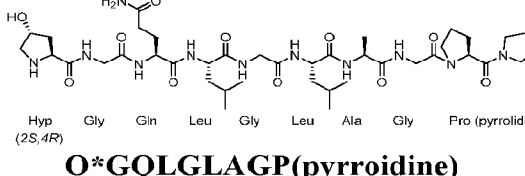
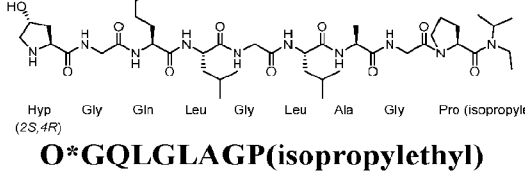
In order to prepare C-terminal modified peptide, Fmoc solid-phase peptide synthesis (SPPS) was conducted, based on a standard procedure described by prior
10 invention WO2018/225961 and further a C-terminal amidation reaction was carried out.

YDE-093 to YDE-107 peptides were synthesized by ANYGEN (Gwangju, Korea) and IRBM (Rome, Italy) by substituting one or more different amino acid residues into the peptide (2S,4R)hydroxyproline-GQLGLAGPK(NH-PEG1-NH-Boc)
15 (Table 1).

Table 1

#	Lot No.	Peptide	Structure / Sequence	M. W.	Purity (%)	Amount (mg)	Solubility in Water (mg/mL)
1	K182-143	YDE-093	Hyp Gly Gln Leu Gly Leu Ala Gly Pro Lys-NH-PEG1-NH-Boc (2S,4R)	1139.4	99.1	10	10.0

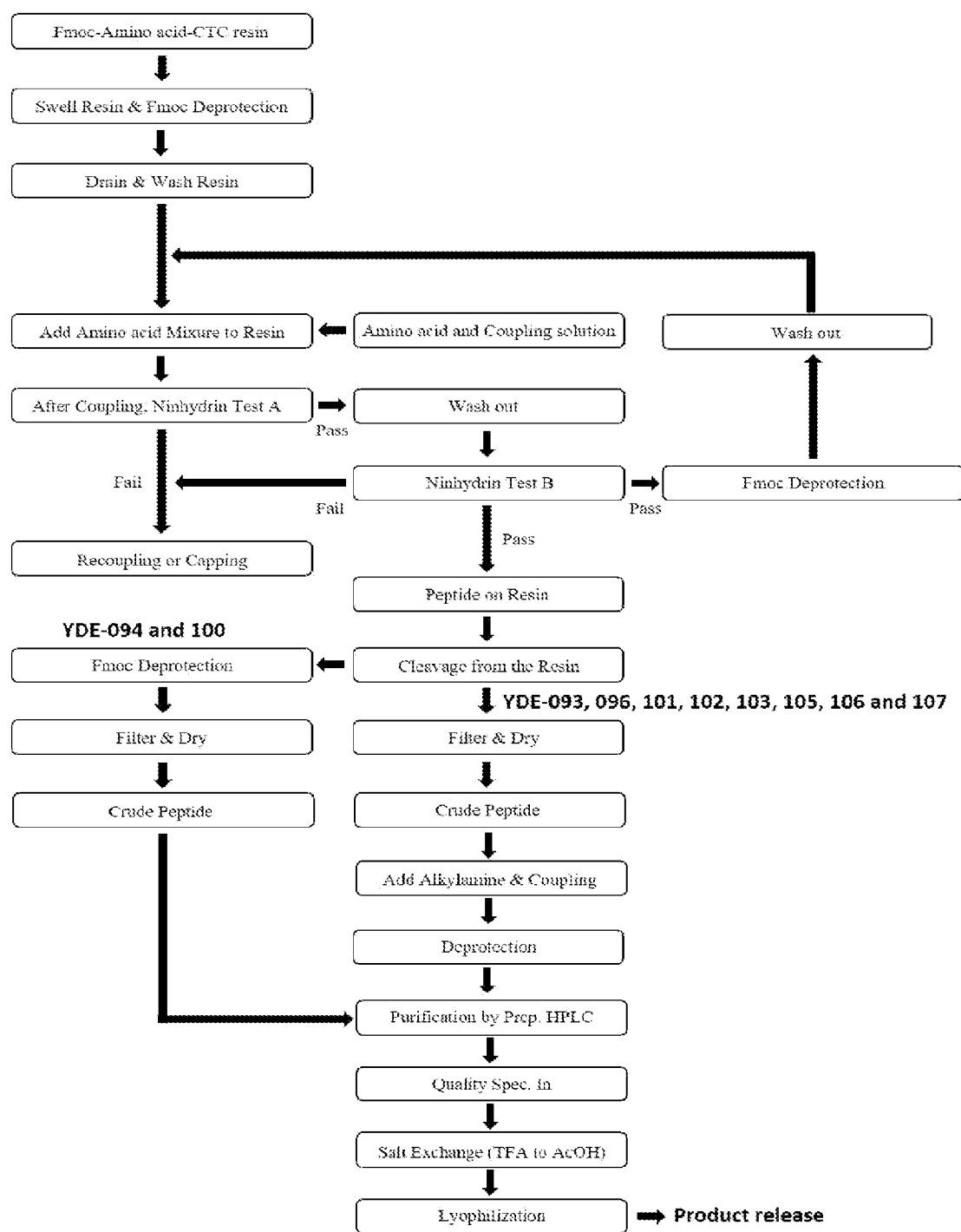
			O*GQLGLAGPK(NH-PEG1-NH-Boc)				
2	K182-472	YDE-094	 Hyp (2S,4R) Gly Gln Asp Gly Leu Ala O*GQDGLA	672.7	97.4	30	10.0
3	I-0417-327-001-001	YDE-096	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro Lys-NH-PEG1-NH-Cbz O*GQLGLAGPK(NH-PEG1-NH-Cbz)	1173.4	95.4	10	10.0
4	K190-638	YDE-100	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro O*GQLGLAGP	824.9	98.7	20	10.0
5	K190-639	YDE-101	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (dimethyl) O*GQLGLAGP(dimethyl)	852.0	96.7	20	10.0
6	K190-640	YDE-102	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (diethyl) O*GQLGLAGP(diethyl)	880.1	97.2	20	10.0

7	K190 641	YDE- 103	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (azetidine) O*GQLGLAGP(azetidine)	864. 0	97. 9	20	10.0
8	K190 643	YDE- 105	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (methylethyl) O*GQLGLAGP(methylethyl)	866. 0	97. 4	20	10.0
9	K190 644	YDE- 106	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (pyrrolidine) O*GQLGLAGP(pyrrolidine)	878. 0	97. 2	20	10.0
10	K190 645	YDE- 107	 Hyp (2S,4R) Gly Gln Leu Gly Leu Ala Gly Pro (isopropylethyl) O*GQLGLAGP(isopropylethyl)	894. 1	98. 2	20	10.0

O* = (2S,4R)hydroxyproline

The process for synthesizing the YDE-093 to YDE-107 peptides and the purification procedure thereof conducted by ANYGEN and IRBM are depicted

5 below.



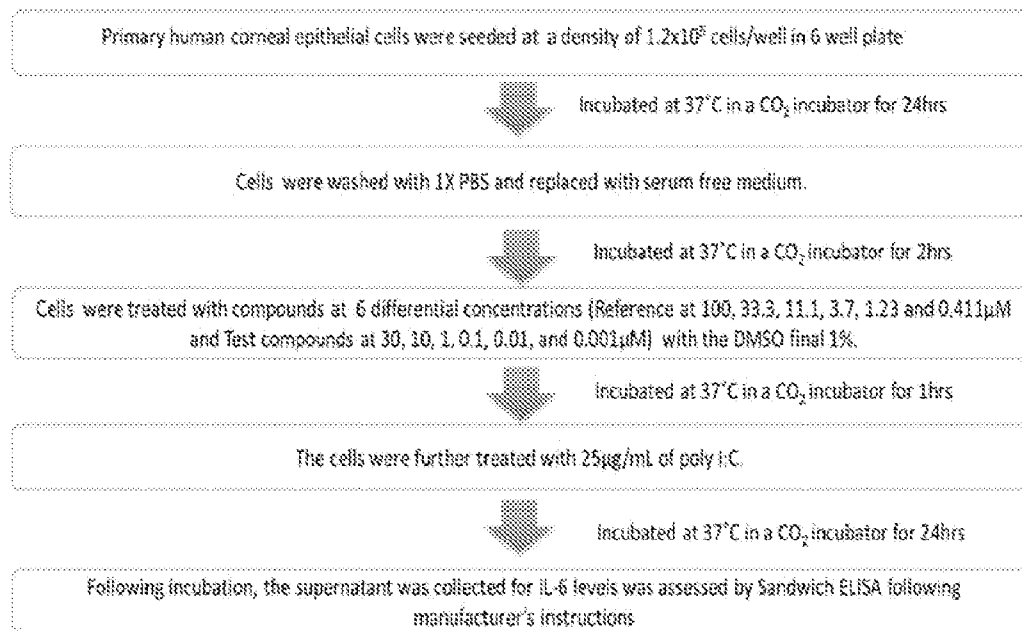
Analysis of YDE peptides

The YDE peptides prepared in Example 1 were analyzed by HPLC. As a result, it was confirmed that the purities of YDE-093, YDE-094, YDE-096, YDE-100, YDE-101, YDE-102, YDE-103, YDE-105, YDE-106 and YDE-107 synthesized were 99.1%, 97.4%, 95.4%, 98.7%, 96.7%, 97.2%, 97.9%, 97.4%, 97.2% and 98.2%, respectively.

In addition, the YDE derivatives prepared in Example 1 were analyzed by Ion-Mass. As a result, it was confirmed that the molecular weights of YDE-093, YDE-094, YDE-096, YDE-100, YDE-101, YDE-102, YDE-103, YDE-105, YDE-106 and YDE-107 synthesized were 1139.0, 673.2, 1173.6, 823.9, 851.9, 880.1, 864.5, 866.1, 878.4 and 894.3, respectively.

Example 2: Evaluation of the effect of peptides on soluble IL-6 cytokine release in poly I:C stimulated Primary Human Corneal Epithelial cells

Assay protocol as shown below was used to determine the significant effect of test compounds. The data was statistically analyzed by one-way ANOVA with a Bonferroni post test comparing all the columns. The significance was represented by the p value.



Selected YDE peptides (YDE-093, -096, -100, -101, -102, -103, -104, -105, -106 and -107) were evaluated by assessing the soluble IL-6 cytokine release in poly I:C stimulated primary human corneal epithelial cells by ELISA (Biolegend, 430504).

Specifically, primary corneal epithelial cells (ATCC, ATCC PCS-700-010) were seeded on a 6-well culture plate containing the Corneal Epithelial Cell Basal Medium (ATCC, ATCC PCS-700-030) in the Corneal Epithelial Cell Growth Kit (ATCC, ATCC PCS-700-040) in an amount of 1.2×10^5 cells per well, which was then cultured for 24 hours under the conditions of 37°C and 5% CO₂. Then, cells were washed with 1X PBS and replaced with serum free medium which was then cultured for 2 hours under the conditions of 37°C and 5% CO₂.

After 2 hours, cells were treated with compounds at 6 differential concentrations (Hinokitiol/YDE peptides at 30, 10, 1, 0.1, 0.01, and 0.001 μM) with the DMSO final 0.5% and then cultured for 1 hour under the conditions of 37°C and 5% CO₂.

After 1 hour, cells were further treated with 25 μg/mL of poly I:C and cultured for 24 hours under the conditions of 37°C and 5% CO₂.

Following incubation, the supernatant was collected for IL-6 levels was assessed by Sandwich ELISA (Enzyme-linked immunosorbent assay) following manufacturer's instructions. The data was statistically analyzed by one-way ANOVA with a Bonferroni post-test comparing all the columns. The significance was represented by the p value.

Results & Conclusion

Human corneal epithelial cells on stimulation with Poly I:C resulted in a significantly increase of IL-6 cytokine levels. Reference compound, Hinokitiol was found to significantly attenuate the Poly I:C stimulated IL-6 cytokine release in a dose dependent manner.

As shown in Figure 1A-1D, test peptides YDE-093 and YDE-096 were found to attenuate Poly I:C induced of IL-6 cytokine release in a dose dependent manner. Test compounds YDE103, and YDE104, were found to attenuate Poly I:C induced IL-6 cytokine release in a dose dependent manner. This was corroborated by the significant attenuation of IL-6 cytokine release at the tested concentrations that included; 30 μM, 10 μM, 1 μM and 0.1 μM respectively. Test compounds YDE101,

YDE102, YDE105, YDE106 and YDE107 were found to attenuate Poly I:C induced IL-6 cytokine release in a dose dependent manner. This was corroborated by the significant attenuation of IL-6 cytokine release at the tested concentrations that included; 30µM, 10µM, and 1µM respectively. Test compound YDE100 was found to attenuate Poly I:C induced IL-6 cytokine release in a dose dependent manner. This was corroborated by the significant attenuation of IL-6 cytokine release at the tested concentrations that included; 30µM, and 10µM respectively.

Example 3: Evaluation of the effect of peptides on cell proliferation using primary corneal epithelial cells

STUDY OBJECTIVE

To determine the cell proliferation assessment of peptides using primary corneal epithelial cells.

STUDY PLAN

- Test System: HCE cells from ATCC.
- Assay Format: 96-well plate format
- Method of Detection: CellTiter-Glo Luminescent Cell Viability Assay (Promega, Cat# G7573)
- Assay Controls: Reference compound (hEGF) and untreated cells
- Test Samples: 57
- Media: Corneal Epithelial Cell Basal Medium + Cell growth kit components

EXPERIMENTAL DESIGN**Assay protocol**

5000 primary corneal epithelial cells/well were seeded in a white opaque plate and incubated for 24hrs in a 37°C incubator supplemented with 5% CO₂



24hrs post cell seeding, test compounds were treated at 8 different



Cells treated with compounds were incubated for 48 & 72hrs at 37°C in a 5% CO₂



Post appropriate incubation time points, CellTiter-Glo luminescent reagent* was added to the plates and incubated at room temperature for 30mins



Luminescence signal was captured using EnVision^{2104®} Multilabel reader

* CellTiter-Glo luminescent reagent procured from, Promega, Cat# G7573

5

Selected YDE peptides (YDE-012, -019, -038, -044, -045, -047, -048, -049, -050, -051, -052, -053, -054, -055, -056, -057, -058, -059, -060, -061, -062, -063, -064, -065, -066, -067, -072, -073, -074, -075, -076, -077, -078, -079, -080, -081, -082, -083, -084, -085, -086, and -087) were evaluated by assessing the effect of peptides on cell proliferation of primary corneal epithelial cells.

10

Specifically, 5000 primary corneal epithelial cells/well were seeded in a white opaque 96-well plate and incubated for 24hrs in a 37°C incubator supplemented with 5% CO₂. After 24 hours, test compounds were treated at 8 different concentrations.

Cells treated with compounds were incubated for 48 & 72hrs at 37°C in a 5% CO₂

15

incubator. Post appropriate incubation time points, CellTiter-Glo luminescent reagent (Promega, Cat# G7573) was added to the plates and incubated at room temperature

for 30 min. Luminescence signal was captured using EnVision^{2104®} Multilabel reader. Assay controls were reference compound (hEGF) and untreated cells.

Results & Conclusion

5 The proliferation effect of YDE-038 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-038 for 48hrs and 72hrs. At concentrations 30, 10, 3 and 1 μ M, no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations (0.03 & 0.01 μ M) an increase in cell
10 proliferation (35-40%) in 72hrs incubation was observed. Whereas after 48hrs incubation there was no proliferation observed, even at lower concentrations (Figure 2A).

 The proliferation effect of YDE-044 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-044 for 48hrs and 72hrs. At
15 concentrations 30 μ M, no significant proliferation of cells (<20% over basal) was observed. At low concentrations of YDE-044, there was proliferation of cells (20-30%). Maximum 30% proliferation was observed at the lowest concentration (0.01 μ M) (Figure 2B).

 The proliferation effect of YDE-045 was assessed using human primary
20 corneal epithelial cells. Cells were incubated with YDE-045 for 48hrs and 72hrs. At concentrations 30, 10, 3 and 1 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated with YDE-045 for 48hrs or 72hrs. However, at lower concentrations an increase in cell proliferation (35-50%) was observed (Figure 2C).

25 The proliferation effect of YDE-049 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-049 for 48hrs and 72hrs. There was no significant proliferation of cells when YDE-049 was incubated at 48hrs incubation. At 30, 10 and 3 μ M the peptide showed toxic effect (~25-40%). However, at 72hrs incubation, at concentrations 30, 10, 3 and 1 μ M, no significant proliferation
30 of cells was observed (<20% over basal). At lower concentrations, an increase in cell proliferation (25-40%) was observed when YDE-049 was incubated with primary corneal epithelial cells for 72hrs (Figure 2D).

The proliferation effect of YDE-053 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-053 for 48hrs and 72hrs. At concentrations 30, 10 and 3 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or
5 72hrs. However, at lower concentrations an increase in cell proliferation (40-60%) was observed (Figure 2E).

The proliferation effect of YDE-054 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-054 for 48hrs and 72hrs. No significant proliferation at 48hrs incubation was observed. At concentrations 30, 10, 3
10 and 1 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 72hrs. However, at lower concentrations an increase in cell proliferation (25-40%) at 72hrs incubation was observed (Figure 2F).

The proliferation effect of YDE-058 was assessed using human primary
15 corneal epithelial cells. Cells were incubated with YDE-058 for 48hrs and 72hrs. No significant proliferation at 48hrs incubation was observed. At concentrations 30 and 10 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 72hrs. However, at lower concentrations moderate increase in cell proliferation (~25%) at 72hrs incubation was
20 observed (Figure 2G).

The proliferation effect of YDE-059 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-059 for 48hrs and 72hrs. At concentrations 30 μ M, no significant proliferation of cells (<20% over basal) was observed. Dose dependent proliferation in tested concentrations in 72hrs incubation
25 with high proliferation at lower dilutions and lower proliferation at high dilutions of peptides was observed. Maximum 40% proliferation resulted in the lowest concentration 0.01 μ M (Figure 2H).

The proliferation effect of YDE-063 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-063 for 48hrs and 72hrs. No
30 significant proliferation of cells in 48 hrs incubation was observed. However, at lower concentrations increase in cell proliferation (~30%) at 72hrs incubation was observed (Figure 2I).

The proliferation effect of YDE-064 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-064 for 48hrs and 72hrs. No significant proliferation of cells in 48 hrs. incubation was observed. However, at lower concentrations (0.03 & 0.01 μ M) an increase in cell proliferation (~35%) at
5 72hrs incubation time point was observed (Figure 2J).

The proliferation effect of YDE-065 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-065 for 48hrs and 72hrs. At concentrations 30, 10, 3 and 1 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for
10 48hrs or 72hrs. However, at lower concentrations an increase in cell proliferation (~35%) at 72hrs incubation was observed (Figure 2K).

The proliferation effect of YDE-066 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-066 for 48hrs and 72hrs. There was no significant increase in cell proliferation when the peptide was incubated
15 with cells for 48hrs or 72hrs (Figure 2L).

The proliferation effect of YDE-067 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-067 for 48hrs and 72hrs. At concentrations 30, 10, 3 and 1 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for
20 48hrs or 72hrs. However, at lower concentrations (0.03 & 0.01 μ M), an increase in cell proliferation (35%) in 72hrs incubation was observed. Whereas 48hrs incubation no significant proliferation was observed even at lower concentrations (Figure 2M).

The proliferation effect of YDE-045 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-045 for 48hrs and 72hrs. At
25 concentrations 30, 10, μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations (0.1, 0.03 & 0.01 μ M) an increase in cell proliferation (35-40%) in 72hrs incubation was observed (Figure 2N).

The proliferation effect of YDE-049 was assessed using human primary
30 corneal epithelial cells. Cells were incubated with YDE-049 for 48hrs and 72hrs. At all tested concentrations, no significant proliferation of cells (<20% over basal) at 48hrs was observed. Proliferation at 0.03 & 0.01 concentrations at 72hrs incubation

was observed. Maximum 30% proliferation was observed at the lowest concentration (0.01 μ M) (Figure 2O).

5 The proliferation effect of YDE-053 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-053 for 48hrs and 72hrs. At concentrations 30, 10 and 3 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations an increase in cell proliferation (40-60%) was observed (Figure 2P).

10 The proliferation effect of YDE-057 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-057 for 48hrs and 72hrs. Significant proliferation at 48hrs incubation with 0.1, 0.03 & 0.01 μ M concentrations was observed. At concentrations 30, 10, 3 and 1 μ M, no significant proliferation of cells (<20% over basal) observed in 48 hrs incubation was observed. However, at lower concentrations an increase in cell proliferation (40-50%) at 72hrs incubation was observed (Figure 2Q).

The proliferation effect of YDE-060 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-060 for 48hrs and 72hrs. At concentrations 30, 10, 3, 1 and 0.3 μ M, significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 72hrs. However, at lower concentrations an increase in cell proliferation (~40-60%) at 72hrs incubation was observed (Figure 2R).

25 The proliferation effect of YDE-065 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-065 for 48hrs and 72hrs. No significant proliferation of cells (<20% over basal) in 48hrs incubation was observed. Dose dependent proliferation in tested concentrations in 72hrs incubation with high proliferation at lower dilutions was observed. Maximum 40% proliferation resulted in the lowest concentration 0.01 μ M (Figure 2S).

30 The proliferation effect of YDE-067 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-067 for 48hrs and 72hrs. No significant proliferation of cells in 48 hrs Incubation. However, at lower concentrations an increase in cell proliferation (~30%) at 72hrs incubation was observed (Figure 2T)

The proliferation effect of YDE-072 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-072 for 48hrs and 72hrs. No significant proliferation of cells in 48 hrs. Incubation except 0.03 & 0.01 μ M concentrations. However, at lower concentrations (0.03 & 0.01 μ M) an increase in cell proliferation (~30%) at 72hrs incubation time point was observed (Figure 2U).

The proliferation effect of YDE-073 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-073 for 48hrs and 72hrs. No significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs. However, at lower concentrations an increase in cell proliferation (~30%) at 72hrs incubation was observed.

The proliferation effect of YDE-074 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-074 for 48hrs and 72hrs. There was no significant increase in cell proliferation when the peptide was incubated with cells for 48hrs or 72hrs (Figure 2W).

The proliferation effect of YDE-075 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-075 for 48hrs and 72hrs. There was no significant increase in cell proliferation when the peptide was incubated with cells for 48hrs. However, at lower concentrations (0.03 & 0.01 μ M) an increase in cell proliferation (~30%) at 72hrs incubation time point was observed (Figure 2X).

The proliferation effect of Diquas was assessed using human primary corneal epithelial cells. Cells were incubated with Diquas for 48hrs and 72hrs. Dose dependent increase in cell proliferation when the peptide was incubated with cells for 48hrs or 72hrs was observed (Figure 2Y).

The proliferation effect of YDE-053 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-053 for 48hrs and 72hrs. An increased proliferation of cells up to 10M (>20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations no significant proliferation (i.e from 0.1nM to 0.0001nM) was observed (Figure 2Z).

The proliferation effect of YDE-067 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-067 for 48hrs and 72hrs. No significant proliferation of cells with 48hrs incubation of compound was observed. Whereas in 72hrs an increased proliferation up to 10nM was observed. However, at

lower concentrations a decrease in cell proliferation (0.1nM to 0.0001nM) was observed (Figure 2AA).

The proliferation effect of Diquas was assessed using human primary corneal epithelial cells. Cells were incubated with Diquas for 48hrs and 72hrs. Dose dependent increase in cell proliferation when the peptide was incubated with cells for 48hrs or 72hrs was observed. There is no significant proliferation observed from 1nM to 0.0001nM (Figure 2AB).

The proliferation effect of YDE-045 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-045 for 48hrs and 72hrs. An increased proliferation of cells up to 10 nM (~35% over basal) was observed. This effect was observed in 48hrs incubation. In 72 hrs incubation concentration dependent increase proliferation observed up to 10nM. However, at lower concentrations no significant proliferation was observed (i.e. 0.001nM & 0.0001nM) (Figure 2AC).

The proliferation effect of YDE-053 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-053 for 48hrs and 72hrs. An increased proliferation of cells up to 10 nM (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations no significant proliferation was observed (i.e. 0.1nM to 0.0001nM) (Figure 2AD).

The proliferation effect of YDE-054 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-054 for 48hrs and 72hrs. An increased proliferation of cells up to 0.1 nM (~30 % over basal) was observed. This effect was observed when the cells were incubated for 48hrs, whereas at 72hrs increased proliferation up to 10nM with 40% proliferation. At higher concentration (1000 nM) there was no significant proliferation was observed (Figure 2AE).

The proliferation effect of YDE-057 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-057 for 48hrs and 72hrs. An increased proliferation of cells upto 10 nM was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations no significant proliferation was observed (i.e. 0.1nM to 0.0001nM) (Figure 2AF).

The proliferation effect of YDE-060 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-060 for 48hrs and 72hrs. Significant proliferation of cells in 48 hrs as well as 72 hrs was observed. Increased

proliferation up to 10nM with ~60% proliferation. However, at lower concentrations no significant cell proliferation was observed (0.01nM to 0.0001nM) (Figure 2AG).

The proliferation effect of Diquas was assessed using human primary corneal epithelial cells. Cells were incubated with Diquas for 48hrs and 72hrs. Dose
5 dependent increase in cell proliferation when the peptide was incubated with cells for 48hrs or 72hrs was observed. There is no significant proliferation observed from 1nM to 0.0001nM (Figure 2AH).

The proliferation effect of YDE-012 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-012 for 48hrs and 72hrs. All
10 tested concentration no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs (Figure 2AI).

The proliferation effect of YDE-019 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-019 for 48hrs and 72hrs. No
15 significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations (0.1, 0.03 & 0.01μM) an increase in cell proliferation (~20%) in 72hrs incubation was observed (Figure 2AJ).

The proliferation effect of YDE-055 was assessed using human primary
20 corneal epithelial cells. Cells were incubated with YDE-055 for 48hrs and 72hrs. No significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations (0.03 & 0.01μM) an increase in cell proliferation (25-30%) in 72hrs incubation was observed (Figure 2AK).

25 The proliferation effect of YDE-076 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-076 for 48hrs and 72hrs. At concentrations 30, 10, μM, significant proliferation of cells was observed (>20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. Other tested concentration no significant proliferation observed (Figure 2AL).

30 The proliferation effect of YDE-077 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-077 for 48hrs and 72hrs. No significant proliferation of cells was observed (<20% over basal). This effect was

observed when the cells were incubated for 48hrs. At 72 hrs incubation an increasing proliferation from 10 μ M to 0.01 μ M was observed (Figure 2AM).

5 The proliferation effect of YDE-078 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-078 for 48hrs and 72hrs. No significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs. At 72 hrs incubation an increasing proliferation from 3 μ M to 0.01 μ M was observed (Figure 2AN).

10 The proliferation effect of YDE-079 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-079 for 48hrs and 72hrs. No significant proliferation of cells (<20% over basal) at higher concentration was observed (30-0.3 μ M). This effect was observed when the cells were incubated for 48hrs. At 72 hrs incubation an increasing significant proliferation from 30 μ M to 0.01 μ M (~35% cell proliferation) was observed (Figure 2AO).

15 The proliferation effect of YDE-080 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-080 for 48hrs and 72hrs. At concentrations 30, 10 & 3 μ M, dependent proliferation of cells was observed (>20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentrations (1.0 to 0.01 μ M) no significant cell proliferation in 48 hrs as well as 72hrs incubation was observed (Figure 2AP).

20 The proliferation effect of YDE-081 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-081 for 48hrs and 72hrs. All tested concentrations no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs (Figure 2AQ).

25 The proliferation effect of YDE-082 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-082 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs. At 72hrs incubation an increasing proliferation from 1 μ M to 0.01 μ M was observed (Figure 30 2AR).

The proliferation effect of YDE-083 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-083 for 48hrs and 72hrs. All tested concentrations no significant proliferation of cells (<20% over basal) was

observed. This effect was observed when the cells were incubated for 48hrs. At 72hrs incubation an increasing proliferation from 1 μ M to 0.01 μ M was observed (Figure 2AS).

5 The proliferation effect of YDE-084 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-084 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs. At 72hrs incubation an increasing proliferation from 10 μ M to 0.01 μ M was observed (Figure 2AT).

10 The proliferation effect of YDE-085 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-085 for 48hrs and 72hrs. Tested concentrations 30 μ M to 0.1 μ M, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs, whereas 0.03 & 0.01 μ M slightly increased proliferation. At 72hrs incubation
15 an increasing proliferation from 1 μ M to 0.01 μ M was observed (Figure 2AU).

 The proliferation effect of YDE-086 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-086 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs. At 72hrs
20 incubation an increasing proliferation from 1 μ M to 0.01 μ M (Figure 2AV).

 The proliferation effect of YDE-087 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-087 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs. At 72hrs
25 incubation an increasing proliferation from 3 μ M to 0.01 μ M was observed (Figure 2AW).

 The proliferation effect of YDE-047 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-047 for 48hrs and 72hrs. No significant proliferation of cells was observed (<20% over basal). This effect was
30 observed when the cells were incubated for 48hrs. At lower concentrations (3 to 0.01 μ M). An increase in cell proliferation (25-30%) in 72hrs incubation was observed. (Figure 2AX).

The proliferation effect of YDE-048 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-048 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs. At 72hrs incubation an increasing proliferation from 1 μ M to 0.01 μ M was observed (Figure 2AY).

The proliferation effect of YDE-050 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-050 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells was observed (<20% over basal). This effect was observed when the cells were incubated for 48hrs or 72hrs. However, at lower concentration 0.01 μ M, an increase in cell proliferation (30%) in 72hrs incubation was observed (Figure 2AZ).

The proliferation effect of YDE-051 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-051 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs (Figure 2BA).

The proliferation effect of YDE-052 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-052 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs or 72hrs (Figure 2BB).

The proliferation effect of YDE-056 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-056 for 48hrs and 72hrs. At concentrations 30 to 0.01, μ M, significant proliferation of cells (>20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs whereas at 72 hrs incubation no significant proliferation was observed (Figure 2BC).

The proliferation effect of YDE-061 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-061 for 48hrs and 72hrs. At concentrations 30 to 0.01, μ M, significant proliferation of cells (>20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs whereas at 72 hrs incubation no significant proliferation was observed (Figure 2BD).

The proliferation effect of YDE-062 was assessed using human primary corneal epithelial cells. Cells were incubated with YDE-062 for 48hrs and 72hrs. All tested concentrations, no significant proliferation of cells (<20% over basal) was observed. This effect was observed when the cells were incubated for 48hrs where as 72hrs showed slightly increase in proliferation (Figure 2BE).

Human epidermal growth factor (hEGF) as used as reference compound to assess the cell proliferation assays. Concentration dependent proliferation of primary corneal epithelial cells was observed. A maximum of ~40% proliferation at highest tested concentration of 30μM at 48hrs incubation was observed (Figure 2BF).

Example 4: Assessment of the effect of YDE053, YDE060, or YDE065 on soluble proteins release in poly I:C stimulated Primary Human Corneal Epithelial cells.

STUDY OBJECTIVE

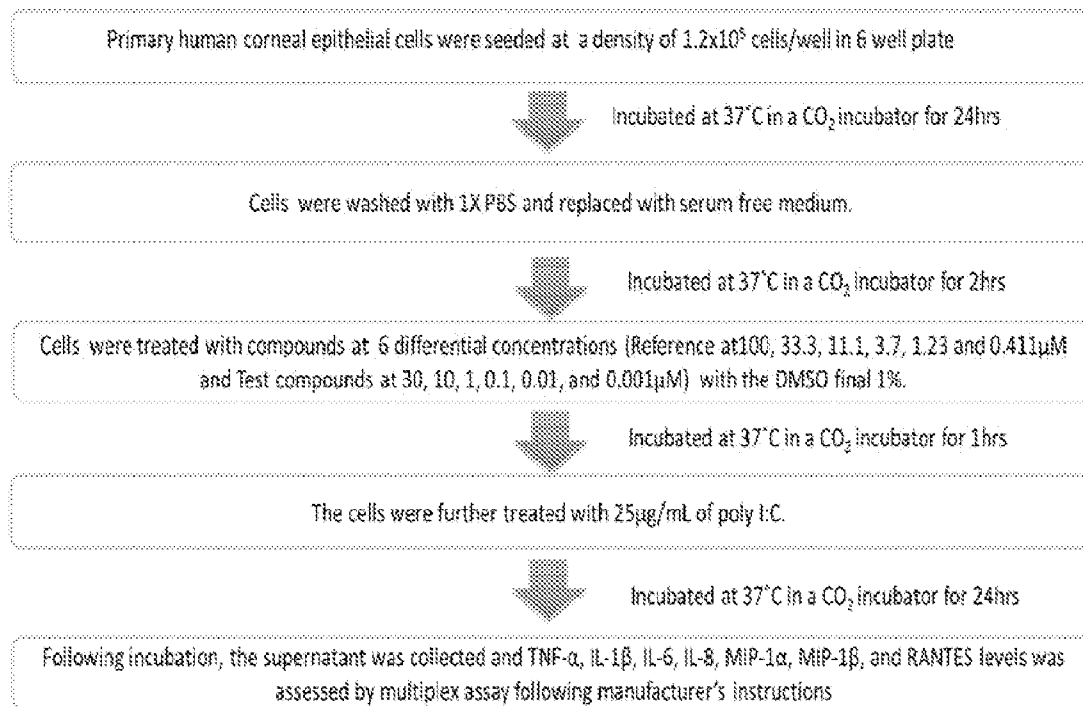
To determine the effect of compound by assessing the panel of soluble proteins release in poly I:C stimulated primary human corneal epithelial cells by Multiplex.

STUDY PLAN

- Test System: Primary Human Corneal Epithelial cells
- Assay Format: 96-well plate format
- Method of Detection: Enzyme-linked immunosorbent assay
- Assay Controls: Hinokitiol

Experimental Design

Assay protocol as described below was used to determine the significant effect of test compounds. The data was statistically analyzed by one-way ANOVA with a Bonferroni post test comparing all the columns. The significance was represented by the p value.



Results & Conclusion

Results are shown in Figure 3. IL-1beta, IL-6, IL-8, MIP-1alpha, MIP-1beta, RANTES, and TNF-alpha cytokine release was observed in human corneal epithelial cells. Stimulation with Poly I:C resulted in a significantly increase of IL-1beta, IL-6, IL-8, MIP-1alpha, MIP-1beta, RANTES, and TNF-alpha cytokine levels.

Reference compound, Hinokitiol, was found to significantly attenuate the Poly I:C stimulated cytokines release (IL-1beta, IL-6, IL-8, MIP-1alpha, MIP-1beta, RANTES, and TNF-alpha) in a dose dependent manner.

Test compounds YDE053, YDE060 and YDE065 were found to attenuate Poly I:C induced IL-6 cytokine release in a dose dependent manner. This was corroborated by the significant attenuation of IL-6 cytokine release at the tested concentrations that included 30µM, 10µM, and 1µM respectively.

Effect of YDE053 on IL-6: Stimulated (MFI Mean $\pm$ SD: 14801 $\pm$ 407) vs Stimulated + 30 µM Hinokitiol (MFI Mean $\pm$ SD: 6759 $\pm$ 500); $p < 0.05$, Stimulated vs Stimulated + 10µM Hinokitiol (MFI Mean $\pm$ SD: 7011 $\pm$ 471) $p < 0.05$, and Stimulated vs. Stimulated + 1µM Hinokitiol (MFI Mean $\pm$ SD: 7004 $\pm$ 376) $p < 0.05$.

Example 5: Determine the effect of YDE053 peptide on NF- κ B (p65) transcription activity in poly I:C stimulated Primary Human Corneal Epithelial cells.

STUDY OBJECTIVE

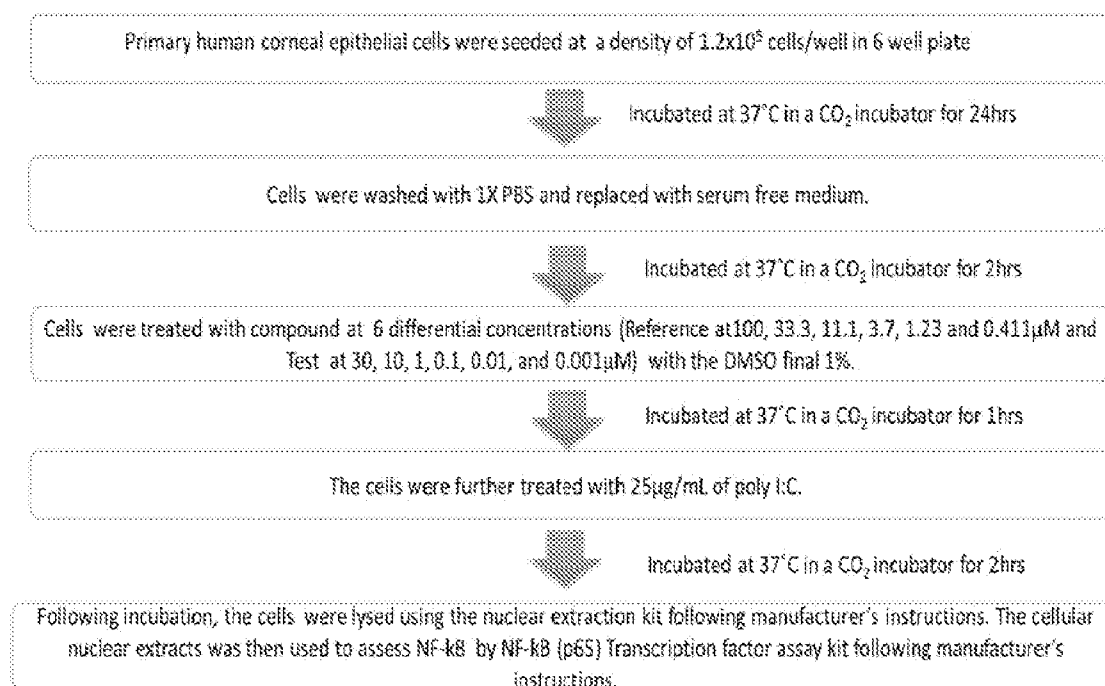
- 5 To determine the effect of YDE053 on NF- κ B (p65) transcription activity in poly I:C stimulated primary human corneal epithelial cells.

STUDY PLAN

- 10
- Test System: Primary Human Corneal Epithelial cells
 - Assay Format: 96-well plate format
 - Method of Detection: Enzyme-linked immunosorbent assay
 - Assay Controls: Hinokitiol

Experimental Design

- 15 Assay protocol as shown below was used to determine the significant effect of test compounds. The data was statistically analyzed by one-way ANOVA with a Bonferroni post test comparing all the columns. The significance was represented by the p value.



20

Results & Conclusion

Results are shown in Figure 4. Poly I:C stimulation on primary human corneal epithelial cells was found to result in the phosphorylation of (p65) NF-kB

(Unstimulated cells: OD Mean $\pm$ SD: 0.047 ± 0.002 vs Stimulated: OD Mean $\pm$ SD:

5 0.121 ± 0.01 ; $p < 0.05$).

Reference compound, Hinokitiol was found to significantly attenuate the phosphorylation of (p65) NF-kB in Poly I:C stimulated cells in a dose dependent manner. The effect of YDE053 was found to significantly attenuate the phosphorylation of (p65) NF-kB in Poly I: C induced cells. This was corroborated by
10 stimulated cells (OD Mean $\pm$ SD: 0.121 ± 0.01) vs cells treated with 30 μ M YDE053 (OD Mean $\pm$ SD: 0.049 ± 0.002); $p < 0.05$, Stimulated cells (OD Mean $\pm$ SD: 0.121 ± 0.01) vs Cells treated with 10 μ M YDE053 (OD Mean $\pm$ SD: 0.06 ± 0.006) $p < 0.05$. Test compound YDE053 reduced (p65) NF-kB transcription activity in a dose dependant manner at the tested concentrations.

15

Example 6: Determine the effect of compounds on soluble IL6 cytokine release in poly I:C stimulated Primary Human Corneal Epithelial cells.

STUDY OBJECTIVE

20

To determine the effect of compound by assessing the soluble IL-6 cytokine release in poly I:C stimulated primary human corneal epithelial cells by ELISA.

STUDY PLAN

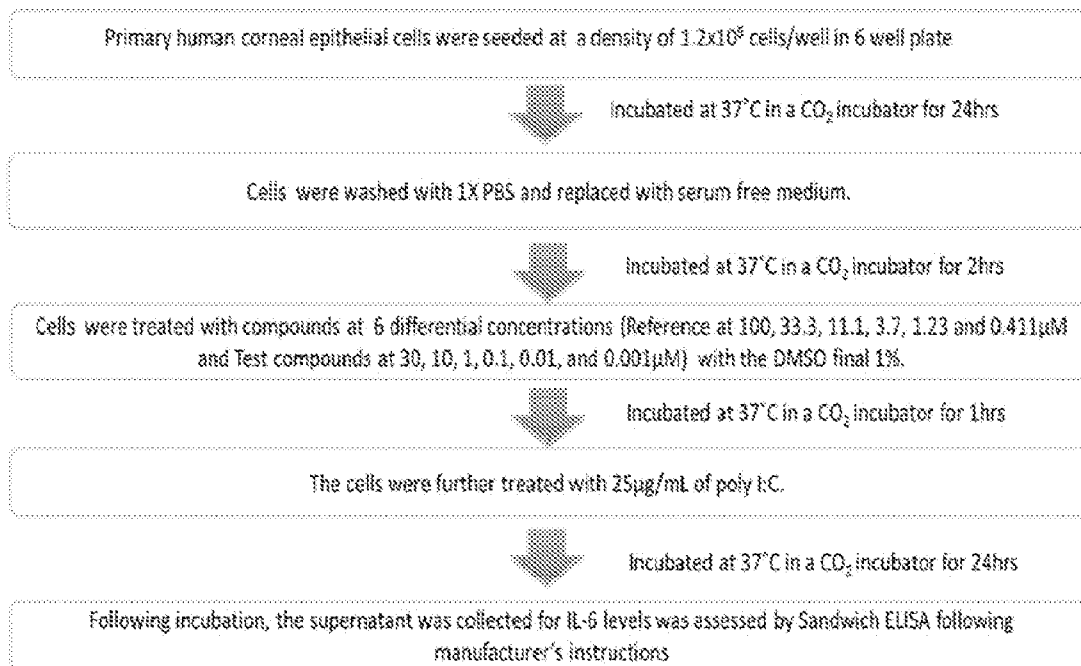
25

- Test System: Primary Human Corneal Epithelial cells
- Assay Format: 96-well plate format
- Method of Detection: Enzyme-linked immunosorbent assay
- Assay Controls: Hinokitiol

30

Experimental Design

Assay protocol as shown below was used to determine the significant effect of test compounds. The data was statistically analyzed by one-way ANOVA with a Bonferroni post test comparing all the columns. The significance was represented by the p value.



Results & Conclusion

Results are shown in Figure 5. Human corneal epithelial cells on stimulation with Poly I:C resulted in a significantly increase of IL-6 cytokine levels. Reference compound, Hinokitiol was found to significantly attenuate the Poly I:C stimulated IL-6 cytokine release in a dose dependent manner. Test compounds; YDE053, YDE048, YDE056, YDE057, YDE058, YDE067, YDE079, YDE011, YDE093, YDE096, YDE043 were found to attenuate Poly I:C induced of IL-6 cytokine release in a dose dependent manner. This was corroborated by the significant attenuation of IL-6 cytokine release at the tested concentrations that included; 30µM, 10µM, 1µM and 0.1µM respectively.

Example 7: In vitro evaluation of test compounds for apparent permeability using 21 day cultured Caco-2 cell monolayer

Study Design & Materials & Methods

5

Table 2

<i>Cell origin</i>	American Type Culture Collection (ATCC)
<i>Test System</i>	Caco-2 cells monolayer in 96 well format
<i>Passage number</i>	36
<i>Test plate</i>	Poly carbonate high pore density from Millipore with 0.4 μm pore size, 0.11 cm^2 active membrane area
<i>Test compound concentration</i>	2 μM
<i>Bidirectional assay (A-B & B-A) time points</i>	0 and 120 minutes
<i>Buffer in Receiver wells</i>	HBSS Buffer
<i>Replicates</i>	Two
<i>End Point</i>	Apparent permeability (Papp)
<i>Bio analysis</i>	LC-MS/MS
<i>QC Compounds</i>	Propranolol (High Permeable) and Atenolol (Low Permeable)
<i>Assay Type</i>	Bi-directional (A-B and B-A)
<i>Cell Density</i>	12,000 cells/well (96 well plate)

Table 3

Test Article	Compound	Molecular weight
1	YDE-011	953.10
2	YDE-043	486.50

Reagent Preparation

Preparation of (Dulbecco's Modified Eagles Medium) DMEM medium pH 7.4:

10 5 mL of 100 mM Sodium pyruvate, 5 mL of 100X non-essential amino acids, 5 mL of Penstrep was added to 100 mL of heat inactivated fetal bovine serum to 385 mL of DMEM aseptically and mixed thoroughly.

Preparation of Hank's Balanced salt solution (HBSS) pH 7.4:

One vial of Hank's balanced salt (Sigma-H1387) was dissolved in 900 mL of milli Q water; pH was adjusted to 7.4 and made up the volume to 1000 mL of water. The solution was filter sterilized and store at 4°C.

5 *Preparation & Dilution of Test Compound:*

10 mM stock solution of test compound was prepared in DMSO. 10 mM stock was diluted with 100% DMSO to prepare 0.2 mM, 0.2 mM stock was diluted with HBSS buffer to a final concentration of 2 µM.

*Assay Procedure*10 *Seeding of the cells:*

Add 250 µL of DMEM to the basal compartment of 96 well multi-screen Caco-2 plates and seed 12000 cells/well (0.16×10^6 cells/ml) in all the apical wells required and 2 wells with only media as blank without cells. Place the Caco-2 plate in CO₂ incubator at 37°C for proliferation of cells.

15 *Media Change:*

The utilized media was replenished every alternate day by fresh medium. On 21st day, utilized medium was removed and washed twice with HBSS Buffer and incubated with HBSS buffer 30 min in incubator and initiated the assay.

Apical to Basal Permeability:

20 75 µL of test compound was added to apical wells and 250 µL of HBSS buffer with 1% DMSO was added to basal wells. Samples were collected at 120 min and processed as stated below.

Basal to Apical Permeability:

25 250 µL of test compound was added to basal wells and 75 µL of HBSS buffer with 1% DMSO was added to apical wells. Samples were collected at 120 min and processed as stated below.

Sampling processing:

30 Single point calibration curve in HBSS buffer was used. 100 µL of supernatant was diluted with 200 µL of water and submitted for LC-MS/MS analysis.

Calculations:

$$P_{app} = dQ/dT \times 1/Co \times 1/A,$$

dQ is amount collected in the basolateral compartment of the 96 well filter plate;

dT is Time of incubation of drug on the cell monolayer;

Co is initial concentration of drug in the apical compartment of the well;

A is surface area of the filter.

Efflux ratio = Papp of basal to apical samples / Papp of apical to basal samples

$$\text{Recovery} = \{(dQ \text{ of Apical} + dQ \text{ of Basal}) / \text{Standard } dQ\} \times 100$$

Results

5 The Caco-2 Permeability results of the test compounds is represented in below Table 4.

Table 4

Compound Name	Average Values					
	Papp (10 ⁻⁶ cm/sec)		Efflux Ratio	A to B % Recovery	B to A % Recovery	Classification
	Apical to Basal	Basal to Apical				
YDE-011	0.00	0.00	NC	15.00	88.50	LOW
YDE-043	0.00	0.00	NC	34.00	67.25	LOW
Propranolol	23.83	37.07	1.56	80.07	90.30	HIGH
Atenolol	0.00	0.57	NC	93.90	85.33	LOW

10 NC: denotes Not calculated

Table 5

15 *Data Interpretation: Criteria for classification of the compounds (Caco-2 Permeability).*

Result of permeability Papp (10 ⁻⁶ cm/s)	Range
< 1	Low permeable
1-10	Medium permeable
>10	High permeable

Example 8: Investigate the effects of YY-101, YDE-011 & YDE-043 Compounds on various cytokine and chemokine release in Human Peripheral Blood Mononuclear Cells (PBMCs) (Study 1)

5 ***Background and Purpose***

The objective of this study was to investigate the effects of YY-101, YDE-011 and YDE-043 compounds on various cytokine and chemokine release in human peripheral blood mononuclear cells (hPBMCs) stimulated by known stimulants such as LPS, poly I:C or PMA/Ionomycin.

10 To achieve this goal, a pilot study was conducted to establish a dose and time-dependent IL-6 cytokine release in hPBMCs by each stimulant. Upon selection of the dose and time point for the best stimulant, the main study was conducted to establish the efficacious dose-response curve of YY-101, YDE-011, YDE-043 on up to 30 cytokine and chemokine release in hPBMC induced by LPS.

15 ***Materials & Methods***

Reagents and Solutions

- Human PBMCs (ATCC, USA)
- Lipopolysaccharides from Escherichia coli (Sigma Aldrich, USA)
- poly (I:C) (Sigma Aldrich, USA)
- 20 • PMA (Sigma Aldrich, USA)
- Ionomycin (Sigma Aldrich, USA)
- Human IL-6 ELISA kit (Thermo fisher, USA)
- Human magnetic Luminex assay kit (R&D System, USA)
- Xiidra® (Shire, USA)
- 25 • Test materials (YY-101, YDE-011, YDE-043) were stored in a deep freezer (-20°C).

Cell Culture

Human PBMCs frozen in a cryopreserve was thawed, washed with Hank's Balanced Salt Solution containing 10% Fetal bovine serum, and seeded onto a 24-well plate at a density of 1×10^6 cells/well with culture RPMI media containing 10% Fetal bovine serum in growth media in a 24 well plate for 12, 24, and 48 hrs and maintained at 37°C in an atmosphere of 95% air and 5% CO₂.

1st Pilot study

Human PBMCs was pretreated with a reference compound; Xiidra® (the final concentration @ 10uM) for 2h before stimulation. An equal volume of 0.5% DMSO was used as a vehicle control. Then, the cells were treated with stimulant(s), poly(I:C) at 25 ug/ml, LPS at 5 and 25 ug/ml at and PMA (5 ng/ml) / Ionomycin (1 ug/ml).

- 5 Triplicates of 100 ul of supernatants from treated cells was harvested at 12, 24, and 48 h and placed in 96 well for Human IL-6 ELISA measurement according to the manufacturer's instructions (Invitrogen, CA, USA).

The pilot study arm with triplicate wells per group in a 24-well plate:

1. PBMC: 0.5% DMSO
- 10 2. PBMC + Poly I:C (25ug/ml)
3. PBMC + LPS (5ug/ml)
4. PBMC + LPS (25ug/ml)
5. PBMC + PMA (5ng/ml)/Ionomycin (1ug/ml)
6. PBMC + Poly I:C (25ug/ml) + Xiidra® 10uM
- 15 7. PBMC + LPS (5ug/ml) + Xiidra® 10uM
8. PBMC + LPS (25ug/ml) + Xiidra® 10uM
9. PBMC + PMA (5ng/ml)/Ionomycin (1ug/ml) + Xiidra® 10uM

2nd Pilot study

- Human PBMCs was pretreated with a test compound; YDE-011 at 30uM, 1µM for 2h before stimulation. An equal volume of 0.5% DMSO was used as a vehicle control. Then, the cells were treated with stimulants, poly(I:C) at 25 ug/ml, LPS at 5 ug/ml at and PMA (5 ng/ml) / Ionomycin (1 ug/ml). The supernatants from treated cells were harvested at 24 h and placed in 96 well for Human IL-6 ELISAS measurement according to the manufacturer's instructions (Invitrogen, CA, USA).

- 25 The pilot study arm with duplicate wells per group in a 24-well plate:

1. PBMC: 0.5% DMSO
2. PBMC + Poly I:C (25ug/ml)
3. PBMC + LPS (5ug/ml)
4. PBMC + PMA (5ng/ml)/Ionomycin (1ug/ml)
- 30 5. PBMC + Poly I:C (25ug/ml) + Xiidra® 30uM
6. PBMC + LPS (5ug/ml) + Xiidra® 30uM
7. PBMC + PMA (5ng/ml)/Ionomycin (1ug/ml) + Xiidra® 30Um
8. PBMC + Poly I:C (25ug/ml) + Xiidra® 1uM

9. PBMC + LPS (5ug/ml) + Xiidra® 1uM

10. PBMC + PMA (5ng/ml)/Ionomycin (1ug/ml) + Xiidra® 1uM

Human IL-6 ELISA

IL-6 measurement was performed by the sandwich ELISA method. The
 5 capture antibody was coated on a 96-well plate (Corning™ Costar™ 9018, NY, USA) at 100ul/well and incubated overnight at 4°C. The interaction was blocked at room temperature for 2 h to prevent non-specific binding of the antigen-antibody. Then, the plate was incubated overnight at 4°C with 1:200 diluted cell supernatants and standard dilute serial dilutions at 100ul/well. Detection antibody was dispensed
 10 into the plate at 100ul/well, and then allowed to incubate at a room temperature for 1 h. Finally, streptavidin-HRP (100ul/well) was incubated at room temperature for 30 min. TMB substrate (100ul/well) was added and allowed to incubate for 15 min until colored reaction was observed in the dark condition. The sample reading was measured at 450nm wavelength and 570nm, and the quantification of the sample was
 15 converted as concentration (ng/ml) based on the standard curve extrapolation.

The Main Study

Human PBMCs were pretreated with YY-101, YDE-011, YDE-043 or reference compound; Xiidra® at various concentration (ranging from 5pM to 500nM) for 2 h before stimulation. An equal volume of 0.5% DMSO was used as a vehicle
 20 control. Then, the cells were treated with LPS at 5ug/ml, which was selected based on the pilot study. The supernatants from treated cells were harvested at 24 h and placed in a 96 well for Luminex cytokine & chemokine profiling using a Luminex 200 multiplex assay (Luminex; R&D system, USA).

The main study arm with triplicate wells per group in a 24-well plate:

- 25
1. Blank
 2. PBMC: 0.5% DMSO
 3. PBMC + LPS (5ug/ml)
 4. PBMC + YY-101 500 nM
 5. PBMC + YY-101 50 nM

30

 6. PBMC + YY-101 5 nM
 7. PBMC + YY-101 0.5 nM
 8. PBMC + LPS (5ug/ml) + Xiidra® 500 nM
 9. PBMC + LPS (5ug/ml) + Xiidra® 50 nM

10. PBMC + LPS (5ug/ml) + Xiidra® 5 nM
11. PBMC + LPS (5ug/ml) + Xiidra® 0.5 nM
12. PBMC + LPS (5ug/ml) + Xiidra® 0.05 nM
13. PBMC + LPS (5ug/ml) + Xiidra® 0.005 nM
- 5 14. PBMC + LPS (5ug/ml) + YY-101 500 nM
15. PBMC + LPS (5ug/ml) + YY-101 50 nM
16. PBMC + LPS (5ug/ml) + YY-101 5 nM
17. PBMC + LPS (5ug/ml) + YY-101 0.5 nM
18. PBMC + LPS (5ug/ml) + YY-101 0.05 nM
- 10 19. PBMC + LPS (5ug/ml) + YY-101 0.005 nM
20. PBMC + LPS (5ug/ml) + YDE-011 500 nM
21. PBMC + LPS (5ug/ml) + YDE-011 50 nM
22. PBMC + LPS (5ug/ml) + YDE-011 5 nM
23. PBMC + LPS (5ug/ml) + YDE-011 0.5 nM
- 15 24. PBMC + LPS (5ug/ml) + YDE-011 0.05 nM
25. PBMC + LPS (5ug/ml) + YDE-011 0.005 nM
26. PBMC + LPS (5ug/ml) + YDE-043 500 nM
27. PBMC + LPS (5ug/ml) + YDE-043 50 nM
28. PBMC + LPS (5ug/ml) + YDE-043 5 nM
- 20 29. PBMC + LPS (5ug/ml) + YDE-043 0.5 nM
30. PBMC + LPS (5ug/ml) + YDE-043 0.05 nM
31. PBMC + LPS (5ug/ml) + YDE-043 0.005 nM

Multiplex assay

Multiplex assay was used to measure 30 cytokines and chemokines. The

25 1:200 diluted cell supernatant and serial dilution of the standard were dispensed into a 96 well plate at 50ul/well. Then, the pre-mixed cocktail of antibody-coated magnetic beads was dispensed at 50ul/well and incubated at room temperature for 2 h in a horizontal orbital microplate shaker at 800± 500 rpm. The beads were washed using a magnetic device to prevent loss. The biotin-antibody was dispensed in 50ul

30 of each well and incubated at room temperature for 1 h in a shaker at 800± 500 rpm. After washing, streptavidin-PE was added at 50ul/well and incubated at room temperature for 30 min in a shaker under the same conditions. Finally, after washing, wash buffer (100ul/well) was added to the plate and incubated in a shaker for 2 min.

The Luminex™ 200 setting were set according to the manufacturer's protocol. The data was calculated with a standard five-parameter logistic nonlinear regression analysis of the data (xPonent software 4.2, USA). Results were presented as concentration (ng/ml or pg/ml).

5 Below is the list of cytokines and chemokines either in 26-plex or 4-plex.

Table 6

26 plex		4 plex	
Human	Cytokine/Chemokine list	Human	Cytokine/Chemokine list
1	MCP-1 (CCL2)	1	MIP-1 beta (CCL4)
2	MIP-1 alpha (CCL3)	2	RANTES (CCL5)
3	MIP-3 alpha (CCL20)	3	TIMP-1
4	Fractalkine (CX3CL1)	4	VEGF-A
5	Fas-L		
6	GM-CSF		
7	ICAM-1		
8	IFN-gamma		
9	IL-1 alpha		
10	IL-1 beta		
11	IL-2		
12	IL-4		
13	IL-5		
14	IL-6		
15	IL-8 (CXCL8)		
16	IL-10		
17	IL-13		

26 plex		4 plex	
18	IL-17A		
19	Leptin		
20	MMP-3		
21	MMP-8		
22	MMP-9		
23	RAGE		
24	L-Selectin		
25	TNF-alpha		
26	VEGF-D		

Compound Delivery & Formulation

The concentration of compound was prepared according to the information provided by the client.

- 5 All compound was serially diluted in from the stock concentrations and the final concentration of DMSO was not exceed 0.5% DMSO. All compounds were prepared on the same day of the treatment.

Statistical Analysis

- 10 All values are presented as mean $\pm$ standard error of mean (SEM). The statistical significance of the results was analyzed using one-way ANOVA with a Bonferroni post hoc. The statistical analyses were performed using the SPSS software (SPSS 22.0, USA). Each compound treated PBMCs was compared to that of the stimulant induced PBMCs. The significant threshold was fixed at 0.05 i.e. p value has to be lower than 0.05 to be significant.

15 **Results**

- Results are shown in Figures 6-22. Human PBMCs frozen purchased from ATCC in a cryopreservative were thawed, washed with Hank's Balanced Salt Solution containing 10% fetal bovine serum, and seeded onto a 24-well plate at a density of 1×10^6 cells/well with culture RPMI media containing 10% fetal bovine serum in growth media in a 24 well plate for 24 hrs and maintained at 37 °C in an atmosphere of 95% air and 5% CO₂. To establish, a pilot study was conducted to establish the timeline and pro-inflammatory stimulant, the cells are treated with stimulant(s), poly(I:C) at 25 ug/mL, LPS at 5 or 25 ug/mL at or PMA (5ng/ml)/ionomycin (1ug/ml), supernatants from treated cells are harvested at 12, 24

& 48 h and placed in 96 well for IL-6 ELISA measurement. For the main study, at the end of 24 hr culture, cells are pretreated with YY-101, YDE-011, YDE-043 or reference compound, Xiidra® at various concentrations for 2h before stimulation. An equal volume of 0.5% DMSO is used as a vehicle control. Then, the cells are treated with LPS. 20 uL of supernatants from treated cells are harvested at 24 hr post-LPS treatment and placed in 96 well for Luminex cytokine & chemokine profiling using a Luminex 200 multiplex assay.

In the pilot studies, all three stimulants (poly I:C, LPS and PMA/Ionomycin) significantly induced IL-6 production in hPBMCs in a time-dependent manner. The reference compound, Xiidra® and YDE-011 significantly reduced IL-6 levels induced by LPS or poly I:C. In the main test, hPBMCs stimulated by LPS at 5 ug/mL for 24 hrs were co-treated with test and reference compounds with various concentrations and from which cytokine release was measured. Among 30 cytokines and chemokines evaluated, YY-101, YDE-011 and YDE-043 at as low as 5pM significantly reduced LPS-induced pro-inflammatory cytokines and chemokines, IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3 and CCL-4. Among the compounds, YDE-043 significantly lowered LPS-induced IL-1a and IL-1b levels. In contrast, Xiidra® up to 500nM didn't affect any of LPS-induced cytokine/chemokine levels. Interestingly, the compound YY-101 didn't affect the basal levels of cytokine production.

IL-6 ELISA in 1st Pilot test:

IL-6 was measured by sandwich ELISA assay. poly I:C, LPS and PMA/Ionomycin significantly induced IL-6 production in hPBMCs in a time-dependent manner. Among all, LPS induced the highest level of IL-6 at 5 and 25 ug/mL equally.

In the presence of Xiidra® at 30 μ M, the reference compound, IL-6 induction was moderately reduced in all stimulants at 24 and 48hr. Based on strong IL-6 stimulation induced by LPS and poly I:C at 24 and 48 hrs and moderate effects of Xiidra® in the first pilot study, the second pilot study was designed to repeat the stimulants' effect and to elucidate the compound, YDE-011's modulatory effects.

IL-6 ELISA in 2nd Pilot test.

Similar to the first pilot study, a similar level of IL-6 induction was observed when hPBMCs were stimulated by poly I:C, LPS at 5 ug/mL or PMA/Ionomycin.

YDE-011 at 1 uM effectively and significantly reduced IL-6 induction in PBMCs stimulated by poly I:C, LPS or PMA/Ionomycin. The positive modulatory effect of YDE-011 was diminished at a higher concentration.

Multi-cytokine assessment in PBMCs stimulated by LPS.

5 In the main test, hPBMCs were stimulated by LPS at 5 ug/mL for 24 hrs and co-treated with vehicle (0.5% DMSO), test articles and reference compound, Xiidra® at various concentrations (500nM to 5pM). After 24 hr treatment, aliquots of hPBMC media were extracted, diluted in 1:200, and measured for cytokine levels using Luminex multiplex system.

10 Among 30 cytokines and chemokines evaluated, levels of 14 cytokines/chemokines passed the detection QC and the levels of 16 cytokines below the detection levels.

Conclusions

LPS effectively induced various pro-inflammatory cytokines in human PBMCs and its induction was potently and significantly reduced by all the compounds. Among those compounds, YDE-043 more effectively lowered cytokine and chemokine production. The reference marketed compound, Xiidra® at similar concentrations didn't modulate any of cytokine/chemokine levels, suggesting that YY and YDE compounds are more potent and effective immunomodulators in lowering pro-inflammatory cytokine/chemokine productions in human PBMCs when stimulated by endotoxins, such as LPS.

25 In conclusion, all of the test compounds, YY-101, YDE-011, YDE-043, potently and significantly reduced pro-inflammatory cytokine/chemokine production in human PBMCs stimulated by LPS.

Annex 1: 1st Pilot Study Raw Data

Table 7

Sample		12hr	24hr	48hr
PBMC+0.5% DMSO	1st	0	0	0
	2nd	0	0	0
	3rd	0	0	0
	Mean	0	0	0
	STDER	0	0	0
PBMC+Poly I:C(25ug/ml)	1st	15338.9	20950.9	26257.3

Sample		12hr	24hr	48hr
	2nd	11022.2	17695.4	21275.3
	3rd	11068.1	18514.6	19606
	Mean	12476.4	19053.6	22379.5
	STDER	1431.3	977.7	1997.9
PBMC+Poly I:C(25ug/ml)+Xiidra® 10uM	1st	16701.1	14320.1	18990.1
	2nd	15193.1	15773	19515.5
	3rd	14460	16445.9	23645
	Mean	15451.4	15513	20716.8
	STDER	659.7	627.3	1471.9
PBMC+LPS(5ug/ml)	1st	14335.4	23909.6	33897.3
	2nd	18694.5	22492.3	31019.9
	3rd	17440.3	21943.3	30259.1
	Mean	16823.4	22781.7	31725.4
	STDER	1295.6	585.8	1107.9
PBMC+LPS(5ug/ml)+Xi dra® 10uM	1st	14546.1	17436.8	23737.8
	2nd	14465.7	18053	24780.7
	3rd	13637.7	17850.2	27375.7
	Mean	14216.5	17780	25298.1
	STDER	290.3	181.3	1081.6
PBMC+LPS(25ug/ml)	1st	16538	21652.8	32026.4
	2nd	16547.8	20628.4	28839.7
	3rd	15060.5	21084.2	31748.5
	Mean	16048.8	21121.8	30871.5
	STDER	494.2	296.3	1019.1
PBMC+LPS(25ug/ml)+Xi idra® 10uM	1st	12065	18166.2	24395.9
	2nd	20113.3	16796.5	24754.1
	3rd	17779.6	17509.3	29892.3
	Mean	16652.7	17490.7	26347.5
	STDER	2390.7	395.5	1775.5
PBMC+PMA(5ng/ml)/Ion omycin(0.5ug/ml)	1st	1265.6	5302.9	12535.4
	2nd	1186.5	4731.7	12151.6
	3rd	1500.8	4977.8	13166.8
	Mean	1317.6	5004.1	12617.9
	STDER	94.4	165.4	296
PBMC+PMA(5ng/ml)/Ion omycin(0.5ug/ml)+Xiidra ® 10uM	1st	1150.9	3528	7815.5
	2nd	1196.5	3455.6	8506.2
	3rd	1096.5	3622.9	9128.3
	Mean	1148	3535.5	8483.3
	STDER	28.9	48.5	379.1

*Annex 2: 2nd Pilot Study Raw Data***Table 8**

Sample	24hr	
PBMC+0.5% DMSO	1st	0
	2nd	0
	Mean	0
	STDER	0
PBMC+Poly I:C(25ug/ml)	1st	24239.8
	2nd	18619.3
	Mean	21429.5
	STDER	2810.2
PBMC+Poly I:C(25ug/ml)+YDE-011 30uM	1st	39230.7
	2nd	30634.7
	Mean	34932.7
	STDER	4298
PBMC+Poly I:C(25ug/ml)+YDE-011 1uM	1st	13701
	2nd	12585.1
	Mean	13143.1
	STDER	557.9
PBMC+LPS(5ug/ml)	1st	29610.6
	2nd	22576
	Mean	26093.3
	STDER	3517.3
PBMC+LPS(5ug/ml)+YDE-011 30uM	1st	23199.5
	2nd	18310.8
	Mean	20755.2
	STDER	2444.3
PBMC+LPS(5ug/ml)+YDE-011 1uM	1st	14532.1
	2nd	12561.2
	Mean	13546.7
	STDER	985.4
PBMC+PMA(1ng/ml)/Ionomycin(0.5ug/ml)	1st	3031.7
	2nd	5119.3
	Mean	4075.5
	STDER	1043.8
PBMC+PMA(1ng/ml)/Ionomycin(0.5ug/ml)+YDE-011 30uM	1st	3114.6
	2nd	3025
	Mean	3069.8
	STDER	44.8
PBMC+PMA(1ng/ml)/Ionomycin(0.5ug/ml)+YDE-011 1uM	1st	2817.2
	2nd	3828.2
	Mean	3322.7

Sample	24hr	
	STDER	505.5

Annex 3: The Main Study Raw Data

Table 9

Bead name : IL-2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	29.0	67.0	1.0	<0.45
	2nd	31.0	67.0	1.0	0.45
	Mean	30.0	67.0	1.0	#DIV/0!
	STDER	1.0	0.0	0.0	#DIV/0!
PBMC + 0.5% DMSO	1st	30.0	87.0	200.0	5.9
	2nd	30.0	86.0	200.0	5.9
	3rd	32.0	107.0	200.0	173.5
	Mean	30.7	93.3	200.0	61.8
	STDER	0.7	6.8	0.0	55.9
PBMC+LPS(5ug/ml)	1st	88.5	68.0	200.0	4607.6
	2nd	74.0	85.0	200.0	3485.4
	3rd	79.0	107.0	200.0	3873.0
	Mean	80.5	86.7	200.0	3988.7
	STDER	4.3	11.3	0.0	329.1
PBMC+YY101 500nM	1st	31.5	86.0	200.0	132.3
	2nd	33.0	102.0	200.0	255.5
	Mean	32.3	94.0	200.0	193.9
	STDER	0.8	8.0	0.0	61.6
PBMC+YY101 50nM	1st	30.5	88.0	200.0	48.8
	2nd	32.0	75.0	200.0	173.5
	Mean	31.3	81.5	200.0	111.2
	STDER	0.8	6.5	0.0	62.4
PBMC+YY101 5nM	1st	32.0	86.0	200.0	173.5
	2nd	32.0	101.0	200.0	173.5
	Mean	32.0	93.5	200.0	173.5
	STDER	0.0	7.5	0.0	0.0
PBMC+YY101 0.5nM	1st	32.0	84.0	200.0	173.5
	2nd	34.0	92.0	200.0	337.0
	Mean	33.0	88.0	200.0	255.2
	STDER	1.0	4.0	0.0	81.7
PBMC+YY101 0.05uM	1st	38.0	105.0	200.0	659.4
	2nd	34.0	92.0	200.0	337.0
	Mean	36.0	98.5	200.0	498.2
	STDER	2.0	6.5	0.0	161.2
PBMC+LPS(5ug/ml)+ Xiidra 500nM	1st	88.0	101.0	200.0	4569.0
	2nd	86.0	97.0	200.0	4414.5
	Mean	87.0	99.0	200.0	4491.8
	STDER	1.0	2.0	0.0	77.3

Bead name : IL-2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+ Xiidra 50nM	1st	90.0	69.0	200.0	4723.4
	2nd	93.0	95.0	200.0	4954.9
	Mean	91.5	82.0	200.0	4839.1
	STDER	1.5	13.0	0.0	115.7
PBMC+LPS(5ug/ml)+ Xiidra 5nM	1st	83.0	70.0	200.0	4182.6
	2nd	95.0	79.0	200.0	5109.1
	Mean	89.0	74.5	200.0	4645.8
	STDER	6.0	4.5	0.0	463.2
PBMC+LPS(5ug/ml)+ Xiidra 0.5nM	1st	76.0	87.0	200.0	3640.5
	2nd	79.5	80.0	200.0	3911.7
	Mean	77.8	83.5	200.0	3776.1
	STDER	1.8	3.5	0.0	135.6
PBMC+LPS(5ug/ml)+ Xiidra 0.05nM	1st	74.0	103.0	200.0	3485.4
	2nd	81.5	94.0	200.0	4066.6
	Mean	77.8	98.5	200.0	3776.0
	STDER	3.8	4.5	0.0	290.6
PBMC+LPS(5ug/ml)+ Xiidra 0.005nM	1st	79.0	74.0	200.0	3873.0
	2nd	72.0	67.0	200.0	3330.1
	Mean	75.5	70.5	200.0	3601.6
	STDER	3.5	3.5	0.0	271.4
PBMC+LPS(5ug/ml)+ YY101 500nM	1st	64.0	68.0	200.0	2707.7
	2nd	66.0	84.0	200.0	2863.5
	3rd	62.0	84.0	200.0	2551.7
	Mean	64.0	78.7	200.0	2707.6
	STDER	1.2	5.3	0.0	90.0
PBMC+LPS(5ug/ml)+ YY101 50nM	1st	61.0	79.0	200.0	2473.6
	2nd	64.0	96.0	200.0	2707.7
	3rd	66.0	99.0	200.0	2863.5
	Mean	63.7	91.3	200.0	2681.6
	STDER	1.5	6.2	0.0	113.3
PBMC+LPS(5ug/ml)+ YY101 5nM	1st	61.0	87.0	200.0	2473.6
	2nd	63.0	83.0	200.0	2629.7
	3rd	67.0	67.0	200.0	2941.4
	Mean	63.7	79.0	200.0	2681.6
	STDER	1.8	6.1	0.0	137.5
PBMC+LPS(5ug/ml)+ YY101 0.5nM	1st	66.0	102.0	200.0	2863.5
	2nd	65.0	87.0	200.0	2785.6
	3rd	65.5	74.0	200.0	2824.6
	Mean	65.5	87.7	200.0	2824.6
	STDER	0.3	8.1	0.0	22.5
PBMC+LPS(5ug/ml)+ YY101 0.05nM	1st	65.0	82.0	200.0	2785.6
	2nd	70.0	87.0	200.0	3174.7
	3rd	68.5	96.0	200.0	3058.1
	Mean	67.8	88.3	200.0	3006.1
	STDER	1.5	4.1	0.0	115.3

Bead name : IL-2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+ YY101 0.005nM	1st	64.5	76.0	200.0	2746.7
	2nd	64.0	61.0	200.0	2707.7
	3rd	62.0	68.0	200.0	2551.7
	Mean	63.5	68.3	200.0	2668.7
	STDER	0.8	4.3	0.0	59.6
PBMC+LPS(5ug/ml)+ YDE011 500nM	1st	67.0	85.0	200.0	2941.4
	2nd	37.0	95.0	200.0	579.2
	3rd	51.5	86.0	200.0	1729.4
	Mean	51.8	88.7	200.0	1750.0
	STDER	8.7	3.2	0.0	682.0
PBMC+LPS(5ug/ml)+ YDE011 50nM	1st	56.0	111.0	200.0	2082.5
	2nd	57.0	71.0	200.0	2160.8
	3rd	38.0	81.0	200.0	659.4
	Mean	50.3	87.7	200.0	1634.3
	STDER	6.2	12.0	0.0	487.9
PBMC+LPS(5ug/ml)+ YDE011 5nM	1st	49.0	80.0	200.0	1532.6
	2nd	50.0	83.0	200.0	1611.3
	3rd	62.0	100.0	200.0	2551.7
	Mean	53.7	87.7	200.0	1898.5
	STDER	4.2	6.2	0.0	327.4
PBMC+LPS(5ug/ml)+ YDE011 0.5nM	1st	58.0	85.0	200.0	2239.1
	2nd	54.0	82.0	200.0	1925.7
	3rd	57.5	92.0	200.0	2200.0
	Mean	56.5	86.3	200.0	2121.6
	STDER	1.3	3.0	0.0	98.6
PBMC+LPS(5ug/ml)+ YDE011 0.05nM	1st	64.0	90.0	200.0	2707.7
	2nd	61.0	86.0	200.0	2473.6
	3rd	65.5	102.0	200.0	2824.6
	Mean	63.5	92.7	200.0	2668.6
	STDER	1.3	4.8	0.0	103.2
PBMC+LPS(5ug/ml)+ YDE011 0.005nM	1st	58.0	79.0	200.0	2239.1
	2nd	56.0	78.0	200.0	2082.5
	3rd	64.0	100.0	200.0	2707.7
	Mean	59.3	85.7	200.0	2343.1
	STDER	2.4	7.2	0.0	187.8
PBMC+LPS(5ug/ml)+ YDE043 500nM	1st	55.0	95.0	200.0	2004.2
	2nd	56.0	84.0	200.0	2082.5
	3rd	58.0	87.0	200.0	2239.1
	Mean	56.3	88.7	200.0	2108.6
	STDER	0.9	3.3	0.0	69.1
PBMC+LPS(5ug/ml)+ YDE043 50nM	1st	62.0	90.0	200.0	2551.7
	2nd	60.0	102.0	200.0	2395.5
	3rd	58.0	87.0	200.0	2239.1
	Mean	60.0	93.0	200.0	2395.4
	STDER	1.2	4.6	0.0	90.2

Bead name : IL-2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+ YDE043 5nM	1st	65.0	76.0	200.0	2785.6
	2nd	60.0	77.0	200.0	2395.5
	3rd	61.0	103.0	200.0	2473.6
	Mean	62.0	85.3	200.0	2551.6
	STDER	1.5	8.8	0.0	119.2
PBMC+LPS(5ug/ml)+ YDE043 0.5nM	1st	56.0	83.0	200.0	2082.5
	2nd	59.0	98.0	200.0	2317.3
	3rd	56.5	92.0	200.0	2121.7
	Mean	57.2	91.0	200.0	2173.8
	STDER	0.9	4.4	0.0	72.6
PBMC+LPS(5ug/ml)+ YDE043 0.05nM	1st	55.0	72.0	200.0	2004.2
	2nd	58.0	80.0	200.0	2239.1
	3rd	58.0	88.0	200.0	2239.1
	Mean	57.0	80.0	200.0	2160.8
	STDER	1.0	4.6	0.0	78.3
PBMC+LPS(5ug/ml)+ YDE043 0.005nM	1st	58.0	82.0	200.0	2239.1
	2nd	59.0	85.0	200.0	2317.3
	3rd	68.5	66.0	200.0	3058.1
	Mean	61.8	77.7	200.0	2538.2
	STDER	3.3	5.9	0.0	260.9

Table 10

Bead name : IL-6					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	20.5	78.0	1.0	<2.65
	2nd	20.0	108.0	1.0	<2.65
	Mean	20.3	93.0	1.0	#DIV/0!
	STDER	0.3	15.0	0.0	#DIV/0!
PBMC + 0.5% DMSO	1st	22.5	94.0	200.0	16.1
	2nd	22.0	93.0	200.0	5.0
	3rd	22.0	111.0	200.0	5.0
	Mean	22.2	99.3	200.0	8.7
	STDER	0.2	5.8	0.0	3.7
PBMC+LPS(5ug/ml)	1st	1407.0	93.0	200.0	32871.0
	2nd	1182.0	74.0	200.0	27467.5
	3rd	1126.5	114.0	200.0	26138.3
	Mean	1238.5	93.7	200.0	28825.6
	STDER	85.8	11.6	0.0	2058.8
PBMC+YY101 500nM	1st	21.0	114.0	200.0	<2.65
	2nd	21.0	122.0	200.0	<2.65
	Mean	21.0	118.0	200.0	#DIV/0!
	STDER	0.0	4.0	0.0	#DIV/0!
PBMC+YY101 50nM	1st	22.0	84.0	200.0	5.0

Bead name : IL-6					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	20.0	106.0	200.0	<2.65
	Mean	21.0	95.0	200.0	5.0
	STDER	1.0	11.0	0.0	#DIV/0!
PBMC+YY101 5nM	1st	22.0	103.0	200.0	5.0
	2nd	22.0	100.0	200.0	5.0
	Mean	22.0	101.5	200.0	5.0
	STDER	0.0	1.5	0.0	0.0
PBMC+YY101 0.5nM	1st	22.0	99.0	200.0	5.0
	2nd	23.0	101.0	200.0	27.3
	Mean	22.5	100.0	200.0	16.2
	STDER	0.5	1.0	0.0	11.1
PBMC+YY101 0.05uM	1st	28.0	80.0	200.0	140.1
	2nd	20.0	106.0	200.0	<2.65
	Mean	24.0	93.0	200.0	140.1
	STDER	4.0	13.0	0.0	#DIV/0!
PBMC+LPS(5ug/ml)+X iidra 500nM	1st	1422.0	94.0	200.0	33232.1
	2nd	1420.0	84.0	200.0	33183.9
	Mean	1421.0	89.0	200.0	33208.0
	STDER	1.0	5.0	0.0	24.1
PBMC+LPS(5ug/ml)+X iidra 50nM	1st	1365.0	97.0	200.0	31860.4
	2nd	1427.5	122.0	200.0	33364.6
	Mean	1396.3	109.5	200.0	32612.5
	STDER	31.3	12.5	0.0	752.1
PBMC+LPS(5ug/ml)+X iidra 5nM	1st	1234.5	114.0	200.0	28726.1
	2nd	1306.0	109.0	200.0	30442.3
	Mean	1270.3	111.5	200.0	29584.2
	STDER	35.8	2.5	0.0	858.1
PBMC+LPS(5ug/ml)+X iidra 0.5nM	1st	1094.5	108.0	200.0	25372.4
	2nd	1188.5	102.0	200.0	27623.3
	Mean	1141.5	105.0	200.0	26497.8
	STDER	47.0	3.0	0.0	1125.4
PBMC+LPS(5ug/ml)+X iidra 0.05nM	1st	1112.0	127.0	200.0	25791.2
	2nd	1129.0	104.0	200.0	26198.1
	Mean	1120.5	115.5	200.0	25994.6
	STDER	8.5	11.5	0.0	203.5
PBMC+LPS(5ug/ml)+X iidra 0.005nM	1st	1131.5	108.0	200.0	26257.9
	2nd	1091.0	94.0	200.0	25288.7
	Mean	1111.3	101.0	200.0	25773.3
	STDER	20.3	7.0	0.0	484.6
PBMC+LPS(5ug/ml)+Y Y101 500nM	1st	749.0	65.0	200.0	17129.3
	2nd	775.0	118.0	200.0	17748.1
	3rd	727.5	84.0	200.0	16617.9
	Mean	750.5	89.0	200.0	17165.1
	STDER	13.7	15.5	0.0	326.8

Bead name : IL-6					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+Y Y101 50nM	1st	715.0	87.0	200.0	16320.6
	2nd	730.5	112.0	200.0	16689.2
	3rd	780.5	98.0	200.0	17879.0
	Mean	742.0	99.0	200.0	16962.9
	STDER	19.8	7.2	0.0	470.2
PBMC+LPS(5ug/ml)+Y Y101 5nM	1st	727.0	95.0	200.0	16606.0
	2nd	720.0	84.0	200.0	16439.5
	3rd	813.0	105.0	200.0	18652.8
	Mean	753.3	94.7	200.0	17232.8
	STDER	29.9	6.1	0.0	711.7
PBMC+LPS(5ug/ml)+Y Y101 0.5nM	1st	788.5	94.0	200.0	18069.4
	2nd	754.0	98.0	200.0	17248.3
	3rd	816.5	96.0	200.0	18736.2
	Mean	786.3	96.0	200.0	18018.0
	STDER	18.1	1.2	0.0	430.3
PBMC+LPS(5ug/ml)+Y Y101 0.05nM	1st	769.0	94.0	200.0	17605.3
	2nd	832.0	99.0	200.0	19105.4
	3rd	803.0	87.0	200.0	18414.7
	Mean	801.3	93.3	200.0	18375.1
	STDER	18.2	3.5	0.0	433.5
PBMC+LPS(5ug/ml)+Y Y101 0.005nM	1st	817.5	106.0	200.0	18760.0
	2nd	772.0	85.0	200.0	17676.7
	3rd	775.0	97.0	200.0	17748.1
	Mean	788.2	96.0	200.0	18061.6
	STDER	14.7	6.1	0.0	349.8
PBMC+LPS(5ug/ml)+Y DE011 500nM	1st	843.0	88.0	200.0	19367.5
	2nd	422.5	96.0	200.0	9383.5
	3rd	657.5	98.0	200.0	14953.9
	Mean	641.0	94.0	200.0	14568.3
	STDER	121.7	3.1	0.0	2888.6
PBMC+LPS(5ug/ml)+Y DE011 50nM	1st	732.0	132.0	200.0	16724.9
	2nd	754.0	97.0	200.0	17248.3
	3rd	444.0	97.0	200.0	9892.0
	Mean	643.3	108.7	200.0	14621.7
	STDER	99.9	11.7	0.0	2369.7
PBMC+LPS(5ug/ml)+Y DE011 5nM	1st	537.0	93.0	200.0	12094.3
	2nd	573.0	105.0	200.0	12947.9
	3rd	684.0	93.0	200.0	15583.6
	Mean	598.0	97.0	200.0	13541.9
	STDER	44.2	4.0	0.0	1050.1
PBMC+LPS(5ug/ml)+Y DE011 0.5nM	1st	673.0	99.0	200.0	15322.2
	2nd	687.0	97.0	200.0	15654.9
	3rd	676.0	104.0	200.0	15393.5
	Mean	678.7	100.0	200.0	15456.8

Bead name : IL-6					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	STDER	4.3	2.1	0.0	101.1
PBMC+LPS(5ug/ml)+Y DE011 0.05nM	1st	821.0	96.0	200.0	18843.4
	2nd	800.0	81.0	200.0	18343.3
	3rd	810.0	84.0	200.0	18581.4
	Mean	810.3	87.0	200.0	18589.3
	STDER	6.1	4.6	0.0	144.4
PBMC+LPS(5ug/ml)+Y DE011 0.005nM	1st	737.0	73.0	200.0	16843.8
	2nd	670.0	89.0	200.0	15250.9
	3rd	712.0	114.0	200.0	16249.2
	Mean	706.3	92.0	200.0	16114.6
	STDER	19.5	11.9	0.0	464.7
PBMC+LPS(5ug/ml)+Y DE043 500nM	1st	612.0	95.0	200.0	13873.4
	2nd	612.0	95.0	200.0	13873.4
	3rd	654.5	86.0	200.0	14882.6
	Mean	626.2	92.0	200.0	14209.8
	STDER	14.2	3.0	0.0	336.4
PBMC+LPS(5ug/ml)+Y DE043 50nM	1st	742.0	89.0	200.0	16962.8
	2nd	725.5	94.0	200.0	16570.3
	3rd	645.5	118.0	200.0	14668.8
	Mean	704.3	100.3	200.0	16067.3
	STDER	29.8	9.0	0.0	708.4
PBMC+LPS(5ug/ml)+Y DE043 5nM	1st	717.5	80.0	200.0	16380.0
	2nd	753.0	73.0	200.0	17224.5
	3rd	698.0	121.0	200.0	15916.4
	Mean	722.8	91.3	200.0	16507.0
	STDER	16.1	15.0	0.0	382.9
PBMC+LPS(5ug/ml)+Y DE043 0.5nM	1st	673.0	83.0	200.0	15322.2
	2nd	663.0	101.0	200.0	15084.6
	3rd	618.5	92.0	200.0	14027.7
	Mean	651.5	92.0	200.0	14811.5
	STDER	16.8	5.2	0.0	397.9
PBMC+LPS(5ug/ml)+Y DE043 0.05nM	1st	591.5	90.0	200.0	13386.9
	2nd	647.5	96.0	200.0	14716.3
	3rd	645.0	99.0	200.0	14657.0
	Mean	628.0	95.0	200.0	14253.4
	STDER	18.3	2.6	0.0	433.6
PBMC+LPS(5ug/ml)+Y DE043 0.005nM	1st	690.0	89.0	200.0	15726.2
	2nd	734.0	87.0	200.0	16772.5
	3rd	892.0	99.0	200.0	20535.6
	Mean	772.0	91.7	200.0	17678.1
	STDER	61.3	3.7	0.0	1460.3

Table 11

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	32.0	76.0	1.0	0.3
	2nd	30.0	90.0	1.0	0.2
	Mean	31.0	83.0	1.0	0.3
	STDE R	1.0	7.0	0.0	0.1
PBMC + 0.5% DMSO	1st	287.5	78.0	200.0	3955.9
	2nd	110.5	86.0	200.0	1155.1
	3rd	113.0	91.0	200.0	1192.3
	Mean	170.3	85.0	200.0	2101.1
	STDE R	58.6	3.8	0.0	927.5
PBMC+LPS(5ug/ml)	1st	4811.0	82.0	200.0	100889.1
	2nd	4193.0	91.0	200.0	84243.2
	3rd	4083.0	83.0	200.0	81501.2
	Mean	4362.3	85.3	200.0	88877.9
	STDE R	226.6	2.8	0.0	6057.6
PBMC+YY101 500nM	1st	120.0	87.0	200.0	1297.1
	2nd	165.0	93.0	200.0	1986.4
	Mean	142.5	90.0	200.0	1641.8
	STDE R	22.5	3.0	0.0	344.6
PBMC+YY101 50nM	1st	166.5	76.0	200.0	2009.8
	2nd	117.0	85.0	200.0	1252.1
	Mean	141.8	80.5	200.0	1630.9
	STDE R	24.8	4.5	0.0	378.8
PBMC+YY101 5nM	1st	281.0	93.0	200.0	3848.8

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	151.0	87.0	200.0	1769.4
	Mean	216.0	90.0	200.0	2809.1
	STDE R	65.0	3.0	0.0	1039.7
PBMC+YY101 0.5nM	1st	164.0	81.0	200.0	1970.8
	2nd	368.0	89.0	200.0	5300.9
	Mean	266.0	85.0	200.0	3635.9
	STDE R	102.0	4.0	0.0	1665.0
PBMC+YY101 0.05uM	1st	836.5	74.0	200.0	13586.7
	2nd	207.0	97.0	200.0	2648.7
	Mean	521.8	85.5	200.0	8117.7
	STDE R	314.8	11.5	0.0	5469.0
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	4811.0	90.0	200.0	100889.1
	2nd	4424.0	73.0	200.0	90193.3
	Mean	4617.5	81.5	200.0	95541.2
	STDE R	193.5	8.5	0.0	5347.9
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	4604.0	66.0	200.0	95040.0
	2nd	4553.0	99.0	200.0	93646.0
	Mean	4578.5	82.5	200.0	94343.0
	STDE R	25.5	16.5	0.0	697.0
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	4476.0	84.0	200.0	91572.9
	2nd	4697.5	74.0	200.0	97642.3
	Mean	4586.8	79.0	200.0	94607.6

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	STDE R	110.8	5.0	0.0	3034.7
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	4067.5	78.0	200.0	81119.1
	2nd	4450.5	96.0	200.0	90894.4
	Mean	4259.0	87.0	200.0	86006.8
	STDE R	191.5	9.0	0.0	4887.6
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	4169.0	109.0	200.0	83640.3
	2nd	4413.0	73.0	200.0	89903.5
	Mean	4291.0	91.0	200.0	86771.9
	STDE R	122.0	18.0	0.0	3131.6
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	4154.0	91.0	200.0	83264.8
	2nd	4103.5	100.0	200.0	82008.2
	Mean	4128.8	95.5	200.0	82636.5
	STDE R	25.3	4.5	0.0	628.3
PBMC+LPS(5ug/ml)+YY101 500nM	1st	3175.0	77.0	200.0	60492.6
	2nd	3150.0	81.0	200.0	59945.6
	3rd	2895.0	68.0	200.0	54438.6
	Mean	3073.3	75.3	200.0	58292.3
	STDE R	89.5	3.8	0.0	1933.3
PBMC+LPS(5ug/ml)+YY101 50nM	1st	2910.0	67.0	200.0	54759.1
	2nd	2830.5	114.0	200.0	53065.0
	3rd	2978.0	91.0	200.0	56217.2
	Mean	2906.2	90.7	200.0	54680.4

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	STDE R	42.6	13.6	0.0	910.8
PBMC+LPS(5ug/ml)+YY101 5nM	1st	2948.5	96.0	200.0	55583.6
	2nd	2967.0	77.0	200.0	55980.8
	3rd	3170.0	75.0	200.0	60383.1
	Mean	3028.5	82.7	200.0	57315.8
	STDE R	71.0	6.7	0.0	1537.9
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	3194.0	89.0	200.0	60909.2
	2nd	3056.0	95.0	200.0	57900.7
	3rd	3241.0	61.0	200.0	61943.2
	Mean	3163.7	81.7	200.0	60251.0
	STDE R	55.5	10.5	0.0	1212.5
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	3031.0	88.0	200.0	57359.8
	2nd	3177.0	77.0	200.0	60536.4
	3rd	3247.0	77.0	200.0	62075.6
	Mean	3151.7	80.7	200.0	59990.6
	STDE R	63.6	3.7	0.0	1388.4
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	3223.0	64.0	200.0	61546.6
	2nd	3009.0	78.0	200.0	56884.9
	3rd	3015.0	75.0	200.0	57014.3
	Mean	3082.3	72.3	200.0	58481.9
	STDE R	70.4	4.3	0.0	1532.8
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	3436.0	70.0	200.0	66288.2

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	1788.0	97.0	200.0	31741.3
	3rd	2708.0	79.0	200.0	50476.2
	Mean	2644.0	82.0	200.0	49501.9
	STDE R	476.8	7.9	0.0	9984.7
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	2885.5	86.0	200.0	54235.8
	2nd	2934.0	74.0	200.0	55272.7
	3rd	1763.5	68.0	200.0	31257.8
	Mean	2527.7	76.0	200.0	46922.1
	STDE R	382.3	5.3	0.0	7837.9
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	2473.5	80.0	200.0	45587.7
	2nd	2353.0	76.0	200.0	43107.6
	3rd	2728.5	94.0	200.0	50907.7
	Mean	2518.3	83.3	200.0	46534.3
	STDE R	110.7	5.5	0.0	2300.9
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	2824.0	110.0	200.0	52927.0
	2nd	2793.0	107.0	200.0	52269.8
	3rd	2767.5	88.0	200.0	51730.5
	Mean	2794.8	101.7	200.0	52309.1
	STDE R	16.3	6.9	0.0	346.0
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	3224.0	105.0	200.0	61568.6
	2nd	3187.0	75.0	200.0	60755.7
	3rd	3203.0	82.0	200.0	61106.8

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	Mean	3204.7	87.3	200.0	61143.7
	STDE R	10.7	9.1	0.0	235.4
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	2963.5	76.0	200.0	55905.6
	2nd	2780.0	84.0	200.0	51994.7
	3rd	2980.0	103.0	200.0	56260.2
	Mean	2907.8	87.7	200.0	54720.2
	STDE R	64.1	8.0	0.0	1366.6
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	2752.5	58.0	200.0	51413.7
	2nd	2670.0	97.0	200.0	49678.2
	3rd	2861.0	86.0	200.0	53713.6
	Mean	2761.2	80.3	200.0	51601.8
	STDE R	55.3	11.6	0.0	1168.7
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	3049.5	72.0	200.0	57759.9
	2nd	3090.0	89.0	200.0	58638.2
	3rd	2701.0	90.0	200.0	50329.0
	Mean	2946.8	83.7	200.0	55575.7
	STDE R	123.5	5.8	0.0	2635.6
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	2993.0	69.0	200.0	56540.0
	2nd	3073.0	69.0	200.0	58269.2
	3rd	2846.0	105.0	200.0	53394.4
	Mean	2970.7	81.0	200.0	56067.9
	STDE R	66.5	12.0	0.0	1426.9

Bead name : IL-8/CXCL8					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	2928.0	66.0	200.0	55144.2
	2nd	2761.0	89.0	200.0	51593.2
	3rd	2697.0	81.0	200.0	50244.9
	Mean	2795.3	78.7	200.0	52327.4
	STDER	68.9	6.7	0.0	1461.2
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	2613.0	77.0	200.0	48485.5
	2nd	2832.5	60.0	200.0	53107.5
	3rd	2773.0	89.0	200.0	51846.7
	Mean	2739.5	75.3	200.0	51146.6
	STDER	65.5	8.4	0.0	1379.4
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	2977.5	86.0	200.0	56206.5
	2nd	2856.0	81.0	200.0	53607.2
	3rd	3484.0	72.0	200.0	67372.3
	Mean	3105.8	79.7	200.0	59062.0
	STDER	192.3	4.1	0.0	4222.4

Table 12

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	63.5	64.0	1.0	<2.59
	2nd	61.0	61.0	1.0	<2.59
	Mean	62.3	62.5	1.0	#DIV/0!
	STDER	1.3	1.5	0.0	#DIV/0!
PBMC + 0.5% DMSO	1st	57.0	61.0	200.0	<2.59
	2nd	55.0	63.0	200.0	<2.59
	3rd	61.0	70.0	200.0	<2.59
	Mean	57.7	64.7	200.0	#DIV/0!
	STDER	1.8	2.7	0.0	#DIV/0!

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)	1st	134.5	54.0	200.0	1536.4
	2nd	127.5	50.0	200.0	1367.3
	3rd	123.5	60.0	200.0	1269.7
	Mean	128.5	54.7	200.0	1391.1
	STDER	3.2	2.9	0.0	77.9
PBMC+YY101 500nM	1st	59.0	50.0	200.0	<2.59
	2nd	67.5	50.0	200.0	<2.59
	Mean	63.3	50.0	200.0	#DIV/0!
	STDER	4.3	0.0	0.0	#DIV/0!
PBMC+YY101 50nM	1st	57.5	70.0	200.0	<2.59
	2nd	59.0	57.0	200.0	<2.59
	Mean	58.3	63.5	200.0	#DIV/0!
	STDER	0.8	6.5	0.0	#DIV/0!
PBMC+YY101 5nM	1st	61.0	72.0	200.0	<2.59
	2nd	66.0	70.0	200.0	<2.59
	Mean	63.5	71.0	200.0	#DIV/0!
	STDER	2.5	1.0	0.0	#DIV/0!
PBMC+YY101 0.5nM	1st	61.0	55.0	200.0	<2.59
	2nd	61.0	55.0	200.0	<2.59
	Mean	61.0	55.0	200.0	#DIV/0!
	STDER	0.0	0.0	0.0	#DIV/0!
PBMC+YY101 0.05uM	1st	59.5	50.0	200.0	<2.59
	2nd	62.5	64.0	200.0	<2.59
	Mean	61.0	57.0	200.0	#DIV/0!
	STDER	1.5	7.0	0.0	#DIV/0!
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	114.0	67.0	200.0	1034.6
	2nd	111.0	62.0	200.0	959.2
	Mean	112.5	64.5	200.0	996.9
	STDER	1.5	2.5	0.0	37.7
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	126.0	51.0	200.0	1330.8
	2nd	147.0	69.0	200.0	1833.9
	Mean	136.5	60.0	200.0	1582.3
	STDER	10.5	9.0	0.0	251.5
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	135.0	70.0	200.0	1548.4

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	139.0	63.0	200.0	1644.1
	Mean	137.0	66.5	200.0	1596.3
	STDER	2.0	3.5	0.0	47.9
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	114.5	66.0	200.0	1047.1
	2nd	129.5	72.0	200.0	1415.8
	Mean	122.0	69.0	200.0	1231.5
	STDER	7.5	3.0	0.0	184.4
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	119.0	78.0	200.0	1158.9
	2nd	130.0	50.0	200.0	1427.9
	Mean	124.5	64.0	200.0	1293.4
	STDER	5.5	14.0	0.0	134.5
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	117.5	50.0	200.0	1121.8
	2nd	128.0	51.0	200.0	1379.4
	Mean	122.8	50.5	200.0	1250.6
	STDER	5.3	0.5	0.0	128.8
PBMC+LPS(5ug/ml)+YY101 500nM	1st	106.0	71.0	200.0	832.3
	2nd	108.0	69.0	200.0	883.3
	3rd	103.0	50.0	200.0	755.1
	Mean	105.7	63.3	200.0	823.5
	STDER	1.5	6.7	0.0	37.3
PBMC+LPS(5ug/ml)+YY101 50nM	1st	99.0	50.0	200.0	651.0
	2nd	106.5	50.0	200.0	845.0
	3rd	104.5	50.0	200.0	793.8
	Mean	103.3	50.0	200.0	763.3
	STDER	2.2	0.0	0.0	58.1
PBMC+LPS(5ug/ml)+YY101 5nM	1st	107.0	65.0	200.0	857.8

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	110.0	52.0	200.0	934.0
	3rd	113.0	50.0	200.0	1009.5
	Mean	110.0	55.7	200.0	933.8
	STDER	1.7	4.7	0.0	43.8
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	107.5	62.0	200.0	870.5
	2nd	101.0	54.0	200.0	703.2
	3rd	101.5	58.0	200.0	716.2
	Mean	103.3	58.0	200.0	763.3
	STDER	2.1	2.3	0.0	53.7
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	105.0	61.0	200.0	806.6
	2nd	117.5	52.0	200.0	1121.8
	3rd	108.0	54.0	200.0	883.3
	Mean	110.2	55.7	200.0	937.2
	STDER	3.8	2.7	0.0	94.9
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	106.0	52.0	200.0	832.3
	2nd	100.0	53.0	200.0	677.1
	3rd	104.0	57.0	200.0	780.9
	Mean	103.3	54.0	200.0	763.4
	STDER	1.8	1.5	0.0	45.6
PBMC+LPS(5ug/ml)+YDE01 1 500nM	1st	108.0	70.0	200.0	883.3
	2nd	60.0	83.0	200.0	<2.59
	3rd	83.5	50.0	200.0	225.5
	Mean	83.8	67.7	200.0	554.4
	STDER	13.9	9.6	0.0	328.9
PBMC+LPS(5ug/ml)+YDE01 1 50nM	1st	94.0	67.0	200.0	518.2
	2nd	106.5	50.0	200.0	845.0
	3rd	58.0	53.0	200.0	<2.59
	Mean	86.2	56.7	200.0	681.6

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	STDER	14.5	5.2	0.0	163.4
PBMC+LPS(5ug/ml)+YDE01 1 5nM	1st	82.0	73.0	200.0	181.1
	2nd	83.0	56.0	200.0	210.8
	3rd	89.0	61.0	200.0	381.9
	Mean	84.7	63.3	200.0	257.9
	STDER	2.2	5.0	0.0	62.6
PBMC+LPS(5ug/ml)+YDE01 1 0.5nM	1st	90.0	51.0	200.0	409.5
	2nd	86.0	67.0	200.0	297.6
	3rd	90.0	63.0	200.0	409.5
	Mean	88.7	60.3	200.0	372.2
	STDER	1.3	4.8	0.0	37.3
PBMC+LPS(5ug/ml)+YDE01 1 0.05nM	1st	102.0	71.0	200.0	729.2
	2nd	97.5	56.0	200.0	611.5
	3rd	99.0	64.0	200.0	651.0
	Mean	99.5	63.7	200.0	663.9
	STDER	1.3	4.3	0.0	34.6
PBMC+LPS(5ug/ml)+YDE01 1 0.005nM	1st	98.0	60.0	200.0	624.7
	2nd	90.0	57.0	200.0	409.5
	3rd	94.5	50.0	200.0	531.7
	Mean	94.2	55.7	200.0	521.9
	STDER	2.3	3.0	0.0	62.3
PBMC+LPS(5ug/ml)+YDE04 3 500nM	1st	92.0	54.0	200.0	464.2
	2nd	95.0	71.0	200.0	545.0
	3rd	91.0	53.0	200.0	436.9
	Mean	92.7	59.3	200.0	482.0
	STDER	1.2	5.8	0.0	32.5
PBMC+LPS(5ug/ml)+YDE04 3 50nM	1st	96.0	64.0	200.0	571.7
	2nd	97.0	56.0	200.0	598.2
	3rd	94.0	72.0	200.0	518.2
	Mean	95.7	64.0	200.0	562.7
	STDER	0.9	4.6	0.0	23.5
PBMC+LPS(5ug/ml)+YDE04 3 5nM	1st	95.0	54.0	200.0	545.0
	2nd	98.5	50.0	200.0	637.8
	3rd	95.5	80.0	200.0	558.4
	Mean	96.3	61.3	200.0	580.4
	STDER	1.1	9.4	0.0	29.0
PBMC+LPS(5ug/ml)+YDE04 3 0.5nM	1st	91.0	55.0	200.0	436.9
	2nd	93.0	61.0	200.0	491.3
	3rd	98.0	65.0	200.0	624.7
	Mean	94.0	60.3	200.0	517.6
	STDER	2.1	2.9	0.0	55.8
PBMC+LPS(5ug/ml)+YDE04 3 0.05nM	1st	91.0	57.0	200.0	436.9
	2nd	94.0	60.0	200.0	518.2
	3rd	89.0	51.0	200.0	381.9

Bead name : IL-10					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 0.005nM	Mean	91.3	56.0	200.0	445.7
	STDER	1.5	2.6	0.0	39.6
	1st	99.0	62.0	200.0	651.0
	2nd	105.0	57.0	200.0	806.6
	3rd	118.0	68.0	200.0	1134.2
	Mean	107.3	62.3	200.0	863.9
	STDER	5.6	3.2	0.0	142.4

Table 13

Bead name : TNF-alpha					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	19.0	79.0	1.0	<7.70
	2nd	21.0	89.0	1.0	<7.70
	Mean	20.0	84.0	1.0	#DIV/0!
	STDER	1.0	5.0	0.0	#DIV/0!
PBMC + 0.5% DMSO	1st	21.0	76.0	200.0	<7.70
	2nd	19.0	77.0	200.0	<7.70
	3rd	19.5	100.0	200.0	<7.70
	Mean	19.8	84.3	200.0	#DIV/0!
	STDER	0.6	7.8	0.0	#DIV/0!
PBMC+LPS(5ug/ml)	1st	78.0	72.0	200.0	3554.3
	2nd	66.0	87.0	200.0	2809.1
	3rd	61.0	104.0	200.0	2495.5
	Mean	68.3	87.7	200.0	2953.0
	STDER	5.0	9.2	0.0	314.0

Bead name : TNF-alpha					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
PBMC+YY101 500nM	1st	19.5	82.0	200.0	<7.70
	2nd	21.0	112.0	200.0	<7.70
	Mean	20.3	97.0	200.0	#DIV/0!
	STDE R	0.8	15.0	0.0	#DIV/0!
PBMC+YY101 50nM	1st	19.0	63.0	200.0	<7.70
	2nd	22.0	70.0	200.0	<7.70
	Mean	20.5	66.5	200.0	#DIV/0!
	STDE R	1.5	3.5	0.0	#DIV/0!
PBMC+YY101 5nM	1st	20.0	84.0	200.0	<7.70
	2nd	21.0	76.0	200.0	<7.70
	Mean	20.5	80.0	200.0	#DIV/0!
	STDE R	0.5	4.0	0.0	#DIV/0!
PBMC+YY101 0.5nM	1st	20.0	85.0	200.0	<7.70
	2nd	19.0	77.0	200.0	<7.70
	Mean	19.5	81.0	200.0	#DIV/0!
	STDE R	0.5	4.0	0.0	#DIV/0!
PBMC+YY101 0.05uM	1st	21.0	83.0	200.0	<7.70
	2nd	22.0	95.0	200.0	<7.70
	Mean	21.5	89.0	200.0	#DIV/0!
	STDE R	0.5	6.0	0.0	#DIV/0!
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	72.0	71.0	200.0	3183.0
	2nd	70.5	74.0	200.0	3089.8

Bead name : TNF-alpha					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
	Mean	71.3	72.5	200.0	3136.4
	STDE R	0.8	1.5	0.0	46.6
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	71.0	85.0	200.0	3120.8
	2nd	73.0	75.0	200.0	3245.0
	Mean	72.0	80.0	200.0	3182.9
	STDE R	1.0	5.0	0.0	62.1
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	63.0	80.0	200.0	2621.2
	2nd	66.0	77.0	200.0	2809.1
	Mean	64.5	78.5	200.0	2715.2
	STDE R	1.5	1.5	0.0	94.0
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	59.0	86.0	200.0	2369.4
	2nd	66.5	100.0	200.0	2840.4
	Mean	62.8	93.0	200.0	2604.9
	STDE R	3.8	7.0	0.0	235.5
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	56.0	79.0	200.0	2179.5
	2nd	64.0	84.0	200.0	2683.9
	Mean	60.0	81.5	200.0	2431.7
	STDE R	4.0	2.5	0.0	252.2
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	61.0	82.0	200.0	2495.5
	2nd	57.0	66.0	200.0	2242.9
	Mean	59.0	74.0	200.0	2369.2
	STDE R	2.0	8.0	0.0	126.3

Bead name : TNF-alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YY101 500nM	1st	56. 0	77.0	200.0	2179.5
	2nd	53. 0	89.0	200.0	1988.8
	3rd	50. 0	88.0	200.0	1797.0
	Mean	53. 0	84.7	200.0	1988.4
	STDE R	1.7	3.8	0.0	110.4
PBMC+LPS(5ug/ml)+YY101 50nM	1st	49. 0	85.0	200.0	1732.8
	2nd	48. 0	83.0	200.0	1668.5
	3rd	53. 0	83.0	200.0	1988.8
	Mean	50. 0	83.7	200.0	1796.7
	STDE R	1.5	0.7	0.0	97.8
PBMC+LPS(5ug/ml)+YY101 5nM	1st	53. 0	69.0	200.0	1988.8
	2nd	52. 0	83.0	200.0	1925.0
	3rd	57. 0	60.0	200.0	2242.9
	Mean	54. 0	70.7	200.0	2052.2
	STDE R	1.5	6.7	0.0	97.1
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	60. 0	72.0	200.0	2432.5
	2nd	57. 0	93.0	200.0	2242.9
	3rd	55. 0	73.0	200.0	2116.1
	Mean	57. 3	79.3	200.0	2263.8
	STDE R	1.5	6.8	0.0	91.9
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	50. 0	78.0	200.0	1797.0
	2nd	63. 0	87.0	200.0	2621.2

Bead name : TNF-alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	57. 0	71.0	200.0	2242.9
	Mean	56. 7	78.7	200.0	2220.4
	STDE R	3.8	4.6	0.0	238.2
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	67. 0	81.0	200.0	2871.6
	2nd	59. 0	79.0	200.0	2369.4
	3rd	56. 0	67.0	200.0	2179.5
	Mean	60. 7	75.7	200.0	2473.5
	STDE R	3.3	4.4	0.0	206.5
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	55. 0	85.0	200.0	2116.1
	2nd	32. 5	84.0	200.0	647.8
	3rd	41. 5	80.0	200.0	1246.7
	Mean	43. 0	83.0	200.0	1336.9
	STDE R	6.5	1.5	0.0	426.2
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	49. 0	91.0	200.0	1732.8
	2nd	56. 0	77.0	200.0	2179.5
	3rd	29. 5	82.0	200.0	442.1
	Mean	44. 8	83.3	200.0	1451.5
	STDE R	7.9	4.1	0.0	520.9
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	34. 0	95.0	200.0	749.3
	2nd	44. 0	87.0	200.0	1409.7
	3rd	48. 0	82.0	200.0	1668.5
	Mean	42. 0	88.0	200.0	1275.8

Bead name : TNF-alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	4.2	3.8	0.0	273.7
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	43. 0	90.0	200.0	1344.6
	2nd	53. 0	83.0	200.0	1988.8
	3rd	50. 0	81.0	200.0	1797.0
	Mean	48. 7	84.7	200.0	1710.1
	STDE R	3.0	2.7	0.0	191.0
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	51. 0	83.0	200.0	1861.0
	2nd	54. 0	85.0	200.0	2052.5
	3rd	54. 0	87.0	200.0	2052.5
	Mean	53. 0	85.0	200.0	1988.7
	STDE R	1.0	1.2	0.0	63.8
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	55. 0	74.0	200.0	2116.1
	2nd	53. 0	71.0	200.0	1988.8
	3rd	51. 0	98.0	200.0	1861.0
	Mean	53. 0	81.0	200.0	1988.6
	STDE R	1.2	8.5	0.0	73.6
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	47. 0	77.0	200.0	1604.0
	2nd	39. 5	82.0	200.0	1115.3
	3rd	43. 0	80.0	200.0	1344.6
	Mean	43. 2	79.7	200.0	1354.6
	STDE R	2.2	1.5	0.0	141.2
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	53. 5	76.0	200.0	2020.6

Bead name : TNF-alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	50. 0	93.0	200.0	1797.0
	3rd	45. 0	88.0	200.0	1474.6
	Mean	49. 5	85.7	200.0	1764.1
	STDE R	2.5	5.0	0.0	158.5
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	44. 5	92.0	200.0	1442.2
	2nd	54. 0	74.0	200.0	2052.5
	3rd	45. 0	120. 0	200.0	1474.6
	Mean	47. 8	95.3	200.0	1656.4
	STDE R	3.1	13.4	0.0	198.2
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	49. 5	54.0	200.0	1764.9
	2nd	44. 0	85.0	200.0	1409.7
	3rd	44. 0	73.0	200.0	1409.7
	Mean	45. 8	70.7	200.0	1528.1
	STDE R	1.8	9.0	0.0	118.4
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	40. 5	82.0	200.0	1181.1
	2nd	46. 0	79.0	200.0	1539.4
	3rd	45. 0	80.0	200.0	1474.6
	Mean	43. 8	80.3	200.0	1398.4
	STDE R	1.7	0.9	0.0	110.2
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	54. 0	80.0	200.0	2052.5
	2nd	50. 0	81.0	200.0	1797.0
	3rd	58. 0	95.0	200.0	2306.2

Bead name : TNF-alpha					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
	Mean	54.0	85.3	200.0	2051.9
	STDE R	2.3	4.8	0.0	147.0

Table 14

Bead name : MMP-3					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
Blank	1st	48.0	55.0	1.0	29.2
	2nd	48.0	65.0	1.0	29.2
	Mean	48.0	60.0	1.0	29.2
	STDE R	0.0	5.0	0.0	0.0
PBMC + 0.5% DMSO	1st	51.0	64.0	200.0	6062.8
	2nd	47.0	67.0	200.0	5771.5
	3rd	49.5	58.0	200.0	5953.3
	Mean	49.2	63.0	200.0	5929.2
	STDE R	1.2	2.6	0.0	84.9
PBMC+LPS(5ug/ml)	1st	96.5	50.0	200.0	9511.1
	2nd	87.0	61.0	200.0	8772.5
	3rd	84.0	53.0	200.0	8541.1
	Mean	89.2	54.7	200.0	8941.6
	STDE R	3.8	3.3	0.0	292.5
PBMC+YY101 500nM	1st	54.0	82.0	200.0	6282.7
	2nd	56.0	81.0	200.0	6429.9
	Mean	55.0	81.5	200.0	6356.3

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	1.0	0.5	0.0	73.6
PBMC+YY101 50nM	1st	54. 0	66.0	200.0	6282.7
	2nd	49. 5	50.0	200.0	5953.3
	Mean	51. 8	58.0	200.0	6118.0
	STDE R	2.3	8.0	0.0	164.7
PBMC+YY101 5nM	1st	52. 5	64.0	200.0	6172.6
	2nd	54. 5	50.0	200.0	6319.4
	Mean	53. 5	57.0	200.0	6246.0
	STDE R	1.0	7.0	0.0	73.4
PBMC+YY101 0.5nM	1st	51. 0	68.0	200.0	6062.8
	2nd	56. 0	59.0	200.0	6429.9
	Mean	53. 5	63.5	200.0	6246.3
	STDE R	2.5	4.5	0.0	183.5
PBMC+YY101 0.05uM	1st	57. 0	53.0	200.0	6503.7
	2nd	53. 5	64.0	200.0	6245.9
	Mean	55. 3	58.5	200.0	6374.8
	STDE R	1.8	5.5	0.0	128.9
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	93. 0	55.0	200.0	9237.9
	2nd	87. 5	56.0	200.0	8811.1
	Mean	90. 3	55.5	200.0	9024.5
	STDE R	2.8	0.5	0.0	213.4
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	93. 0	54.0	200.0	9237.9

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	99. 0	61.0	200.0	9707.0
	Mean	96. 0	57.5	200.0	9472.4
	STDE R	3.0	3.5	0.0	234.5
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	90. 0	73.0	200.0	9004.8
	2nd	97. 0	67.0	200.0	9550.2
	Mean	93. 5	70.0	200.0	9277.5
	STDE R	3.5	3.0	0.0	272.7
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	79. 0	84.0	200.0	8157.7
	2nd	87. 0	63.0	200.0	8772.5
	Mean	83. 0	73.5	200.0	8465.1
	STDE R	4.0	10.5	0.0	307.4
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	81. 0	70.0	200.0	8310.7
	2nd	85. 0	73.0	200.0	8618.2
	Mean	83. 0	71.5	200.0	8464.4
	STDE R	2.0	1.5	0.0	153.7
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	81. 0	53.0	200.0	8310.7
	2nd	83. 5	64.0	200.0	8502.7
	Mean	82. 3	58.5	200.0	8406.7
	STDE R	1.3	5.5	0.0	96.0
PBMC+LPS(5ug/ml)+YY101 500nM	1st	77. 5	60.0	200.0	8043.1
	2nd	72. 5	68.0	200.0	7663.2
	3rd	71. 0	62.0	200.0	7549.7

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	73. 7	63.3	200.0	7752.0
	STDE R	2.0	2.4	0.0	149.2
PBMC+LPS(5ug/ml)+YY101 50nM	1st	71. 0	53.0	200.0	7549.7
	2nd	73. 0	61.0	200.0	7701.1
	3rd	78. 0	57.0	200.0	8081.3
	Mean	74. 0	57.0	200.0	7777.4
	STDE R	2.1	2.3	0.0	158.1
PBMC+LPS(5ug/ml)+YY101 5nM	1st	71. 0	78.0	200.0	7549.7
	2nd	71. 0	54.0	200.0	7549.7
	3rd	85. 0	52.0	200.0	8618.2
	Mean	75. 7	61.3	200.0	7905.9
	STDE R	4.7	8.4	0.0	356.1
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	73. 0	87.0	200.0	7701.1
	2nd	74. 0	60.0	200.0	7776.9
	3rd	74. 0	53.0	200.0	7776.9
	Mean	73. 7	66.7	200.0	7751.6
	STDE R	0.3	10.4	0.0	25.3
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	74. 0	53.0	200.0	7776.9
	2nd	84. 0	51.0	200.0	8541.1
	3rd	76. 0	67.0	200.0	7928.9
	Mean	78. 0	57.0	200.0	8082.3
	STDE R	3.1	5.0	0.0	233.6

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	71. 0	51.0	200.0	7549.7
	2nd	70. 0	60.0	200.0	7474.3
	3rd	72. 0	69.0	200.0	7625.3
	Mean	71. 0	60.0	200.0	7549.8
	STDE R	0.6	5.2	0.0	43.6
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	74. 0	50.0	200.0	7776.9
	2nd	41. 5	50.0	200.0	5374.6
	3rd	60. 0	55.0	200.0	6725.8
	Mean	58. 5	51.7	200.0	6625.8
	STDE R	9.4	1.7	0.0	695.3
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	67. 0	63.0	200.0	7248.5
	2nd	70. 0	53.0	200.0	7474.3
	3rd	43. 0	63.0	200.0	5482.5
	Mean	60. 0	59.7	200.0	6735.1
	STDE R	8.5	3.3	0.0	629.7
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	54. 0	50.0	200.0	6282.7
	2nd	61. 0	58.0	200.0	6800.1
	3rd	68. 0	63.0	200.0	7323.6
	Mean	61. 0	57.0	200.0	6802.1
	STDE R	4.0	3.8	0.0	300.5
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	67. 0	87.0	200.0	7248.5
	2nd	65. 0	50.0	200.0	7098.6

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	64. 5	70.0	200.0	7061.2
	Mean	65. 5	69.0	200.0	7136.1
	STDE R	0.8	10.7	0.0	57.2
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	70. 0	67.0	200.0	7474.3
	2nd	76. 0	57.0	200.0	7928.9
	3rd	70. 5	50.0	200.0	7512.0
	Mean	72. 2	58.0	200.0	7638.4
	STDE R	1.9	4.9	0.0	145.7
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	70. 5	66.0	200.0	7512.0
	2nd	68. 0	67.0	200.0	7323.6
	3rd	66. 0	63.0	200.0	7173.5
	Mean	68. 2	65.3	200.0	7336.4
	STDE R	1.3	1.2	0.0	97.9
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	65. 0	57.0	200.0	7098.6
	2nd	72. 5	56.0	200.0	7663.2
	3rd	66. 0	71.0	200.0	7173.5
	Mean	67. 8	61.3	200.0	7311.7
	STDE R	2.4	4.8	0.0	177.0
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	73. 0	53.0	200.0	7701.1
	2nd	69. 0	51.0	200.0	7398.9
	3rd	62. 5	50.0	200.0	6911.8
	Mean	68. 2	51.3	200.0	7337.3

Bead name : MMP-3					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	3.1	0.9	0.0	229.9
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	70. 0	55.0	200.0	7474.3
	2nd	70. 0	61.0	200.0	7474.3
	3rd	68. 0	75.0	200.0	7323.6
	Mean	69. 3	63.7	200.0	7424.0
	STDE R	0.7	5.9	0.0	50.2
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	65. 0	58.0	200.0	7098.6
	2nd	67. 0	69.0	200.0	7248.5
	3rd	66. 0	65.0	200.0	7173.5
	Mean	66. 0	64.0	200.0	7173.5
	STDE R	0.6	3.2	0.0	43.3
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	64. 5	60.0	200.0	7061.2
	2nd	67. 0	50.0	200.0	7248.5
	3rd	65. 0	73.0	200.0	7098.6
	Mean	65. 5	61.0	200.0	7136.1
	STDE R	0.8	6.7	0.0	57.2
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	66. 0	55.0	200.0	7173.5
	2nd	74. 0	50.0	200.0	7776.9
	3rd	78. 0	61.0	200.0	8081.3
	Mean	72. 7	55.3	200.0	7677.2
	STDE R	3.5	3.2	0.0	266.8

Table 15

Bead name : CCL2/MCP-1					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
Blank	1st	18.0	79.0	1.0	21.6
	2nd	19.0	96.0	1.0	22.1
	Mean	18.5	87.5	1.0	21.9
	STDE R	0.5	8.5	0.0	0.3
PBMC + 0.5% DMSO	1st	17.0	73.0	200.0	4216.3
	2nd	18.0	81.0	200.0	4321.5
	3rd	18.0	107.0	200.0	4321.5
	Mean	17.7	87.0	200.0	4286.5
	STDE R	0.3	10.3	0.0	35.1
PBMC+LPS(5ug/ml)	1st	36.0	78.0	200.0	6053.2
	2nd	31.0	86.0	200.0	5597.9
	3rd	28.0	93.0	200.0	5316.3
	Mean	31.7	85.7	200.0	5655.8
	STDE R	2.3	4.3	0.0	214.7
PBMC+YY101 500nM	1st	18.0	83.0	200.0	4321.5
	2nd	21.0	111.0	200.0	4630.2
	Mean	19.5	97.0	200.0	4475.9
	STDE R	1.5	14.0	0.0	154.4
PBMC+YY101 50nM	1st	18.0	86.0	200.0	4321.5
	2nd	19.0	87.0	200.0	4425.5
	Mean	18.5	86.5	200.0	4373.5
	STDE R	0.5	0.5	0.0	52.0

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+YY101 5nM	1st	19.0	106.0	200.0	4425.5
	2nd	19.0	93.0	200.0	4425.5
	Mean	19.0	99.5	200.0	4425.5
	STDE R	0.0	6.5	0.0	0.0
PBMC+YY101 0.5nM	1st	20.0	78.0	200.0	4528.4
	2nd	23.0	90.0	200.0	4830.8
	Mean	21.5	84.0	200.0	4679.6
	STDE R	1.5	6.0	0.0	151.2
PBMC+YY101 0.05uM	1st	33.0	69.0	200.0	5782.0
	2nd	17.5	96.0	200.0	4269.1
	Mean	25.3	82.5	200.0	5025.5
	STDE R	7.8	13.5	0.0	756.4
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	34.0	94.0	200.0	5873.0
	2nd	32.0	76.0	200.0	5690.3
	Mean	33.0	85.0	200.0	5781.6
	STDE R	1.0	9.0	0.0	91.4
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	35.0	88.0	200.0	5963.4
	2nd	36.0	101.0	200.0	6053.2
	Mean	35.5	94.5	200.0	6008.3
	STDE R	0.5	6.5	0.0	44.9
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	27.0	90.0	200.0	5220.9
	2nd	35.5	90.0	200.0	6008.4

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	31. 3	90.0	200.0	5614.6
	STDE R	4.3	0.0	0.0	393.7
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	28. 0	92.0	200.0	5316.3
	2nd	27. 5	90.0	200.0	5268.7
	Mean	27. 8	91.0	200.0	5292.5
	STDE R	0.3	1.0	0.0	23.8
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	30. 0	91.0	200.0	5504.7
	2nd	28. 0	86.0	200.0	5316.3
	Mean	29. 0	88.5	200.0	5410.5
	STDE R	1.0	2.5	0.0	94.2
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	27. 0	93.0	200.0	5220.9
	2nd	28. 0	70.0	200.0	5316.3
	Mean	27. 5	81.5	200.0	5268.6
	STDE R	0.5	11.5	0.0	47.7
PBMC+LPS(5ug/ml)+YY101 500nM	1st	19. 0	69.0	200.0	4425.5
	2nd	19. 0	94.0	200.0	4425.5
	3rd	20. 0	107. 0	200.0	4528.4
	Mean	19. 3	90.0	200.0	4459.8
	STDE R	0.3	11.2	0.0	34.3
PBMC+LPS(5ug/ml)+YY101 50nM	1st	20. 5	82.0	200.0	4579.5
	2nd	21. 0	81.0	200.0	4630.2
	3rd	21. 0	85.0	200.0	4630.2

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	20. 8	82.7	200.0	4613.3
	STDE R	0.2	1.2	0.0	16.9
PBMC+LPS(5ug/ml)+YY101 5nM	1st	21. 0	106. 0	200.0	4630.2
	2nd	20. 0	81.0	200.0	4528.4
	3rd	22. 0	71.0	200.0	4731.0
	Mean	21. 0	86.0	200.0	4629.9
	STDE R	0.6	10.4	0.0	58.5
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	21. 0	98.0	200.0	4630.2
	2nd	20. 0	82.0	200.0	4528.4
	3rd	21. 0	85.0	200.0	4630.2
	Mean	20. 7	88.3	200.0	4596.3
	STDE R	0.3	4.9	0.0	33.9
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	20. 0	87.0	200.0	4528.4
	2nd	22. 0	86.0	200.0	4731.0
	3rd	20. 0	94.0	200.0	4528.4
	Mean	20. 7	89.0	200.0	4596.0
	STDE R	0.7	2.5	0.0	67.5
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	20. 0	89.0	200.0	4528.4
	2nd	21. 0	88.0	200.0	4630.2
	3rd	19. 0	74.0	200.0	4425.5
	Mean	20. 0	83.7	200.0	4528.1
	STDE R	0.6	4.8	0.0	59.1

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	22. 0	89.0	200.0	4731.0
	2nd	12. 0	101. 0	200.0	3670.6
	3rd	16. 0	91.0	200.0	4109.9
	Mean	16. 7	93.7	200.0	4170.5
	STDE R	2.9	3.7	0.0	307.6
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	18. 0	89.0	200.0	4321.5
	2nd	20. 0	79.0	200.0	4528.4
	3rd	12. 0	74.0	200.0	3670.6
	Mean	16. 7	80.7	200.0	4173.5
	STDE R	2.4	4.4	0.0	258.5
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	14. 0	92.0	200.0	3893.1
	2nd	18. 0	88.0	200.0	4321.5
	3rd	18. 0	103. 0	200.0	4321.5
	Mean	16. 7	94.3	200.0	4178.7
	STDE R	1.3	4.5	0.0	142.8
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	19. 0	115. 0	200.0	4425.5
	2nd	17. 5	86.0	200.0	4269.1
	3rd	17. 0	97.0	200.0	4216.3
	Mean	17. 8	99.3	200.0	4303.7
	STDE R	0.6	8.5	0.0	62.8
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	19. 0	95.0	200.0	4425.5
	2nd	19. 0	71.0	200.0	4425.5

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	19. 5	94.0	200.0	4477.1
	Mean	19. 2	86.7	200.0	4442.7
	STDE R	0.2	7.8	0.0	17.2
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	19. 0	69.0	200.0	4425.5
	2nd	20. 0	92.0	200.0	4528.4
	3rd	18. 0	101. 0	200.0	4321.5
	Mean	19. 0	87.3	200.0	4425.2
	STDE R	0.6	9.5	0.0	59.7
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	21. 0	90.0	200.0	4630.2
	2nd	21. 0	92.0	200.0	4630.2
	3rd	21. 0	88.0	200.0	4630.2
	Mean	21. 0	90.0	200.0	4630.2
	STDE R	0.0	1.2	0.0	0.0
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	20. 0	92.0	200.0	4528.4
	2nd	22. 0	90.0	200.0	4731.0
	3rd	19. 5	72.0	200.0	4477.1
	Mean	20. 5	84.7	200.0	4578.9
	STDE R	0.8	6.4	0.0	77.5
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	20. 5	74.0	200.0	4579.5
	2nd	19. 5	68.0	200.0	4477.1
	3rd	21. 0	103. 0	200.0	4630.2
	Mean	20. 3	81.7	200.0	4562.3

Bead name : CCL2/MCP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.4	10.8	0.0	45.0
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	19. 0	71.0	200.0	4425.5
	2nd	18. 0	86.0	200.0	4321.5
	3rd	19. 0	91.0	200.0	4425.5
	Mean	18. 7	82.7	200.0	4390.9
	STDE R	0.3	6.0	0.0	34.7
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	20. 0	95.0	200.0	4528.4
	2nd	19. 5	76.0	200.0	4477.1
	3rd	21. 0	93.0	200.0	4630.2
	Mean	20. 2	88.0	200.0	4545.3
	STDE R	0.4	6.0	0.0	45.0
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	19. 0	71.0	200.0	4425.5
	2nd	22. 0	78.0	200.0	4731.0
	3rd	22. 0	99.0	200.0	4731.0
	Mean	21. 0	82.7	200.0	4629.2
	STDE R	1.0	8.4	0.0	101.8

Table 16

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
Blank	1st	17. 0	64.0	1.0	70.1
	2nd	16. 0	70.0	1.0	65.0
	Mean	16. 5	67.0	1.0	67.5

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.5	3.0	0.0	2.6
PBMC + 0.5% DMSO	1st	18. 0	67.0	200.0	14981.7
	2nd	18. 5	58.0	200.0	15447.9
	3rd	19. 5	62.0	200.0	16349.6
	Mean	18. 7	62.3	200.0	15593.1
	STDE R	0.4	2.6	0.0	401.5
PBMC+LPS(5ug/ml)	1st	96. 0	55.0	200.0	54195.6
	2nd	66. 0	55.0	200.0	42643.2
	3rd	67. 0	59.0	200.0	43065.7
	Mean	76. 3	56.3	200.0	46634.8
	STDE R	9.8	1.3	0.0	3782.4
PBMC+YY101 500nM	1st	17. 0	77.0	200.0	14014.0
	2nd	17. 0	87.0	200.0	14014.0
	Mean	17. 0	82.0	200.0	14014.0
	STDE R	0.0	5.0	0.0	0.0
PBMC+YY101 50nM	1st	16. 5	50.0	200.0	13510.6
	2nd	18. 0	54.0	200.0	14981.7
	Mean	17. 3	52.0	200.0	14246.1
	STDE R	0.8	2.0	0.0	735.6
PBMC+YY101 5nM	1st	17. 0	54.0	200.0	14014.0
	2nd	17. 5	62.0	200.0	14504.0
	Mean	17. 3	58.0	200.0	14259.0

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.3	4.0	0.0	245.0
PBMC+YY101 0.5nM	1st	19. 0	50.0	200.0	15903.7
	2nd	20. 0	61.0	200.0	16786.4
	Mean	19. 5	55.5	200.0	16345.0
	STDE R	0.5	5.5	0.0	441.4
PBMC+YY101 0.05uM	1st	19. 0	58.0	200.0	15903.7
	2nd	15. 0	50.0	200.0	11904.9
	Mean	17. 0	54.0	200.0	13904.3
	STDE R	2.0	4.0	0.0	1999.4
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	81. 0	63.0	200.0	48681.5
	2nd	77. 5	54.0	200.0	47325.4
	Mean	79. 3	58.5	200.0	48003.4
	STDE R	1.8	4.5	0.0	678.0
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	77. 0	56.0	200.0	47129.3
	2nd	79. 5	50.0	200.0	48103.9
	Mean	78. 3	53.0	200.0	47616.6
	STDE R	1.3	3.0	0.0	487.3
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	69. 0	61.0	200.0	43901.3
	2nd	70. 0	50.0	200.0	44314.5
	Mean	69. 5	55.5	200.0	44107.9
	STDE R	0.5	5.5	0.0	206.6
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	61. 0	65.0	200.0	40481.0

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	69.5	54.0	200.0	44108.3
	Mean	65.3	59.5	200.0	42294.6
	STDE R	4.3	5.5	0.0	1813.6
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	66.5	50.0	200.0	42854.8
	2nd	67.0	59.0	200.0	43065.7
	Mean	66.8	54.5	200.0	42960.3
	STDE R	0.3	4.5	0.0	105.4
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	61.5	60.0	200.0	40701.1
	2nd	61.0	71.0	200.0	40481.0
	Mean	61.3	65.5	200.0	40591.0
	STDE R	0.3	5.5	0.0	110.1
PBMC+LPS(5ug/ml)+YY101 500nM	1st	46.5	66.0	200.0	33635.0
	2nd	49.0	75.0	200.0	34887.9
	3rd	46.0	53.0	200.0	33380.1
	Mean	47.2	64.7	200.0	33967.7
	STDE R	0.9	6.4	0.0	466.0
PBMC+LPS(5ug/ml)+YY101 50nM	1st	43.0	69.0	200.0	31818.4
	2nd	52.0	50.0	200.0	36347.5
	3rd	45.0	67.0	200.0	32865.8
	Mean	46.7	62.0	200.0	33677.2
	STDE R	2.7	6.0	0.0	1368.9
PBMC+LPS(5ug/ml)+YY101 5nM	1st	46.0	65.0	200.0	33380.1

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	51. 0	61.0	200.0	35866.0
	3rd	48. 0	61.0	200.0	34390.9
	Mean	48. 3	62.3	200.0	34545.7
	STDE R	1.5	1.3	0.0	721.8
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	51. 5	50.0	200.0	36107.4
	2nd	46. 0	57.0	200.0	33380.1
	3rd	50. 0	50.0	200.0	35379.6
	Mean	49. 2	52.3	200.0	34955.7
	STDE R	1.6	2.3	0.0	815.3
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	51. 0	58.0	200.0	35866.0
	2nd	54. 5	72.0	200.0	37530.4
	3rd	51. 0	60.0	200.0	35866.0
	Mean	52. 2	63.3	200.0	36420.8
	STDE R	1.2	4.4	0.0	554.8
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	49. 5	50.0	200.0	35134.4
	2nd	46. 0	56.0	200.0	33380.1
	3rd	45. 0	59.0	200.0	32865.8
	Mean	46. 8	55.0	200.0	33793.5
	STDE R	1.4	2.6	0.0	686.7
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	48. 0	61.0	200.0	34390.9
	2nd	23. 0	73.0	200.0	19244.9
	3rd	39. 5	50.0	200.0	29918.7

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
	Mean	36.8	61.3	200.0	27851.5
	STDE R	7.3	6.6	0.0	4492.8
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	41.5	50.0	200.0	31015.1
	2nd	45.0	57.0	200.0	32865.8
	3rd	25.5	50.0	200.0	21122.8
	Mean	37.3	52.3	200.0	28334.6
	STDE R	6.0	2.3	0.0	3645.3
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	32.0	69.0	200.0	25497.0
	2nd	33.0	56.0	200.0	26119.3
	3rd	40.5	50.0	200.0	30470.7
	Mean	35.2	58.3	200.0	27362.3
	STDE R	2.7	5.6	0.0	1564.5
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	42.0	71.0	200.0	31284.6
	2nd	39.0	50.0	200.0	29639.8
	3rd	40.5	58.0	200.0	30470.7
	Mean	40.5	59.7	200.0	30465.1
	STDE R	0.9	6.1	0.0	474.8
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	48.0	59.0	200.0	34390.9
	2nd	45.0	50.0	200.0	32865.8
	3rd	50.5	70.0	200.0	35623.4
	Mean	47.8	59.7	200.0	34293.4
	STDE R	1.6	5.8	0.0	797.5

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	43. 0	51.0	200.0	31818.4
	2nd	37. 5	50.0	200.0	28790.7
	3rd	42. 0	69.0	200.0	31284.6
	Mean	40. 8	56.7	200.0	30631.2
	STDE R	1.7	6.2	0.0	933.1
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	37. 0	50.0	200.0	28503.4
	2nd	33. 5	54.0	200.0	26426.3
	3rd	38. 5	64.0	200.0	29358.9
	Mean	36. 3	56.0	200.0	28096.2
	STDE R	1.5	4.2	0.0	870.7
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	46. 0	55.0	200.0	33380.1
	2nd	46. 0	58.0	200.0	33380.1
	3rd	37. 0	70.0	200.0	28503.4
	Mean	43. 0	61.0	200.0	31754.6
	STDE R	3.0	4.6	0.0	1625.6
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	43. 0	54.0	200.0	31818.4
	2nd	45. 0	59.0	200.0	32865.8
	3rd	41. 0	68.0	200.0	30743.9
	Mean	43. 0	60.3	200.0	31809.4
	STDE R	1.2	4.1	0.0	612.6
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	39. 0	53.0	200.0	29639.8
	2nd	42. 0	57.0	200.0	31284.6

Bead name : CCL3/MIP-1 alpha					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	38. 0	54.0	200.0	29075.9
	Mean	39. 7	54.7	200.0	30000.1
	STDE R	1.2	1.2	0.0	662.6
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	36. 5	56.0	200.0	28213.9
	2nd	40. 0	70.0	200.0	30195.7
	3rd	40. 0	52.0	200.0	30195.7
	Mean	38. 8	59.3	200.0	29535.1
	STDE R	1.2	5.5	0.0	660.6
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	44. 0	50.0	200.0	32345.4
	2nd	54. 0	63.0	200.0	37296.1
	3rd	74. 0	59.0	200.0	45939.1
	Mean	57. 3	57.3	200.0	38526.9
	STDE R	8.8	3.8	0.0	3972.1

Table 17

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
Blank	1st	6.0	1.0	65.0	<148.02
	2nd	6.0	1.0	58.0	<148.02
	Mean	6.0	1.0	61.5	#DIV/0!
	STDE R	0.0	0.0	3.5	#DIV/0!
PBMC + 0.5% DMSO	1st	6.0	200. 0	70.0	<148.02
	2nd	6.0	200. 0	70.0	<148.02
	3rd	6.0	200. 0	94.0	<148.02
	Mean	6.0	200. 0	78.0	#DIV/0!

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
	STDE R	0.0	0.0	8.0	#DIV/0!
PBMC+LPS(5ug/ml)	1st	20.0	200.0	73.0	36796.9
	2nd	17.0	200.0	73.0	31897.6
	3rd	18.0	200.0	104.0	33639.0
	Mean	18.3	200.0	83.3	34111.2
	STDE R	0.9	0.0	10.3	1433.9
PBMC+YY101 500nM	1st	6.0	200.0	59.0	<148.02
	2nd	7.0	200.0	67.0	<148.02
	Mean	6.5	200.0	63.0	#DIV/0!
	STDE R	0.5	0.0	4.0	#DIV/0!
PBMC+YY101 50nM	1st	8.0	200.0	62.0	<148.02
	2nd	7.0	200.0	110.0	<148.02
	Mean	7.5	200.0	86.0	#DIV/0!
	STDE R	0.5	0.0	24.0	#DIV/0!
PBMC+YY101 5nM	1st	7.0	200.0	107.0	<148.02
	2nd	6.0	200.0	95.0	<148.02
	Mean	6.5	200.0	101.0	#DIV/0!
	STDE R	0.5	0.0	6.0	#DIV/0!
PBMC+YY101 0.5nM	1st	6.0	200.0	73.0	<148.02
	2nd	6.0	200.0	98.0	<148.02
	Mean	6.0	200.0	85.5	#DIV/0!
	STDE R	0.0	0.0	12.5	#DIV/0!

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
PBMC+YY101 0.05uM	1st	6.0	200.0	72.0	<148.02
	2nd	5.0	200.0	77.0	<148.02
	Mean	5.5	200.0	74.5	#DIV/0!
	STDE R	0.5	0.0	2.5	#DIV/0!
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	20.0	200.0	66.0	36796.9
	2nd	18.0	200.0	70.0	33639.0
	Mean	19.0	200.0	68.0	35218.0
	STDE R	1.0	0.0	2.0	1578.9
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	15.0	200.0	63.0	27945.2
	2nd	16.0	200.0	68.0	30013.2
	Mean	15.5	200.0	65.5	28979.2
	STDE R	0.5	0.0	2.5	1034.0
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	16.0	200.0	70.0	30013.2
	2nd	16.0	200.0	90.0	30013.2
	Mean	16.0	200.0	80.0	30013.2
	STDE R	0.0	0.0	10.0	0.0
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	16.0	200.0	81.0	30013.2
	2nd	17.0	200.0	62.0	31897.6
	Mean	16.5	200.0	71.5	30955.4
	STDE R	0.5	0.0	9.5	942.2
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	15.5	200.0	88.0	29005.5
	2nd	17.0	200.0	97.0	31897.6

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	16. 3	200. 0	92.5	30451.5
	STDE R	0.8	0.0	4.5	1446.1
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	16. 0	200. 0	85.0	30013.2
	2nd	14. 0	200. 0	62.0	25629.7
	Mean	15. 0	200. 0	73.5	27821.4
	STDE R	1.0	0.0	11.5	2191.8
PBMC+LPS(5ug/ml)+YY101 500nM	1st	11. 0	200. 0	60.0	15257.5
	2nd	12. 0	200. 0	71.0	19701.2
	3rd	12. 0	200. 0	72.0	19701.2
	Mean	11. 7	200. 0	67.7	18220.0
	STDE R	0.3	0.0	3.8	1481.3
PBMC+LPS(5ug/ml)+YY101 50nM	1st	11. 0	200. 0	65.0	15257.5
	2nd	12. 0	200. 0	104.0	19701.2
	3rd	11. 0	200. 0	90.0	15257.5
	Mean	11. 3	200. 0	86.3	16738.7
	STDE R	0.3	0.0	11.4	1481.3
PBMC+LPS(5ug/ml)+YY101 5nM	1st	11. 5	200. 0	76.0	17703.4
	2nd	11. 0	200. 0	92.0	15257.5
	3rd	11. 0	200. 0	79.0	15257.5
	Mean	11. 2	200. 0	82.3	16072.8
	STDE R	0.2	0.0	4.9	815.3
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	11. 5	200. 0	98.0	17703.4

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	14. 0	200. 0	85.0	25629.7
	3rd	12. 0	200. 0	73.0	19701.2
	Mean	12. 5	200. 0	85.3	21011.4
	STDE R	0.8	0.0	7.2	2380.0
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	14. 0	200. 0	50.0	25629.7
	2nd	11. 5	200. 0	74.0	17703.4
	3rd	12. 0	200. 0	83.0	19701.2
	Mean	12. 5	200. 0	69.0	21011.4
	STDE R	0.8	0.0	9.8	2380.0
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	14. 0	200. 0	84.0	25629.7
	2nd	12. 0	200. 0	70.0	19701.2
	3rd	12. 0	200. 0	70.0	19701.2
	Mean	12. 7	200. 0	74.7	21677.4
	STDE R	0.7	0.0	4.7	1976.1
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	12. 0	200. 0	61.0	19701.2
	2nd	10. 0	200. 0	89.0	1874.9
	3rd	12. 0	200. 0	61.0	19701.2
	Mean	11. 3	200. 0	70.3	13759.1
	STDE R	0.7	0.0	9.3	5942.1
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	13. 0	200. 0	77.0	22956.0
	2nd	14. 0	200. 0	102.0	25629.7
	3rd	13. 0	200. 0	74.0	22956.0

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Count	Dilution	Concentration (pg/ml)
	Mean	13.3	200.0	84.3	23847.2
	STDE R	0.3	0.0	8.9	891.2
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	11.0	200.0	64.0	15257.5
	2nd	12.0	200.0	95.0	19701.2
	3rd	11.0	200.0	103.0	15257.5
	Mean	11.3	200.0	87.3	16738.7
	STDE R	0.3	0.0	11.9	1481.3
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	13.0	200.0	95.0	22956.0
	2nd	13.0	200.0	75.0	22956.0
	3rd	13.0	200.0	76.0	22956.0
	Mean	13.0	200.0	82.0	22956.0
	STDE R	0.0	0.0	6.5	0.0
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	13.0	200.0	53.0	22956.0
	2nd	13.0	200.0	62.0	22956.0
	3rd	13.0	200.0	92.0	22956.0
	Mean	13.0	200.0	69.0	22956.0
	STDE R	0.0	0.0	11.8	0.0
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	12.0	200.0	87.0	19701.2
	2nd	13.0	200.0	97.0	22956.0
	3rd	12.0	200.0	74.0	19701.2
	Mean	12.3	200.0	86.0	20786.2
	STDE R	0.3	0.0	6.7	1084.9

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	14. 0	200. 0	79.0	25629.7
	2nd	13. 0	200. 0	65.0	22956.0
	3rd	12. 0	200. 0	74.0	19701.2
	Mean	13. 0	200. 0	72.7	22762.3
	STDE R	0.6	0.0	4.1	1714.1
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	13. 0	200. 0	79.0	22956.0
	2nd	13. 0	200. 0	76.0	22956.0
	3rd	11. 5	200. 0	96.0	17703.4
	Mean	12. 5	200. 0	83.7	21205.1
	STDE R	0.5	0.0	6.2	1750.9
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	12. 0	200. 0	77.0	19701.2
	2nd	13. 0	200. 0	73.0	22956.0
	3rd	12. 0	200. 0	85.0	19701.2
	Mean	12. 3	200. 0	78.3	20786.2
	STDE R	0.3	0.0	3.5	1084.9
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	13. 0	200. 0	80.0	22956.0
	2nd	13. 0	200. 0	74.0	22956.0
	3rd	12. 0	200. 0	57.0	19701.2
	Mean	12. 7	200. 0	70.3	21871.1
	STDE R	0.3	0.0	6.9	1084.9
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	12. 0	200. 0	92.0	19701.2
	2nd	12. 0	200. 0	96.0	19701.2

Bead name : CCL4/MIP-1 beta					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	12. 0	200. 0	78.0	19701.2
	Mean	12. 0	200. 0	88.7	19701.2
	STDE R	0.0	0.0	5.5	0.0
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	13. 0	200. 0	69.0	22956.0
	2nd	16. 0	200. 0	73.0	30013.2
	3rd	12. 0	200. 0	78.0	19701.2
	Mean	13. 7	200. 0	73.3	24223.5
	STDE R	1.2	0.0	2.6	3043.5

Table 18

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
Blank	1st	20. 0	57.0	1.0	0.8
	2nd	16. 0	66.0	1.0	0.0
	Mean	18. 0	61.5	1.0	0.4
	STDE R	2.0	4.5	0.0	0.4
PBMC + 0.5% DMSO	1st	18. 0	63.0	200.0	84.2
	2nd	18. 5	62.0	200.0	102.5
	3rd	18. 0	89.0	200.0	84.2
	Mean	18. 2	71.3	200.0	90.3
	STDE R	0.2	8.8	0.0	6.1
PBMC+LPS(5ug/ml)	1st	39. 0	64.0	200.0	740.9
	2nd	31. 0	63.0	200.0	505.6

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	31. 0	73.0	200.0	505.6
	Mean	33. 7	66.7	200.0	584.0
	STDE R	2.7	3.2	0.0	78.4
PBMC+YY101 500nM	1st	18. 0	57.0	200.0	84.2
	2nd	18. 0	81.0	200.0	84.2
	Mean	18. 0	69.0	200.0	84.2
	STDE R	0.0	12.0	0.0	0.0
PBMC+YY101 50nM	1st	19. 5	64.0	200.0	138.1
	2nd	18. 0	53.0	200.0	84.2
	Mean	18. 8	58.5	200.0	111.1
	STDE R	0.8	5.5	0.0	27.0
PBMC+YY101 5nM	1st	20. 0	75.0	200.0	155.5
	2nd	20. 0	60.0	200.0	155.5
	Mean	20. 0	67.5	200.0	155.5
	STDE R	0.0	7.5	0.0	0.0
PBMC+YY101 0.5nM	1st	20. 0	70.0	200.0	155.5
	2nd	20. 0	66.0	200.0	155.5
	Mean	20. 0	68.0	200.0	155.5
	STDE R	0.0	2.0	0.0	0.0
PBMC+YY101 0.05uM	1st	17. 0	74.0	200.0	45.8
	2nd	19. 5	54.0	200.0	138.1
	Mean	18. 3	64.0	200.0	92.0

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	1.3	10.0	0.0	46.2
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	38. 0	73.0	200.0	712.0
	2nd	37. 0	50.0	200.0	683.0
	Mean	37. 5	61.5	200.0	697.5
	STDE R	0.5	11.5	0.0	14.5
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	37. 5	74.0	200.0	697.5
	2nd	40. 0	82.0	200.0	769.6
	Mean	38. 8	78.0	200.0	733.6
	STDE R	1.3	4.0	0.0	36.1
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	32. 5	66.0	200.0	550.5
	2nd	35. 5	66.0	200.0	639.2
	Mean	34. 0	66.0	200.0	594.9
	STDE R	1.5	0.0	0.0	44.3
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	28. 5	64.0	200.0	429.6
	2nd	32. 0	61.0	200.0	535.6
	Mean	30. 3	62.5	200.0	482.6
	STDE R	1.8	1.5	0.0	53.0
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	29. 0	89.0	200.0	444.9
	2nd	30. 0	70.0	200.0	475.3
	Mean	29. 5	79.5	200.0	460.1
	STDE R	0.5	9.5	0.0	15.2
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	30. 0	66.0	200.0	475.3

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	27. 0	62.0	200.0	383.2
	Mean	28. 5	64.0	200.0	429.3
	STDE R	1.5	2.0	0.0	46.1
PBMC+LPS(5ug/ml)+YY101 500nM	1st	29. 5	56.0	200.0	460.1
	2nd	31. 0	74.0	200.0	505.6
	3rd	27. 0	71.0	200.0	383.2
	Mean	29. 2	67.0	200.0	449.6
	STDE R	1.2	5.6	0.0	35.7
PBMC+LPS(5ug/ml)+YY101 50nM	1st	27. 0	69.0	200.0	383.2
	2nd	27. 5	58.0	200.0	398.7
	3rd	31. 0	69.0	200.0	505.6
	Mean	28. 5	65.3	200.0	429.2
	STDE R	1.3	3.7	0.0	38.5
PBMC+LPS(5ug/ml)+YY101 5nM	1st	29. 0	64.0	200.0	444.9
	2nd	30. 0	64.0	200.0	475.3
	3rd	32. 0	57.0	200.0	535.6
	Mean	30. 3	61.7	200.0	485.3
	STDE R	0.9	2.3	0.0	26.7
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	29. 5	72.0	200.0	460.1
	2nd	29. 0	80.0	200.0	444.9
	3rd	29. 5	60.0	200.0	460.1
	Mean	29. 3	70.7	200.0	455.0

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.2	5.8	0.0	5.1
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	28. 0	74.0	200.0	414.2
	2nd	34. 5	66.0	200.0	609.8
	3rd	28. 0	61.0	200.0	414.2
	Mean	30. 2	67.0	200.0	479.4
	STDE R	2.2	3.8	0.0	65.2
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	28. 0	58.0	200.0	414.2
	2nd	27. 0	55.0	200.0	383.2
	3rd	30. 0	61.0	200.0	475.3
	Mean	28. 3	58.0	200.0	424.2
	STDE R	0.9	1.7	0.0	27.1
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	32. 0	60.0	200.0	535.6
	2nd	16. 0	67.0	200.0	1.9
	3rd	24. 0	56.0	200.0	288.4
	Mean	24. 0	61.0	200.0	275.3
	STDE R	4.6	3.2	0.0	154.2
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	28. 5	74.0	200.0	429.6
	2nd	25. 0	59.0	200.0	320.3
	3rd	18. 0	63.0	200.0	84.2
	Mean	23. 8	65.3	200.0	278.0
	STDE R	3.1	4.5	0.0	101.9
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	23. 0	75.0	200.0	256.0

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	24. 0	74.0	200.0	288.4
	3rd	28. 5	70.0	200.0	429.6
	Mean	25. 2	73.0	200.0	324.6
	STDE R	1.7	1.5	0.0	53.3
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	28. 5	84.0	200.0	429.6
	2nd	27. 0	86.0	200.0	383.2
	3rd	27. 5	70.0	200.0	398.7
	Mean	27. 7	80.0	200.0	403.8
	STDE R	0.4	5.0	0.0	13.6
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	32. 0	74.0	200.0	535.6
	2nd	32. 5	70.0	200.0	550.5
	3rd	29. 0	66.0	200.0	444.9
	Mean	31. 2	70.0	200.0	510.3
	STDE R	1.1	2.3	0.0	33.0
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	34. 0	60.0	200.0	595.1
	2nd	29. 5	68.0	200.0	460.1
	3rd	30. 0	86.0	200.0	475.3
	Mean	31. 2	71.3	200.0	510.2
	STDE R	1.4	7.7	0.0	42.7
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	30. 0	67.0	200.0	475.3
	2nd	28. 0	55.0	200.0	414.2
	3rd	27. 0	60.0	200.0	383.2

Bead name : IL-1 alpha/IL-1F1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	28. 3	60.7	200.0	424.2
	STDE R	0.9	3.5	0.0	27.1
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	30. 0	76.0	200.0	475.3
	2nd	29. 0	62.0	200.0	444.9
	3rd	27. 0	83.0	200.0	383.2
	Mean	28. 7	73.7	200.0	434.5
	STDE R	0.9	6.2	0.0	27.1
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	31. 0	64.0	200.0	505.6
	2nd	29. 0	54.0	200.0	444.9
	3rd	29. 0	70.0	200.0	444.9
	Mean	29. 7	62.7	200.0	465.1
	STDE R	0.7	4.7	0.0	20.2
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	26. 0	57.0	200.0	351.9
	2nd	26. 5	50.0	200.0	367.6
	3rd	25. 5	64.0	200.0	336.2
	Mean	26. 0	57.0	200.0	351.9
	STDE R	0.3	4.0	0.0	9.1
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	26. 0	74.0	200.0	351.9
	2nd	25. 0	64.0	200.0	320.3
	3rd	25. 0	78.0	200.0	320.3
	Mean	25. 3	72.0	200.0	330.9
	STDE R	0.3	4.2	0.0	10.5

Bead name : IL-1 alpha/IL-1F1					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	27.0	71.0	200.0	383.2
	2nd	30.5	50.0	200.0	490.5
	3rd	34.0	60.0	200.0	595.1
	Mean	30.5	60.3	200.0	489.6
	STDE R	2.0	6.1	0.0	61.2

Table 19

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	14.0	55.0	1.0	2.1
	2nd	13.0	69.0	1.0	1.8
	Mean	13.5	62.0	1.0	2.0
	STDE R	0.5	7.0	0.0	0.1
PBMC + 0.5% DMSO	1st	12.0	71.0	200.0	304.1
	2nd	12.0	79.0	200.0	304.1
	3rd	14.0	84.0	200.0	420.1
	Mean	12.7	78.0	200.0	342.8
	STDE R	0.7	3.8	0.0	38.7
PBMC+LPS(5ug/ml)	1st	141.5	74.0	200.0	7972.5
	2nd	117.0	69.0	200.0	6511.1
	3rd	106.0	72.0	200.0	5855.9
	Mean	121.5	71.7	200.0	6779.8
	STDE R	10.5	1.5	0.0	625.6
PBMC+YY101 500nM	1st	14.0	100.0	200.0	420.1
	2nd	14.0	101.0	200.0	420.1
	Mean	14.0	100.5	200.0	420.1
	STDE R	0.0	0.5	0.0	0.0

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+YY101 50nM	1st	13.0	80.0	200.0	362.0
	2nd	13.0	78.0	200.0	362.0
	Mean	13.0	79.0	200.0	362.0
	STDE R	0.0	1.0	0.0	0.0
PBMC+YY101 5nM	1st	13.0	80.0	200.0	362.0
	2nd	14.0	77.0	200.0	420.1
	Mean	13.5	78.5	200.0	391.1
	STDE R	0.5	1.5	0.0	29.0
PBMC+YY101 0.5nM	1st	13.0	63.0	200.0	362.0
	2nd	14.0	84.0	200.0	420.1
	Mean	13.5	73.5	200.0	391.1
	STDE R	0.5	10.5	0.0	29.0
PBMC+YY101 0.05uM	1st	14.0	89.0	200.0	420.1
	2nd	14.0	67.0	200.0	420.1
	Mean	14.0	78.0	200.0	420.1
	STDE R	0.0	11.0	0.0	0.0
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	144.5	96.0	200.0	8151.7
	2nd	149.0	69.0	200.0	8420.4
	Mean	146.8	82.5	200.0	8286.0
	STDE R	2.3	13.5	0.0	134.4
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	141.0	71.0	200.0	7942.7
	2nd	152.0	84.0	200.0	8599.7
	Mean	146.5	77.5	200.0	8271.2
	STDE R	5.5	6.5	0.0	328.5
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	125.0	73.0	200.0	6988.0
	2nd	142.0	62.0	200.0	8002.4
	Mean	133.5	67.5	200.0	7495.2
	STDE R	8.5	5.5	0.0	507.2

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	108.0	99.0	200.0	5975.0
	2nd	124.0	78.0	200.0	6928.3
	Mean	116.0	88.5	200.0	6451.7
	STDE R	8.0	10.5	0.0	476.7
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	116.5	82.0	200.0	6481.3
	2nd	113.0	95.0	200.0	6272.8
	Mean	114.8	88.5	200.0	6377.0
	STDE R	1.8	6.5	0.0	104.3
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	118.0	71.0	200.0	6570.7
	2nd	104.0	67.0	200.0	5736.8
	Mean	111.0	69.0	200.0	6153.8
	STDE R	7.0	2.0	0.0	416.9
PBMC+LPS(5ug/ml)+YY101 500nM	1st	96.0	73.0	200.0	5260.9
	2nd	107.0	95.0	200.0	5915.4
	3rd	101.0	81.0	200.0	5558.3
	Mean	101.3	83.0	200.0	5578.2
	STDE R	3.2	6.4	0.0	189.2
PBMC+LPS(5ug/ml)+YY101 50nM	1st	95.0	76.0	200.0	5201.4
	2nd	95.0	67.0	200.0	5201.4
	3rd	115.5	66.0	200.0	6421.7
	Mean	101.8	69.7	200.0	5608.2
	STDE R	6.8	3.2	0.0	406.8
PBMC+LPS(5ug/ml)+YY101 5nM	1st	100.0	78.0	200.0	5498.8
	2nd	101.0	63.0	200.0	5558.3

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	3rd	118.0	75.0	200.0	6570.7
	Mean	106.3	72.0	200.0	5875.9
	STDE R	5.8	4.6	0.0	347.8
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	104.0	85.0	200.0	5736.8
	2nd	108.0	86.0	200.0	5975.0
	3rd	115.5	74.0	200.0	6421.7
	Mean	109.2	81.7	200.0	6044.5
	STDE R	3.4	3.8	0.0	200.7
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	104.0	85.0	200.0	5736.8
	2nd	117.0	74.0	200.0	6511.1
	3rd	104.5	78.0	200.0	5766.6
	Mean	108.5	79.0	200.0	6004.8
	STDE R	4.3	3.2	0.0	253.3
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	108.0	71.0	200.0	5975.0
	2nd	108.5	64.0	200.0	6004.7
	3rd	99.0	58.0	200.0	5439.3
	Mean	105.2	64.3	200.0	5806.3
	STDE R	3.1	3.8	0.0	183.7
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	105.0	81.0	200.0	5796.4
	2nd	52.5	74.0	200.0	2681.1
	3rd	80.0	70.0	200.0	4310.2
	Mean	79.2	75.0	200.0	4262.6
	STDE R	15.2	3.2	0.0	899.6
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	101.0	81.0	200.0	5558.3

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	2nd	102.0	81.0	200.0	5617.8
	3rd	61.0	63.0	200.0	3183.9
	Mean	88.0	75.0	200.0	4786.7
	STDEV	13.5	6.0	0.0	801.6
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	67.0	74.0	200.0	3539.2
	2nd	79.0	61.0	200.0	4250.8
	3rd	96.0	70.0	200.0	5260.9
	Mean	80.7	68.3	200.0	4350.3
	STDEV	8.4	3.8	0.0	499.5
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	89.0	89.0	200.0	4844.7
	2nd	91.0	79.0	200.0	4963.6
	3rd	88.0	79.0	200.0	4785.3
	Mean	89.3	82.3	200.0	4864.5
	STDEV	0.9	3.3	0.0	52.4
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	105.0	82.0	200.0	5796.4
	2nd	110.0	62.0	200.0	6094.1
	3rd	102.0	83.0	200.0	5617.8
	Mean	105.7	75.7	200.0	5836.1
	STDEV	2.3	6.8	0.0	138.9
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	97.5	60.0	200.0	5350.1
	2nd	92.0	86.0	200.0	5023.0
	3rd	94.0	85.0	200.0	5141.9
	Mean	94.5	77.0	200.0	5171.7
	STDEV	1.6	8.5	0.0	95.6
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	82.0	70.0	200.0	4428.9
	2nd	78.0	86.0	200.0	4191.5
	3rd	90.0	76.0	200.0	4904.1
	Mean	83.3	77.3	200.0	4508.2
	STDEV	3.5	4.7	0.0	209.5
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	101.5	78.0	200.0	5588.1
	2nd	99.5	78.0	200.0	5469.1
	3rd	88.0	88.0	200.0	4785.3
	Mean	96.3	81.3	200.0	5280.8

Bead name : IL-1 beta/IL-1F2					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
	STDER	4.2	3.3	0.0	250.1
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	98.0	59.0	200.0	5379.8
	2nd	101.0	74.0	200.0	5558.3
	3rd	95.0	86.0	200.0	5201.4
	Mean	98.0	73.0	200.0	5379.8
	STDER	1.7	7.8	0.0	103.0
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	91.0	71.0	200.0	4963.6
	2nd	88.0	83.0	200.0	4785.3
	3rd	82.0	65.0	200.0	4428.9
	Mean	87.0	73.0	200.0	4725.9
	STDER	2.6	5.3	0.0	157.2
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	83.0	73.0	200.0	4488.3
	2nd	82.0	71.0	200.0	4428.9
	3rd	82.5	80.0	200.0	4458.6
	Mean	82.5	74.7	200.0	4458.6
	STDER	0.3	2.7	0.0	17.1
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	84.0	76.0	200.0	4547.7
	2nd	97.0	65.0	200.0	5320.3
	3rd	119.0	61.0	200.0	6630.3
	Mean	100.0	67.3	200.0	5499.4
	STDER	10.2	4.5	0.0	607.8

Table 20

Bead name : TIMP-1					
Sample		MFI	Count	Dilution	Concentration (pg/ml)
Blank	1st	13.0	1.0	50.0	11.8
	2nd	13.0	1.0	52.0	11.8
	Mean	13.0	1.0	51.0	11.8
	STDER	0.0	0.0	1.0	0.0
PBMC + 0.5% DMSO	1st	26.5	200.0	50.0	6531.0

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	23. 5	200. 0	50.0	5800.6
	3rd	22. 0	200. 0	52.0	5411.1
	Mean	24. 0	200. 0	50.7	5914.2
	STDE R	1.3	0.0	0.7	328.2
PBMC+LPS(5ug/ml)	1st	26. 5	200. 0	50.0	6531.0
	2nd	25. 5	200. 0	50.0	6293.9
	3rd	25. 5	200. 0	50.0	6293.9
	Mean	25. 8	200. 0	50.0	6372.9
	STDE R	0.3	0.0	0.0	79.0
PBMC+YY101 500nM	1st	29. 0	200. 0	50.0	7100.2
	2nd	30. 0	200. 0	50.0	7319.6
	Mean	29. 5	200. 0	50.0	7209.9
	STDE R	0.5	0.0	0.0	109.7
PBMC+YY101 50nM	1st	29. 5	200. 0	50.0	7210.4
	2nd	27. 0	200. 0	68.0	6647.4
	Mean	28. 3	200. 0	59.0	6928.9
	STDE R	1.3	0.0	9.0	281.5
PBMC+YY101 5nM	1st	26. 5	200. 0	50.0	6531.0
	2nd	24. 0	200. 0	52.0	5926.6
	Mean	25. 3	200. 0	51.0	6228.8
	STDE R	1.3	0.0	1.0	302.2
PBMC+YY101 0.5nM	1st	25. 0	200. 0	50.0	6173.1

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	28. 5	200. 0	64.0	6988.8
	Mean	26. 8	200. 0	57.0	6580.9
	STDE R	1.8	0.0	7.0	407.8
PBMC+YY101 0.05uM	1st	46. 0	200. 0	54.0	10402.5
	2nd	29. 0	200. 0	50.0	7100.2
	Mean	37. 5	200. 0	52.0	8751.3
	STDE R	8.5	0.0	2.0	1651.2
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	25. 0	200. 0	50.0	6173.1
	2nd	23. 0	200. 0	57.0	5672.8
	Mean	24. 0	200. 0	53.5	5923.0
	STDE R	1.0	0.0	3.5	250.1
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	23. 0	200. 0	50.0	5672.8
	2nd	22. 5	200. 0	50.0	5543.0
	Mean	22. 8	200. 0	50.0	5607.9
	STDE R	0.3	0.0	0.0	64.9
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	25. 0	200. 0	58.0	6173.1
	2nd	26. 0	200. 0	52.0	6413.2
	Mean	25. 5	200. 0	55.0	6293.1
	STDE R	0.5	0.0	3.0	120.0
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	24. 5	200. 0	50.0	6050.7
	2nd	25. 0	200. 0	50.0	6173.1
	Mean	24. 8	200. 0	50.0	6111.9

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.3	0.0	0.0	61.2
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	23. 5	200. 0	50.0	5800.6
	2nd	24. 0	200. 0	55.0	5926.6
	Mean	23. 8	200. 0	52.5	5863.6
	STDE R	0.3	0.0	2.5	63.0
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	24. 0	200. 0	50.0	5926.6
	2nd	22. 5	200. 0	50.0	5543.0
	Mean	23. 3	200. 0	50.0	5734.8
	STDE R	0.8	0.0	0.0	191.8
PBMC+LPS(5ug/ml)+YY101 500nM	1st	17. 0	200. 0	52.0	3935.4
	2nd	17. 0	200. 0	67.0	3935.4
	3rd	15. 0	200. 0	50.0	3220.1
	Mean	16. 3	200. 0	56.3	3696.9
	STDE R	0.7	0.0	5.4	238.4
PBMC+LPS(5ug/ml)+YY101 50nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	15. 0	200. 0	50.0	3220.1
	3rd	17. 0	200. 0	54.0	3935.4
	Mean	16. 3	200. 0	51.3	3696.9
	STDE R	0.7	0.0	1.3	238.4
PBMC+LPS(5ug/ml)+YY101 5nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	17. 0	200. 0	57.0	3935.4
	3rd	15. 0	200. 0	50.0	3220.1

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	16. 3	200. 0	52.3	3696.9
	STDE R	0.7	0.0	2.3	238.4
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	16. 0	200. 0	50.0	3590.9
	3rd	20. 0	200. 0	50.0	4859.3
	Mean	17. 7	200. 0	50.0	4128.5
	STDE R	1.2	0.0	0.0	378.7
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	17. 0	200. 0	55.0	3935.4
	2nd	16. 0	200. 0	50.0	3590.9
	3rd	17. 0	200. 0	56.0	3935.4
	Mean	16. 7	200. 0	53.7	3820.5
	STDE R	0.3	0.0	1.9	114.8
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	18. 0	200. 0	50.0	4259.2
	2nd	15. 0	200. 0	54.0	3220.1
	3rd	18. 0	200. 0	57.0	4259.2
	Mean	17. 0	200. 0	53.7	3912.8
	STDE R	1.0	0.0	2.0	346.4
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	16. 0	200. 0	50.0	3590.9
	3rd	17. 0	200. 0	52.0	3935.4
	Mean	16. 7	200. 0	50.7	3820.5
	STDE R	0.3	0.0	0.7	114.8

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	18. 0	200. 0	50.0	4259.2
	3rd	19. 0	200. 0	55.0	4566.3
	Mean	18. 0	200. 0	51.7	4253.6
	STDE R	0.6	0.0	1.7	182.1
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	20. 0	200. 0	50.0	4859.3
	2nd	17. 0	200. 0	50.0	3935.4
	3rd	16. 0	200. 0	50.0	3590.9
	Mean	17. 7	200. 0	50.0	4128.5
	STDE R	1.2	0.0	0.0	378.7
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	16. 0	200. 0	50.0	3590.9
	2nd	17. 0	200. 0	50.0	3935.4
	3rd	19. 5	200. 0	54.0	4714.4
	Mean	17. 5	200. 0	51.3	4080.2
	STDE R	1.0	0.0	1.3	332.3
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	18. 5	200. 0	50.0	4414.6
	2nd	16. 0	200. 0	50.0	3590.9
	3rd	20. 0	200. 0	50.0	4859.3
	Mean	18. 2	200. 0	50.0	4288.3
	STDE R	1.2	0.0	0.0	371.6
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	18. 0	200. 0	50.0	4259.2
	2nd	16. 0	200. 0	50.0	3590.9

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	18. 0	200. 0	50.0	4259.2
	Mean	17. 3	200. 0	50.0	4036.4
	STDE R	0.7	0.0	0.0	222.8
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	19. 0	200. 0	60.0	4566.3
	2nd	16. 5	200. 0	50.0	3766.0
	3rd	19. 0	200. 0	50.0	4566.3
	Mean	18. 2	200. 0	53.3	4299.5
	STDE R	0.8	0.0	3.3	266.7
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	20. 0	200. 0	50.0	4859.3
	3rd	18. 0	200. 0	58.0	4259.2
	Mean	18. 3	200. 0	52.7	4351.3
	STDE R	0.9	0.0	2.7	270.6
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	19. 0	200. 0	58.0	4566.3
	2nd	19. 0	200. 0	60.0	4566.3
	3rd	18. 0	200. 0	54.0	4259.2
	Mean	18. 7	200. 0	57.3	4463.9
	STDE R	0.3	0.0	1.8	102.3
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	18. 0	200. 0	56.0	4259.2
	2nd	18. 5	200. 0	50.0	4414.6
	3rd	17. 0	200. 0	51.0	3935.4
	Mean	17. 8	200. 0	52.3	4203.1

Bead name : TIMP-1					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.4	0.0	1.9	141.2
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	18. 0	200. 0	50.0	4259.2
	2nd	18. 5	200. 0	50.0	4414.6
	3rd	16. 0	200. 0	50.0	3590.9
	Mean	17. 5	200. 0	50.0	4088.2
	STDE R	0.8	0.0	0.0	252.7
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	17. 0	200. 0	50.0	3935.4
	2nd	22. 5	200. 0	50.0	5543.0
	3rd	19. 0	200. 0	54.0	4566.3
	Mean	19. 5	200. 0	51.3	4681.6
	STDE R	1.6	0.0	1.3	467.7

Table 21

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
Blank	1st	24. 0	71.0	1.0	110.4
	2nd	23. 0	63.0	1.0	99.0
	Mean	23. 5	67.0	1.0	104.7
	STDE R	0.5	4.0	0.0	5.7
PBMC + 0.5% DMSO	1st	23. 0	63.0	200.0	19789.4
	2nd	24. 0	77.0	200.0	22079.2
	3rd	22. 0	73.0	200.0	17222.7
	Mean	23. 0	71.0	200.0	19697.1

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.6	4.2	0.0	1402.7
PBMC+LPS(5ug/ml)	1st	23. 0	56.0	200.0	19789.4
	2nd	22. 0	51.0	200.0	17222.7
	3rd	24. 0	64.0	200.0	22079.2
	Mean	23. 0	57.0	200.0	19697.1
	STDE R	0.6	3.8	0.0	1402.7
PBMC+YY101 500nM	1st	23. 0	88.0	200.0	19789.4
	2nd	23. 5	84.0	200.0	20963.1
	Mean	23. 3	86.0	200.0	20376.3
	STDE R	0.3	2.0	0.0	586.9
PBMC+YY101 50nM	1st	26. 0	73.0	200.0	26106.3
	2nd	24. 0	63.0	200.0	22079.2
	Mean	25. 0	68.0	200.0	24092.8
	STDE R	1.0	5.0	0.0	2013.5
PBMC+YY101 5nM	1st	22. 0	74.0	200.0	17222.7
	2nd	23. 5	58.0	200.0	20963.1
	Mean	22. 8	66.0	200.0	19092.9
	STDE R	0.8	8.0	0.0	1870.2
PBMC+YY101 0.5nM	1st	21. 0	55.0	200.0	14234.9
	2nd	22. 0	62.0	200.0	17222.7
	Mean	21. 5	58.5	200.0	15728.8
	STDE R	0.5	3.5	0.0	1493.9

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+YY101 0.05uM	1st	23. 0	72.0	200.0	19789.4
	2nd	22. 0	61.0	200.0	17222.7
	Mean	22. 5	66.5	200.0	18506.0
	STDE R	0.5	5.5	0.0	1283.3
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	26. 0	50.0	200.0	26106.3
	2nd	22. 0	60.0	200.0	17222.7
	Mean	24. 0	55.0	200.0	21664.5
	STDE R	2.0	5.0	0.0	4441.8
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	25. 0	53.0	200.0	24169.3
	2nd	22. 0	92.0	200.0	17222.7
	Mean	23. 5	72.5	200.0	20696.0
	STDE R	1.5	19.5	0.0	3473.3
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	22. 0	77.0	200.0	17222.7
	2nd	22. 0	50.0	200.0	17222.7
	Mean	22. 0	63.5	200.0	17222.7
	STDE R	0.0	13.5	0.0	0.0
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	20. 0	72.0	200.0	10481.4
	2nd	20. 0	66.0	200.0	10481.4
	Mean	20. 0	69.0	200.0	10481.4
	STDE R	0.0	3.0	0.0	0.0
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	22. 0	81.0	200.0	17222.7
	2nd	22. 5	58.0	200.0	18547.4

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	22. 3	69.5	200.0	17885.0
	STDE R	0.3	11.5	0.0	662.3
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	21. 0	66.0	200.0	14234.9
	2nd	22. 0	55.0	200.0	17222.7
	Mean	21. 5	60.5	200.0	15728.8
	STDE R	0.5	5.5	0.0	1493.9
PBMC+LPS(5ug/ml)+YY101 500nM	1st	23. 0	53.0	200.0	19789.4
	2nd	22. 0	72.0	200.0	17222.7
	3rd	23. 0	66.0	200.0	19789.4
	Mean	22. 7	63.7	200.0	18933.8
	STDE R	0.3	5.6	0.0	855.5
PBMC+LPS(5ug/ml)+YY101 50nM	1st	22. 0	59.0	200.0	17222.7
	2nd	21. 0	65.0	200.0	14234.9
	3rd	21. 0	71.0	200.0	14234.9
	Mean	21. 3	65.0	200.0	15230.8
	STDE R	0.3	3.5	0.0	995.9
PBMC+LPS(5ug/ml)+YY101 5nM	1st	24. 0	60.0	200.0	22079.2
	2nd	22. 0	74.0	200.0	17222.7
	3rd	25. 0	63.0	200.0	24169.3
	Mean	23. 7	65.7	200.0	21157.1
	STDE R	0.9	4.3	0.0	2057.6
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	22. 0	52.0	200.0	17222.7

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	22. 0	71.0	200.0	17222.7
	3rd	21. 0	81.0	200.0	14234.9
	Mean	21. 7	68.0	200.0	16226.8
	STDE R	0.3	8.5	0.0	995.9
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	22. 0	56.0	200.0	17222.7
	2nd	21. 5	70.0	200.0	15795.3
	3rd	22. 0	52.0	200.0	17222.7
	Mean	21. 8	59.3	200.0	16746.9
	STDE R	0.2	5.5	0.0	475.8
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	23. 0	62.0	200.0	19789.4
	2nd	20. 0	54.0	200.0	10481.4
	3rd	23. 0	59.0	200.0	19789.4
	Mean	22. 0	58.3	200.0	16686.7
	STDE R	1.0	2.3	0.0	3102.7
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	23. 0	63.0	200.0	19789.4
	2nd	13. 0	79.0	200.0	<98.95
	3rd	19. 5	62.0	200.0	8003.2
	Mean	18. 5	68.0	200.0	13896.3
	STDE R	2.9	5.5	0.0	5893.1
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	20. 0	66.0	200.0	10481.4
	2nd	21. 0	65.0	200.0	14234.9
	3rd	12. 0	60.0	200.0	<98.95

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	17. 7	63.7	200.0	12358.1
	STDE R	2.8	1.9	0.0	1876.7
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	17. 0	52.0	200.0	<98.95
	2nd	19. 0	60.0	200.0	4332.6
	3rd	22. 0	62.0	200.0	17222.7
	Mean	19. 3	58.0	200.0	10777.7
	STDE R	1.5	3.1	0.0	6445.0
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	20. 0	76.0	200.0	10481.4
	2nd	19. 0	91.0	200.0	4332.6
	3rd	21. 0	67.0	200.0	14234.9
	Mean	20. 0	78.0	200.0	9683.0
	STDE R	0.6	7.0	0.0	2886.3
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	23. 0	74.0	200.0	19789.4
	2nd	20. 0	80.0	200.0	10481.4
	3rd	21. 0	81.0	200.0	14234.9
	Mean	21. 3	78.3	200.0	14835.2
	STDE R	0.9	2.2	0.0	2703.7
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	22. 0	50.0	200.0	17222.7
	2nd	22. 0	59.0	200.0	17222.7
	3rd	20. 0	75.0	200.0	10481.4
	Mean	21. 3	61.3	200.0	14975.6
	STDE R	0.7	7.3	0.0	2247.1

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	22. 0	63.0	200.0	17222.7
	2nd	19. 0	65.0	200.0	4332.6
	3rd	20. 0	50.0	200.0	10481.4
	Mean	20. 3	59.3	200.0	10678.9
	STDE R	0.9	4.7	0.0	3722.4
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	21. 5	54.0	200.0	15795.3
	2nd	23. 0	65.0	200.0	19789.4
	3rd	23. 0	70.0	200.0	19789.4
	Mean	22. 5	63.0	200.0	18458.0
	STDE R	0.5	4.7	0.0	1331.4
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	23. 0	55.0	200.0	19789.4
	2nd	20. 5	60.0	200.0	12493.0
	3rd	21. 0	79.0	200.0	14234.9
	Mean	21. 5	64.7	200.0	15505.7
	STDE R	0.8	7.3	0.0	2200.0
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	20. 5	54.0	200.0	12493.0
	2nd	22. 0	64.0	200.0	17222.7
	3rd	22. 0	63.0	200.0	17222.7
	Mean	21. 5	60.3	200.0	15646.1
	STDE R	0.5	3.2	0.0	1576.6
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	20. 0	63.0	200.0	10481.4
	2nd	18. 5	60.0	200.0	<98.95

Bead name : Leptin					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	18. 0	62.0	200.0	<98.95
	Mean	18. 8	61.7	200.0	10481.4
	STDE R	0.6	0.9	0.0	#DIV/0!
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	22. 5	58.0	200.0	18547.4
	2nd	24. 0	60.0	200.0	22079.2
	3rd	22. 5	56.0	200.0	18547.4
	Mean	23. 0	58.0	200.0	19724.6
	STDE R	0.5	1.2	0.0	1177.3

Table 22

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
Blank	1st	29. 5	50.0	1.0	20.7
	2nd	34. 0	64.0	1.0	27.8
	Mean	31. 8	57.0	1.0	24.3
	STDE R	2.3	7.0	0.0	3.5
PBMC + 0.5% DMSO	1st	56. 0	66.0	200.0	12836.1
	2nd	39. 0	76.0	200.0	7158.5
	3rd	37. 0	93.0	200.0	6512.8
	Mean	44. 0	78.3	200.0	8835.8
	STDE R	6.0	7.9	0.0	2008.8
PBMC+LPS(5ug/ml)	1st	33. 0	87.0	200.0	5239.4
	2nd	35. 0	77.0	200.0	5872.9

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	3rd	33. 0	83.0	200.0	5239.4
	Mean	33. 7	82.3	200.0	5450.5
	STDE R	0.7	2.9	0.0	211.2
PBMC+YY101 500nM	1st	48. 0	69.0	200.0	10126.8
	2nd	54. 0	92.0	200.0	12153.3
	Mean	51. 0	80.5	200.0	11140.0
	STDE R	3.0	11.5	0.0	1013.3
PBMC+YY101 50nM	1st	53. 0	89.0	200.0	11813.2
	2nd	46. 0	70.0	200.0	9459.2
	Mean	49. 5	79.5	200.0	10636.2
	STDE R	3.5	9.5	0.0	1177.0
PBMC+YY101 5nM	1st	67. 5	78.0	200.0	16823.6
	2nd	52. 0	81.0	200.0	11474.0
	Mean	59. 8	79.5	200.0	14148.8
	STDE R	7.8	1.5	0.0	2674.8
PBMC+YY101 0.5nM	1st	56. 0	82.0	200.0	12836.1
	2nd	77. 0	73.0	200.0	20186.4
	Mean	66. 5	77.5	200.0	16511.2
	STDE R	10. 5	4.5	0.0	3675.1
PBMC+YY101 0.05uM	1st	79. 0	69.0	200.0	20901.3
	2nd	57. 0	74.0	200.0	13178.7
	Mean	68. 0	71.5	200.0	17040.0

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	11. 0	2.5	0.0	3861.3
PBMC+LPS(5ug/ml)+Xiidra 500nM	1st	35. 0	73.0	200.0	5872.9
	2nd	35. 0	65.0	200.0	5872.9
	Mean	35. 0	69.0	200.0	5872.9
	STDE R	0.0	4.0	0.0	0.0
PBMC+LPS(5ug/ml)+Xiidra 50nM	1st	35. 0	63.0	200.0	5872.9
	2nd	37. 0	79.0	200.0	6512.8
	Mean	36. 0	71.0	200.0	6192.8
	STDE R	1.0	8.0	0.0	319.9
PBMC+LPS(5ug/ml)+Xiidra 5nM	1st	32. 0	76.0	200.0	4925.2
	2nd	37. 0	85.0	200.0	6512.8
	Mean	34. 5	80.5	200.0	5719.0
	STDE R	2.5	4.5	0.0	793.8
PBMC+LPS(5ug/ml)+Xiidra 0.5nM	1st	27. 5	72.0	200.0	3535.8
	2nd	31. 0	83.0	200.0	4612.9
	Mean	29. 3	77.5	200.0	4074.3
	STDE R	1.8	5.5	0.0	538.5
PBMC+LPS(5ug/ml)+Xiidra 0.05nM	1st	30. 0	102. 0	200.0	4302.5
	2nd	31. 5	78.0	200.0	4768.8
	Mean	30. 8	90.0	200.0	4535.6
	STDE R	0.8	12.0	0.0	233.2
PBMC+LPS(5ug/ml)+Xiidra 0.005nM	1st	30. 0	77.0	200.0	4302.5

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	30. 0	76.0	200.0	4302.5
	Mean	30. 0	76.5	200.0	4302.5
	STDE R	0.0	0.5	0.0	0.0
PBMC+LPS(5ug/ml)+YY101 500nM	1st	31. 0	64.0	200.0	4612.9
	2nd	33. 0	71.0	200.0	5239.4
	3rd	34. 0	64.0	200.0	5555.3
	Mean	32. 7	66.3	200.0	5135.8
	STDE R	0.9	2.3	0.0	276.9
PBMC+LPS(5ug/ml)+YY101 50nM	1st	33. 0	80.0	200.0	5239.4
	2nd	32. 0	76.0	200.0	4925.2
	3rd	34. 0	76.0	200.0	5555.3
	Mean	33. 0	77.3	200.0	5239.9
	STDE R	0.6	1.3	0.0	181.9
PBMC+LPS(5ug/ml)+YY101 5nM	1st	33. 0	76.0	200.0	5239.4
	2nd	30. 0	74.0	200.0	4302.5
	3rd	35. 0	79.0	200.0	5872.9
	Mean	32. 7	76.3	200.0	5138.2
	STDE R	1.5	1.5	0.0	456.1
PBMC+LPS(5ug/ml)+YY101 0.5nM	1st	33. 0	73.0	200.0	5239.4
	2nd	33. 0	74.0	200.0	5239.4
	3rd	33. 0	60.0	200.0	5239.4
	Mean	33. 0	69.0	200.0	5239.4

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	STDE R	0.0	4.5	0.0	0.0
PBMC+LPS(5ug/ml)+YY101 0.05nM	1st	33. 0	69.0	200.0	5239.4
	2nd	32. 0	77.0	200.0	4925.2
	3rd	31. 5	68.0	200.0	4768.8
	Mean	32. 2	71.3	200.0	4977.8
	STDE R	0.4	2.8	0.0	138.4
PBMC+LPS(5ug/ml)+YY101 0.005nM	1st	28. 0	76.0	200.0	3688.0
	2nd	32. 0	69.0	200.0	4925.2
	3rd	33. 0	57.0	200.0	5239.4
	Mean	31. 0	67.3	200.0	4617.5
	STDE R	1.5	5.5	0.0	473.5
PBMC+LPS(5ug/ml)+YDE011 500nM	1st	31. 0	75.0	200.0	4612.9
	2nd	18. 5	76.0	200.0	931.9
	3rd	25. 0	77.0	200.0	2784.3
	Mean	24. 8	76.0	200.0	2776.4
	STDE R	3.6	0.6	0.0	1062.6
PBMC+LPS(5ug/ml)+YDE011 50nM	1st	24. 5	74.0	200.0	2636.1
	2nd	28. 0	71.0	200.0	3688.0
	3rd	20. 0	62.0	200.0	1342.1
	Mean	24. 2	69.0	200.0	2555.4
	STDE R	2.3	3.6	0.0	678.4
PBMC+LPS(5ug/ml)+YDE011 5nM	1st	22. 0	77.0	200.0	1907.3

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	2nd	28. 0	65.0	200.0	3688.0
	3rd	30. 0	77.0	200.0	4302.5
	Mean	26. 7	73.0	200.0	3299.3
	STDE R	2.4	4.0	0.0	718.2
PBMC+LPS(5ug/ml)+YDE011 0.5nM	1st	27. 0	92.0	200.0	3384.2
	2nd	28. 0	80.0	200.0	3688.0
	3rd	26. 5	66.0	200.0	3233.2
	Mean	27. 2	79.3	200.0	3435.2
	STDE R	0.4	7.5	0.0	133.7
PBMC+LPS(5ug/ml)+YDE011 0.05nM	1st	31. 0	65.0	200.0	4612.9
	2nd	31. 0	79.0	200.0	4612.9
	3rd	30. 0	80.0	200.0	4302.5
	Mean	30. 7	74.7	200.0	4509.4
	STDE R	0.3	4.8	0.0	103.5
PBMC+LPS(5ug/ml)+YDE011 0.005nM	1st	29. 5	60.0	200.0	4148.1
	2nd	31. 0	60.0	200.0	4612.9
	3rd	29. 0	82.0	200.0	3994.2
	Mean	29. 8	67.3	200.0	4251.7
	STDE R	0.6	7.3	0.0	186.0
PBMC+LPS(5ug/ml)+YDE043 500nM	1st	28. 0	72.0	200.0	3688.0
	2nd	32. 0	70.0	200.0	4925.2
	3rd	28. 0	85.0	200.0	3688.0

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
	Mean	29. 3	75.7	200.0	4100.4
	STDE R	1.3	4.7	0.0	412.4
PBMC+LPS(5ug/ml)+YDE043 50nM	1st	28. 0	75.0	200.0	3688.0
	2nd	28. 0	70.0	200.0	3688.0
	3rd	30. 0	81.0	200.0	4302.5
	Mean	28. 7	75.3	200.0	3892.8
	STDE R	0.7	3.2	0.0	204.8
PBMC+LPS(5ug/ml)+YDE043 5nM	1st	30. 0	50.0	200.0	4302.5
	2nd	28. 0	67.0	200.0	3688.0
	3rd	27. 5	72.0	200.0	3535.8
	Mean	28. 5	63.0	200.0	3842.1
	STDE R	0.8	6.7	0.0	234.3
PBMC+LPS(5ug/ml)+YDE043 0.5nM	1st	28. 0	60.0	200.0	3688.0
	2nd	28. 0	86.0	200.0	3688.0
	3rd	26. 5	64.0	200.0	3233.2
	Mean	27. 5	70.0	200.0	3536.4
	STDE R	0.5	8.1	0.0	151.6
PBMC+LPS(5ug/ml)+YDE043 0.05nM	1st	29. 0	75.0	200.0	3994.2
	2nd	29. 5	70.0	200.0	4148.1
	3rd	28. 0	76.0	200.0	3688.0
	Mean	28. 8	73.7	200.0	3943.4
	STDE R	0.4	1.9	0.0	135.2

Bead name : MMP-9					
Sample		MF I	Cou nt	Diluti on	Concentration (pg/ml)
PBMC+LPS(5ug/ml)+YDE043 0.005nM	1st	29. 0	53.0	200.0	3994.2
	2nd	34. 0	69.0	200.0	5555.3
	3rd	36. 0	79.0	200.0	6192.0
	Mean	33. 0	67.0	200.0	5247.2
	STDE R	2.1	7.6	0.0	652.9

Example 9: Investigate the effects of YY-101, YDE-011 & YDE-043 Compounds on various cytokine and chemokine release in Human Peripheral Blood Mononuclear Cells (PBMCs) (Study 2)

Background and Purpose

The objective of this study was to investigate the effects of YY-101, YDE-011 and YDE-043 compound on various cytokine and chemokine release in human peripheral blood mononuclear cells (hPBMCs) stimulated by known stimulants LPS.

To achieve this goal, this study was conducted to establish the efficacious dose-response curve of YY-101, YDE-011 and YDE-043 up to 30 cytokine and chemokine release in hPBMC induced by LPS.

Materials & Methods

Human PBMCs frozen purchased from ATCC in a cryo-preserved were thawed, washed with Hank's Balanced Salt Solution containing 10% fetal bovine serum, and seeded onto a 24-well plate at a density of 0.5×10^6 cells/well with culture RPMI media containing 10% fetal bovine serum in growth media in a 24 well plate for 24 hrs and maintained at 37 °C in an atmosphere of 95% air and 5% CO₂. At the end of 24 hr culture, cells are pretreated with YY-101, YDE-011 and YDE-043 or reference compound, Xiidra® at various concentrations for 2h before stimulation. An equal volume of 0.5% DMSO is used as a vehicle control. Then, the cells are treated with LPS. Supernatants from treated cells are harvested at 24 hr post-LPS treatment and placed in 96 well for Luminex cytokine & chemokine profiling using a Luminex 200 multiplex assay.

Reagents and Solutions

- Human PBMCs (ATCC, USA)
- Lipopolysaccharides from Escherichia coli (Sigma Aldrich, USA)
- Human magnetic Luminex assay kit (R&D System, USA)
- 5 • Xiidra® (Shire, USA)
- Test materials (YY-101, YDE-011 and YDE-043) were stored in a deep freezer (-20°C).

Cell Culture

Human PBMCs frozen in a cryopreserve was thawed, washed with Hank's
 10 Balanced Salt Solution containing 10% Fetal bovine serum, and seeded onto a 24-
 well plate at a density of 0.5×10^6 cells/well with culture RPMI media containing
 10% Fetal bovine serum in growth media in a 24 well plate for 24 hrs and maintained
 at 37°C in an atmosphere of 95% air and 5% CO₂.

Treatment

15 Human PBMCs were pretreated with YY-101, YDE-011 and YDE-043 or
 reference compound; Xiidra® at various concentration (ranging from 1nM to
 100uM) for 2 h before stimulation. An equal volume of 0.5% DMSO was used as a
 vehicle control. Then, the cells were treated with LPS at 5ug/ml. The supernatants
 from treated cells were harvested at 24 h and placed in a 96 well for Luminex
 20 cytokine & chemokine profiling using a Luminex 200 multiplex assay (Luminex;
 R&D system, USA).

The main study arm with triplicate wells per group in a 24-well plate:

1. Blank
2. PBMC: 0.5% DMSO
- 25 3. PBMC + LPS (5ug/ml)
4. PBMC + YY-101 100 uM
5. PBMC + YY-101 10 uM
6. PBMC + YY-101 1 uM
7. PBMC + YY-101 0.1uM
- 30 8. PBMC + YY-101 0.01uM
9. PBMC + LPS (5ug/ml) + Xiidra®100 uM
10. PBMC + LPS (5ug/ml) + Xiidra®10 uM
11. PBMC + LPS (5ug/ml) + Xiidra®1 uM
12. PBMC + LPS (5ug/ml) + Xiidra®0.1 uM
- 35 13. PBMC + LPS (5ug/ml) + Xiidra®0.01 uM
14. PBMC + LPS (5ug/ml) + Xiidra®0.001 uM
15. PBMC + LPS (5ug/ml) + YY-101 100 uM

16. PBMC + LPS (5ug/ml) + YY-101 10 uM
17. PBMC + LPS (5ug/ml) + YY-101 1 uM
18. PBMC + LPS (5ug/ml) + YY-101 0.1 uM
19. PBMC + LPS (5ug/ml) + YY-101 0.01 uM
- 5 20. PBMC + LPS (5ug/ml) + YY-101 0.001 uM
21. PBMC + LPS (5ug/ml) + YDE-011 100 uM
22. PBMC + LPS (5ug/ml) + YDE-011 10 uM
23. PBMC + LPS (5ug/ml) + YDE-011 1 uM
24. PBMC + LPS (5ug/ml) + YDE-011 0.1 uM
- 10 25. PBMC + LPS (5ug/ml) + YDE-011 0.01 uM
26. PBMC + LPS (5ug/ml) + YDE-011 0.001 uM
27. PBMC + LPS (5ug/ml) + YDE-043 100 uM
28. PBMC + LPS (5ug/ml) + YDE-043 10 uM
29. PBMC + LPS (5ug/ml) + YDE-043 1 uM
- 15 30. PBMC + LPS (5ug/ml) + YDE-043 0.1 uM
31. PBMC + LPS (5ug/ml) + YDE-043 0.01 uM
32. PBMC + LPS (5ug/ml) + YDE-043 0.001 uM

Cell Count

- 20 The number of PBMCs was measured after 24hr of treatment. The culture both and trypan blue were diluted 1:1 and 10ul was added to Countess cell counting chamber (Thermo fisher, USA). The number of PBMCs was measured using a Countess automated cell counter (Thermo fisher, USA).

25 *Multiplex Assay*

- Multiplex assay was used to measure 30 cytokines and chemokines. The 1:2, 1:10 and 1:200 diluted cell supernatant and serial dilution of the standard were dispensed into a 96 well plate at 50ul/well. Then, the pre-mixed cocktail of antibody-coated magnetic beads was dispensed at 50ul/well and incubated at room temperature for 2 h in a horizontal orbital microplate shaker at 800± 500 rpm. The beads were washed using a magnetic device to prevent loss. The biotin-antibody was dispensed in 50ul of each well and incubated at room temperature for 1 h in a shaker at 800± 500 rpm. After washing, streptavidin-PE was added at 50ul/well and incubated at room temperature for 30 min in a shaker under the same conditions.
- 30 Finally, after washing, wash buffer (100ul/well) was added to the plate and incubated in a shaker for 2 min. The Luminex™ 200 setting were set according to the manufacturer's protocol. The data was calculated with a standard five-parameter logistic nonlinear regression analysis of the data (xPonent software 4.2, USA). The
- 35

levels of cytokine/chemokine are normalized to the live cell counts (1×10^5 cells/mL) and presented as concentrations per mL (pg/mL or ng/mL).

Below is the list of cytokines and chemokines either in 21-plex, 5-plex and two 2-plex (Table 23).

5 **Table 23**

21 plex	1:2 dilution	5 plex	1:10 dilution
Human	Cytokine/Chemokine	Human	Cytokine/Chemokine
1	MCP-1 (CCL2)	1	MIP-1 alpha (CCL3)
2	RANTES (CCL5)	2	MIP-1 beta (CCL4)
3	MIP-3alpha (CCL20)	3	IL-1 beta
4	Fractalkine (CX3CL1)	4	IL-10
5	Fas-L	5	TNF-alpha
6	GM-CSF		
7	ICAM-1		
8	IFN-gamma		
9	IL-1 alpha		
10	IL-2		
11	IL-4		
12	IL-5		
13	IL-13		
14	IL-17A		
15	Leptin		
16	MMP-3		
17	MMP-8		
18	MMP-9		
19	RAGE		
20	L-Selectin		

21	VEGF-D		

2-plex	1:2 dilution	2-plex	1:200 dilution
Human	Cytokine/Chemokine list	Human	Cytokine/Chemokine
1	TIMP-1	1	IL-6
2	VEGF-A	2	IL-8 (CXCL8)

Compound Delivery & Formulation

The concentration of compound was prepared according to the information provided by the client.

All compound was serially diluted in from the stock concentrations and the final concentration of DMSO was not exceed 0.5% DMSO. All compounds were prepared on the same day of the treatment.

Results

Results are shown in Figures 23-42. hPBMCs stimulated by LPS at 5 ug/mL for 24 hrs were co-treated with test and reference compounds with various concentrations and from which cytokine release was measured. Among 30 cytokines and chemokines evaluated, similar to the previous study (NS-Y0119 1st main test), all of the compounds, YY-101, YDE-011 and YDE-043 effectively and potently reduced LPS-induced various pro-inflammatory cytokines and chemokines in human PBMCs at as low as 1 nM. Among the compounds, both YDE-011 and YDE-043 significantly reduced various pro-inflammatory cytokines and chemokines such as IL-6, IL-8, IL-10, TNF- α , IFN-gamma, CCL2, CCL4, CCL5, CCL20, Fas, TIMP-1 more than 50% and CCL-3 over 70%. Interestingly, the compound, YY-101 didn't affect the basal levels of most of cytokine/chemokine production or the viability of hPBMCs.

Human PBMCs were stimulated by LPS at 5 ug/mL for 24 hrs and co-treated with vehicle (0.5% DMSO), test articles and reference compound, Xiidra® at various concentrations (100uM to 1nM). After 24 hr treatment, aliquots of hPBMC media were extracted, diluted in 1:2, 1:10 and 1:200, and measured for cytokine levels using a Luminex multiplex system. Additional aliquots were extracted to count the number of total and live PBMCs.

hPBMC cell counts with or without LPS and test articles

A range of the total and live cells after 24-hour treatment was between $5.8-13.0 \times 10^5$ and $4.6-7.2 \times 10^5$ cells per well (1mL), respectively. The percentage of live over the total cells was between 54-89.5%, of which the majority falls within 70-80% range (Table 1). Although some variability among groups exists, when compared to each treatment groups, little or no difference in the total and live cells or viability % was observed in any groups. In other words, none of LPS alone or YY-101 alone, LPS + Xiidra®, LPS + YY-101, LPS + YDE-011, or LPS + YDE-043 consistently affected the total and live number of PBMCs up to 100 μ M. Neither did the percent viability.

Multi-cytokine assessment in PBMCs stimulated by LPS

Among 30 cytokines & chemokines evaluated, 15 of 30 were detected within the standard curve range, 5 below the range and 10 were below the level of detection & quantification even though the sample dilution was minimized (Table 2).

Among those 15 detectable cytokines/chemokines, similar to the previous study (NS-Y0119 1st main test), all of the compounds, YY-101, YDE-011 and YDE-043, effectively and potently reduced LPS-induced various pro-inflammatory cytokines and chemokines in human PBMCs at as low as 1 nM. Among the compounds, both YDE-011 and YDE-043 significantly reduced various pro-inflammatory cytokines and chemokines such as IL-6, IL-8, IL-10, TNF- α , IFN- γ , CCL2, CCL4, CCL5, CCL20, Fas, TIMP-1 more than 50% and CCL-3 over 70%. YY-101 also significantly reduced LPS-induced various cytokines and chemokines (IL-10, TNF- α , CCL4) in human PBMCs at as low as 1 nM.

CCL3 is a chemokine ligand 3 known as macrophage inflammatory protein 1- α (MIP-1- α), which is involved in the acute inflammatory state in the recruitment and activation of leukocytes through binding to the receptors CCR1, CCR4 and CCR5. CCL3 has known to interact with CCL4 and attracts macrophages, monocytes and neutrophils. Interestingly, CCL3 concentrations were significantly increased in Sjögren's syndrome patients and CCL3 and CCL4 levels correlated significantly with basal tear secretion, tear clearance rate, keratoepitheliopathy score, and goblet cell density. The level correlates with various tear film and ocular surface parameters. (Choi et al., Curr Eye Res. 2012 37:12-7).

Although the detection level was low, all of the compounds potently reduced LPS-induced IL2, IL-4 and IL-17A levels in a dose-dependent manner. In contrast, YY-101 also further increased LPS-induced IL-1a, IL-I3, CCL20 and GM-CSF levels at 100.iM, which may due to the YY-101 mediated cellular toxicity.

- 5 However, it is unlikely as YY-101 at 100.iM didn't affect any viability or the total number of PBMCs (Table 1). Similar to the previous finding, YY-101, even up to 100.iM didn't affect the basal levels of cytokine production except TIMP-1.

When the reference compound, Xiidra® was tested at higher concentrations than the previous study, it began to reduce some of cytokines induced by LPS.

- 10 Xiidra® significantly reduced IL-10, CCL3, CCL4, IFN-y.

Table 24*PBMC Cell Counts with and without LPS and test articles.*

	Total cell (10⁵/ml)	Live cell (10⁵/ml)	Viability (%)
PBMC + 0.5% DMSO	8.2±0.4	7.2±0.3	87.3±0.9
PBMC+LPS(5ug/ml)	6.8±.	5.8±0.2	85.0±0.6
PBMC+YY101 0.01uM	5.9±0.4	5.0±0.2	85.0±2.0
PBMC+YY101 0.1uM	6.1±0.8	5.1±0.2	84.0±0.0
PBMC+YY101 1uM	6.1±0.2	5.5±0.0	89.5±2.5
PBMC+YY101 10uM	7.4±0.3	6.3±0.2	86.0±1.0
PBMC+YY101 100uM	7.8±0.5	6.7±0.3	86.5±1.5
PBMC+LPS(5ug/ml)+Xiidra® 0.001uM	13.0±3.0	6.9±0.7	54.0±8.0
PBMC+LPS(5ug/ml)+Xiidra® 0.01uM	6.9±0.6	5.5±0.3	80.0±2.0
PBMC+LPS(5ug/ml)+Xiidra® 0.1uM	7.1±0.7	6.2±0.5	86.5±1.5
PBMC+LPS(5ug/ml)+Xiidra® 1uM	5.8±0.3	4.6±0.2	80.5±0.5
PBMC+LPS(5ug/ml)+Xiidra® 10uM	6.9±0.2	6.1±0.3	89.0±2.0
PBMC+LPS(5ug/ml)+Xiidra® 100uM	7.5±0.9	6.5±0.7	86.5±1.5
PBMC+LPS(5ug/ml)+YY-101 0.001uM	7.7±0.6	6.5±0.4	84.3±2.6
PBMC+LPS(5ug/ml)+YY-101 0.01uM	8.1±0.6	6.2±0.1	77.3±5.0
PBMC+LPS(5ug/ml)+YY-101 0.1uM	7.8±0.8	5.9±0.3	75.7±4.7
PBMC+LPS(5ug/ml)+YY-101 1uM	9.8±0.6	6.5±0.3	66.7±5.8
PBMC+LPS(5ug/ml)+YY-101 10uM	9.1±1.1	6.7±0.5	73.7±4.8
PBMC+LPS(5ug/ml)+YY-101 100uM	7.8±1.0	5.8±0.4	76.7±5.2
PBMC+LPS(5ug/ml)+YDE-011 0.001uM	6.3±0.2	5.4±0.4	85.0±5.1
PBMC+LPS(5ug/ml)+YDE-011 0.01uM	7.3±0.4	5.9±0.4	81.0±1.2
PBMC+LPS(5ug/ml)+YDE-011 0.1uM	7.1±0.7	5.8±0.5	82.0±4.0
PBMC+LPS(5ug/ml)+YDE-011 1uM	6.4±0.3	5.0±0.2	79.7±5.8
PBMC+LPS(5ug/ml)+YDE-011 10uM	6.0±0.4	5.3±0.3	88.3±1.5
PBMC+LPS(5ug/ml)+YDE-011 100uM	8.2±0.4	6.1±0.0	74.3±4.1
PBMC+LPS(5ug/ml)+YDE-043 0.001uM	6.3±0.7	5.0±0.5	79.3±1.5
PBMC+LPS(5ug/ml)+YDE-043 0.01uM	6.9±0.4	5.4±0.6	77.3±6.9
PBMC+LPS(5ug/ml)+YDE-043 0.1uM	6.6±0.1	5.4±0.2	82.0±4.0
PBMC+LPS(5ug/ml)+YDE-043 1uM	6.8±0.6	5.3±0.3	78.0±5.0
PBMC+LPS(5ug/ml)+YDE-043 10uM	6.4±0.1	5.4±0.1	83.3±3.3
PBMC+LPS(5ug/ml)+YDE-043 100uM	7.6±0.6	6.3±0.1	84.5±4.5

All values are presented as mean $\pm$ standard error of mean (SEM). The statistical significance of the results was analyzed using one-way ANOVA with a Bonferroni post hoc. The statistical analyses were performed using the SPSS software (SPSS 22.0, USA). Each compound treated PBMCs was compared to that of the stimulant induced PBMCs. The significant threshold was fixed at 0.05 i.e. p value has to be lower than 0.05 to be significant.

Conclusions

LPS effectively induced various pro-inflammatory cytokines in human PBMCs and its induction was potently and significantly reduced by all compounds as low as 1 nM; whereas, the reference compound, Xiidra® was not as effective as the compounds. This finding is consistent with Example 8, suggesting that the compounds, especially YDE-011 and YDE043, are more potent and effective immunomodulators in lowering pro-inflammatory cytokine/chemokine productions in human PBMCs when stimulated by an endotoxin, LPS.

Table 25

A list of cytokines/chemokines and QC results

No.	Cytokines	Dilution factor	Result	No.	CycleNo	Dilution factor	Result
1	IL-10	1:10	Within standard curve range	15	16.2	1:2	Below standard curve range
2	IL-8	1:200	Within standard curve range	17	18.174	1:2	Below standard curve range
3	IL-6	1:200	Within standard curve range	18	13.4	1:2	Below standard curve range
4	TGF- α	1:10	Within standard curve range	19	16.03.8	1:2	Below standard curve range
5	CCL2/MIP-1 α	1:10	Within standard curve range	20	16.03.9	1:2	Below standard curve range
6	CCL4/MIP-1 β	1:10	Within standard curve range	21	16.03.3	1:2	BLQ
7	CCL5/RANTES	1:2	Within standard curve range	22	16.03.8	1:2	BLQ
8	IP-10	1:2	Within standard curve range	23	1.56e6.11	1:2	BLQ
9	CCL20/MIP-3 α	1:2	Within standard curve range	24	16.03	1:2	BLQ
10	Far1/GM-CSF	1:2	Within standard curve range	25	16.03.11.9	1:2	BLQ
11	CCL20/MIP-3 α	1:2	Within standard curve range	26	0.5	1:2	BLQ
12	IL-1 α	1:2	Within standard curve range	27	16.13	1:2	BLQ
13	IL-1 β /IL-1 β 2	1:10	Within standard curve range	28	16.03.5	1:2	BLQ
14	TGF- β 1	1:2	Within standard curve range	29	16.03.1	1:2	BLQ
15	CCL5/R	1:2	Within standard curve range	30	16.03.10	1:2	BLQ

Table 26: Annex 1 – The count of PBMCs raw data

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
PBMC + 0.5% DMSO	1st	8.7	7.5	86.0
	2nd	8.5	7.4	87.0
	3rd	7.5	6.6	89.0
	Mean	8.2	7.2	87.3
	STDER	0.4	0.3	0.9
PBMC+LPS(5ug/ml)	1st	7.3	6.1	84.0
	2nd	6.7	5.8	86.0
	3rd	6.4	5.5	85.0
	Mean	6.8	5.8	85.0
	STDER	0.3	0.2	0.6
PBMC+YY101 0.01uM	1st	6.3	5.2	83.0
	2nd	5.5	4.8	87.0
	Mean	5.9	5.0	85.0
	STDER	0.4	0.2	2.0
PBMC+YY101 0.1uM	1st	5.2	4.4	84.0
	2nd	6.9	5.8	84.0
	Mean	6.1	5.1	84.0
	STDER	0.8	0.7	0.0
PBMC+YY101 1uM	1st	5.9	5.5	92.0
	2nd	6.3	5.5	87.0
	Mean	6.1	5.5	89.5
	STDER	0.2	0.0	2.5
PBMC+YY101 10uM	1st	7.6	6.4	85.0
	2nd	7.1	6.1	87.0
	Mean	7.4	6.3	86.0
	STDER	0.3	0.2	1.0
PBMC+YY101 100uM	1st	7.3	6.4	88.0

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
	2nd	8.2	7.0	85.0
	Mean	7.8	6.7	86.5
	STDER	0.5	0.3	1.5
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	1st	10.0	6.2	62.0
	2nd	16.0	7.6	46.0
	Mean	13.0	6.9	54.0
	STDER	3.0	0.7	8.0
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	1st	6.3	5.2	82.0
	2nd	7.4	5.8	78.0
	Mean	6.9	5.5	80.0
	STDER	0.6	0.3	2.0
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	1st	7.8	6.6	85.0
	2nd	6.4	5.7	88.0
	Mean	7.1	6.2	86.5
	STDER	0.7	0.5	1.5
PBMC+LPS(5ug/ml)+Xiidra 1uM	1st	6.0	4.8	81.0
	2nd	5.5	4.4	80.0
	Mean	5.8	4.6	80.5
	STDER	0.3	0.2	0.5
PBMC+LPS(5ug/ml)+Xiidra 10uM	1st	6.7	5.8	87.0
	2nd	7.1	6.4	91.0
	Mean	6.9	6.1	89.0
	STDER	0.2	0.3	2.0
PBMC+LPS(5ug/ml)+Xiidra 100uM	1st	8.3	7.1	85.0
	2nd	6.6	5.8	88.0
	Mean	7.5	6.5	86.5
	STDER	0.9	0.7	1.5
	1st	6.7	5.7	84.0

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
PBMC+LPS(5ug/ml)+YY101 0.001uM	2nd	8.8	7.1	80.0
	3rd	7.5	6.6	89.0
	Mean	7.7	6.5	84.3
	STDER	0.6	0.4	2.6
PBMC+LPS(5ug/ml)+YY101 0.01uM	1st	9.2	6.4	70.0
	2nd	8.1	6.0	75.0
	3rd	7.0	6.1	87.0
	Mean	8.1	6.2	77.3
	STDER	0.6	0.1	5.0
PBMC+LPS(5ug/ml)+YY101 0.1uM	1st	9.3	6.2	67.0
	2nd	6.7	5.2	77.0
	3rd	7.5	6.2	83.0
	Mean	7.8	5.9	75.7
	STDER	0.8	0.3	4.7
PBMC+LPS(5ug/ml)+YY101 1uM	1st	8.8	6.3	72.0
	2nd	9.7	7.1	73.0
	3rd	11.0	6.2	55.0
	Mean	9.8	6.5	66.7
	STDER	0.6	0.3	5.8
PBMC+LPS(5ug/ml)+YY101 10uM	1st	7.3	6.0	83.0
	2nd	9.0	6.4	71.0
	3rd	11.0	7.6	67.0
	Mean	9.1	6.7	73.7
	STDER	1.1	0.5	4.8
PBMC+LPS(5ug/ml)+YY101 100uM	1st	8.7	6.3	73.0
	2nd	8.8	6.2	70.0
	3rd	5.8	5.0	87.0
	Mean	7.8	5.8	76.7

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
	STDER	1.0	0.4	5.2
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	5.9	4.5	75.0
	2nd	6.3	5.8	92.0
	3rd	6.6	5.8	88.0
	Mean	6.3	5.4	85.0
	STDER	0.2	0.4	5.1
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	7.6	6.3	83.0
	2nd	7.8	6.2	81.0
	3rd	6.4	5.1	79.0
	Mean	7.3	5.9	81.0
	STDER	0.4	0.4	1.2
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	7.8	6.6	85.0
	2nd	5.7	5.0	87.0
	3rd	7.7	5.7	74.0
	Mean	7.1	5.8	82.0
	STDER	0.7	0.5	4.0
PBMC+LPS(5ug/ml)+YDE011 1uM	1st	6.2	5.5	89.0
	2nd	7.0	4.8	69.0
	3rd	5.9	4.8	81.0
	Mean	6.4	5.0	79.7
	STDER	0.3	0.2	5.8
PBMC+LPS(5ug/ml)+YDE011 10uM	1st	5.9	5.4	91.0
	2nd	6.7	5.8	86.0
	3rd	5.4	4.7	88.0
	Mean	6.0	5.3	88.3
	STDER	0.4	0.3	1.5
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	7.6	6.1	81.0
	2nd	8.1	6.1	75.0

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
	3rd	9.0	6.0	67.0
	Mean	8.2	6.1	74.3
	STDER	0.4	0.0	4.1
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	5.6	4.4	79.0
	2nd	7.8	6.0	77.0
	3rd	5.6	4.6	82.0
	Mean	6.3	5.0	79.3
	STDER	0.7	0.5	1.5
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	6.2	4.5	72.0
	2nd	7.3	6.6	91.0
	3rd	7.2	5.0	69.0
	Mean	6.9	5.4	77.3
	STDER	0.4	0.6	6.9
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	6.8	5.0	74.0
	2nd	6.4	5.6	87.0
	3rd	6.5	5.6	85.0
	Mean	6.6	5.4	82.0
	STDER	0.1	0.2	4.0
PBMC+LPS(5ug/ml)+YDE043 1uM	1st	6.9	5.8	83.0
	2nd	5.7	4.8	83.0
	3rd	7.8	5.3	68.0
	Mean	6.8	5.3	78.0
	STDER	0.6	0.3	5.0
PBMC+LPS(5ug/ml)+YDE043 10uM	1st	6.4	5.2	80.0
	2nd	6.7	5.4	80.0
	3rd	6.2	5.6	90.0
	Mean	6.4	5.4	83.3
	STDER	0.1	0.1	3.3

PBMCs count				
Sample		Total cell count (10 ⁵ /ml)	Live cell (10 ⁵ /ml)	Viability (%)
PBMC+LPS(5ug/ml)+YDE043 100uM	1st	7.0	6.2	89.0
	2nd	8.1	6.4	80.0
	Mean	7.6	6.3	84.5
	STDER	0.6	0.1	4.5

Table 27: Annex 2 – The main study raw data

Bead name : IL-10							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc./live cell (pg/10 ⁵)	
Blank	1st	-0.3	10.0	NaN			
	2nd	0.3	10.0	NaN			
	Mean	0.0	10.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.3	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	-0.3	10.0		7.5	0.0	
	2nd	-0.3	10.0		7.4	0.0	
	3rd	-0.3	10.0		6.6	0.0	
	Mean	-0.3	10.0	#DIV/0!	7.2	0.0	
	STDER	0.0	0.0	#DIV/0!	0.3	0.0	
PBMC+LPS(5ug/ml)	1st	503.8	10.0	743.5	6.1	121.9	
	2nd	445.8	10.0	670.5	5.8	115.6	
	3rd	467.8	10.0	698.3	5.5	127.0	
	Mean	472.4	10.0	704.1	5.8	121.5	
	STDER	16.9	0.0	21.3	0.2	3.3	
PBMC+YY101 0.01uM	1st	0.8	10.0		5.2	0.0	

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	1.8	10.0	4.3	4.8	0.9
	Mean	1.3	10.0	4.3	5.0	0.5
	STDER	0.5	0.0	#DIV/0!	0.2	0.5
	1st	0.8	10.0		4.4	0.0
PBMIC+YY101 0.1uM	2nd	1.8	10.0	4.3	5.8	0.7
	Mean	1.3	10.0	4.3	5.1	0.4
	STDER	0.5	0.0	#DIV/0!	0.7	0.4
	1st	0.8	10.0		5.5	0.0
PBMIC+YY101 1uM	2nd	0.8	10.0		5.5	0.0
	Mean	0.8	10.0	#DIV/0!	5.5	0.0
	STDER	0.0	0.0	#DIV/0!	0.0	0.0
	1st	7.8	10.0	23.2	6.4	3.6
PBMIC+YY101 10uM	2nd	1.3	10.0	2.0	6.1	0.3
	Mean	4.5	10.0	12.6	6.3	2.0
	STDER	3.3	0.0	10.6	0.2	1.6
	1st	2.8	10.0	8.2	6.4	1.3

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	-0.3	10.0		7.0	0.0
	Mean	1.3	10.0	8.2	6.7	0.6
	STDER	1.5	0.0	#DIV/0!	0.3	0.6
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	1st	319.8	10.0	507.4	6.2	81.8
	2nd	310.3	10.0	494.8	7.6	65.1
	Mean	315.0	10.0	501.1	6.9	73.5
	STDER	4.8	0.0	6.3	0.7	8.4
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	1st	298.8	10.0	479.5	5.2	92.2
	2nd	327.3	10.0	517.4	5.8	89.2
	Mean	313.0	10.0	498.4	5.5	90.7
	STDER	14.3	0.0	18.9	0.3	1.5
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	1st	257.3	10.0	423.5	6.6	64.2
	2nd	223.3	10.0	376.6	5.7	66.1
	Mean	240.3	10.0	400.0	6.2	65.1
	STDER	17.0	0.0	23.4	0.5	1.0
PBMIC+LPS(5ug/ml)+Xiidra 1uM	1st	305.8	10.0	488.8	4.8	101.8

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	219.3	10.0	371.0	4.4	84.3
	Mean	262.5	10.0	429.9	4.6	93.1
	STDER	43.3	0.0	58.9	0.2	8.8
	1st	311.8	10.0	496.8	5.8	85.7
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	335.3	10.0	527.9	6.4	82.5
	Mean	323.5	10.0	512.4	6.1	84.1
	STDER	11.8	0.0	15.5	0.3	1.6
	1st	329.8	10.0	520.7	7.1	73.3
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	318.8	10.0	506.1	5.8	87.3
	Mean	324.3	10.0	513.4	6.5	80.3
	STDER	5.5	0.0	7.3	0.7	7.0
	1st	315.3	10.0	501.5	5.7	88.0
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	305.8	10.0	488.8	7.1	68.9
	3rd	275.3	10.0	447.9	6.6	67.9
	Mean	298.8	10.0	479.4	6.5	74.9
	STDER	12.1	0.0	16.2	0.4	6.5

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	308.8	10.0	492.8	6.4	77.0
	2nd	313.8	10.0	499.5	6.0	83.2
	3rd	319.8	10.0	507.4	6.1	83.2
	Mean	314.1	10.0	499.9	6.2	81.1
	STDER	3.2	0.0	4.2	0.1	2.1
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	259.8	10.0	426.9	6.2	68.9
	2nd	283.8	10.0	459.4	5.2	88.3
	3rd	277.3	10.0	450.6	6.2	72.7
	Mean	273.6	10.0	445.6	5.9	76.6
	STDER	7.2	0.0	9.7	0.3	6.0
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	357.3	10.0	556.7	6.3	88.4
	2nd	302.8	10.0	484.8	7.1	68.3
	3rd	327.8	10.0	518.0	6.2	83.6
	Mean	329.3	10.0	519.9	6.5	80.1
	STDER	15.8	0.0	20.8	0.3	6.1
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	287.8	10.0	464.8	6.0	77.5

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	342.3	10.0	537.1	6.4	83.9
	3rd	255.8	10.0	421.4	7.6	55.4
	Mean	295.3	10.0	474.4	6.7	72.3
	STDER	25.3	0.0	33.7	0.5	8.6
PBMC+LPS(5ug/ml)+YY101 100uM	1st	86.8	10.0	173.5	6.3	27.5
	2nd	83.8	10.0	168.6	6.2	27.2
	3rd	87.8	10.0	175.1	5.0	35.0
	Mean	86.1	10.0	172.4	5.8	29.9
	STDER	1.2	0.0	2.0	0.4	2.6
	1st	163.3	10.0	291.0	4.5	64.7
PBMC+LPS(5ug/ml)+YDE011 0.001uM	2nd	179.3	10.0	314.2	5.8	54.2
	3rd	173.8	10.0	306.3	5.8	52.8
	Mean	172.1	10.0	303.8	5.4	57.2
	STDER	4.7	0.0	6.8	0.4	3.7
	1st	192.8	10.0	333.6	6.3	52.9
	2nd	186.8	10.0	325.0	6.2	52.4

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	3rd	166.3	10.0	295.4	5.1	57.9
	Mean	181.9	10.0	318.0	5.9	54.4
	STDER	8.0	0.0	11.6	0.4	1.7
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	168.8	10.0	299.0	6.6	45.3
	2nd	181.8	10.0	317.8	5.0	63.6
	3rd	176.3	10.0	309.9	5.7	54.4
	Mean	175.6	10.0	308.9	5.8	54.4
	STDER	3.8	0.0	5.5	0.5	5.3
	1st	179.3	10.0	314.2	5.5	57.1
PBMIC+LPS(5ug/ml)+YDE011 1uM	2nd	182.8	10.0	319.3	4.8	66.5
	3rd	176.8	10.0	310.6	4.8	64.7
	Mean	179.6	10.0	314.7	5.0	62.8
	STDER	1.7	0.0	2.5	0.2	2.9
	1st	168.8	10.0	299.0	5.4	55.4
	2nd	166.3	10.0	295.4	5.8	50.9
PBMIC+LPS(5ug/ml)+YDE011 10uM	3rd	174.8	10.0	307.7	4.7	65.5

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	Mean	169.9	10.0	300.7	5.3	57.3
	STDER	2.5	0.0	3.7	0.3	4.3
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	43.8	10.0	99.4	6.1	16.3
	2nd	51.8	10.0	113.9	6.1	18.7
	3rd	55.8	10.0	121.1	6.0	20.2
	Mean	50.4	10.0	111.4	6.1	18.4
	STDER	3.5	0.0	6.4	0.0	1.1
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	194.3	10.0	335.7	4.4	76.3
	2nd	168.3	10.0	298.3	6.0	49.7
	3rd	157.8	10.0	282.9	4.6	61.5
	Mean	173.4	10.0	305.6	5.0	62.5
	STDER	10.8	0.0	15.7	0.5	7.7
PBMIC+LPS(5ug/ml)+YDE043 0.01uM	1st	200.8	10.0	344.9	4.5	76.7
	2nd	213.3	10.0	362.6	6.6	54.9
	3rd	188.3	10.0	327.1	5.0	65.4
	Mean	200.8	10.0	344.9	5.4	65.7

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	STDER	7.2	0.0	10.2	0.6	6.3
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	190.3	10.0	330.0	5.0	66.0
	2nd	178.3	10.0	312.8	5.6	55.9
	3rd	186.3	10.0	324.3	5.6	57.9
	Mean	184.9	10.0	322.4	5.4	59.9
	STDER	3.5	0.0	5.1	0.2	3.1
	1st	189.3	10.0	328.6	5.8	56.7
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	178.3	10.0	312.8	4.8	65.2
	3rd	198.3	10.0	341.4	5.3	64.4
	Mean	188.6	10.0	327.6	5.3	62.1
	STDER	5.8	0.0	8.3	0.3	2.7
	1st	182.3	10.0	318.5	5.2	61.3
	2nd	153.8	10.0	277.0	5.4	51.3
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	167.8	10.0	297.5	5.6	53.1
	Mean	167.9	10.0	297.7	5.4	55.2
	STDER	8.2	0.0	12.0	0.1	3.1

Bead name : IL-10						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	47.8	10.0	106.7	6.2	17.2
	2nd	50.8	10.0	112.1	6.4	17.5
	Mean	49.3	10.0	109.4	6.3	17.4
	STDER	1.5	0.0	2.7	0.1	0.2

Table 28

Bead name : IL-8						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	-0.5	200.0	NaN		
	2nd	0.5	200.0	NaN		
	Mean	0.0	200.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	68.0	200.0	2052.8	7.5	273.7
	2nd	70.5	200.0	2126.4	7.4	287.4
	3rd	89.0	200.0	2671.9	6.6	404.8

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	75.8	200.0	2283.7	7.2	322.0	
	STDER	6.6	0.0	195.3	0.3	41.6	
	1st	1590.5	200.0	48853.0	6.1	8008.7	
	2nd	1546.5	200.0	47437.7	5.8	8178.9	
	3rd	1575.5	200.0	48370.0	5.5	8794.5	
	Mean	1570.8	200.0	48220.2	5.8	8327.4	
	STDER	12.9	0.0	415.4	0.2	238.7	
	1st	95.5	200.0	2863.8	5.2	550.7	
	2nd	230.0	200.0	6854.4	4.8	1428.0	
	Mean	162.8	200.0	4859.1	5.0	989.4	
PBMC+YY101 0.01uM	STDER	67.3	0.0	1995.3	0.2	438.6	
	1st	90.0	200.0	2701.4	4.4	614.0	
	2nd	205.5	200.0	6125.1	5.8	1056.0	
	Mean	147.8	200.0	4413.2	5.1	835.0	
	STDER	57.8	0.0	1711.8	0.7	221.0	
	1st	149.5	200.0	4461.8	5.5	811.2	
PBMC+YY101 0.1uM							
PBMC+YY101 1uM							

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	157.5	200.0	4699.1	5.5	854.4	
	Mean	153.5	200.0	4580.5	5.5	832.8	
	STDER	4.0	0.0	118.6	0.0	21.6	
	1st	1227.5	200.0	37311.2	6.4	5829.9	
PBMC+YY101 10uM	2nd	166.5	200.0	4966.2	6.1	814.1	
	Mean	697.0	200.0	21138.7	6.3	3322.0	
	STDER	530.5	0.0	16172.5	0.2	2507.9	
	1st	664.5	200.0	19929.7	6.4	3114.0	
PBMC+YY101 100uM	2nd	358.5	200.0	10693.9	7.0	1527.7	
	Mean	511.5	200.0	15311.8	6.7	2320.9	
	STDER	153.0	0.0	4617.9	0.3	793.2	
	1st	1631.5	200.0	50176.1	6.2	8092.9	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	1424.5	200.0	43537.7	7.6	5728.6	
	Mean	1528.0	200.0	46856.9	6.9	6910.8	
	STDER	103.5	0.0	3319.2	0.7	1182.1	
	1st	1533.0	200.0	47004.4	5.2	9039.3	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1638.0	200.0	50386.3	5.8	8687.3	
	Mean	1585.5	200.0	48695.3	5.5	8863.3	
	STDER	52.5	0.0	1691.0	0.3	176.0	
	1st	1396.5	200.0	42647.5	6.6	6461.7	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	1433.5	200.0	43824.2	5.7	7688.5	
	Mean	1415.0	200.0	43235.9	6.2	7075.1	
	STDER	18.5	0.0	588.4	0.5	613.4	
	1st	1382.5	200.0	42203.1	4.8	8792.3	
PBMC+LPS(5ug/ml)+Xiidra 1uM	2nd	1548.0	200.0	47485.8	4.4	10792.2	
	Mean	1465.3	200.0	44844.5	4.6	9792.3	
	STDER	82.8	0.0	2641.4	0.2	1000.0	
	1st	1418.5	200.0	43346.8	5.8	7473.6	
PBMC+LPS(5ug/ml)+Xiidra 10uM	2nd	1370.5	200.0	41822.5	6.4	6534.8	
	Mean	1394.5	200.0	42584.6	6.1	7004.2	
	STDER	24.0	0.0	762.2	0.3	469.4	
	1st	1356.0	200.0	41363.0	7.1	5825.8	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1346.5	200.0	41062.3	5.8	7079.7	
	Mean	1351.3	200.0	41212.6	6.5	6452.7	
	STDER	4.8	0.0	150.4	0.7	627.0	
	1st	1479.5	200.0	45291.5	5.7	7945.9	
	2nd	1465.5	200.0	44844.4	7.1	6316.1	
	3rd	1677.0	200.0	51649.5	6.6	7825.7	
PBMCLPS(5ug/ml)+YY101 0.001uM	Mean	1540.7	200.0	47261.8	6.5	7362.6	
	STDER	68.3	0.0	2197.6	0.4	524.4	
	1st	1486.0	200.0	45499.3	6.4	7109.3	
	2nd	1465.5	200.0	44844.4	6.0	7474.1	
	3rd	1515.5	200.0	46443.3	6.1	7613.7	
	Mean	1489.0	200.0	45595.7	6.2	7399.0	
PBMCLPS(5ug/ml)+YY101 0.01uM	STDER	14.5	0.0	464.1	0.1	150.4	
	1st	1353.5	200.0	41283.9	6.2	6658.7	
	2nd	1407.5	200.0	42997.0	5.2	8268.7	
	3rd	1359.5	200.0	41473.9	6.2	6689.3	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	1373.5	200.0	41918.3	5.9	7205.6	
	STDER	17.1	0.0	542.2	0.3	531.6	
	1st	1476.5	200.0	45195.7	6.3	7173.9	
	2nd	1478.5	200.0	45259.6	7.1	6374.6	
	3rd	1560.0	200.0	47871.4	6.2	7721.2	
	Mean	1505.0	200.0	46108.9	6.5	7089.9	
	STDER	27.5	0.0	881.4	0.3	391.0	
	1st	1511.5	200.0	46315.2	6.0	7719.2	
	2nd	1649.0	200.0	50742.2	6.4	7928.5	
	3rd	1407.0	200.0	42981.1	7.6	5655.4	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	1522.5	200.0	46679.5	6.7	7101.0	
	STDER	70.1	0.0	2247.8	0.5	725.3	
	1st	1574.5	200.0	48337.8	6.3	7672.7	
	2nd	1532.5	200.0	46988.3	6.2	7578.8	
	3rd	1444.5	200.0	44174.7	5.0	8834.9	
	Mean	1517.2	200.0	46500.3	5.8	8028.8	
PBMC+LPS(5ug/ml)+YY101 100uM	Mean	1517.2	200.0	46500.3	5.8	8028.8	
	STDER	70.1	0.0	2247.8	0.5	725.3	
	1st	1574.5	200.0	48337.8	6.3	7672.7	
	2nd	1532.5	200.0	46988.3	6.2	7578.8	
	3rd	1444.5	200.0	44174.7	5.0	8834.9	
	Mean	1517.2	200.0	46500.3	5.8	8028.8	
	STDER	70.1	0.0	2247.8	0.5	725.3	
	1st	1574.5	200.0	48337.8	6.3	7672.7	
	2nd	1532.5	200.0	46988.3	6.2	7578.8	
	3rd	1444.5	200.0	44174.7	5.0	8834.9	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	38.3	0.0	1226.3	0.4	404.0	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	861.5	200.0	25949.1	4.5	5766.5	
	2nd	838.5	200.0	25243.2	5.8	4352.3	
	3rd	906.5	200.0	27333.0	5.8	4712.6	
	Mean	868.8	200.0	26175.1	5.4	4943.8	
	STDER	20.0	0.0	613.8	0.4	424.3	
	1st	906.0	200.0	27317.6	6.3	4336.1	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	964.0	200.0	29106.4	6.2	4694.6	
	3rd	900.5	200.0	27148.3	5.1	5323.2	
	Mean	923.5	200.0	27857.4	5.9	4784.6	
	STDER	20.3	0.0	626.4	0.4	288.5	
	1st	852.5	200.0	25672.8	6.6	3889.8	
	2nd	870.5	200.0	26225.6	5.0	5245.1	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	853.5	200.0	25703.5	5.7	4509.4	
	Mean	858.8	200.0	25867.3	5.8	4548.1	
	STDER	5.8	0.0	179.4	0.5	391.7	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 1uM	1st	872.0	200.0	26271.7	5.5	4776.7	
	2nd	875.5	200.0	26379.3	4.8	5495.7	
	3rd	805.5	200.0	24231.7	4.8	5048.3	
	Mean	851.0	200.0	25627.6	5.0	5106.9	
	STDER	22.8	0.0	698.6	0.2	209.6	
PBMC+LPS(5ug/ml)+YDE011 10uM	1st	851.0	200.0	25626.7	5.4	4745.7	
	2nd	841.5	200.0	25335.2	5.8	4368.1	
	3rd	809.5	200.0	24354.2	4.7	5181.8	
	Mean	834.0	200.0	25105.4	5.3	4765.2	
	STDER	12.6	0.0	384.9	0.3	235.1	
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	918.5	200.0	27702.6	6.1	4541.4	
	2nd	881.5	200.0	26563.8	6.1	4354.7	
	3rd	793.0	200.0	23849.1	6.0	3974.8	
	Mean	864.3	200.0	26038.5	6.1	4290.3	
	STDER	37.2	0.0	1143.0	0.0	166.7	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	841.0	200.0	25319.8	4.4	5754.5	

Bead name : IL-8							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	932.5	200.0	28134.2	6.0	4689.0	
	3rd	973.0	200.0	29384.5	4.6	6387.9	
	Mean	915.5	200.0	27612.8	5.0	5610.5	
	STDER	39.0	0.0	1202.0	0.5	495.7	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	928.5	200.0	28010.8	4.5	6224.6	
	2nd	897.5	200.0	27056.0	6.6	4099.4	
	3rd	939.5	200.0	28350.1	5.0	5670.0	
	Mean	921.8	200.0	27805.6	5.4	5331.3	
	STDER	12.6	0.0	387.4	0.6	636.4	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	912.0	200.0	27502.4	5.0	5500.5	
	2nd	822.0	200.0	24737.2	5.6	4417.4	
	3rd	926.5	200.0	27949.2	5.6	4990.9	
	Mean	886.8	200.0	26729.6	5.4	4969.6	
	STDER	32.7	0.0	1004.5	0.2	312.9	
PBMC+LPS(5ug/ml)+YDE043 1uM	1st	912.5	200.0	27517.8	5.8	4744.4	
	2nd	765.5	200.0	23008.1	4.8	4793.4	

Bead name : IL-8						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	3rd	954.0	200.0	28797.5	5.3	5433.5
	Mean	877.3	200.0	26441.2	5.3	4990.4
	STDER	57.2	0.0	1755.8	0.3	222.0
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	960.5	200.0	28998.3	5.2	5576.6
	2nd	1141.5	200.0	34618.6	5.4	6410.8
	3rd	812.5	200.0	24446.1	5.6	4365.4
	Mean	971.5	200.0	29354.3	5.4	5450.9
	STDER	95.1	0.0	2941.9	0.1	593.8
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	895.5	200.0	26994.4	6.2	4353.9
	2nd	798.5	200.0	24017.4	6.4	3752.7
	Mean	847.0	200.0	25505.9	6.3	4053.3
	STDER	48.5	0.0	1488.5	0.1	300.6

Table 29

Bead name : IL-6						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.3	200.0	NaN		
	2nd	-0.3	200.0	NaN		
	Mean	0.0	200.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.3	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMC + 0.5% DMSO	1st	2.3	200.0		7.5	0.0
	2nd	3.8	200.0		7.4	0.0
	3rd	2.3	200.0		6.6	0.0
	Mean	2.8	200.0	#DIV/0!	7.2	0.0
	STDER	0.5	0.0	#DIV/0!	0.3	0.0
PBMC+LPS(5ug/ml)	1st	431.3	200.0	15083.7	6.1	2472.7
	2nd	423.3	200.0	14810.7	5.8	2553.6
	3rd	407.3	200.0	14264.9	5.5	2593.6
	Mean	420.6	200.0	14719.8	5.8	2540.0
	STDER	7.1	0.0	240.7	0.2	35.5
PBMC+YY101 0.01uM	1st	4.3	200.0		5.2	0.0

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	2.3	200.0		4.8	0.0	
	Mean	3.3	200.0	#DIV/0!	5.0	0.0	
	STDER	1.0	0.0	#DIV/0!	0.2	0.0	
	1st	1.3	200.0		4.4	0.0	
PBMCMC+YY101 0.1uM	2nd	1.3	200.0		5.8	0.0	
	Mean	1.3	200.0	#DIV/0!	5.1	0.0	
	STDER	0.0	0.0	#DIV/0!	0.7	0.0	
	1st	2.3	200.0		5.5	0.0	
PBMCMC+YY101 1uM	2nd	1.3	200.0		5.5	0.0	
	Mean	1.8	200.0	#DIV/0!	5.5	0.0	
	STDER	0.5	0.0	#DIV/0!	0.0	0.0	
	1st	27.3	200.0	880.7	6.4	137.6	
PBMCMC+YY101 10uM	2nd	3.3	200.0		6.1	0.0	
	Mean	15.3	200.0	880.7	6.3	68.8	
	STDER	12.0	0.0	#DIV/0!	0.2	68.8	
	1st	19.8	200.0	524.7	6.4	82.0	

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	11.8	200.0		7.0	0.0	
	Mean	15.8	200.0	524.7	6.7	41.0	
	STDER	4.0	0.0	#DIV/0!	0.3	41.0	
	1st	415.8	200.0	14554.8	6.2	2347.5	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	365.3	200.0	12833.4	7.6	1688.6	
	Mean	390.5	200.0	13694.1	6.9	2018.1	
	STDER	25.3	0.0	860.7	0.7	329.5	
	1st	427.3	200.0	14947.2	5.2	2874.5	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	380.3	200.0	13344.5	5.8	2300.8	
	Mean	403.8	200.0	14145.8	5.5	2587.6	
	STDER	23.5	0.0	801.4	0.3	286.8	
	1st	367.8	200.0	12918.6	6.6	1957.4	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	384.3	200.0	13480.8	5.7	2365.0	
	Mean	376.0	200.0	13199.7	6.2	2161.2	
	STDER	8.3	0.0	281.1	0.5	203.8	
	1st	405.8	200.0	14213.7	4.8	2961.2	

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	428.8	200.0	14998.4	4.4	3408.7	
	Mean	417.3	200.0	14606.0	4.6	3185.0	
	STDER	11.5	0.0	392.3	0.2	223.8	
	1st	431.3	200.0	15083.7	5.8	2600.6	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	400.3	200.0	14026.2	6.4	2191.6	
	Mean	415.8	200.0	14554.9	6.1	2396.1	
	STDER	15.5	0.0	528.8	0.3	204.5	
	1st	407.8	200.0	14281.9	7.1	2011.5	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	426.3	200.0	14913.1	5.8	2571.2	
	Mean	417.0	200.0	14597.5	6.5	2291.4	
	STDER	9.3	0.0	315.6	0.7	279.8	
	1st	371.3	200.0	13037.8	5.7	2287.3	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	359.8	200.0	12646.1	7.1	1781.1	
	3rd	335.3	200.0	11811.7	6.6	1789.6	
	Mean	355.4	200.0	12498.5	6.5	1952.7	
	STDER	10.6	0.0	361.6	0.4	167.3	

Bead name : IL-6						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	378.3	200.0	13276.3	6.4	2074.4
	2nd	385.8	200.0	13531.9	6.0	2255.3
	3rd	373.3	200.0	13106.0	6.1	2148.5
	Mean	379.1	200.0	13304.7	6.2	2159.4
	STDER	3.6	0.0	123.8	0.1	52.5
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	353.8	200.0	12441.7	6.2	2006.7
	2nd	374.8	200.0	13157.1	5.2	2530.2
	3rd	365.8	200.0	12850.5	6.2	2072.7
	Mean	364.8	200.0	12816.4	5.9	2203.2
	STDER	6.1	0.0	207.2	0.3	164.6
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	377.3	200.0	13242.2	6.3	2101.9
	2nd	366.3	200.0	12867.5	7.1	1812.3
	3rd	368.8	200.0	12952.6	6.2	2089.1
	Mean	370.8	200.0	13020.8	6.5	2001.1
	STDER	3.3	0.0	113.4	0.3	94.5
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	398.8	200.0	13975.0	6.0	2329.2

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	430.3	200.0	15049.6	6.4	2351.5	
	3rd	371.3	200.0	13037.8	7.6	1715.5	
	Mean	400.1	200.0	14020.8	6.7	2132.1	
	STDER	17.0	0.0	581.2	0.5	208.4	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	462.3	200.0	16142.7	6.3	2562.3	
	2nd	442.3	200.0	15459.3	6.2	2493.4	
	3rd	428.8	200.0	14998.4	5.0	2999.7	
	Mean	444.4	200.0	15533.5	5.8	2685.2	
	STDER	9.7	0.0	332.4	0.4	158.5	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	179.8	200.0	6493.4	4.5	1443.0	
	2nd	185.3	200.0	6683.4	5.8	1152.3	
	3rd	194.8	200.0	7011.0	5.8	1208.8	
	Mean	186.6	200.0	6729.3	5.4	1268.0	
	STDER	4.4	0.0	151.1	0.4	89.0	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	201.3	200.0	7234.7	6.3	1148.4	
	2nd	198.3	200.0	7131.5	6.2	1150.2	

Bead name : IL-6						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	3rd	192.3	200.0	6924.8	5.1	1357.8
	Mean	197.3	200.0	7097.0	5.9	1218.8
	STDER	2.6	0.0	91.1	0.4	69.5
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	178.8	200.0	6458.9	6.6	978.6
	2nd	191.8	200.0	6907.6	5.0	1381.5
	3rd	186.8	200.0	6735.2	5.7	1181.6
	Mean	185.8	200.0	6700.6	5.8	1180.6
	STDER	3.8	0.0	130.7	0.5	116.3
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	189.3	200.0	6821.4	5.5	1240.3
	2nd	200.8	200.0	7217.5	4.8	1503.6
	3rd	179.3	200.0	6476.2	4.8	1349.2
	Mean	189.8	200.0	6838.4	5.0	1364.4
	STDER	6.2	0.0	214.2	0.2	76.4
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	191.3	200.0	6890.4	5.4	1276.0
	2nd	185.8	200.0	6700.7	5.8	1155.3
	3rd	186.3	200.0	6717.9	4.7	1429.3

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	187.8	200.0	6769.7	5.3	1286.9	
	STDER	1.8	0.0	60.6	0.3	79.3	
	1st	217.8	200.0	7801.4	6.1	1278.9	
	2nd	215.3	200.0	7715.7	6.1	1264.9	
	3rd	200.3	200.0	7200.3	6.0	1200.1	
	Mean	211.1	200.0	7572.5	6.1	1247.9	
	STDER	5.5	0.0	187.7	0.0	24.3	
	1st	175.8	200.0	6355.1	4.4	1444.3	
	2nd	211.3	200.0	7578.4	6.0	1263.1	
	3rd	204.3	200.0	7337.9	4.6	1595.2	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	197.1	200.0	7090.4	5.0	1434.2	
	STDER	10.9	0.0	374.2	0.5	96.0	
	1st	196.3	200.0	7062.6	4.5	1569.5	
	2nd	194.8	200.0	7011.0	6.6	1062.3	
	3rd	187.3	200.0	6752.4	5.0	1350.5	
	Mean	192.8	200.0	6942.0	5.4	1327.4	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	192.8	200.0	6942.0	5.4	1327.4	
	STDER	10.9	0.0	374.2	0.5	96.0	
	1st	196.3	200.0	7062.6	4.5	1569.5	
	2nd	194.8	200.0	7011.0	6.6	1062.3	
	3rd	187.3	200.0	6752.4	5.0	1350.5	
	Mean	192.8	200.0	6942.0	5.4	1327.4	
	STDER	10.9	0.0	374.2	0.5	96.0	
	1st	196.3	200.0	7062.6	4.5	1569.5	
	2nd	194.8	200.0	7011.0	6.6	1062.3	
	3rd	187.3	200.0	6752.4	5.0	1350.5	

Bead name : IL-6							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	2.8	0.0	96.0	0.6	146.9	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	180.8	200.0	6528.0	5.0	1305.6	
	2nd	169.8	200.0	6147.3	5.6	1097.7	
	3rd	197.3	200.0	7097.1	5.6	1267.3	
	Mean	182.6	200.0	6590.8	5.4	1223.6	
	STDER	8.0	0.0	276.0	0.2	63.9	
	1st	198.3	200.0	7131.5	5.8	1229.6	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	170.3	200.0	6164.6	4.8	1284.3	
	3rd	214.3	200.0	7681.3	5.3	1449.3	
	Mean	194.3	200.0	6992.5	5.3	1321.1	
	STDER	12.9	0.0	443.3	0.3	66.0	
	1st	203.3	200.0	7303.5	5.2	1404.5	
	2nd	415.8	200.0	14554.8	5.4	2695.3	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	185.3	200.0	6683.4	5.6	1193.5	
	Mean	268.1	200.0	9513.9	5.4	1764.4	
	STDER	74.0	0.0	2526.8	0.1	469.4	

Bead name : IL-6						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	205.8	200.0	7389.4	6.2	1191.8
	2nd	199.8	200.0	7183.1	6.4	1122.4
	Mean	202.8	200.0	7286.3	6.3	1157.1
	STDER	3.0	0.0	103.2	0.1	34.7

Table 30

Bead name : TNF-alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.0	10.0	NaN		
	2nd	0.0	10.0	NaN		
	Mean	0.0	10.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	1.0	10.0	16.4	7.5	2.2
	2nd	2.0	10.0	19.0	7.4	2.6
	3rd	1.5	10.0	17.7	6.6	2.7

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	1.5	10.0	17.7	7.2	2.5	
	STDER	0.3	0.0	0.7	0.3	0.1	
	1st	1068.5	10.0	3196.1	6.1	524.0	
	2nd	986.0	10.0	2941.3	5.8	507.1	
	3rd	943.5	10.0	2810.4	5.5	511.0	
	Mean	999.3	10.0	2982.6	5.8	514.0	
	STDER	36.7	0.0	113.2	0.2	5.1	
	1st	5.0	10.0	26.8	5.2	5.1	
	2nd	6.0	10.0	29.4	4.8	6.1	
	Mean	5.5	10.0	28.1	5.0	5.6	
PBMC+YY101 0.01uM	STDER	0.5	0.0	1.3	0.2	0.5	
	1st	5.0	10.0	26.8	4.4	6.1	
	2nd	7.0	10.0	32.0	5.8	5.5	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
PBMC+YY101 0.1uM	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
PBMC+YY101 1uM	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	
	Mean	6.0	10.0	29.4	5.1	5.8	
	STDER	1.0	0.0	2.6	0.7	0.3	
	1st	7.0	10.0	32.0	5.5	5.8	

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	8.0	10.0	34.6	5.5	6.3	
	Mean	7.5	10.0	33.3	5.5	6.1	
	STDER	0.5	0.0	1.3	0.0	0.2	
PBMC+YY101 10uM	1st	29.0	10.0	90.9	6.4	14.2	
	2nd	7.0	10.0	32.0	6.1	5.2	
	Mean	18.0	10.0	61.4	6.3	9.7	
	STDER	11.0	0.0	29.4	0.2	4.5	
PBMC+YY101 100uM	1st	30.5	10.0	95.0	6.4	14.8	
	2nd	14.0	10.0	50.5	7.0	7.2	
	Mean	22.3	10.0	72.7	6.7	11.0	
	STDER	8.3	0.0	22.2	0.3	3.8	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	1st	861.0	10.0	2557.1	6.2	412.4	
	2nd	841.0	10.0	2495.8	7.6	328.4	
	Mean	851.0	10.0	2526.4	6.9	370.4	
	STDER	10.0	0.0	30.6	0.7	42.0	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	1st	1000.0	10.0	2984.4	5.2	573.9	

Bead name : TNF- α pha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10^5 /ml)	conc/live cell (pg/ 10^5)	
	2nd	837.0	10.0	2483.6	5.8	428.2	
	Mean	918.5	10.0	2734.0	5.5	501.1	
	STDER	81.5	0.0	250.4	0.3	72.9	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	1st	869.0	10.0	2581.6	6.6	391.1	
	2nd	751.0	10.0	2221.0	5.7	389.6	
	Mean	810.0	10.0	2401.3	6.2	390.4	
	STDER	59.0	0.0	180.3	0.5	0.8	
PBMC+LPS(5ug/ml)+Xiidra 1uM	1st	942.5	10.0	2807.3	4.8	584.9	
	2nd	670.0	10.0	1974.8	4.4	448.8	
	Mean	806.3	10.0	2391.0	4.6	516.8	
	STDER	136.3	0.0	416.3	0.2	68.0	
PBMC+LPS(5ug/ml)+Xiidra 10uM	1st	1003.5	10.0	2995.2	5.8	516.4	
	2nd	964.0	10.0	2873.5	6.4	449.0	
	Mean	983.8	10.0	2934.4	6.1	482.7	
	STDER	19.8	0.0	60.9	0.3	33.7	
PBMC+LPS(5ug/ml)+Xiidra 100uM	1st	802.0	10.0	2376.5	7.1	334.7	

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	778.0	10.0	2303.3	5.8	397.1	
	Mean	790.0	10.0	2339.9	6.5	365.9	
	STDER	12.0	0.0	36.6	0.7	31.2	
PBMC+LPS(5ug/ml)+YY101 0.001uM	1st	854.5	10.0	2537.1	5.7	445.1	
	2nd	878.0	10.0	2609.2	7.1	367.5	
	3rd	729.0	10.0	2154.0	6.6	326.4	
	Mean	820.5	10.0	2433.4	6.5	379.7	
	STDER	46.3	0.0	141.3	0.4	34.8	
	1st	946.5	10.0	2819.6	6.4	440.6	
PBMC+LPS(5ug/ml)+YY101 0.01uM	2nd	935.0	10.0	2784.2	6.0	464.0	
	3rd	887.0	10.0	2636.8	6.1	432.3	
	Mean	922.8	10.0	2746.9	6.2	445.6	
	STDER	18.2	0.0	56.0	0.1	9.5	
	1st	937.5	10.0	2791.9	6.2	450.3	
	2nd	963.0	10.0	2870.4	5.2	552.0	
PBMC+LPS(5ug/ml)+YY101 0.1uM	3rd	971.0	10.0	2895.0	6.2	466.9	

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	957.2	10.0	2852.4	5.9	489.7	
	STDER	10.1	0.0	31.1	0.3	31.5	
	1st	920.0	10.0	2738.1	6.3	434.6	
	2nd	844.5	10.0	2506.5	7.1	353.0	
	3rd	814.0	10.0	2413.2	6.2	389.2	
	Mean	859.5	10.0	2552.6	6.5	392.3	
	STDER	31.5	0.0	96.6	0.3	23.6	
	1st	921.0	10.0	2741.2	6.0	456.9	
	2nd	942.5	10.0	2807.3	6.4	438.6	
	3rd	905.0	10.0	2692.0	7.6	354.2	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	922.8	10.0	2746.8	6.7	416.6	
	STDER	10.9	0.0	33.4	0.5	31.6	
	1st	865.0	10.0	2569.3	6.3	407.8	
	2nd	783.0	10.0	2318.5	6.2	374.0	
	3rd	823.5	10.0	2442.3	5.0	488.5	
	Mean	823.8	10.0	2443.4	5.8	423.4	
PBMC+LPS(5ug/ml)+YY101 100uM							

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	23.7	0.0	72.4	0.4	34.0	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	427.5	10.0	1245.3	4.5	276.7	
	2nd	426.0	10.0	1240.9	5.8	213.9	
	3rd	441.0	10.0	1285.6	5.8	221.7	
	Mean	431.5	10.0	1257.3	5.4	237.4	
	STDER	4.8	0.0	14.2	0.4	19.8	
	1st	449.0	10.0	1309.5	6.3	207.9	
	2nd	441.0	10.0	1285.6	6.2	207.4	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	3rd	441.0	10.0	1285.6	5.1	252.1	
	Mean	443.7	10.0	1293.5	5.9	222.4	
	STDER	2.7	0.0	8.0	0.4	14.8	
	1st	437.0	10.0	1273.7	6.6	193.0	
	2nd	438.0	10.0	1276.6	5.0	255.3	
	3rd	432.0	10.0	1258.7	5.7	220.8	
	Mean	435.7	10.0	1269.7	5.8	223.0	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	STDER	1.9	0.0	5.5	0.5	18.0	

Bead name : TNF- α							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	440.0	10.0	1282.6	5.5	233.2	
	2nd	415.0	10.0	1208.1	4.8	251.7	
	3rd	439.0	10.0	1279.6	4.8	266.6	
	Mean	431.3	10.0	1256.8	5.0	250.5	
	STDER	8.2	0.0	24.4	0.2	9.7	
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	479.0	10.0	1399.2	5.4	259.1	
	2nd	431.0	10.0	1255.8	5.8	216.5	
	3rd	458.0	10.0	1336.4	4.7	284.3	
	Mean	456.0	10.0	1330.4	5.3	253.3	
	STDER	13.9	0.0	41.5	0.3	19.8	
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	340.0	10.0	985.6	6.1	161.6	
	2nd	331.5	10.0	960.5	6.1	157.5	
	3rd	331.0	10.0	959.0	6.0	159.8	
	Mean	334.2	10.0	968.4	6.1	159.6	
	STDER	2.9	0.0	8.6	0.0	1.2	
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	428.5	10.0	1248.3	4.4	283.7	

Bead name : TNF- α							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10^5 /ml)	conc/live cell (pg/ 10^5)	
	2nd	481.0	10.0	1405.1	6.0	234.2	
	3rd	453.0	10.0	1321.4	4.6	287.3	
	Mean	454.2	10.0	1325.0	5.0	268.4	
	STDER	15.2	0.0	45.3	0.5	17.1	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	440.0	10.0	1282.6	4.5	285.0	
	2nd	453.5	10.0	1322.9	6.6	200.4	
	3rd	471.5	10.0	1376.7	5.0	275.3	
	Mean	455.0	10.0	1327.4	5.4	253.6	
	STDER	9.1	0.0	27.3	0.6	26.7	
	1st	430.5	10.0	1254.3	5.0	250.9	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	457.0	10.0	1333.4	5.6	238.1	
	3rd	469.0	10.0	1369.2	5.6	244.5	
	Mean	452.2	10.0	1319.0	5.4	244.5	
	STDER	11.4	0.0	34.0	0.2	3.7	
	1st	456.0	10.0	1330.4	5.8	229.4	
	2nd	391.0	10.0	1136.7	4.8	236.8	

Bead name : TNF-alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	451.0	10.0	1315.4	5.3	248.2	
	Mean	432.7	10.0	1260.8	5.3	238.1	
	STDER	20.9	0.0	62.2	0.3	5.5	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	404.0	10.0	1175.4	5.2	226.0	
	2nd	429.0	10.0	1249.8	5.4	231.4	
	3rd	452.0	10.0	1318.4	5.6	235.4	
	Mean	428.3	10.0	1247.9	5.4	231.0	
	STDER	13.9	0.0	41.3	0.1	2.7	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	330.0	10.0	956.0	6.2	154.2	
	2nd	293.0	10.0	847.0	6.4	132.4	
	Mean	311.5	10.0	901.5	6.3	143.3	
	STDER	18.5	0.0	54.5	0.1	10.9	

Table 31

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.5	10.0	NaN			
	2nd	-0.5	10.0	NaN			
	Mean	0.0	10.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	-0.5	10.0		7.5	0.0	
	2nd	-0.5	10.0		7.4	0.0	
	3rd	-0.5	10.0		6.6	0.0	
	Mean	-0.5	10.0	#DIV/0!	7.2	0.0	
	STDER	0.0	0.0	#DIV/0!	0.3	0.0	
PBMC+LPS(5ug/ml)	1st	2832.5	10.0	33012.9	6.1	5411.9	
	2nd	2469.5	10.0	30553.0	5.8	5267.8	
	3rd	2329.0	10.0	29577.8	5.5	5377.8	
	Mean	2543.7	10.0	31047.9	5.8	5352.5	
	STDER	150.0	0.0	1022.0	0.2	43.5	
PBMC+YY101 0.01uM	1st	0.5	10.0		5.2	0.0	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	-1.0	10.0		4.8	0.0	
	Mean	-0.3	10.0	#DIV/0!	5.0	0.0	
	STDER	0.8	0.0	#DIV/0!	0.2	0.0	
	1st	-0.5	10.0		4.4	0.0	
PBMCMC+YY101 0.1uM	2nd	-0.5	10.0		5.8	0.0	
	Mean	-0.5	10.0	#DIV/0!	5.1	0.0	
	STDER	0.0	0.0	#DIV/0!	0.7	0.0	
	1st	1.5	10.0	588.0	5.5	106.9	
PBMCMC+YY101 1uM	2nd	0.5	10.0		5.5	0.0	
	Mean	1.0	10.0	588.0	5.5	53.5	
	STDER	0.5	0.0	#DIV/0!	0.0	53.5	
	1st	7.5	10.0	1997.0	6.4	312.0	
PBMCMC+YY101 10uM	2nd	-0.5	10.0		6.1	0.0	
	Mean	3.5	10.0	1997.0	6.3	156.0	
	STDER	4.0	0.0	#DIV/0!	0.2	156.0	
	1st	2.5	10.0	1030.2	6.4	161.0	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	-0.5	10.0		7.0	0.0	
	Mean	1.0	10.0	1030.2	6.7	80.5	
	STDER	1.5	0.0	#DIV/0!	0.3	80.5	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	1st	2391.5	10.0	30013.4	6.2	4840.9	
	2nd	2296.5	10.0	29350.1	7.6	3861.9	
	Mean	2344.0	10.0	29681.8	6.9	4351.4	
	STDER	47.5	0.0	331.7	0.7	489.5	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	1st	2786.0	10.0	32701.9	5.2	6288.8	
	2nd	2444.5	10.0	30380.5	5.8	5238.0	
	Mean	2615.3	10.0	31541.2	5.5	5763.4	
	STDER	170.8	0.0	1160.7	0.3	525.4	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	1st	2010.0	10.0	27301.7	6.6	4136.6	
	2nd	1672.5	10.0	24770.7	5.7	4345.7	
	Mean	1841.3	10.0	26036.2	6.2	4241.2	
	STDER	168.8	0.0	1265.5	0.5	104.6	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	1st	1962.5	10.0	26954.1	4.8	5615.4	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1468.5	10.0	23157.9	4.4	5263.2	
	Mean	1715.5	10.0	25056.0	4.6	5439.3	
	STDER	247.0	0.0	1898.1	0.2	176.1	
	1st	1875.5	10.0	26310.6	5.8	4536.3	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	1893.5	10.0	26444.5	6.4	4131.9	
	Mean	1884.5	10.0	26377.5	6.1	4334.1	
	STDER	9.0	0.0	66.9	0.3	202.2	
	1st	1943.0	10.0	26810.6	7.1	3776.1	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	1557.5	10.0	23870.5	5.8	4115.6	
	Mean	1750.3	10.0	25340.6	6.5	3945.9	
	STDER	192.8	0.0	1470.0	0.7	169.7	
	1st	2104.5	10.0	27986.1	5.7	4909.8	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	1995.5	10.0	27195.8	7.1	3830.4	
	3rd	1764.5	10.0	25475.7	6.6	3860.0	
	Mean	1954.8	10.0	26885.9	6.5	4200.1	
	STDER	100.2	0.0	741.1	0.4	355.0	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	2293.5	10.0	29329.0	6.4	4582.7	
	2nd	2303.0	10.0	29395.7	6.0	4899.3	
	3rd	2116.5	10.0	28072.3	6.1	4602.0	
	Mean	2237.7	10.0	28932.4	6.2	4694.7	
	STDER	60.6	0.0	430.4	0.1	102.5	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	2157.0	10.0	28362.4	6.2	4574.6	
	2nd	2199.5	10.0	28665.1	5.2	5512.5	
	3rd	2154.5	10.0	28344.5	6.2	4571.7	
	Mean	2170.3	10.0	28457.4	5.9	4886.3	
	STDER	14.6	0.0	104.0	0.3	313.1	
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	2206.5	10.0	28714.8	6.3	4557.9	
	2nd	2029.0	10.0	27440.0	7.1	3864.8	
	3rd	2109.5	10.0	28022.0	6.2	4519.7	
	Mean	2115.0	10.0	28059.0	6.5	4314.1	
	STDER	51.3	0.0	368.5	0.3	224.9	
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	2406.5	10.0	30117.5	6.0	5019.6	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	2501.0	10.0	30769.7	6.4	4807.8	
	3rd	2251.0	10.0	29029.8	7.6	3819.7	
	Mean	2386.2	10.0	29972.3	6.7	4549.0	
	STDER	72.9	0.0	507.5	0.5	369.7	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	3190.5	10.0	35374.6	6.3	5615.0	
	2nd	2648.5	10.0	31775.7	6.2	5125.1	
	3rd	2798.0	10.0	32782.2	5.0	6556.4	
	Mean	2879.0	10.0	33310.8	5.8	5765.5	
	STDER	161.6	0.0	1072.0	0.4	420.0	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	134.5	10.0	7525.9	4.5	1672.4	
	2nd	126.5	10.0	7321.9	5.8	1262.4	
	3rd	137.0	10.0	7588.4	5.8	1308.3	
	Mean	132.7	10.0	7478.7	5.4	1414.4	
	STDER	3.2	0.0	80.5	0.4	129.7	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	138.5	10.0	7625.5	6.3	1210.4	
	2nd	137.5	10.0	7600.8	6.2	1225.9	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	134.5	10.0	7525.9	5.1	1475.7	
	Mean	136.8	10.0	7584.1	5.9	1304.0	
	STDER	1.2	0.0	29.9	0.4	86.0	
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	113.5	10.0	6974.8	6.6	1056.8	
	2nd	127.0	10.0	7334.8	5.0	1467.0	
	3rd	114.5	10.0	7002.2	5.7	1228.5	
	Mean	118.3	10.0	7103.9	5.8	1250.7	
	STDER	4.3	0.0	115.7	0.5	118.9	
	1st	129.5	10.0	7399.2	5.5	1345.3	
PBMIC+LPS(5ug/ml)+YDE011 1uM	2nd	138.0	10.0	7613.2	4.8	1586.1	
	3rd	137.5	10.0	7600.8	4.8	1583.5	
	Mean	135.0	10.0	7537.7	5.0	1505.0	
	STDER	2.8	0.0	69.4	0.2	79.8	
	1st	152.5	10.0	7962.5	5.4	1474.5	
	2nd	128.5	10.0	7373.5	5.8	1271.3	
PBMIC+LPS(5ug/ml)+YDE011 10uM	3rd	148.5	10.0	7868.0	4.7	1674.0	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	143.2	10.0	7734.7	5.3	1473.3	
	STDER	7.4	0.0	182.6	0.3	116.3	
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	164.5	10.0	8238.4	6.1	1350.6	
	2nd	157.0	10.0	8067.3	6.1	1322.5	
	3rd	137.5	10.0	7600.8	6.0	1266.8	
	Mean	153.0	10.0	7968.8	6.1	1313.3	
	STDER	8.0	0.0	190.5	0.0	24.6	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	139.0	10.0	7637.9	4.4	1735.9	
	2nd	163.0	10.0	8204.6	6.0	1367.4	
	3rd	152.5	10.0	7962.5	4.6	1731.0	
	Mean	151.5	10.0	7935.0	5.0	1611.4	
	STDER	6.9	0.0	164.2	0.5	122.0	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	145.5	10.0	7796.2	4.5	1732.5	
	2nd	153.5	10.0	7985.9	6.6	1210.0	
	3rd	148.5	10.0	7868.0	5.0	1573.6	
	Mean	149.2	10.0	7883.4	5.4	1505.4	

Bead name : CCL3/MIP-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	2.3	0.0	55.3	0.6	154.6	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	134.0	10.0	7513.4	5.0	1502.7	
	2nd	138.5	10.0	7625.5	5.6	1361.7	
	3rd	145.5	10.0	7796.2	5.6	1392.2	
	Mean	139.3	10.0	7645.0	5.4	1418.9	
	STDER	3.3	0.0	82.2	0.2	42.8	
	1st	152.5	10.0	7962.5	5.8	1372.8	
	2nd	110.5	10.0	6891.7	4.8	1435.8	
PBMC+LPS(5ug/ml)+YDE043 1uM	3rd	156.5	10.0	8055.7	5.3	1520.0	
	Mean	139.8	10.0	7636.6	5.3	1442.9	
	STDER	14.7	0.0	373.5	0.3	42.6	
	1st	133.5	10.0	7500.8	5.2	1442.5	
	2nd	131.5	10.0	7450.2	5.4	1379.7	
	3rd	148.5	10.0	7868.0	5.6	1405.0	
	Mean	137.8	10.0	7606.3	5.4	1409.0	
PBMC+LPS(5ug/ml)+YDE043 10uM	STDER	5.4	0.0	131.6	0.1	18.2	

Bead name : CCL3/MIP-1 alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	152.5	10.0	7962.5	6.2	1284.3
	2nd	136.5	10.0	7575.9	6.4	1183.7
	Mean	144.5	10.0	7769.2	6.3	1234.0
	STDER	8.0	0.0	193.3	0.1	50.3

Table 32

Bead name : CCL4/MIP-1 beta						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.0	10.0	NaN		
	2nd	0.0	10.0	NaN		
	Mean	0.0	10.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	0.0	10.0		7.5	0.0
	2nd	0.0	10.0		7.4	0.0
	3rd	0.0	10.0		6.6	0.0

	Mean	0.0	10.0	#DIV/0!	7.2	0.0
	STDER	0.0	0.0	#DIV/0!	0.3	0.0
PBM C+LPS(5ug/ml)	1st	794.0	10.0	18382.1	6.1	3013.5
	2nd	724.0	10.0	17299.3	5.8	2982.6
	3rd	697.5	10.0	16886.0	5.5	3070.2
	Mean	738.5	10.0	17522.4	5.8	3022.1
	STDER	28.8	0.0	446.1	0.2	25.6
PBM C+YY101 0.01uM	1st	0.0	10.0		5.2	0.0
	2nd	0.0	10.0		4.8	0.0
	Mean	0.0	10.0	#DIV/0!	5.0	0.0
	STDER	0.0	0.0	#DIV/0!	0.2	0.0
	1st	0.0	10.0		4.4	0.0
PBM C+YY101 0.1uM	2nd	0.0	10.0		5.8	0.0
	Mean	0.0	10.0	#DIV/0!	5.1	0.0
	STDER	0.0	0.0	#DIV/0!	0.7	0.0
	1st	-1.0	10.0		5.5	0.0
	2nd	-0.5	10.0		5.5	0.0
PBM C+YY101 1uM	Mean	-0.8	10.0	#DIV/0!	5.5	0.0
	STDER	0.3	0.0	#DIV/0!	0.0	0.0

PBMC+YY101 10uM	1st	10.0	10.0	10.0	1948.5	6.4	304.4
	2nd	1.0	10.0			6.1	0.0
	Mean	5.5	10.0		1948.5	6.3	152.2
	STDER	4.5	0.0		#DIV/0!	0.2	152.2
PBMC+YY101 100uM	1st	10.0	10.0	10.0	1948.5	6.4	304.4
	2nd	3.0	10.0		772.9	7.0	110.4
	Mean	6.5	10.0		1360.7	6.7	207.4
	STDER	3.5	0.0		587.8	0.3	97.0
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	1st	615.0	10.0		15584.4	6.2	2513.6
	2nd	573.0	10.0		14911.0	7.6	1962.0
	Mean	594.0	10.0		15247.7	6.9	2237.8
	STDER	21.0	0.0		336.7	0.7	275.8
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	1st	700.0	10.0		16925.1	5.2	3254.8
	2nd	628.0	10.0		15791.2	5.8	2722.6
	Mean	664.0	10.0		16358.1	5.5	2988.7
	STDER	36.0	0.0		566.9	0.3	266.1
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	1st	524.0	10.0		14113.8	6.6	2138.5
	2nd	442.0	10.0		12744.4	5.7	2235.9
	Mean	483.0	10.0		13429.1	6.2	2187.2

	STDER	41.0	0.0	684.7	0.5	48.7
PBMC+LPS(5ug/ml)+Xiidra 1uM	1st	599.0	10.0	15328.8	4.8	3193.5
	2nd	397.0	10.0	11968.5	4.4	2720.1
	Mean	498.0	10.0	13648.6	4.6	2956.8
	STDER	101.0	0.0	1680.2	0.2	236.7
PBMC+LPS(5ug/ml)+Xiidra 10uM	1st	630.0	10.0	15822.9	5.8	2728.1
	2nd	629.0	10.0	15807.1	6.4	2469.9
	Mean	629.5	10.0	15815.0	6.1	2599.0
	STDER	0.5	0.0	7.9	0.3	129.1
PBMC+LPS(5ug/ml)+Xiidra 100uM	1st	631.5	10.0	15846.7	7.1	2231.9
	2nd	565.5	10.0	14789.8	5.8	2550.0
	Mean	598.5	10.0	15318.3	6.5	2391.0
	STDER	33.0	0.0	528.5	0.7	159.0
PBMC+LPS(5ug/ml)+YY101 0.001uM	1st	551.5	10.0	14562.9	5.7	2554.9
	2nd	527.0	10.0	14163.0	7.1	1994.8
	3rd	469.0	10.0	13200.9	6.6	2000.1
	Mean	515.8	10.0	13975.6	6.5	2183.3
PBMC+LPS(5ug/ml)+YY101 0.01uM	STDER	24.5	0.0	404.2	0.4	185.8
	1st	611.0	10.0	15520.6	6.4	2425.1

	2nd	596.5	10.0	15288.8	6.0	2548.1
	3rd	560.0	10.0	14700.8	6.1	2410.0
	Mean	589.2	10.0	15170.0	6.2	2461.1
	STDER	15.2	0.0	244.0	0.1	43.8
PBMC+LPS(5ug/ml)+YY101 0.1uM	1st	576.0	10.0	14959.4	6.2	2412.8
	2nd	592.0	10.0	15216.6	5.2	2926.3
	3rd	584.0	10.0	15088.1	6.2	2433.6
	Mean	584.0	10.0	15088.0	5.9	2590.9
	STDER	4.6	0.0	74.3	0.3	167.8
	1st	594.0	10.0	15248.7	6.3	2420.4
	2nd	556.5	10.0	14644.0	7.1	2062.5
	3rd	547.0	10.0	14489.7	6.2	2337.0
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	565.8	10.0	14794.1	6.5	2273.3
	STDER	14.3	0.0	231.6	0.3	108.1
	1st	614.0	10.0	15568.4	6.0	2594.7
	2nd	651.0	10.0	16155.4	6.4	2524.3
PBMC+LPS(5ug/ml)+YY101 10uM	3rd	560.0	10.0	14700.8	7.6	1934.3
	Mean	608.3	10.0	15474.9	6.7	2351.1
	STDER	26.4	0.0	422.5	0.5	209.4

PBMC+LPS(5ug/ml)+YY101 100uM	1st	537.0	10.0	14326.7	6.3	2274.1
	2nd	474.5	10.0	13293.2	6.2	2144.1
	3rd	488.0	10.0	13518.7	5.0	2703.7
	Mean	499.8	10.0	13712.9	5.8	2374.0
	STDER	19.0	0.0	313.7	0.4	169.1
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	158.0	10.0	7267.3	4.5	1615.0
	2nd	156.0	10.0	7220.3	5.8	1244.9
	3rd	158.0	10.0	7267.3	5.8	1253.0
	Mean	157.3	10.0	7251.7	5.4	1370.9
	STDER	0.7	0.0	15.7	0.4	122.0
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	167.5	10.0	7487.6	6.3	1188.5
	2nd	164.0	10.0	7407.0	6.2	1194.7
	3rd	159.0	10.0	7290.8	5.1	1429.6
	Mean	163.5	10.0	7395.1	5.9	1270.9
	STDER	2.5	0.0	57.1	0.4	79.3
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	152.0	10.0	7125.7	6.6	1079.6
	2nd	151.0	10.0	7101.9	5.0	1420.4
	3rd	141.0	10.0	6860.2	5.7	1203.6
	Mean	148.0	10.0	7029.3	5.8	1234.5

	STDER	3.5	0.0	84.8	0.5	99.6
PBMC+LPS(5ug/ml)+YDE011 1uM	1st	151.0	10.0	7101.9	5.5	1291.2
	2nd	152.0	10.0	7125.7	4.8	1484.5
	3rd	158.0	10.0	7267.3	4.8	1514.0
	Mean	153.7	10.0	7165.0	5.0	1429.9
	STDER	2.2	0.0	51.7	0.2	69.9
PBMC+LPS(5ug/ml)+YDE011 10uM	1st	166.0	10.0	7453.1	5.4	1380.2
	2nd	153.5	10.0	7161.3	5.8	1234.7
	3rd	161.5	10.0	7349.0	4.7	1563.6
	Mean	160.3	10.0	7321.1	5.3	1392.8
	STDER	3.7	0.0	85.4	0.3	95.2
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	119.0	10.0	6303.5	6.1	1033.4
	2nd	121.5	10.0	6368.7	6.1	1044.1
	3rd	115.0	10.0	6197.9	6.0	1033.0
	Mean	118.5	10.0	6290.1	6.1	1036.8
	STDER	1.9	0.0	49.8	0.0	3.6
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	165.5	10.0	7441.6	4.4	1691.3
	2nd	185.0	10.0	7881.5	6.0	1313.6
	3rd	182.5	10.0	7826.1	4.6	1701.3

	Mean	177.7	10.0	7716.4	5.0	1568.7
	STDER	6.1	0.0	138.3	0.5	127.6
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	178.0	10.0	7725.6	4.5	1716.8
	2nd	177.0	10.0	7703.2	6.6	1167.1
	3rd	183.0	10.0	7837.2	5.0	1567.4
	Mean	179.3	10.0	7755.3	5.4	1483.8
	STDER	1.9	0.0	41.4	0.6	164.1
	1st	153.5	10.0	7161.3	5.0	1432.3
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	159.5	10.0	7302.4	5.6	1304.0
	3rd	173.0	10.0	7612.9	5.6	1359.5
	Mean	162.0	10.0	7358.9	5.4	1365.2
	STDER	5.8	0.0	133.4	0.2	37.1
	1st	175.0	10.0	7658.2	5.8	1320.4
	2nd	137.0	10.0	6761.7	4.8	1408.7
PBMC+LPS(5ug/ml)+YDE043 1uM	3rd	175.0	10.0	7658.2	5.3	1444.9
	Mean	162.3	10.0	7359.3	5.3	1391.3
	STDER	12.7	0.0	298.8	0.3	37.0
	1st	159.0	10.0	7290.8	5.2	1402.1
	2nd	158.0	10.0	7267.3	5.4	1345.8

PBMC+LPS(5ug/ml)+YDE043 100uM	3rd	161.0	10.0	7337.4	5.6	1310.3
	Mean	159.3	10.0	7298.5	5.4	1352.7
	STDER	0.9	0.0	20.6	0.1	26.7
	1st	118.5	10.0	6290.4	6.2	1014.6
	2nd	104.0	10.0	5899.5	6.4	921.8
	Mean	111.3	10.0	6094.9	6.3	968.2
	STDER	7.3	0.0	195.4	0.1	46.4

Table 33

Bead name : CCL5/RANTES						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.5	2.0	NaN		
	2nd	-0.5	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMC + 0.5% DMSO	1st	49.5	2.0	35.7	7.5	4.8
	2nd	42.5	2.0	31.0	7.4	4.2
	3rd	31.0	2.0	22.5	6.6	3.4

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	41.0	2.0	29.7	7.2	4.1	
	STDER	5.4	0.0	3.9	0.3	0.4	
	1st	1262.5	2.0	448.6	6.1	73.5	
	2nd	1084.5	2.0	396.8	5.8	68.4	
	3rd	1296.0	2.0	458.2	5.5	83.3	
	Mean	1214.3	2.0	434.5	5.8	75.1	
	STDER	65.6	0.0	19.1	0.2	4.4	
	1st	37.5	2.0	27.5	5.2	5.3	
	2nd	66.5	2.0	46.1	4.8	9.6	
	Mean	52.0	2.0	36.8	5.0	7.4	
PBMC+YY101 0.01uM	STDER	14.5	0.0	9.3	0.2	2.2	
	1st	43.5	2.0	31.7	4.4	7.2	
	2nd	57.5	2.0	40.7	5.8	7.0	
	Mean	50.5	2.0	36.2	5.1	7.1	
	STDER	7.0	0.0	4.5	0.7	0.1	
	1st	45.5	2.0	33.0	5.5	6.0	
PBMC+YY101 0.1uM							
PBMC+YY101 1uM							

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	52.5	2.0	37.6	5.5	6.8	
	Mean	49.0	2.0	35.3	5.5	6.4	
	STDER	3.5	0.0	2.3	0.0	0.4	
	1st	201.5	2.0	109.6	6.4	17.1	
PBMCMC+YY101 10uM	2nd	70.5	2.0	48.3	6.1	7.9	
	Mean	136.0	2.0	79.0	6.3	12.5	
	STDER	65.5	0.0	30.6	0.2	4.6	
	1st	131.5	2.0	79.2	6.4	12.4	
PBMCMC+YY101 100uM	2nd	82.5	2.0	55.0	7.0	7.9	
	Mean	107.0	2.0	67.1	6.7	10.1	
	STDER	24.5	0.0	12.1	0.3	2.3	
	1st	1222.5	2.0	437.0	6.2	70.5	
PBMCMC+LPS(5ug/ml)+Xiindra 0.001uM	2nd	1145.5	2.0	414.6	7.6	54.6	
	Mean	1184.0	2.0	425.8	6.9	62.5	
	STDER	38.5	0.0	11.2	0.7	8.0	
	1st	1212.5	2.0	434.1	5.2	83.5	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1054.0	2.0	387.9	5.8	66.9	
	Mean	1133.3	2.0	411.0	5.5	75.2	
	STDER	79.3	0.0	23.1	0.3	8.3	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	1st	904.5	2.0	343.6	6.6	52.1	
	2nd	898.0	2.0	341.6	5.7	59.9	
	Mean	901.3	2.0	342.6	6.2	56.0	
	STDER	3.3	0.0	1.0	0.5	3.9	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	1st	1248.5	2.0	444.5	4.8	92.6	
	2nd	763.5	2.0	300.9	4.4	68.4	
	Mean	1006.0	2.0	372.7	4.6	80.5	
	STDER	242.5	0.0	71.8	0.2	12.1	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	1st	959.5	2.0	360.0	5.8	62.1	
	2nd	1078.5	2.0	395.1	6.4	61.7	
	Mean	1019.0	2.0	377.5	6.1	61.9	
	STDER	59.5	0.0	17.5	0.3	0.2	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	1st	903.5	2.0	343.3	7.1	48.4	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	947.5	2.0	356.4	5.8	61.5	
	Mean	925.5	2.0	349.9	6.5	54.9	
	STDER	22.0	0.0	6.6	0.7	6.6	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	1120.5	2.0	407.4	5.7	71.5	
	2nd	1139.5	2.0	412.9	7.1	58.2	
	3rd	1049.5	2.0	386.6	6.6	58.6	
	Mean	1103.2	2.0	402.3	6.5	62.7	
	STDER	27.4	0.0	8.0	0.4	4.4	
	1st	1358.5	2.0	476.2	6.4	74.4	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	2nd	1246.5	2.0	443.9	6.0	74.0	
	3rd	1240.5	2.0	442.2	6.1	72.5	
	Mean	1281.8	2.0	454.1	6.2	73.6	
	STDER	38.4	0.0	11.0	0.1	0.6	
	1st	1206.5	2.0	432.4	6.2	69.7	
	2nd	1188.5	2.0	427.1	5.2	82.1	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	3rd	1179.5	2.0	424.5	6.2	68.5	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	1191.5	2.0	428.0	5.9	73.5	
	STDER	7.9	0.0	2.3	0.3	4.4	
	1st	1289.0	2.0	456.2	6.3	72.4	
	2nd	1161.5	2.0	419.3	7.1	59.1	
	3rd	1151.5	2.0	416.4	6.2	67.2	
	Mean	1200.7	2.0	430.6	6.5	66.2	
	STDER	44.3	0.0	12.8	0.3	3.9	
	1st	1173.5	2.0	422.8	6.0	70.5	
	2nd	1264.5	2.0	449.1	6.4	70.2	
	3rd	1158.5	2.0	418.4	7.6	55.1	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	1198.8	2.0	430.1	6.7	65.2	
	STDER	33.1	0.0	9.6	0.5	5.1	
	1st	875.0	2.0	334.7	6.3	53.1	
	2nd	860.5	2.0	330.4	6.2	53.3	
	3rd	909.5	2.0	345.1	5.0	69.0	
	Mean	881.7	2.0	336.7	5.8	58.5	
PBMC+LPS(5ug/ml)+YY101 100uM							

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	14.5	0.0	4.4	0.4	5.3	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	455.5	2.0	202.5	4.5	45.0	
	2nd	455.5	2.0	202.5	5.8	34.9	
	3rd	520.5	2.0	224.1	5.8	38.6	
	Mean	477.2	2.0	209.7	5.4	39.5	
	STDER	21.7	0.0	7.2	0.4	2.9	
	1st	476.0	2.0	209.4	6.3	33.2	
	2nd	497.5	2.0	216.5	6.2	34.9	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	3rd	508.5	2.0	220.2	5.1	43.2	
	Mean	494.0	2.0	215.3	5.9	37.1	
	STDER	9.5	0.0	3.2	0.4	3.1	
	1st	468.0	2.0	206.7	6.6	31.3	
	2nd	463.5	2.0	205.2	5.0	41.0	
	3rd	475.0	2.0	209.0	5.7	36.7	
	Mean	468.8	2.0	207.0	5.8	36.3	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	STDER	3.3	0.0	1.1	0.5	2.8	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 1uM	1st	464.5	2.0	205.5	5.5	37.4	
	2nd	446.5	2.0	199.5	4.8	41.6	
	3rd	431.5	2.0	194.4	4.8	40.5	
	Mean	447.5	2.0	199.8	5.0	39.8	
	STDER	9.5	0.0	3.2	0.2	1.3	
PBMC+LPS(5ug/ml)+YDE011 10uM	1st	492.0	2.0	214.7	5.4	39.8	
	2nd	453.5	2.0	201.8	5.8	34.8	
	3rd	442.5	2.0	198.1	4.7	42.1	
	Mean	462.7	2.0	204.9	5.3	38.9	
	STDER	15.0	0.0	5.0	0.3	2.2	
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	362.5	2.0	170.4	6.1	27.9	
	2nd	315.5	2.0	153.5	6.1	25.2	
	3rd	337.5	2.0	161.5	6.0	26.9	
	Mean	338.5	2.0	161.8	6.1	26.7	
	STDER	13.6	0.0	4.9	0.0	0.8	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	445.5	2.0	199.1	4.4	45.3	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	497.5	2.0	216.5	6.0	36.1	
	3rd	465.0	2.0	205.7	4.6	44.7	
	Mean	469.3	2.0	207.1	5.0	42.0	
	STDER	15.2	0.0	5.1	0.5	3.0	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	506.0	2.0	219.3	4.5	48.7	
	2nd	486.5	2.0	212.9	6.6	32.3	
	3rd	483.0	2.0	211.7	5.0	42.3	
	Mean	491.8	2.0	214.6	5.4	41.1	
	STDER	7.2	0.0	2.4	0.6	4.8	
	1st	508.5	2.0	220.2	5.0	44.0	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	448.5	2.0	200.1	5.6	35.7	
	3rd	530.5	2.0	227.4	5.6	40.6	
	Mean	495.8	2.0	215.9	5.4	40.1	
	STDER	24.5	0.0	8.1	0.2	2.4	
	1st	502.5	2.0	218.2	5.8	37.6	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	486.5	2.0	212.9	4.8	44.3	

Bead name : CCL5/RANTES							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	484.5	2.0	212.2	5.3	40.0	
	Mean	491.2	2.0	214.4	5.3	40.7	
	STDER	5.7	0.0	1.9	0.3	2.0	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	486.5	2.0	212.9	5.2	40.9	
	2nd	429.5	2.0	193.7	5.4	35.9	
	3rd	453.5	2.0	201.8	5.6	36.0	
	Mean	456.5	2.0	202.8	5.4	37.6	
	STDER	16.5	0.0	5.6	0.1	1.7	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	353.0	2.0	167.0	6.2	26.9	
	2nd	330.5	2.0	159.0	6.4	24.8	
	Mean	341.8	2.0	163.0	6.3	25.9	
	STDER	11.3	0.0	4.0	0.1	1.1	

Table 34

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.0	2.0	NaN			
	2nd	0.0	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	1.0	2.0		7.5	0.0	
	2nd	1.0	2.0		7.4	0.0	
	3rd	0.0	2.0		6.6	0.0	
	Mean	0.7	2.0	#DIV/0!	7.2	0.0	
	STDER	0.3	0.0	#DIV/0!	0.3	0.0	
PBMC+LPS(5ug/ml)	1st	473.0	2.0	1833.4	6.1	300.6	
	2nd	476.0	2.0	1844.0	5.8	317.9	
	3rd	552.5	2.0	2113.7	5.5	384.3	
	Mean	500.5	2.0	1930.4	5.8	334.3	
	STDER	26.0	0.0	91.7	0.2	25.5	
PBMC+YY101 0.01uM	1st	5.0	2.0	12.5	5.2	2.4	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	8.0	2.0	29.1	4.8	6.1	
	Mean	6.5	2.0	20.8	5.0	4.2	
	STDER	1.5	0.0	8.3	0.2	1.8	
PBMCMC+YY101 0.1uM	1st	5.0	2.0	12.5	4.4	2.8	
	2nd	8.0	2.0	29.1	5.8	5.0	
	Mean	6.5	2.0	20.8	5.1	3.9	
	STDER	1.5	0.0	8.3	0.7	1.1	
PBMCMC+YY101 1uM	1st	5.0	2.0	12.5	5.5	2.3	
	2nd	7.0	2.0	23.7	5.5	4.3	
	Mean	6.0	2.0	18.1	5.5	3.3	
	STDER	1.0	0.0	5.6	0.0	1.0	
PBMCMC+YY101 10uM	1st	15.5	2.0	67.3	6.4	10.5	
	2nd	9.0	2.0	34.4	6.1	5.6	
	Mean	12.3	2.0	50.9	6.3	8.1	
	STDER	3.3	0.0	16.5	0.2	2.4	
PBMCMC+YY101 100uM	1st	12.0	2.0	49.9	6.4	7.8	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	7.0	2.0	23.7	7.0	3.4	
	Mean	9.5	2.0	36.8	6.7	5.6	
	STDER	2.5	0.0	13.1	0.3	2.2	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	1st	635.0	2.0	2400.7	6.2	387.2	
	2nd	634.5	2.0	2399.0	7.6	315.7	
	Mean	634.8	2.0	2399.8	6.9	351.4	
	STDER	0.3	0.0	0.9	0.7	35.8	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	1st	690.0	2.0	2590.1	5.2	498.1	
	2nd	498.5	2.0	1923.7	5.8	331.7	
	Mean	594.3	2.0	2256.9	5.5	414.9	
	STDER	95.8	0.0	333.2	0.3	83.2	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	1st	360.0	2.0	1427.4	6.6	216.3	
	2nd	428.0	2.0	1672.9	5.7	293.5	
	Mean	394.0	2.0	1550.1	6.2	254.9	
	STDER	34.0	0.0	122.8	0.5	38.6	
PBMC+LPS(5ug/ml)+Xiidra 1uM	1st	344.0	2.0	1369.0	4.8	285.2	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	285.0	2.0	1151.6	4.4	261.7	
	Mean	314.5	2.0	1260.3	4.6	273.5	
	STDER	29.5	0.0	108.7	0.2	11.7	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	1st	208.0	2.0	861.4	5.8	148.5	
	2nd	269.0	2.0	1092.0	6.4	170.6	
	Mean	238.5	2.0	976.7	6.1	159.6	
	STDER	30.5	0.0	115.3	0.3	11.0	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	1st	123.0	2.0	529.0	7.1	74.5	
	2nd	146.0	2.0	620.6	5.8	107.0	
	Mean	134.5	2.0	574.8	6.5	90.8	
	STDER	11.5	0.0	45.8	0.7	16.2	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	619.0	2.0	2345.3	5.7	411.5	
	2nd	724.0	2.0	2706.6	7.1	381.2	
	3rd	596.0	2.0	2265.5	6.6	343.3	
	Mean	646.3	2.0	2439.1	6.5	378.6	
	STDER	39.4	0.0	135.7	0.4	19.7	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 0.01uM	1st	940.0	2.0	3435.7	6.4	536.8	
	2nd	906.0	2.0	3322.0	6.0	553.7	
	3rd	705.0	2.0	2641.6	6.1	433.0	
	Mean	850.3	2.0	3133.1	6.2	507.8	
	STDER	73.3	0.0	247.9	0.1	37.7	
PBMC+LPS(5ug/ml)+YY101 0.1uM	1st	527.0	2.0	2024.2	6.2	326.5	
	2nd	408.0	2.0	1601.1	5.2	307.9	
	3rd	491.5	2.0	1899.0	6.2	306.3	
	Mean	475.5	2.0	1841.4	5.9	313.6	
	STDER	35.3	0.0	125.5	0.3	6.5	
PBMC+LPS(5ug/ml)+YY101 1uM	1st	658.0	2.0	2480.1	6.3	393.7	
	2nd	645.5	2.0	2437.0	7.1	343.2	
	3rd	531.0	2.0	2038.3	6.2	328.8	
	Mean	611.5	2.0	2318.4	6.5	355.2	
	STDER	40.4	0.0	140.6	0.3	19.7	
PBMC+LPS(5ug/ml)+YY101 10uM	1st	827.5	2.0	3058.1	6.0	509.7	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	691.0	2.0	2593.6	6.4	405.2	
	3rd	609.5	2.0	2312.4	7.6	304.3	
	Mean	709.3	2.0	2654.7	6.7	406.4	
	STDER	63.6	0.0	217.4	0.5	59.3	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	504.0	2.0	1943.2	6.3	308.4	
	2nd	555.0	2.0	2122.4	6.2	342.3	
	3rd	450.0	2.0	1751.5	5.0	350.3	
	Mean	503.0	2.0	1939.0	5.8	333.7	
	STDER	30.3	0.0	107.1	0.4	12.8	
	1st	147.0	2.0	624.6	4.5	138.8	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	2nd	174.0	2.0	730.3	5.8	125.9	
	3rd	235.0	2.0	964.1	5.8	166.2	
	Mean	185.3	2.0	773.0	5.4	143.6	
	STDER	26.0	0.0	100.3	0.4	11.9	
	1st	205.0	2.0	849.9	6.3	134.9	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	185.0	2.0	773.0	6.2	124.7	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	180.0	2.0	753.6	5.1	147.8	
	Mean	190.0	2.0	792.2	5.9	135.8	
	STDER	7.6	0.0	29.4	0.4	6.7	
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	216.0	2.0	892.0	6.6	135.1	
	2nd	180.0	2.0	753.6	5.0	150.7	
	3rd	190.0	2.0	792.3	5.7	139.0	
	Mean	195.3	2.0	812.6	5.8	141.6	
	STDER	10.7	0.0	41.2	0.5	4.7	
	1st	268.0	2.0	1088.2	5.5	197.9	
PBMIC+LPS(5ug/ml)+YDE011 1uM	2nd	220.5	2.0	909.1	4.8	189.4	
	3rd	235.0	2.0	964.1	4.8	200.9	
	Mean	241.2	2.0	987.2	5.0	196.0	
	STDER	14.1	0.0	53.0	0.2	3.4	
	1st	237.5	2.0	973.6	5.4	180.3	
	2nd	208.0	2.0	861.4	5.8	148.5	
PBMIC+LPS(5ug/ml)+YDE011 10uM	3rd	163.5	2.0	689.4	4.7	146.7	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	203.0	2.0	841.5	5.3	158.5	
	STDER	21.5	0.0	82.6	0.3	10.9	
	1st	142.0	2.0	604.8	6.1	99.1	
	2nd	114.0	2.0	492.8	6.1	80.8	
	3rd	117.0	2.0	504.9	6.0	84.1	
	Mean	124.3	2.0	534.1	6.1	88.0	
	STDER	8.9	0.0	35.5	0.0	5.6	
	1st	208.5	2.0	863.3	4.4	196.2	
	2nd	230.0	2.0	945.2	6.0	157.5	
	3rd	185.5	2.0	774.9	4.6	168.5	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	208.0	2.0	861.2	5.0	174.1	
	STDER	12.8	0.0	49.2	0.5	11.5	
	1st	207.0	2.0	857.6	4.5	190.6	
	2nd	190.0	2.0	792.3	6.6	120.0	
	3rd	211.5	2.0	874.8	5.0	175.0	
	Mean	202.8	2.0	841.6	5.4	161.9	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	203.0	2.0	841.5	5.3	158.5	
	STDER	21.5	0.0	82.6	0.3	10.9	
	1st	142.0	2.0	604.8	6.1	99.1	
	2nd	114.0	2.0	492.8	6.1	80.8	
	3rd	117.0	2.0	504.9	6.0	84.1	
	Mean	124.3	2.0	534.1	6.1	88.0	
	STDER	8.9	0.0	35.5	0.0	5.6	
	1st	208.5	2.0	863.3	4.4	196.2	
	2nd	230.0	2.0	945.2	6.0	157.5	
	3rd	185.5	2.0	774.9	4.6	168.5	

Bead name : IFN-gamma							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	6.5	0.0	25.1	0.6	21.4	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	216.0	2.0	892.0	5.0	178.4	
	2nd	148.0	2.0	628.5	5.6	112.2	
	3rd	211.0	2.0	872.9	5.6	155.9	
	Mean	191.7	2.0	797.8	5.4	148.8	
	STDER	21.9	0.0	84.8	0.2	19.4	
	1st	175.0	2.0	734.2	5.8	126.6	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	201.0	2.0	834.6	4.8	173.9	
	3rd	241.5	2.0	988.7	5.3	186.5	
	Mean	205.8	2.0	852.5	5.3	162.3	
	STDER	19.3	0.0	74.0	0.3	18.2	
	1st	199.5	2.0	828.9	5.2	159.4	
	2nd	199.0	2.0	826.9	5.4	153.1	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	209.0	2.0	865.3	5.6	154.5	
	Mean	202.5	2.0	840.3	5.4	155.7	
	STDER	3.3	0.0	12.5	0.1	1.9	

Bead name : IFN-gamma						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	111.0	2.0	480.6	6.2	77.5
	2nd	102.0	2.0	444.0	6.4	69.4
	Mean	106.5	2.0	462.3	6.3	73.4
	STDER	4.5	0.0	18.3	0.1	4.1

Table 35

Bead name : CCCL2/JE/MCP-1						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.0	2.0	NaN		
	2nd	0.0	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	56.0	2.0	109.1	7.5	14.5
	2nd	176.0	2.0	202.1	7.4	27.3
	3rd	181.0	2.0	205.3	6.6	31.1

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	137.7	2.0	172.2	7.2	24.3	
	STDER	40.9	0.0	31.5	0.3	5.0	
	1st	10850.5	2.0	3125.9	6.1	512.4	
	2nd	10117.0	2.0	2900.2	5.8	500.0	
	3rd	10150.0	2.0	2910.1	5.5	529.1	
	Mean	10372.5	2.0	2978.7	5.8	513.9	
	STDER	239.2	0.0	73.7	0.2	8.4	
	1st	4825.5	2.0	1522.2	5.2	292.7	
	2nd	16019.0	2.0	5242.2	4.8	1092.1	
	Mean	10422.3	2.0	3382.2	5.0	692.4	
PBMC+YY101 0.01uM	STDER	5596.8	0.0	1860.0	0.2	399.7	
	1st	4052.5	2.0	1338.6	4.4	304.2	
	2nd	9626.0	2.0	2755.6	5.8	475.1	
	Mean	6839.3	2.0	2047.1	5.1	389.7	
	STDER	2786.8	0.0	708.5	0.7	85.4	
	1st	4611.0	2.0	1471.3	5.5	267.5	
PBMC+YY101 0.1uM							
PBMC+YY101 1uM							

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	7230.0	2.0	2108.8	5.5	383.4	
	Mean	5920.5	2.0	1790.1	5.5	325.5	
	STDER	1309.5	0.0	318.8	0.0	58.0	
PBM C+YY101 10uM	1st	22755.0	2.0	12584.2	6.4	1966.3	
	2nd	10032.5	2.0	2874.9	6.1	471.3	
	Mean	16393.8	2.0	7729.5	6.3	1218.8	
	STDER	6361.3	0.0	4854.6	0.2	747.5	
PBM C+YY101 100uM	1st	4286.0	2.0	1394.1	6.4	217.8	
	2nd	1867.5	2.0	796.7	7.0	113.8	
	Mean	3076.8	2.0	1095.4	6.7	165.8	
	STDER	1209.3	0.0	298.7	0.3	52.0	
PBM C+LPS(5ug/ml)+Xiidra 0.001uM	1st	14536.5	2.0	4509.4	6.2	727.3	
	2nd	13875.0	2.0	4222.1	7.6	555.5	
	Mean	14205.8	2.0	4365.8	6.9	641.4	
	STDER	330.8	0.0	143.7	0.7	85.9	
PBM C+LPS(5ug/ml)+Xiidra 0.01uM	1st	12993.5	2.0	3869.5	5.2	744.1	

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	14776.0	2.0	4619.0	5.8	796.4	
	Mean	13884.8	2.0	4244.3	5.5	770.3	
	STDER	891.3	0.0	374.7	0.3	26.1	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	1st	10785.0	2.0	3105.2	6.6	470.5	
	2nd	10732.0	2.0	3088.6	5.7	541.9	
	Mean	10758.5	2.0	3096.9	6.2	506.2	
	STDER	26.5	0.0	8.3	0.5	35.7	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	1st	10830.0	2.0	3119.4	4.8	649.9	
	2nd	11231.0	2.0	3248.1	4.4	738.2	
	Mean	11030.5	2.0	3183.8	4.6	694.0	
	STDER	200.5	0.0	64.4	0.2	44.2	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	1st	8984.0	2.0	2573.5	5.8	443.7	
	2nd	10594.0	2.0	3045.6	6.4	475.9	
	Mean	9789.0	2.0	2809.5	6.1	459.8	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	STDER	805.0	0.0	236.0	0.3	16.1	
	1st	8030.0	2.0	2315.5	7.1	326.1	

Bead name : CCL2/JE/MCP-1						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	8710.5	2.0	2498.1	5.8	430.7
	Mean	8370.3	2.0	2406.8	6.5	378.4
	STDER	340.3	0.0	91.3	0.7	52.3
PBMCLPS(5ug/ml)+YY101 0.001uM	1st	12717.0	2.0	3765.3	5.7	660.6
	2nd	12912.0	2.0	3838.5	7.1	540.6
	3rd	13837.0	2.0	4206.2	6.6	637.3
	Mean	13155.3	2.0	3936.7	6.5	612.8
	STDER	345.5	0.0	136.4	0.4	36.7
	1st	13686.0	2.0	4143.7	6.4	647.5
PBMCLPS(5ug/ml)+YY101 0.01uM	2nd	13444.5	2.0	4045.9	6.0	674.3
	3rd	13067.0	2.0	3897.7	6.1	639.0
	Mean	13399.2	2.0	4029.1	6.2	653.6
	STDER	180.1	0.0	71.5	0.1	10.7
	1st	12267.0	2.0	3601.3	6.2	580.9
	2nd	12562.0	2.0	3708.0	5.2	713.1
PBMCLPS(5ug/ml)+YY101 0.1uM	3rd	11811.0	2.0	3442.0	6.2	555.2

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	12213.3	2.0	3583.8	5.9	616.4	
	STDER	218.4	0.0	77.3	0.3	48.9	
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	13078.5	2.0	3902.2	6.3	619.4	
	2nd	13103.0	2.0	3911.6	7.1	550.9	
	3rd	13960.0	2.0	4257.8	6.2	686.7	
	Mean	13380.5	2.0	4023.9	6.5	619.0	
	STDER	289.8	0.0	117.0	0.3	39.2	
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	11415.0	2.0	3308.6	6.0	551.4	
	2nd	12533.0	2.0	3697.4	6.4	577.7	
	3rd	11609.0	2.0	3373.4	7.6	443.9	
	Mean	11852.3	2.0	3459.8	6.7	524.3	
	STDER	344.9	0.0	120.3	0.5	40.9	
PBMIC+LPS(5ug/ml)+YY101 100uM	1st	992.0	2.0	541.0	6.3	85.9	
	2nd	1275.0	2.0	629.1	6.2	101.5	
	3rd	1263.0	2.0	625.5	5.0	125.1	
	Mean	1176.7	2.0	598.6	5.8	104.2	

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	92.4	0.0	28.8	0.4	11.4	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	6216.5	2.0	1856.7	4.5	412.6	
	2nd	6415.5	2.0	1905.5	5.8	328.5	
	3rd	6318.0	2.0	1881.6	5.8	324.4	
	Mean	6316.7	2.0	1881.3	5.4	355.2	
	STDER	57.5	0.0	14.1	0.4	28.7	
	1st	6375.0	2.0	1895.6	6.3	300.9	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	7050.0	2.0	2063.3	6.2	332.8	
	3rd	6660.0	2.0	1965.9	5.1	385.5	
	Mean	6695.0	2.0	1974.9	5.9	339.7	
	STDER	195.6	0.0	48.6	0.4	24.7	
	1st	5566.0	2.0	1699.1	6.6	257.4	
	2nd	5817.0	2.0	1759.6	5.0	351.9	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	5428.0	2.0	1666.0	5.7	292.3	
	Mean	5603.7	2.0	1708.3	5.8	300.6	
	STDER	113.9	0.0	27.4	0.5	27.6	

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	5965.5	2.0	1795.6	5.5	326.5	
	2nd	6315.0	2.0	1880.8	4.8	391.8	
	3rd	5630.0	2.0	1714.5	4.8	357.2	
	Mean	5970.2	2.0	1797.0	5.0	358.5	
	STDER	197.8	0.0	48.0	0.2	18.9	
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	4743.0	2.0	1502.6	5.4	278.3	
	2nd	5215.5	2.0	1615.2	5.8	278.5	
	3rd	5049.0	2.0	1575.4	4.7	335.2	
	Mean	5002.5	2.0	1564.4	5.3	297.3	
	STDER	138.4	0.0	33.0	0.3	18.9	
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	262.0	2.0	252.0	6.1	41.3	
	2nd	360.0	2.0	301.1	6.1	49.4	
	3rd	342.0	2.0	292.6	6.0	48.8	
	Mean	321.3	2.0	281.9	6.1	46.5	
	STDER	30.1	0.0	15.2	0.0	2.6	
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	7127.0	2.0	2082.8	4.4	473.4	

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	7646.5	2.0	2215.5	6.0	369.2	
	3rd	6916.0	2.0	2029.7	4.6	441.2	
	Mean	7229.8	2.0	2109.3	5.0	427.9	
	STDER	217.1	0.0	55.2	0.5	30.8	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	6942.0	2.0	2036.2	4.5	452.5	
	2nd	6650.0	2.0	1963.4	6.6	297.5	
	3rd	7082.0	2.0	2071.4	5.0	414.3	
	Mean	6891.3	2.0	2023.7	5.4	388.1	
	STDER	127.3	0.0	31.8	0.6	46.6	
	1st	7234.0	2.0	2109.9	5.0	422.0	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	5852.5	2.0	1768.2	5.6	315.8	
	3rd	6350.5	2.0	1889.5	5.6	337.4	
	Mean	6479.0	2.0	1922.5	5.4	358.4	
	STDER	403.9	0.0	100.0	0.2	32.4	
	1st	7486.0	2.0	2174.1	5.8	374.9	
	2nd	7253.0	2.0	2114.7	4.8	440.6	

Bead name : CCL2/JE/MCP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	7122.0	2.0	2081.5	5.3	392.7	
	Mean	7287.0	2.0	2123.4	5.3	402.7	
	STDER	106.4	0.0	27.1	0.3	19.6	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	6348.5	2.0	1889.0	5.2	363.3	
	2nd	5845.0	2.0	1766.4	5.4	327.1	
	3rd	5753.0	2.0	1744.2	5.6	311.5	
	Mean	5982.2	2.0	1799.9	5.4	333.9	
	STDER	185.1	0.0	45.0	0.1	15.3	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	275.0	2.0	258.9	6.2	41.8	
	2nd	364.0	2.0	303.0	6.4	47.3	
	Mean	319.5	2.0	281.0	6.3	44.6	
	STDER	44.5	0.0	22.1	0.1	2.8	

Table 36

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.0	2.0	NaN			
	2nd	0.0	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	4.0	2.0	4.6	7.5	0.6	
	2nd	4.0	2.0	4.6	7.4	0.6	
	3rd	4.0	2.0	4.6	6.6	0.7	
	Mean	4.0	2.0	4.6	7.2	0.6	
	STDER	0.0	0.0	0.0	0.3	0.0	
PBMC+LPS(5ug/ml)	1st	32.0	2.0	23.1	6.1	3.8	
	2nd	47.0	2.0	33.4	5.8	5.8	
	3rd	45.0	2.0	32.0	5.5	5.8	
	Mean	41.3	2.0	29.5	5.8	5.1	
	STDER	4.7	0.0	3.2	0.2	0.7	
PBMC+YY101 0.01uM	1st	7.0	2.0	6.5	5.2	1.3	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	10.5	2.0	8.8	4.8	1.8	
	Mean	8.8	2.0	7.7	5.0	1.5	
	STDER	1.8	0.0	1.1	0.2	0.3	
	1st	7.0	2.0	6.5	4.4	1.5	
PBMCMC+YY101 0.1uM	2nd	9.0	2.0	7.8	5.8	1.3	
	Mean	8.0	2.0	7.2	5.1	1.4	
	STDER	1.0	0.0	0.6	0.7	0.1	
	1st	7.0	2.0	6.5	5.5	1.2	
PBMCMC+YY101 1uM	2nd	10.0	2.0	8.5	5.5	1.5	
	Mean	8.5	2.0	7.5	5.5	1.4	
	STDER	1.5	0.0	1.0	0.0	0.2	
	1st	18.5	2.0	14.0	6.4	2.2	
PBMCMC+YY101 10uM	2nd	16.0	2.0	12.4	6.1	2.0	
	Mean	17.3	2.0	13.2	6.3	2.1	
	STDER	1.3	0.0	0.8	0.2	0.1	
	1st	9.0	2.0	7.8	6.4	1.2	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	6.0	2.0	5.9	7.0	0.8	
	Mean	7.5	2.0	6.9	6.7	1.0	
	STDER	1.5	0.0	1.0	0.3	0.2	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	1st	77.0	2.0	54.4	6.2	8.8	
	2nd	45.0	2.0	32.0	7.6	4.2	
	Mean	61.0	2.0	43.2	6.9	6.5	
	STDER	16.0	0.0	11.2	0.7	2.3	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	1st	56.0	2.0	39.7	5.2	7.6	
	2nd	41.0	2.0	29.3	5.8	5.0	
	Mean	48.5	2.0	34.5	5.5	6.3	
	STDER	7.5	0.0	5.2	0.3	1.3	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	1st	36.5	2.0	26.2	6.6	4.0	
	2nd	37.5	2.0	26.9	5.7	4.7	
	Mean	37.0	2.0	26.5	6.2	4.3	
	STDER	0.5	0.0	0.3	0.5	0.4	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	1st	37.0	2.0	26.5	4.8	5.5	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	24.5	2.0	18.1	4.4	4.1	
	Mean	30.8	2.0	22.3	4.6	4.8	
	STDER	6.3	0.0	4.2	0.2	0.7	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	1st	34.0	2.0	24.5	5.8	4.2	
	2nd	44.5	2.0	31.7	6.4	5.0	
	Mean	39.3	2.0	28.1	6.1	4.6	
	STDER	5.3	0.0	3.6	0.3	0.4	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	1st	42.0	2.0	30.0	7.1	4.2	
	2nd	40.0	2.0	28.6	5.8	4.9	
	Mean	41.0	2.0	29.3	6.5	4.6	
	STDER	1.0	0.0	0.7	0.7	0.4	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	50.5	2.0	35.8	5.7	6.3	
	2nd	46.0	2.0	32.7	7.1	4.6	
	3rd	33.5	2.0	24.1	6.6	3.7	
	Mean	43.3	2.0	30.9	6.5	4.9	
	STDER	5.1	0.0	3.5	0.4	0.8	

Bead name : Fas Ligand						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	43.0	2.0	30.7	6.4	4.8
	2nd	55.5	2.0	39.3	6.0	6.6
	3rd	44.0	2.0	31.3	6.1	5.1
	Mean	47.5	2.0	33.8	6.2	5.5
	STDER	4.0	0.0	2.8	0.1	0.5
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	46.0	2.0	32.7	6.2	5.3
	2nd	43.0	2.0	30.7	5.2	5.9
	3rd	35.0	2.0	25.2	6.2	4.1
	Mean	41.3	2.0	29.5	5.9	5.1
	STDER	3.3	0.0	2.3	0.3	0.5
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	50.0	2.0	35.5	6.3	5.6
	2nd	51.0	2.0	36.2	7.1	5.1
	3rd	44.5	2.0	31.7	6.2	5.1
	Mean	48.5	2.0	34.5	6.5	5.3
	STDER	2.0	0.0	1.4	0.3	0.2
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	82.0	2.0	58.0	6.0	9.7

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	76.0	2.0	53.7	6.4	8.4	
	3rd	40.0	2.0	28.6	7.6	3.8	
	Mean	66.0	2.0	46.7	6.7	7.3	
	STDER	13.1	0.0	9.2	0.5	1.8	
PBMCLPS(5ug/ml)+YY101 100uM	1st	55.0	2.0	39.0	6.3	6.2	
	2nd	21.5	2.0	16.0	6.2	2.6	
	3rd	29.0	2.0	21.1	5.0	4.2	
	Mean	35.2	2.0	25.4	5.8	4.3	
	STDER	10.2	0.0	7.0	0.4	1.0	
PBMCLPS(5ug/ml)+YDE011 0.001uM	1st	21.0	2.0	15.7	4.5	3.5	
	2nd	25.0	2.0	18.4	5.8	3.2	
	3rd	22.0	2.0	16.4	5.8	2.8	
	Mean	22.7	2.0	16.8	5.4	3.2	
	STDER	1.2	0.0	0.8	0.4	0.2	
PBMCLPS(5ug/ml)+YDE011 0.01uM	1st	23.0	2.0	17.1	6.3	2.7	
	2nd	18.0	2.0	13.7	6.2	2.2	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	21.0	2.0	15.7	5.1	3.1	
	Mean	20.7	2.0	15.5	5.9	2.7	
	STDER	1.5	0.0	1.0	0.4	0.3	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	26.0	2.0	19.1	6.6	2.9	
	2nd	24.0	2.0	17.7	5.0	3.5	
	3rd	20.0	2.0	15.0	5.7	2.6	
	Mean	23.3	2.0	17.3	5.8	3.0	
	STDER	1.8	0.0	1.2	0.5	0.3	
	1st	23.5	2.0	17.4	5.5	3.2	
PBMC+LPS(5ug/ml)+YDE011 1uM	2nd	20.5	2.0	15.4	4.8	3.2	
	3rd	20.0	2.0	15.0	4.8	3.1	
	Mean	21.3	2.0	15.9	5.0	3.2	
	STDER	1.1	0.0	0.7	0.2	0.0	
	1st	27.0	2.0	19.7	5.4	3.7	
	2nd	24.0	2.0	17.7	5.8	3.1	
PBMC+LPS(5ug/ml)+YDE011 10uM	3rd	19.0	2.0	14.4	4.7	3.1	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	23.3	2.0	17.3	5.3	3.3	
	STDER	2.3	0.0	1.6	0.3	0.2	
	1st	15.0	2.0	11.7	6.1	1.9	
	2nd	17.0	2.0	13.1	6.1	2.1	
	3rd	20.0	2.0	15.0	6.0	2.5	
	Mean	17.3	2.0	13.3	6.1	2.2	
	STDER	1.5	0.0	1.0	0.0	0.2	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	23.0	2.0	17.1	4.4	3.9	
	2nd	28.0	2.0	20.4	6.0	3.4	
	3rd	17.0	2.0	13.1	4.6	2.8	
	Mean	22.7	2.0	16.8	5.0	3.4	
	STDER	3.2	0.0	2.1	0.5	0.3	
	1st	26.0	2.0	19.1	4.5	4.2	
	2nd	21.0	2.0	15.7	6.6	2.4	
	3rd	43.5	2.0	31.0	5.0	6.2	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	30.2	2.0	21.9	5.4	4.3	

Bead name : Fas Ligand							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	6.8	0.0	4.6	0.6	1.1	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	19.0	2.0	14.4	5.0	2.9	
	2nd	16.5	2.0	12.7	5.6	2.3	
	3rd	16.0	2.0	12.4	5.6	2.2	
	Mean	17.2	2.0	13.2	5.4	2.5	
	STDER	0.9	0.0	0.6	0.2	0.2	
	1st	18.0	2.0	13.7	5.8	2.4	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	21.0	2.0	15.7	4.8	3.3	
	3rd	28.0	2.0	20.4	5.3	3.9	
	Mean	22.3	2.0	16.6	5.3	3.2	
	STDER	3.0	0.0	2.0	0.3	0.4	
	1st	22.0	2.0	16.4	5.2	3.2	
	2nd	23.0	2.0	17.1	5.4	3.2	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	21.0	2.0	15.7	5.6	2.8	
	Mean	22.0	2.0	16.4	5.4	3.0	
	STDER	0.6	0.0	0.4	0.1	0.1	

Bead name : Fas Ligand						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMc+LPS(5ug/ml)+YDE043 100uM	1st	20.0	2.0	15.0	6.2	2.4
	2nd	14.5	2.0	11.4	6.4	1.8
	Mean	17.3	2.0	13.2	6.3	2.1
	STDER	2.8	0.0	1.8	0.1	0.3

Table 37

Bead name : CCCL20/MIP-3 alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.5	2.0	NaN		
	2nd	-0.5	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMc + 0.5% DMSO	1st	3.5	2.0		7.5	0.0
	2nd	2.0	2.0		7.4	0.0
	3rd	3.5	2.0		6.6	0.0

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBM C+LPS(5ug/ml)	Mean	3.0	2.0	#DIV/0!	7.2	0.0	
	STDER	0.5	0.0	#DIV/0!	0.3	0.0	
	1st	432.0	2.0	384.5	6.1	63.0	
	2nd	390.5	2.0	351.1	5.8	60.5	
	3rd	428.5	2.0	381.7	5.5	69.4	
	Mean	417.0	2.0	372.4	5.8	64.3	
	STDER	13.3	0.0	10.7	0.2	2.6	
	1st	7.5	2.0	7.3	5.2	1.4	
	2nd	14.5	2.0	16.8	4.8	3.5	
	Mean	11.0	2.0	12.1	5.0	2.5	
PBM C+YY101 0.01uM	STDER	3.5	0.0	4.7	0.2	1.0	
	1st	7.5	2.0	7.3	4.4	1.7	
	2nd	10.5	2.0	11.6	5.8	2.0	
	Mean	9.0	2.0	9.5	5.1	1.8	
PBM C+YY101 0.1uM	STDER	1.5	0.0	2.1	0.7	0.2	
	1st	7.5	2.0	7.3	5.5	1.3	
	2nd	10.5	2.0	11.6	5.8	2.0	
	Mean	9.0	2.0	9.5	5.1	1.8	
PBM C+YY101 1uM	STDER	1.5	0.0	2.1	0.7	0.2	
	1st	7.5	2.0	7.3	5.5	1.3	
	2nd	10.5	2.0	11.6	5.8	2.0	
	Mean	9.0	2.0	9.5	5.1	1.8	

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	9.5	2.0	10.2	5.5	1.9	
	Mean	8.5	2.0	8.8	5.5	1.6	
	STDER	1.0	0.0	1.4	0.0	0.3	
PBMCMC+YY101 10uM	1st	51.5	2.0	57.4	6.4	9.0	
	2nd	21.5	2.0	25.3	6.1	4.1	
	Mean	36.5	2.0	41.3	6.3	6.6	
	STDER	15.0	0.0	16.1	0.2	2.4	
PBMCMC+YY101 100uM	1st	25.5	2.0	29.8	6.4	4.7	
	2nd	13.0	2.0	14.9	7.0	2.1	
	Mean	19.3	2.0	22.4	6.7	3.4	
	STDER	6.3	0.0	7.5	0.3	1.3	
PBMCMC+LPS(5ug/ml)+Xiidra 0.001uM	1st	453.5	2.0	401.8	6.2	64.8	
	2nd	392.5	2.0	352.7	7.6	46.4	
	Mean	423.0	2.0	377.2	6.9	55.6	
	STDER	30.5	0.0	24.5	0.7	9.2	
PBMCMC+LPS(5ug/ml)+Xiidra 0.01uM	1st	485.5	2.0	427.3	5.2	82.2	

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	377.5	2.0	340.5	5.8	58.7	
	Mean	431.5	2.0	383.9	5.5	70.4	
	STDER	54.0	0.0	43.4	0.3	11.7	
	1st	306.5	2.0	282.4	6.6	42.8	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	248.5	2.0	234.1	5.7	41.1	
	Mean	277.5	2.0	258.3	6.2	41.9	
	STDER	29.0	0.0	24.2	0.5	0.9	
	1st	459.5	2.0	406.6	4.8	84.7	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	2nd	258.5	2.0	242.5	4.4	55.1	
	Mean	359.0	2.0	324.5	4.6	69.9	
	STDER	100.5	0.0	82.0	0.2	14.8	
	1st	356.5	2.0	323.4	5.8	55.8	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	353.0	2.0	320.6	6.4	50.1	
	Mean	354.8	2.0	322.0	6.1	52.9	
	STDER	1.8	0.0	1.4	0.3	2.8	
	1st	228.5	2.0	217.2	7.1	30.6	

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	253.0	2.0	237.9	5.8	41.0	
	Mean	240.8	2.0	227.6	6.5	35.8	
	STDER	12.3	0.0	10.3	0.7	5.2	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	329.0	2.0	301.0	5.7	52.8	
	2nd	315.5	2.0	289.9	7.1	40.8	
	3rd	395.5	2.0	355.1	6.6	53.8	
	Mean	346.7	2.0	315.3	6.5	49.1	
	STDER	24.7	0.0	20.2	0.4	4.2	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	431.0	2.0	383.7	6.4	60.0	
	2nd	375.5	2.0	338.9	6.0	56.5	
	3rd	464.5	2.0	410.6	6.1	67.3	
	Mean	423.7	2.0	377.7	6.2	61.2	
	STDER	26.0	0.0	20.9	0.1	3.2	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	424.5	2.0	378.5	6.2	61.0	
	2nd	407.0	2.0	364.4	5.2	70.1	
	3rd	388.5	2.0	349.4	6.2	56.4	

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	406.7	2.0	364.1	5.9	62.5	
	STDER	10.4	0.0	8.4	0.3	4.0	
	1st	356.0	2.0	323.0	6.3	51.3	
	2nd	364.5	2.0	330.0	7.1	46.5	
	3rd	404.5	2.0	362.4	6.2	58.4	
	Mean	375.0	2.0	338.5	6.5	52.1	
	STDER	15.0	0.0	12.1	0.3	3.5	
	1st	357.5	2.0	324.3	6.0	54.0	
	2nd	423.5	2.0	377.7	6.4	59.0	
	3rd	454.5	2.0	402.6	7.6	53.0	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	411.8	2.0	368.2	6.7	55.3	
	STDER	28.6	0.0	23.1	0.5	1.9	
	1st	692.5	2.0	590.1	6.3	93.7	
	2nd	694.5	2.0	591.7	6.2	95.4	
	3rd	646.0	2.0	553.9	5.0	110.8	
	Mean	677.7	2.0	578.6	5.8	100.0	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	692.5	2.0	590.1	6.3	93.7	
	2nd	694.5	2.0	591.7	6.2	95.4	
	3rd	646.0	2.0	553.9	5.0	110.8	
	Mean	677.7	2.0	578.6	5.8	100.0	
	1st	692.5	2.0	590.1	6.3	93.7	
	2nd	694.5	2.0	591.7	6.2	95.4	

Bead name : CCL20/MIP-3 alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	STDER	15.8	0.0	12.4	0.4	5.4
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	284.5	2.0	264.2	4.5	58.7
	2nd	235.5	2.0	223.2	5.8	38.5
	3rd	270.0	2.0	252.1	5.8	43.5
	Mean	263.3	2.0	246.5	5.4	46.9
	STDER	14.5	0.0	12.2	0.4	6.1
	1st	247.5	2.0	233.3	6.3	37.0
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	278.0	2.0	258.8	6.2	41.7
	3rd	297.0	2.0	274.6	5.1	53.8
	Mean	274.2	2.0	255.6	5.9	44.2
	STDER	14.4	0.0	12.0	0.4	5.0
	1st	253.5	2.0	238.3	6.6	36.1
	2nd	245.5	2.0	231.6	5.0	46.3
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	265.5	2.0	248.4	5.7	43.6
	Mean	254.8	2.0	239.4	5.8	42.0
	STDER	5.8	0.0	4.9	0.5	3.1

Bead name : CCL20/MIP-3 alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	212.5	2.0	203.6	5.5	37.0
	2nd	218.5	2.0	208.7	4.8	43.5
	3rd	233.5	2.0	221.5	4.8	46.1
	Mean	221.5	2.0	211.3	5.0	42.2
	STDER	6.2	0.0	5.3	0.2	2.7
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	248.5	2.0	234.1	5.4	43.4
	2nd	234.5	2.0	222.3	5.8	38.3
	3rd	249.0	2.0	234.5	4.7	49.9
	Mean	244.0	2.0	230.3	5.3	43.9
	STDER	4.8	0.0	4.0	0.3	3.4
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	379.5	2.0	342.2	6.1	56.1
	2nd	351.5	2.0	319.4	6.1	52.4
	3rd	338.5	2.0	308.7	6.0	51.5
	Mean	356.5	2.0	323.4	6.1	53.3
	STDER	12.1	0.0	9.9	0.0	1.4
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	252.5	2.0	237.5	4.4	54.0

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	225.0	2.0	214.3	6.0	35.7	
	3rd	225.5	2.0	214.7	4.6	46.7	
	Mean	234.3	2.0	222.1	5.0	45.5	
	STDER	9.1	0.0	7.7	0.5	5.3	
PBMIC+LPS(5ug/ml)+YDE043 0.01uM	1st	294.0	2.0	272.1	4.5	60.5	
	2nd	250.5	2.0	235.8	6.6	35.7	
	3rd	284.5	2.0	264.2	5.0	52.8	
	Mean	276.3	2.0	257.4	5.4	49.7	
	STDER	13.2	0.0	11.0	0.6	7.3	
	1st	291.0	2.0	269.6	5.0	53.9	
PBMIC+LPS(5ug/ml)+YDE043 0.1uM	2nd	287.5	2.0	266.7	5.6	47.6	
	3rd	294.0	2.0	272.1	5.6	48.6	
	Mean	290.8	2.0	269.5	5.4	50.0	
	STDER	1.9	0.0	1.6	0.2	2.0	
	1st	288.0	2.0	267.1	5.8	46.1	
PBMIC+LPS(5ug/ml)+YDE043 1uM	2nd	269.5	2.0	251.7	4.8	52.4	

Bead name : CCL20/MIP-3 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	272.5	2.0	254.2	5.3	48.0	
	Mean	276.7	2.0	257.7	5.3	48.8	
	STDER	5.7	0.0	4.8	0.3	1.9	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	279.5	2.0	260.1	5.2	50.0	
	2nd	280.5	2.0	260.9	5.4	48.3	
	3rd	306.5	2.0	282.4	5.6	50.4	
	Mean	288.8	2.0	267.8	5.4	49.6	
	STDER	8.8	0.0	7.3	0.1	0.6	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	428.5	2.0	381.7	6.2	61.6	
	2nd	370.5	2.0	334.8	6.4	52.3	
	Mean	399.5	2.0	358.3	6.3	56.9	
	STDER	29.0	0.0	23.4	0.1	4.6	

Table 38

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.5	2.0	NaN			
	2nd	-0.5	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	0.0	2.0	3.3	7.5	0.4	
	2nd	-1.0	2.0	1.0	7.4	0.1	
	3rd	-1.0	2.0	1.0	6.6	0.1	
	Mean	-0.7	2.0	1.8	7.2	0.2	
	STDER	0.3	0.0	0.8	0.3	0.1	
PBMC+LPS(5ug/ml)	1st	516.5	2.0	435.0	6.1	71.3	
	2nd	483.0	2.0	410.3	5.8	70.7	
	3rd	466.5	2.0	398.1	5.5	72.4	
	Mean	488.7	2.0	414.5	5.8	71.5	
	STDER	14.7	0.0	10.9	0.2	0.5	
PBMC+YY101 0.01uM	1st	-1.0	2.0	1.0	5.2	0.2	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1.0	2.0	5.3	4.8	1.1	
	Mean	0.0	2.0	3.1	5.0	0.6	
	STDER	1.0	0.0	2.2	0.2	0.5	
	1st	-1.0	2.0	1.0	4.4	0.2	
PBMCMC+YY101 0.1uM	2nd	1.0	2.0	5.3	5.8	0.9	
	Mean	0.0	2.0	3.1	5.1	0.6	
	STDER	1.0	0.0	2.2	0.7	0.3	
	1st	1.0	2.0	5.3	5.5	1.0	
PBMCMC+YY101 1uM	2nd	1.0	2.0	5.3	5.5	1.0	
	Mean	1.0	2.0	5.3	5.5	1.0	
	STDER	0.0	0.0	0.0	0.0	0.0	
	1st	20.0	2.0	31.7	6.4	5.0	
PBMCMC+YY101 10uM	2nd	2.0	2.0	7.1	6.1	1.2	
	Mean	11.0	2.0	19.4	6.3	3.1	
	STDER	9.0	0.0	12.3	0.2	1.9	
	1st	4.0	2.0	10.4	6.4	1.6	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1.0	2.0	5.3	7.0	0.8	
	Mean	2.5	2.0	7.9	6.7	1.2	
	STDER	1.5	0.0	2.5	0.3	0.4	
	1st	599.0	2.0	495.8	6.2	80.0	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	545.0	2.0	456.0	7.6	60.0	
	Mean	572.0	2.0	475.9	6.9	70.0	
	STDER	27.0	0.0	19.9	0.7	10.0	
	1st	651.0	2.0	534.1	5.2	102.7	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	539.0	2.0	451.6	5.8	77.9	
	Mean	595.0	2.0	492.8	5.5	90.3	
	STDER	56.0	0.0	41.3	0.3	12.4	
	1st	471.0	2.0	401.4	6.6	60.8	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	473.5	2.0	403.3	5.7	70.8	
	Mean	472.3	2.0	402.4	6.2	65.8	
	STDER	1.3	0.0	0.9	0.5	5.0	
	1st	619.0	2.0	510.5	4.8	106.4	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	421.0	2.0	364.4	4.4	82.8	
	Mean	520.0	2.0	437.5	4.6	94.6	
	STDER	99.0	0.0	73.0	0.2	11.8	
	1st	493.5	2.0	418.0	5.8	72.1	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	528.0	2.0	443.5	6.4	69.3	
	Mean	510.8	2.0	430.8	6.1	70.7	
	STDER	17.3	0.0	12.7	0.3	1.4	
	1st	378.0	2.0	332.4	7.1	46.8	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	397.5	2.0	346.9	5.8	59.8	
	Mean	387.8	2.0	339.7	6.5	53.3	
	STDER	9.8	0.0	7.3	0.7	6.5	
	1st	504.5	2.0	426.2	5.7	74.8	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	553.0	2.0	461.9	7.1	65.1	
	3rd	496.0	2.0	419.9	6.6	63.6	
	Mean	517.8	2.0	436.0	6.5	67.8	
	STDER	17.8	0.0	13.1	0.4	3.5	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 0.01uM	1st	613.0	2.0	506.1	6.4	79.1	
	2nd	572.0	2.0	475.9	6.0	79.3	
	3rd	584.0	2.0	484.7	6.1	79.5	
	Mean	589.7	2.0	488.9	6.2	79.3	
	STDER	12.2	0.0	9.0	0.1	0.1	
PBMC+LPS(5ug/ml)+YY101 0.1uM	1st	593.0	2.0	491.3	6.2	79.2	
	2nd	580.0	2.0	481.8	5.2	92.6	
	3rd	581.0	2.0	482.5	6.2	77.8	
	Mean	584.7	2.0	485.2	5.9	83.2	
	STDER	4.2	0.0	3.1	0.3	4.7	
PBMC+LPS(5ug/ml)+YY101 1uM	1st	538.5	2.0	451.2	6.3	71.6	
	2nd	506.0	2.0	427.3	7.1	60.2	
	3rd	515.5	2.0	434.3	6.2	70.0	
	Mean	520.0	2.0	437.6	6.5	67.3	
	STDER	9.6	0.0	7.1	0.3	3.6	
PBMC+LPS(5ug/ml)+YY101 10uM	1st	568.5	2.0	473.3	6.0	78.9	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	565.0	2.0	470.7	6.4	73.6	
	3rd	582.5	2.0	483.6	7.6	63.6	
	Mean	572.0	2.0	475.9	6.7	72.0	
	STDER	5.3	0.0	3.9	0.5	4.5	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	816.0	2.0	656.9	6.3	104.3	
	2nd	762.0	2.0	616.5	6.2	99.4	
	3rd	759.0	2.0	614.2	5.0	122.8	
	Mean	779.0	2.0	629.2	5.8	108.8	
	STDER	18.5	0.0	13.9	0.4	7.1	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	383.0	2.0	336.1	4.5	74.7	
	2nd	382.0	2.0	335.4	5.8	57.8	
	3rd	416.5	2.0	361.1	5.8	62.3	
	Mean	393.8	2.0	344.2	5.4	64.9	
	STDER	11.3	0.0	8.4	0.4	5.0	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	392.0	2.0	342.8	6.3	54.4	
	2nd	414.0	2.0	359.2	6.2	57.9	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	444.5	2.0	381.8	5.1	74.9	
	Mean	416.8	2.0	361.3	5.9	62.4	
	STDER	15.2	0.0	11.3	0.4	6.3	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	378.0	2.0	332.4	6.6	50.4	
	2nd	352.0	2.0	312.9	5.0	62.6	
	3rd	398.0	2.0	347.3	5.7	60.9	
	Mean	376.0	2.0	330.9	5.8	58.0	
	STDER	13.3	0.0	10.0	0.5	3.8	
	1st	400.5	2.0	349.2	5.5	63.5	
PBMC+LPS(5ug/ml)+YDE011 1uM	2nd	363.0	2.0	321.1	4.8	66.9	
	3rd	396.0	2.0	345.8	4.8	72.0	
	Mean	386.5	2.0	338.7	5.0	67.5	
	STDER	11.8	0.0	8.8	0.2	2.5	
	1st	410.0	2.0	356.2	5.4	66.0	
	2nd	372.0	2.0	327.9	5.8	56.5	
PBMC+LPS(5ug/ml)+YDE011 10uM	3rd	396.0	2.0	345.8	4.7	73.6	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	392.7	2.0	343.3	5.3	65.4	
	STDER	11.1	0.0	8.3	0.3	4.9	
	1st	532.0	2.0	446.4	6.1	73.2	
	2nd	472.0	2.0	402.2	6.1	65.9	
	3rd	518.0	2.0	436.1	6.0	72.7	
	Mean	507.3	2.0	428.2	6.1	70.6	
	STDER	18.1	0.0	13.4	0.0	2.3	
	1st	387.0	2.0	339.1	4.4	77.1	
	2nd	2522.0	2.0	369.6	6.0	61.6	
	3rd	412.0	2.0	357.7	4.6	77.8	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	1107.0	2.0	355.5	5.0	72.1	
	STDER	707.5	0.0	8.9	0.5	5.3	
	1st	405.0	2.0	352.5	4.5	78.3	
	2nd	391.5	2.0	342.5	6.6	51.9	
	3rd	429.0	2.0	370.4	5.0	74.1	
	Mean	408.5	2.0	355.1	5.4	68.1	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	408.5	2.0	355.1	5.4	68.1	
	STDER	707.5	0.0	8.9	0.5	5.3	
	1st	405.0	2.0	352.5	4.5	78.3	
	2nd	391.5	2.0	342.5	6.6	51.9	
	3rd	429.0	2.0	370.4	5.0	74.1	
	Mean	408.5	2.0	355.1	5.4	68.1	
	STDER	707.5	0.0	8.9	0.5	5.3	
	1st	405.0	2.0	352.5	4.5	78.3	
	2nd	391.5	2.0	342.5	6.6	51.9	
	3rd	429.0	2.0	370.4	5.0	74.1	

Bead name : IL-1 alpha							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	11.0	0.0	8.2	0.6	8.2	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	417.0	2.0	361.4	5.0	72.3	
	2nd	373.5	2.0	329.0	5.6	58.8	
	3rd	445.5	2.0	382.6	5.6	68.3	
	Mean	412.0	2.0	357.7	5.4	66.5	
	STDER	20.9	0.0	15.6	0.2	4.0	
	1st	394.5	2.0	344.7	5.8	59.4	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	378.0	2.0	332.4	4.8	69.2	
	3rd	386.5	2.0	338.7	5.3	63.9	
	Mean	386.3	2.0	338.6	5.3	64.2	
	STDER	4.8	0.0	3.6	0.3	2.8	
	1st	411.5	2.0	357.4	5.2	68.7	
	2nd	391.0	2.0	342.1	5.4	63.3	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	403.0	2.0	351.0	5.6	62.7	
	Mean	401.8	2.0	350.2	5.4	64.9	
	STDER	5.9	0.0	4.4	0.1	1.9	

Bead name : IL-1 alpha						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	543.0	2.0	454.5	6.2	73.3
	2nd	488.5	2.0	414.4	6.4	64.7
	Mean	515.8	2.0	434.4	6.3	69.0
	STDER	27.3	0.0	20.1	0.1	4.3

Table 39

Bead name : IL-1 beta/IL-1F2						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.5	10.0	NaN		
	2nd	-0.5	10.0	NaN		
	Mean	0.0	10.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	1.5	10.0		7.5	0.0
	2nd	1.5	10.0		7.4	0.0
	3rd	1.5	10.0		6.6	0.0

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	1.5	10.0	#DIV/0!	7.2	0.0	
	STDER	0.0	0.0	#DIV/0!	0.3	0.0	
PBMIC+LPS(5ug/ml)	1st	1906.0	10.0	7351.0	6.1	1205.1	
	2nd	1803.0	10.0	6969.3	5.8	1201.6	
	3rd	1657.5	10.0	6432.1	5.5	1169.5	
	Mean	1788.8	10.0	6917.5	5.8	1192.1	
	STDER	72.1	0.0	266.5	0.2	11.3	
PBMIC+YY101 0.01uM	1st	0.5	10.0		5.2	0.0	
	2nd	4.5	10.0	5.5	4.8	1.2	
	Mean	2.5	10.0	5.5	5.0	0.6	
	STDER	2.0	0.0	#DIV/0!	0.2	0.6	
PBMIC+YY101 0.1uM	1st	1.5	10.0		4.4	0.0	
	2nd	1.5	10.0		5.8	0.0	
	Mean	1.5	10.0	#DIV/0!	5.1	0.0	
	STDER	0.0	0.0	#DIV/0!	0.7	0.0	
PBMIC+YY101 1uM	1st	3.5	10.0		5.5	0.0	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	0.5	10.0		5.5	0.0	
	Mean	2.0	10.0	#DIV/0!	5.5	0.0	
	STDER	1.5	0.0	#DIV/0!	0.0	0.0	
	1st	23.5	10.0	122.9	6.4	19.2	
PBMC+YY101 10uM	2nd	2.5	10.0		6.1	0.0	
	Mean	13.0	10.0	122.9	6.3	9.6	
	STDER	10.5	0.0	#DIV/0!	0.2	9.6	
	1st	53.5	10.0	278.4	6.4	43.5	
PBMC+YY101 100uM	2nd	9.5	10.0	40.7	7.0	5.8	
	Mean	31.5	10.0	159.6	6.7	24.7	
	STDER	22.0	0.0	118.9	0.3	18.8	
	1st	2154.5	10.0	8278.0	6.2	1335.2	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	2155.5	10.0	8281.8	7.6	1089.7	
	Mean	2155.0	10.0	8279.9	6.9	1212.4	
	STDER	0.5	0.0	1.9	0.7	122.7	
	1st	2558.5	10.0	9809.5	5.2	1886.4	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	2145.5	10.0	8244.3	5.8	1421.4	
	Mean	2352.0	10.0	9026.9	5.5	1653.9	
	STDER	206.5	0.0	782.6	0.3	232.5	
	1st	2013.5	10.0	7750.8	6.6	1174.4	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	1975.5	10.0	7609.3	5.7	1335.0	
	Mean	1994.5	10.0	7680.1	6.2	1254.7	
	STDER	19.0	0.0	70.8	0.5	80.3	
	1st	1857.5	10.0	7171.1	4.8	1494.0	
PBMIC+LPS(5ug/ml)+Xiidra 1uM	2nd	1850.0	10.0	7143.3	4.4	1623.5	
	Mean	1853.8	10.0	7157.2	4.6	1558.7	
	STDER	3.8	0.0	13.9	0.2	64.7	
	1st	1858.0	10.0	7172.9	5.8	1236.7	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	1864.5	10.0	7197.0	6.4	1124.5	
	Mean	1861.3	10.0	7185.0	6.1	1180.6	
	STDER	3.3	0.0	12.0	0.3	56.1	
	1st	1437.5	10.0	5623.1	7.1	792.0	

Bead name : IL-1 beta/IL-1F2						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	1392.5	10.0	5457.9	5.8	941.0
	Mean	1415.0	10.0	5540.5	6.5	866.5
	STDER	22.5	0.0	82.6	0.7	74.5
PBMC+LPS(5ug/ml)+YY101 0.001uM	1st	2055.5	10.0	7907.5	5.7	1387.3
	2nd	2063.0	10.0	7935.5	7.1	1117.7
	3rd	1811.5	10.0	7000.7	6.6	1060.7
	Mean	1976.7	10.0	7614.6	6.5	1188.6
	STDER	82.6	0.0	307.0	0.4	100.7
PBMC+LPS(5ug/ml)+YY101 0.01uM	1st	2188.5	10.0	8405.7	6.4	1313.4
	2nd	2227.5	10.0	8552.3	6.0	1425.4
	3rd	2137.0	10.0	8212.4	6.1	1346.3
	Mean	2184.3	10.0	8390.1	6.2	1361.7
	STDER	26.2	0.0	98.4	0.1	33.2
PBMC+LPS(5ug/ml)+YY101 0.1uM	1st	2151.5	10.0	8266.8	6.2	1333.4
	2nd	2277.5	10.0	8740.8	5.2	1680.9
	3rd	2220.5	10.0	8526.0	6.2	1375.2

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	2216.5	10.0	8511.2	5.9	1463.1	
	STDER	36.4	0.0	137.0	0.3	109.6	
PBMC+LPS(5ug/ml)+YY101 1uM	1st	2138.5	10.0	8218.0	6.3	1304.4	
	2nd	2032.5	10.0	7821.7	7.1	1101.6	
	3rd	1939.5	10.0	7475.4	6.2	1205.7	
	Mean	2036.8	10.0	7838.4	6.5	1203.9	
	STDER	57.5	0.0	214.5	0.3	58.6	
PBMC+LPS(5ug/ml)+YY101 10uM	1st	2218.5	10.0	8518.5	6.0	1419.7	
	2nd	2297.5	10.0	8816.3	6.4	1377.5	
	3rd	2251.5	10.0	8642.7	7.6	1137.2	
	Mean	2255.8	10.0	8659.2	6.7	1311.5	
	STDER	22.9	0.0	86.4	0.5	88.0	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	3353.5	10.0	12944.3	6.3	2054.7	
	2nd	3064.5	10.0	11783.1	6.2	1900.5	
	3rd	3071.5	10.0	11811.0	5.0	2362.2	
	Mean	3163.2	10.0	12179.5	5.8	2105.8	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	95.2	0.0	382.5	0.4	135.7	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	1675.5	10.0	6498.5	4.5	1444.1	
	2nd	1688.0	10.0	6544.6	5.8	1128.4	
	3rd	1649.5	10.0	6402.7	5.8	1103.9	
	Mean	1671.0	10.0	6481.9	5.4	1225.5	
	STDER	11.3	0.0	41.8	0.4	109.5	
	1st	1721.5	10.0	6668.1	6.3	1058.4	
	2nd	1691.5	10.0	6557.5	6.2	1057.7	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	3rd	1669.5	10.0	6476.4	5.1	1269.9	
	Mean	1694.2	10.0	6567.3	5.9	1128.7	
	STDER	15.1	0.0	55.6	0.4	70.6	
	1st	1623.0	10.0	6305.1	6.6	955.3	
	2nd	1642.5	10.0	6376.9	5.0	1275.4	
	3rd	1636.5	10.0	6354.8	5.7	1114.9	
	Mean	1634.0	10.0	6345.6	5.8	1115.2	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	STDER	5.8	0.0	21.2	0.5	92.4	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	1690.5	10.0	6553.8	5.5	1191.6	
	2nd	1663.5	10.0	6454.2	4.8	1344.6	
	3rd	1744.5	10.0	6753.1	4.8	1406.9	
	Mean	1699.5	10.0	6587.0	5.0	1314.4	
	STDER	23.8	0.0	87.8	0.2	64.0	
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	1814.0	10.0	7010.0	5.4	1298.1	
	2nd	1752.5	10.0	6782.6	5.8	1169.4	
	3rd	1813.0	10.0	7006.3	4.7	1490.7	
	Mean	1793.2	10.0	6933.0	5.3	1319.4	
	STDER	20.3	0.0	75.2	0.3	93.4	
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	2213.0	10.0	8497.8	6.1	1393.1	
	2nd	2324.5	10.0	8918.4	6.1	1462.0	
	3rd	2242.5	10.0	8608.8	6.0	1434.8	
	Mean	2260.0	10.0	8675.0	6.1	1430.0	
	STDER	33.4	0.0	125.8	0.0	20.1	
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	1640.5	10.0	6369.5	4.4	1447.6	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1821.5	10.0	7037.7	6.0	1173.0	
	3rd	1673.5	10.0	6491.1	4.6	1411.1	
	Mean	1711.8	10.0	6632.8	5.0	1343.9	
	STDER	55.7	0.0	205.5	0.5	86.1	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	1657.5	10.0	6432.1	4.5	1429.4	
	2nd	1718.0	10.0	6655.2	6.6	1008.4	
	3rd	1708.5	10.0	6620.2	5.0	1324.0	
	Mean	1694.7	10.0	6569.2	5.4	1253.9	
	STDER	18.8	0.0	69.3	0.6	126.5	
	1st	1553.5	10.0	6049.3	5.0	1209.9	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	1644.5	10.0	6384.2	5.6	1140.0	
	3rd	1686.5	10.0	6539.0	5.6	1167.7	
	Mean	1628.2	10.0	6324.2	5.4	1172.5	
	STDER	39.3	0.0	144.5	0.2	20.3	
	1st	1622.5	10.0	6303.2	5.8	1086.8	
	2nd	1524.5	10.0	5942.7	4.8	1238.1	

Bead name : IL-1 beta/IL-1F2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	1632.5	10.0	6340.0	5.3	1196.2	
	Mean	1593.2	10.0	6195.3	5.3	1173.7	
	STDER	34.5	0.0	126.8	0.3	45.1	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	1644.0	10.0	6382.4	5.2	1227.4	
	2nd	1712.5	10.0	6634.9	5.4	1228.7	
	3rd	1717.5	10.0	6653.4	5.6	1188.1	
	Mean	1691.3	10.0	6556.9	5.4	1214.7	
	STDER	23.7	0.0	87.4	0.1	13.3	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	2278.5	10.0	8744.5	6.2	1410.4	
	2nd	1993.0	10.0	7674.4	6.4	1199.1	
	Mean	2135.8	10.0	8209.5	6.3	1304.8	
	STDER	142.8	0.0	535.0	0.1	105.6	

Table 40

Bead name : TIMP-1						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.0	2.0	NaN		
	2nd	0.0	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMC + 0.5% DMSO	1st	2918.0	2.0	4364.2	7.5	581.9
	2nd	3072.0	2.0	4558.5	7.4	616.0
	3rd	2936.5	2.0	4387.5	6.6	664.8
	Mean	2975.5	2.0	4436.7	7.2	620.9
	STDER	48.5	0.0	61.3	0.3	24.1
PBMC+LPS(5ug/ml)	1st	2018.0	2.0	3219.0	6.1	527.7
	2nd	2060.5	2.0	3273.7	5.8	564.4
	3rd	2159.5	2.0	3400.7	5.5	618.3
	Mean	2079.3	2.0	3297.8	5.8	570.1
	STDER	41.9	0.0	53.8	0.2	26.3
PBMC+YY101 0.01uM	1st	3456.0	2.0	5042.4	5.2	969.7

Bead name : T1MP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	3876.0	2.0	5571.4	4.8	1160.7	
	Mean	3666.0	2.0	5306.9	5.0	1065.2	
	STDER	210.0	0.0	264.5	0.2	95.5	
	1st	3084.0	2.0	4573.6	4.4	1039.5	
PBMC+YY101 0.1uM	2nd	3614.5	2.0	5242.0	5.8	903.8	
	Mean	3349.3	2.0	4907.8	5.1	971.6	
	STDER	265.3	0.0	334.2	0.7	67.8	
	1st	3546.0	2.0	5155.8	5.5	937.4	
PBMC+YY101 1uM	2nd	3491.5	2.0	5087.1	5.5	924.9	
	Mean	3518.8	2.0	5121.4	5.5	931.2	
	STDER	27.3	0.0	34.3	0.0	6.2	
	1st	5828.5	2.0	8049.3	6.4	1257.7	
PBMC+YY101 10uM	2nd	3505.0	2.0	5104.1	6.1	836.7	
	Mean	4666.8	2.0	6576.7	6.3	1047.2	
	STDER	1161.8	0.0	1472.6	0.2	210.5	
	1st	4917.0	2.0	6886.9	6.4	1076.1	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	4391.5	2.0	6221.7	7.0	888.8	
	Mean	4654.3	2.0	6554.3	6.7	982.4	
	STDER	262.8	0.0	332.6	0.3	93.6	
	1st	1751.5	2.0	2874.2	6.2	463.6	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	1703.0	2.0	2810.9	7.6	369.9	
	Mean	1727.3	2.0	2842.6	6.9	416.7	
	STDER	24.3	0.0	31.6	0.7	46.9	
	1st	1905.5	2.0	3073.9	5.2	591.1	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	1832.5	2.0	2979.4	5.8	513.7	
	Mean	1869.0	2.0	3026.7	5.5	552.4	
	STDER	36.5	0.0	47.3	0.3	38.7	
	1st	1721.0	2.0	2834.4	6.6	429.5	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	1669.0	2.0	2766.5	5.7	485.4	
	Mean	1695.0	2.0	2800.5	6.2	457.4	
	STDER	26.0	0.0	34.0	0.5	27.9	
	1st	1780.5	2.0	2911.9	4.8	606.6	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1783.0	2.0	2915.2	4.4	662.5	
	Mean	1781.8	2.0	2913.5	4.6	634.6	
	STDER	1.3	0.0	1.6	0.2	27.9	
	1st	1805.0	2.0	2943.7	5.8	507.5	
PBMC+LPS(5ug/ml)+Xiidra 10uM	2nd	1994.0	2.0	3188.1	6.4	498.1	
	Mean	1899.5	2.0	3065.9	6.1	502.8	
	STDER	94.5	0.0	122.2	0.3	4.7	
	1st	2052.5	2.0	3263.4	7.1	459.6	
PBMC+LPS(5ug/ml)+Xiidra 100uM	2nd	1981.5	2.0	3172.0	5.8	546.9	
	Mean	2017.0	2.0	3217.7	6.5	503.3	
	STDER	35.5	0.0	45.7	0.7	43.6	
	1st	1596.0	2.0	2670.8	5.7	468.6	
PBMC+LPS(5ug/ml)+YY101 0.001uM	2nd	1464.5	2.0	2497.3	7.1	351.7	
	3rd	1648.5	2.0	2739.7	6.6	415.1	
	Mean	1569.7	2.0	2635.9	6.5	411.8	
	STDER	54.7	0.0	72.1	0.4	33.8	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	1569.5	2.0	2636.0	6.4	411.9	
	2nd	1506.0	2.0	2552.3	6.0	425.4	
	3rd	1668.0	2.0	2765.2	6.1	453.3	
	Mean	1581.2	2.0	2651.1	6.2	430.2	
	STDER	47.1	0.0	61.9	0.1	12.2	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	1634.5	2.0	2721.3	6.2	438.9	
	2nd	1465.5	2.0	2498.6	5.2	480.5	
	3rd	1526.0	2.0	2578.7	6.2	415.9	
	Mean	1542.0	2.0	2599.6	5.9	445.1	
	STDER	49.4	0.0	65.1	0.3	18.9	
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	1553.5	2.0	2614.9	6.3	415.1	
	2nd	1585.0	2.0	2656.4	7.1	374.1	
	3rd	1654.5	2.0	2747.5	6.2	443.2	
	Mean	1597.7	2.0	2672.9	6.5	410.8	
	STDER	29.8	0.0	39.2	0.3	20.0	
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	1650.0	2.0	2741.7	6.0	456.9	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1695.5	2.0	2801.1	6.4	437.7	
	3rd	1495.5	2.0	2538.4	7.6	334.0	
	Mean	1613.7	2.0	2693.7	6.7	409.5	
	STDER	60.5	0.0	79.6	0.5	38.2	
	1st	2179.0	2.0	3425.7	6.3	543.8	
PBMC+LPS(5ug/ml)+YY101 100uM	2nd	2135.0	2.0	3369.3	6.2	543.4	
	3rd	1987.0	2.0	3179.1	5.0	635.8	
	Mean	2100.3	2.0	3324.7	5.8	574.3	
	STDER	58.1	0.0	74.6	0.4	30.7	
	1st	974.0	2.0	1831.6	4.5	407.0	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	2nd	852.5	2.0	1659.9	5.8	286.2	
	3rd	1013.5	2.0	1886.6	5.8	325.3	
	Mean	946.7	2.0	1792.7	5.4	339.5	
	STDER	48.4	0.0	68.3	0.4	35.6	
	1st	936.0	2.0	1778.3	6.3	282.3	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	959.5	2.0	1811.3	6.2	292.1	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	1132.0	2.0	2050.0	5.1	402.0	
	Mean	1009.2	2.0	1879.9	5.9	325.5	
	STDER	61.8	0.0	85.6	0.4	38.4	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	1008.5	2.0	1879.7	6.6	284.8	
	2nd	865.0	2.0	1677.8	5.0	335.6	
	3rd	1049.0	2.0	1935.9	5.7	339.6	
	Mean	974.2	2.0	1831.1	5.8	320.0	
	STDER	55.8	0.0	78.4	0.5	17.6	
	1st	1001.5	2.0	1869.9	5.5	340.0	
PBMC+LPS(5ug/ml)+YDE011 1uM	2nd	916.5	2.0	1750.8	4.8	364.7	
	3rd	918.5	2.0	1753.6	4.8	365.3	
	Mean	945.5	2.0	1791.4	5.0	356.7	
	STDER	28.0	0.0	39.3	0.2	8.4	
	1st	966.0	2.0	1820.4	5.4	337.1	
PBMC+LPS(5ug/ml)+YDE011 10uM	2nd	947.5	2.0	1794.4	5.8	309.4	
	3rd	873.5	2.0	1689.9	4.7	359.5	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	929.0	2.0	1768.2	5.3	335.3	
	STDER	28.3	0.0	39.9	0.3	14.5	
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	1336.5	2.0	2326.8	6.1	381.4	
	2nd	1184.5	2.0	2121.7	6.1	347.8	
	3rd	1172.0	2.0	2104.6	6.0	350.8	
	Mean	1231.0	2.0	2184.4	6.1	360.0	
	STDER	52.9	0.0	71.4	0.0	10.7	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	1st	1014.0	2.0	1887.3	4.4	428.9	
	2nd	1129.5	2.0	2046.6	6.0	341.1	
	3rd	1147.0	2.0	2070.5	4.6	450.1	
	Mean	1096.8	2.0	2001.5	5.0	406.7	
	STDER	41.7	0.0	57.5	0.5	33.4	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	1101.0	2.0	2007.5	4.5	446.1	
	2nd	1089.5	2.0	1991.7	6.6	301.8	
	3rd	1067.0	2.0	1960.7	5.0	392.1	
	Mean	1085.8	2.0	1986.7	5.4	380.0	

Bead name : TIMP-1							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	10.0	0.0	13.7	0.6	42.1	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	987.5	2.0	1850.4	5.0	370.1	
	2nd	893.5	2.0	1718.3	5.6	306.8	
	3rd	1037.5	2.0	1919.9	5.6	342.8	
	Mean	972.8	2.0	1829.5	5.4	339.9	
	STDER	42.2	0.0	59.2	0.2	18.3	
	1st	1043.5	2.0	1928.2	5.8	332.5	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	958.5	2.0	1809.9	4.8	377.1	
	3rd	935.0	2.0	1776.9	5.3	335.3	
	Mean	979.0	2.0	1838.3	5.3	348.3	
	STDER	33.0	0.0	46.0	0.3	14.4	
	1st	990.0	2.0	1853.9	5.2	356.5	
	2nd	1032.0	2.0	1912.3	5.4	354.1	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	929.0	2.0	1768.4	5.6	315.8	
	Mean	983.7	2.0	1844.9	5.4	342.1	
	STDER	29.9	0.0	41.8	0.1	13.2	

Bead name : T1MP-1						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	1277.5	2.0	2247.5	6.2	362.5
	2nd	1143.0	2.0	2065.1	6.4	322.7
	Mean	1210.3	2.0	2156.3	6.3	342.6
	STDER	67.3	0.0	91.2	0.1	19.9

Table 41

Bead name : GM-CSF						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	-1.5	2.0	NaN		
	2nd	1.5	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	1.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	1.5	2.0		7.5	0.0
	2nd	3.5	2.0		7.4	0.0
	3rd	2.5	2.0		6.6	0.0

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	2.5	2.0	#DIV/0!	7.2	0.0	
	STDER	0.6	0.0	#DIV/0!	0.3	0.0	
	1st	142.5	2.0	123.7	6.1	20.3	
	2nd	133.5	2.0	116.3	5.8	20.0	
	3rd	132.5	2.0	115.4	5.5	21.0	
	Mean	136.2	2.0	118.5	5.8	20.4	
	STDER	3.2	0.0	2.6	0.2	0.3	
	1st	8.5	2.0	5.3	5.2	1.0	
	2nd	9.5	2.0	6.3	4.8	1.3	
	Mean	9.0	2.0	5.8	5.0	1.2	
PBMC+YY101 0.01uM	STDER	0.5	0.0	0.5	0.2	0.2	
	1st	5.5	2.0	1.9	4.4	0.4	
	2nd	10.0	2.0	6.9	5.8	1.2	
	Mean	7.8	2.0	4.4	5.1	0.8	
PBMC+YY101 1uM	STDER	2.3	0.0	2.5	0.7	0.4	
	1st	8.0	2.0	4.7	5.5	0.9	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	7.5	2.0	4.2	5.5	0.8	
	Mean	7.8	2.0	4.4	5.5	0.8	
	STDER	0.3	0.0	0.3	0.0	0.1	
	1st	37.5	2.0	33.5	6.4	5.2	
PBMCMC+YY101 10uM	2nd	16.5	2.0	13.5	6.1	2.2	
	Mean	27.0	2.0	23.5	6.3	3.7	
	STDER	10.5	0.0	10.0	0.2	1.5	
	1st	17.5	2.0	14.5	6.4	2.3	
PBMCMC+YY101 100uM	2nd	10.5	2.0	7.4	7.0	1.1	
	Mean	14.0	2.0	11.0	6.7	1.7	
	STDER	3.5	0.0	3.6	0.3	0.6	
	1st	174.5	2.0	149.9	6.2	24.2	
PBMCMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	160.5	2.0	138.5	7.6	18.2	
	Mean	167.5	2.0	144.2	6.9	21.2	
	STDER	7.0	0.0	5.7	0.7	3.0	
	1st	193.5	2.0	165.2	5.2	31.8	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	189.5	2.0	162.0	5.8	27.9	
	Mean	191.5	2.0	163.6	5.5	29.9	
	STDER	2.0	0.0	1.6	0.3	1.9	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	1st	124.5	2.0	108.8	6.6	16.5	
	2nd	133.0	2.0	115.9	5.7	20.3	
	Mean	128.8	2.0	112.3	6.2	18.4	
	STDER	4.3	0.0	3.5	0.5	1.9	
PBMC+LPS(5ug/ml)+Xiidra 1uM	1st	125.5	2.0	109.6	4.8	22.8	
	2nd	109.0	2.0	95.8	4.4	21.8	
	Mean	117.3	2.0	102.7	4.6	22.3	
	STDER	8.3	0.0	6.9	0.2	0.5	
PBMC+LPS(5ug/ml)+Xiidra 10uM	1st	97.5	2.0	86.1	5.8	14.9	
	2nd	103.5	2.0	91.2	6.4	14.3	
	Mean	100.5	2.0	88.7	6.1	14.6	
	STDER	3.0	0.0	2.5	0.3	0.3	
PBMC+LPS(5ug/ml)+Xiidra 100uM	1st	96.5	2.0	85.3	7.1	12.0	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	98.5	2.0	87.0	5.8	15.0	
	Mean	97.5	2.0	86.1	6.5	13.5	
	STDER	1.0	0.0	0.8	0.7	1.5	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	161.0	2.0	138.9	5.7	24.4	
	2nd	187.5	2.0	160.4	7.1	22.6	
	3rd	212.0	2.0	180.1	6.6	27.3	
	Mean	186.8	2.0	159.8	6.5	24.7	
	STDER	14.7	0.0	11.9	0.4	1.4	
	1st	192.5	2.0	164.4	6.4	25.7	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	2nd	186.5	2.0	159.6	6.0	26.6	
	3rd	178.5	2.0	153.1	6.1	25.1	
	Mean	185.8	2.0	159.0	6.2	25.8	
	STDER	4.1	0.0	3.3	0.1	0.4	
	1st	175.5	2.0	150.7	6.2	24.3	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	2nd	157.0	2.0	135.6	5.2	26.1	
	3rd	153.5	2.0	132.7	6.2	21.4	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	162.0	2.0	139.7	5.9	23.9	
	STDER	6.8	0.0	5.6	0.3	1.4	
	1st	159.0	2.0	137.2	6.3	21.8	
	2nd	154.0	2.0	133.1	7.1	18.8	
	3rd	178.5	2.0	153.1	6.2	24.7	
	Mean	163.8	2.0	141.2	6.5	21.7	
	STDER	7.5	0.0	6.1	0.3	1.7	
	1st	178.5	2.0	153.1	6.0	25.5	
	2nd	167.0	2.0	143.8	6.4	22.5	
	3rd	171.5	2.0	147.4	7.6	19.4	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	172.3	2.0	148.1	6.7	22.5	
	STDER	3.3	0.0	2.7	0.5	1.8	
	1st	287.0	2.0	239.6	6.3	38.0	
	2nd	257.5	2.0	216.3	6.2	34.9	
	3rd	257.5	2.0	216.3	5.0	43.3	
	Mean	267.3	2.0	224.0	5.8	38.7	
PBMC+LPS(5ug/ml)+YY101 100uM	Mean	267.3	2.0	224.0	5.8	38.7	
	STDER	3.3	0.0	2.7	0.5	1.8	
	1st	287.0	2.0	239.6	6.3	38.0	
	2nd	257.5	2.0	216.3	6.2	34.9	
	3rd	257.5	2.0	216.3	5.0	43.3	
	Mean	267.3	2.0	224.0	5.8	38.7	
	STDER	3.3	0.0	2.7	0.5	1.8	
	1st	287.0	2.0	239.6	6.3	38.0	
	2nd	257.5	2.0	216.3	6.2	34.9	
	3rd	257.5	2.0	216.3	5.0	43.3	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	9.8	0.0	7.8	0.4	2.4	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	105.0	2.0	92.5	4.5	20.6	
	2nd	109.5	2.0	96.3	5.8	16.6	
	3rd	116.5	2.0	102.1	5.8	17.6	
	Mean	110.3	2.0	97.0	5.4	18.3	
	STDER	3.3	0.0	2.8	0.4	1.2	
	1st	102.5	2.0	90.4	6.3	14.3	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	123.5	2.0	108.0	6.2	17.4	
	3rd	127.5	2.0	111.3	5.1	21.8	
	Mean	117.8	2.0	103.2	5.9	17.9	
	STDER	7.8	0.0	6.5	0.4	2.2	
	1st	114.5	2.0	100.5	6.6	15.2	
	2nd	103.0	2.0	90.8	5.0	18.2	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	108.5	2.0	95.4	5.7	16.7	
	Mean	108.7	2.0	95.6	5.8	16.7	
	STDER	3.3	0.0	2.8	0.5	0.8	

Bead name : GM-CSF						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	109.5	2.0	96.3	5.5	17.5
	2nd	105.0	2.0	92.5	4.8	19.3
	3rd	105.5	2.0	92.9	4.8	19.4
	Mean	106.7	2.0	93.9	5.0	18.7
	STDER	1.4	0.0	1.2	0.2	0.6
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	117.5	2.0	103.0	5.4	19.1
	2nd	105.5	2.0	92.9	5.8	16.0
	3rd	112.5	2.0	98.8	4.7	21.0
	Mean	111.8	2.0	98.2	5.3	18.7
	STDER	3.5	0.0	2.9	0.3	1.5
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	173.5	2.0	149.0	6.1	24.4
	2nd	147.5	2.0	127.8	6.1	21.0
	3rd	150.5	2.0	130.3	6.0	21.7
	Mean	157.2	2.0	135.7	6.1	22.4
	STDER	8.2	0.0	6.7	0.0	1.1
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	96.5	2.0	85.3	4.4	19.4

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	118.5	2.0	103.8	6.0	17.3	
	3rd	115.5	2.0	101.3	4.6	22.0	
	Mean	110.2	2.0	96.8	5.0	19.6	
	STDER	6.9	0.0	5.8	0.5	1.4	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	107.5	2.0	94.6	4.5	21.0	
	2nd	97.5	2.0	86.1	6.6	13.1	
	3rd	111.5	2.0	97.9	5.0	19.6	
	Mean	105.5	2.0	92.9	5.4	17.9	
	STDER	4.2	0.0	3.5	0.6	2.5	
	1st	99.5	2.0	87.8	5.0	17.6	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	103.5	2.0	91.2	5.6	16.3	
	3rd	112.0	2.0	98.4	5.6	17.6	
	Mean	105.0	2.0	92.5	5.4	17.1	
	STDER	3.7	0.0	3.1	0.2	0.4	
	1st	101.5	2.0	89.5	5.8	15.4	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	104.5	2.0	92.1	4.8	19.2	

Bead name : GM-CSF							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	106.0	2.0	93.3	5.3	17.6	
	Mean	104.0	2.0	91.6	5.3	17.4	
	STDER	1.3	0.0	1.1	0.3	1.1	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	116.5	2.0	102.1	5.2	19.6	
	2nd	109.5	2.0	96.3	5.4	17.8	
	3rd	119.5	2.0	104.6	5.6	18.7	
	Mean	115.2	2.0	101.0	5.4	18.7	
	STDER	3.0	0.0	2.5	0.1	0.5	
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	162.5	2.0	140.1	6.2	22.6	
	2nd	155.5	2.0	134.4	6.4	21.0	
	Mean	159.0	2.0	137.2	6.3	21.8	
	STDER	3.5	0.0	2.9	0.1	0.8	

Table 42

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.0	2.0	NaN			
	2nd	0.0	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	11.5	2.0	2.3	7.5	0.3	
	2nd	14.5	2.0	4.4	7.4	0.6	
	3rd	12.0	2.0	2.6	6.6	0.4	
	Mean	12.7	2.0	3.1	7.2	0.4	
	STDER	0.9	0.0	0.7	0.3	0.1	
PBMC+LPS(5ug/ml)	1st	26.0	2.0	12.5	6.1	2.1	
	2nd	23.5	2.0	10.8	5.8	1.9	
	3rd	26.0	2.0	12.5	5.5	2.3	
	Mean	25.2	2.0	11.9	5.8	2.1	
	STDER	0.8	0.0	0.6	0.2	0.1	
PBMC+YY101 0.01uM	1st	92.5	2.0	56.9	5.2	10.9	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	94.0	2.0	57.9	4.8	12.1	
	Mean	93.3	2.0	57.4	5.0	11.5	
	STDER	0.8	0.0	0.5	0.2	0.6	
	1st	75.0	2.0	45.4	4.4	10.3	
PBMCMC+YY101 0.1uM	2nd	117.5	2.0	73.2	5.8	12.6	
	Mean	96.3	2.0	59.3	5.1	11.5	
	STDER	21.3	0.0	13.9	0.7	1.1	
	1st	97.0	2.0	59.8	5.5	10.9	
PBMCMC+YY101 1uM	2nd	106.0	2.0	65.7	5.5	11.9	
	Mean	101.5	2.0	62.8	5.5	11.4	
	STDER	4.5	0.0	2.9	0.0	0.5	
	1st	112.0	2.0	69.6	6.4	10.9	
PBMCMC+YY101 10uM	2nd	115.0	2.0	71.5	6.1	11.7	
	Mean	113.5	2.0	70.6	6.3	11.3	
	STDER	1.5	0.0	1.0	0.2	0.4	
	1st	27.0	2.0	13.2	6.4	2.1	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	31.0	2.0	16.0	7.0	2.3	
	Mean	29.0	2.0	14.6	6.7	2.2	
	STDER	2.0	0.0	1.4	0.3	0.1	
	1st	25.0	2.0	11.8	6.2	1.9	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	16.0	2.0	5.5	7.6	0.7	
	Mean	20.5	2.0	8.7	6.9	1.3	
	STDER	4.5	0.0	3.2	0.7	0.6	
	1st	14.0	2.0	4.1	5.2	0.8	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	9.0	2.0	0.4	5.8	0.1	
	Mean	11.5	2.0	2.2	5.5	0.4	
	STDER	2.5	0.0	1.9	0.3	0.4	
	1st	6.0	2.0		6.6	0.0	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	10.0	2.0	1.1	5.7	0.2	
	Mean	8.0	2.0	1.1	6.2	0.1	
	STDER	2.0	0.0	#DIV/0!	0.5	0.1	
	1st	6.0	2.0		4.8	0.0	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	3.0	2.0		4.4	0.0	
	Mean	4.5	2.0	#DIV/0!	4.6	0.0	
	STDER	1.5	0.0	#DIV/0!	0.2	0.0	
	1st	5.0	2.0		5.8	0.0	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	4.0	2.0		6.4	0.0	
	Mean	4.5	2.0	#DIV/0!	6.1	0.0	
	STDER	0.5	0.0	#DIV/0!	0.3	0.0	
	1st	2.0	2.0		7.1	0.0	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	3.0	2.0		5.8	0.0	
	Mean	2.5	2.0	#DIV/0!	6.5	0.0	
	STDER	0.5	0.0	#DIV/0!	0.7	0.0	
	1st	13.0	2.0		5.7	0.6	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	19.0	2.0		7.1	1.1	
	3rd	17.0	2.0		6.6	0.9	
	Mean	16.3	2.0		6.5	0.9	
	STDER	1.8	0.0		0.4	0.1	

Bead name : IL-2						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	18.0	2.0	6.9	6.4	1.1
	2nd	25.0	2.0	11.8	6.0	2.0
	3rd	18.0	2.0	6.9	6.1	1.1
	Mean	20.3	2.0	8.6	6.2	1.4
	STDER	2.3	0.0	1.6	0.1	0.3
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	8.0	2.0		6.2	0.0
	2nd	3.0	2.0		5.2	0.0
	3rd	8.0	2.0		6.2	0.0
	Mean	6.3	2.0	#DIV/0!	5.9	0.0
	STDER	1.7	0.0	#DIV/0!	0.3	0.0
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	15.5	2.0	5.2	6.3	0.8
	2nd	13.5	2.0	3.7	7.1	0.5
	3rd	12.0	2.0	2.6	6.2	0.4
	Mean	13.7	2.0	3.8	6.5	0.6
	STDER	1.0	0.0	0.7	0.3	0.1
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	19.5	2.0	8.0	6.0	1.3

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	14.0	2.0	4.1	6.4	0.6	
	3rd	13.5	2.0	3.7	7.6	0.5	
	Mean	15.7	2.0	5.3	6.7	0.8	
	STDER	1.9	0.0	1.4	0.5	0.3	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	11.0	2.0	1.9	6.3	0.3	
	2nd	9.0	2.0	0.4	6.2	0.1	
	3rd	7.0	2.0		5.0	0.0	
	Mean	9.0	2.0	1.1	5.8	0.1	
	STDER	1.2	0.0	0.8	0.4	0.1	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	4.0	2.0		4.5	0.0	
	2nd	4.0	2.0		5.8	0.0	
	3rd	4.0	2.0		5.8	0.0	
	Mean	4.0	2.0	#DIV/0!	5.4	0.0	
	STDER	0.0	0.0	#DIV/0!	0.4	0.0	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	1st	5.0	2.0		6.3	0.0	
	2nd	5.0	2.0		6.2	0.0	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	5.0	2.0		5.1	0.0	
	Mean	5.0	2.0	#DIV/0!	5.9	0.0	
	STDER	0.0	0.0	#DIV/0!	0.4	0.0	
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	7.0	2.0		6.6	0.0	
	2nd	8.0	2.0		5.0	0.0	
	3rd	5.0	2.0		5.7	0.0	
	Mean	6.7	2.0	#DIV/0!	5.8	0.0	
	STDER	0.9	0.0	#DIV/0!	0.5	0.0	
	1st	6.0	2.0		5.5	0.0	
PBMIC+LPS(5ug/ml)+YDE011 1uM	2nd	4.0	2.0		4.8	0.0	
	3rd	6.0	2.0		4.8	0.0	
	Mean	5.3	2.0	#DIV/0!	5.0	0.0	
	STDER	0.7	0.0	#DIV/0!	0.2	0.0	
	1st	6.0	2.0		5.4	0.0	
	2nd	5.0	2.0		5.8	0.0	
PBMIC+LPS(5ug/ml)+YDE011 10uM	3rd	5.0	2.0		4.7	0.0	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	5.3	2.0	#DIV/0!	5.3	0.0	
	STDER	0.3	0.0	#DIV/0!	0.3	0.0	
	1st	4.0	2.0		6.1	0.0	
	2nd	2.0	2.0		6.1	0.0	
	3rd	6.0	2.0		6.0	0.0	
	Mean	4.0	2.0	#DIV/0!	6.1	0.0	
	STDER	1.2	0.0	#DIV/0!	0.0	0.0	
	1st	3.0	2.0		4.4	0.0	
	2nd	8.0	2.0		6.0	0.0	
	3rd	8.0	2.0		4.6	0.0	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	6.3	2.0	#DIV/0!	5.0	0.0	
	STDER	1.7	0.0	#DIV/0!	0.5	0.0	
	1st	6.0	2.0		4.5	0.0	
	2nd	4.0	2.0		6.6	0.0	
	3rd	4.0	2.0		5.0	0.0	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	4.7	2.0	#DIV/0!	5.4	0.0	

Bead name : IL-2							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	STDER	0.7	0.0	#DIV/0!	0.6	0.0	
	1st	6.0	2.0		5.0	0.0	
	2nd	3.0	2.0		5.6	0.0	
	3rd	8.0	2.0		5.6	0.0	
	Mean	5.7	2.0	#DIV/0!	5.4	0.0	
	STDER	1.5	0.0	#DIV/0!	0.2	0.0	
	1st	3.0	2.0		5.8	0.0	
	2nd	2.0	2.0		4.8	0.0	
PBMC+LPS(5ug/ml)+YDE043 1uM	3rd	4.0	2.0		5.3	0.0	
	Mean	3.0	2.0	#DIV/0!	5.3	0.0	
	STDER	0.6	0.0	#DIV/0!	0.3	0.0	
	1st	3.0	2.0		5.2	0.0	
	2nd	2.0	2.0		5.4	0.0	
	3rd	5.0	2.0		5.6	0.0	
	Mean	3.3	2.0	#DIV/0!	5.4	0.0	
	STDER	0.9	0.0	#DIV/0!	0.1	0.0	
PBMC+LPS(5ug/ml)+YDE043 10uM							

Bead name : IL-2						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	2.0	2.0		6.2	0.0
	2nd	2.0	2.0		6.4	0.0
	Mean	2.0	2.0	#DIV/0!	6.3	0.0
	STDER	0.0	0.0	#DIV/0!	0.1	0.0

Table 43

Bead name : IL-17A						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	0.5	2.0	NaN		
	2nd	-0.5	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	0.5	2.0	1.0	7.5	0.1
	2nd	2.5	2.0	4.3	7.4	0.6
	3rd	1.5	2.0	2.7	6.6	0.4

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)	Mean	1.5	2.0	2.7	7.2	0.4	
	STDER	0.6	0.0	1.0	0.3	0.1	
	1st	4.5	2.0	7.5	6.1	1.2	
	2nd	3.5	2.0	6.0	5.8	1.0	
	3rd	4.5	2.0	7.5	5.5	1.4	
	Mean	4.2	2.0	7.0	5.8	1.2	
	STDER	0.3	0.0	0.5	0.2	0.1	
	1st	4.5	2.0	7.5	5.2	1.5	
	2nd	4.5	2.0	7.5	4.8	1.6	
	Mean	4.5	2.0	7.5	5.0	1.5	
PBMC+YY101 0.01uM	STDER	0.0	0.0	0.0	0.2	0.1	
	1st	2.5	2.0	4.3	4.4	1.0	
	2nd	7.5	2.0	12.2	5.8	2.1	
	Mean	5.0	2.0	8.3	5.1	1.5	
	STDER	2.5	0.0	3.9	0.7	0.6	
	1st	3.5	2.0	6.0	5.5	1.1	
PBMC+YY101 0.1uM							
PBMC+YY101 1uM							

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	2.5	2.0	4.3	5.5	0.8	
	Mean	3.0	2.0	5.2	5.5	0.9	
	STDER	0.5	0.0	0.8	0.0	0.1	
PBMIC+YY101 10uM	1st	14.5	2.0	22.9	6.4	3.6	
	2nd	8.5	2.0	13.8	6.1	2.3	
	Mean	11.5	2.0	18.3	6.3	2.9	
	STDER	3.0	0.0	4.6	0.2	0.7	
PBMIC+YY101 100uM	1st	1.5	2.0	2.7	6.4	0.4	
	2nd	2.5	2.0	4.3	7.0	0.6	
	Mean	2.0	2.0	3.5	6.7	0.5	
	STDER	0.5	0.0	0.8	0.3	0.1	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	1st	7.5	2.0	12.2	6.2	2.0	
	2nd	2.5	2.0	4.3	7.6	0.6	
	Mean	5.0	2.0	8.3	6.9	1.3	
	STDER	2.5	0.0	3.9	0.7	0.7	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	1st	3.5	2.0	6.0	5.2	1.1	

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	3.5	2.0	6.0	5.8	1.0	
	Mean	3.5	2.0	6.0	5.5	1.1	
	STDER	0.0	0.0	0.0	0.3	0.1	
	1st	3.5	2.0	6.0	6.6	0.9	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	2.5	2.0	4.3	5.7	0.8	
	Mean	3.0	2.0	5.2	6.2	0.8	
	STDER	0.5	0.0	0.8	0.5	0.1	
	1st	0.5	2.0	1.0	4.8	0.2	
PBMC+LPS(5ug/ml)+Xiidra 1uM	2nd	1.0	2.0	1.9	4.4	0.4	
	Mean	0.8	2.0	1.5	4.6	0.3	
	STDER	0.3	0.0	0.4	0.2	0.1	
	1st	1.5	2.0	2.7	5.8	0.5	
PBMC+LPS(5ug/ml)+Xiidra 10uM	2nd	1.5	2.0	2.7	6.4	0.4	
	Mean	1.5	2.0	2.7	6.1	0.4	
	STDER	0.0	0.0	0.0	0.3	0.0	
	1st	1.5	2.0	2.7	7.1	0.4	

Bead name : IL-17A						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
	2nd	1.5	2.0	2.7	5.8	0.5
	Mean	1.5	2.0	2.7	6.5	0.4
	STDER	0.0	0.0	0.0	0.7	0.0
PBMC+LPS(5ug/ml)+YY101 0.001uM	1st	2.5	2.0	4.3	5.7	0.8
	2nd	2.5	2.0	4.3	7.1	0.6
	3rd	1.5	2.0	2.7	6.6	0.4
	Mean	2.2	2.0	3.8	6.5	0.6
	STDER	0.3	0.0	0.5	0.4	0.1
	1st	3.5	2.0	6.0	6.4	0.9
PBMC+LPS(5ug/ml)+YY101 0.01uM	2nd	3.5	2.0	6.0	6.0	1.0
	3rd	1.5	2.0	2.7	6.1	0.4
	Mean	2.8	2.0	4.9	6.2	0.8
	STDER	0.7	0.0	1.1	0.1	0.2
	1st	3.5	2.0	6.0	6.2	1.0
	2nd	0.5	2.0	1.0	5.2	0.2
PBMC+LPS(5ug/ml)+YY101 0.1uM	3rd	3.5	2.0	6.0	6.2	1.0

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 1uM	Mean	2.5	2.0	4.3	5.9	0.7	
	STDER	1.0	0.0	1.6	0.3	0.3	
	1st	2.5	2.0	4.3	6.3	0.7	
	2nd	2.5	2.0	4.3	7.1	0.6	
	3rd	4.5	2.0	7.5	6.2	1.2	
	Mean	3.2	2.0	5.4	6.5	0.8	
	STDER	0.7	0.0	1.1	0.3	0.2	
	1st	2.5	2.0	4.3	6.0	0.7	
	2nd	1.5	2.0	2.7	6.4	0.4	
	3rd	1.5	2.0	2.7	7.6	0.4	
PBMC+LPS(5ug/ml)+YY101 10uM	Mean	1.8	2.0	3.3	6.7	0.5	
	STDER	0.3	0.0	0.5	0.5	0.1	
	1st	0.5	2.0	1.0	6.3	0.2	
	2nd	1.5	2.0	2.7	6.2	0.4	
	3rd	0.5	2.0	1.0	5.0	0.2	
	Mean	0.8	2.0	1.6	5.8	0.3	
PBMC+LPS(5ug/ml)+YY101 100uM	Mean	0.5	2.0	1.0	6.3	0.2	
	STDER	0.3	0.0	0.5	0.5	0.1	
	1st	0.5	2.0	1.0	6.3	0.2	
	2nd	1.5	2.0	2.7	6.2	0.4	
	3rd	0.5	2.0	1.0	5.0	0.2	
	Mean	0.8	2.0	1.6	5.8	0.3	

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	0.3	0.0	0.6	0.4	0.1	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	1st	2.5	2.0	4.3	4.5	1.0	
	2nd	1.5	2.0	2.7	5.8	0.5	
	3rd	1.5	2.0	2.7	5.8	0.5	
	Mean	1.8	2.0	3.3	5.4	0.6	
	STDER	0.3	0.0	0.5	0.4	0.2	
	1st	0.5	2.0	1.0	6.3	0.2	
PBMC+LPS(5ug/ml)+YDE011 0.01uM	2nd	0.5	2.0	1.0	6.2	0.2	
	3rd	2.5	2.0	4.3	5.1	0.9	
	Mean	1.2	2.0	2.1	5.9	0.4	
	STDER	0.7	0.0	1.1	0.4	0.2	
	1st	1.5	2.0	2.7	6.6	0.4	
	2nd	0.5	2.0	1.0	5.0	0.2	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	0.5	2.0	1.0	5.7	0.2	
	Mean	0.8	2.0	1.6	5.8	0.3	
	STDER	0.3	0.0	0.6	0.5	0.1	

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	2.5	2.0	4.3	5.5	0.8	
	2nd	2.5	2.0	4.3	4.8	0.9	
	3rd	1.5	2.0	2.7	4.8	0.6	
	Mean	2.2	2.0	3.8	5.0	0.8	
	STDER	0.3	0.0	0.5	0.2	0.1	
PBMIC+LPS(5ug/ml)+YDE011 10uM	1st	1.5	2.0	2.7	5.4	0.5	
	2nd	1.5	2.0	2.7	5.8	0.5	
	3rd	-0.5	2.0		4.7	0.0	
	Mean	0.8	2.0	2.7	5.3	0.3	
	STDER	0.7	0.0	0.0	0.3	0.2	
PBMIC+LPS(5ug/ml)+YDE011 100uM	1st	0.5	2.0	1.0	6.1	0.2	
	2nd	0.5	2.0	1.0	6.1	0.2	
	3rd	-0.5	2.0		6.0	0.0	
	Mean	0.2	2.0	1.0	6.1	0.1	
	STDER	0.3	0.0	0.0	0.0	0.1	
PBMIC+LPS(5ug/ml)+YDE043 0.001uM	1st	0.5	2.0	1.0	4.4	0.2	

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	-0.5	2.0		6.0	0.0	
	3rd	0.5	2.0	1.0	4.6	0.2	
	Mean	0.2	2.0	1.0	5.0	0.2	
	STDER	0.3	0.0	0.0	0.5	0.1	
PBMIC+LPS(5ug/ml)+YDE043 0.01uM	1st	0.5	2.0	1.0	4.5	0.2	
	2nd	0.5	2.0	1.0	6.6	0.2	
	3rd	0.5	2.0	1.0	5.0	0.2	
	Mean	0.5	2.0	1.0	5.4	0.2	
	STDER	0.0	0.0	0.0	0.6	0.0	
PBMIC+LPS(5ug/ml)+YDE043 0.1uM	1st	1.5	2.0	2.7	5.0	0.5	
	2nd	0.5	2.0	1.0	5.6	0.2	
	3rd	0.5	2.0	1.0	5.6	0.2	
	Mean	0.8	2.0	1.6	5.4	0.3	
PBMIC+LPS(5ug/ml)+YDE043 1uM	STDER	0.3	0.0	0.6	0.2	0.1	
	1st	0.5	2.0	1.0	5.8	0.2	
	2nd	-0.5	2.0		4.8	0.0	

Bead name : IL-17A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	1.5	2.0	2.7	5.3	0.5	
	Mean	0.5	2.0	1.9	5.3	0.2	
	STDER	0.6	0.0	0.8	0.3	0.2	
	1st	0.0	2.0	0.1	5.2	0.0	
PBMIC+LPS(5ug/ml)+YDE043 10uM	2nd	1.5	2.0	2.7	5.4	0.5	
	3rd	0.5	2.0	1.0	5.6	0.2	
	Mean	0.7	2.0	1.3	5.4	0.2	
	STDER	0.4	0.0	0.8	0.1	0.1	
	1st	-0.5	2.0		6.2	0.0	
	2nd	-0.5	2.0		6.4	0.0	
	Mean	-0.5	2.0	#DIV/0!	6.3	0.0	
	STDER	0.0	0.0	#DIV/0!	0.1	0.0	
PBMIC+LPS(5ug/ml)+YDE043 100uM							

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Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	0.0	2.0	NaN			
	2nd	0.0	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.0	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	-1.0	2.0	7.7	7.5	1.0	
	2nd	-0.5	2.0	13.6	7.4	1.8	
	3rd	-1.0	2.0	7.7	6.6	1.2	
	Mean	-0.8	2.0	9.7	7.2	1.3	
	STDER	0.2	0.0	2.0	0.3	0.3	
PBMC+LPS(5ug/ml)	1st	2.0	2.0	33.2	6.1	5.4	
	2nd	3.0	2.0	39.4	5.8	6.8	
	3rd	2.0	2.0	33.2	5.5	6.0	
	Mean	2.3	2.0	35.3	5.8	6.1	
	STDER	0.3	0.0	2.1	0.2	0.4	
PBMC+YY101 0.01uM	1st	0.5	2.0	22.6	5.2	4.3	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	2.0	2.0	33.2	4.8	6.9	
	Mean	1.3	2.0	27.9	5.0	5.6	
	STDER	0.8	0.0	5.3	0.2	1.3	
PBMCMC+YY101 0.1uM	1st	1.0	2.0	26.4	4.4	6.0	
	2nd	2.0	2.0	33.2	5.8	5.7	
	Mean	1.5	2.0	29.8	5.1	5.9	
	STDER	0.5	0.0	3.4	0.7	0.1	
PBMCMC+YY101 1uM	1st	0.0	2.0	18.4	5.5	3.3	
	2nd	0.0	2.0	18.4	5.5	3.3	
	Mean	0.0	2.0	18.4	5.5	3.3	
	STDER	0.0	0.0	0.0	0.0	0.0	
PBMCMC+YY101 10uM	1st	6.0	2.0	55.5	6.4	8.7	
	2nd	3.0	2.0	39.4	6.1	6.5	
	Mean	4.5	2.0	47.4	6.3	7.6	
	STDER	1.5	0.0	8.1	0.2	1.1	
PBMCMC+YY101 100uM	1st	-1.0	2.0	7.7	6.4	1.2	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	0.0	2.0	18.4	7.0	2.6	
	Mean	-0.5	2.0	13.0	6.7	1.9	
	STDER	0.5	0.0	5.3	0.3	0.7	
	1st	2.0	2.0	33.2	6.2	5.4	
PBMIC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	2.0	2.0	33.2	7.6	4.4	
	Mean	2.0	2.0	33.2	6.9	4.9	
	STDER	0.0	0.0	0.0	0.7	0.5	
	1st	2.0	2.0	33.2	5.2	6.4	
PBMIC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	3.0	2.0	39.4	5.8	6.8	
	Mean	2.5	2.0	36.3	5.5	6.6	
	STDER	0.5	0.0	3.1	0.3	0.2	
	1st	1.0	2.0	26.4	6.6	4.0	
PBMIC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	0.0	2.0	18.4	5.7	3.2	
	Mean	0.5	2.0	22.4	6.2	3.6	
	STDER	0.5	0.0	4.0	0.5	0.4	
	1st	2.0	2.0	33.2	4.8	6.9	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1.0	2.0	26.4	4.4	6.0	
	Mean	1.5	2.0	29.8	4.6	6.5	
	STDER	0.5	0.0	3.4	0.2	0.5	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	1st	2.0	2.0	33.2	5.8	5.7	
	2nd	1.0	2.0	26.4	6.4	4.1	
	Mean	1.5	2.0	29.8	6.1	4.9	
	STDER	0.5	0.0	3.4	0.3	0.8	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	1st	0.0	2.0	18.4	7.1	2.6	
	2nd	2.0	2.0	33.2	5.8	5.7	
	Mean	1.0	2.0	25.8	6.5	4.2	
	STDER	1.0	0.0	7.4	0.7	1.6	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	1st	0.0	2.0	18.4	5.7	3.2	
	2nd	2.0	2.0	33.2	7.1	4.7	
	3rd	1.0	2.0	26.4	6.6	4.0	
	Mean	1.0	2.0	26.0	6.5	4.0	
	STDER	0.6	0.0	4.3	0.4	0.4	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	2.0	2.0	33.2	6.4	5.2	
	2nd	2.0	2.0	33.2	6.0	5.5	
	3rd	2.0	2.0	33.2	6.1	5.4	
	Mean	2.0	2.0	33.2	6.2	5.4	
	STDER	0.0	0.0	0.0	0.1	0.1	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	3.0	2.0	39.4	6.2	6.4	
	2nd	4.0	2.0	45.1	5.2	8.7	
	3rd	2.0	2.0	33.2	6.2	5.4	
	Mean	3.0	2.0	39.2	5.9	6.8	
	STDER	0.6	0.0	3.4	0.3	1.0	
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	2.0	2.0	33.2	6.3	5.3	
	2nd	2.0	2.0	33.2	7.1	4.7	
	3rd	2.0	2.0	33.2	6.2	5.4	
	Mean	2.0	2.0	33.2	6.5	5.1	
	STDER	0.0	0.0	0.0	0.3	0.2	
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	1.0	2.0	26.4	6.0	4.4	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1.0	2.0	26.4	6.4	4.1	
	3rd	0.0	2.0	18.4	7.6	2.4	
	Mean	0.7	2.0	23.7	6.7	3.6	
	STDER	0.3	0.0	2.7	0.5	0.6	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	0.0	2.0	18.4	6.3	2.9	
	2nd	0.0	2.0	18.4	6.2	3.0	
	3rd	-1.0	2.0	7.7	5.0	1.5	
	Mean	-0.3	2.0	14.8	5.8	2.5	
	STDER	0.3	0.0	3.6	0.4	0.5	
	1st	0.0	2.0	18.4	4.5	4.1	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	2nd	-1.0	2.0	7.7	5.8	1.3	
	3rd	-0.5	2.0	13.6	5.8	2.3	
	Mean	-0.5	2.0	13.2	5.4	2.6	
	STDER	0.3	0.0	3.1	0.4	0.8	
	1st	0.0	2.0	18.4	6.3	2.9	
	2nd	1.0	2.0	26.4	6.2	4.3	
PBMC+LPS(5ug/ml)+YDE011 0.01uM							

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	3rd	1.0	2.0	26.4	5.1	5.2	
	Mean	0.7	2.0	23.7	5.9	4.1	
	STDER	0.3	0.0	2.7	0.4	0.7	
	1st	0.0	2.0	18.4	6.6	2.8	
	2nd	-2.0	2.0		5.0	0.0	
	3rd	1.0	2.0	26.4	5.7	4.6	
	Mean	-0.3	2.0	22.4	5.8	2.5	
	STDER	0.9	0.0	4.0	0.5	1.3	
	1st	0.0	2.0	18.4	5.5	3.3	
PBMC+LPS(5ug/ml)+YDE011 1uM	2nd	-1.5	2.0		4.8	0.0	
	3rd	0.0	2.0	18.4	4.8	3.8	
	Mean	-0.5	2.0	18.4	5.0	2.4	
	STDER	0.5	0.0	0.0	0.2	1.2	
	1st	0.0	2.0	18.4	5.4	3.4	
	2nd	-0.5	2.0	13.6	5.8	2.3	
	3rd	0.0	2.0	18.4	4.7	3.9	
PBMC+LPS(5ug/ml)+YDE011 10uM							

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	-0.2	2.0	16.8	5.3	3.2	
	STDER	0.2	0.0	1.6	0.3	0.5	
	1st	-1.0	2.0	7.7	6.1	1.3	
	2nd	-1.5	2.0		6.1	0.0	
	3rd	-1.0	2.0	7.7	6.0	1.3	
	Mean	-1.2	2.0	7.7	6.1	0.8	
	STDER	0.2	0.0	0.0	0.0	0.4	
	1st	1.0	2.0	26.4	4.4	6.0	
	2nd	2.0	2.0	33.2	6.0	5.5	
	3rd	0.0	2.0	18.4	4.6	4.0	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	1.0	2.0	26.0	5.0	5.2	
	STDER	0.6	0.0	4.3	0.5	0.6	
	1st	-1.0	2.0	7.7	4.5	1.7	
	2nd	-1.0	2.0	7.7	6.6	1.2	
	3rd	0.0	2.0	18.4	5.0	3.7	
	Mean	-0.7	2.0	11.3	5.4	2.2	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	-0.2	2.0	16.8	5.3	3.2	
	STDER	0.2	0.0	1.6	0.3	0.5	
	1st	-1.0	2.0	7.7	6.1	1.3	
	2nd	-1.5	2.0		6.1	0.0	
	3rd	-1.0	2.0	7.7	6.0	1.3	
	Mean	-1.2	2.0	7.7	6.1	0.8	
	STDER	0.2	0.0	0.0	0.0	0.4	
	1st	1.0	2.0	26.4	4.4	6.0	
	2nd	2.0	2.0	33.2	6.0	5.5	
	3rd	0.0	2.0	18.4	4.6	4.0	

Bead name : IL-4							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	0.3	0.0	3.6	0.6	0.8	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	1.0	2.0	26.4	5.0	5.3	
	2nd	0.0	2.0	18.4	5.6	3.3	
	3rd	-1.0	2.0	7.7	5.6	1.4	
	Mean	0.0	2.0	17.5	5.4	3.3	
	STDER	0.6	0.0	5.4	0.2	1.1	
	1st	-1.5	2.0		5.8	0.0	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	1.0	2.0	26.4	4.8	5.5	
	3rd	1.0	2.0	26.4	5.3	5.0	
	Mean	0.2	2.0	26.4	5.3	3.5	
	STDER	0.8	0.0	0.0	0.3	1.8	
	1st	0.0	2.0	18.4	5.2	3.5	
	2nd	-1.0	2.0	7.7	5.4	1.4	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	0.0	2.0	18.4	5.6	3.3	
	Mean	-0.3	2.0	14.8	5.4	2.7	
	STDER	0.3	0.0	3.6	0.1	0.7	

Bead name : IL-4						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
PBMIC+LPS(5ug/ml)+YDE043 100uM	1st	-1.0	2.0	7.7	6.2	1.2
	2nd	-1.0	2.0	7.7	6.4	1.2
	Mean	-1.0	2.0	7.7	6.3	1.2
	STDER	0.0	0.0	0.0	0.1	0.0

Bead name : VEGF-A						
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)
Blank	1st	-0.3	2.0	NaN		
	2nd	0.3	2.0	NaN		
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!
	STDER	0.3	0.0	#DIV/0!	#DIV/0!	#DIV/0!
PBMIC + 0.5% DMSO	1st	2.3	2.0	10.7	7.5	1.4
	2nd	2.3	2.0	10.7	7.4	1.4
	3rd	1.3	2.0	8.5	6.6	1.3
	Mean	1.9	2.0	10.0	7.2	1.4

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	0.3	0.0	0.7	0.3	0.1	
PBMC+LPS(5ug/ml)	1st	0.3	2.0	6.1	6.1	1.0	
	2nd	0.3	2.0	6.1	5.8	1.1	
	3rd	-0.8	2.0	3.6	5.5	0.7	
	Mean	-0.1	2.0	5.3	5.8	0.9	
	STDER	0.3	0.0	0.8	0.2	0.1	
	1st	2.3	2.0	10.7	5.2	2.1	
PBMC+YY101 0.01uM	2nd	0.3	2.0	6.1	4.8	1.3	
	Mean	1.3	2.0	8.4	5.0	1.7	
	STDER	1.0	0.0	2.3	0.2	0.4	
	1st	0.3	2.0	6.1	4.4	1.4	
PBMC+YY101 0.1uM	2nd	1.3	2.0	8.5	5.8	1.5	
	Mean	0.8	2.0	7.3	5.1	1.4	
	STDER	0.5	0.0	1.2	0.7	0.0	
	1st	1.3	2.0	8.5	5.5	1.5	
PBMC+YY101 1uM	2nd	0.3	2.0	6.1	5.5	1.1	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+YY101 10uM	Mean	0.8	2.0	7.3	5.5	1.3	
	STDER	0.5	0.0	1.2	0.0	0.2	
	1st	0.8	2.0	7.3	6.4	1.1	
	2nd	1.3	2.0	8.5	6.1	1.4	
	Mean	1.0	2.0	7.9	6.3	1.3	
	STDER	0.3	0.0	0.6	0.2	0.1	
	1st	-0.8	2.0	3.6	6.4	0.6	
	2nd	-0.8	2.0	3.6	7.0	0.5	
PBMC+YY101 100uM	Mean	-0.8	2.0	3.6	6.7	0.5	
	STDER	0.0	0.0	0.0	0.3	0.0	
	1st	0.3	2.0	6.1	6.2	1.0	
	2nd	-0.8	2.0	3.6	7.6	0.5	
	Mean	-0.3	2.0	4.9	6.9	0.7	
	STDER	0.5	0.0	1.3	0.7	0.3	
	1st	-0.3	2.0	4.9	5.2	0.9	
	2nd	-0.8	2.0	3.6	5.8	0.6	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	Mean	-0.3	2.0	4.9	6.9	0.7	
	STDER	0.5	0.0	1.3	0.7	0.3	
	1st	-0.3	2.0	4.9	5.2	0.9	
	2nd	-0.8	2.0	3.6	5.8	0.6	
	Mean	-0.3	2.0	4.9	6.9	0.7	
	STDER	0.5	0.0	1.3	0.7	0.3	
	1st	-0.3	2.0	4.9	5.2	0.9	
	2nd	-0.8	2.0	3.6	5.8	0.6	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	Mean	-0.3	2.0	4.9	6.9	0.7	
	STDER	0.5	0.0	1.3	0.7	0.3	
	1st	-0.3	2.0	4.9	5.2	0.9	
	2nd	-0.8	2.0	3.6	5.8	0.6	
	Mean	-0.3	2.0	4.9	6.9	0.7	
	STDER	0.5	0.0	1.3	0.7	0.3	
	1st	-0.3	2.0	4.9	5.2	0.9	
	2nd	-0.8	2.0	3.6	5.8	0.6	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	Mean	-0.5	2.0	4.2	5.5	0.8	
	STDER	0.3	0.0	0.6	0.3	0.2	
	1st	0.3	2.0	6.1	6.6	0.9	
	2nd	-2.8	2.0		5.7	0.0	
	Mean	-1.3	2.0	6.1	6.2	0.5	
	STDER	1.5	0.0	#DIV/0!	0.5	0.5	
	1st	-0.8	2.0	3.6	4.8	0.7	
	2nd	-2.3	2.0		4.4	0.0	
PBMC+LPS(5ug/ml)+Xiidra 1uM	Mean	-1.5	2.0	3.6	4.6	0.4	
	STDER	0.8	0.0	#DIV/0!	0.2	0.4	
	1st	-0.8	2.0	3.6	5.8	0.6	
	2nd	-1.8	2.0	0.6	6.4	0.1	
	Mean	-1.3	2.0	2.1	6.1	0.4	
	STDER	0.5	0.0	1.5	0.3	0.3	
	1st	-0.8	2.0	3.6	7.1	0.5	
	2nd	-0.8	2.0	3.6	5.8	0.6	
PBMC+LPS(5ug/ml)+Xiidra 10uM	Mean	-1.3	2.0	2.1	6.1	0.4	
	STDER	0.5	0.0	1.5	0.3	0.3	
	1st	-0.8	2.0	3.6	7.1	0.5	
	2nd	-0.8	2.0	3.6	5.8	0.6	
	Mean	-1.3	2.0	2.1	6.1	0.4	
	STDER	0.5	0.0	1.5	0.3	0.3	
	1st	-0.8	2.0	3.6	7.1	0.5	
	2nd	-0.8	2.0	3.6	5.8	0.6	
PBMC+LPS(5ug/ml)+Xiidra 100uM	Mean	-1.3	2.0	2.1	6.1	0.4	
	STDER	0.5	0.0	1.5	0.3	0.3	
	1st	-0.8	2.0	3.6	7.1	0.5	
	2nd	-0.8	2.0	3.6	5.8	0.6	
	Mean	-1.3	2.0	2.1	6.1	0.4	
	STDER	0.5	0.0	1.5	0.3	0.3	
	1st	-0.8	2.0	3.6	7.1	0.5	
	2nd	-0.8	2.0	3.6	5.8	0.6	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YY101 0.001uM	Mean	-0.8	2.0	3.6	6.5	0.6	
	STDER	0.0	0.0	0.0	0.7	0.1	
	1st	-1.3	2.0	2.2	5.7	0.4	
	2nd	0.3	2.0	6.1	7.1	0.9	
	3rd	-1.8	2.0	0.6	6.6	0.1	
	Mean	-0.9	2.0	3.0	6.5	0.4	
	STDER	0.6	0.0	1.6	0.4	0.2	
	1st	-1.8	2.0	0.6	6.4	0.1	
	2nd	-3.8	2.0		6.0	0.0	
	3rd	-3.8	2.0		6.1	0.0	
PBMC+LPS(5ug/ml)+YY101 0.01uM	Mean	-3.1	2.0	0.6	6.2	0.0	
	STDER	0.7	0.0	#DIV/0!	0.1	0.0	
	1st	-0.8	2.0	3.6	6.2	0.6	
	2nd	-1.8	2.0	0.6	5.2	0.1	
	3rd	-0.8	2.0	3.6	6.2	0.6	
	Mean	-1.1	2.0	2.6	5.9	0.4	
PBMC+LPS(5ug/ml)+YY101 0.1uM	Mean	-0.8	2.0	3.6	6.2	0.6	
	STDER	0.7	0.0	#DIV/0!	0.1	0.0	
	1st	-0.8	2.0	3.6	6.2	0.6	
	2nd	-1.8	2.0	0.6	5.2	0.1	
	3rd	-0.8	2.0	3.6	6.2	0.6	
	Mean	-1.1	2.0	2.6	5.9	0.4	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	0.3	0.0	1.0	0.3	0.2	
PBMC+LPS(5ug/ml)+YY101 1uM	1st	-2.3	2.0		6.3	0.0	
	2nd	-1.3	2.0	2.2	7.1	0.3	
	3rd	-0.8	2.0	3.6	6.2	0.6	
	Mean	-1.4	2.0	2.9	6.5	0.3	
	STDER	0.4	0.0	0.7	0.3	0.2	
	1st	-1.3	2.0	2.2	6.0	0.4	
PBMC+LPS(5ug/ml)+YY101 10uM	2nd	-1.3	2.0	2.2	6.4	0.3	
	3rd	-0.8	2.0	3.6	7.6	0.5	
	Mean	-1.1	2.0	2.7	6.7	0.4	
	STDER	0.2	0.0	0.5	0.5	0.0	
	1st	0.3	2.0	6.1	6.3	1.0	
	2nd	0.3	2.0	6.1	6.2	1.0	
PBMC+LPS(5ug/ml)+YY101 100uM	3rd	-1.8	2.0	0.6	5.0	0.1	
	Mean	-0.4	2.0	4.3	5.8	0.7	
	STDER	0.7	0.0	1.8	0.4	0.3	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YDE011 0.001uM	1st	0.3	2.0	6.1	4.5	1.4	
	2nd	-1.8	2.0	0.6	5.8	0.1	
	3rd	0.3	2.0	6.1	5.8	1.1	
	Mean	-0.4	2.0	4.3	5.4	0.8	
	STDER	0.7	0.0	1.8	0.4	0.4	
PBMIC+LPS(5ug/ml)+YDE011 0.01uM	1st	-0.3	2.0	4.9	6.3	0.8	
	2nd	-2.8	2.0		6.2	0.0	
	3rd	-1.8	2.0	0.6	5.1	0.1	
	Mean	-1.6	2.0	2.8	5.9	0.3	
	STDER	0.7	0.0	2.1	0.4	0.2	
PBMIC+LPS(5ug/ml)+YDE011 0.1uM	1st	-1.8	2.0	0.6	6.6	0.1	
	2nd	-2.8	2.0		5.0	0.0	
	3rd	-1.8	2.0	0.6	5.7	0.1	
	Mean	-2.1	2.0	0.6	5.8	0.1	
	STDER	0.3	0.0	0.0	0.5	0.0	
PBMIC+LPS(5ug/ml)+YDE011 1uM	1st	-0.3	2.0	4.9	5.5	0.9	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	-2.8	2.0		4.8	0.0	
	3rd	-1.8	2.0	0.6	4.8	0.1	
	Mean	-1.6	2.0	2.8	5.0	0.3	
	STDER	0.7	0.0	2.1	0.2	0.3	
PBMC+LPS(5ug/ml)+YDE011 10uM	1st	-0.8	2.0	3.6	5.4	0.7	
	2nd	-2.8	2.0		5.8	0.0	
	3rd	-1.8	2.0	0.6	4.7	0.1	
	Mean	-1.8	2.0	2.1	5.3	0.3	
	STDER	0.6	0.0	1.5	0.3	0.2	
PBMC+LPS(5ug/ml)+YDE011 100uM	1st	-2.8	2.0		6.1	0.0	
	2nd	-2.3	2.0		6.1	0.0	
	3rd	-2.3	2.0		6.0	0.0	
	Mean	-2.4	2.0	#DIV/0!	6.1	0.0	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	STDER	0.2	0.0	#DIV/0!	0.0	0.0	
	1st	-0.8	2.0	3.6	4.4	0.8	
	2nd	-0.8	2.0	3.6	6.0	0.6	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	-0.8	2.0	3.6	4.6	0.8	
	Mean	-0.8	2.0	3.6	5.0	0.7	
	STDER	0.0	0.0	0.0	0.5	0.1	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	1st	-1.8	2.0	0.6	4.5	0.1	
	2nd	-1.8	2.0	0.6	6.6	0.1	
	3rd	-1.8	2.0	0.6	5.0	0.1	
	Mean	-1.8	2.0	0.6	5.4	0.1	
	STDER	0.0	0.0	0.0	0.6	0.0	
	1st	-1.8	2.0	0.6	5.0	0.1	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	2nd	-1.8	2.0	0.6	5.6	0.1	
	3rd	-1.8	2.0	0.6	5.6	0.1	
	Mean	-1.8	2.0	0.6	5.4	0.1	
	STDER	0.0	0.0	0.0	0.2	0.0	
	1st	0.3	2.0	6.1	5.8	1.1	
	2nd	-0.8	2.0	3.6	4.8	0.7	
PBMC+LPS(5ug/ml)+YDE043 1uM	3rd	-0.8	2.0	3.6	5.3	0.7	

Bead name : VEGF-A							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	Mean	-0.4	2.0	4.4	5.3	0.8	
	STDER	0.3	0.0	0.8	0.3	0.1	
PBMIC+LPS(5ug/ml)+YDE043 10uM	1st	-2.3	2.0		5.2	0.0	
	2nd	0.3	2.0	6.1	5.4	1.1	
	3rd	-0.3	2.0	4.9	5.6	0.9	
	Mean	-0.8	2.0	5.5	5.4	0.7	
	STDER	0.8	0.0	0.6	0.1	0.3	
	1st	-0.3	2.0	4.9	6.2	0.8	
PBMIC+LPS(5ug/ml)+YDE043 100uM	2nd	-2.8	2.0		6.4	0.0	
	Mean	-1.5	2.0	4.9	6.3	0.4	
	STDER	1.3	0.0	#DIV/0!	0.1	0.4	

Table 45

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
Blank	1st	-0.5	2.0	NaN			
	2nd	0.5	2.0	NaN			
	Mean	0.0	2.0	#DIV/0!	#DIV/0!	#DIV/0!	
	STDER	0.5	0.0	#DIV/0!	#DIV/0!	#DIV/0!	
PBMC + 0.5% DMSO	1st	337.5	2.0	1614.0	7.5	215.2	
	2nd	556.5	2.0	2589.3	7.4	349.9	
	3rd	755.5	2.0	3475.0	6.6	526.5	
	Mean	549.8	2.0	2559.4	7.2	363.9	
	STDER	120.7	0.0	537.4	0.3	90.1	
PBMC+LPS(5ug/ml)	1st	29.5	2.0	109.0	6.1	17.9	
	2nd	29.5	2.0	109.0	5.8	18.8	
	3rd	27.5	2.0	94.9	5.5	17.3	
	Mean	28.8	2.0	104.3	5.8	18.0	
	STDER	0.7	0.0	4.7	0.2	0.4	
PBMC+YY101 0.01uM	1st	1408.5	2.0	6464.0	5.2	1243.1	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1612.0	2.0	7431.3	4.8	1548.2	
	Mean	1510.3	2.0	6947.7	5.0	1395.6	
	STDER	101.8	0.0	483.7	0.2	152.6	
	1st	1206.5	2.0	5521.9	4.4	1255.0	
PBMCMC+YY101 0.1uM	2nd	1844.5	2.0	8560.2	5.8	1475.9	
	Mean	1525.5	2.0	7041.0	5.1	1365.4	
	STDER	319.0	0.0	1519.1	0.7	110.5	
	1st	1451.5	2.0	6666.8	5.5	1212.2	
PBMCMC+YY101 1uM	2nd	1598.5	2.0	7366.6	5.5	1339.4	
	Mean	1525.0	2.0	7016.7	5.5	1275.8	
	STDER	73.5	0.0	349.9	0.0	63.6	
	1st	2812.5	2.0	13551.9	6.4	2117.5	
PBMCMC+YY101 10uM	2nd	1599.0	2.0	7369.0	6.1	1208.0	
	Mean	2205.8	2.0	10460.4	6.3	1662.8	
	STDER	606.8	0.0	3091.5	0.2	454.7	
	1st	1309.5	2.0	6000.1	6.4	937.5	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	1013.0	2.0	4635.0	7.0	662.1	
	Mean	1161.3	2.0	5317.6	6.7	799.8	
	STDER	148.3	0.0	682.5	0.3	137.7	
	1st	37.5	2.0	161.5	6.2	26.1	
PBMC+LPS(5ug/ml)+Xiidra 0.001uM	2nd	38.5	2.0	167.8	7.6	22.1	
	Mean	38.0	2.0	164.7	6.9	24.1	
	STDER	0.5	0.0	3.1	0.7	2.0	
	1st	34.5	2.0	142.4	5.2	27.4	
PBMC+LPS(5ug/ml)+Xiidra 0.01uM	2nd	42.0	2.0	189.4	5.8	32.7	
	Mean	38.3	2.0	165.9	5.5	30.0	
	STDER	3.8	0.0	23.5	0.3	2.6	
	1st	28.5	2.0	102.0	6.6	15.5	
PBMC+LPS(5ug/ml)+Xiidra 0.1uM	2nd	28.5	2.0	102.0	5.7	17.9	
	Mean	28.5	2.0	102.0	6.2	16.7	
	STDER	0.0	0.0	0.0	0.5	1.2	
	1st	21.5	2.0	48.9	4.8	10.2	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	30.5	2.0	115.8	4.4	26.3	
	Mean	26.0	2.0	82.3	4.6	18.3	
	STDER	4.5	0.0	33.5	0.2	8.1	
	1st	20.5	2.0	40.2	5.8	6.9	
PBMIC+LPS(5ug/ml)+Xiidra 10uM	2nd	21.5	2.0	48.9	6.4	7.6	
	Mean	21.0	2.0	44.5	6.1	7.3	
	STDER	0.5	0.0	4.3	0.3	0.4	
	1st	24.0	2.0	69.0	7.1	9.7	
PBMIC+LPS(5ug/ml)+Xiidra 100uM	2nd	24.5	2.0	72.8	5.8	12.6	
	Mean	24.3	2.0	70.9	6.5	11.1	
	STDER	0.3	0.0	1.9	0.7	1.4	
	1st	36.0	2.0	152.0	5.7	26.7	
PBMIC+LPS(5ug/ml)+YY101 0.001uM	2nd	36.5	2.0	155.2	7.1	21.9	
	3rd	50.5	2.0	239.8	6.6	36.3	
	Mean	41.0	2.0	182.3	6.5	28.3	
	STDER	4.8	0.0	28.7	0.4	4.3	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMIC+LPS(5ug/ml)+YY101 0.01uM	1st	37.5	2.0	161.5	6.4	25.2	
	2nd	36.5	2.0	155.2	6.0	25.9	
	3rd	33.5	2.0	135.8	6.1	22.3	
	Mean	35.8	2.0	150.9	6.2	24.5	
	STDER	1.2	0.0	7.7	0.1	1.1	
PBMIC+LPS(5ug/ml)+YY101 0.1uM	1st	28.5	2.0	102.0	6.2	16.5	
	2nd	31.0	2.0	119.2	5.2	22.9	
	3rd	31.5	2.0	122.6	6.2	19.8	
	Mean	30.3	2.0	114.6	5.9	19.7	
	STDER	0.9	0.0	6.4	0.3	1.9	
PBMIC+LPS(5ug/ml)+YY101 1uM	1st	36.5	2.0	155.2	6.3	24.6	
	2nd	37.5	2.0	161.5	7.1	22.8	
	3rd	41.5	2.0	186.3	6.2	30.1	
	Mean	38.5	2.0	167.7	6.5	25.8	
	STDER	1.5	0.0	9.5	0.3	2.2	
PBMIC+LPS(5ug/ml)+YY101 10uM	1st	37.5	2.0	161.5	6.0	26.9	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	2nd	38.5	2.0	167.8	6.4	26.2	
	3rd	34.5	2.0	142.4	7.6	18.7	
	Mean	36.8	2.0	157.2	6.7	24.0	
	STDER	1.2	0.0	7.7	0.5	2.6	
PBMC+LPS(5ug/ml)+YY101 100uM	1st	28.0	2.0	98.5	6.3	15.6	
	2nd	28.5	2.0	102.0	6.2	16.5	
	3rd	26.5	2.0	87.7	5.0	17.5	
	Mean	27.7	2.0	96.1	5.8	16.5	
	STDER	0.6	0.0	4.3	0.4	0.6	
	1st	48.5	2.0	228.2	4.5	50.7	
PBMC+LPS(5ug/ml)+YDE011 0.001uM	2nd	41.5	2.0	186.3	5.8	32.1	
	3rd	44.5	2.0	204.5	5.8	35.3	
	Mean	44.8	2.0	206.3	5.4	39.4	
	STDER	2.0	0.0	12.1	0.4	5.7	
	1st	39.5	2.0	174.0	6.3	27.6	
	2nd	39.5	2.0	174.0	6.2	28.1	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	3rd	42.5	2.0	192.4	5.1	37.7	
	Mean	40.5	2.0	180.2	5.9	31.1	
	STDER	1.0	0.0	6.1	0.4	3.3	
PBMC+LPS(5ug/ml)+YDE011 0.1uM	1st	42.5	2.0	192.4	6.6	29.2	
	2nd	39.5	2.0	174.0	5.0	34.8	
	3rd	39.5	2.0	174.0	5.7	30.5	
	Mean	40.5	2.0	180.2	5.8	31.5	
	STDER	1.0	0.0	6.1	0.5	1.7	
	1st	42.5	2.0	192.4	5.5	35.0	
PBMC+LPS(5ug/ml)+YDE011 1uM	2nd	40.5	2.0	180.2	4.8	37.5	
	3rd	42.5	2.0	192.4	4.8	40.1	
	Mean	41.8	2.0	188.3	5.0	37.5	
	STDER	0.7	0.0	4.1	0.2	1.5	
	1st	41.5	2.0	186.3	5.4	34.5	
	2nd	43.5	2.0	198.5	5.8	34.2	
PBMC+LPS(5ug/ml)+YDE011 10uM	3rd	41.5	2.0	186.3	4.7	39.6	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE011 100uM	Mean	42.2	2.0	190.4	5.3	36.1	
	STDER	0.7	0.0	4.0	0.3	1.8	
	1st	38.5	2.0	167.8	6.1	27.5	
	2nd	39.5	2.0	174.0	6.1	28.5	
	3rd	37.5	2.0	161.5	6.0	26.9	
	Mean	38.5	2.0	167.8	6.1	27.7	
	STDER	0.6	0.0	3.6	0.0	0.5	
	1st	39.0	2.0	170.9	4.4	38.8	
	2nd	49.5	2.0	234.0	6.0	39.0	
	3rd	54.5	2.0	262.8	4.6	57.1	
PBMC+LPS(5ug/ml)+YDE043 0.001uM	Mean	47.7	2.0	222.6	5.0	45.0	
	STDER	4.6	0.0	27.1	0.5	6.1	
	1st	40.5	2.0	180.2	4.5	40.0	
	2nd	41.5	2.0	186.3	6.6	28.2	
	3rd	42.5	2.0	192.4	5.0	38.5	
	Mean	41.5	2.0	186.3	5.4	35.6	
PBMC+LPS(5ug/ml)+YDE043 0.01uM	Mean	42.2	2.0	190.4	5.3	36.1	
	STDER	0.7	0.0	4.0	0.3	1.8	
	1st	38.5	2.0	167.8	6.1	27.5	
	2nd	39.5	2.0	174.0	6.1	28.5	
	3rd	37.5	2.0	161.5	6.0	26.9	
	Mean	38.5	2.0	167.8	6.1	27.7	
	STDER	0.6	0.0	3.6	0.0	0.5	
	1st	39.0	2.0	170.9	4.4	38.8	
	2nd	49.5	2.0	234.0	6.0	39.0	
	3rd	54.5	2.0	262.8	4.6	57.1	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
	STDER	0.6	0.0	3.5	0.6	3.7	
PBMC+LPS(5ug/ml)+YDE043 0.1uM	1st	42.5	2.0	192.4	5.0	38.5	
	2nd	36.5	2.0	155.2	5.6	27.7	
	3rd	39.5	2.0	174.0	5.6	31.1	
	Mean	39.5	2.0	173.9	5.4	32.4	
	STDER	1.7	0.0	10.7	0.2	3.2	
	1st	43.5	2.0	198.5	5.8	34.2	
PBMC+LPS(5ug/ml)+YDE043 1uM	2nd	36.5	2.0	155.2	4.8	32.3	
	3rd	40.5	2.0	180.2	5.3	34.0	
	Mean	40.2	2.0	178.0	5.3	33.5	
	STDER	2.0	0.0	12.5	0.3	0.6	
	1st	43.5	2.0	198.5	5.2	38.2	
	2nd	42.5	2.0	192.4	5.4	35.6	
PBMC+LPS(5ug/ml)+YDE043 10uM	3rd	40.0	2.0	177.1	5.6	31.6	
	Mean	42.0	2.0	189.3	5.4	35.1	
	STDER	1.0	0.0	6.4	0.1	1.9	

Bead name : MMP-9							
Sample		MFI	Dilution	Concentration (pg/ml)	Live cell (10 ⁵ /ml)	conc/live cell (pg/10 ⁵)	
PBMC+LPS(5ug/ml)+YDE043 100uM	1st	35.5	2.0	148.8	6.2	24.0	
	2nd	32.5	2.0	129.2	6.4	20.2	
	Mean	34.0	2.0	139.0	6.3	22.1	
	STDER	1.5	0.0	9.8	0.1	1.9	

Example 10: Establish effects of YY-101, YDE-011, YDE-043, YDE-048 and YDE-060 compounds on 25 selected cytokine and chemokine release in tears from rats with ELGE dry eye condition

Objective:

- 5 • To establish effects of YY-101, YDE-011, YDE-043, YDE-048 and YDE-060 compounds on 25 selected cytokine and chemokine release in tears from rats with ELGE dry eye condition.

Materials:

- Rat IL-6 ELISA kit (Thermo fisher, USA)
- 10 • Rat magnetic Luminex assay kit - Procartaplex (Thermo fisher, USA)

Reference compound used:

- Xiidra® (Shire, USA)

Test Compound

- 0.3 % YY-101, 0.3 % YDE-011, 0.3 % YDE-043, 0.3 % YDE-048 and 0.3 %
- 15 YDE-060.

Summary of the protocol

1. Rats with ELGE were treated with YY & YDE compound in 5ul eye drops twice a day for 2 weeks.
2. Tear samples were collected using a capillary tube and stored in -80°C
- 20 freezer until analysis.
3. Tear samples were combined within the group and protein were quantified using the BCA assay.
4. Cytokines level is assessed by multiplex assay following manufacturer's instructions.

25 *Statistical Analysis*

- All values are presented as mean $\pm$ standard deviation (SD).

Results

The results are shown in Figures 43-51 and are presented as concentration (pg/mg protein). All data was normalized to their protein levels. Out of 25 cytokines

30 & chemokines evaluated, 14 of them were within the standard curve range, 3 were below the range, 1 over the range and 7 were below the level of detection & quantification. Since the amount of sample was very small (2-10 uL), each dilution factor was selected in order to generate min. volume for Luminex measurement.

Table 46

No.	Group	Dilution factor
1	Sham	1/12
2	ELGE	1/12
3	Xiidra	1/12
4	YY-101	1/12
5	YDE-011	1/14/75
6	YDE-043	1/12
5	YDE-048	1/19/33
8	YDE-060	1/12

Table 47

No.	Cytokine	Result	No.	Cytokine	Result
1	Eotaxin	Within standard curve range	14	VEGF-A	Within standard curve range
2	Gro- α _KC	Within standard curve range	15	bNGF	Below standard curve range
3	IL-17A	Within standard curve range	16	Leptin	Below standard curve range
4	IL-1 13	Within standard curve range	17	RANTES	Below standard curve range
5	IL-21	Within standard curve range	18	CRP	OLQ
6	IL-4	Within standard curve range	19	TGF-13	BLQ
7	MCP-1	Within standard curve range	20	IFN- γ	BLQ
8	MCP-3	Within standard curve range	21	IL-10	BLQ
9	sVCAM-1	Within standard curve range	22	IL-2	BLQ
10	TNF- α	Within standard curve range	23	IL-6	BLQ
11	IL-12p70	Within standard curve range	24	MIP-1 α	BLQ
12	IL-1 α	Within standard curve range	25	sRANKL	BLQ
13	IP-10	Within standard curve range			

Key:

- OLQ = Over the level of quantification
- BLQ = Below the level of Quantification

5 *Summary & Conclusion*

- Due to small samples of tears, all individual samples were pooled within the groups, thus, the statistical analysis was not performed. Despite of the small sample amount, most of selected cytokine and chemokine levels in the conjunctival epithelial cells were detected within the normal standard range.
- 10 • As expected, a 2 week ELGE induced dry eye condition in rats led to a significant increase of proinflammatory cytokine/chemokine levels in tears of ELGE animals compared to those in the sham control groups.
- Both the test compounds and the reference compound, Xiidra, significantly reduced most of Th1, Th2 & Th17 derived cytokines and proinflammatory chemokines, suggesting that improvement of corneal damages in ELGE rat dry
15 condition is, at least partly, due to the effective treatment in reducing the proinflammatory cytokine and chemokines in the eye.

20 **Example 11: Establish effects of YDE-048 and YDE-043 compounds on 25 selected cytokine and chemokine release from conjunctival epithelial cells (including goblet cells) of rats with ELGE dry eye condition**

Objective

- To establish effects of YDE-048 and YDE-043 compounds on 25 selected cytokine and chemokine release from conjunctival epithelial cells (including
25 goblet cells) of rats with ELGE dry eye condition (from NSY0319 study).

Materials

- Rat IL-6 ELISA kit (Thermo fisher, USA, cat no: BMS625)
- Rat magnetic Luminex assay kit - Procartaplex (Thermo fisher, USA, cat no: PPX-25-MX9HJJU)

30 *Test Compound*

- 0.1%, 0.3%, 1%, 3% of YDE-048 & 1% of YDE-043.

Statistical Analysis

- All values are presented as mean $\pm$ standard deviation (SD).

- All values were statistically analyzed by one-way ANOVA with a Tukey, Dunnett's post test comparing all the groups.

Results

The results are shown in Figures 52-61 and are presented as concentration (pg/mg protein). All data was normalized to their protein levels. Out of 25 cytokines & chemokines evaluated, 14 of them were within the standard curve range, 4 were below the range, 1 over the range and 6 were below the level of detection & quantification.

Table 48

No.	Cytokine	Dilution factor	Result	No.	Cytokine	Dilution factor	Result
1	Gro- α _KC	1:01	Within standard curve range	14	TNF- α	1:01	Within standard curve range
2	IL-1 α	1:01	Within standard curve range	15	IL-12p70	1:01	Below standard curve range
3	IL-1 13	1:01	Within standard curve range	16	IL-21	1:01	Below standard curve range
4	Leptin	1:01	Within standard curve range	17	bNGF	1:01	Below standard curve range
5	IP-10	1:01	Within standard curve range	18	IL-4	1:01	Below standard curve range
6	VEGF-A	1:01	Within standard curve range	19	CRP	1:01	OLQ
7	Eotaxin	1:01	Within standard curve range	20	IFN- γ	1:01	BLQ
8	IL-17A	1:01	Within standard curve range	21	IL-10	1:01	BLQ

9	MCP-1	1:01	Within standard curve range	22	IL-2	1:01	BLQ
10	MCP-3	1:01	Within standard curve range	23	IL-6	1:01	BLQ
11	RANTES	1:01	Within standard curve range	24	MIP-1 α	1:01	BLQ
12	sVCAM-1	1:01	Within standard curve range	25	sRANKL	1:01	BLQ
13	TGF-13	1:01	Within standard curve range				

Key:

- OLQ = Over the level of quantification
- BLQ = Below the level of Quantification

Summary & Conclusion

- 5
- Most of selected cytokine and chemokine levels in the conjunctival epithelial cells were detected within the normal standard range.
 - Literature suggests that the dry eye condition leads to increase the level of proinflammatory cytokines (e.g., TNF-alpha, IL-6, IL-17) in the conjunctival epithelial cells dry eye disease. However, a 2 week ELGE induced dry eye condition in rats didn't elicit proinflammatory cytokine/chemokine induction in conjunctival epithelial cells in ELGE animals compared to those in the sham control groups.
- 10
- None of the compounds significantly affected cytokine/chemokine production, suggesting that the compounds have little or no effect the basal level of proinflammatory cytokine/chemokines (including IL-6 levels) in conjunctival epithelial cells although YDE-048 and YDE-043 were effective in improving corneal damaged induced by ELGE.
- 15

Example 12: Efficacy Evaluation of the Compounds of the Invention in Mouse IBD Model

DSS induced colitis:

5 Experimental schematic timeline is shown in Figure 62.

Table 49

Group		mpk	N	Route	
1	Control (No DSS)		6+2	SC	B.I.D
2	DSS		6+2	SC	
3	DSS + Cyclosporin A	20	6+2	PO	
4	DSS + YDE-048	10	6+2	SC	
5	DSS + YDE-048	100	6+2	SC	

YDE-048 is soluble in saline

- 10 End-point termination – tissue and handling hours after last dosing, collect terminal blood sample, colon
- Blood chemistry evaluation (i.e., CRP)
 - Histology and pathology evaluation – H&E
 - Inflammation and oxidative markers (e.g, TNF-a, nitrotyrosine)

15

Table 50

<u>Body weight (BW) loss (%) score:</u>	
0-1%	= 0
1-5%	= 1
5-10%	= 2
10-20%	= 3
20%	= 4
<u>Stool consistency (SC) score:</u>	

Normal	= 0
Soft, but still formed	= 1
Very soft	= 2
Diarrhea	= 4
<u>Fecal blood occurrence (FB) score:</u>	
Normal	= 0
Visible traces of blood - slight	= 1
Visible traces of blood - critical	= 2
Gross rectal bleeding	= 4
<u>Disease Activity Index (DAI)</u>	= BW score + SC score + FB score

Table 51

Group		Mpk	N
G1	Control (No DSS)		4
G2	DSS		8
G3	DSS + Cyclosporin A	20	8
G4	DSS + YDE-048	10	5
G5	DSS + YDE-048	100	8

DSS induced colitis

- 5
 - Histology pathology evaluation – H&E
 - Inflammation and oxidative markers – TNF- α , Nitrotyrosine
 - TNF- α : 3 image (different 3 layer of on direction) per sample (area : Intestinal villus)
 - Nitrotyrosine : 2 image (including all layer in Right, Left) per sample

10 **Summary**

- 3% DSS for five days induced body weight loss, increased disease activity index (DAI) in mice
- Increased disease index includes body weight loss and increased appearance of loose stools and fecal blood

- A positive reference compound, cyclosporin A, significantly reduced DSS-induced body weight and increased DSI.
 - YDE-048 at 100mg/kg significantly reduced DSS-induced increased DSI. In particular, YDE-048 reduced DSS-induced occurrence of loose stools and fecal blood.
 - The level of C-reactive protein (pro-inflammation marker) is highly elevated in plasma of mice with IBD, and YDE-048 partially reduced the level.
 - Future studies will focus on increased sample size, higher dose (e.g., 300 mg/kg) and/or alternative drug delivery (Alzet pump or Matrigel)
- Immunohistological evaluation on intestines show that TNF- α level is significantly elevated in mice with IBD, and YDE-048 significantly reduced both TNF- α (pro-inflammatory cytokine) and nitrotyrosine (a marker for protein oxidation) levels.

The data and results are shown in Figures 62-65 and Figures 77-79.

Example 13: Mouse Rheumatoid Arthritis Model

Summary:

- CII injection led to marked induction of arthritis-like symptoms in mice as early as one day after a CII booster injection and continued to escalated symptoms up to 3 weeks.
- A reference compound, dexamethasone, strongly reduced inflammation and clinical scores in hind paws although it also lead to a decrease in body weight in mice.
- YDE-048 reduced the clinical symptoms and scores in the first week (an early phase of inflammation)
- Recommend to repeat the study with increased sample size, higher dose (e.g., 300 mg/kg) and/or alternative drug delivery (Alzet pump or Matrigel)

The data and results are shown in Figures 66-68.

Example 14: Mouse Osteoporosis Model

OVX induced Osteoporosis disease model in C57bL6 mouse

Experiment schematic timeline is shown in Figure 69.

Study scheme and group information:

- 12 week old C57bl6/J Female and generate OVX-induced osteoporosis model
 - Study Length: 9 Weeks (1 week model generation + 8 weeks of Test article dosing)
- 5
- Acclimation: 1 week
 - Dosing: B.I.D / 8 weeks
 - Body Weight and General observation: 8 weeks
- Report preparation: 7 days
 - Formulation and test article handling and storage (according to client MSDS)
- 10
- Body weight measurement (weekly); uterus weight at the end of experiment
 - End-point termination:
 - Lumbar vertebrae bone strength test
 - Femurs fixed in 4% paraformaldehyde for μ -CT (e.g., bone mineral density, bone structure, bone quality and volume)
- 15
- Fixed femurs decalcified in 12% EDTA2Na at RT for approximately 3 weeks and embedded in paraffin. Their slices used for TRAP staining, H&E (hematoxylin and eosin) staining, and immunohistochemical staining.
 - Body weight
- 20
- • Total N = 28
 - 4 groups, n = 7 in each group, total 28 mice:
 - Vehicle, Test article 1, Test article 2
 - WT N = 7
 - Osteoporosis model N = 21

25

End point sampling:

- body weight
 - sampling time after 1hr compound injection
 - serum
- 30
- saline perfusion
 - uterus -> weight, gross
 - femur (L/R)
 - L - in 4% PFA for u-CT (get a sample back)

- R - in 10% NBF for staining
- Lumbar vertebrae in PBS for bone test

Table 52

Group		mpk	N	Route	
1	WT		7	S.C	B.I.D
2	OVX + Vehicle		7	S.C	
3	OVX + YDE-048	10	7	S.C	
4	OVX + YDE-048	100	7	S.C	

5 YDE-048 is soluble in saline

Summary

- Ovariectomy (OVX) led to a body weight increase, uterus weight loss in female C57BL/6 mice.
- 10 • Micro-CT scan showed OVX also led to trabecular bone density and connectivity loss in femur with little loss in cortical bone loss in 2 months.
- OVX didn't affect lumbar vertebrae bone strength within 2 months.
- YDE-048 significantly protected trabecular bone loss (both density and volume) in a dose-dependent manner
- 15 • Recommend to repeat the study with increased sample size, higher dose (e.g., 300 mg/kg) and/or alternative drug delivery (Alzet pump or Matrigel)

The data and results are shown in Figures 69-76.

Incorporation by Reference

- 20 All publications and patents mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference. In case of conflict, the present application, including any definitions herein, will control.

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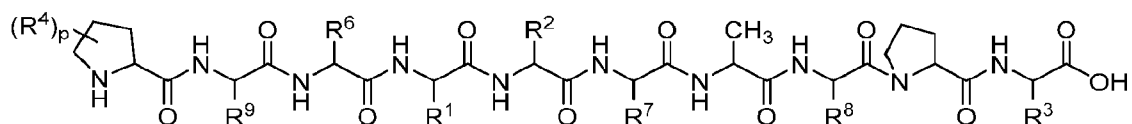
Equivalents

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and
5 the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

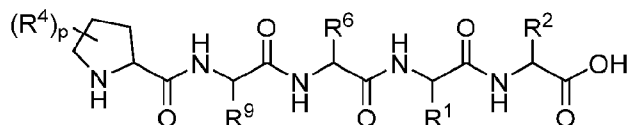
We claim:

1. A method of preventing or treating an IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine mediated disease or disorder in a subject, comprising administering to the subject

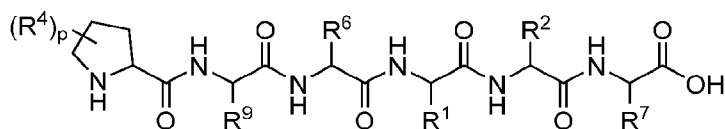
i) a compound represented by Formula (I), (V), (VI), (VII), (IX) or (X-am) or a pharmaceutically acceptable salt and/or prodrug thereof:



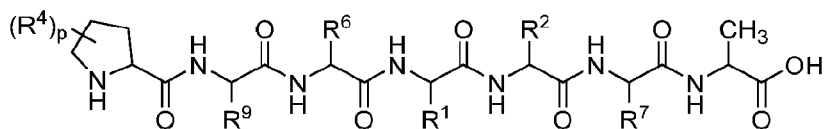
(I),



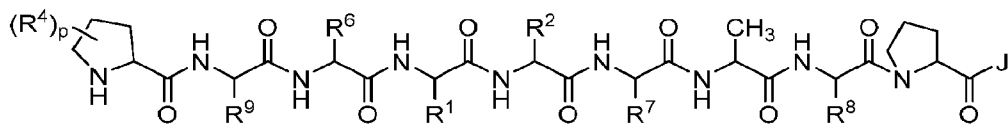
(V),



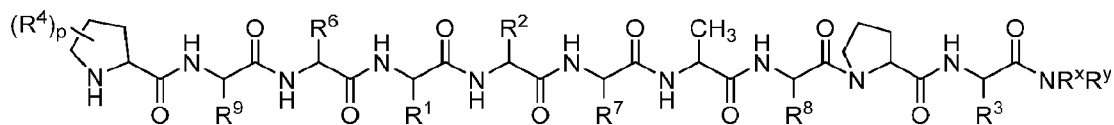
(VI),



(VII),



(IX), or



(X-am),

wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

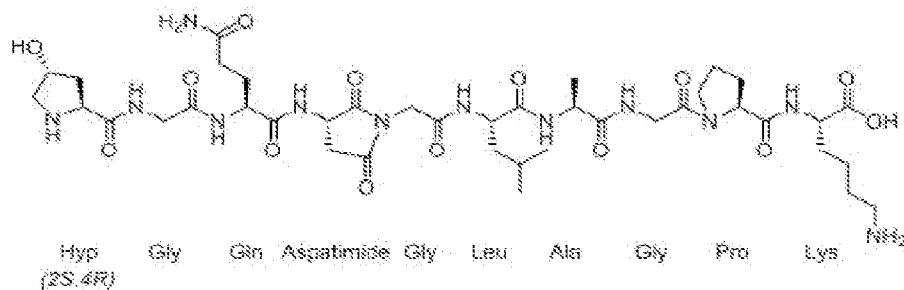
R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-NR^xR^y$; and

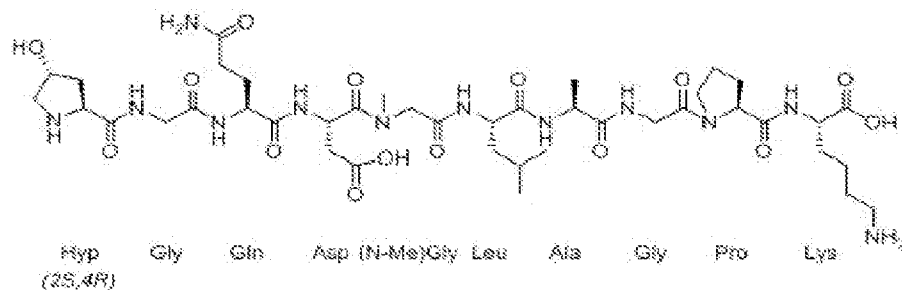
R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring,

ii) a compound represented by Formula (8) or (10)

or a pharmaceutically acceptable salt and/or prodrug thereof:



[Formula 8];



[Formula 10]

iii) a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xcc or Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys,

or a pharmaceutically acceptable salt and/or stereoisomer thereof,
wherein:

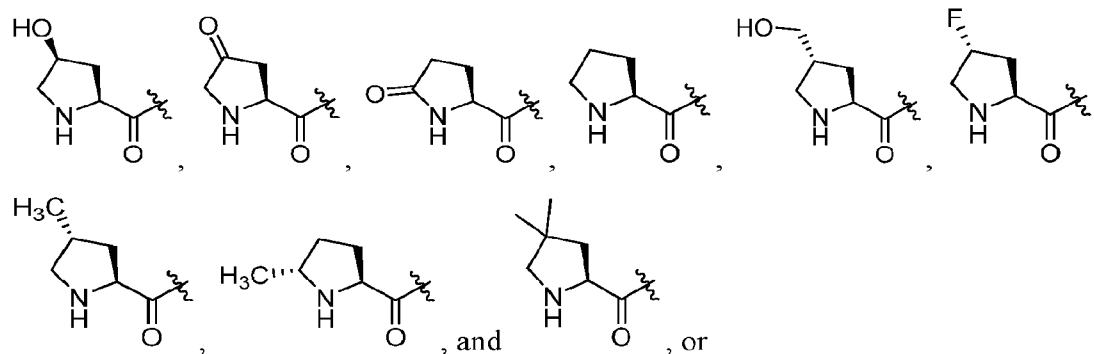
Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr,

Trp, homo-Ser, Asp(Me), and Asn(Me);

Xbb is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly;

Xcc is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH); and

Xdd is selected from:



iv) a peptide having any one amino acid sequence selected from:

Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;

Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys;

HyP-Gly-Gln-Leu-Gly-Leu-Ala;

HyP-Gly-Gln-Glu-Gly-Leu-Gly;

HyP-Gly-Gln-Leu-Gly-Leu;

D-HyP(2R, 4S)-Gly-D-Gln-D-Leu-Gly-D-Leu;

HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-D-Leu-Gly; and

D-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

2. The method of claim 1, wherein the subject has elevated levels of IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine.

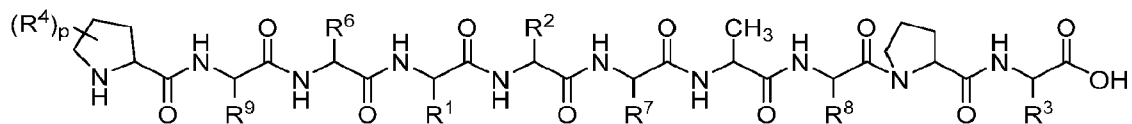
3. The method of claim 1 or 2, wherein the IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine mediated disease is an autoimmune disease, an inflammatory disease, or a cancer.

4. The method of any one of claims 1-3, wherein the disease or disorder is Acute posterior multifocal placoid pigment epitheliopathy (APMPPE), Agammaglobulinemia, Alopecia Areata, Amyloidosis, Amyotrophic lateral sclerosis (ALS), Aniridia, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune hepatitis, Autoimmune inner ear disease, Autoimmune Lymphoproliferative Syndrome, Atopic dermatitis, Asthma, Behçet's Disease, Best Disease, Birdshot Chorioretinopathy, Blepharitis, Bronchiolitis, Cancer (Chondrosarcoma, Cervical, Breast, Lung), Capillary Leak Syndrome, Castleman disease, Celiac disease, Chagas disease, Chalazia and Sty, Chandler's syndrome, Cholesteatoma of Middle Ear, Choroideremia, Chronic recurrent multifocal osteomyelitis, Cogan's syndrome, Collagen Induced Arthritis (CIA), Cold agglutinin disease, Cone Rod Dystrophies, Conjunctivitis, Corneal Wound Healing, CREST syndrome, Crohn's disease, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dry Eye Disease (DED), Dry macular degeneration (Dry AMD), Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Essential Iris Atrophy, Evan's syndrome, Farmer's Lung, Fibromyalgia, Giant cell arteritis, Giant cell myocarditis, Giant Papillary Conjunctivitis, Glomerulonephritis, Goodpasture's syndrome, Graft-Versus-Host Disease, Granulomatosis with polyangiitis, Graves' disease, Guillain-Barre syndrome, Gyrate Atrophy, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Hypogammaglobulinemia, Hypoproliferative anemia, IgA Nephropathy, Inclusion body myositis, Interstitial cystitis, Inflammatory Bowel Disease, Iritis, Irritant Dermatitis, Juvenile arthritis, Juvenile/Type 1 Diabetes, Juvenile macular degeneration, Juvenile myositis, Juvenile X-linked Retinoschisis, Kawasaki syndrome, Keratitis, Keratoconjunctivitis sicca (Dry Eye), Late-Onset Retinal Degeneration (L-ORD), Lichen planus, Lichen sclerosus, Lupus (SLE), Macular Edema, Meniere's disease, Multiple sclerosis, Myasthenia gravis, Microscopic polyangiitis, Neuropathic Corneal Pain, Neurotropic Keratitis, Ocular Allergy, Ocular Inflammation (uveitis), Ocular Pain, Ocular Neurodegeneration, Optic Nerve Atrophy, Optic neuritis, Oral Submucous Fibrosis, Osteoarthritis (OA), Osteoporosis, Parkinson's disease, Pars Planitis, Pemphigus, Photokeratitis, Polyarteritis nodosa, Polymyalgia rheumatica, Polymyositis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleritis, Sjogren's syndrome,

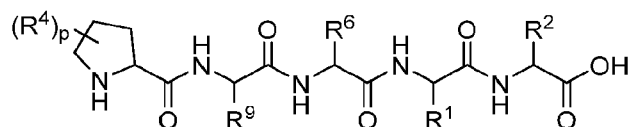
Stargardt Disease, Stickler Syndrome, Temporal arteritis/Giant cell arteritis, Thyroid Eye Disease, Trachoma, Transverse myelitis, Trichiasis, Ulcerative colitis, Usher Syndrome, Uveitis, Vasculitis, Vitiligo, Viral myocarditis, Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)), Wet macular degeneration, or Wound Healing.

5. A method of reducing production of IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF- α , MMP3, CCL-2, CCL-3, CCL-4, Fas, TIMP-1, or a Th1, Th2, and/or Th17 derived cytokine or proinflammatory chemokine in cells of a subject, comprising administering to a subject

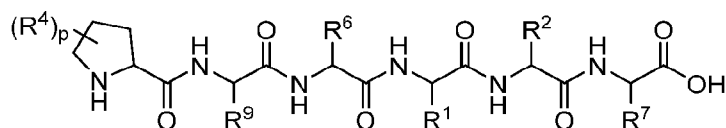
i) a compound represented by Formula (I), (V), (VI), (VII), (IX) or (X-am) or a pharmaceutically acceptable salt and/or prodrug thereof:



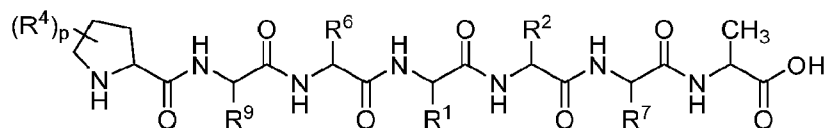
(I),



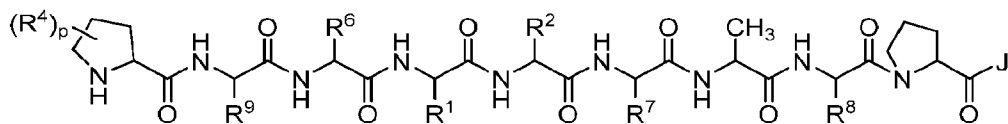
(V),



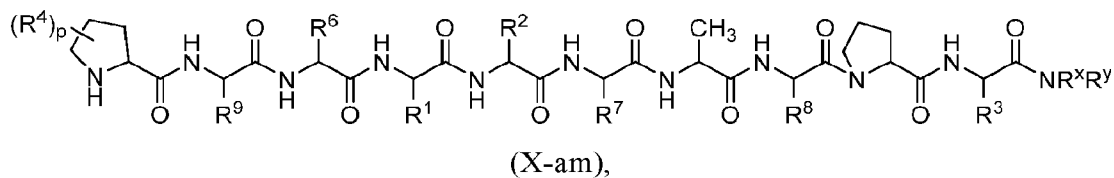
(VI),



(VII),



(IX), or



wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

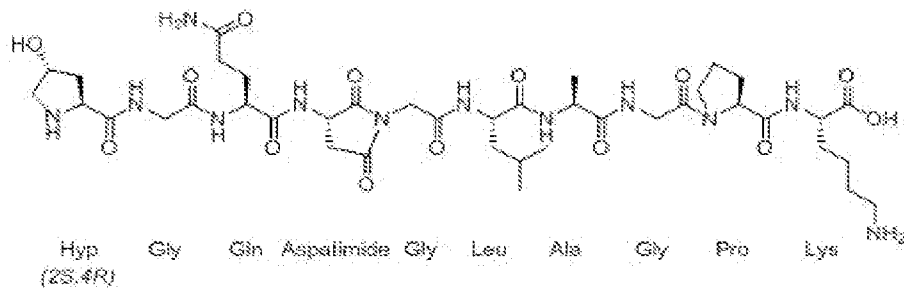
R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-NR^xR^y$; and

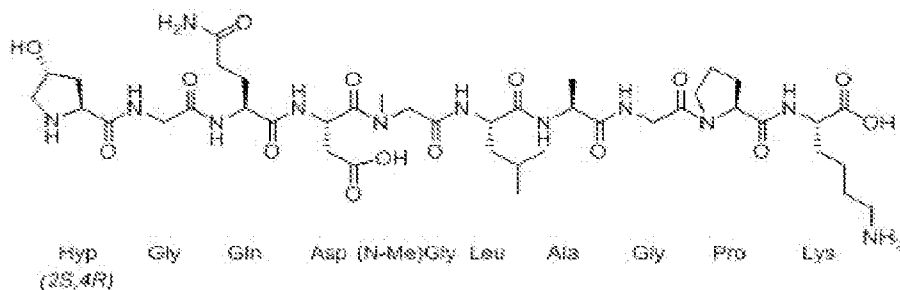
R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring,

ii) a compound represented by Formula (8) or (10)

or a pharmaceutically acceptable salt and/or prodrug thereof:



[Formula 8];



[Formula 10]

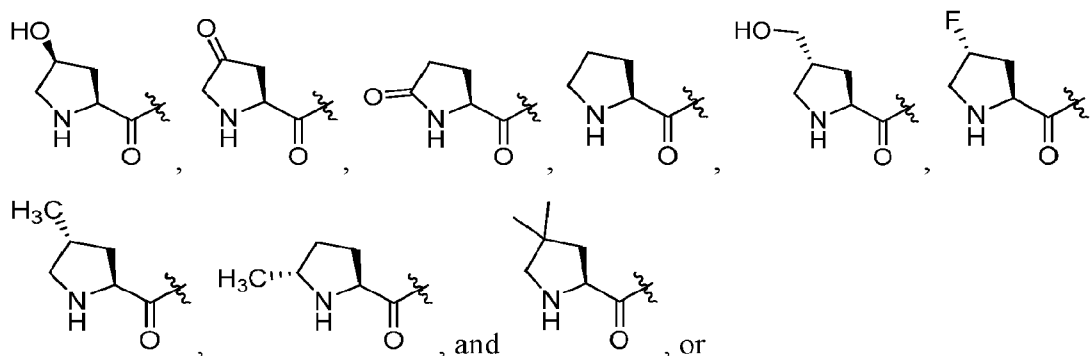
iii) a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xcc or Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, or a pharmaceutically acceptable salt and/or stereoisomer thereof, wherein:

Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me);

Xbb is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly;

Xcc is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH); and

Xdd is selected from:



iv) a peptide having any one amino acid sequence selected from:

Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;

Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys;

HyP-Gly-Gln-Leu-Gly-Leu-Ala;

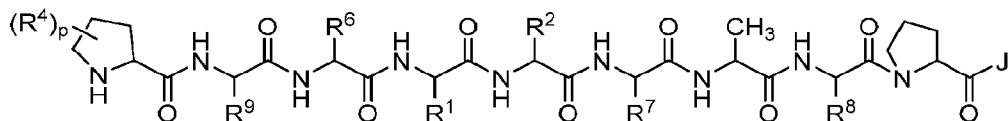
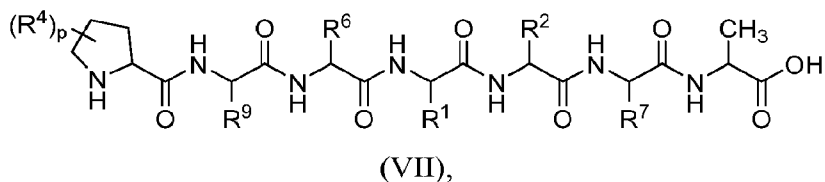
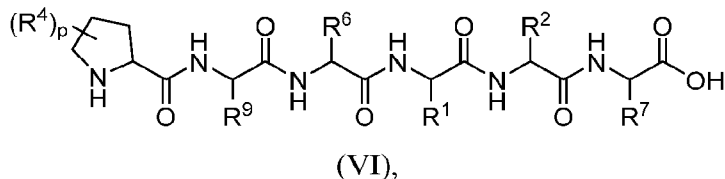
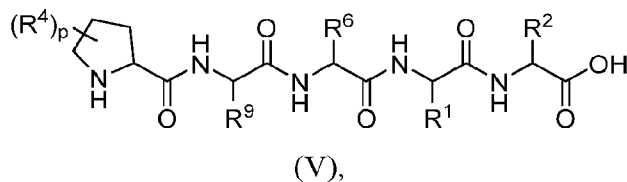
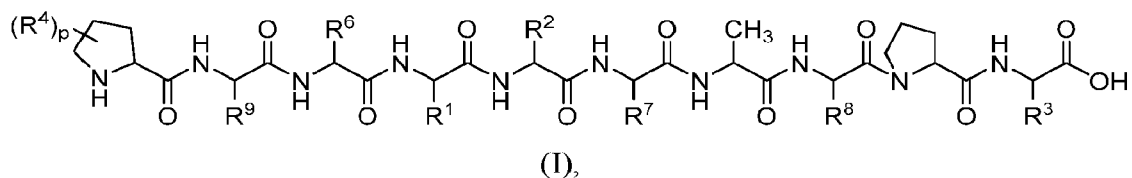
HyP-Gly-Gln-Glu-Gly-Leu-Gly;

HyP-Gly-Gln-Leu-Gly-Leu;

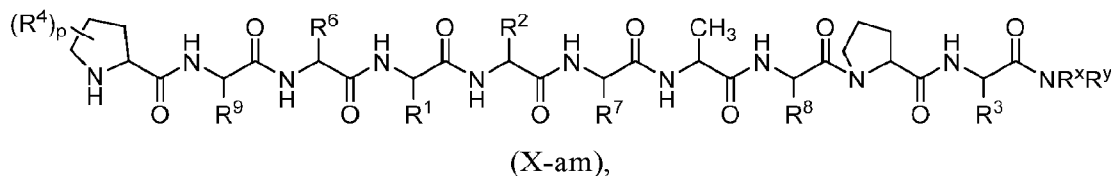
D-HyP(2R, 4S)-Gly-D-Gln-D-Leu-Gly-D-Leu;

HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-D-Leu-Gly; and
D-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

6. The method of claim 5, wherein administering the compound reduces the cytokine and/or chemokine levels by at least 30% compared to the untreated control.
7. The method of claim 5, wherein administering the compound reduces the cytokine and/or chemokine levels by at least 50% compared to the untreated control.
8. The method of claim 5, wherein administering the compound reduces the cytokine and/or chemokine levels by at least 70% compared to the untreated control.
9. A method of reducing NF- κ B transcription activity in cells of a subject, comprising administering to a subject
 - i) a compound represented by Formula (I), (V), (VI), (VII), (IX) or (X-am) or a pharmaceutically acceptable salt and/or prodrug thereof:



(IX), or



wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

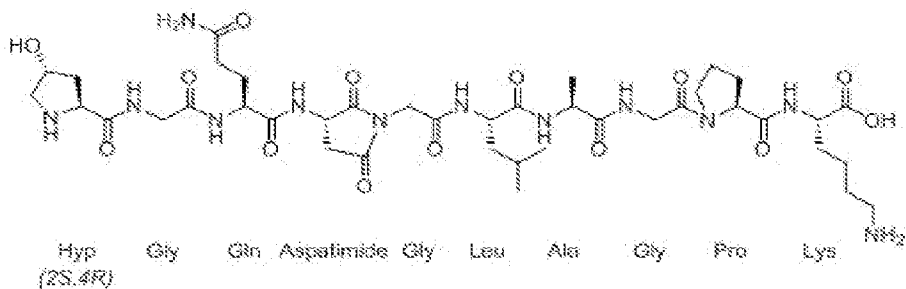
R^6 is hydrogen or substituted or unsubstituted alkyl;

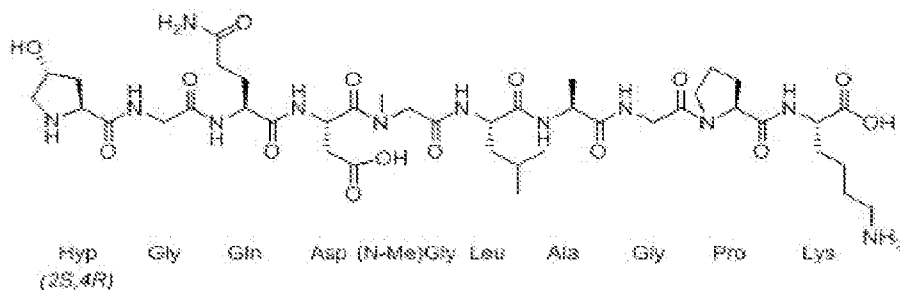
R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-NR^xR^y$; and

R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring,

ii) a compound represented by Formula 8 or 10
or a pharmaceutically acceptable salt and/or prodrug thereof:





[Formula 10]

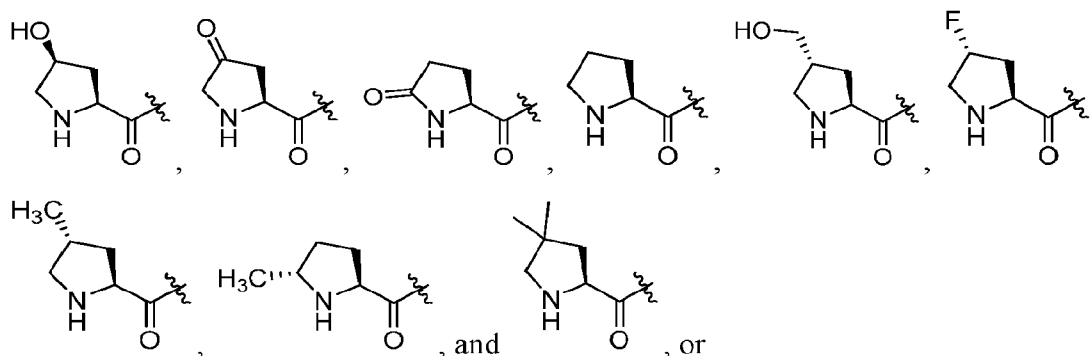
iii) a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xcc or Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, or a pharmaceutically acceptable salt and/or stereoisomer thereof, wherein:

Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me);

Xbb is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly;

Xcc is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH); and

Xdd is selected from:



iv) a peptide having any one amino acid sequence selected from:

Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;

Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys;

HyP-Gly-Gln-Leu-Gly-Leu-Ala;

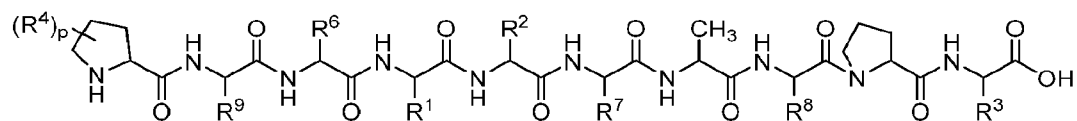
HyP-Gly-Gln-Glu-Gly-Leu-Gly;

HyP-Gly-Gln-Leu-Gly-Leu;

D-HyP(2R, 4S)-Gly-D-Gln-D-Leu-Gly-D-Leu;

HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-D-Leu-Gly; and
D-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

10. The method of any one of claims 1-9, wherein the subject is a mammal.
11. The method of claim 10, wherein the mammal is a mouse or a human.
12. The method of claim 11, wherein the mammal is a human.
13. The method of any one of claims 1-12, wherein the compound is represented by Formula (I):



(I),

or a pharmaceutically acceptable salt and/or prodrug thereof,

wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

14. The method of claim 13, wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, arylalkyl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, oxo, hydroxyl, $-OR^b$, hydroxyalkyl, $-CH_2OR^b$, and halo;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

15. The method of claim 13 or 14, wherein, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, or heteroaryl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, -CN, -NO₂, =N-OH, -N₃, -R^a, -OR^a, -SR^a, -N(R^a)₂, -N(R^a)₃⁺, =NR^a, -NHC(=O)R^c, -C(=O)R^c, -C(=O)N(R^a)₂, -S(=O)₂R^c, -OS(=O)₂OR^a, -S(=O)₂OR^a, -S(=O)₂N(R^a)₂, -S(=O)R^c, -OP(=O)(OR^a)₂, - (alkylene)-C(=O)R^c, -C(=S)R^c, -C(=O)OR^a, -(alkylene)-C(=O)OR^a, -C(=S)OR^a, -C(=O)SR^a, -C(=S)SR^a, -(alkylene)-C(=O)N(R^a)₂, -C(=S)N(R^a)₂, and -C(-NR^a)N(R^a)₂;

R_a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, cycloalkyl, or (cycloalkyl)alkyl.

16. The method of any one of claims 13-15, wherein, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, or heteroaryl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, -R^a, -OR^a, -N(R^a)₂, -N(R^a)₃⁺, -NHC(=O)R^c, -C(=O)R^c, -C(=O)N(R^a)₂, -C(=O)OR^a, - (alkylene)-C(=O)OR^a, and -(alkylene)-C(=O)N(R^a)₂; and

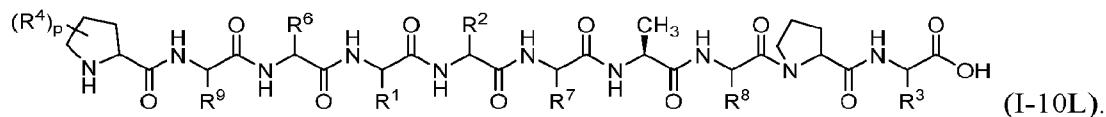
R_a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, cycloalkyl, or (cycloalkyl)alkyl.

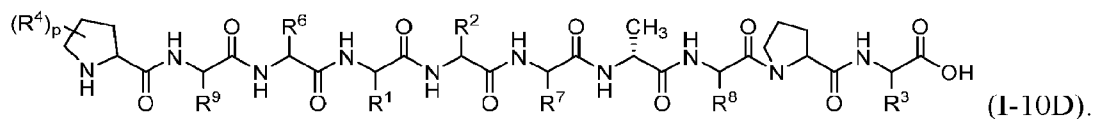
17. The method of claim 15 or 16, wherein R_a , independently for each occurrence, is hydrogen, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, or (heterocycloalkyl)alkyl; and

R^c, independently for each occurrence, is alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl.

18. The method of any one of claims 13-17, wherein the compound has the structure of formula (I-10L):

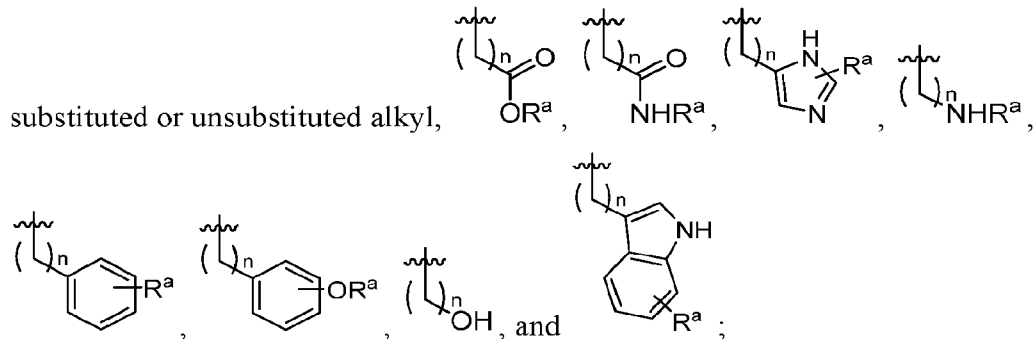


19. The method of any one of claims 13-17, wherein the compound has the structure of formula (I-10D):



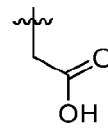
20. The method of any one of claims 13-19, wherein R¹ is substituted or unsubstituted alkyl, arylalkyl, or heteroarylalkyl.

21. The method of any one of claims 13-20, wherein R¹ is selected from

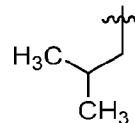
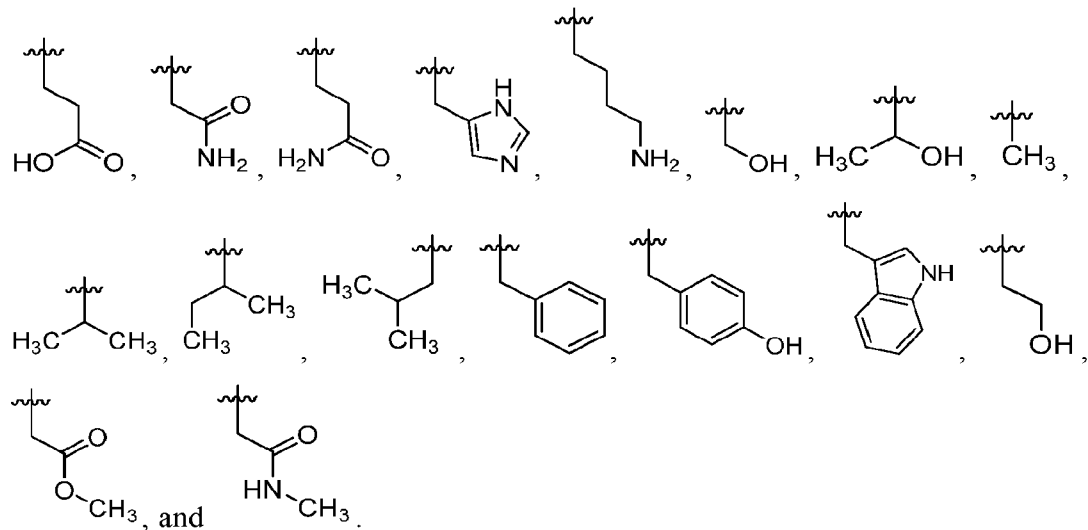


R^a is hydrogen or alkyl; and

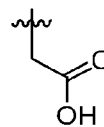
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.



22. The method of any one of claims 13-21, wherein R^1 is selected from

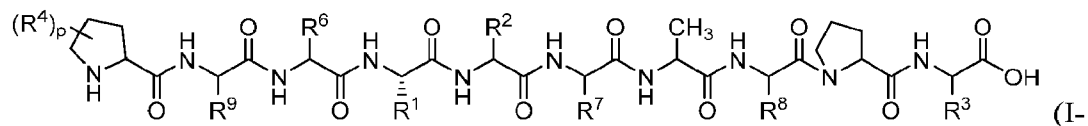


23. The method of any one of claims 13-22, wherein R^1 is



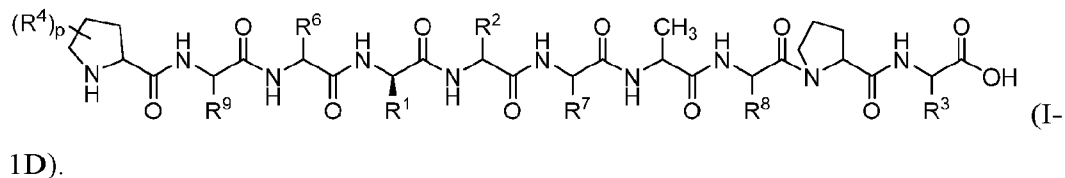
24. The method of any one of claims 13-22, wherein R^1 is

25. The method of any one of claims 13-24, wherein the compound has the structure of formula (I-1L)



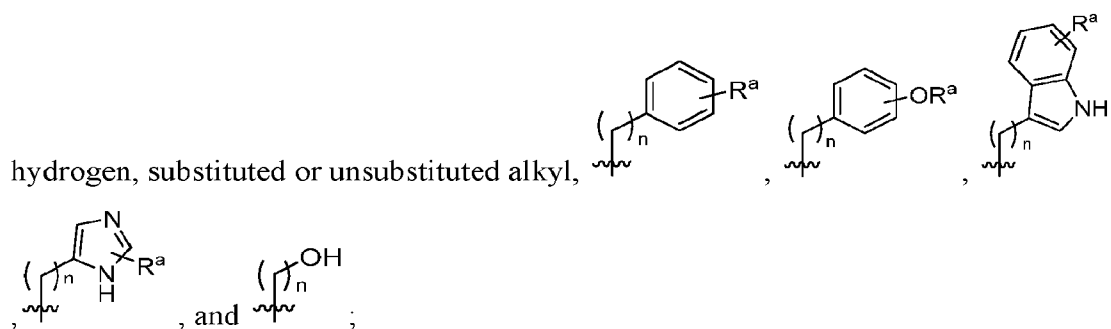
- 1L).

26. The method of any one of claims 13-24, wherein the compound has the structure of formula (I-1D)



27. The method of any one of claims 13-26, wherein R^2 is H or substituted or unsubstituted alkyl, arylalkyl, or heteroarylalkyl.

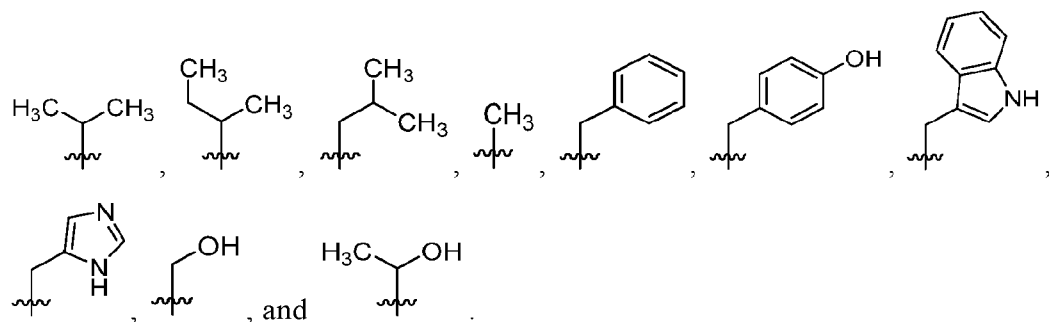
28. The method of any one of claims 13-27, wherein R^2 is selected from



R^a is hydrogen or alkyl; and

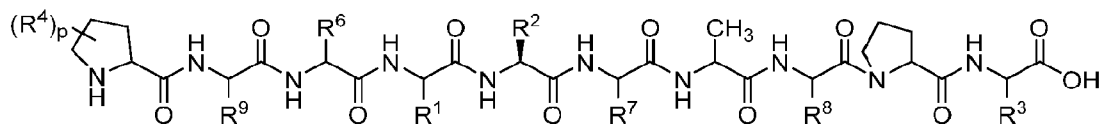
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

29. The method of any one of claims 13-28, wherein R^2 is selected from ,



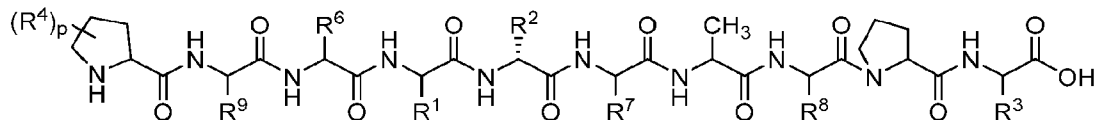
30. The method of any one of claims 13-29, wherein R^2 is hydrogen.

31. The method of any one of claims 13-30, wherein the compound has the structure of formula (I-2L):



(I-2L).

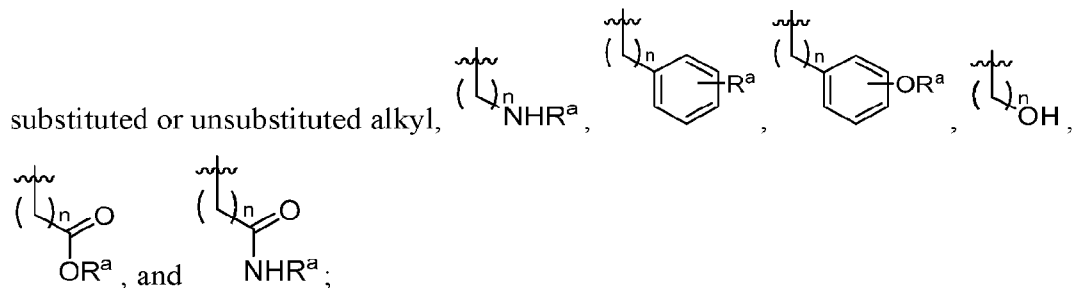
32. The method of any one of claims 13-30, wherein the compound has the structure of formula (I-2D):



(I-2D).

33. The method of any one of claims 13-32, wherein R^3 is substituted or unsubstituted alkyl or arylalkyl.

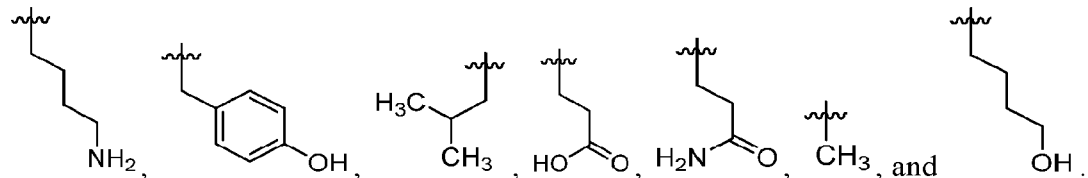
34. The method of any one of claims 13-33, wherein R^3 is selected from

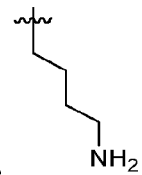


R^a is hydrogen or alkyl; and

n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

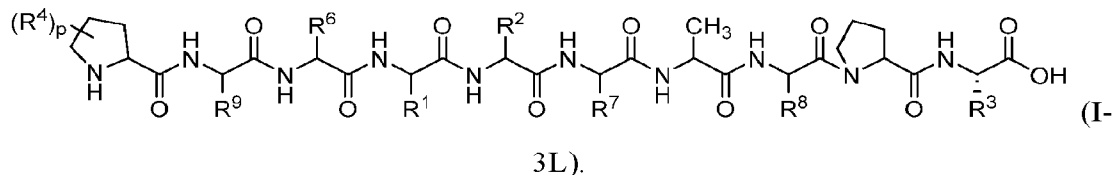
35. The method of any one of claims 13-34, wherein R^3 is selected from



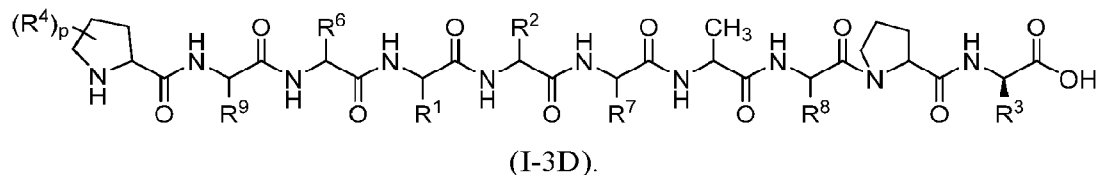


36. The method of any one of claims 13-35, wherein R^3 is

37. The method of any one of claims 13-36, wherein the compound has the structure of formula (I-3L):



38. The method of any one of claims 13-36, wherein the compound has the structure of formula (I-3D):



39. The method of any one of claims 13-38, wherein p is 1 or 2; and R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, $-\text{OR}^b$, $-\text{CH}_2\text{OR}^b$, halo, hydroxyl, and hydroxyalkyl.

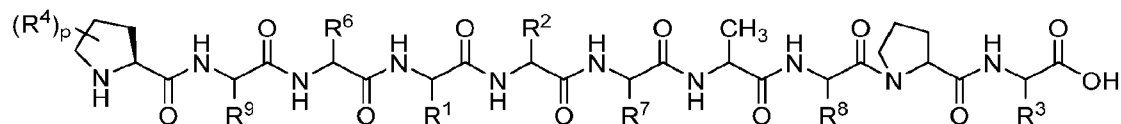
40. The method of any one of claims 13-39, wherein p is 1 or 2; and R^4 , independently for each occurrence, is selected from $-\text{CH}_3$, halo, hydroxyl, and hydroxyalkyl.

41. The method of claim 40, wherein R^4 is hydroxyl.

42. The method of claim 40, wherein R^4 is $-\text{CH}_3$.

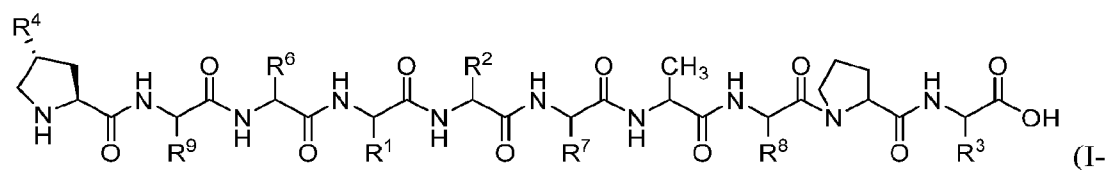
43. The method of any one of claims 39-42, wherein p is 1.

44. The method of any one of claims 13-43, wherein the compound has the structure of formula (I-4Lg):



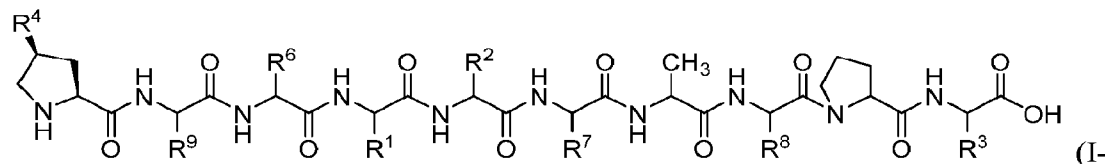
(I-4Lg).

45. The method of any one of claims 13-43, wherein the compound has the structure of formula (I-4La):



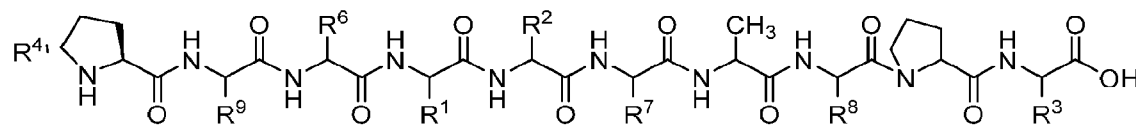
(I-4La).

46. The method of any one of claims 13-43, wherein the compound has the structure of formula (I-4Lb):



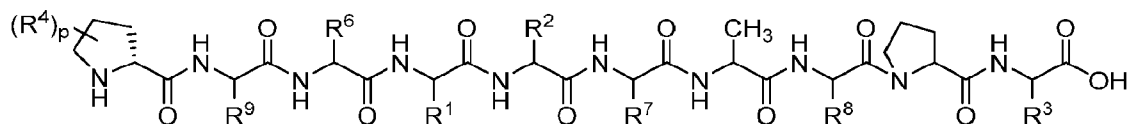
(I-4Lb).

47. The method of any one of claims 13-40, 42, and 43, wherein the compound has the structure of formula (I-4Lc):



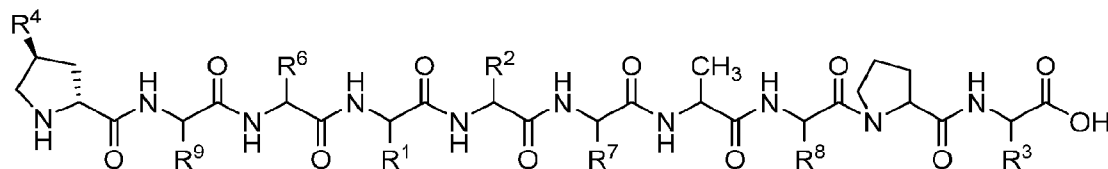
(I-4Lc).

48. The method of any one of claims 13-43, wherein the compound has the structure of formula (I-4Dg):



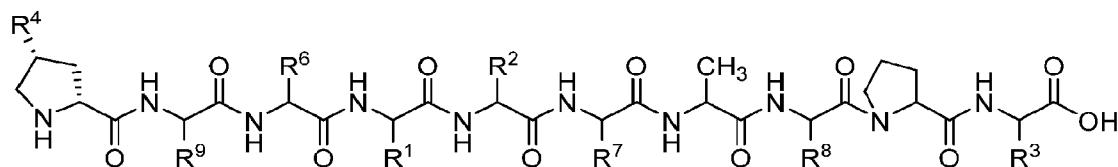
(I-4Dg).

49. The method of any one of claims 13-43 and 48, wherein the compound has the structure of formula (I-4Da):



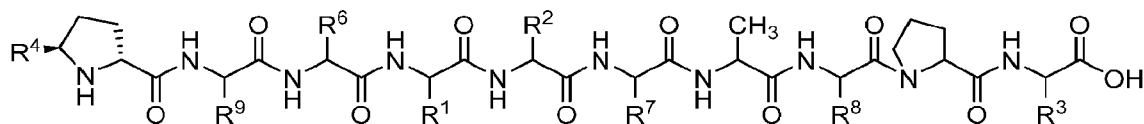
(I-4Da).

50. The method of any one of claims 13-43 and 48, wherein the compound has the structure of formula (I-4Db):



(I-4Db).

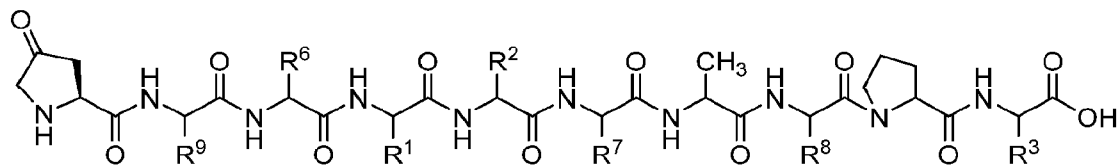
51. The method of any one of claims 13-40, 42, 43, and 48, wherein the compound has the structure of formula (I-4Dc):



(I-4Dc).

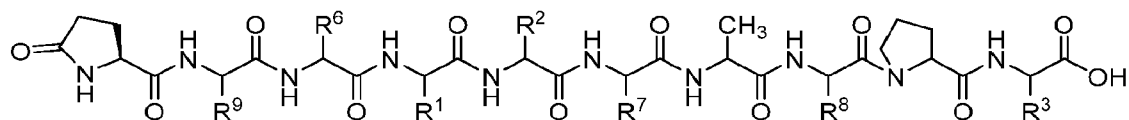
52. The method of any one of claims 13-38, wherein R^4 is oxo.

53. The method of claim 52, wherein the compound has the structure of formula (I-4Ld):



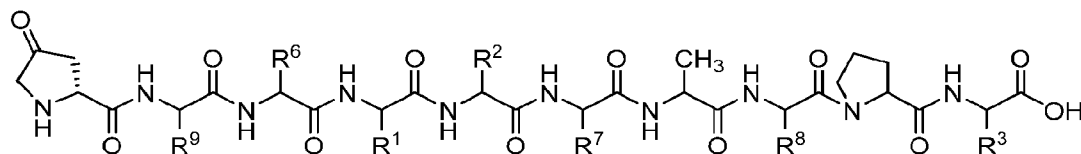
(I-4Ld).

54. The method of claim 52, wherein the compound has the structure of formula (I-4Le):



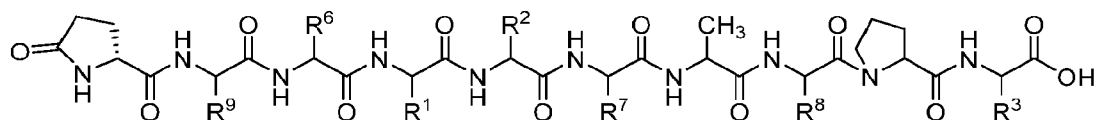
(I-4Le).

55. The method of claim 52, wherein the compound has the structure of formula (I-4Dd):



(I-4Dd).

56. The method of claim 52, wherein the compound has the structure of formula (I-4De):

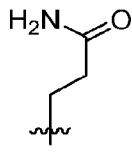


(I-4De).

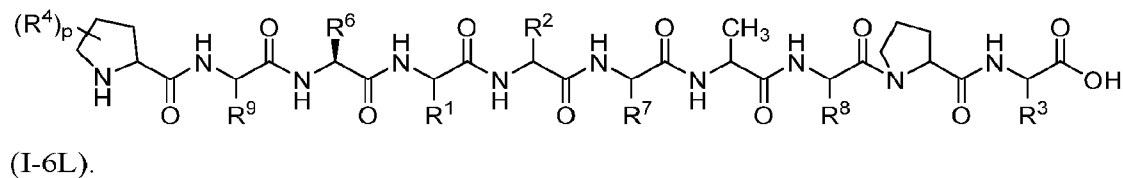
57. The method of any one of claims 1-56, wherein R^6 is hydrogen or alkyl, wherein the alkyl is optionally substituted with one occurrence of $-C(=O)NH_2$.

58. The method of any one of claims 1-57, wherein R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$.

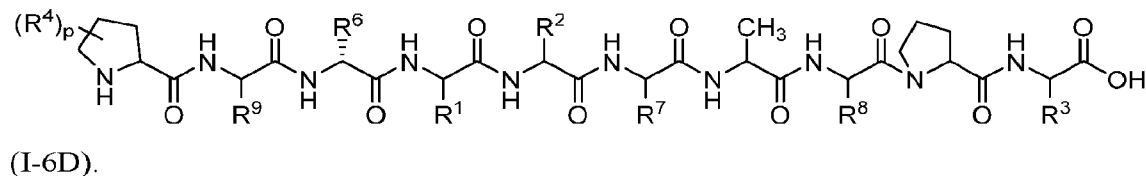
59. The method of any one of claims 1-58, wherein R^6 is $-\text{CH}_3$.

60. The method of any one of claims 1-58, wherein R^6 is .

61. The method of any one of claims 1-60, wherein the compound has the structure of formula (I-6L):

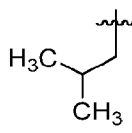


62. The method of any one of claims 1-60, wherein the compound has the structure of formula (I-6D):

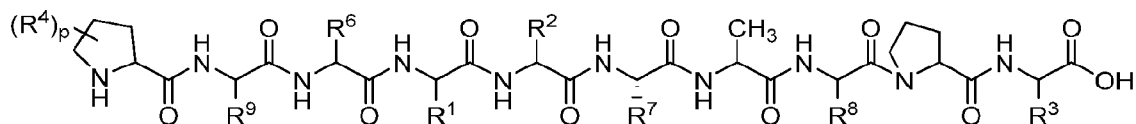


63. The method of any one of claims 1-62, wherein R^7 is $(\text{C}_1\text{-C}_{10})\text{alkyl}$.

64. The method of any one of claims 1-63, wherein R^7 is .

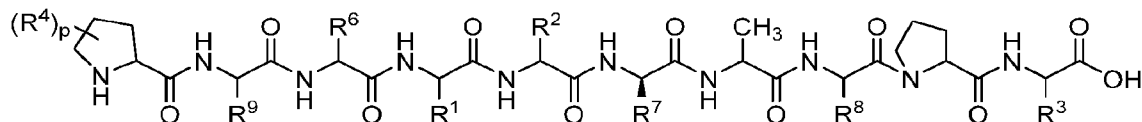
65. The method of any one of claims 1-63, wherein R^7 is .

66. The method of any one of claims 1-65, wherein the compound has the structure of formula (I-7L):



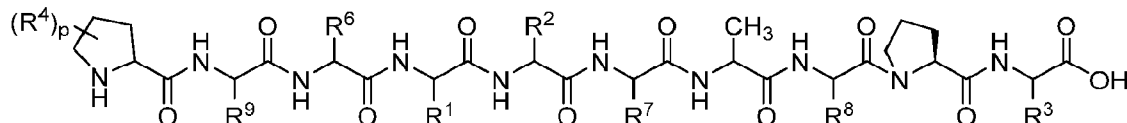
(I-7L).

67. The method of any one of claims 1-65, wherein the compound has the structure of formula (I-7D):



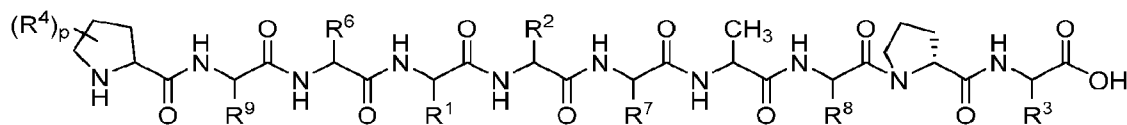
(I-7D).

68. The method of any one of claims 1-67, wherein the compound has the structure of formula (I-11L):



(I-11L).

69. The method of any one of claims 1-67, wherein the compound has the structure of formula (I-11D):



(I-11D).

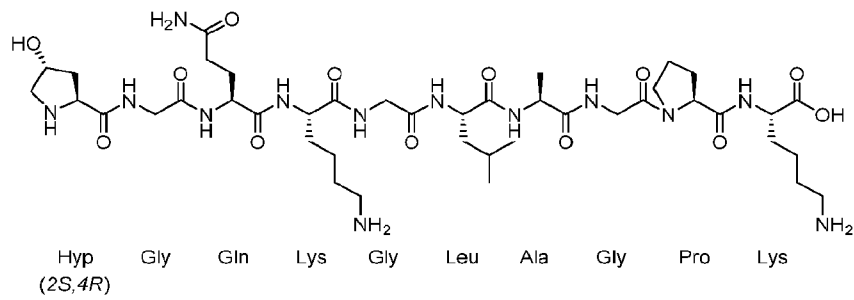
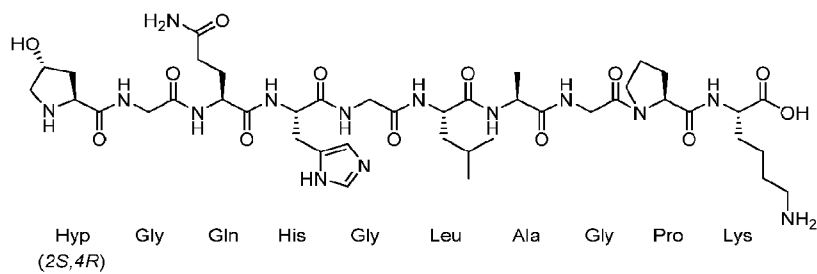
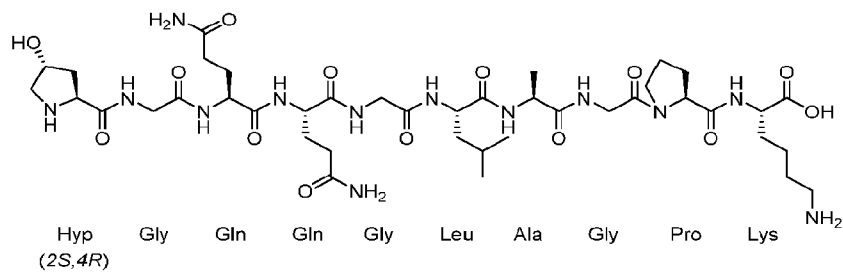
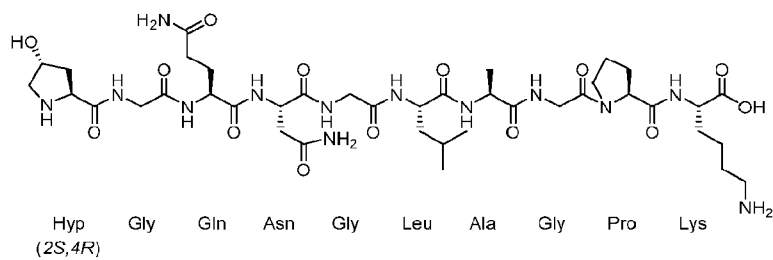
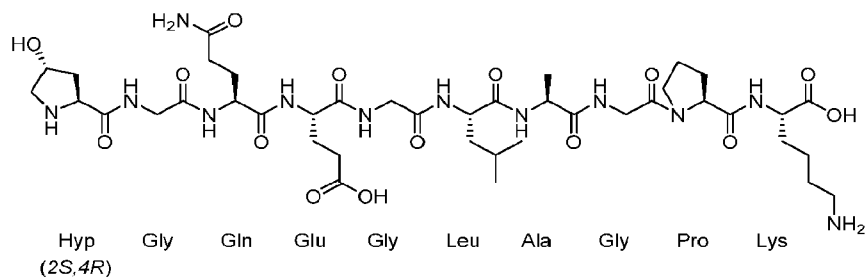
70. The method of any one of claims 1-69, wherein R^8 is $-CH_3$ or $-H$.

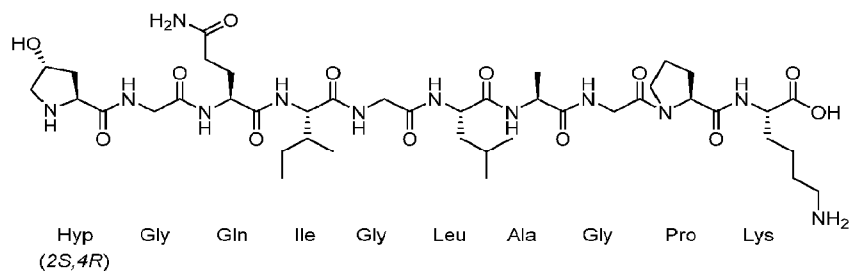
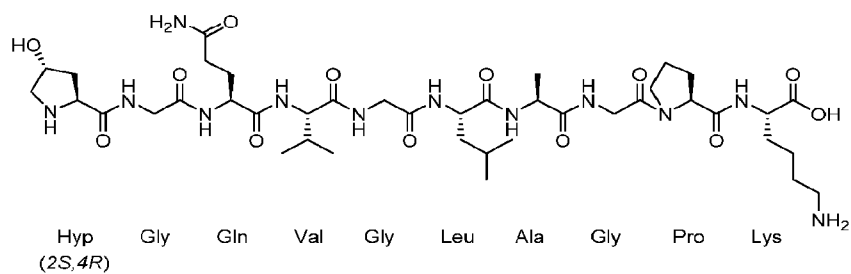
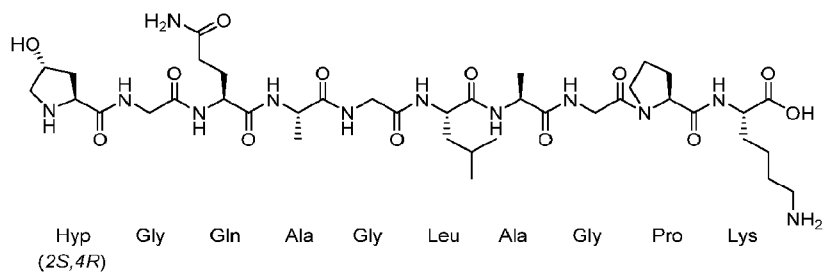
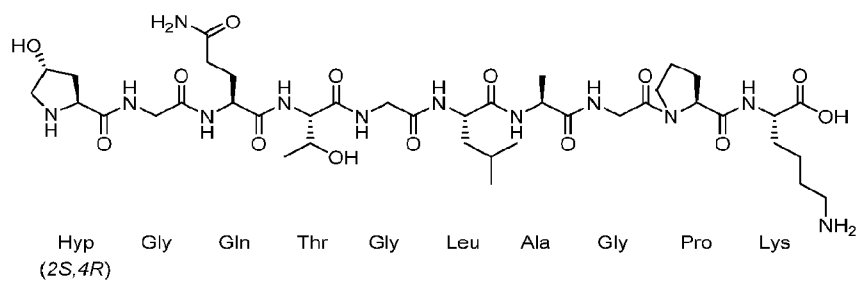
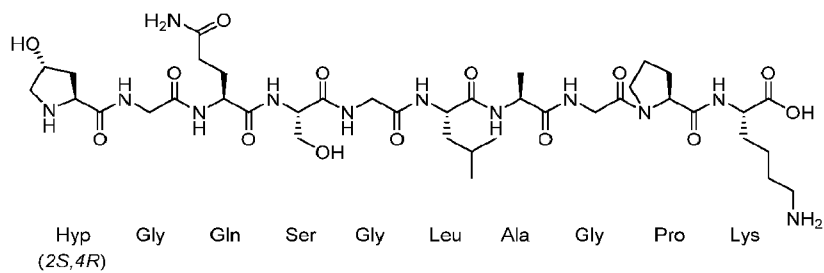
71. The method of any one of claims 1-70, wherein R^8 is $-H$.

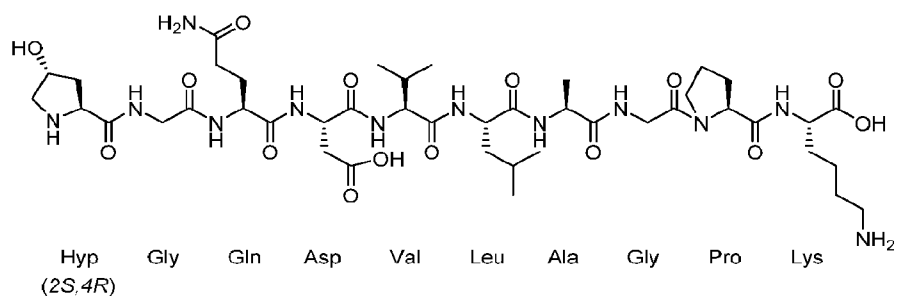
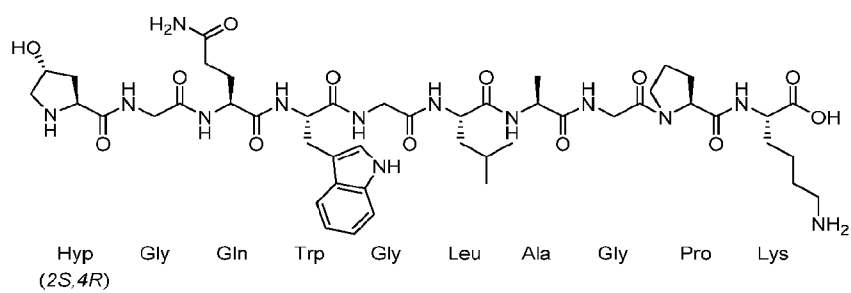
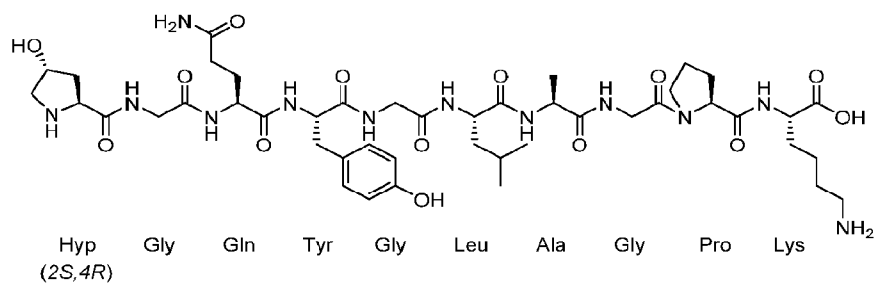
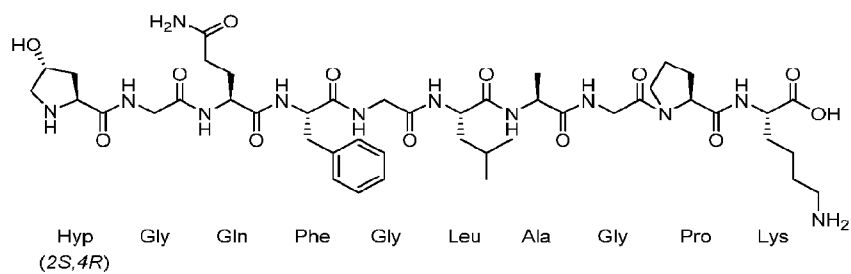
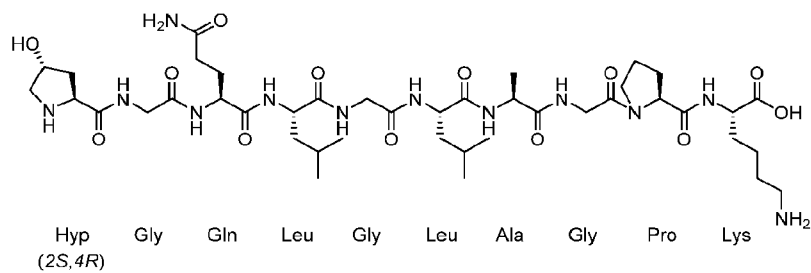
72. The method of any one of claims 1-71, wherein R^9 is $-CH_3$ or $-H$.

73. The method of any one of claims 1-72, wherein R^9 is $-H$.

74. The method of claim 13, wherein the compound is selected from the following:

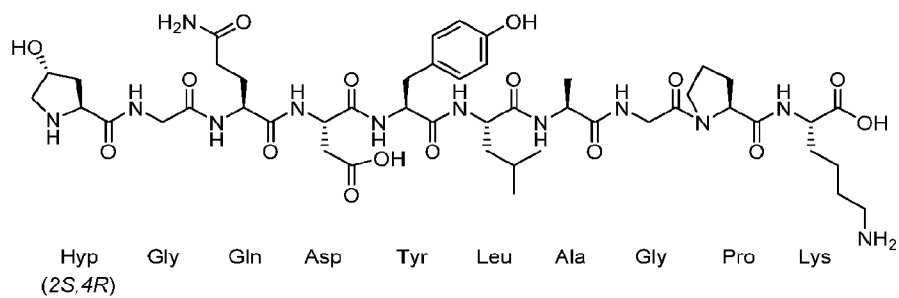
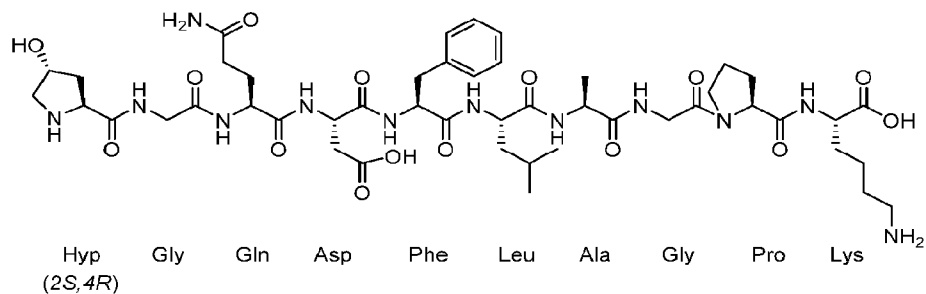
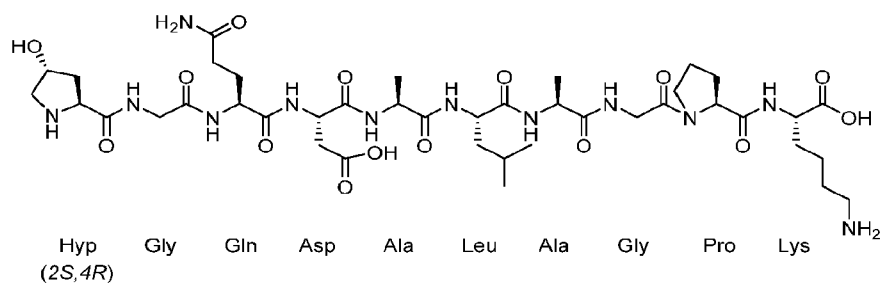
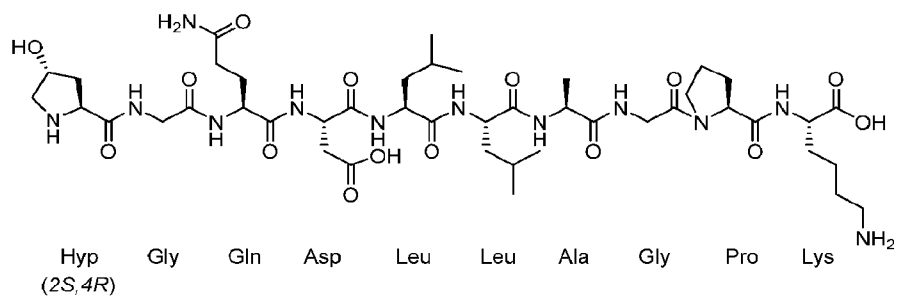
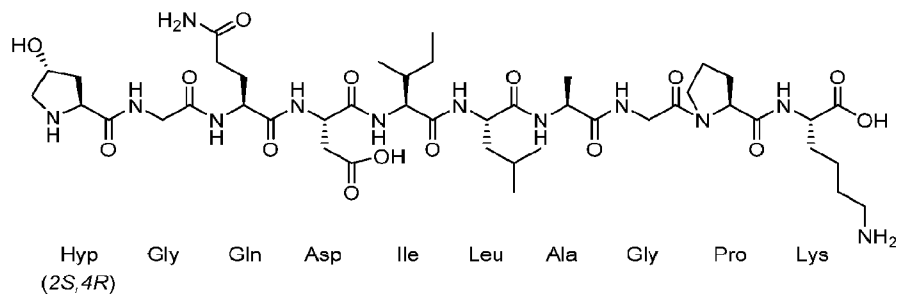


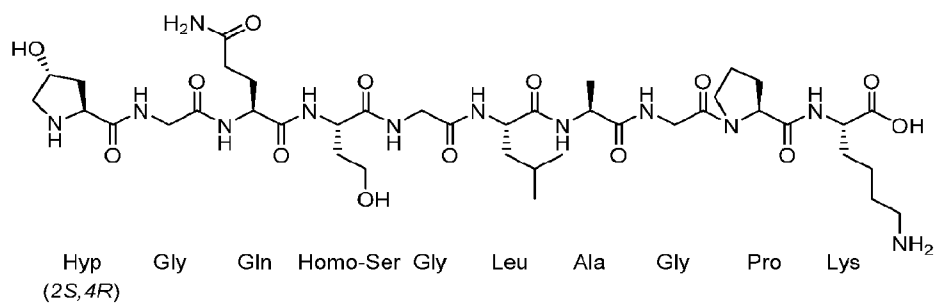
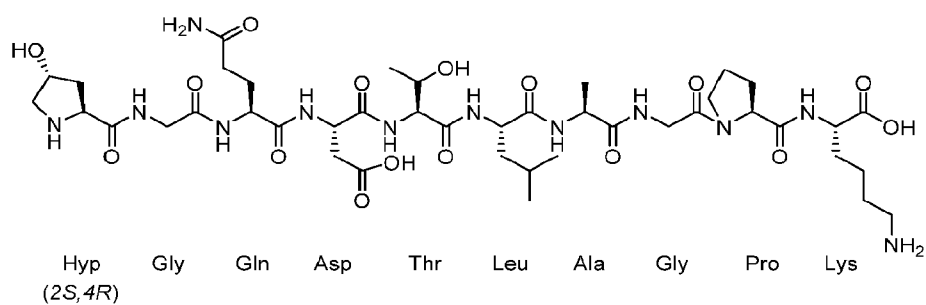
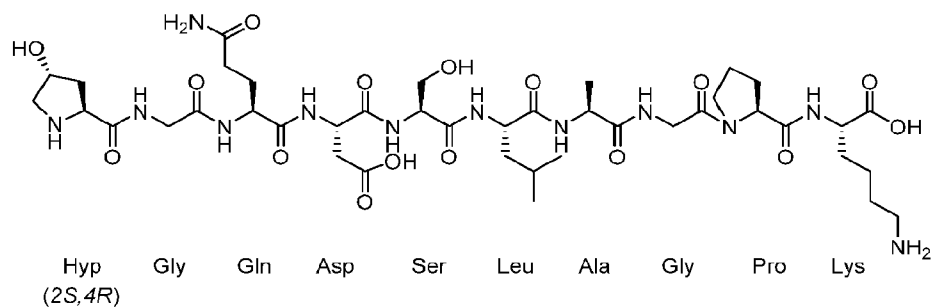
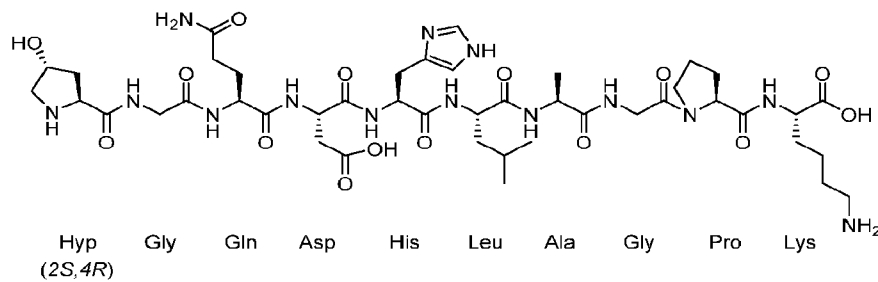
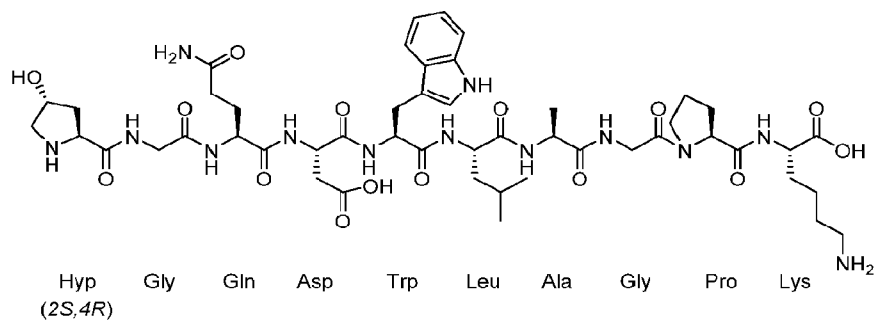


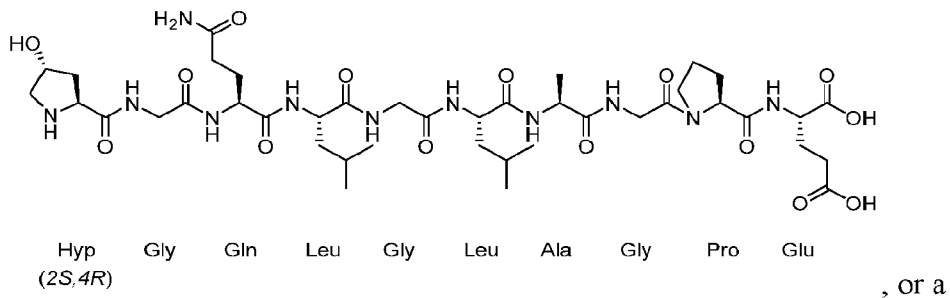
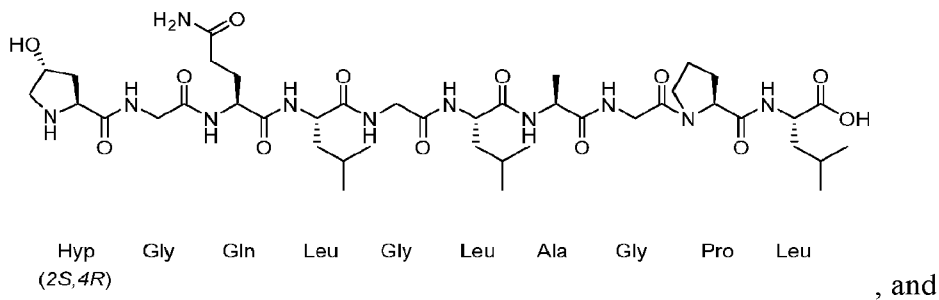
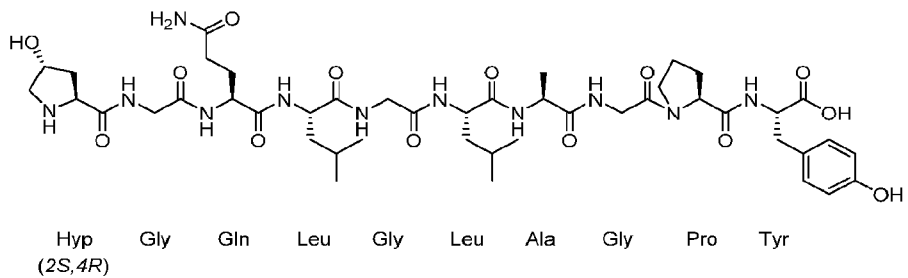
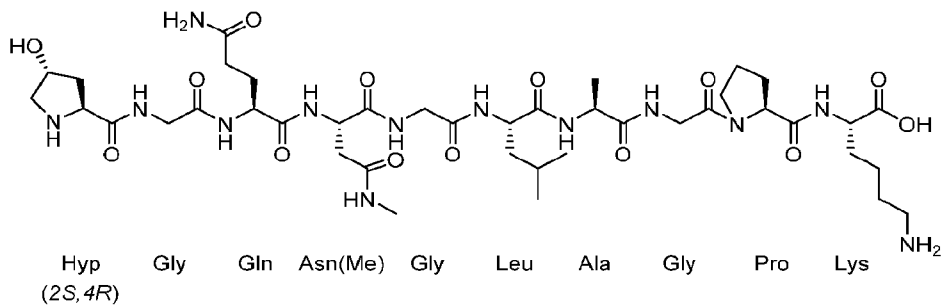
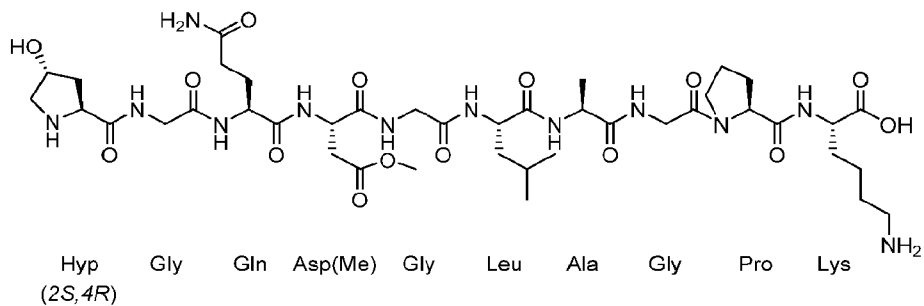


pharmaceutically acceptable salt thereof.

75. The method of claim 13, wherein the compound is selected from the following:

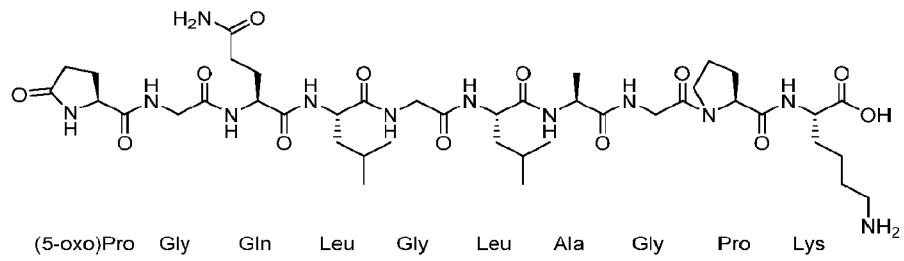
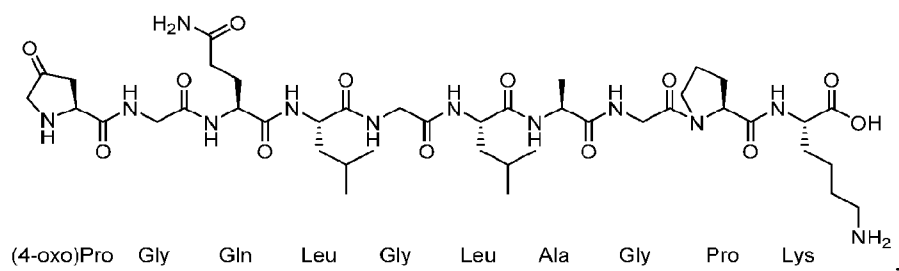
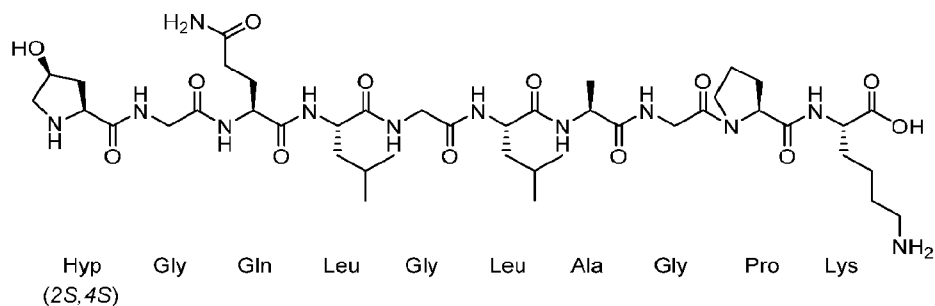
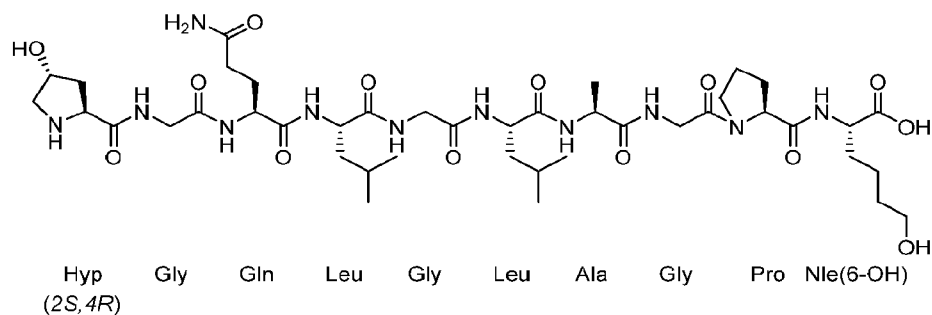
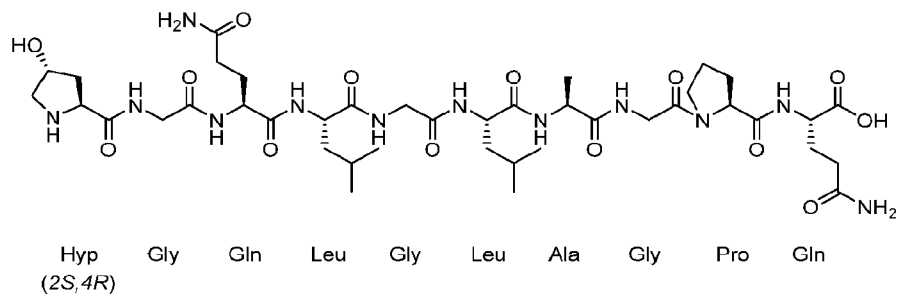


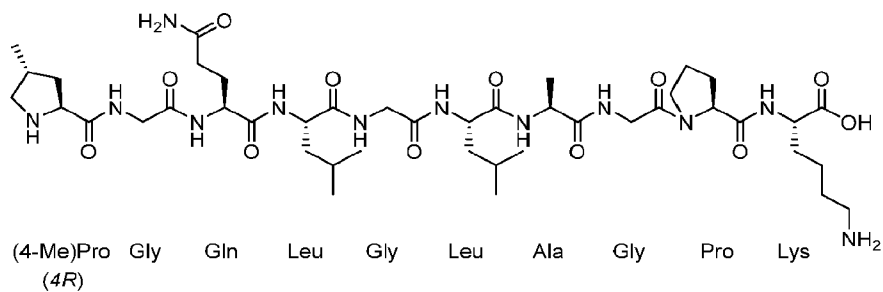
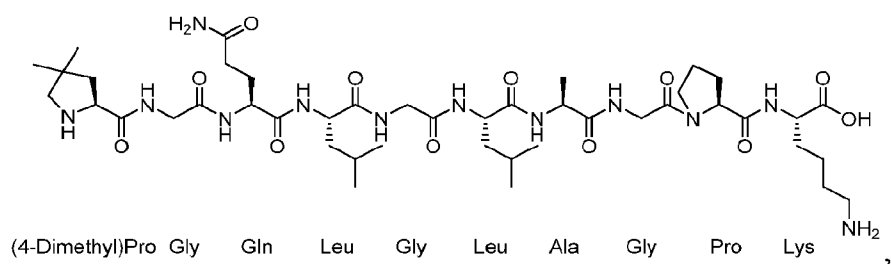
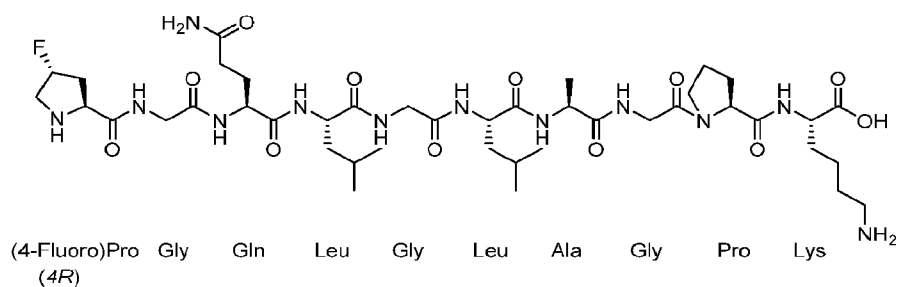
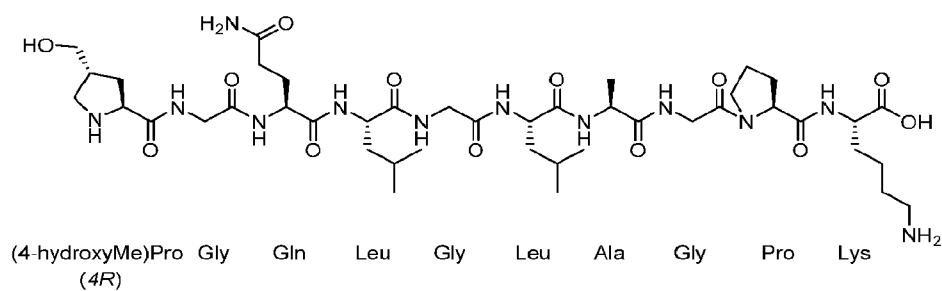
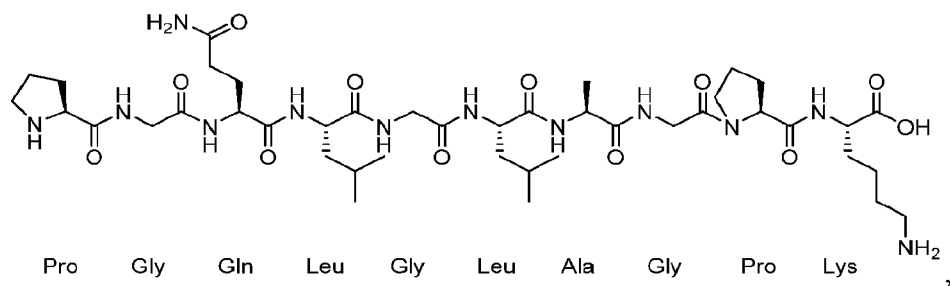


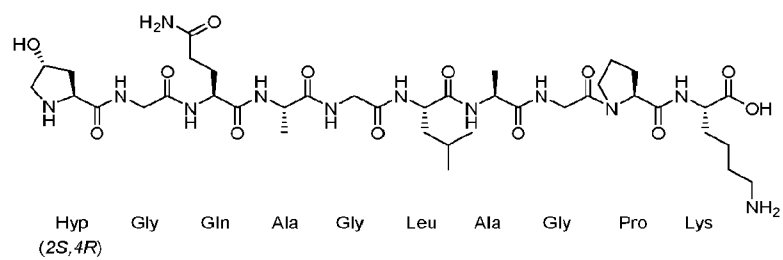
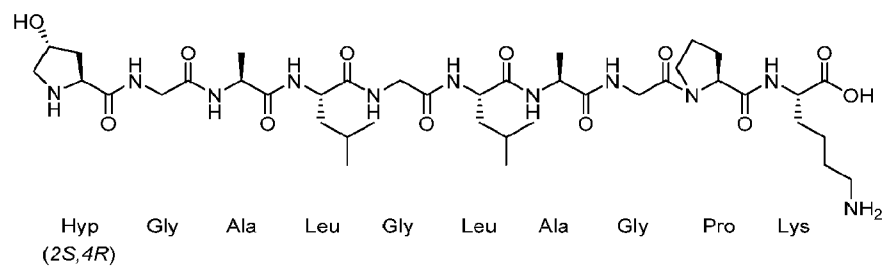
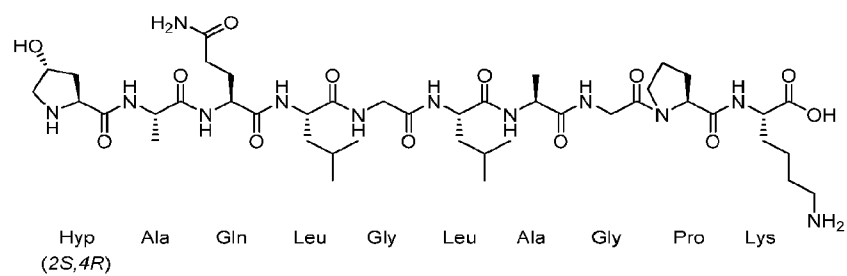
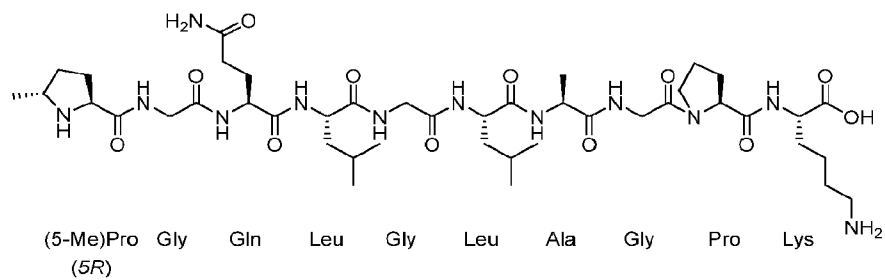


pharmaceutically acceptable salt thereof.

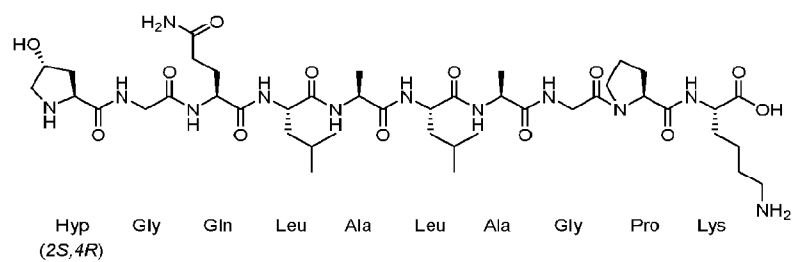
76. The method of claim 13, wherein the compound is selected from the following:







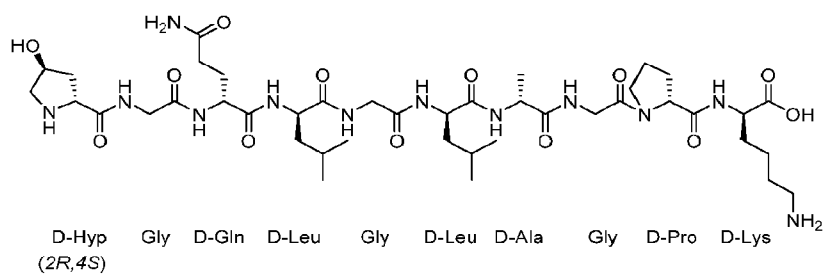
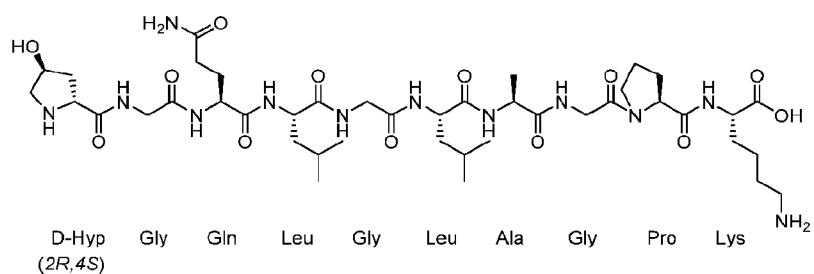
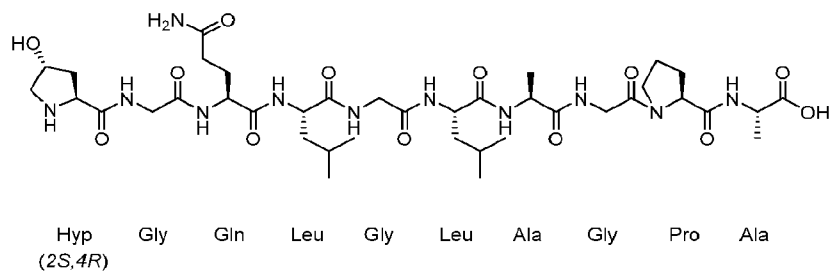
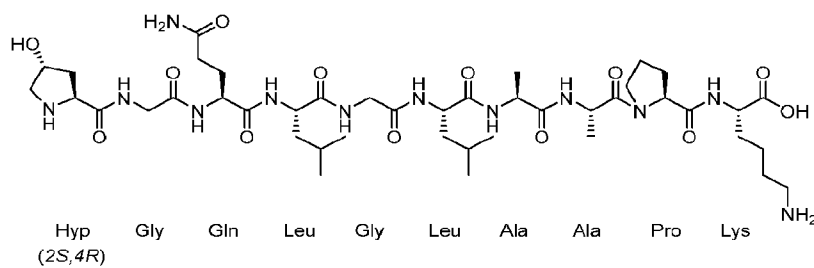
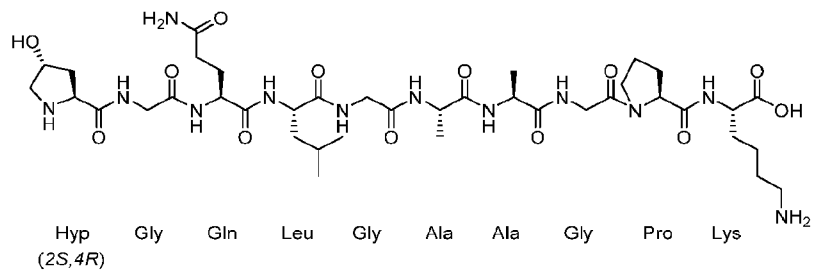
, and

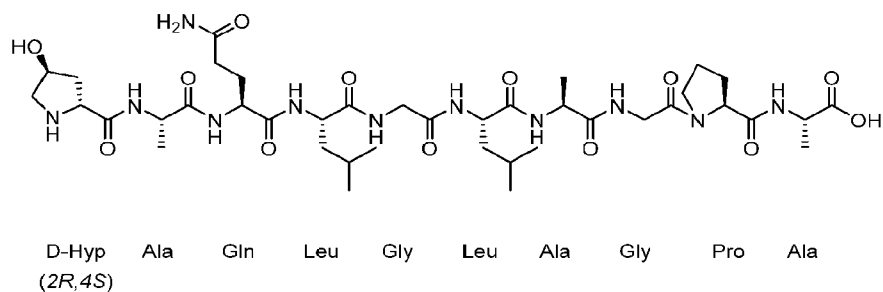
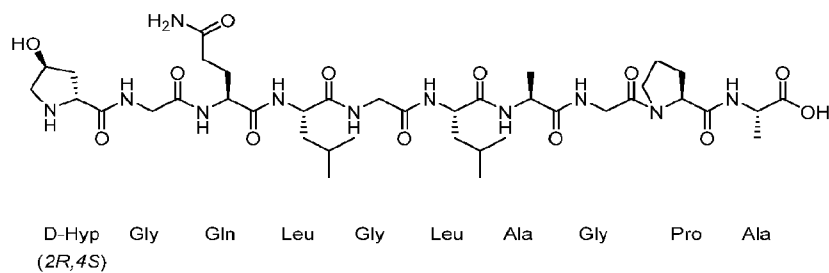
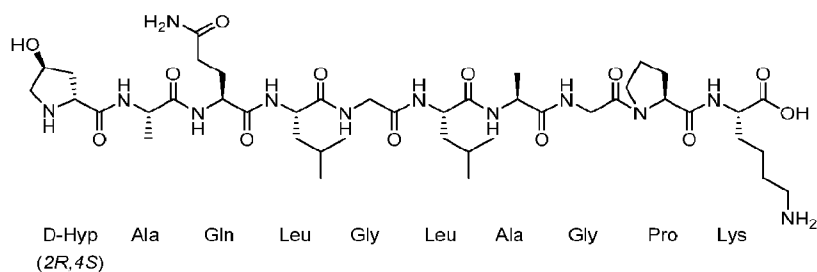
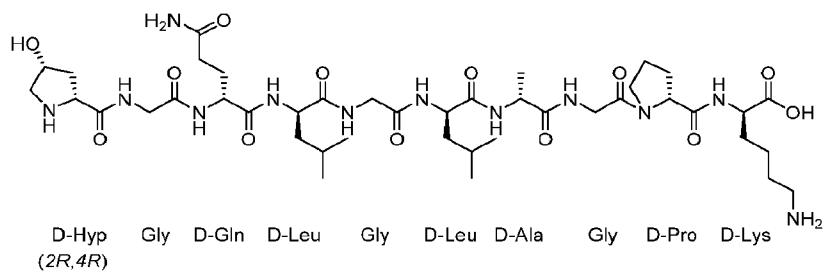


, or a pharmaceutically

acceptable salt thereof.

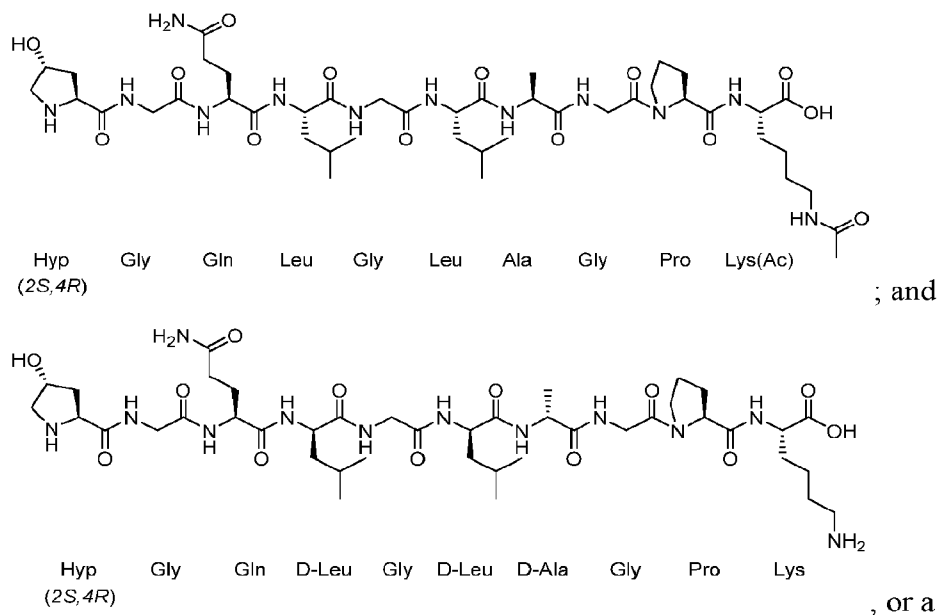
77. The method of claim 13, wherein the compound is selected from the following:





pharmaceutically acceptable salt thereof.

78. The method of claim 13, wherein the compound is selected from the following:



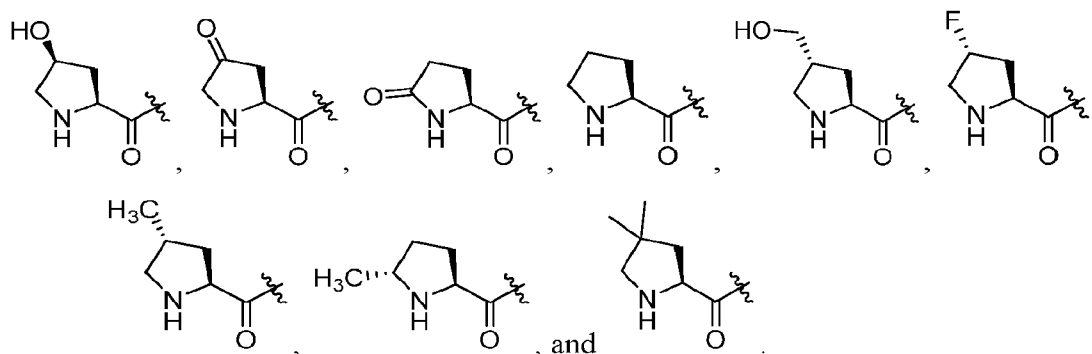
pharmaceutically acceptable salt thereof.

79. The method of any one of claims 1-12, wherein the peptide has an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys; or a pharmaceutically acceptable salt and/or stereoisomer thereof; wherein Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me).

80. The method of any one of claims 1-12, wherein the peptide has an amino acid sequence represented by HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys; or a pharmaceutically acceptable salt and/or stereoisomer thereof; wherein Xbb is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly.

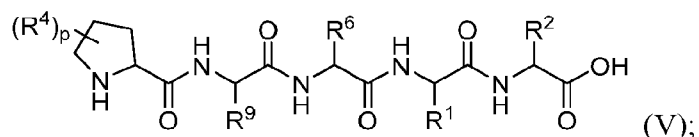
81. The method of any one of claims 1-12, wherein the peptide has an amino acid sequence represented by HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro- Xcc; or a pharmaceutically acceptable salt and/or stereoisomer thereof; wherein Xcc is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH).

82. The method of any one of claims 1-20, wherein the peptide has an amino acid sequence represented by Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;
or a pharmaceutically acceptable salt and/or stereoisomer thereof;
wherein Xdd is selected from:



83. The peptide of any one of claims 1-73, wherein at least one, at least two, at least three, at least four, at least five, at least six, or at least seven amino acid residues in the peptide are D-amino acid residues.

84. The method of any one of claims 1-20, wherein the compound is represented by Formula (V):



or a pharmaceutically acceptable salt thereof; wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^9 is hydrogen or alkyl.

85. The method of claim 84, wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

R^4 for each occurrence is hydroxyl;

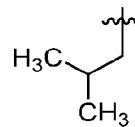
p is 1;

R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

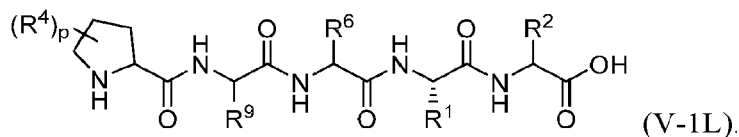
R^9 is hydrogen.

86. The method of claim 84 or 85, wherein R^1 is substituted or unsubstituted alkyl.

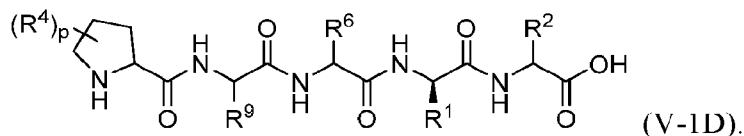
87. The method of any one of claims 84-86, wherein R^1 is



88. The method of any one of claims 84-87, wherein the compound has the structure of formula (V-1L)



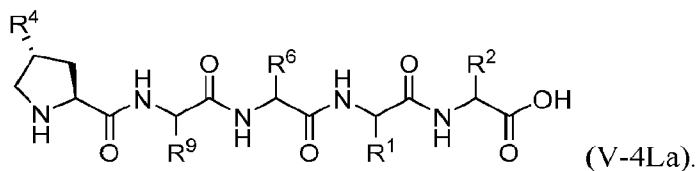
89. The method of any one of claims 84-87, wherein the compound has the structure of formula (V-1D)



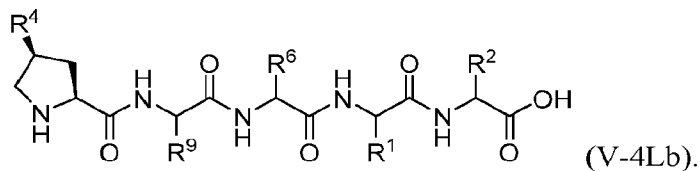
90. The method of any one of claims 84-89, wherein R^2 is H.

91. The method of any one of claims 84-90, wherein p is 1 and R^4 is hydroxyl.

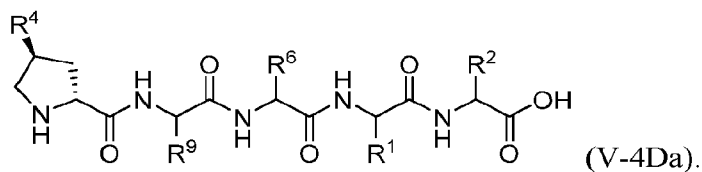
92. The method of any one of claims 84-91, wherein the compound has the structure of formula (V-4La):



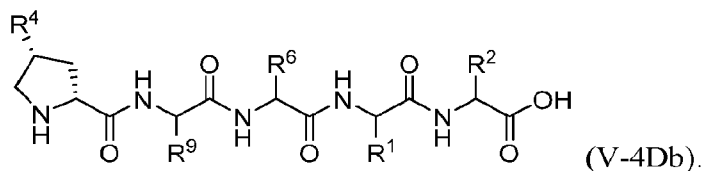
93. The method of any one of claims 84-91, wherein the compound has the structure of formula (V-4Lb):



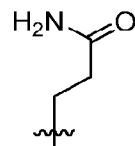
94. The method of any one of claims 84-91, wherein the compound has the structure of formula (V-4Da):



95. The method of any one of claims 84-91, wherein the compound has the structure of formula (V-4Db):

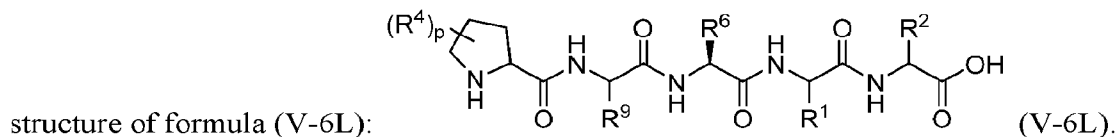


96. The method of any one of claims 84-95, wherein R^6 is alkyl substituted with one occurrence of $-C(=O)NH_2$.

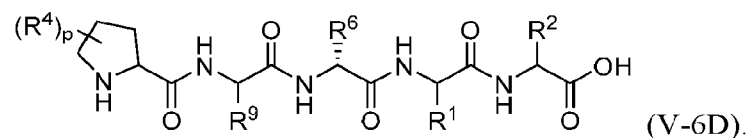


97. The method of any one of claims 84-96, wherein R^6 is

98. The method of any one of claims 84-97, wherein the compound has the

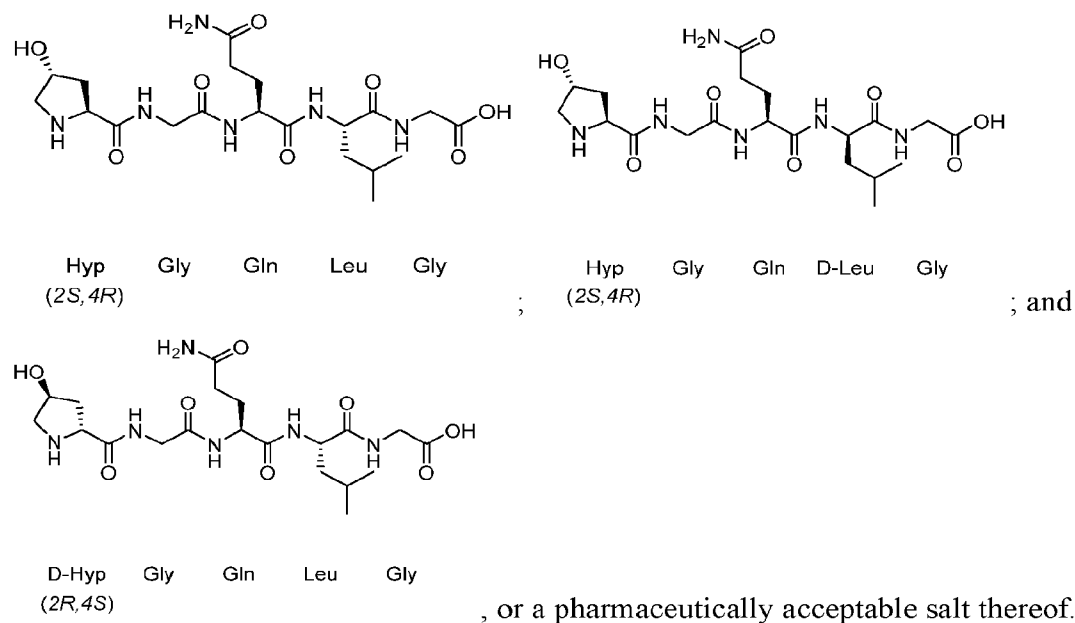


99. The method of any one of claims 84-97, wherein the compound has the structure of formula (V-6D):

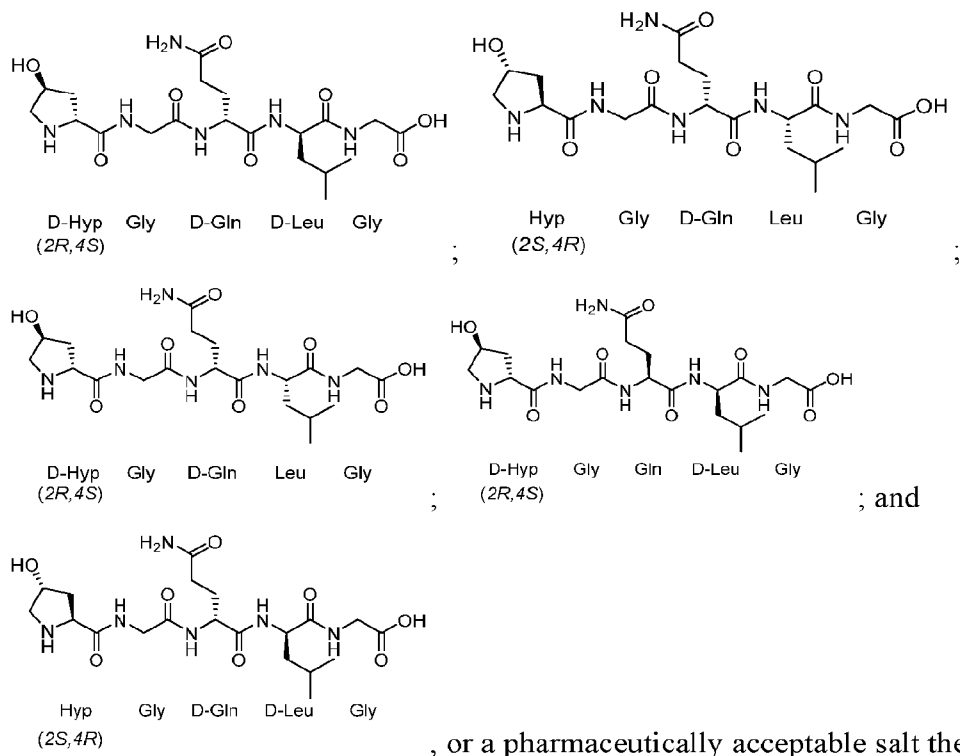


100. The method of any one of claims 84-99, wherein R⁹ is -H.

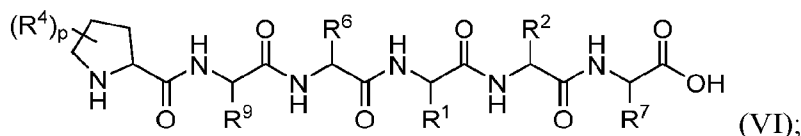
101. The method of claim 84, wherein the compound is selected from the following:



102. The method of claim 84, wherein the compound is selected from the following:



103. The method of any one of claims 1-20, wherein the compound is represented by Formula (VI):



or a pharmaceutically acceptable salt thereof; wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 is hydrogen or alkyl; and

R^9 is hydrogen or alkyl.

104. The method of claim 103, wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

R^4 for each occurrence is hydroxyl;

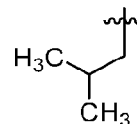
p is 1;

R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

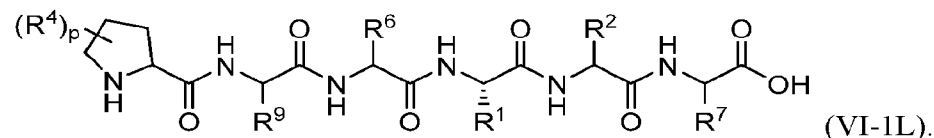
R^9 is hydrogen.

105. The method of claim 103 or 104, wherein R^1 is substituted or unsubstituted alkyl.

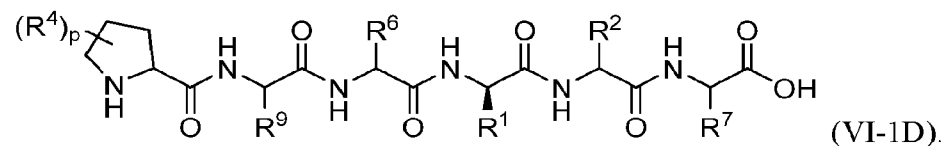
106. The method of any one of claims 103-105, wherein R^1 is



107. The method of any one of claims 103-106, wherein the compound has the structure of formula (VI-1L)



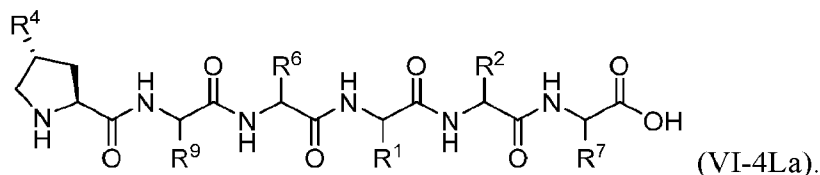
108. The method of any one of claims 103-106, wherein the compound has the structure of formula (VI-1D)



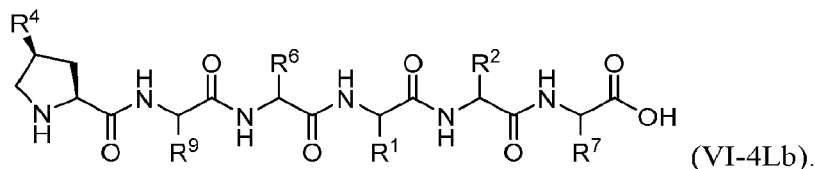
109. The method of any one of claims 103-108, wherein R^2 is H.

110. The method of any one of claims 103-109, wherein p is 1 and R^4 is hydroxyl.

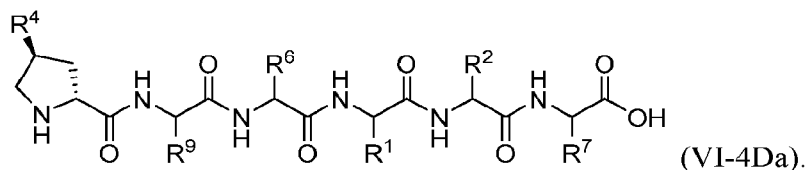
111. The method of any one of claims 103-110, wherein the compound has the structure of formula (VI-4La):



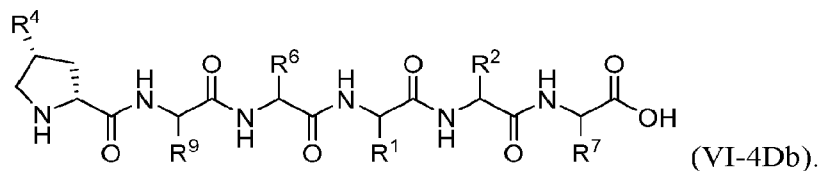
112. The method of any one of claims 103-110, wherein the compound has the structure of formula (VI-4Lb):



113. The method of any one of claims 103-110, wherein the compound has the structure of formula (VI-4Da):

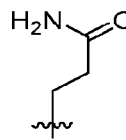


114. The method of any one of claims 103-110, wherein the compound has the structure of formula (VI-4Db):

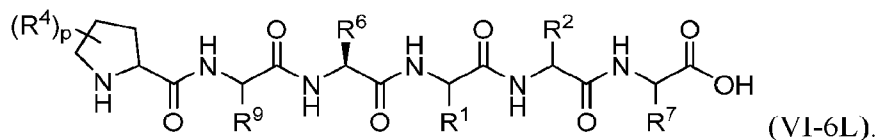


115. The method of any one of claims 103-114, wherein R⁶ is alkyl substituted with one occurrence of -C(=O)NH₂.

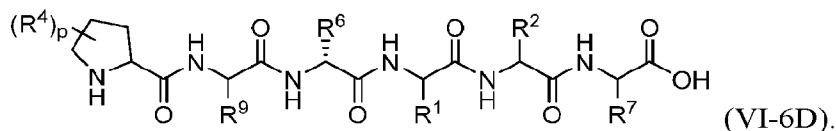
116. The method of any one of claims 103-115, wherein R⁶ is



117. The method of any one of claims 103-116, wherein the compound has the structure of formula (VI-6L):



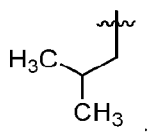
118. The method of any one of claims 103-116, wherein the compound has the structure of formula (VI-6D):



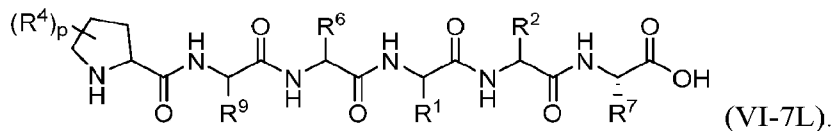
119. The method of any one of claims 103-118, wherein R⁹ is H.

120. The method of any one of claims 103-119, wherein R⁷ is (C₁-C₁₀)alkyl.

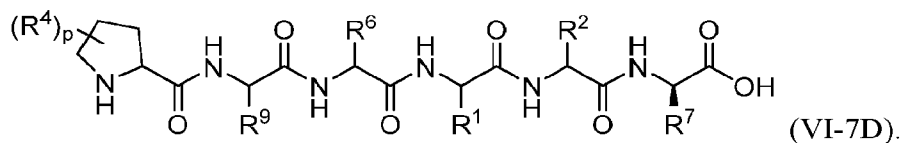
121. The method of any one of claims 103-120, wherein R⁷ is .

122. The method of any one of claims 103-120, wherein R⁷ is .

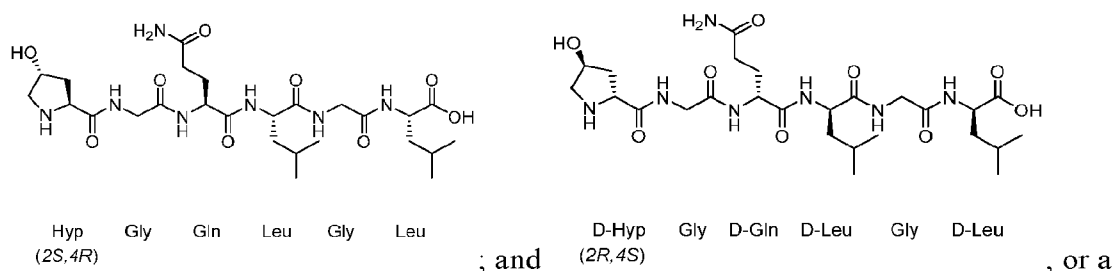
123. The method of any one of claims 103-122, wherein the compound has the structure of formula (VI-7L):



124. The method of any one of claims 103-122, wherein the compound has the structure of formula (VI-7D):

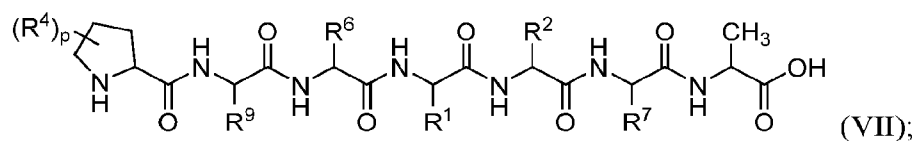


125. The method of claim 103, wherein the compound is selected from the following:



pharmaceutically acceptable salt thereof.

126. The method of any one of claims 1-20, wherein the compound is represented by Formula (VII):



or a pharmaceutically acceptable salt thereof; wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 is hydrogen or alkyl; and

R^9 is hydrogen or alkyl.

127. The method of claim 126, wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

R^4 for each occurrence is hydroxyl;

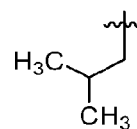
p is 1;

R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

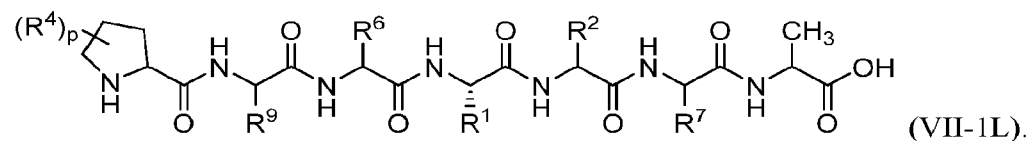
R^9 is hydrogen.

128. The method of claim 126 or 127, wherein R^1 is substituted or unsubstituted alkyl.

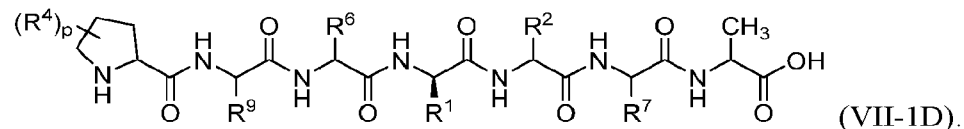
129. The method of any one of claims 126-128, wherein R^1 is



130. The method of any one of claims 126-129, wherein the compound has the structure of formula (VII-1L)



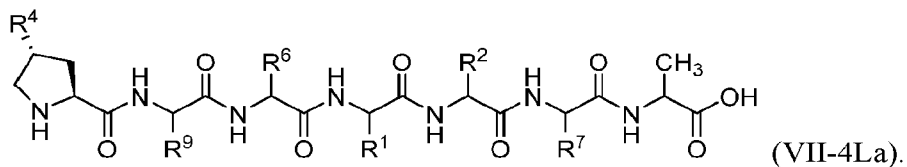
131. The method of any one of claims 126-129, wherein the compound has the structure of formula (VII-1D)



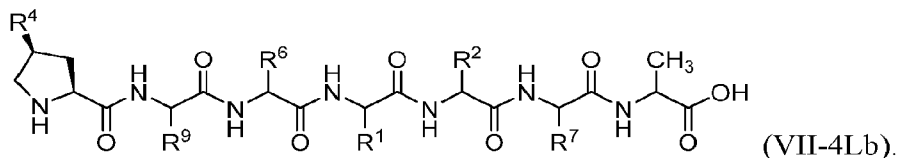
132. The method of any one of claims 126-131, wherein R^2 is H.

133. The method of any one of claims 126-132, wherein p is 1 and R^4 is hydroxyl.

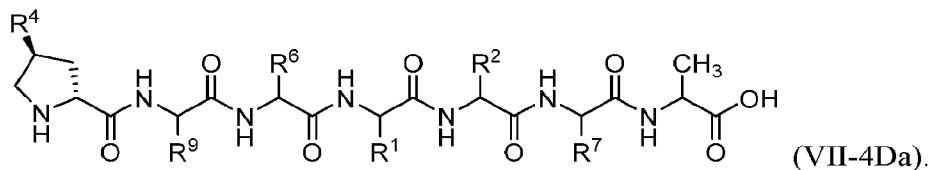
134. The method of any one of claims 126-133, wherein the compound has the structure of formula (VII-4La):



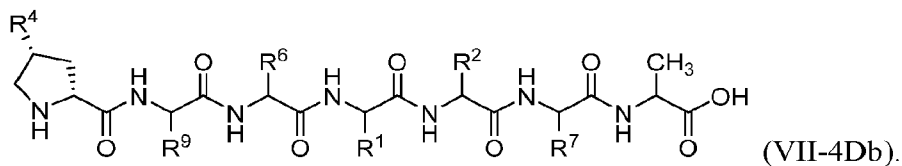
135. The method of any one of claims 126-133, wherein the compound has the structure of formula (VII-4Lb):



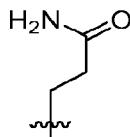
136. The method of any one of claims 126-133, wherein the compound has the structure of formula (VII-4Da):



137. The method of any one of claims 126-133, wherein the compound has the structure of formula (VII-4Db):

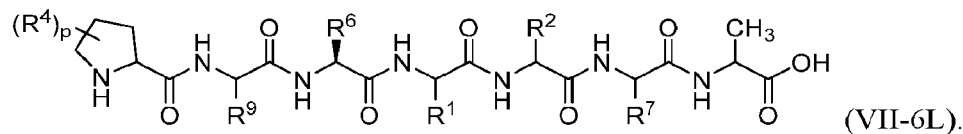


138. The method of any one of claims 126-137, wherein R⁶ is alkyl substituted with one occurrence of -C(=O)NH₂.

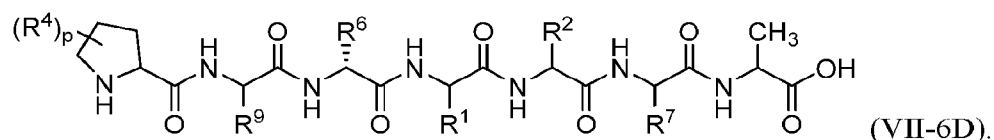


139. The method of any one of claims 126-138, wherein R⁶ is

140. The method of any one of claims 126-139, wherein the compound has the structure of formula (VII-6L):



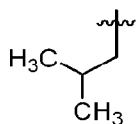
141. The method of any one of claims 126-139, wherein the compound has the structure of formula (VII-6D):



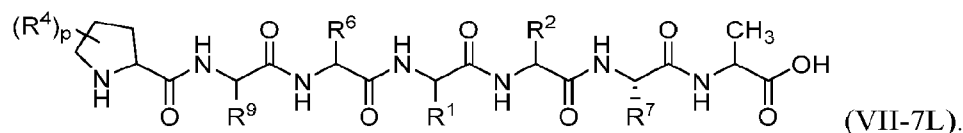
142. The method of any one of claims 126-141, wherein R^9 is $-H$.

143. The method of any one of claims 126-142, wherein R^7 is $(C_1-C_{10})alkyl$.

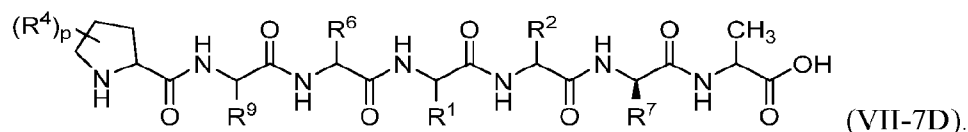
144. The method of any one of claims 126-143, wherein R^7 is .

145. The method of any one of claims 126-143, wherein R^7 is .

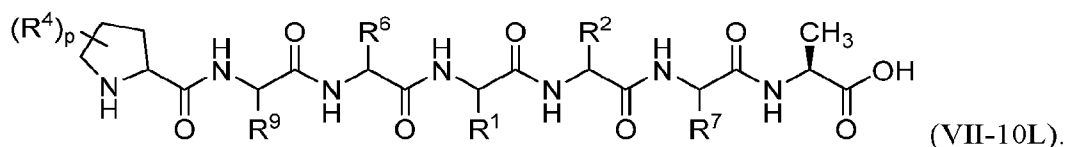
146. The method of any one of claims 126-145, wherein the compound has the structure of formula (VII-7L):



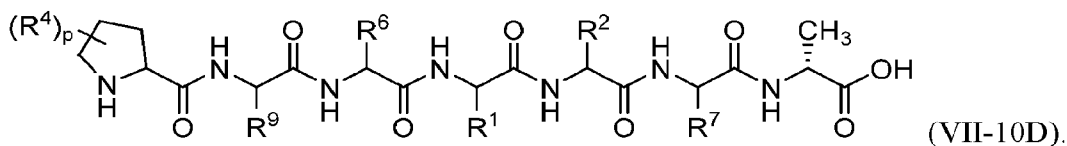
147. The method of any one of claims 126-145, wherein the compound has the structure of formula (VII-7D):



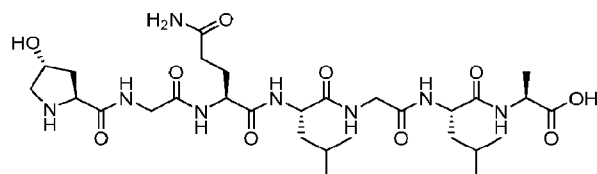
148. The method of any one of claims 126-147, wherein the compound has the structure of formula (VII-10L):



149. The method of any one of claims 126-147, wherein the compound has the structure of formula (VII-10D):



150. The method of claim 126, wherein the compound has the structure:



Hyp Gly Gln Leu Gly Leu Ala
(2S,4R)

, or a pharmaceutically acceptable salt

thereof.

151. The method of any one of claims 1-12, wherein the peptide has any one amino acid sequence selected from:

Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;

Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys;

HyP-Gly-Gln-Leu-Gly-Leu-Ala;

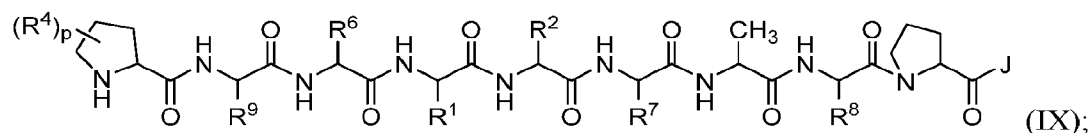
HyP-Gly-Gln-Glu-Gly-Leu-Gly;

HyP-Gly-Gln-Leu-Gly-Leu;

D-HyP(2R, 4S)-Gly-D-Gln-D-Leu-Gly-D-Leu;

HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-D-Leu-Gly; and
 D-HyP(2R, 4S)-Gly-Gln-Leu-Gly;
 or a pharmaceutically acceptable salt thereof.

152. The method of any one of claims 1-12, wherein the compound is represented by Formula (IX):



or a pharmaceutically acceptable salt thereof;

wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-NR^xR^y$; and

R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring.

153. The method of claim 152, wherein:

R^1 and R^2 are each independently H or substituted or unsubstituted alkyl;

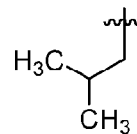
R^4 for each occurrence is hydroxyl;

p is 1;

R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$; and

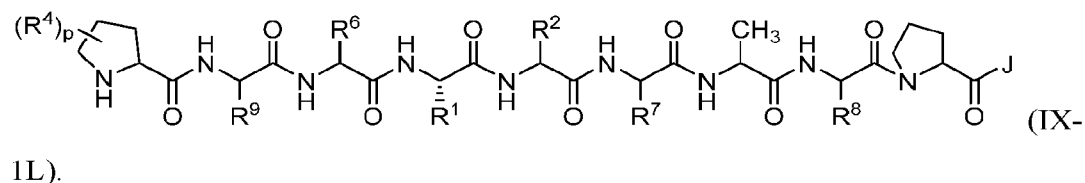
R^9 is hydrogen.

154. The method of claim 152 or 153, wherein R^1 is substituted or unsubstituted alkyl.

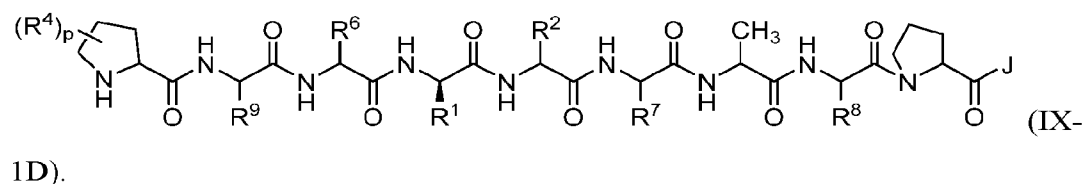


155. The method of any one of claims 152-154, wherein R^1 is

156. The method of any one of claims 152-155, wherein the compound has the structure of formula (IX-1L)



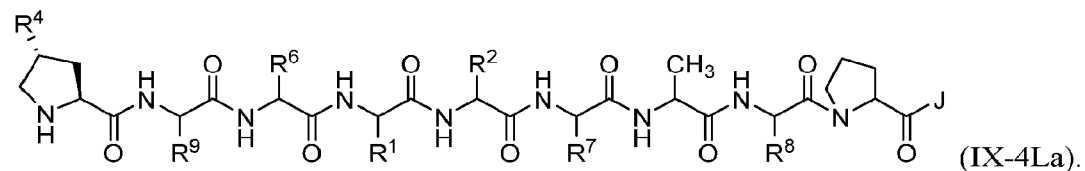
157. The method of any one of claims 152-155, wherein the compound has the structure of formula (IX-1D)



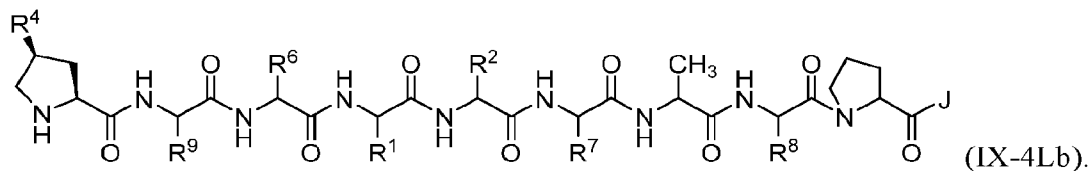
158. The method of any one of claims 152-157, wherein R^2 is H.

159. The method of any one of claims 152-158, wherein p is 1 and R^4 is hydroxyl.

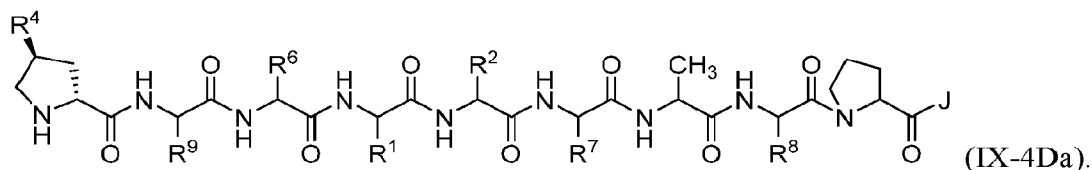
160. The method of any one of claims 152-159, wherein the compound has the structure of formula (IX-4La):



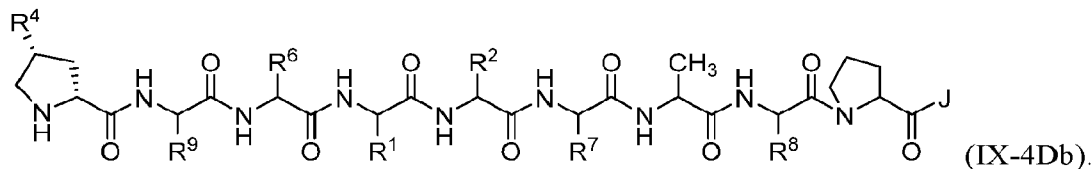
161. The method of any one of claims 152-159, wherein the compound has the structure of formula (IX-4Lb):



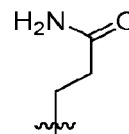
162. The method of any one of claims 152-159, wherein the compound has the structure of formula (IX-4Da):



163. The method of any one of claims 152-159, wherein the compound has the structure of formula (IX-4Db):

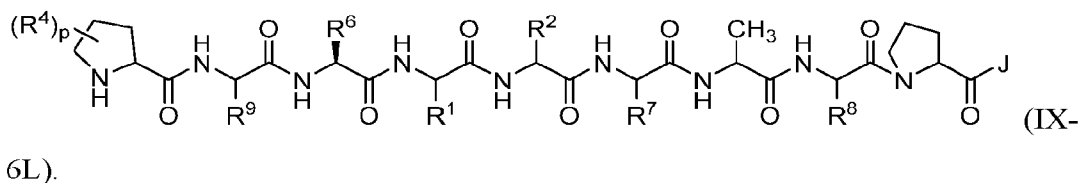


164. The method of any one of claims 152-163, wherein R^6 is alkyl substituted with one occurrence of $-C(=O)NH_2$.

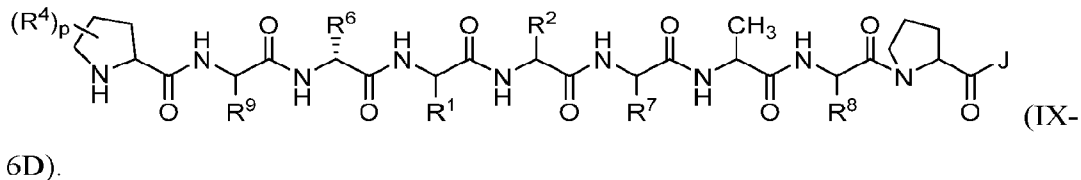


165. The method of any one of claims 152-164, wherein R^6 is

166. The method of any one of claims 152-165, wherein the compound has the structure of formula (IX-6L):



167. The method of any one of claims 152-165, wherein the compound has the structure of formula (IX-6D):



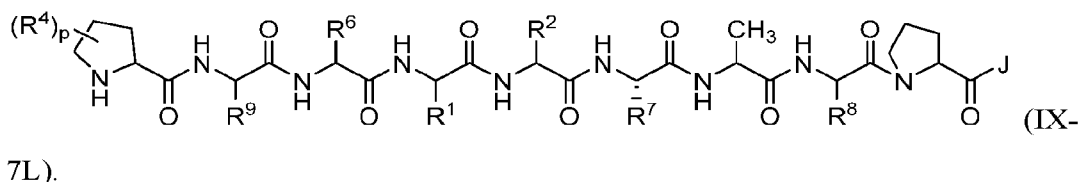
168. The method of any one of claims 152-167, wherein R⁹ is -H.

169. The method of any one of claims 152-168, wherein R⁷ is (C₁-C₁₀)alkyl.

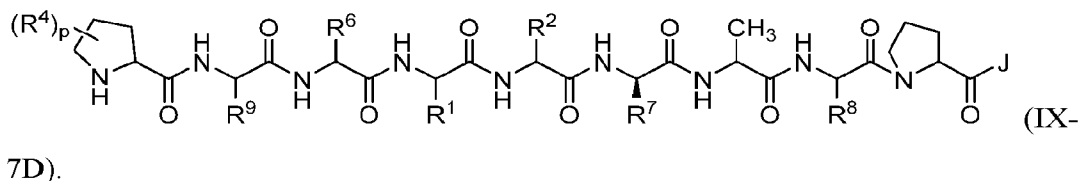
170. The method of any one of claims 152-169, wherein R⁷ is .

171. The method of any one of claims 152-169, wherein R⁷ is .

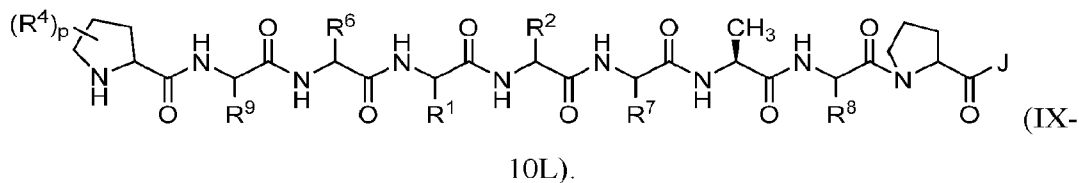
172. The method of any one of claims 152-171, wherein the compound has the structure of formula (IX-7L):



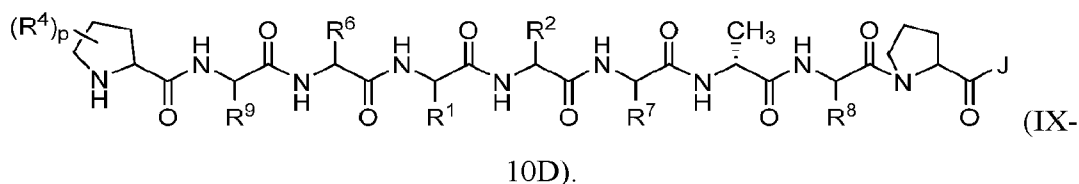
173. The method of any one of claims 152-171, wherein the compound has the structure of formula (IX-7D):



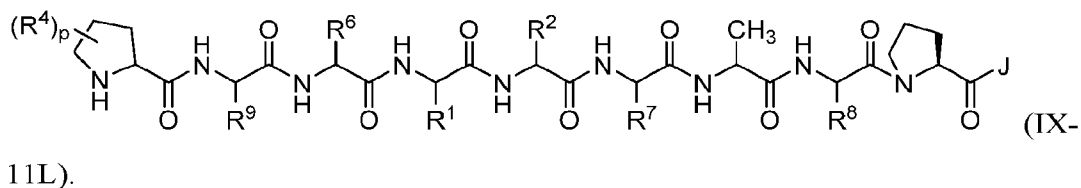
174. The method of any one of claims 152-173, wherein the compound has the structure of formula (IX-10L):



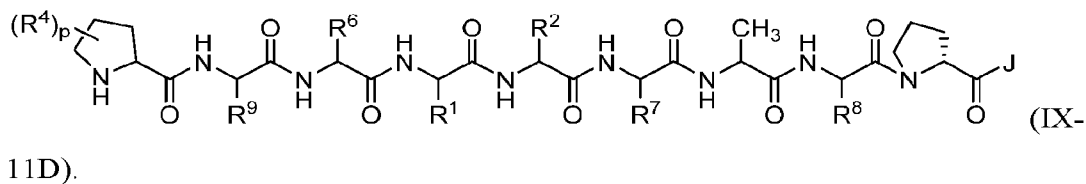
175. The method of any one of claims 152-173, wherein the compound has the structure of formula (IX-10D):



176. The method of any one of claims 152-175, wherein the compound has the structure of formula (IX-11L):



177. The method of any one of claims 152-175, wherein the compound has the structure of formula (IX-11D):



178. The method of any one of claims 152-177, wherein R^8 is $-\text{CH}_3$ or $-\text{H}$.

179. The method of any one of claims 152-178, wherein R^8 is $-\text{H}$.

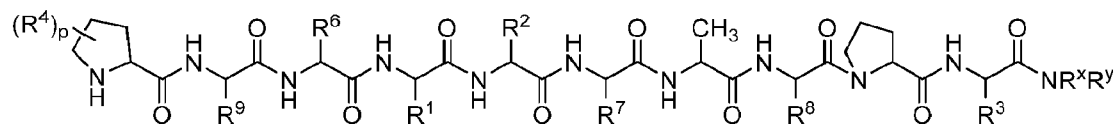
180. The method of any one of claims 152-179, wherein J is OH.

181. The method of any one of claims 152-179, wherein J is $-\text{NR}^x\text{R}^y$.

182. The method of claim 181, wherein R^x and R^y are each independently alkyl.

183. The method of claim 181, wherein R^x and R^y taken together with the intervening nitrogen atom form a ring.

184. The method of any one of claims 1-12, wherein the compound is represented by Formula (X-am):



(X-am);

or a pharmaceutically acceptable salt thereof;

wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclyl, or heterocyclalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, oxo, $-\text{OR}^b$, $-\text{CH}_2\text{OR}^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-\text{NR}^x\text{R}^y$; and

R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring.

185. The method of claim 184, wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, oxo, hydroxyl, $-OR^b$, hydroxyalkyl, $-CH_2OR^b$, and halo;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocyclalkyl;

R^6 is hydrogen or substituted or unsubstituted alkyl; and

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl.

186. The method of claim 184 or 185, wherein, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclalkyl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-CN$, $-NO_2$, $=N-OH$, $-N_3$, $-R^a$, $-OR^a$, $-SR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $=NR^a$, $-NHC(=O)R^c$, $-C(=O)R^c$, $-C(=O)N(R^a)_2$, $-S(=O)_2R^c$, $-OS(=O)_2OR^a$, $-S(=O)_2OR^a$, $-S(=O)_2N(R^a)_2$, $-S(=O)R^c$, $-OP(=O)(OR^a)_2$, $-(alkylene)-C(=O)R^c$, $-C(=S)R^c$, $-C(=O)OR^a$, $-(alkylene)-C(=O)OR^a$, $-C(=S)OR^a$, $-C(=O)SR^a$, $-C(=S)SR^a$, $-(alkylene)-C(=O)N(R^a)_2$, $-C(=S)N(R^a)_2$, and $-C(-NR^a)N(R^a)_2$; and

R^a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclalkyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclalkyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

187. The method of any one of claims 184-177, wherein, where indicated, alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocyclalkyl, or heterocyclalkyl is unsubstituted or is substituted with one or more substituents selected from halo, haloalkyl, oxo, $-R^a$, $-OR^a$, $-N(R^a)_2$, $-N(R^a)_3^+$, $-NHC(=O)R^c$, $-C(=O)R^c$, $-C(=O)N(R^a)_2$, $-C(=O)OR^a$, $-(alkylene)-C(=O)OR^a$, and $-(alkylene)-C(=O)N(R^a)_2$; and

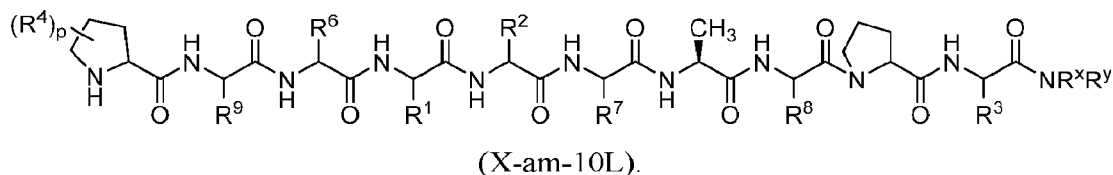
R^a , independently for each occurrence, is hydrogen, or substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclalkyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl; and

R^c , independently for each occurrence, is substituted or unsubstituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclalkyl, cycloalkyl, or (cycloalkyl)alkyl.

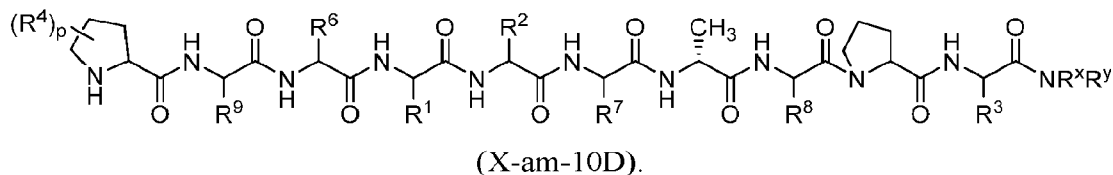
188. The method of claim 186 or 187, wherein R^a , independently for each occurrence, is hydrogen, alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl; and

R^c , independently for each occurrence, is alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclalkyl.

189. The method of any one of claims 184-188, wherein the compound has the structure of formula (X-am-10L):



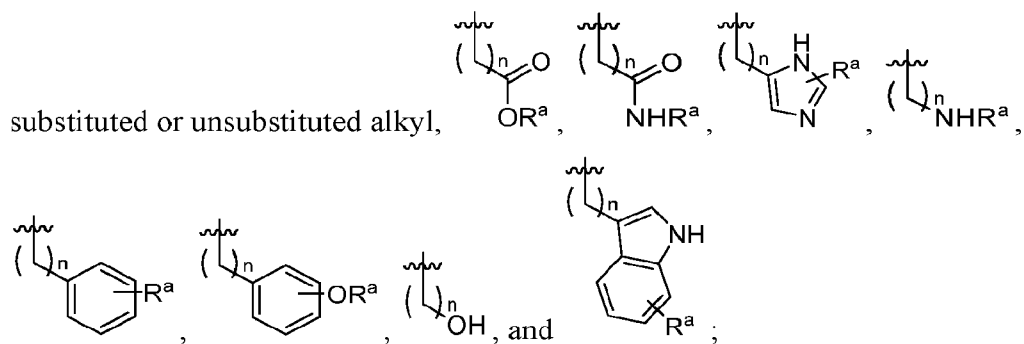
190. The method of any one of claims 184-188, wherein the compound has the structure of formula (X-am-10D):



191. The method of any one of claims 184-190, wherein R^1 is substituted or unsubstituted (C₂-C₁₀)haloalkyl.

192. The method of any one of claims 184-190, wherein R^1 is substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

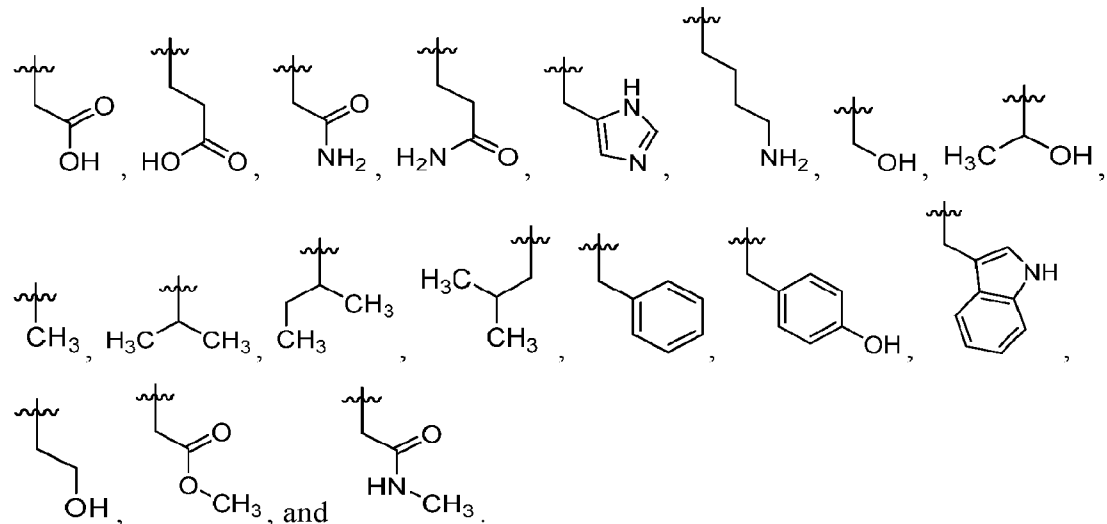
193. The method of any one of claims 184-190, wherein R^1 is selected from



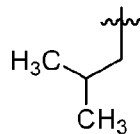
R^a is hydrogen or alkyl; and

n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

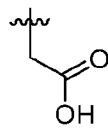
194. The method of any one of claims 184-190, wherein R^1 is selected from



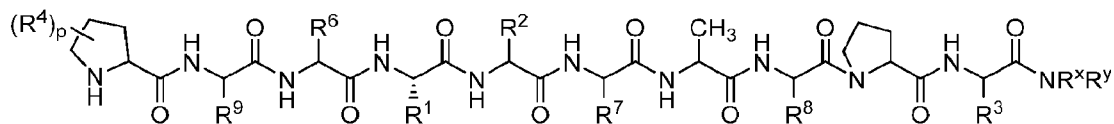
195. The method of any one of claims 184-190, wherein R^1 is



196. The method of any one of claims 184-190, wherein R^1 is

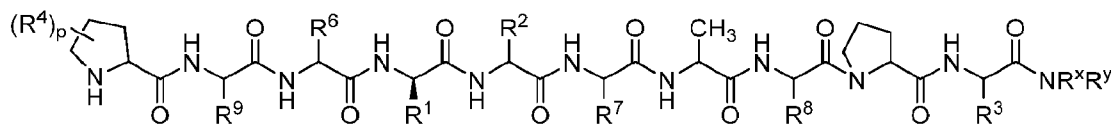


197. The method of any one of claims 184-196, wherein the compound has the structure of formula (X-am-1L)



(X-am-1L).

198. The method of any one of claims 184-196, wherein the compound has the structure of formula (X-am-1D)

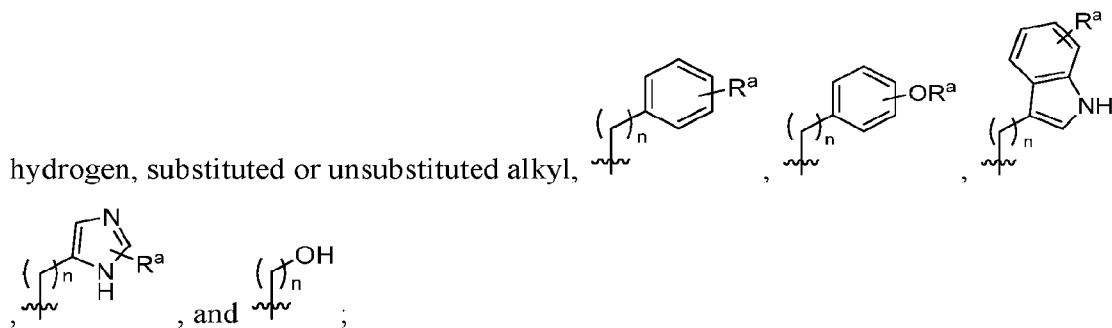


(X-am-1D).

199. The method of any one of claims 184-198, wherein R^2 is substituted or unsubstituted (C_2-C_{10}) haloalkyl.

200. The method of any one of claims 184-198, wherein R^2 is H or substituted or unsubstituted alkyl, arylalkyl, or heterocyclalkyl.

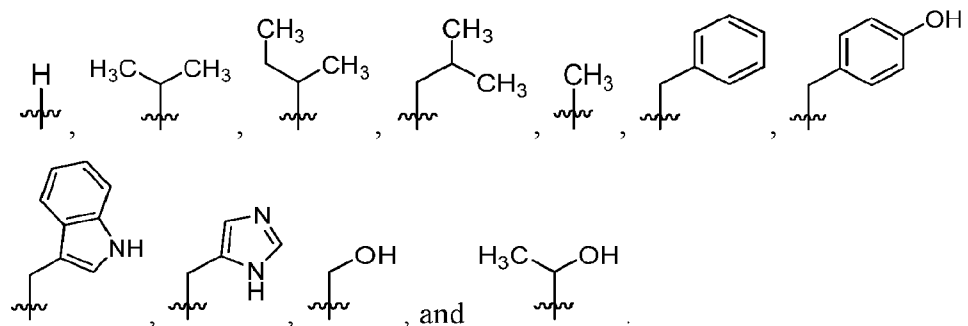
201. The method of any one of claims 184-198, wherein R^2 is selected from



R^a is hydrogen or alkyl; and

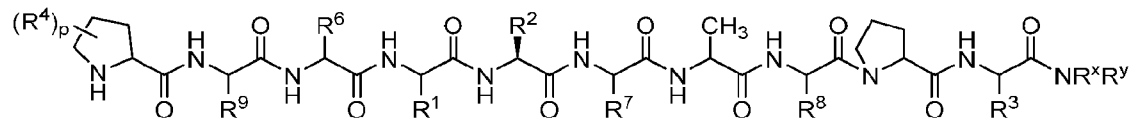
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

202. The method of any one of claims 184-198, wherein R^2 is selected from



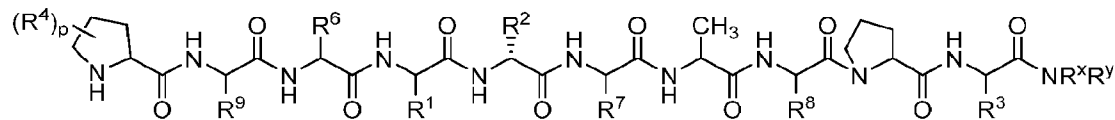
203. The method of any one of claims 184-198, wherein R^2 is hydrogen.

204. The method of any one of claims 184-203, wherein the compound has the structure of formula (X-am-2L):



(X-am-2L).

205. The method of any one of claims 184-203, wherein the compound has the structure of formula (X-am-2D):

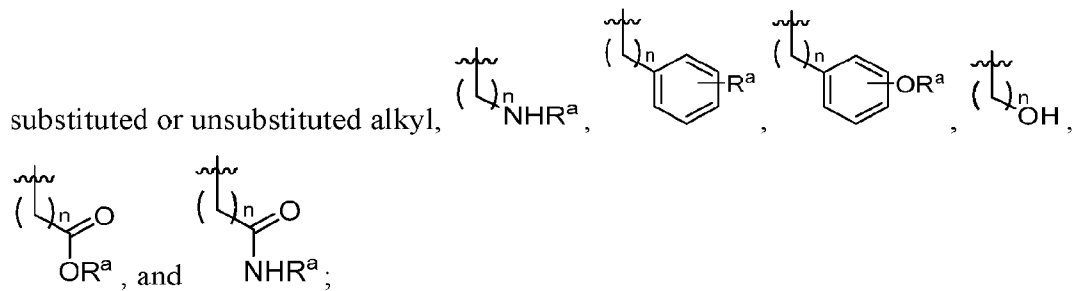


(X-am-2D).

206. The method of any one of claims 184-205, wherein R^3 is substituted or unsubstituted (C_2-C_{10}) haloalkyl.

207. The method of any one of claims 184-205, wherein R^3 is substituted or unsubstituted alkyl or arylalkyl.

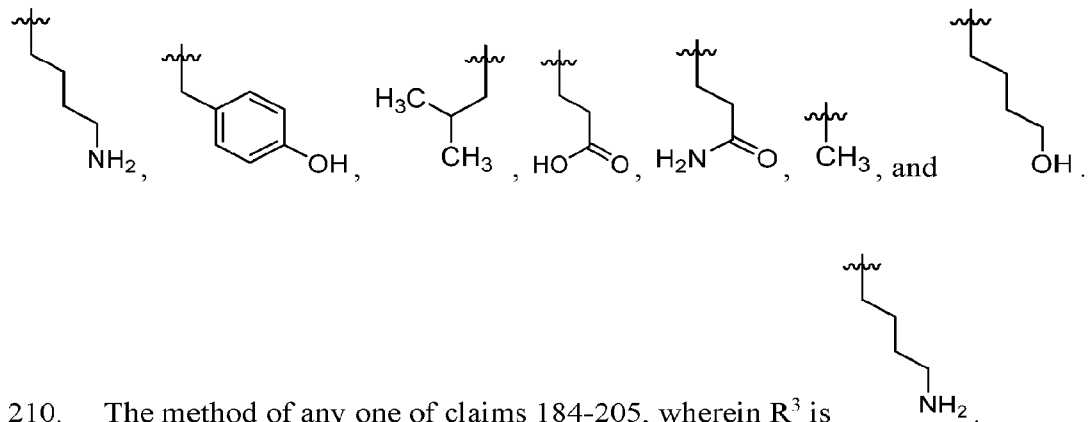
208. The method of any one of claims 184-205, wherein R^3 is selected from



R^a is hydrogen or alkyl; and

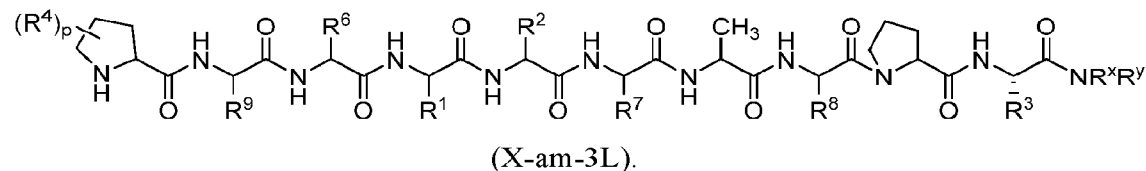
n is an integer from 1 to 10, preferably 1-5, more preferably 1-3.

209. The method of any one of claims 184-205, wherein R^3 is selected from

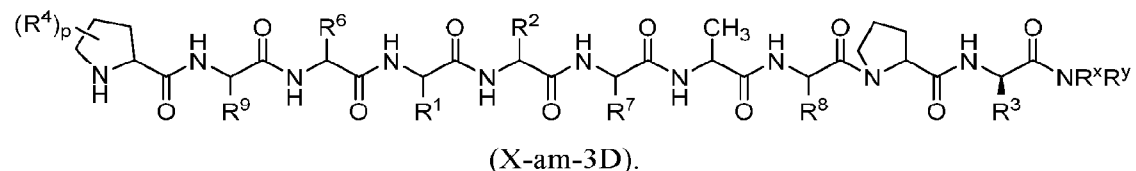


210. The method of any one of claims 184-205, wherein R^3 is

211. The method of any one of claims 184-210, wherein the compound has the structure of formula (X-am-3L):



212. The method of any one of claims 184-210, wherein the compound has the structure of formula (X-am-3D):



213. The method of any one of claims 184-212, wherein p is 1 or 2; and R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl.

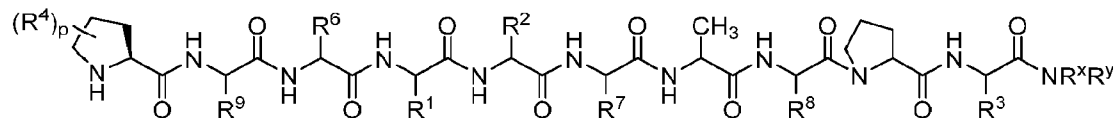
214. The method of any one of claims 184-212, wherein p is 1 or 2; and R^4 , independently for each occurrence, is selected from $-CH_3$, halo, hydroxyl, and hydroxyalkyl.

215. The method of claim 214, wherein R^4 is hydroxyl.

216. The method of claim 214, wherein R^4 is $-CH_3$.

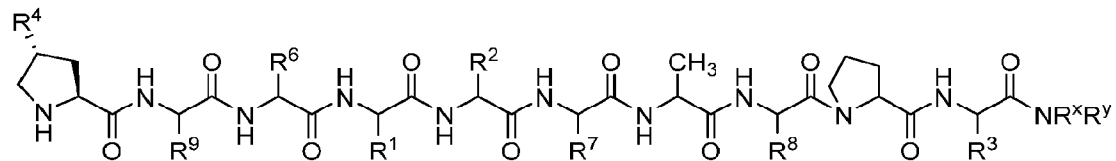
217. The method of any one of claims 213-216, wherein p is 1.

218. The method of any one of claims 184-217, wherein the compound has the structure of formula (X-am-4Lg):



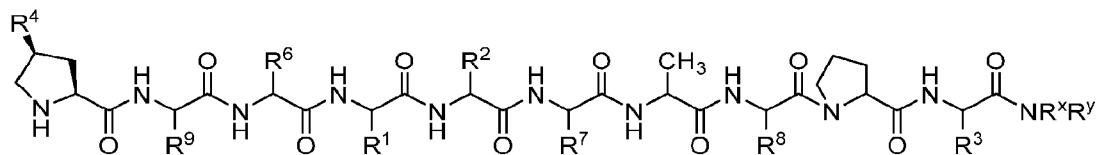
(X-am-4Lg).

219. The method of any one of claims 184-218, wherein the compound has the structure of formula (X-am-4La):



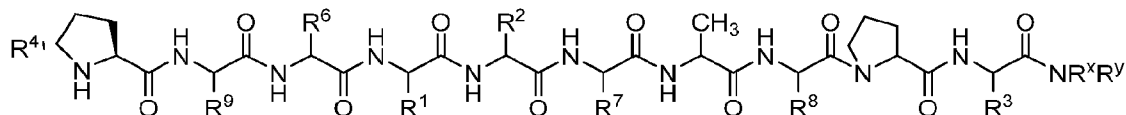
(X-am-4La).

220. The method of any one of claims 184-218, wherein the compound has the structure of formula (X-am-4Lb):



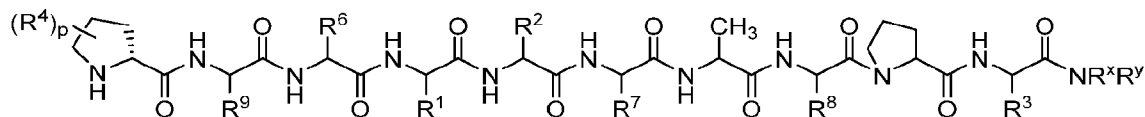
(X-am-4Lb).

221. The method of any one of claims 184-214 and 216-218, wherein the compound has the structure of formula (X-am-4Lc):



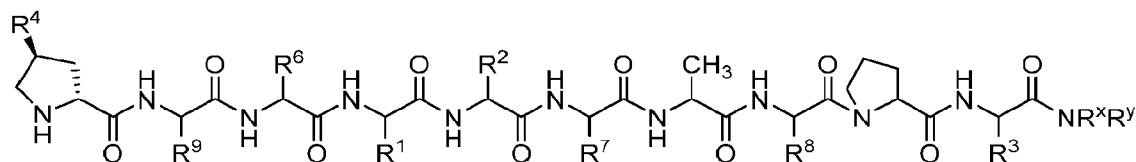
(X-am-4Lc).

222. The method of any one of claims 184-217, wherein the compound has the structure of formula (X-am-4Dg):



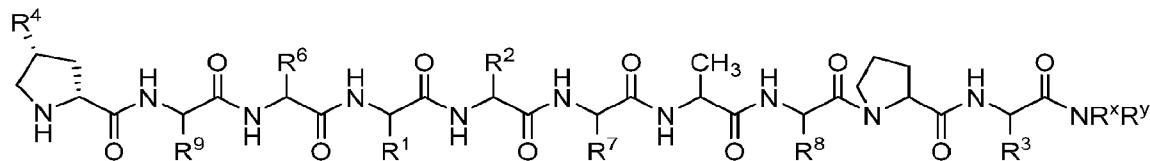
(X-am-4Dg).

223. The method of any one of claims 184-217 and 222, wherein the compound has the structure of formula (X-am-4Da):



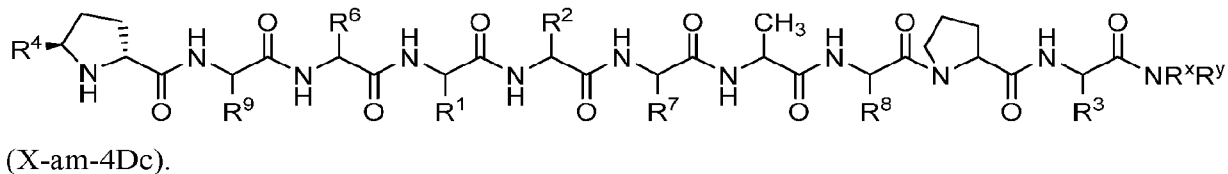
(X-am-4Da).

224. The method of any one of claims 184-217 and 222, wherein the compound has the structure of formula (X-am-4Db):



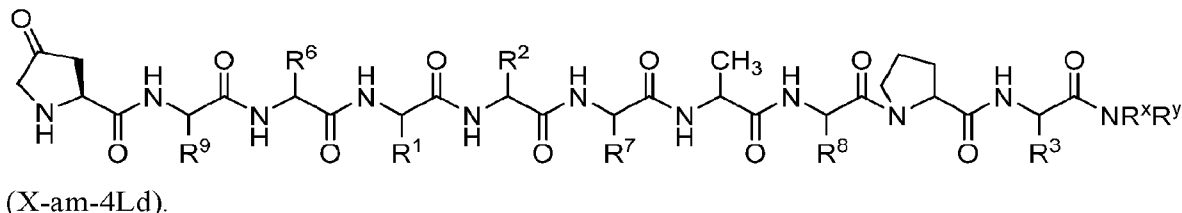
(X-am-4Db).

225. The method of any one of claims 184-214, 216-218, and 222, wherein the compound has the structure of formula (X-am-4Dc):

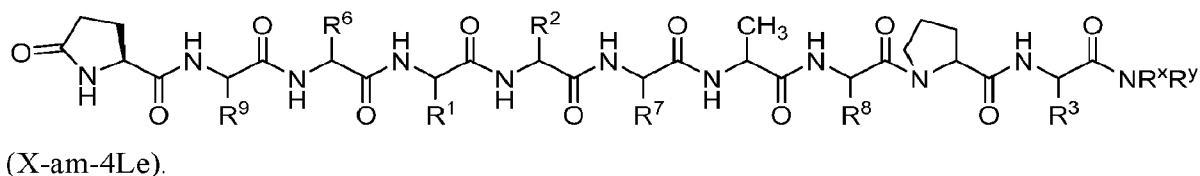


226. The method of any one of claims 184-225, wherein R⁴ is oxo.

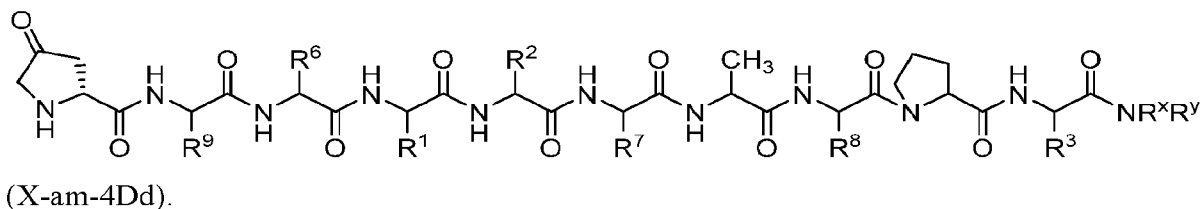
227. The method of claim 226, wherein the compound has the structure of formula (X-am-4Ld):



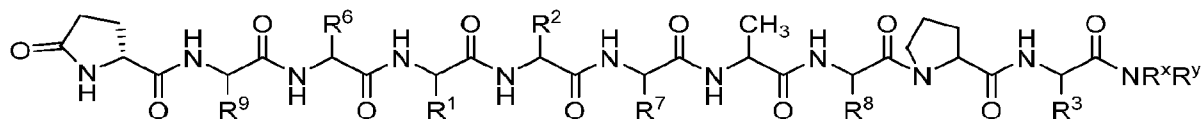
228. The method of claim 226, wherein the compound has the structure of formula (X-am-4Le):



229. The method of claim 226, wherein the compound has the structure of formula (X-am-4Dd):



230. The method of claim 226, wherein the compound has the structure of formula (X-am-4De):



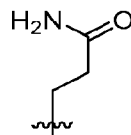
(X-am-4De).

231. The method of any one of claims 184-230, wherein R^6 is hydrogen or alkyl, wherein the alkyl is optionally substituted with one occurrence of $-C(=O)NH_2$.

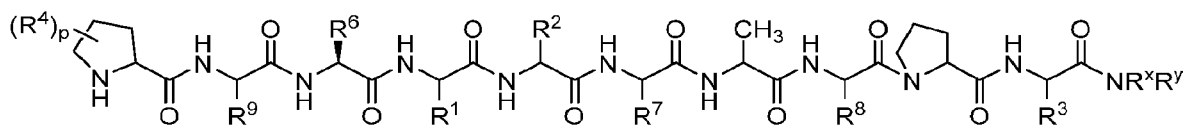
232. The method of any one of claims 184-231, wherein R^6 is alkyl optionally substituted with one occurrence of $-C(=O)NH_2$.

233. The method of any one of claims 184-232, wherein R^6 is $-CH_3$.

234. The method of any one of claims 184-232, wherein R^6 is

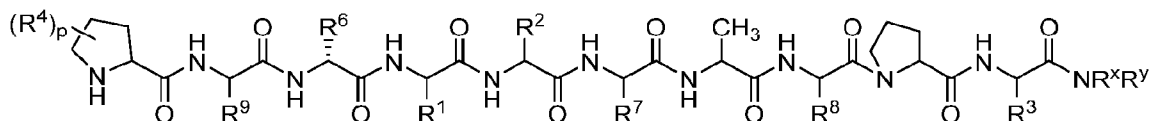


235. The method of any one of claims 184-234, wherein the compound has the structure of formula (X-am-6L):



(X-am-6L).

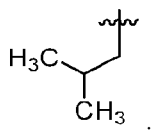
236. The method of any one of claims 184-234, wherein the compound has the structure of formula (X-am-6D):



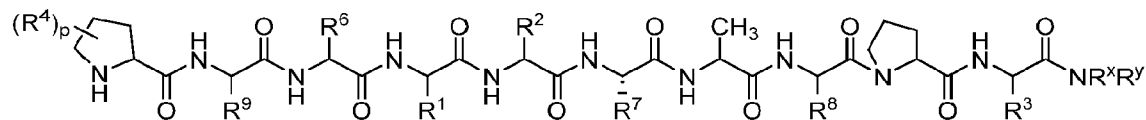
(X-am-6D).

237. The method of any one of claims 184-236, wherein R^7 is (C_1-C_{10}) alkyl.

238. The method of any one of claims 184-237, wherein R^7 is .

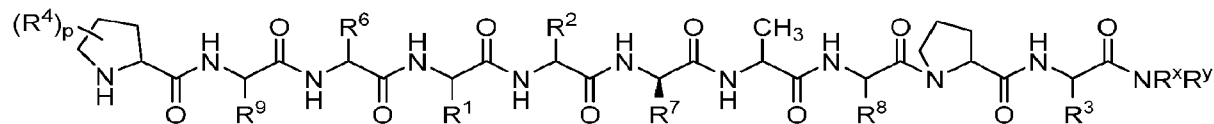
239. The method of any one of claims 184-237, wherein R^7 is .

240. The method of any one of claims 184-239, wherein the compound has the structure of formula (X-am-7L):



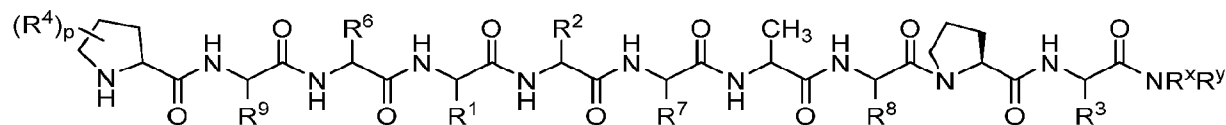
(X-am-7L).

241. The method of any one of claims 184-239, wherein the compound has the structure of formula (X-am-7D):



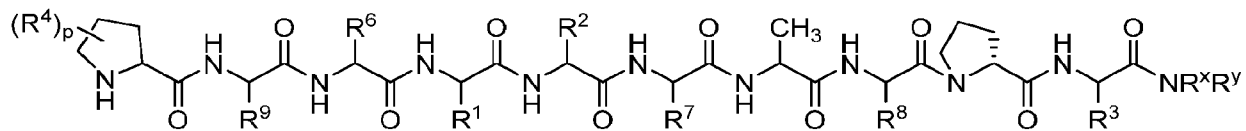
(X-am-7D).

242. The method of any one of claims 184-241, wherein the compound has the structure of formula (X-am-11L):



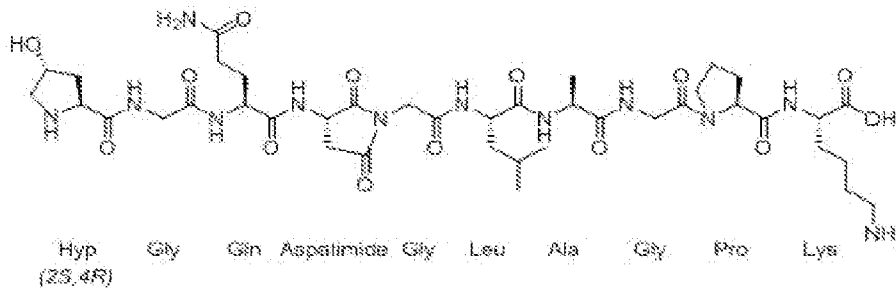
(X-am-11L).

243. The method of any one of claims 184-241, wherein the compound has the structure of formula (X-am-11D):



(X-am-11D).

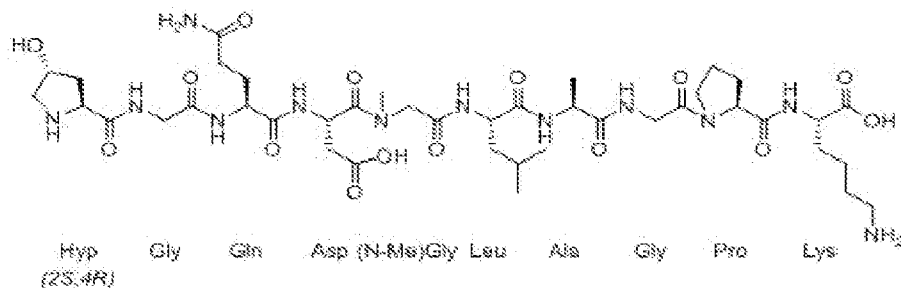
244. The method of any one of claims 184-243, wherein R^8 is $-CH_3$ or $-H$.
245. The method of any one of claims 184-243, wherein R^8 is $-H$.
246. The method of any one of claims 184-245, wherein R^9 is $-CH_3$ or $-H$.
247. The method of any one of claims 184-245, wherein R^9 is $-H$.
248. The method of any one of claims 184-247, wherein R^x and R^y are each independently optionally substituted alkyl.
249. The method of any one of claims 184-247, wherein R^x and R^y are each independently optionally substituted alkoxyalkyl.
250. The method of any one of claims 184-247, wherein R^x and R^y taken together with the intervening nitrogen atom form a ring.
251. The method of any one of claims 1-12, wherein the compound is represented by Formula 8:



[Formula]

8],
or a pharmaceutically acceptable salt thereof.

252. The method of any one of claims 1-12, wherein the compound is represented by Formula 10:



[Formula

10],

or a pharmaceutically acceptable salt thereof.

253. The method of claim 4, wherein the disease or disorder is Acute posterior multifocal placoid pigment epitheliopathy (APMPPE), Agammaglobulinemia, Alopecia Areata, Amyloidosis, Amyotrophic lateral sclerosis (ALS), Aniridia, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune hepatitis, Autoimmune inner ear disease, Autoimmune Lymphoproliferative Syndrome, Atopic dermatitis, Asthma, Behçet's Disease, Best Disease, Birdshot Chorioretinopathy, Blepharitis, Bronchiolitis, Cancer (Chondrosarcoma, Cervical, Breast, Lung), Capillary Leak Syndrome, Castleman disease, Celiac disease, Chagas disease, Chalazia and Sty, Chandler's syndrome, Cholesteatoma of Middle Ear, Choroideremia, Chronic recurrent multifocal osteomyelitis, Cogan's syndrome, Collagen Induced Arthritis (CIA), Cold agglutinin disease, Cone Rod Dystrophies, Conjunctivitis, Corneal Wound Healing, CREST syndrome, Crohn's disease, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dry macular degeneration (Dry AMD), Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Essential Iris Atrophy, Evan's syndrome, Farmer's Lung, Fibromyalgia, Giant cell arteritis, Giant cell myocarditis, Giant Papillary Conjunctivitis, Glomerulonephritis, Goodpasture's syndrome, Graft-Versus-Host Disease, Granulomatosis with polyangiitis, Graves' disease, Guillain-Barre syndrome, Gyrate Atrophy, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Hypogammaglobulinemia, Hypoproliferative anemia, IgA Nephropathy, Inclusion body myositis, Interstitial cystitis, Inflammatory Bowel Disease, Iritis, Irritant Dermatitis, Juvenile arthritis, Juvenile/Type 1 Diabetes, Juvenile macular

degeneration, Juvenile myositis, Juvenile X-linked Retinoschisis, Kawasaki syndrome, Keratitis, Late-Onset Retinal Degeneration (L-ORD), Lichen planus, Lichen sclerosus, Lupus (SLE), Macular Edema, Meniere's disease, Multiple sclerosis, Myasthenia gravis, Microscopic polyangiitis, Neuropathic Corneal Pain, Neurotropic Keratitis, Ocular Allergy, Ocular Inflammation (uveitis), Ocular Pain, Ocular Neurodegeneration, Optic Nerve Atrophy, Optic neuritis, Oral Submucous Fibrosis, Osteoarthritis (OA), Osteoporosis, Parkinson's disease, Pars Planitis, Pemphigus, Photokeratitis, Polyarteritis nodosa, Polymyalgia rheumatica, Polymyositis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleritis, Sjogren's syndrome, Stargardt Disease, Stickler Syndrome, Temporal arteritis/Giant cell arteritis, Thyroid Eye Disease, Trachoma, Transverse myelitis, Trichiasis, Ulcerative colitis, Usher Syndrome, Uveitis, Vasculitis, Vitiligo, Viral myocarditis, or Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)), or Wound Healing.

254. The method of claim 4, wherein the disease or disorder is Dry Eye Disease (DED), Inflammatory Bowel Disease, Keratoconjunctivitis sicca (Dry Eye), Osteoporosis, or Rheumatoid arthritis.

255. The method of claim 4, wherein the disease or disorder is Inflammatory Bowel Disease.

256. The method of claim 4, wherein the disease or disorder is Keratoconjunctivitis sicca (Dry Eye).

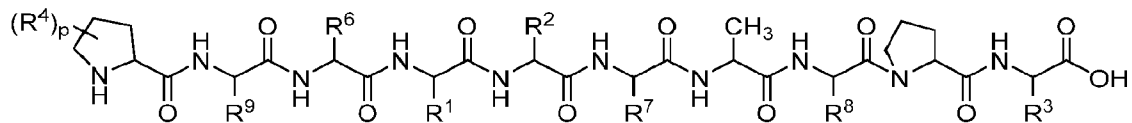
257. The method of claim 4, wherein the disease or disorder is Osteoporosis.

258. The method of claim 4, wherein the disease or disorder is Rheumatoid arthritis.

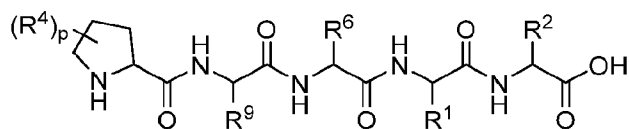
259. The method of claim 4, wherein the disease or disorder is Dry Eye Disease (DED).

260. A method of preventing or treating Keratoconjunctivitis sicca (Dry Eye) in a subject, comprising administering to the subject

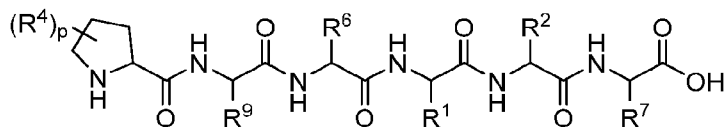
i) a compound represented by Formula (I), (V), (VI), (VII), (IX) or (X-am) or a pharmaceutically acceptable salt and/or prodrug thereof:



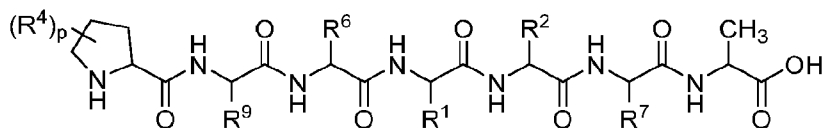
(I),



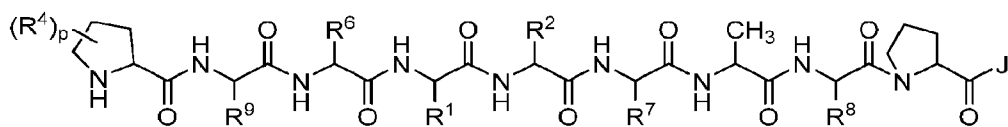
(V),



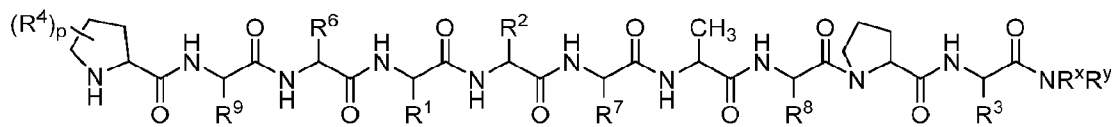
(VI),



(VII),



(IX), or



(X-am),

wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

R^6 is hydrogen or substituted or unsubstituted alkyl;

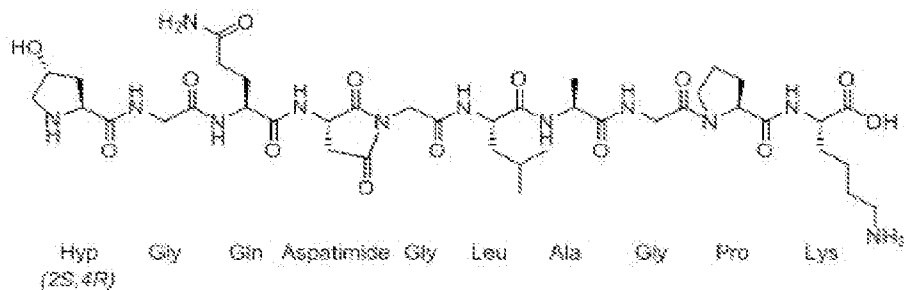
R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

J is OH or $-NR^xR^y$; and

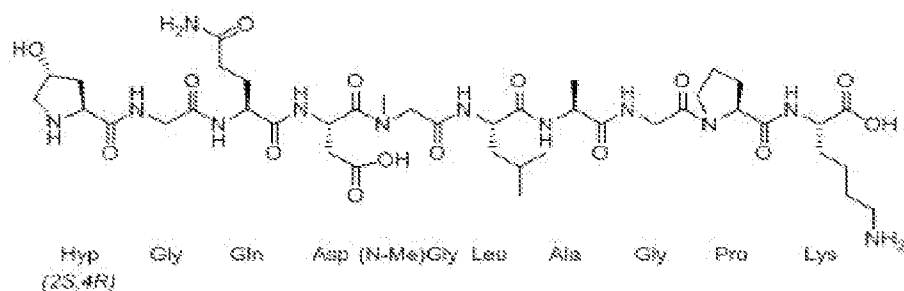
R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring,

ii) a compound represented by Formula (8) or (10)

or a pharmaceutically acceptable salt and/or prodrug thereof:

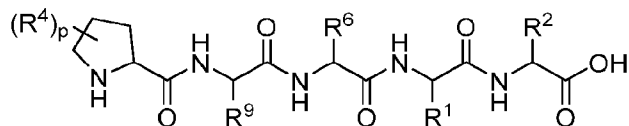


[Formula 8];

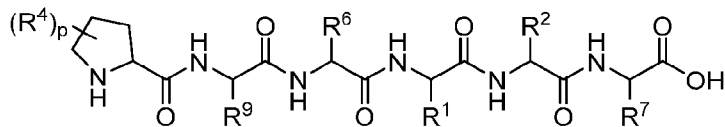


[Formula 10]

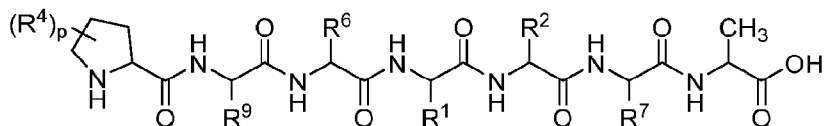
iii) a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xcc or Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, or a pharmaceutically acceptable salt and/or stereoisomer thereof, wherein:



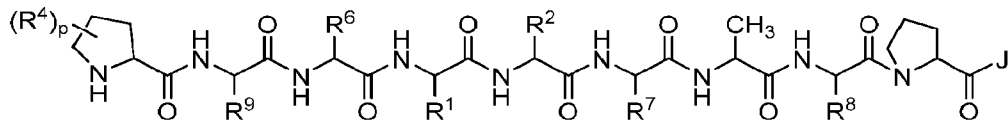
(V),



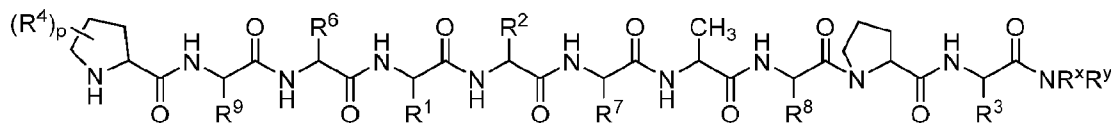
(VI),



(VII),



(IX), or



(X-am),

wherein:

R^1 , R^2 , and R^3 are each independently H or substituted or unsubstituted alkyl, alkoxy, haloalkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, heteroaryl, or heteroarylalkyl;

R^4 , independently for each occurrence, is selected from substituted or unsubstituted alkyl, aryl, arylalkyl, heterocycloalkyl, oxo, $-OR^b$, $-CH_2OR^b$, halo, hydroxyl, and hydroxyalkyl;

R^b is substituted or unsubstituted alkyl, aryl, arylalkyl, or heterocycloalkyl;

p is 0, 1, or 2;

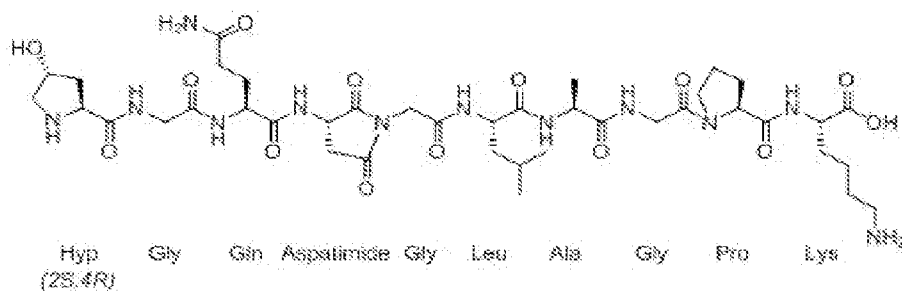
R^6 is hydrogen or substituted or unsubstituted alkyl;

R^7 , R^8 , and R^9 are each independently hydrogen or alkyl;

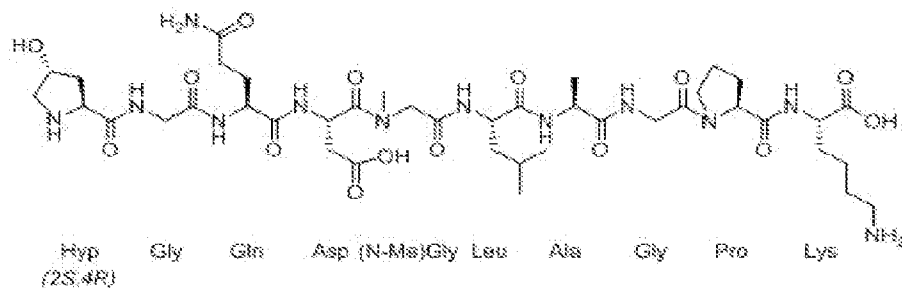
J is OH or $-NR^xR^y$; and

R^x and R^y are each independently selected from H, optionally substituted alkyl, optionally substituted alkoxyalkyl, or R^x and R^y taken together with the intervening nitrogen atom form a ring,

- ii) a compound represented by Formula (8) or (10)
or a pharmaceutically acceptable salt and/or prodrug thereof:



[Formula 8];



[Formula 10]

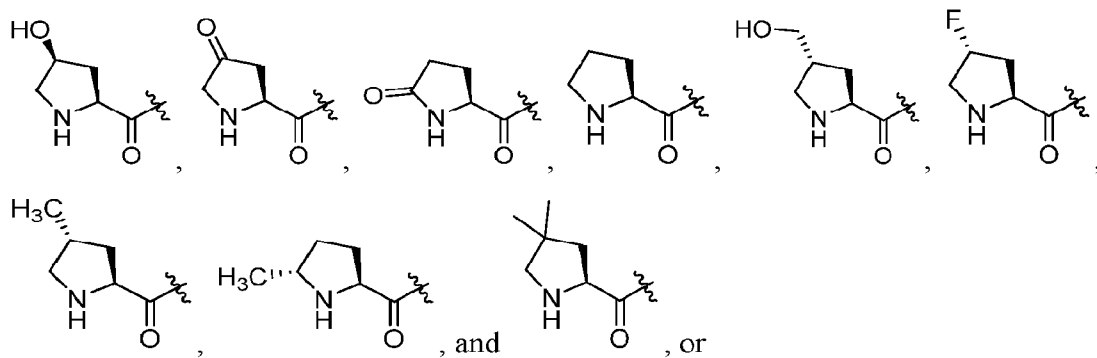
- iii) a peptide having an amino acid sequence represented by HyP-Gly-Gln-Xaa-Gly-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Asp-Xbb-Leu-Ala-Gly-Pro-Lys, HyP-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Xcc or Xdd-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys, or a pharmaceutically acceptable salt and/or stereoisomer thereof, wherein:

Xaa is selected from Glu, Asn, Gln, His, Lys, Ser, Thr, Ala, Val, Ile, Leu, Phe, Tyr, Trp, homo-Ser, Asp(Me), and Asn(Me);

Xbb is selected from Val, Ile, Leu, Ala, Phe, Tyr, Trp, Ser, Thr, and (N-Me)Gly;

Xcc is selected from Tyr, Leu, Glu, Gln, Ala, and Nle(6-OH); and

Xdd is selected from:



iv) a peptide having any one amino acid sequence selected from:

Ala-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Pro-Lys;

Hyp-Gly-Gln-Leu-Gly-Leu-Ala-Gly-Ala-Lys;

HyP-Gly-Gln-Leu-Gly-Leu-Ala;

HyP-Gly-Gln-Glu-Gly-Leu-Gly;

HyP-Gly-Gln-Leu-Gly-Leu;

D-HyP(2R, 4S)-Gly-D-Gln-D-Leu-Gly-D-Leu;

HyP-Gly-Gln-Leu-Gly, HyP-Gly-Gln-D-Leu-Gly; and

D-HyP(2R, 4S)-Gly-Gln-Leu-Gly.

Figure 1A

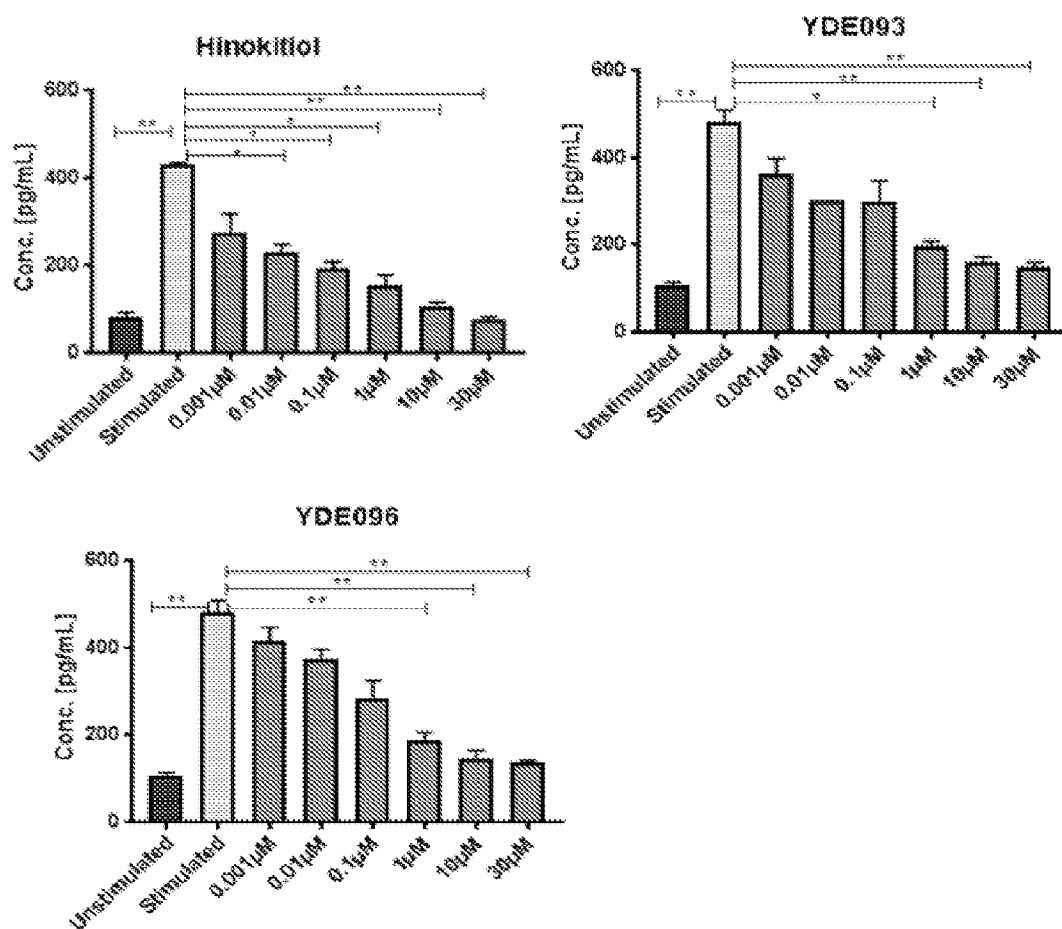


Figure 1B

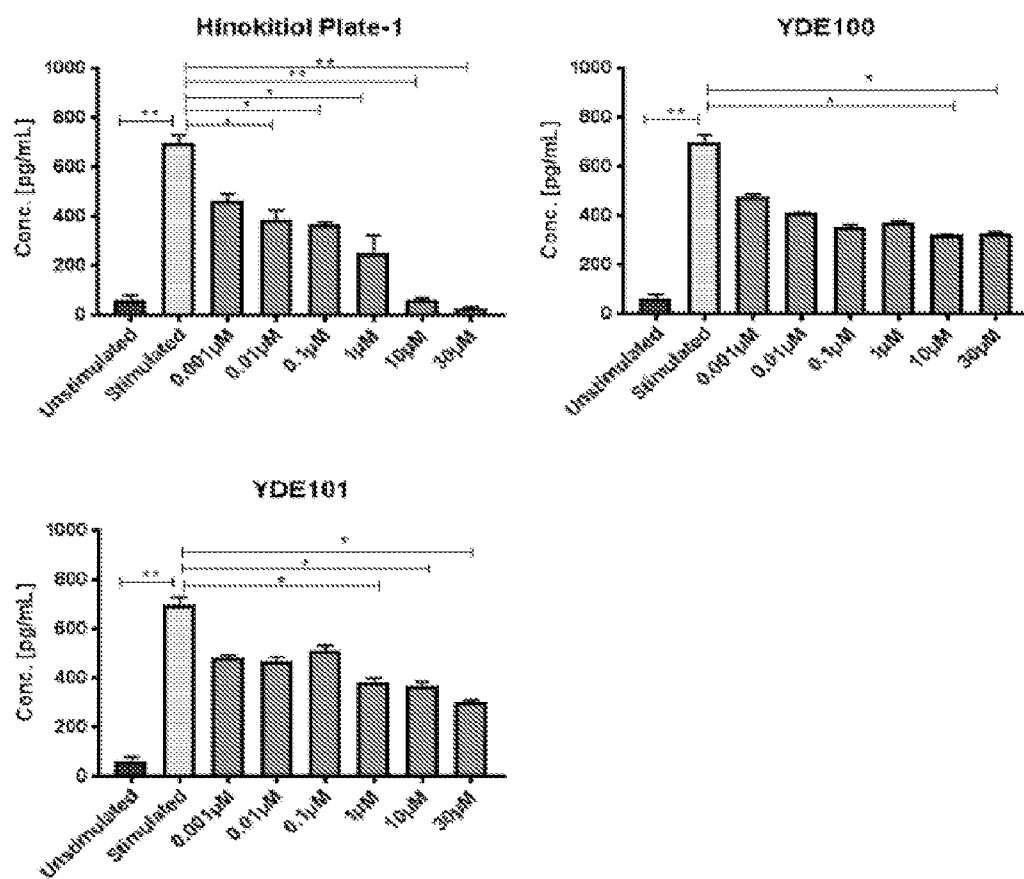


Figure 1C

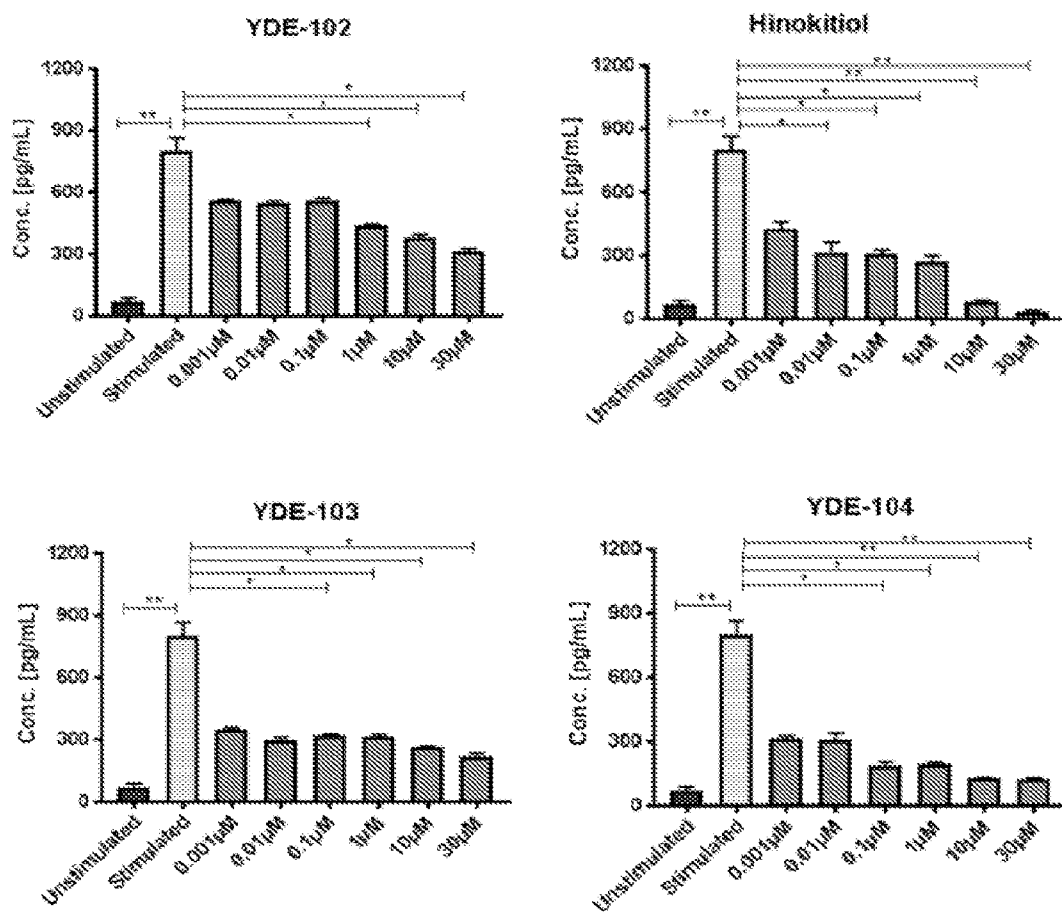


Figure 1D

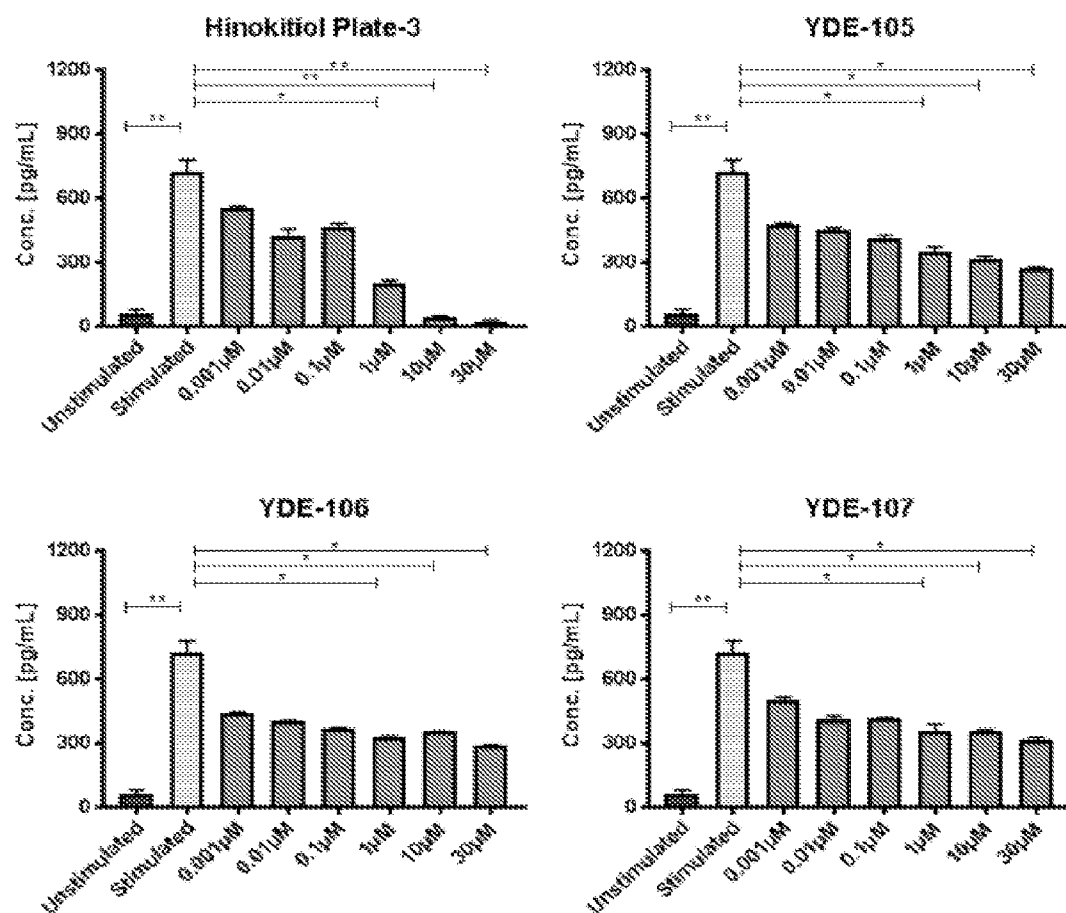


Figure 2A

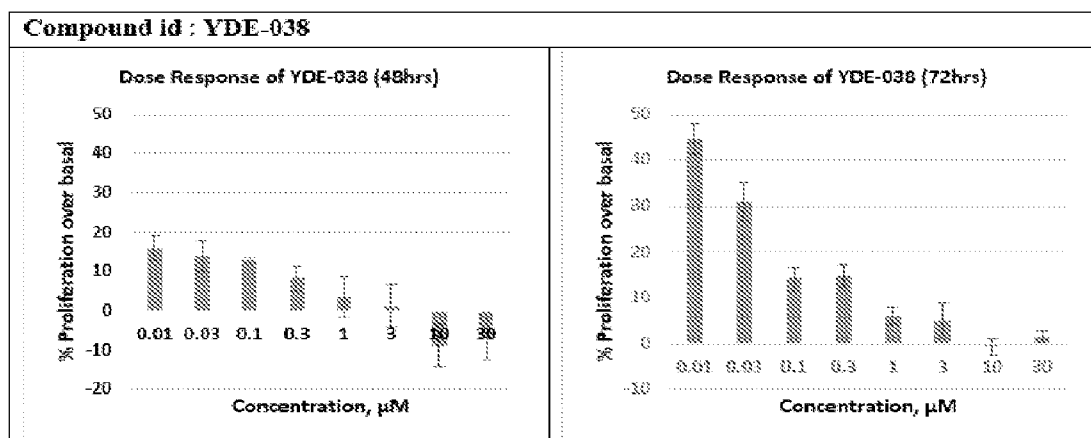


Figure 2B

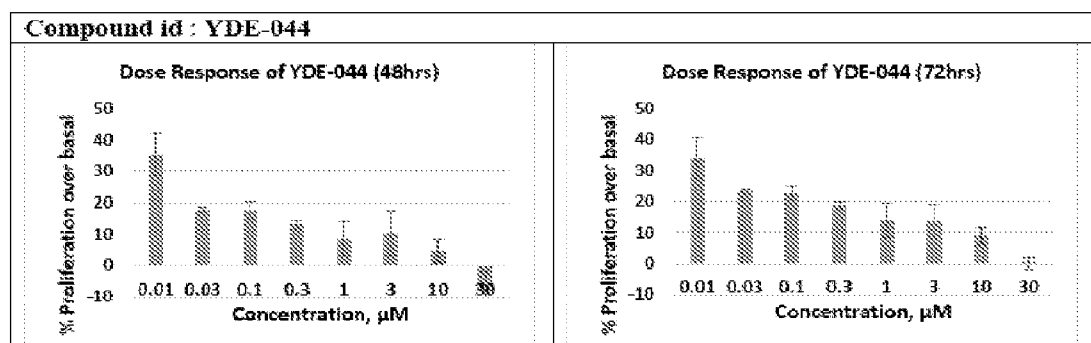


Figure 2C

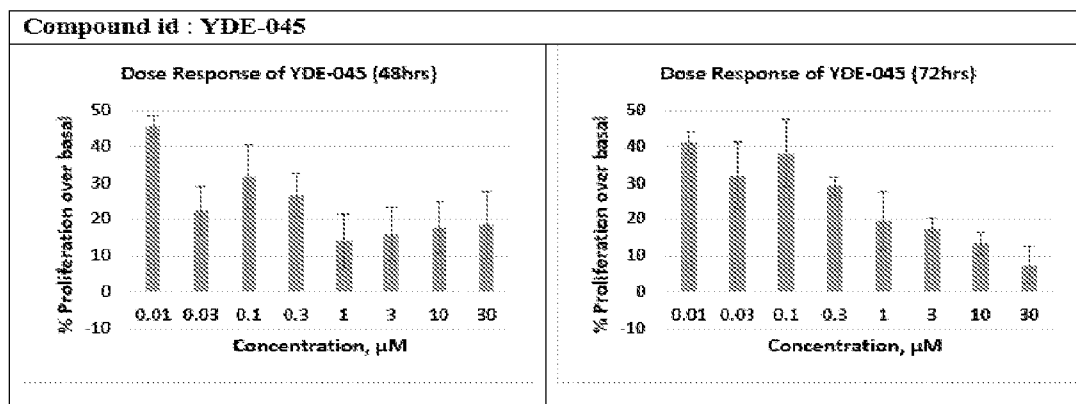


Figure 2D

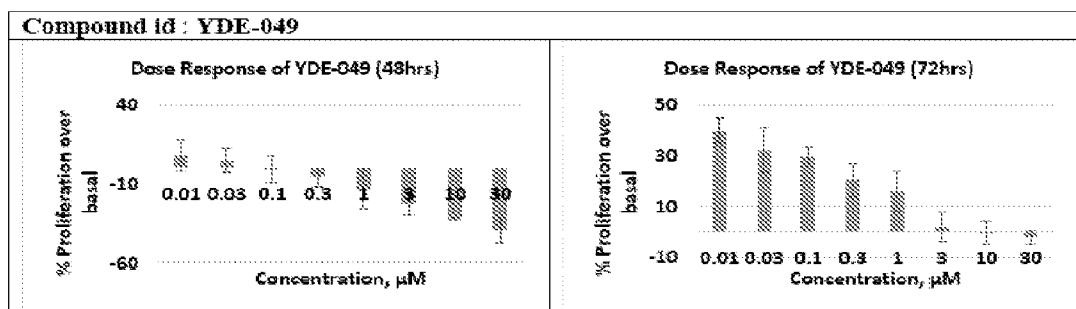


Figure 2E

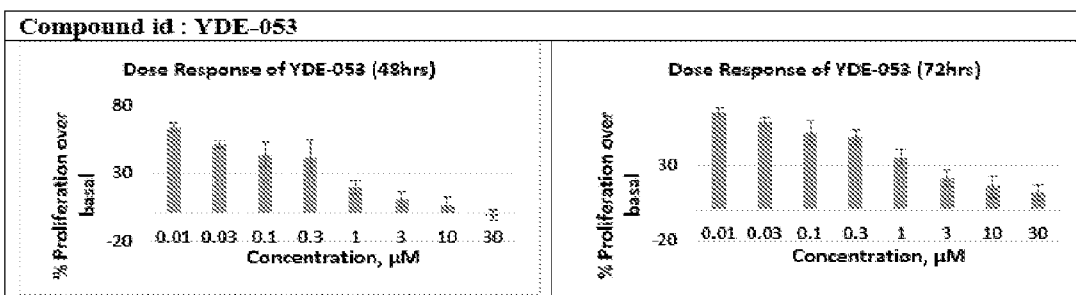


Figure 2F

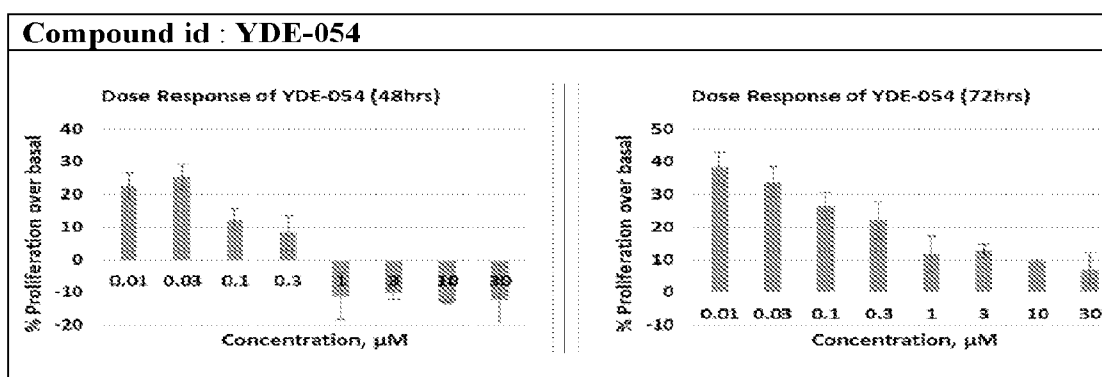


Figure 2G

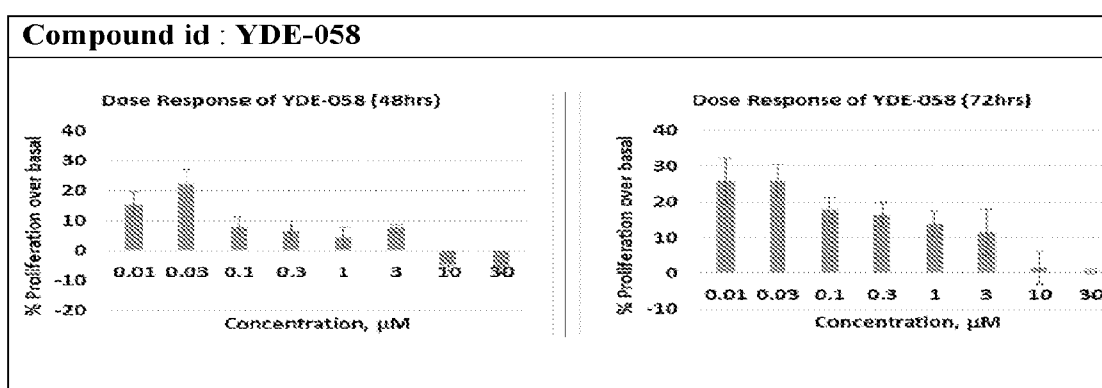


Figure 2H

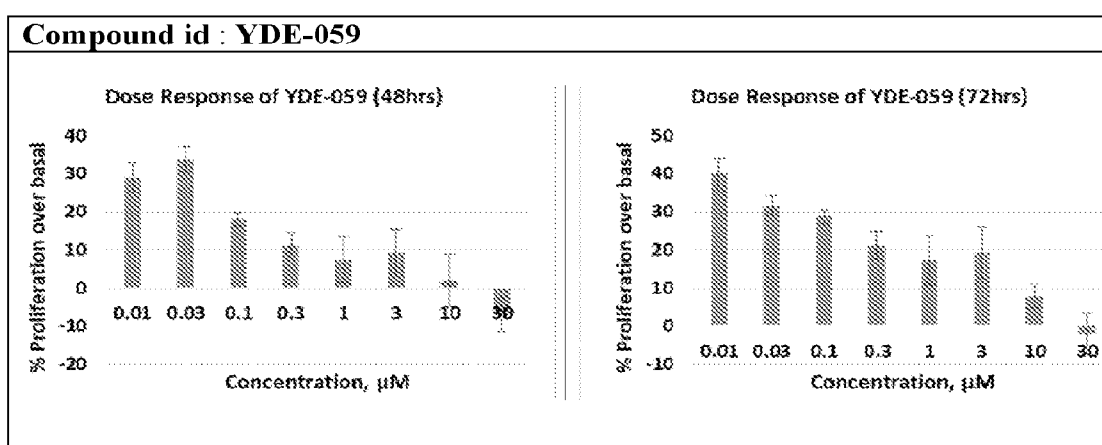


Figure 2I

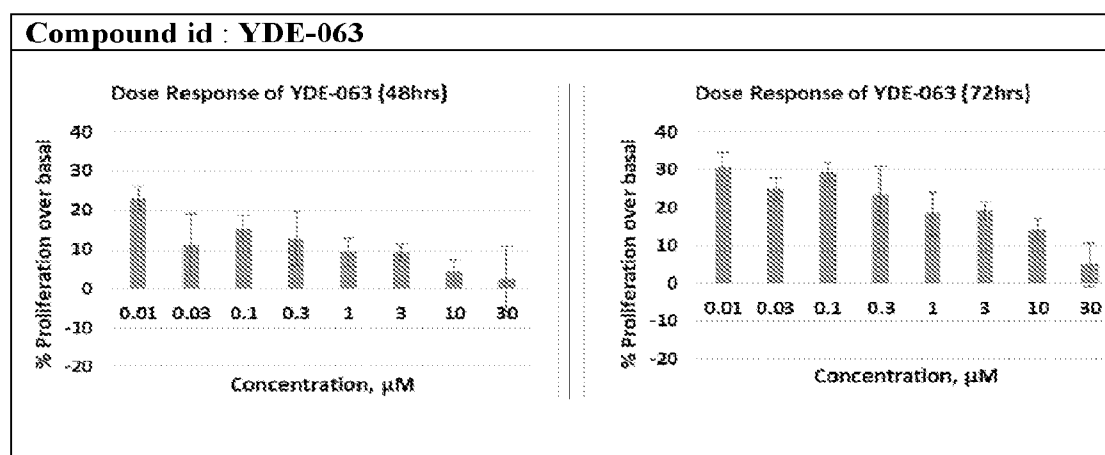


Figure 2J

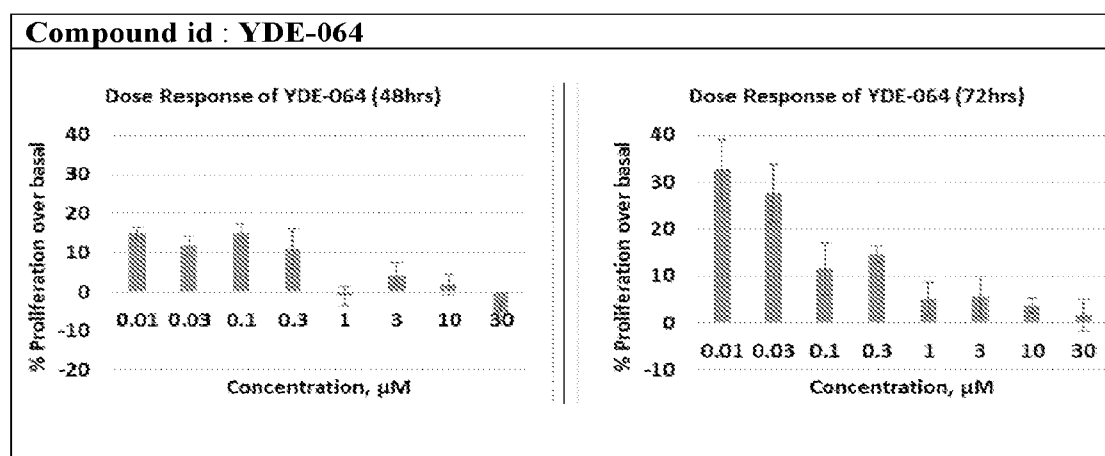


Figure 2K

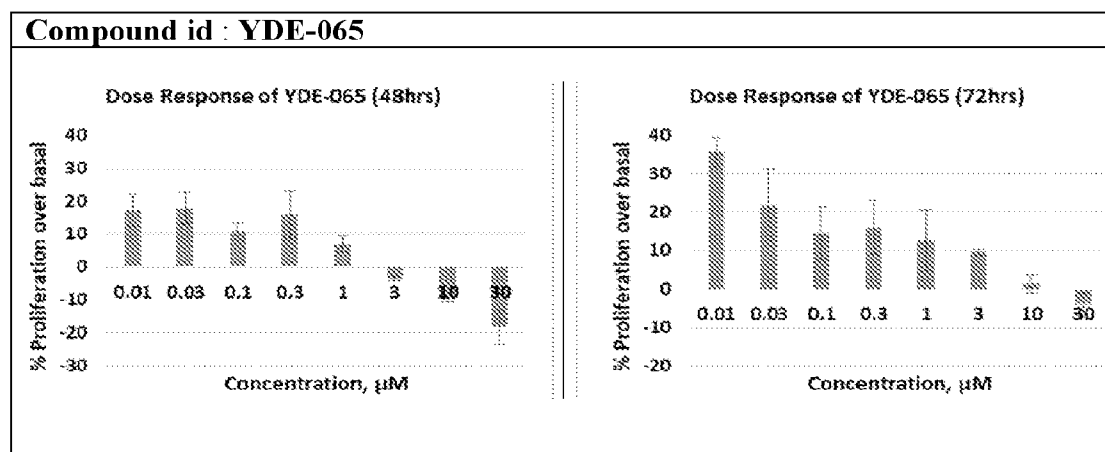


Figure 2L

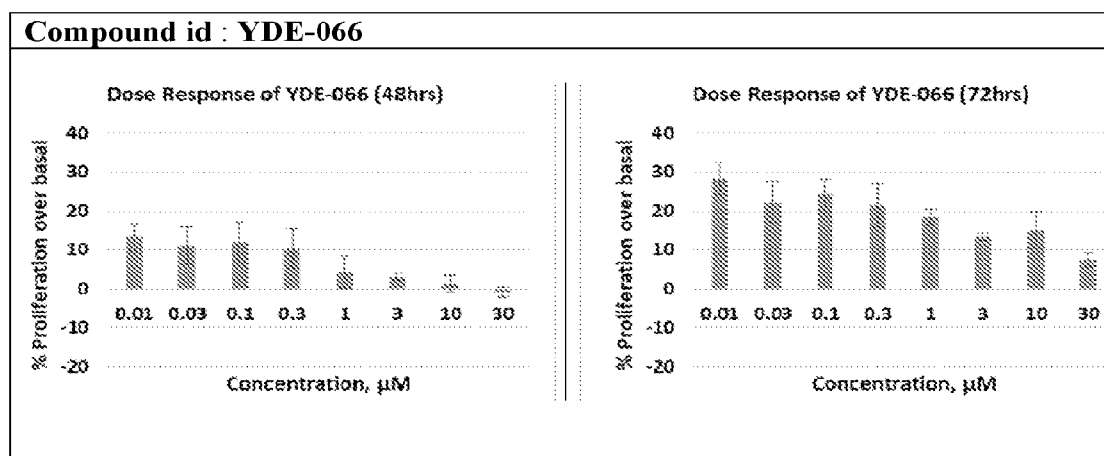


Figure 2M

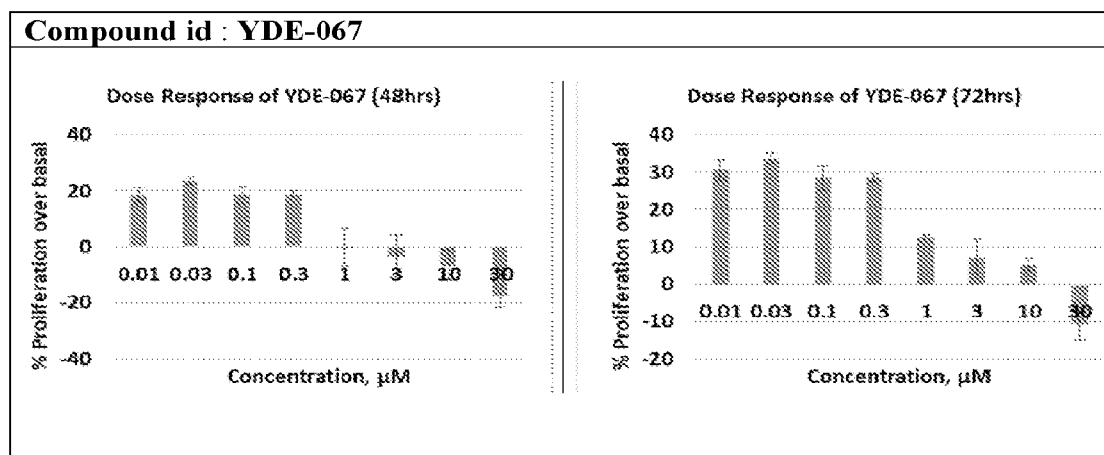


Figure 2N

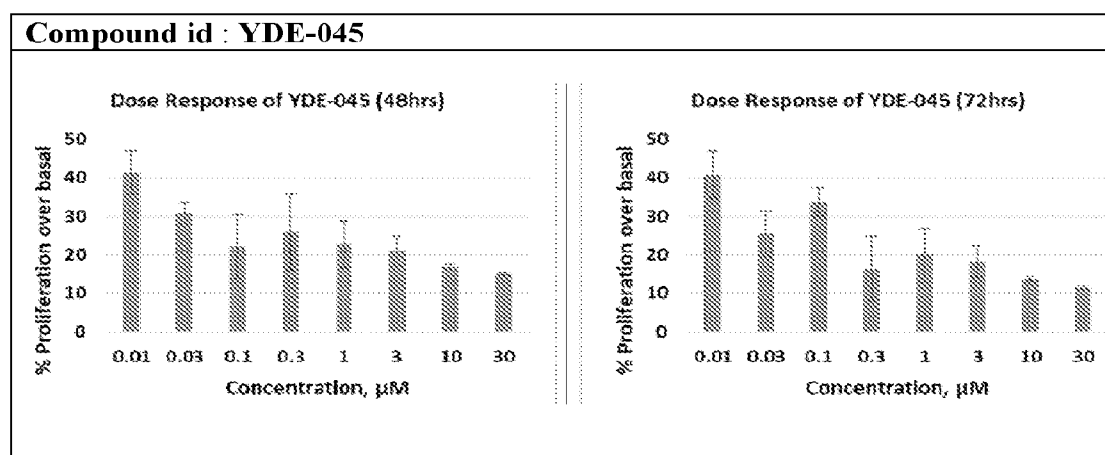


Figure 2O

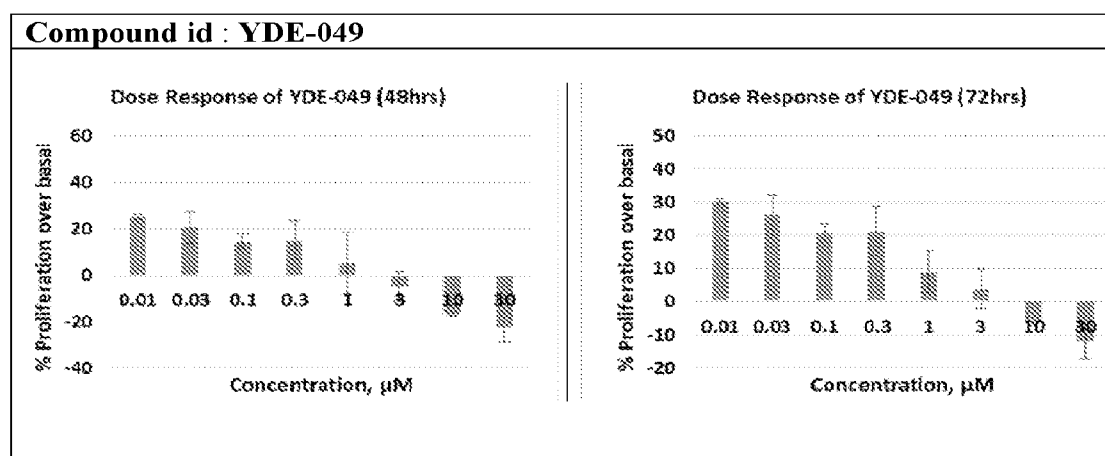


Figure 2P

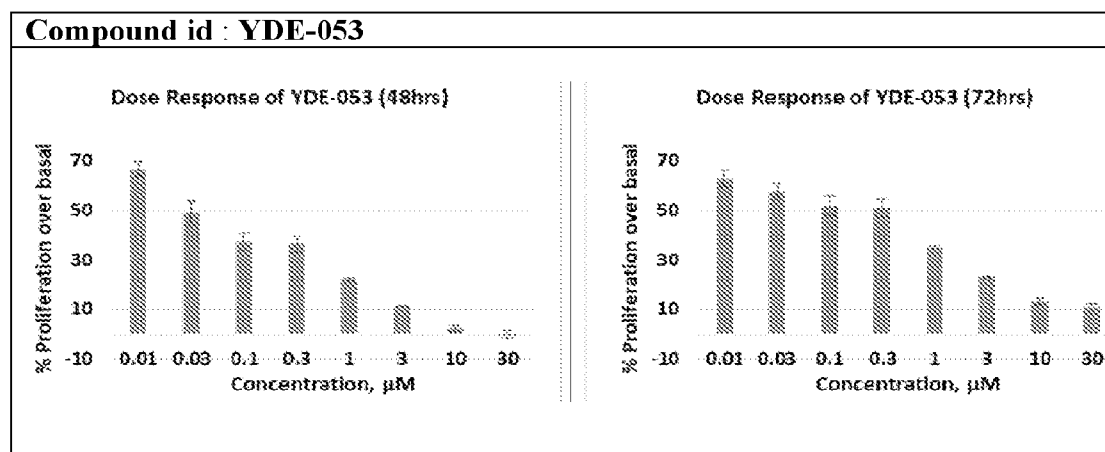


Figure 2Q

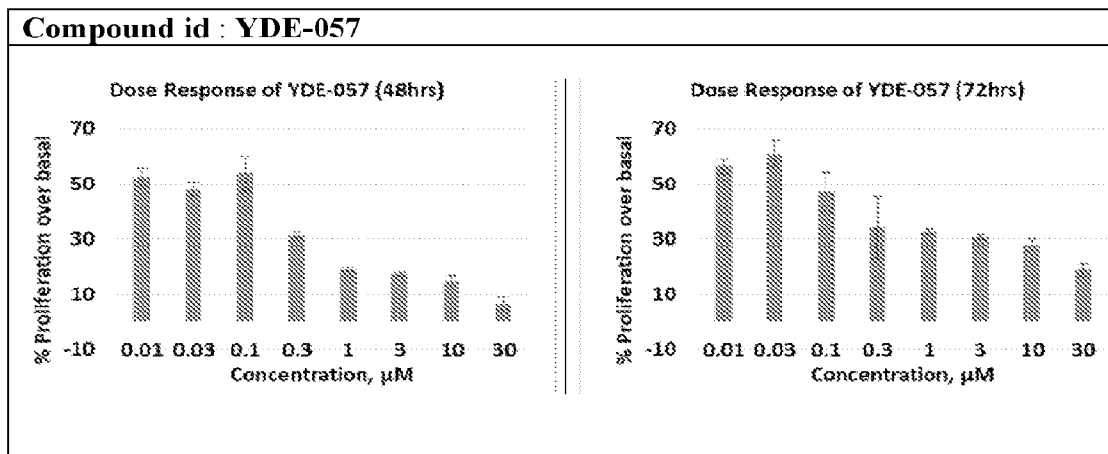


Figure 2R

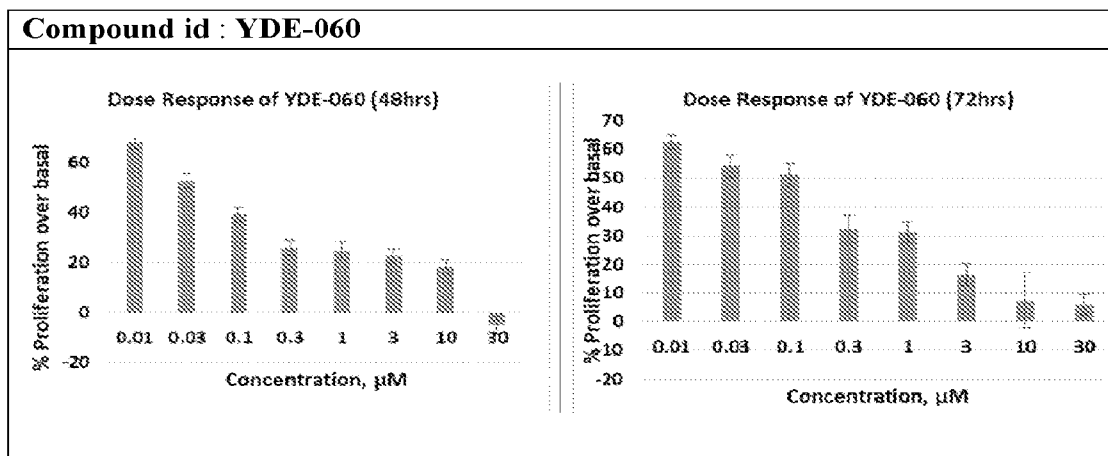


Figure 2S

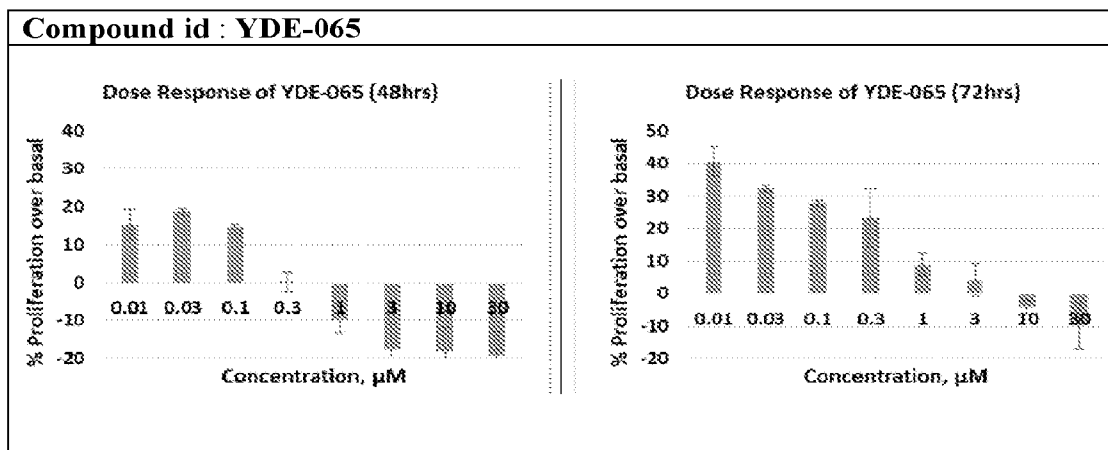


Figure 2T

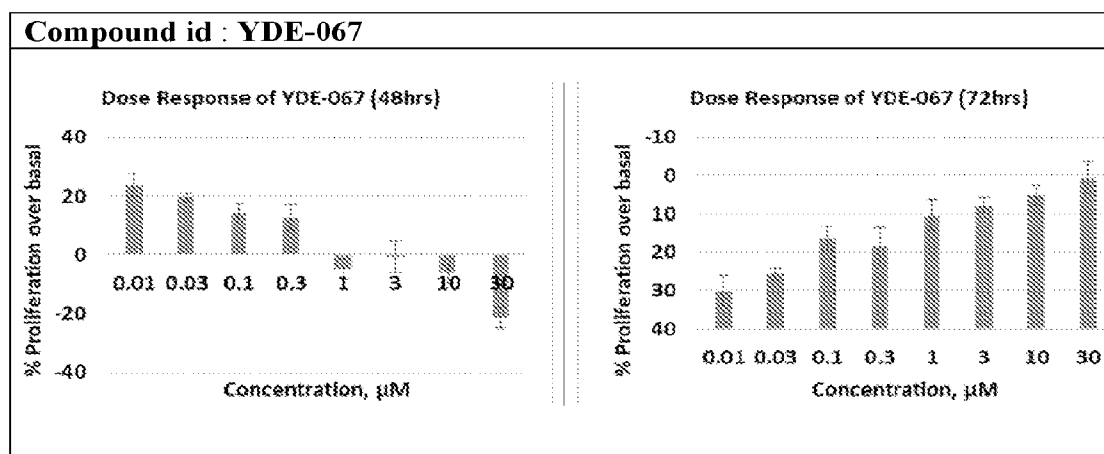


Figure 2U

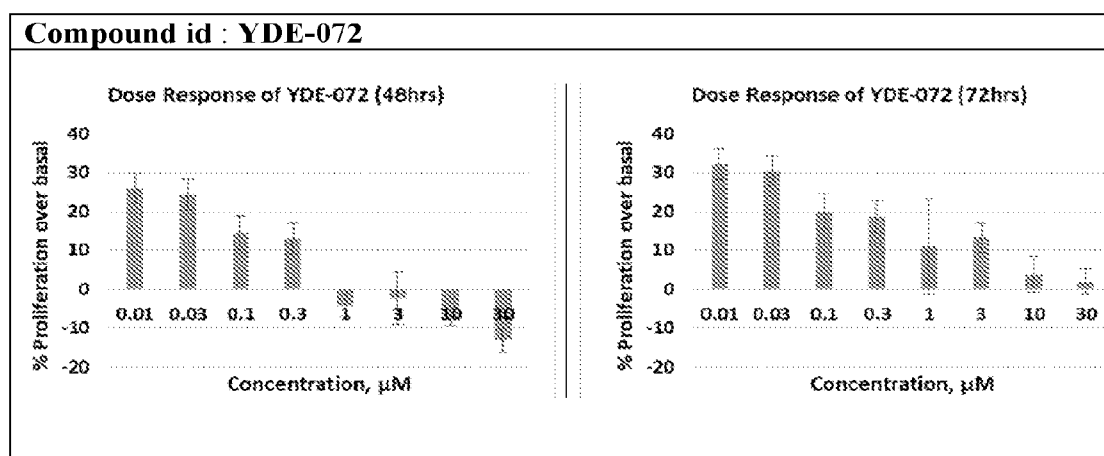


Figure 2V

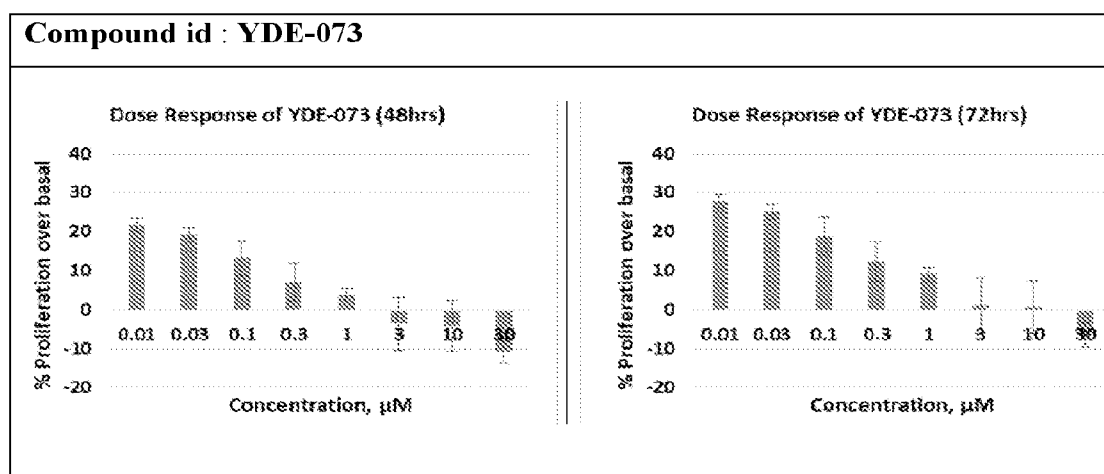


Figure 2W

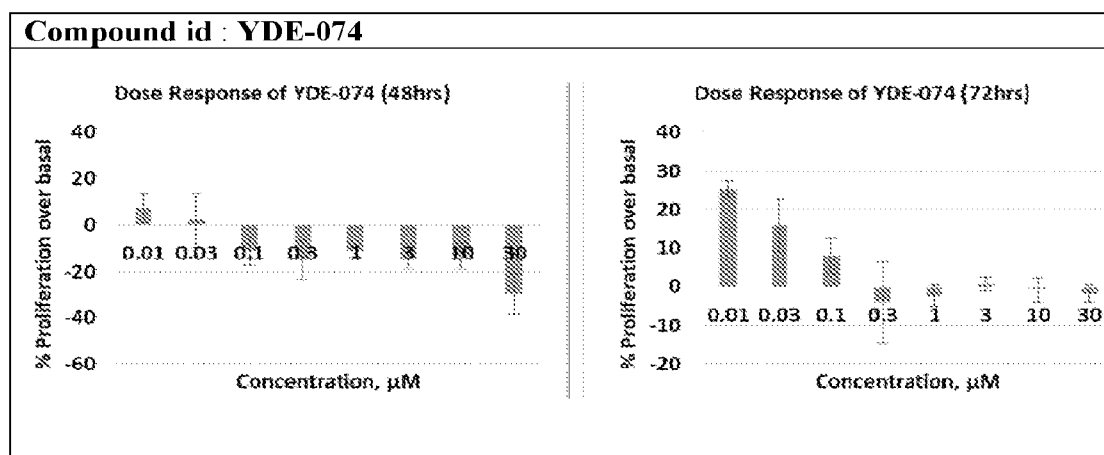


Figure 2X

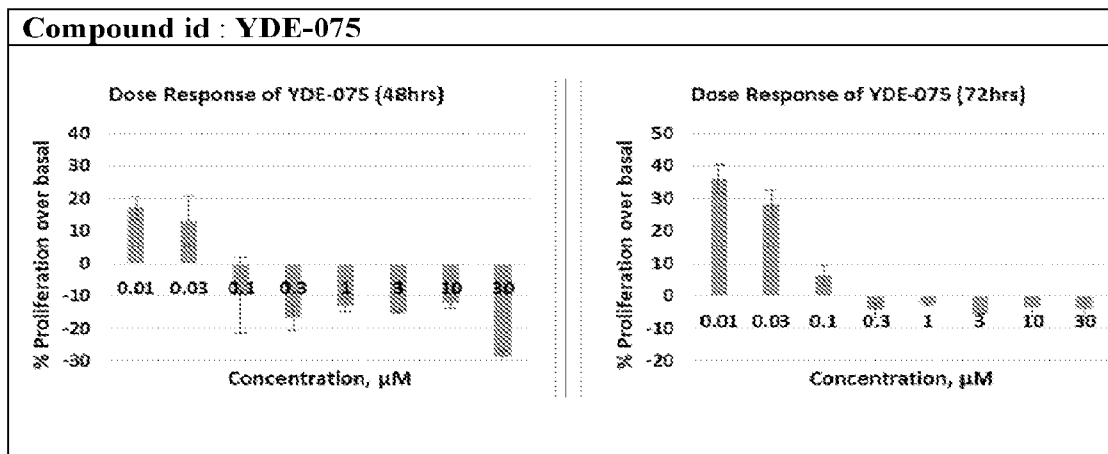


Figure 2Y

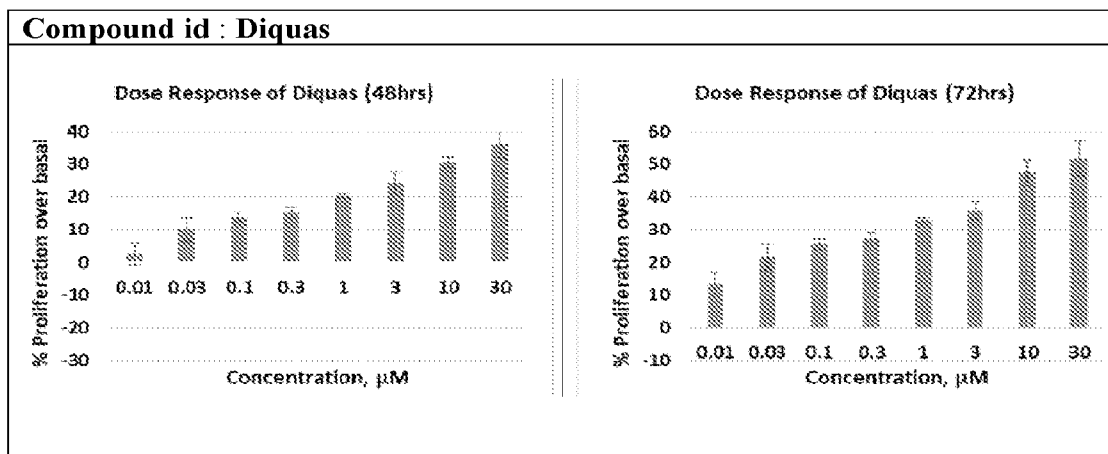


Figure 2Z

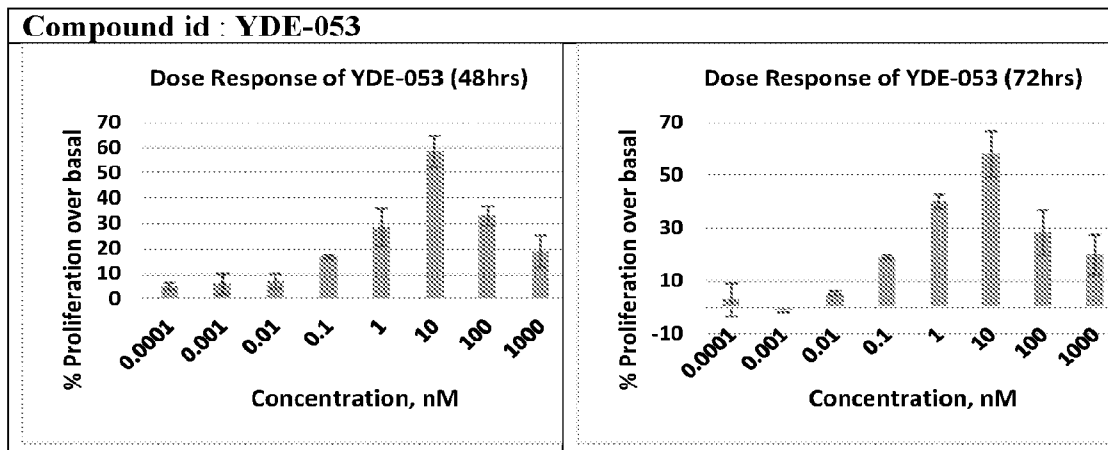


Figure 2AA

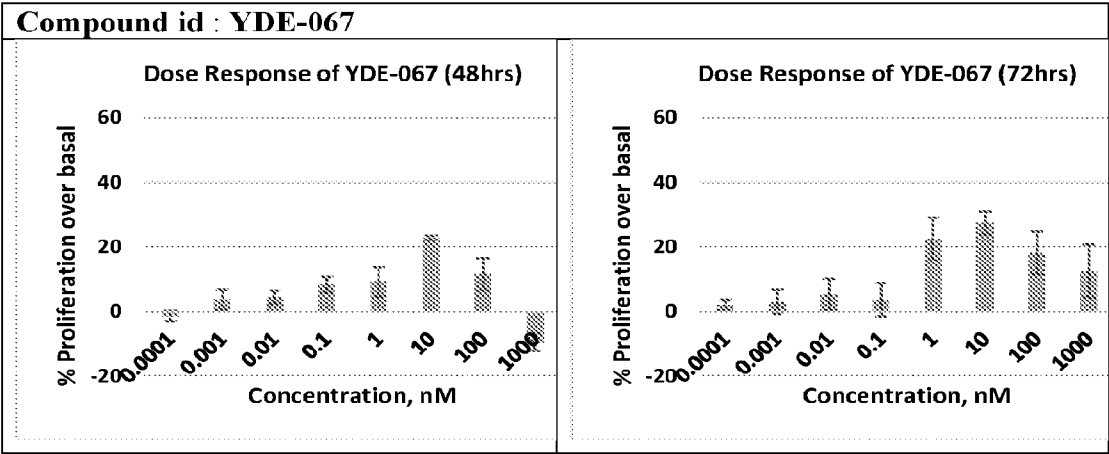


Figure 2AB

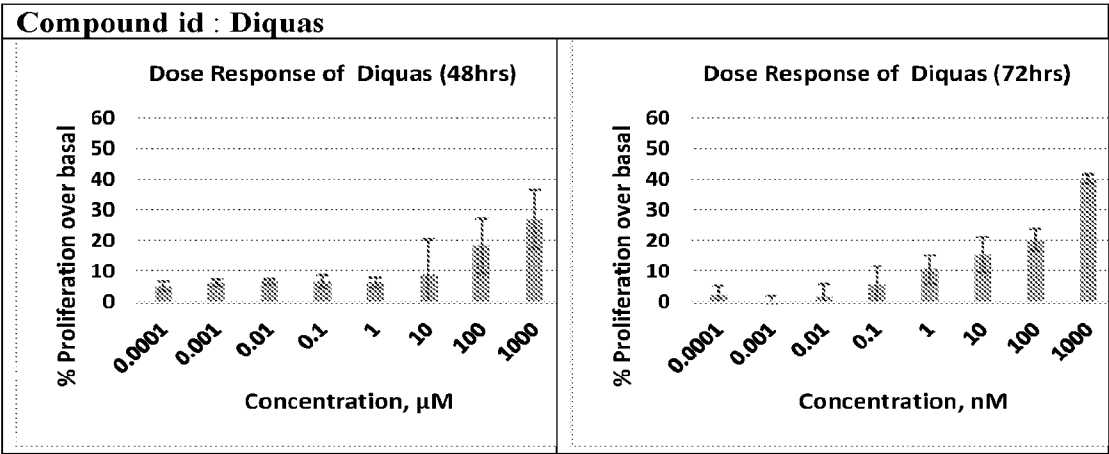


Figure 2AC

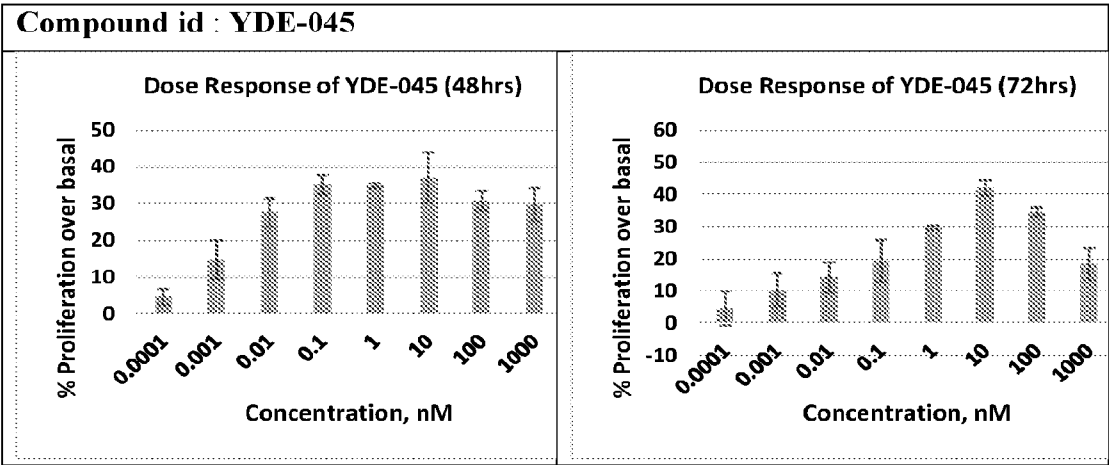


Figure 2AD

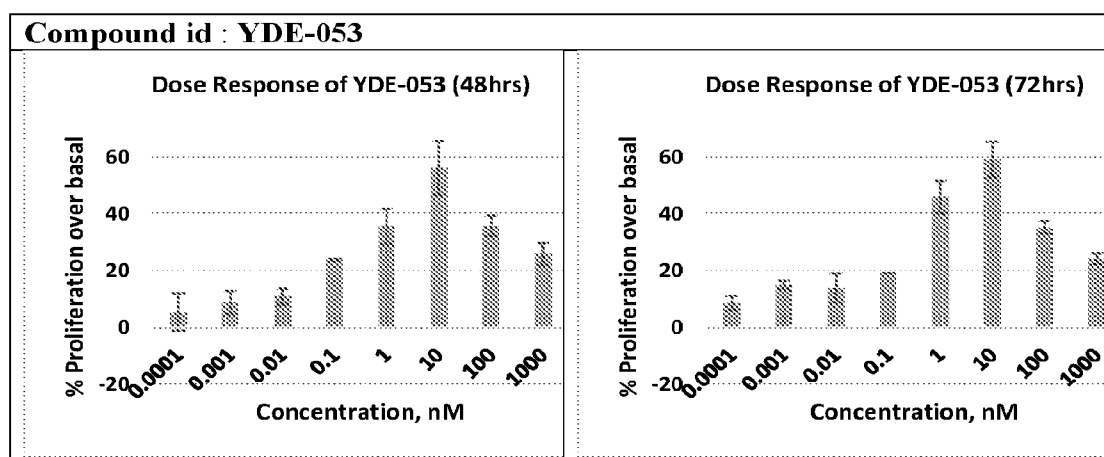


Figure 2AE

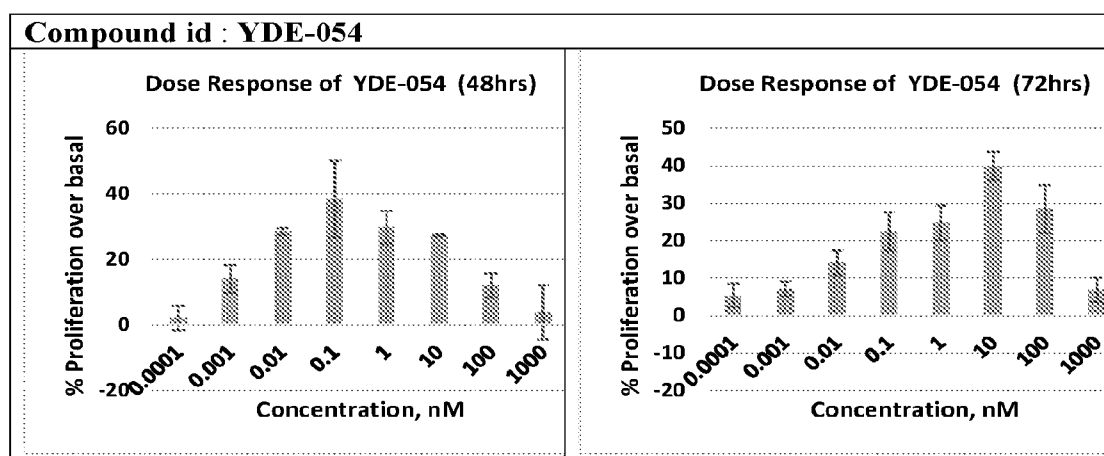


Figure 2AF

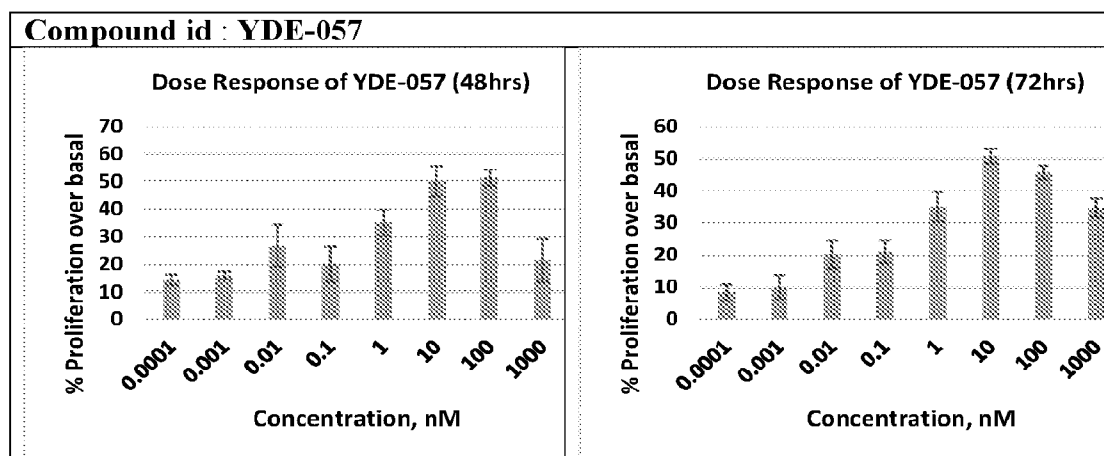


Figure 2AG

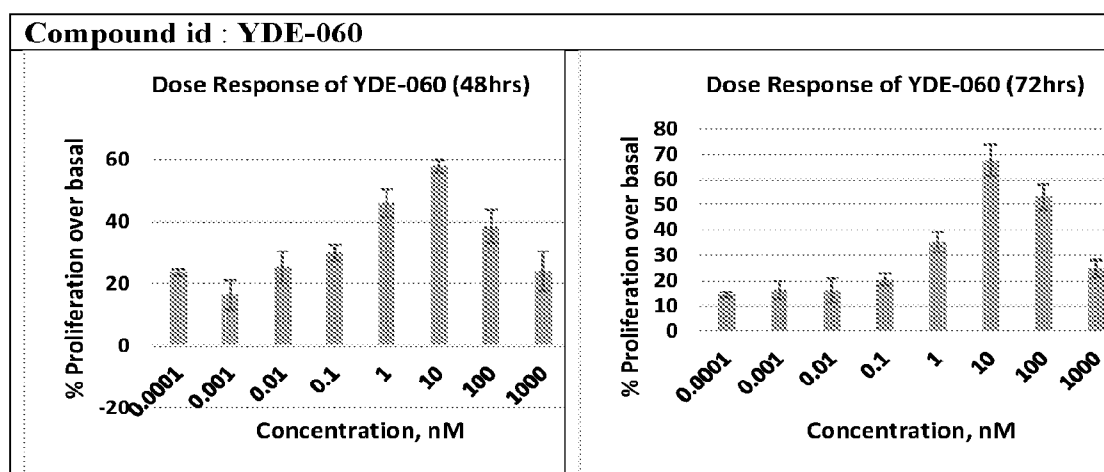


Figure 2AH

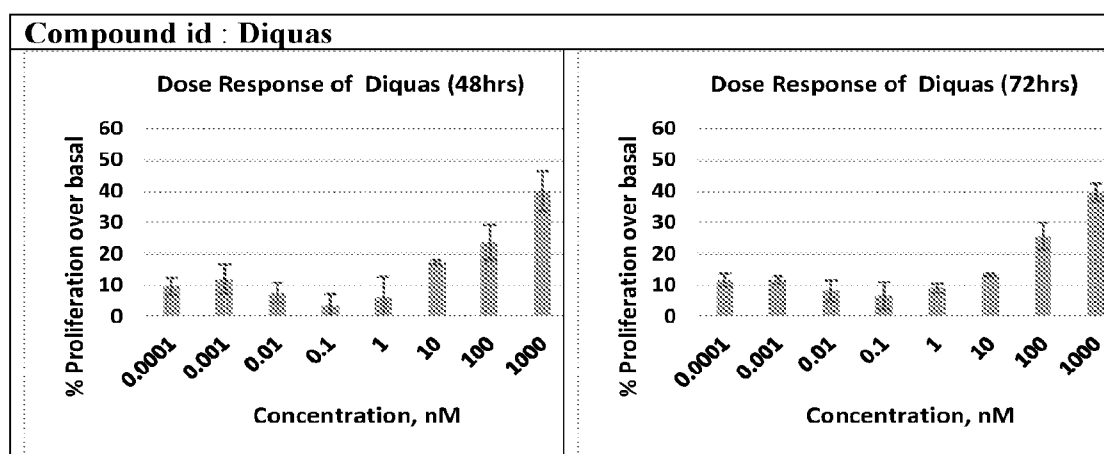


Figure 2AI

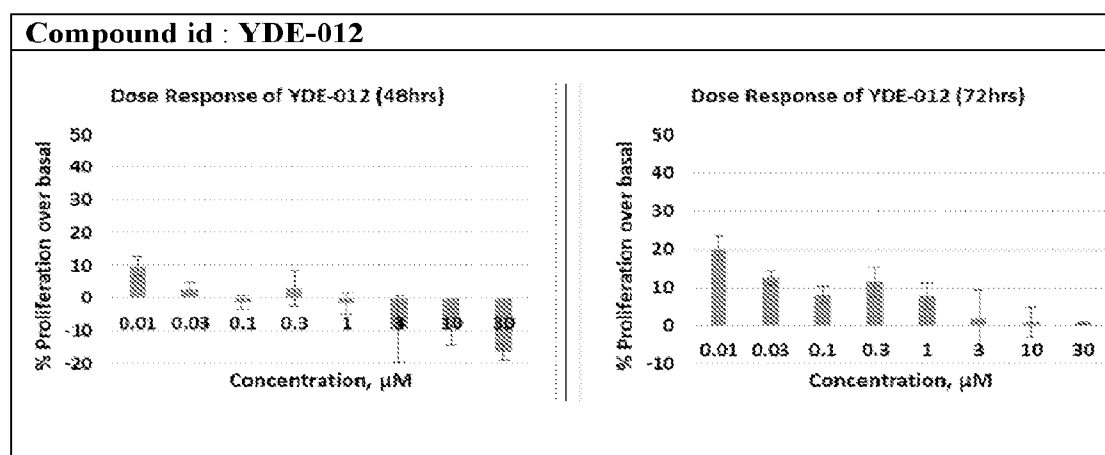


Figure 2AJ

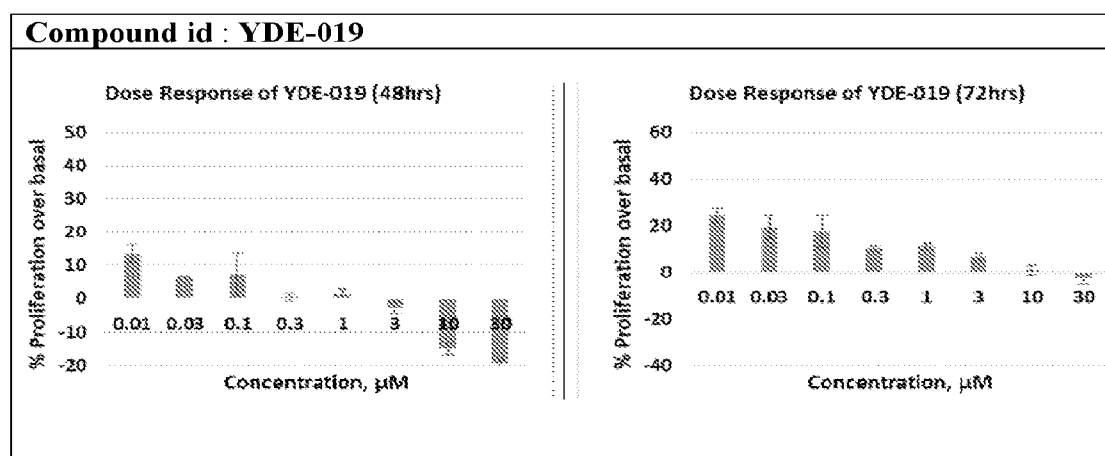


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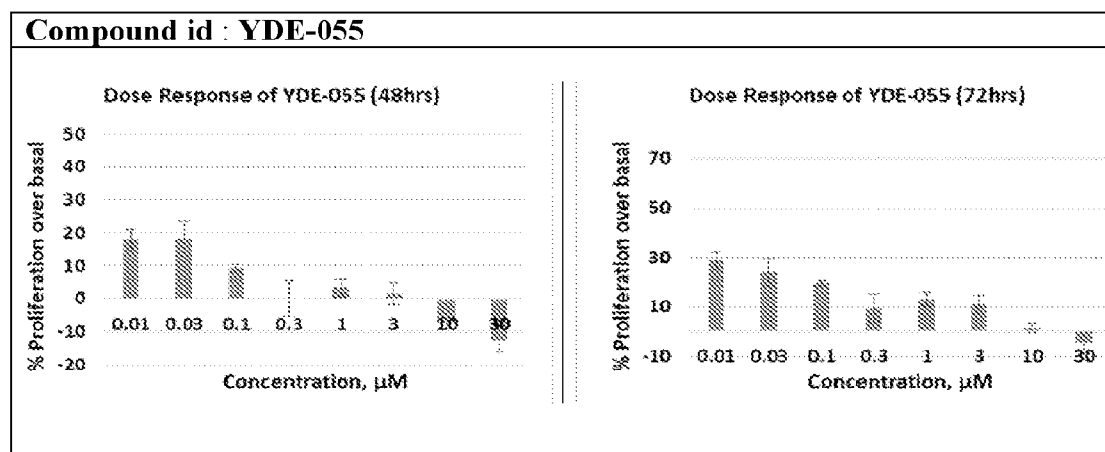


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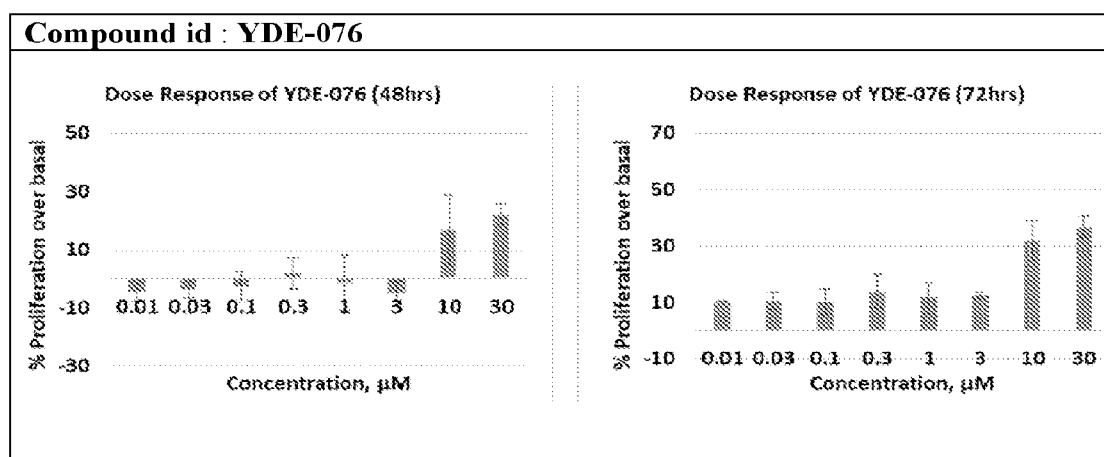


Figure 2AM

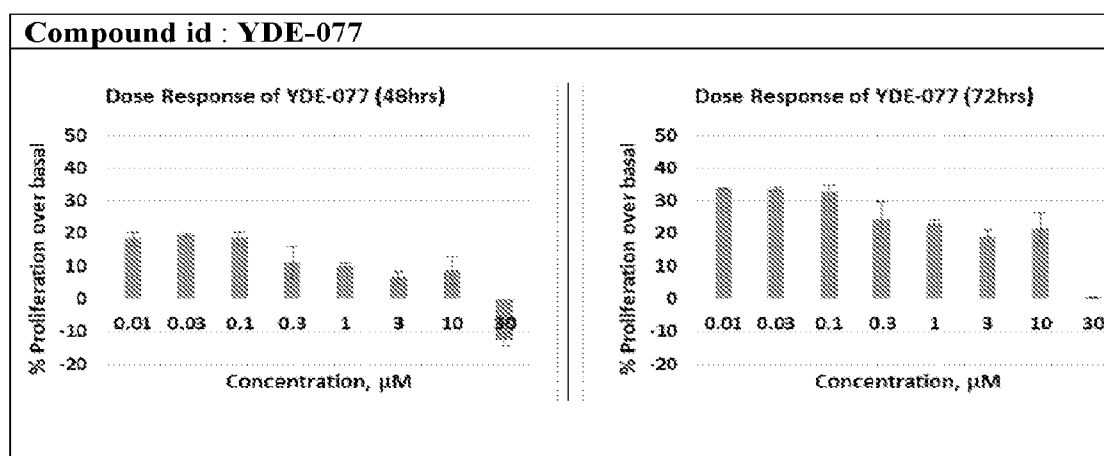


Figure 2AN

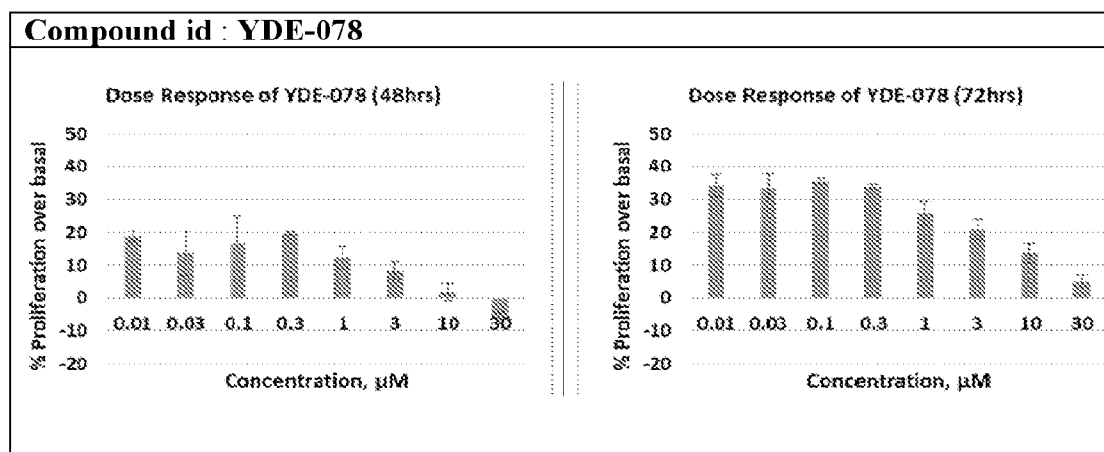


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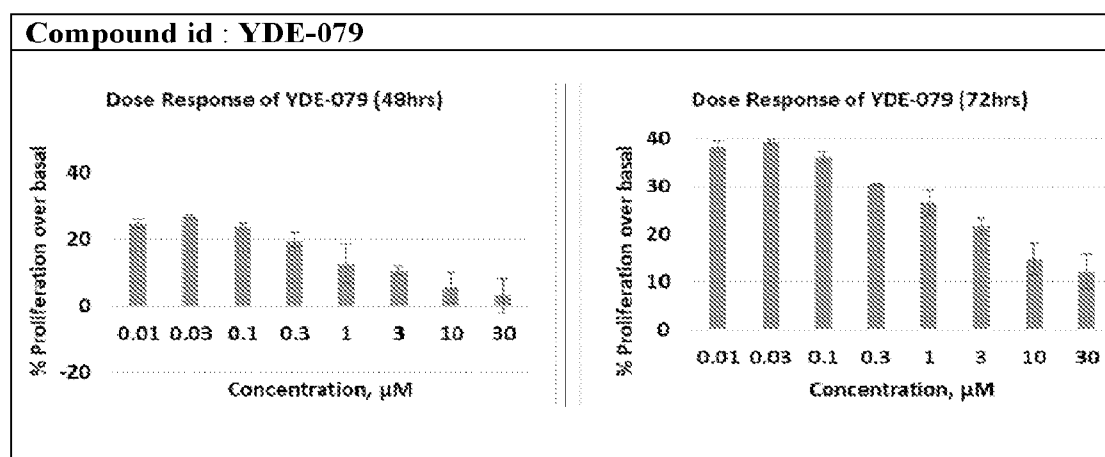


Figure 2AP

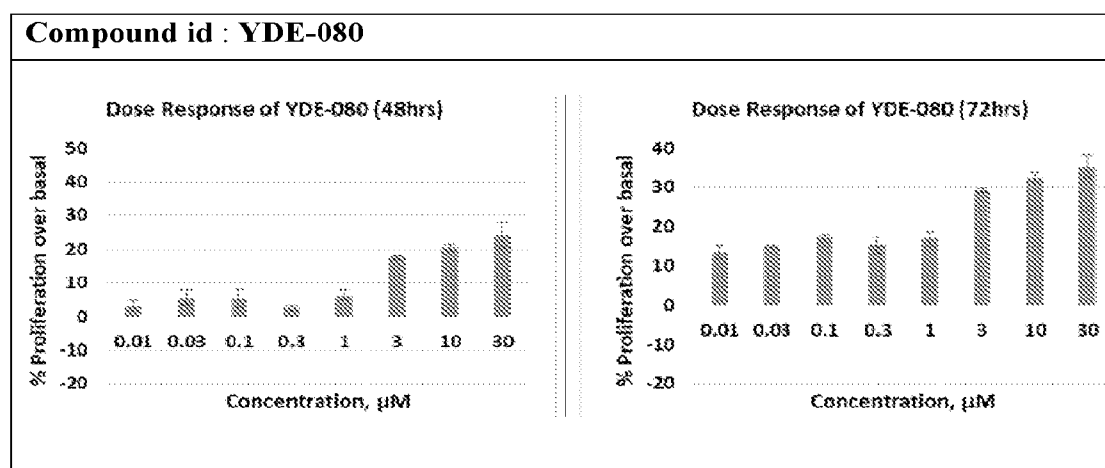


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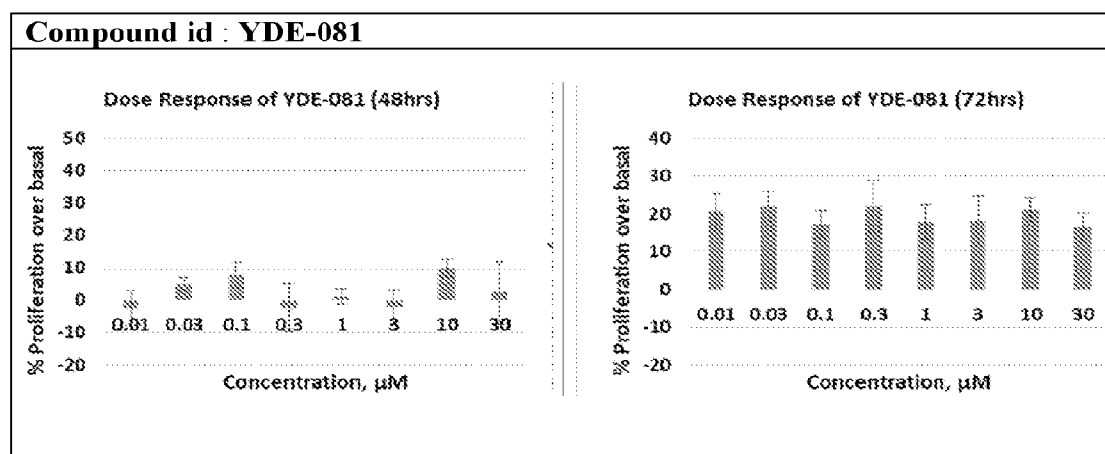


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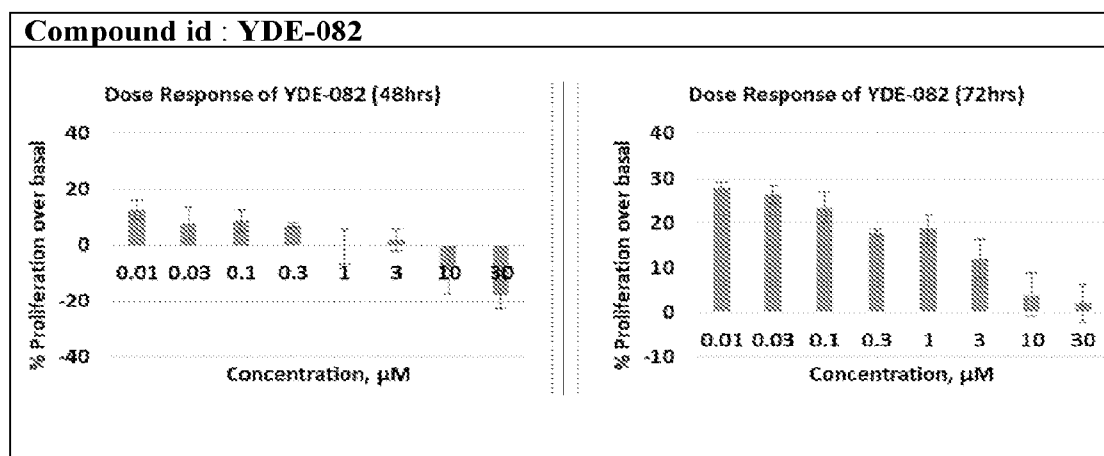


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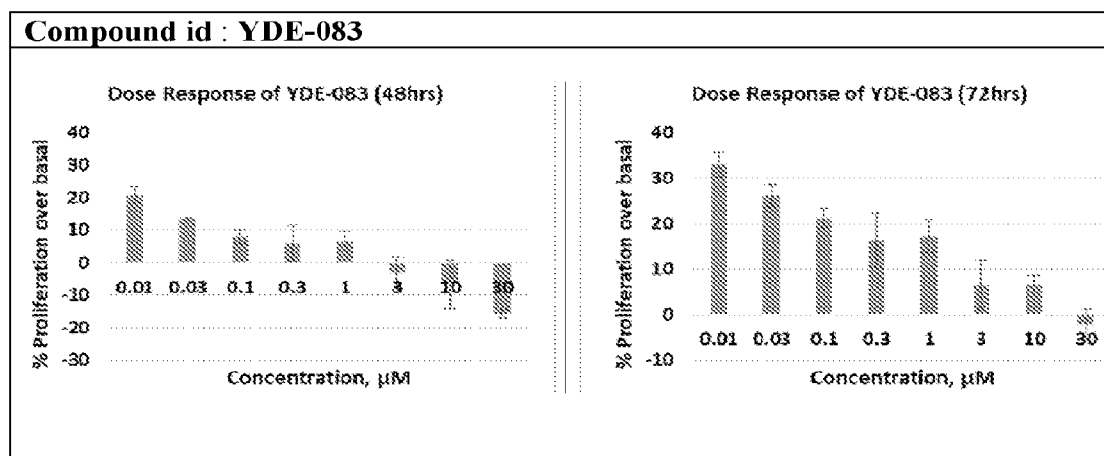


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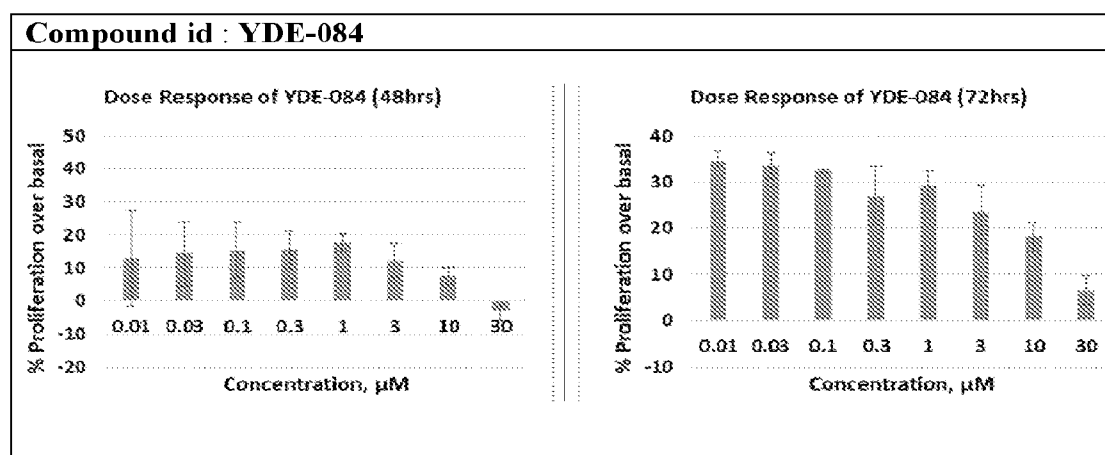


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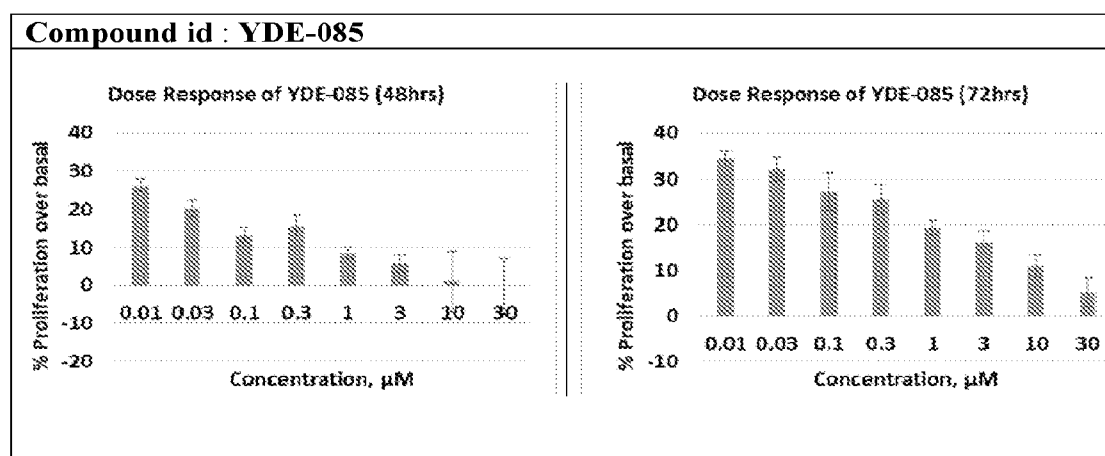


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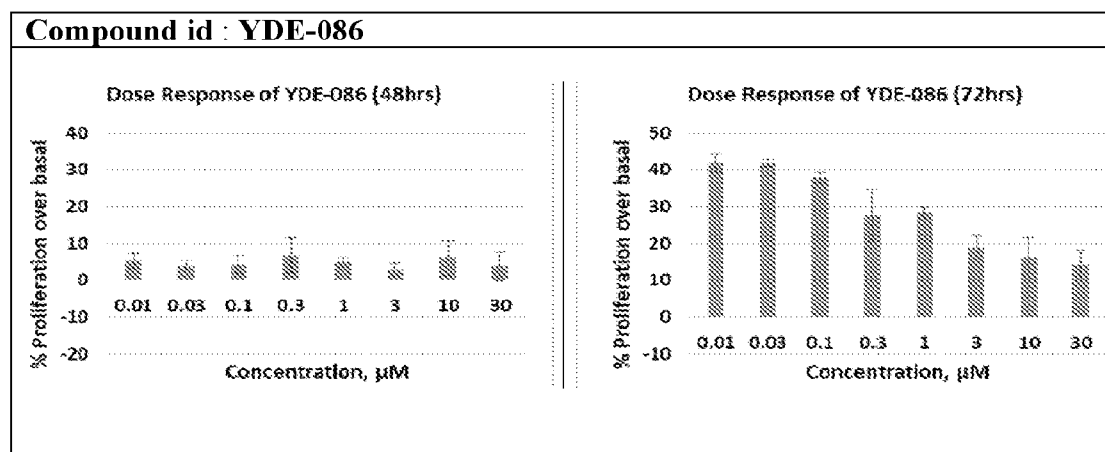


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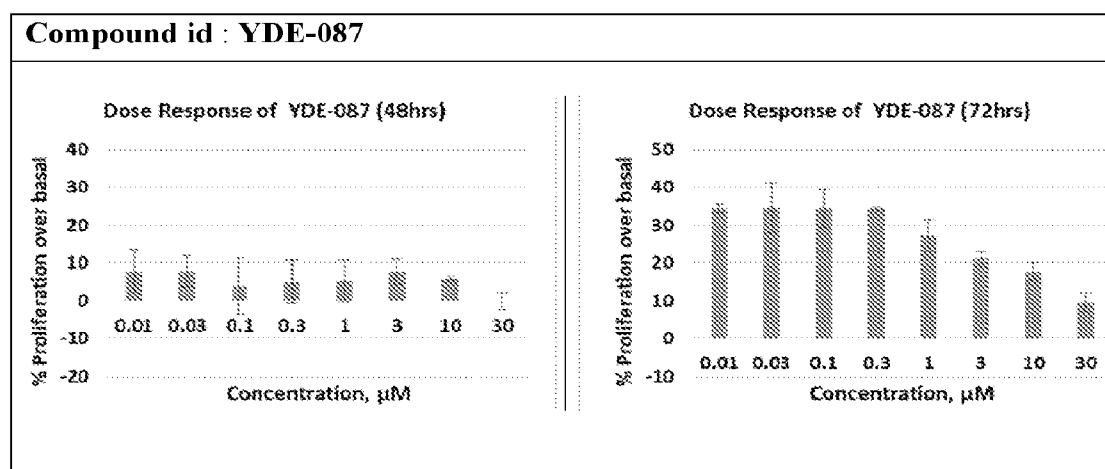


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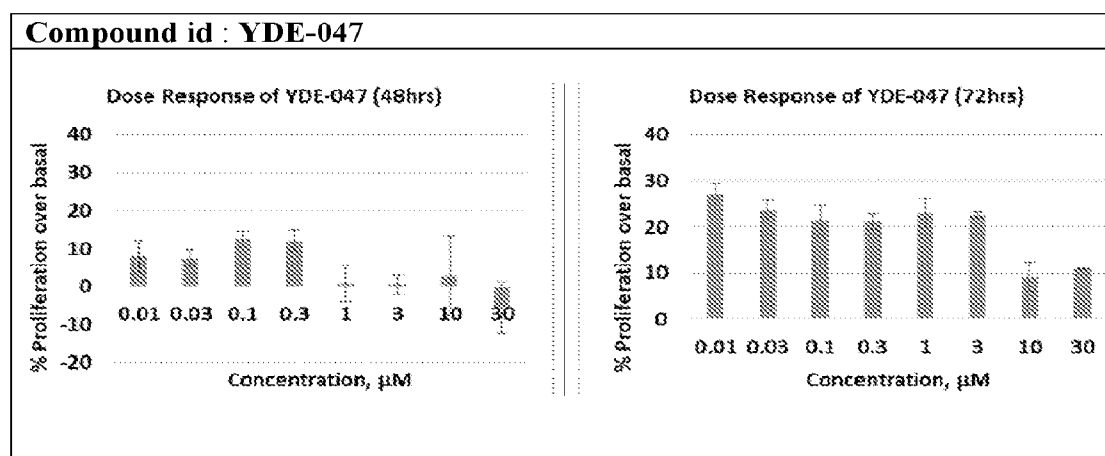


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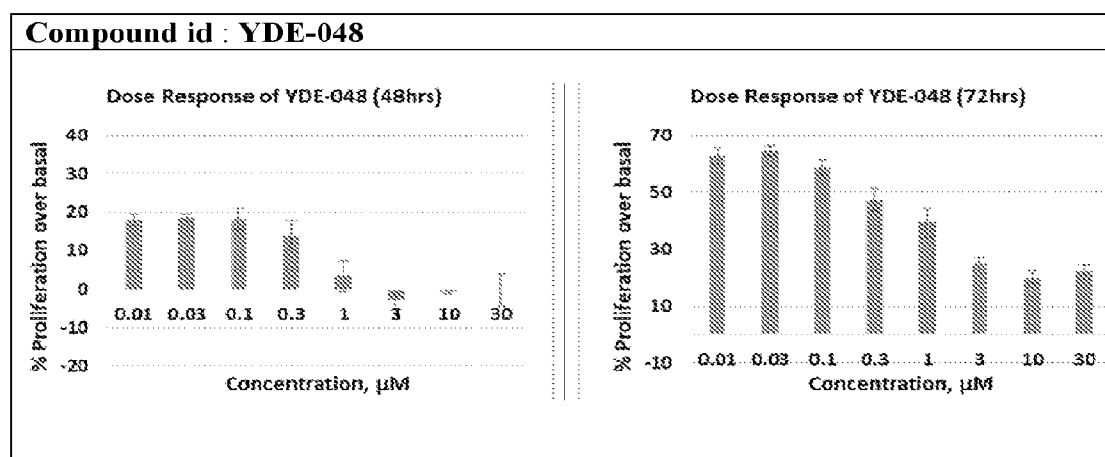


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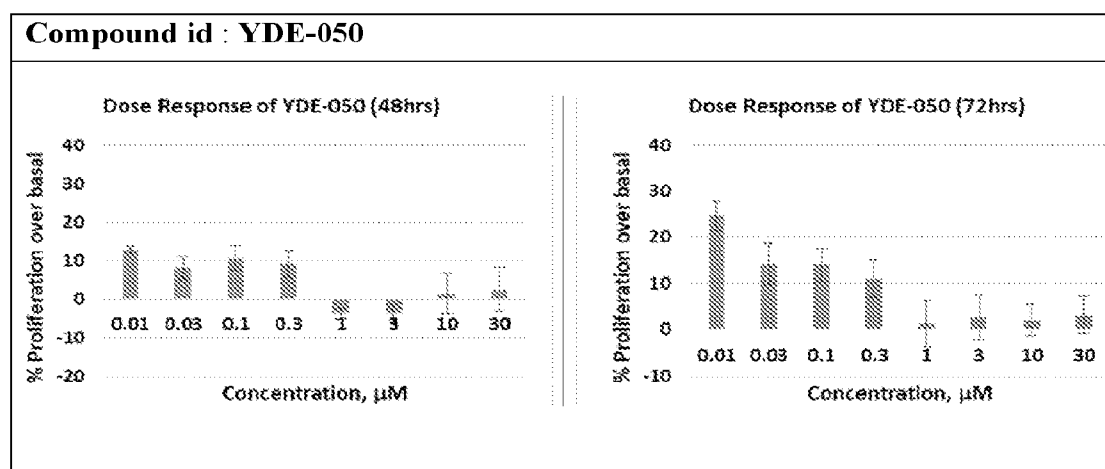


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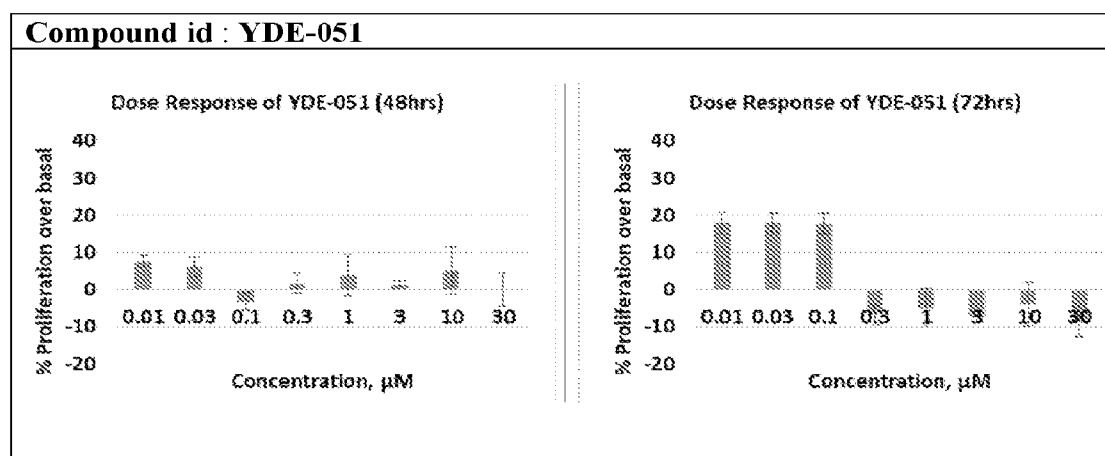


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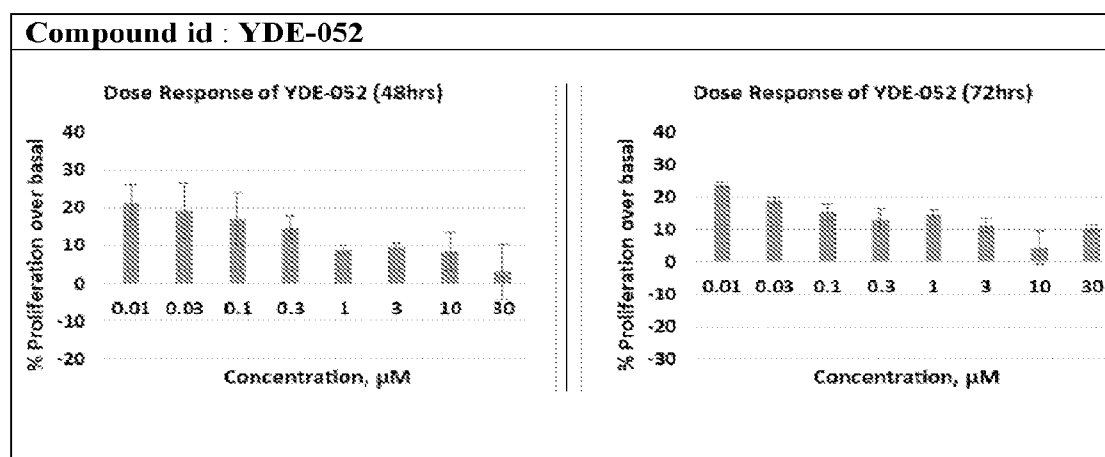


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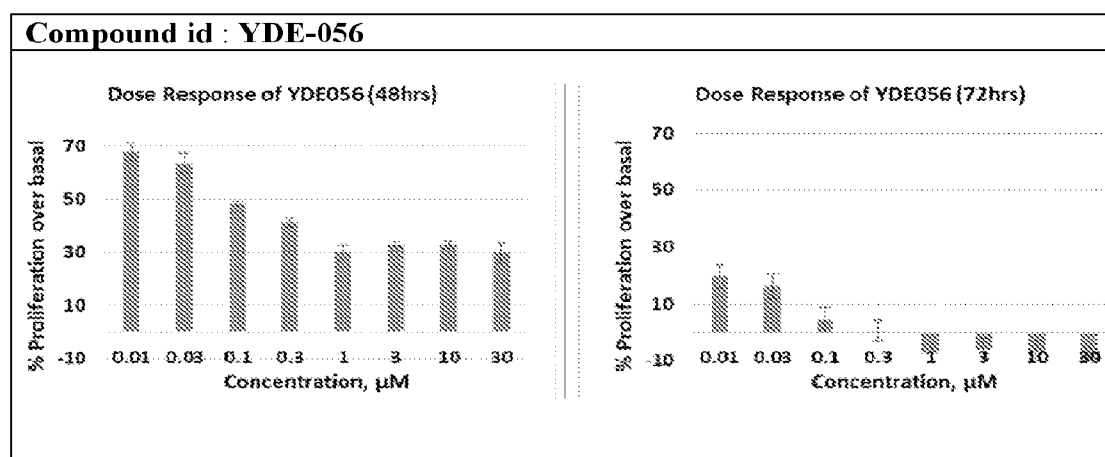


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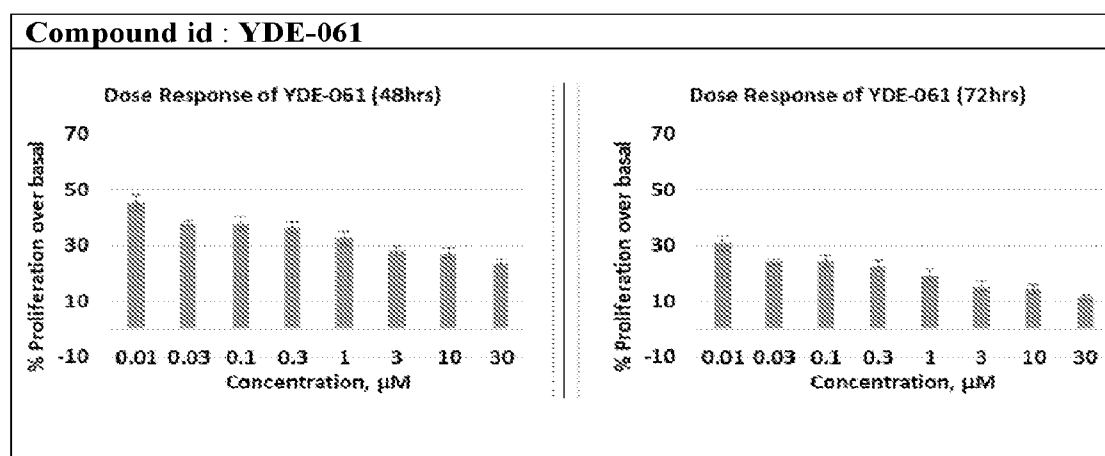


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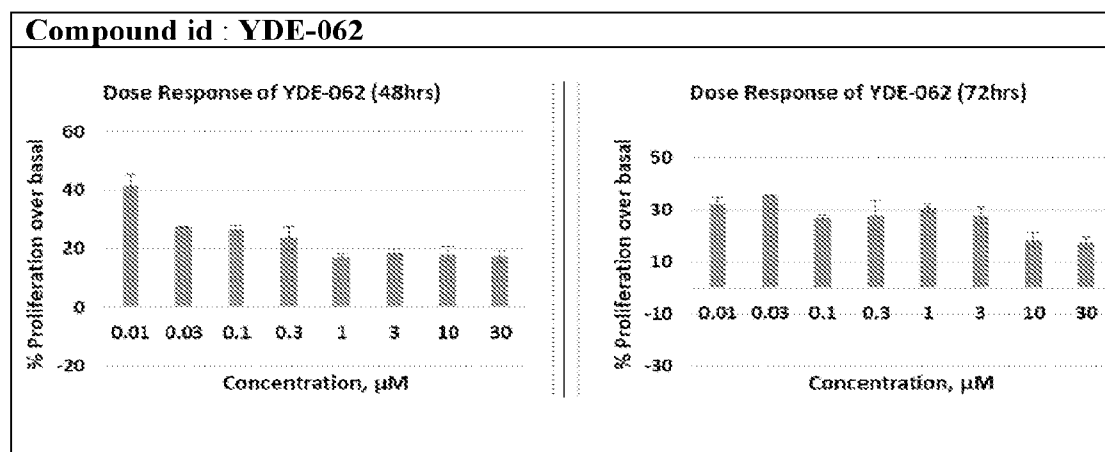


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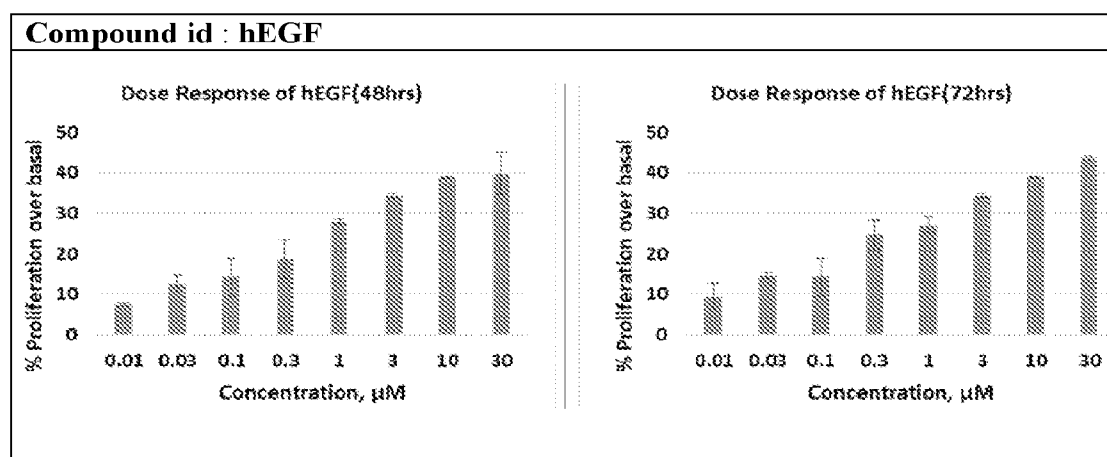


Figure 3

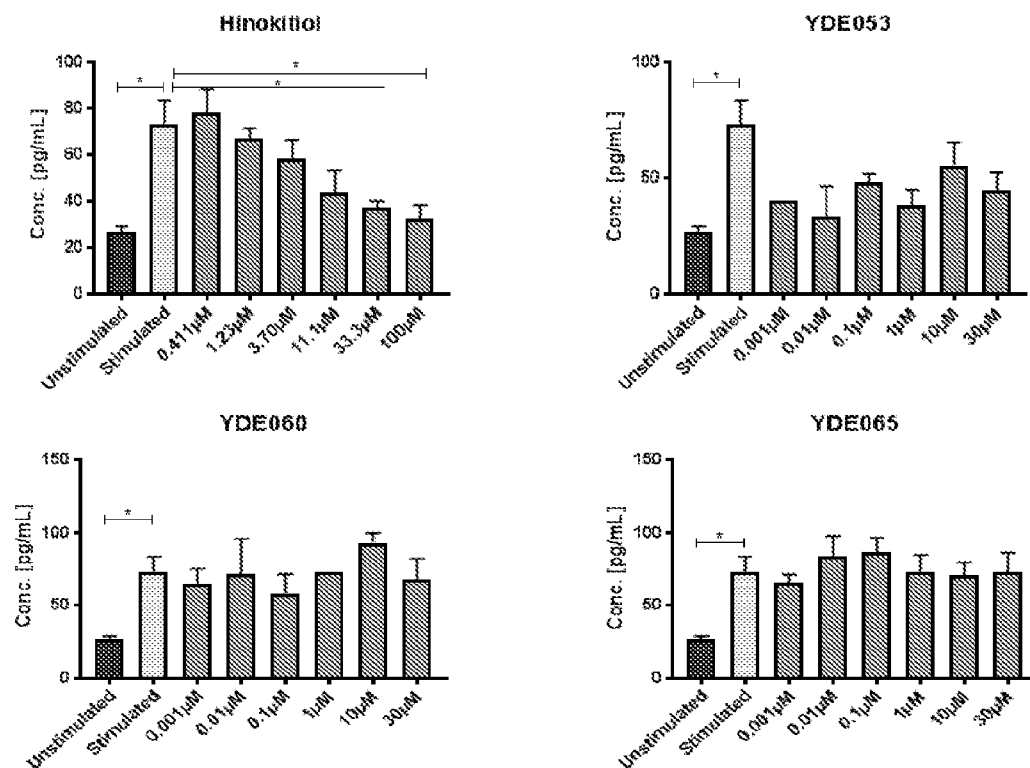


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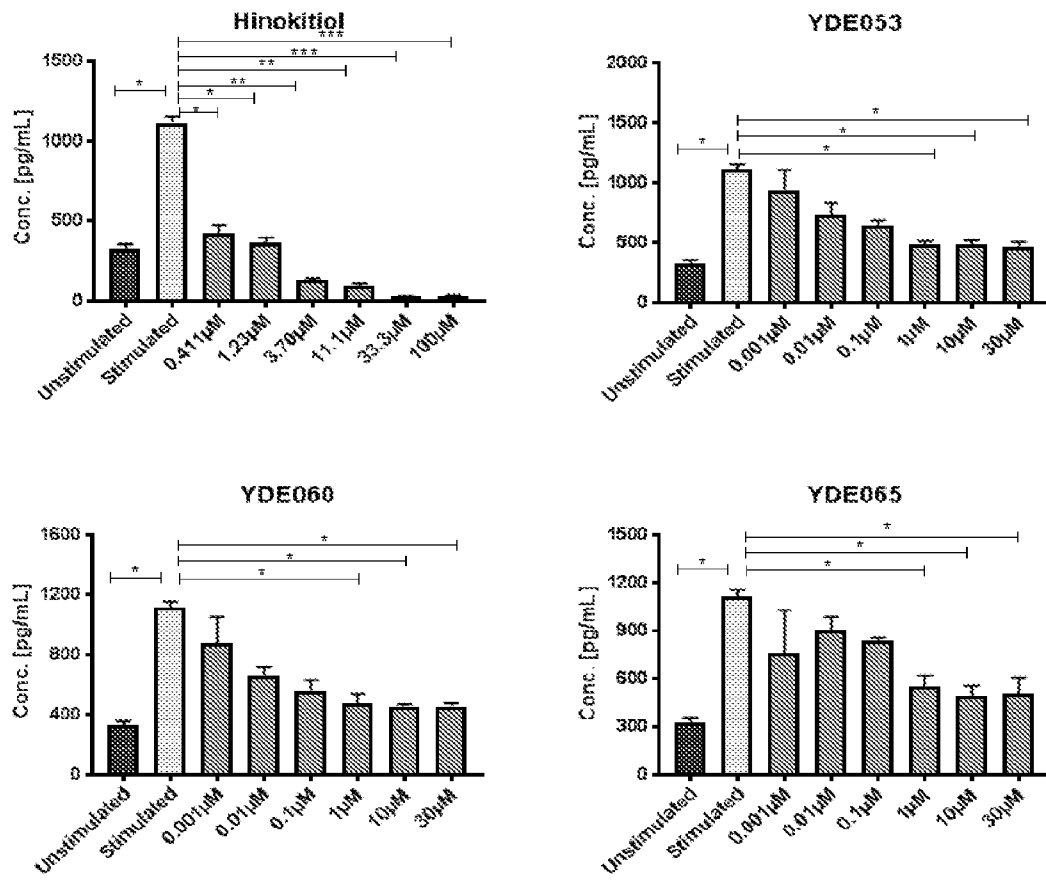


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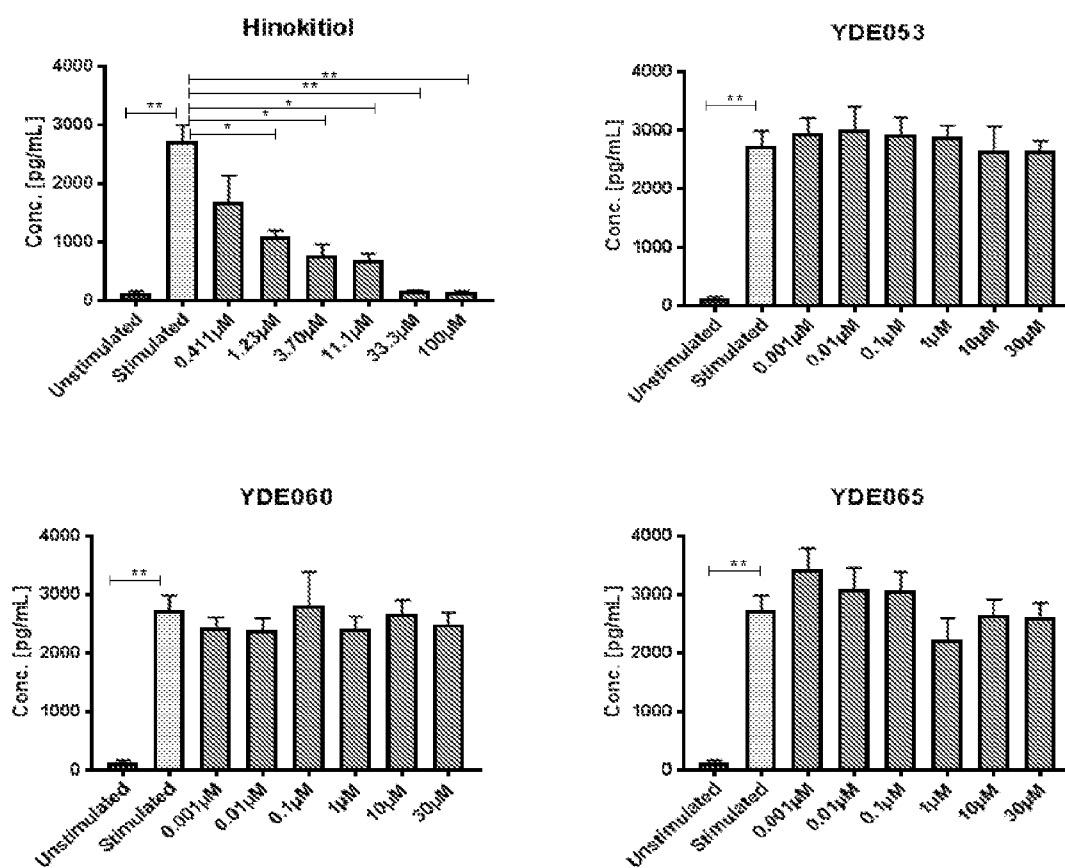


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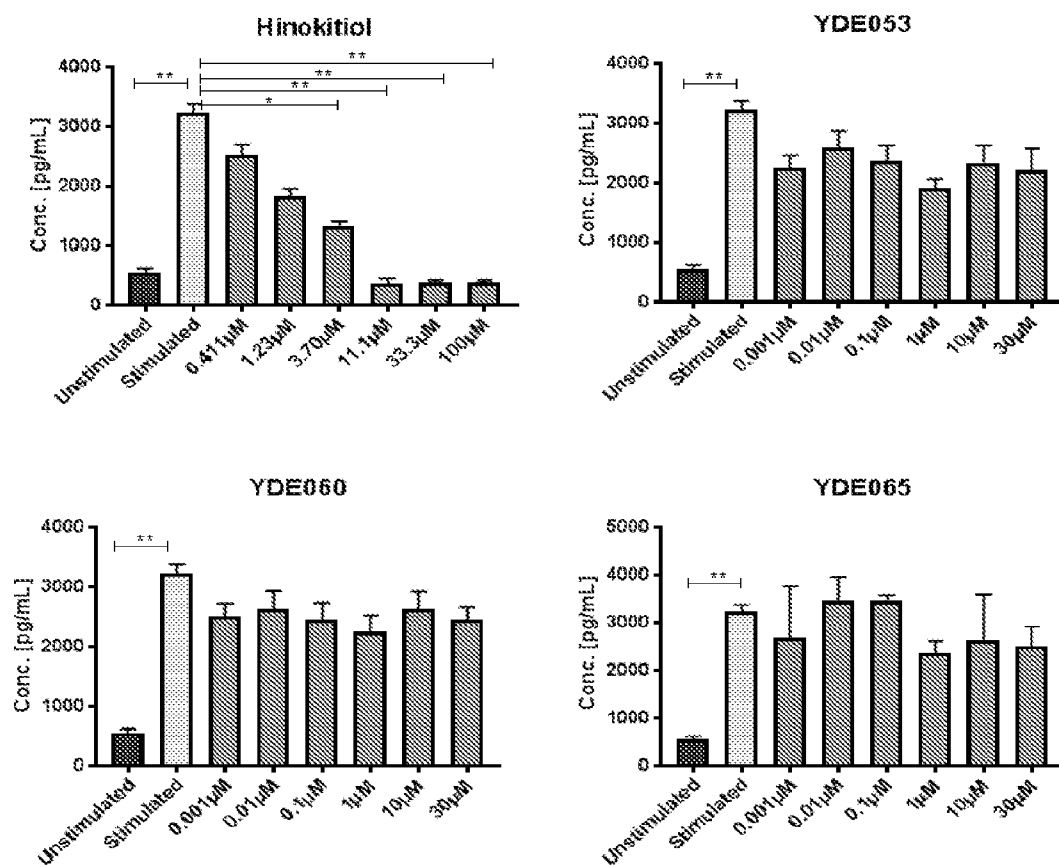


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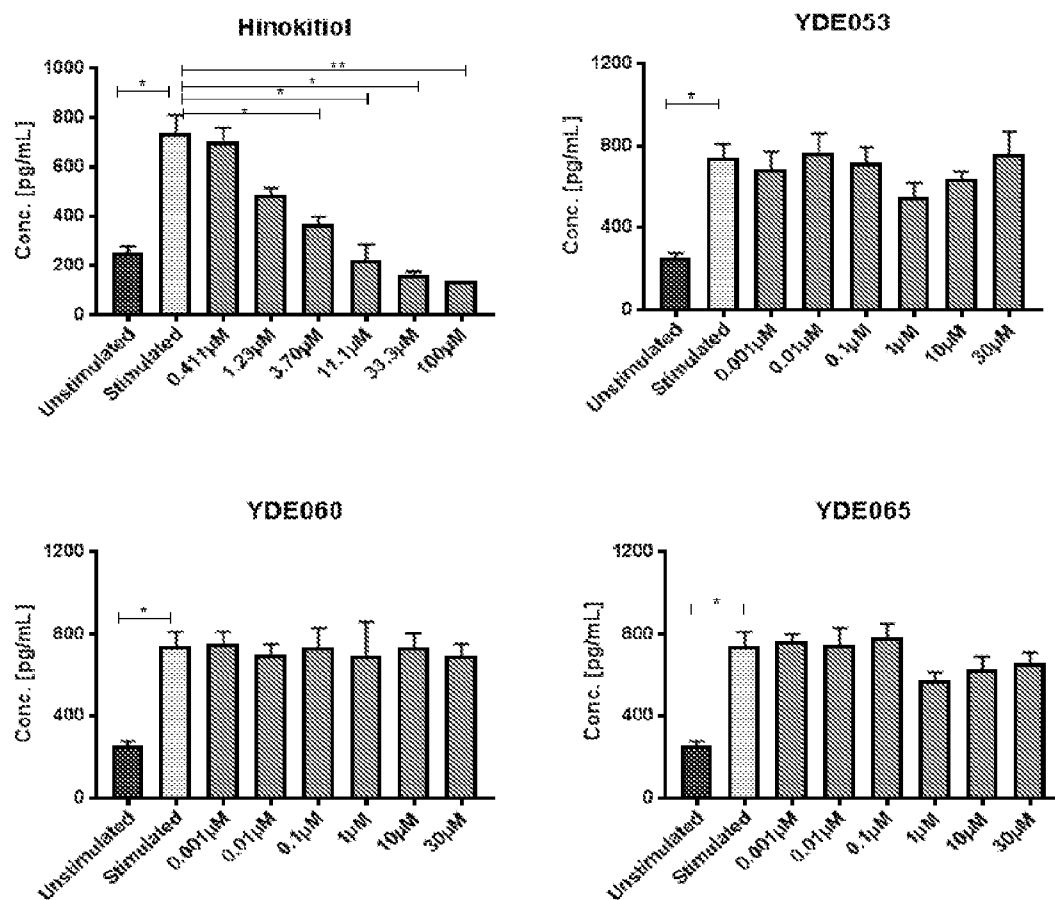


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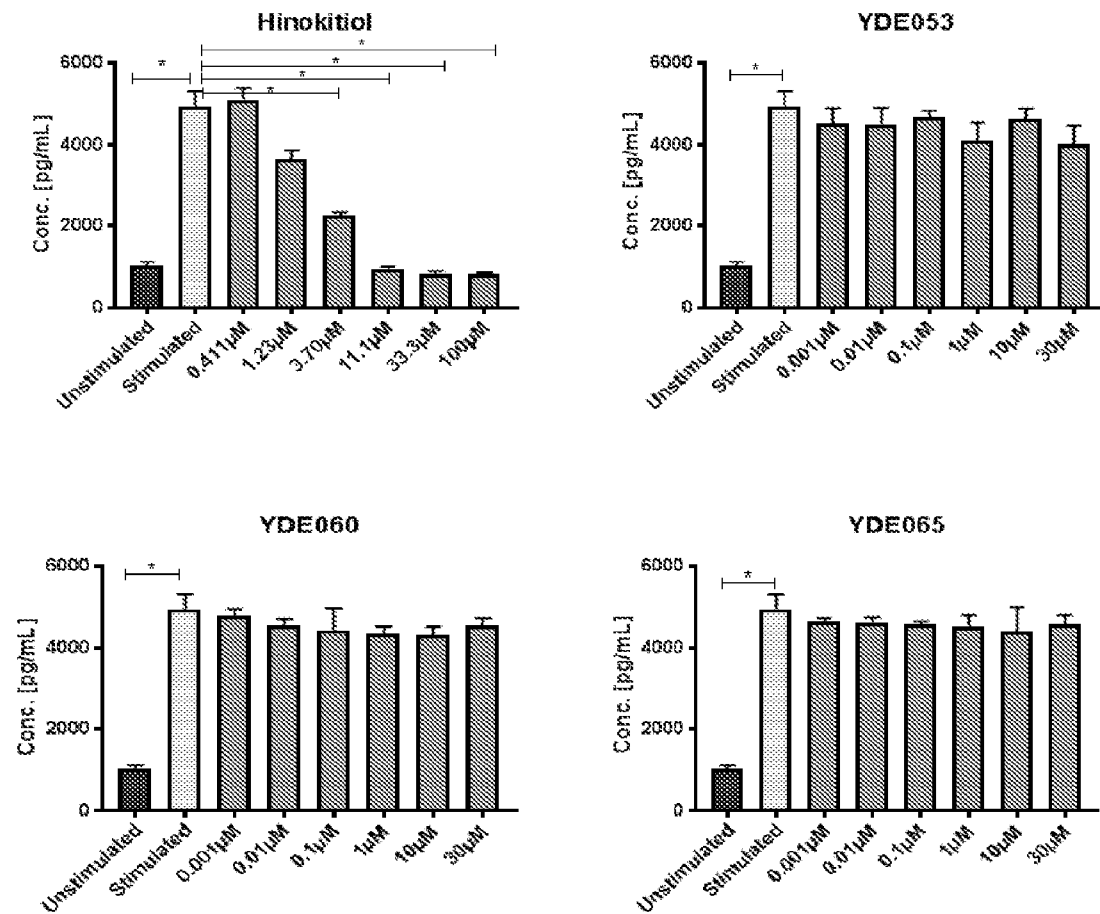


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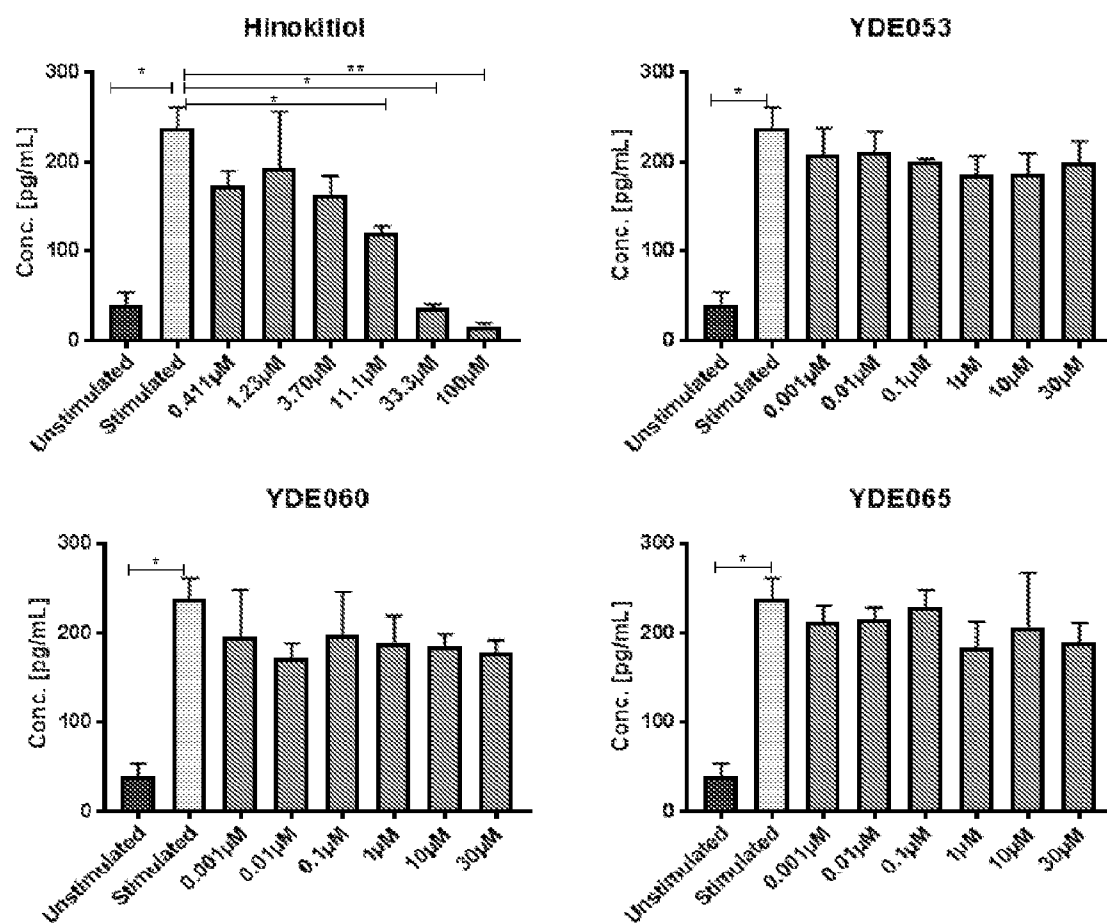


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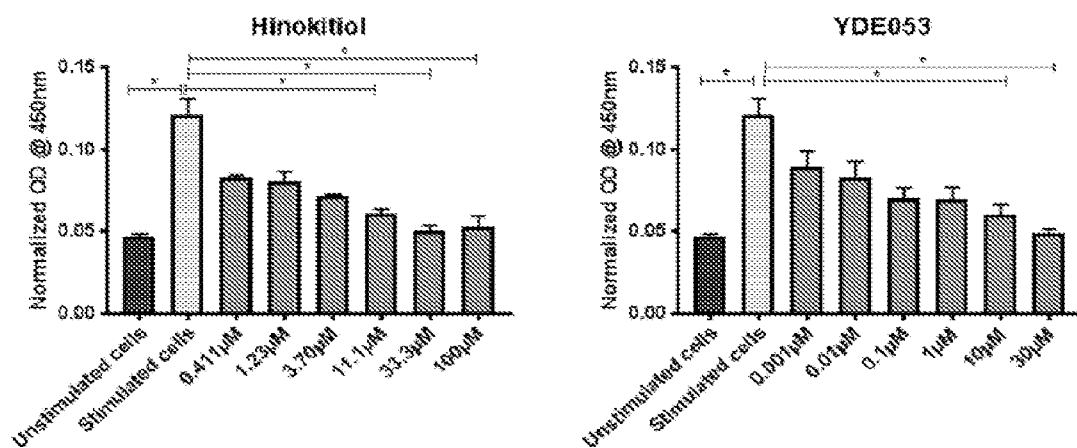


Figure 5

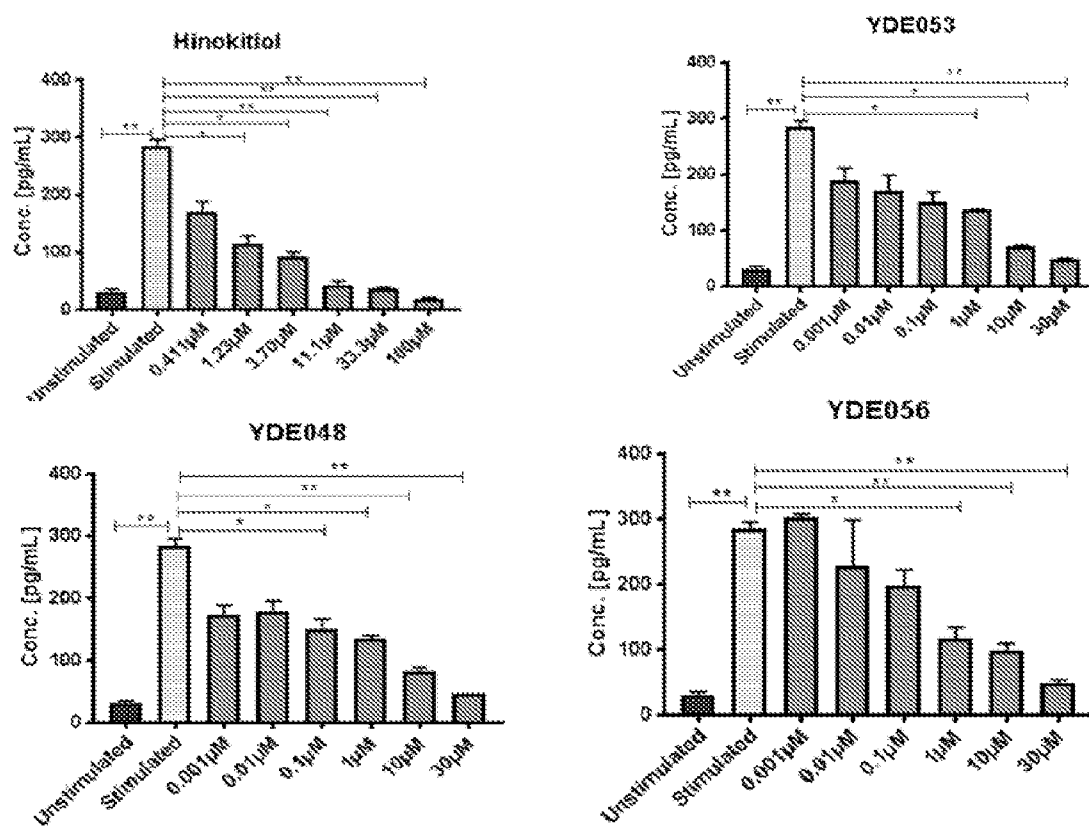


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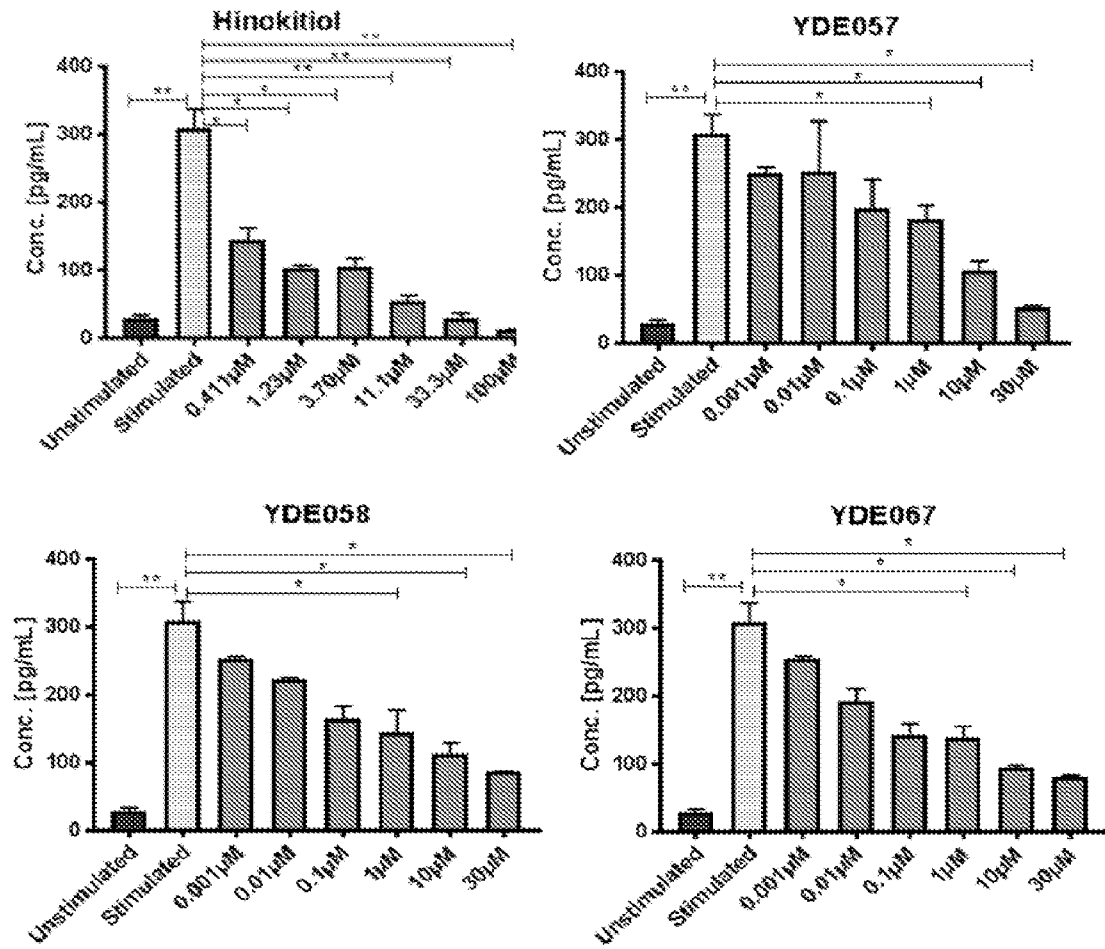


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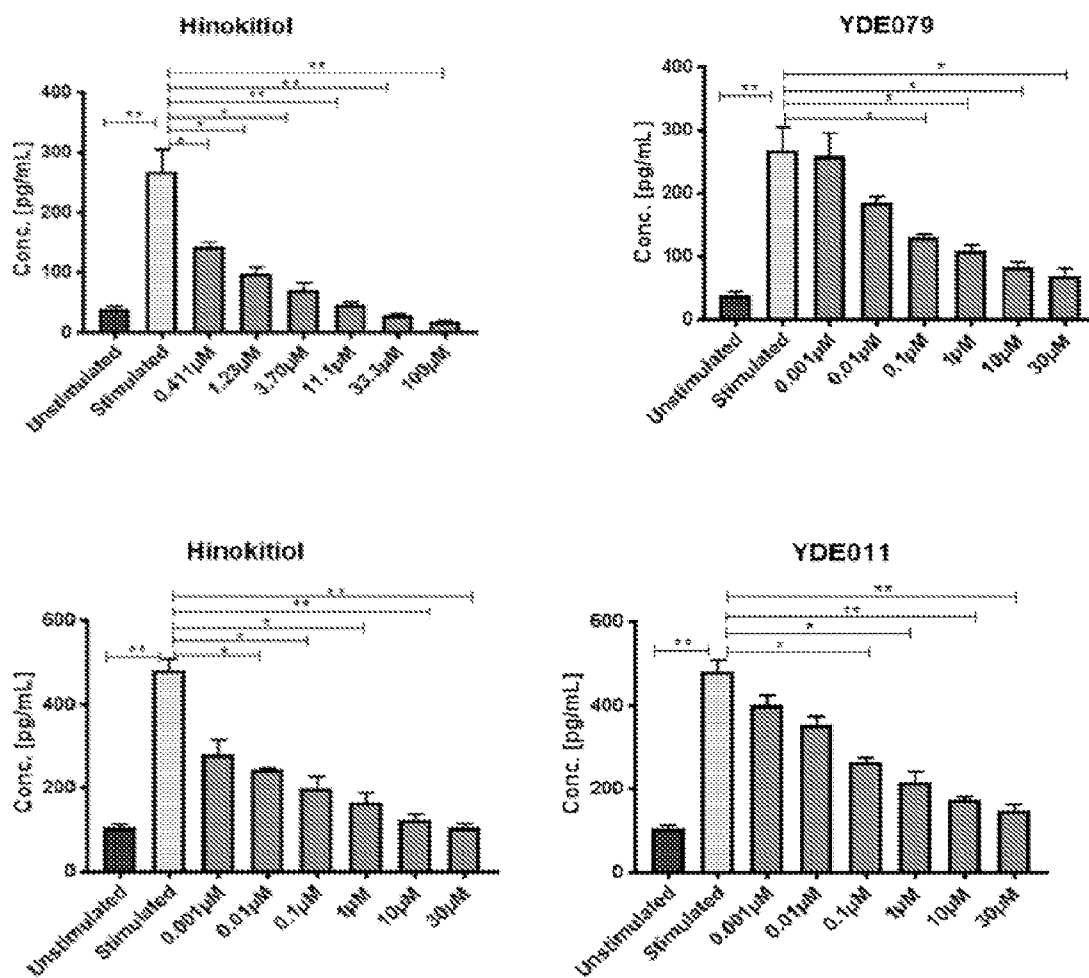


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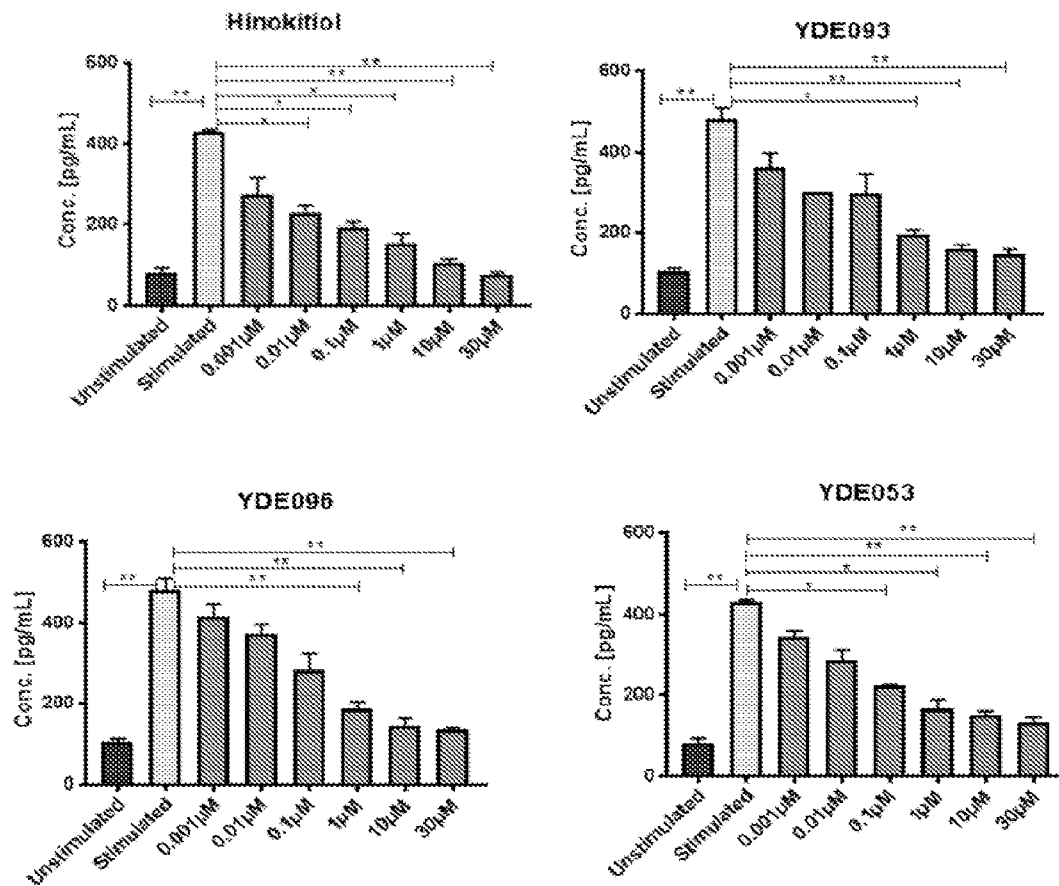


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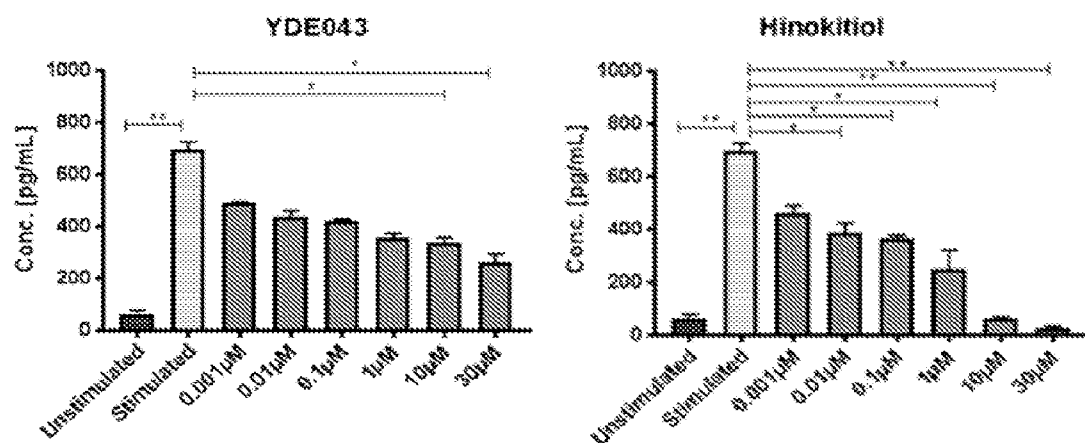


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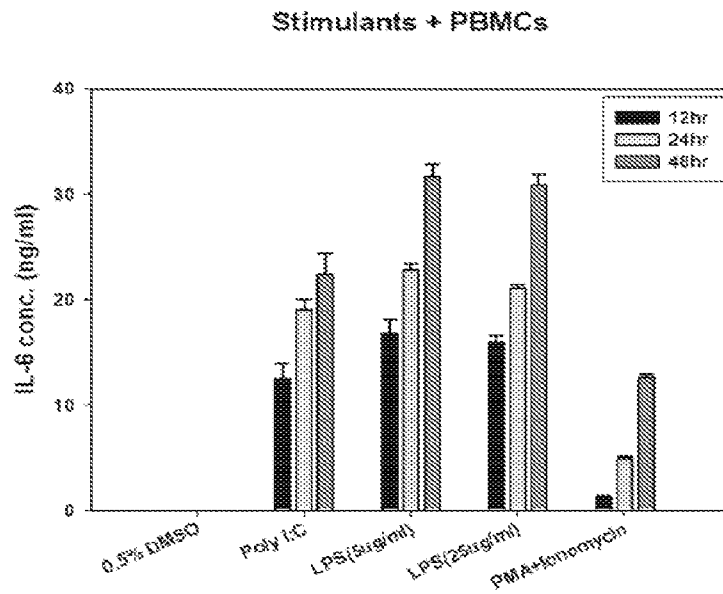


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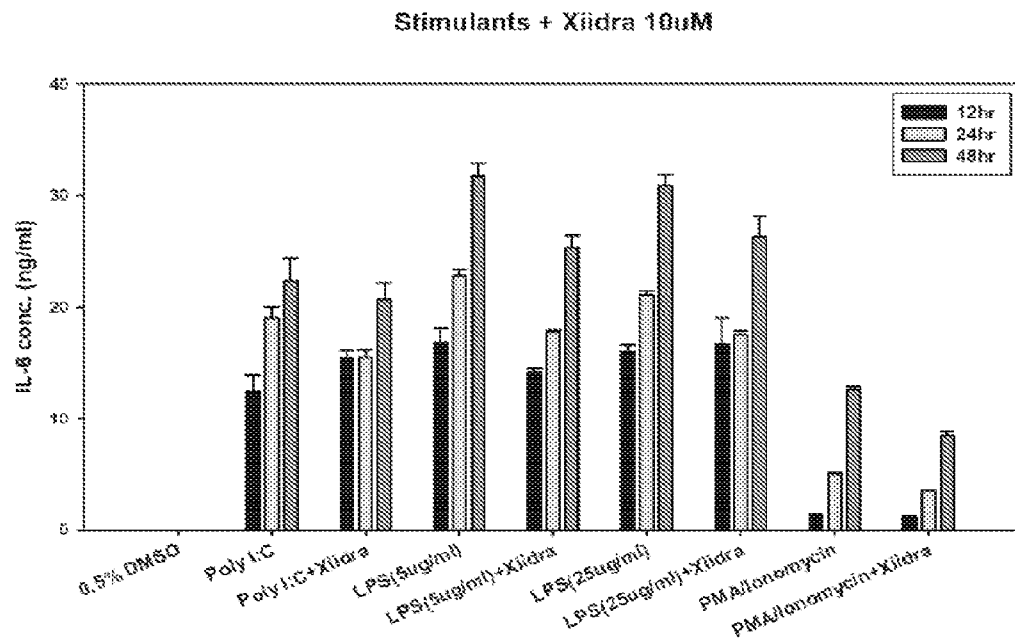


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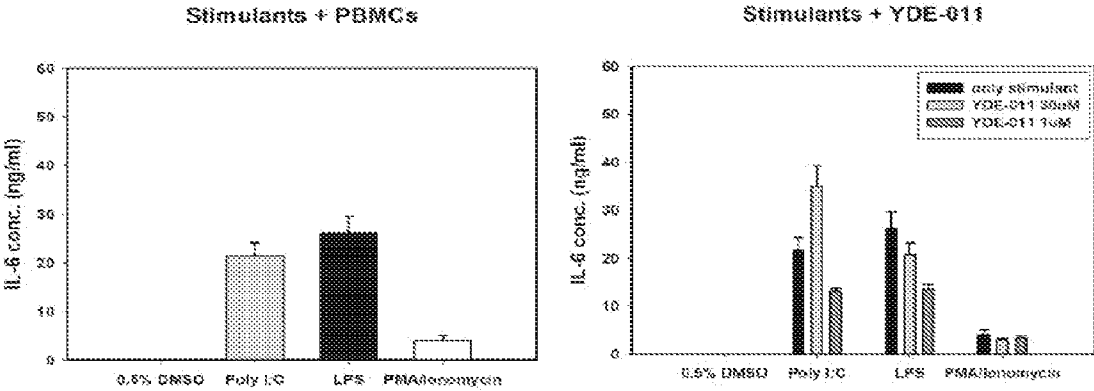


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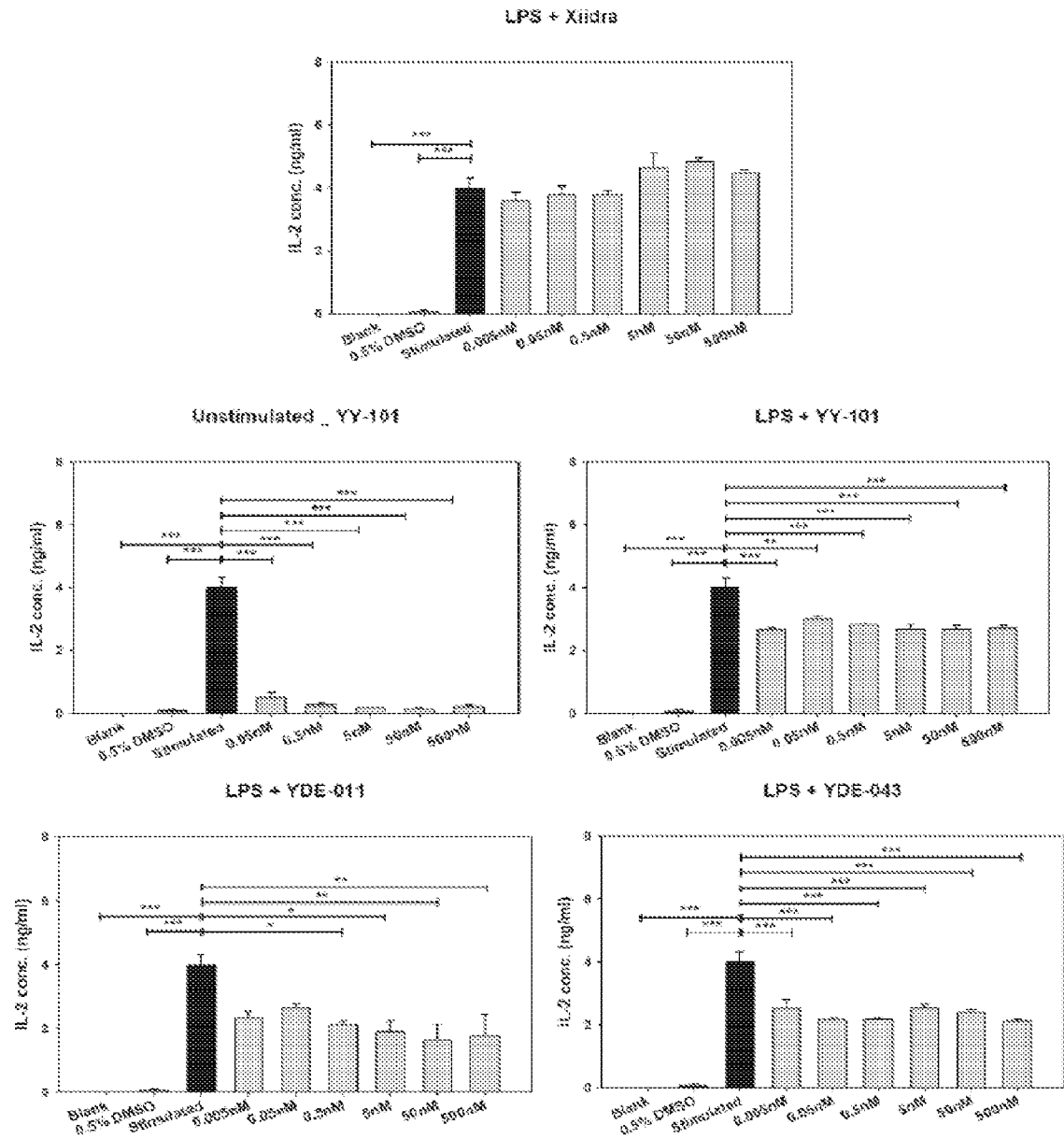


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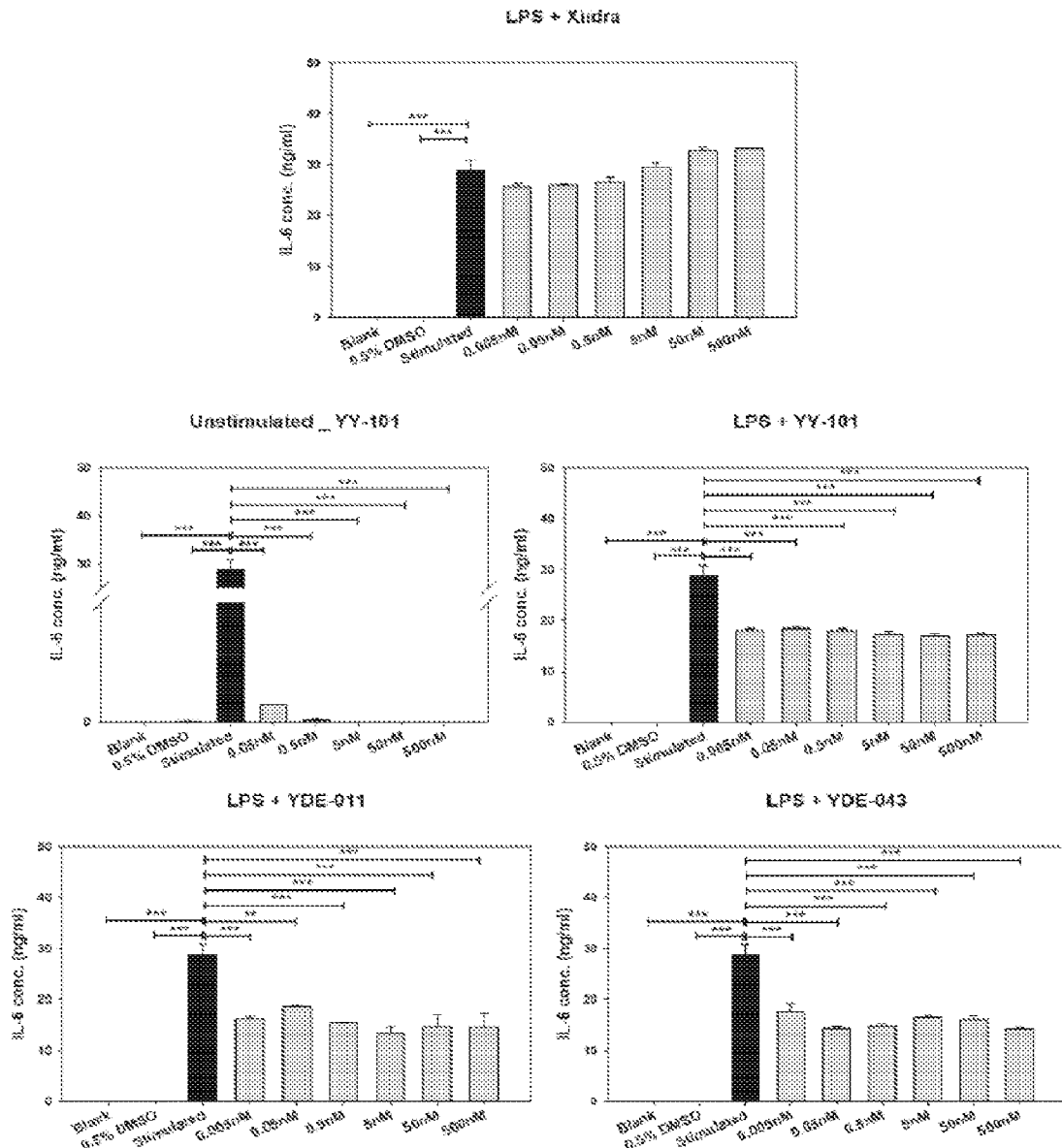


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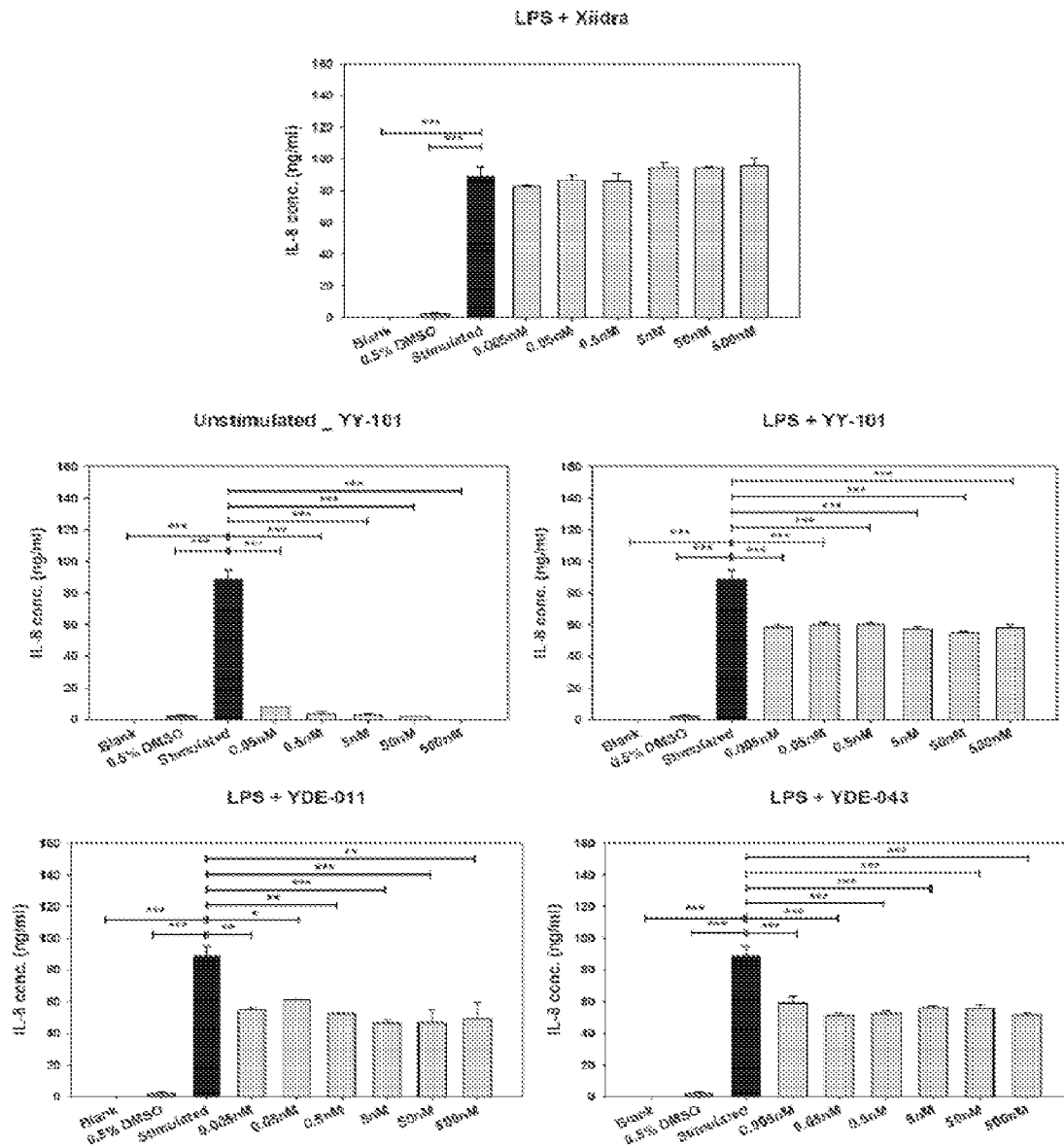


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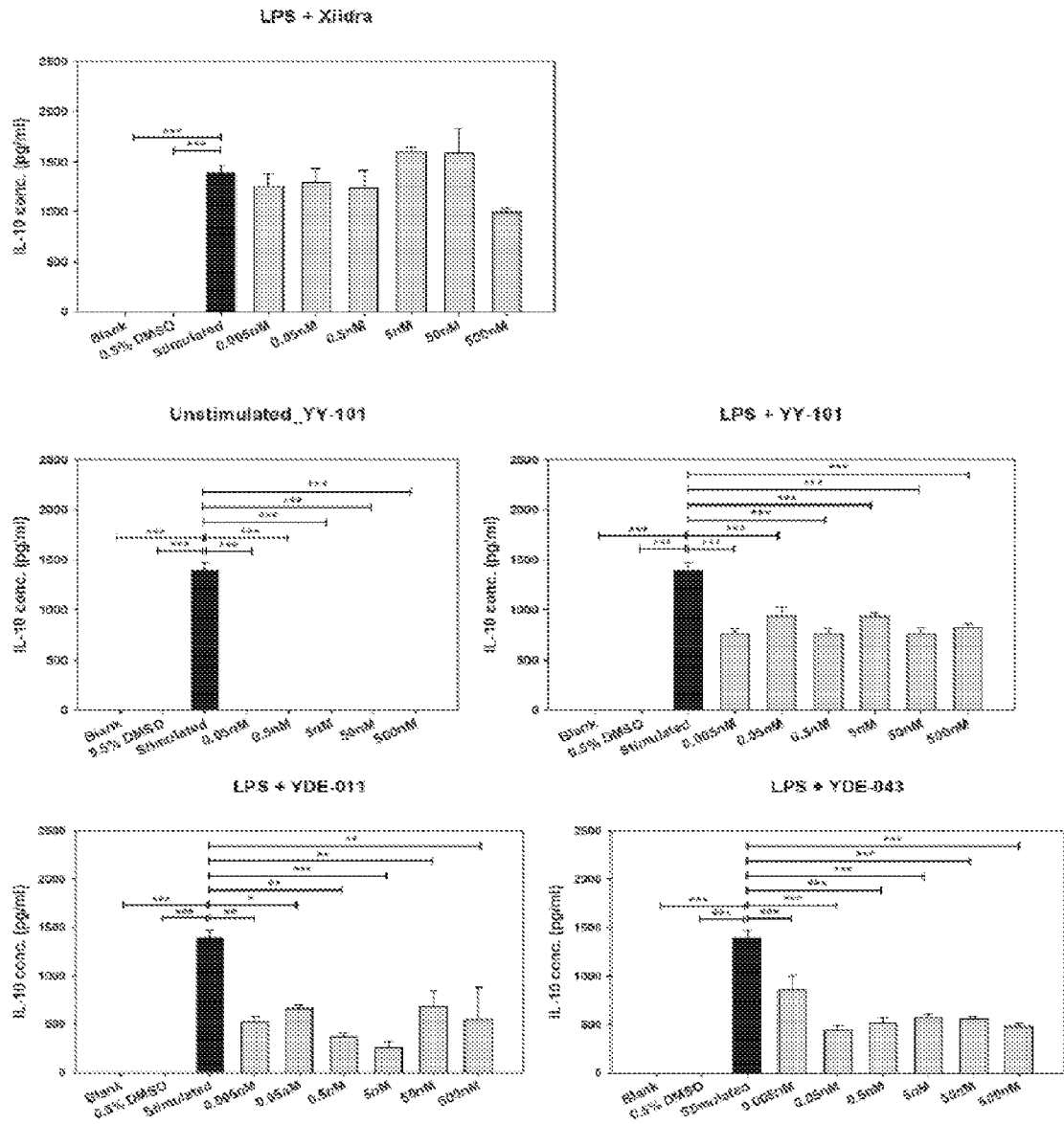


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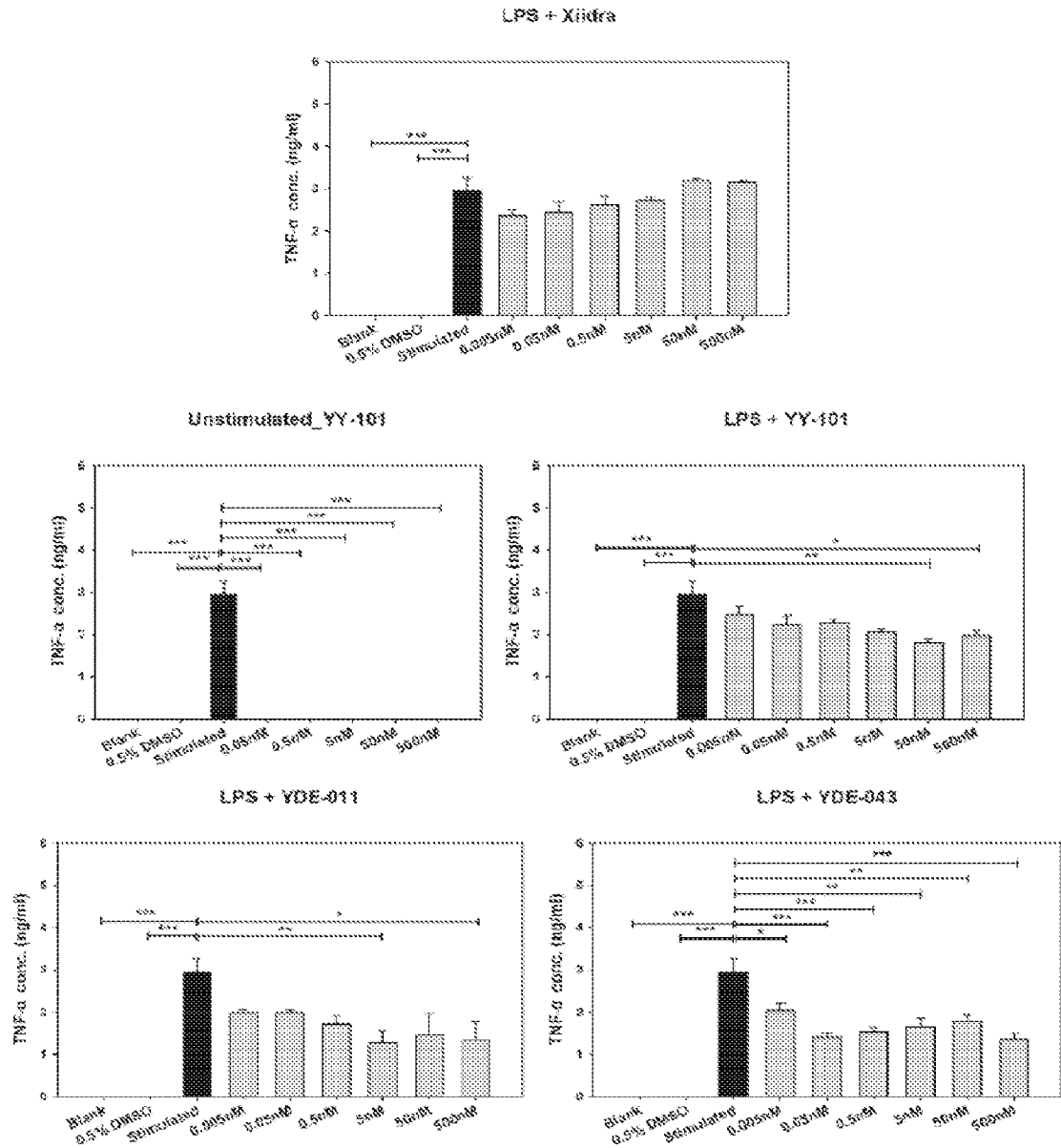


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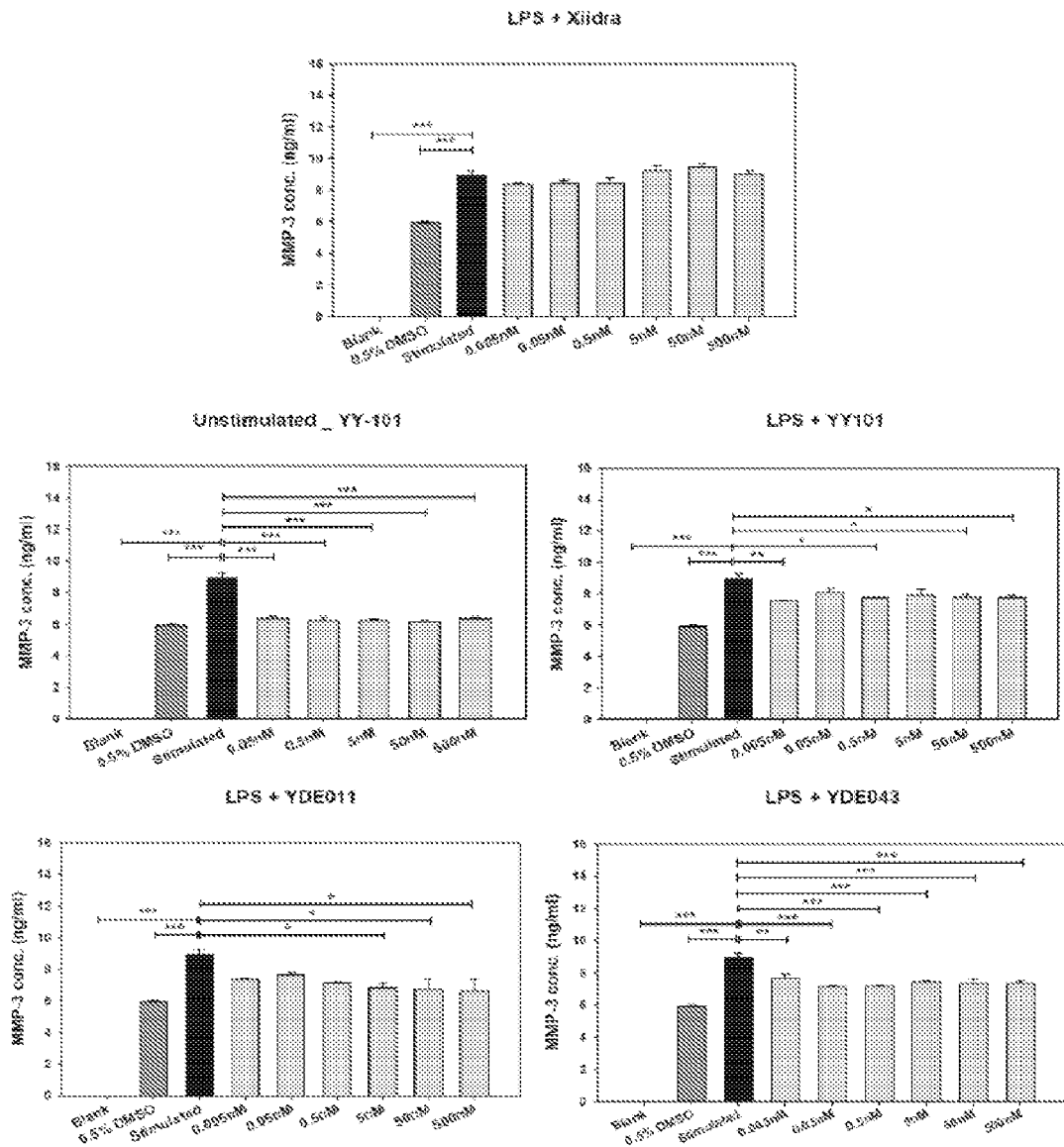


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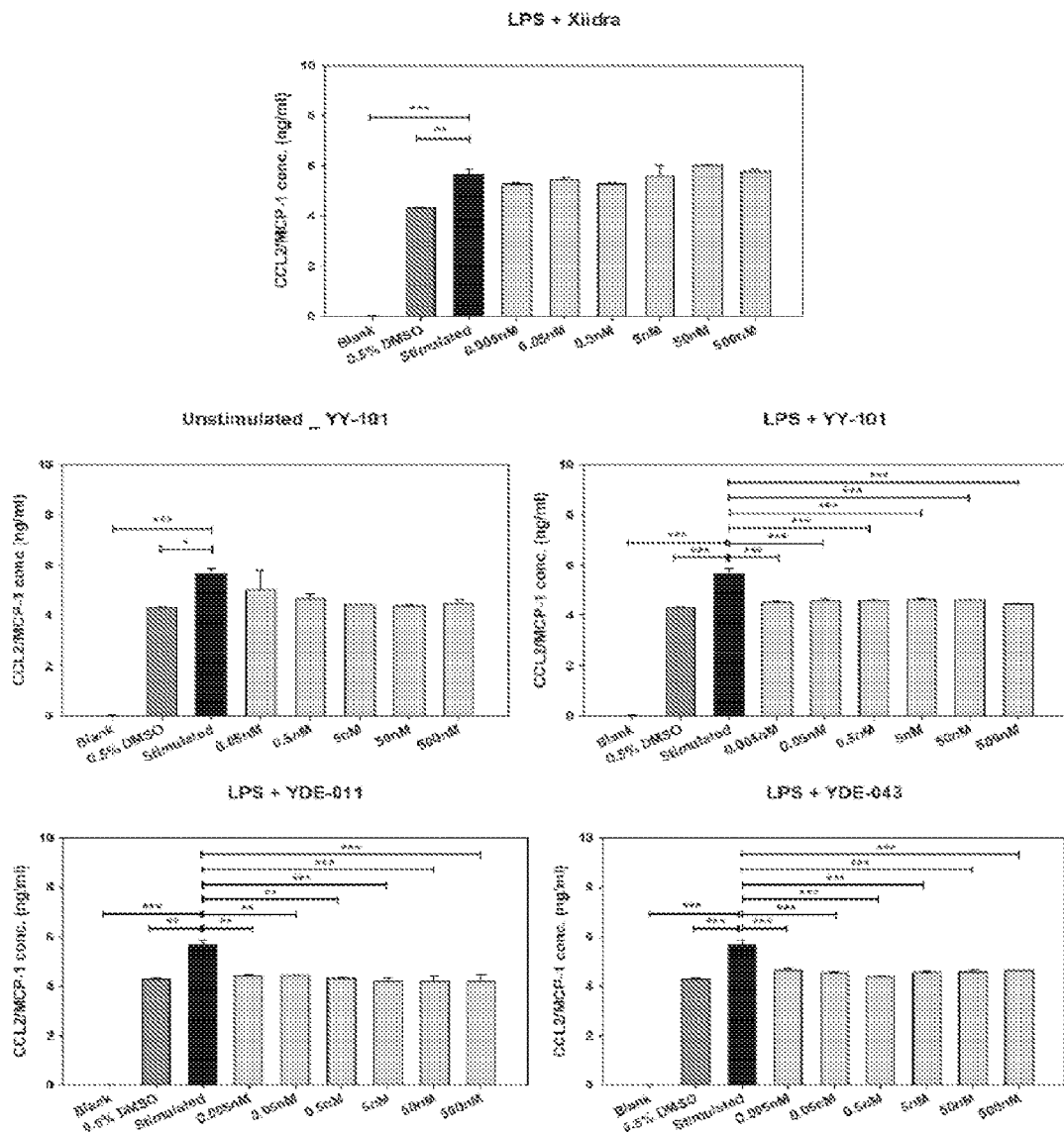


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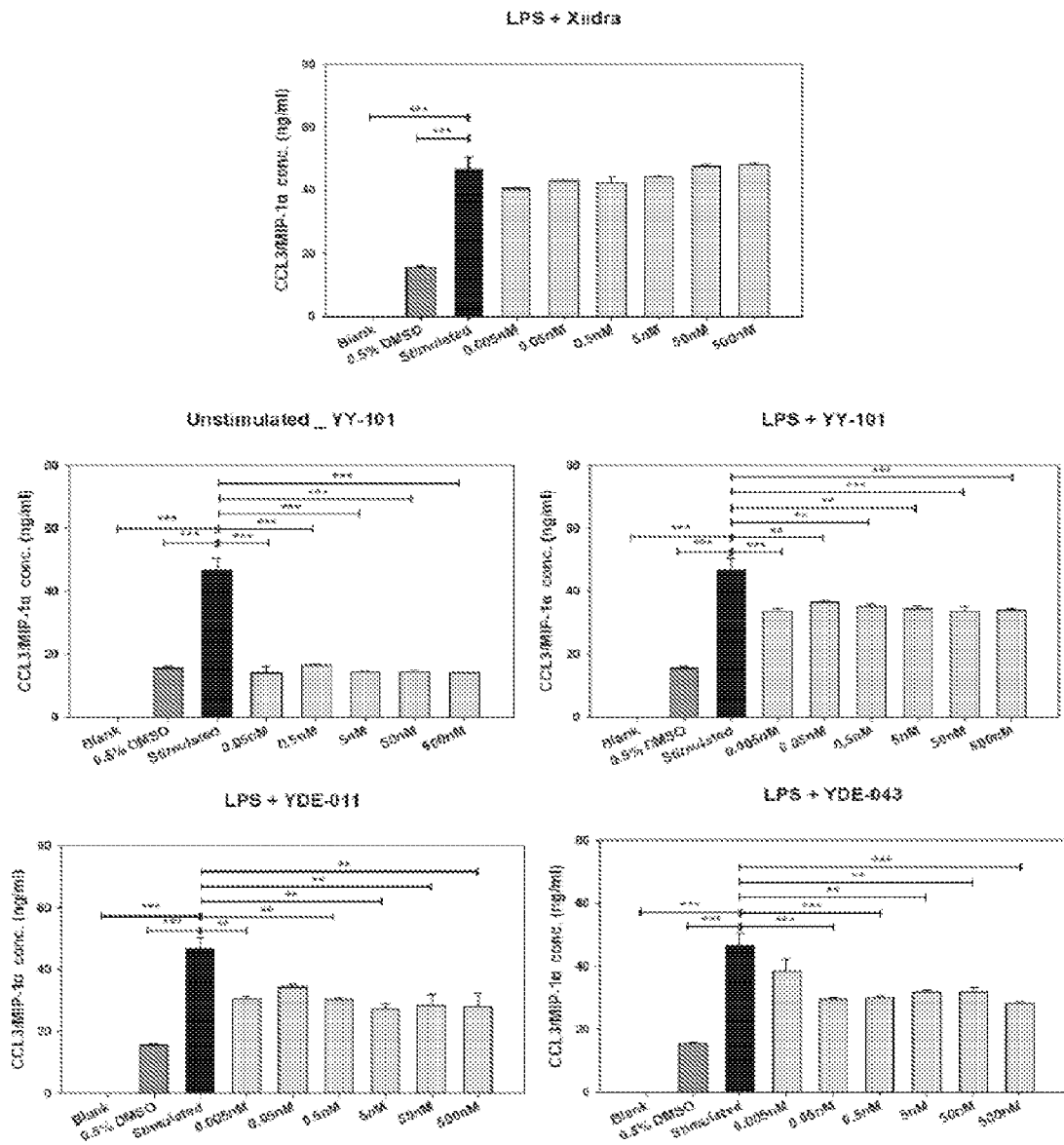


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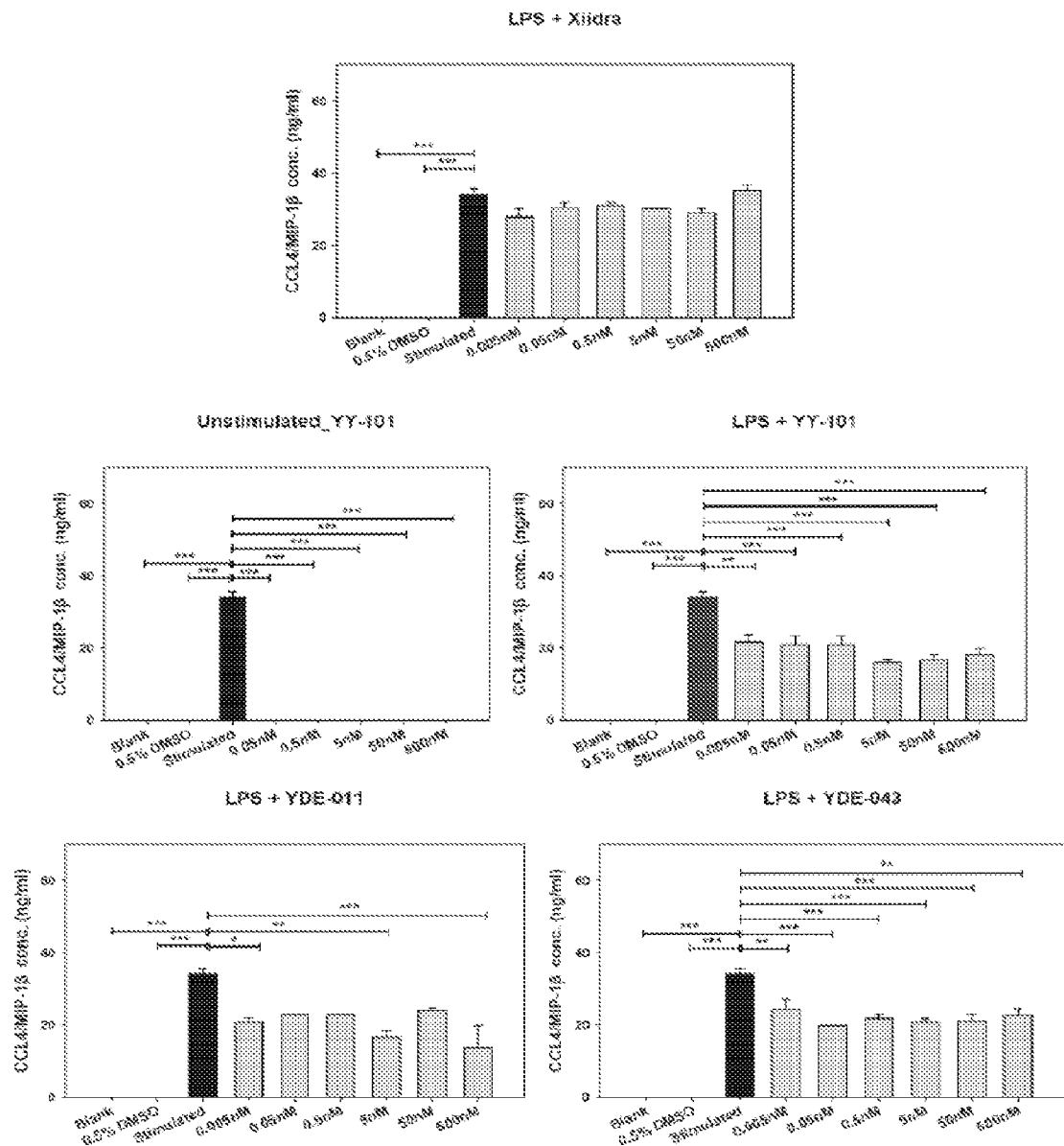


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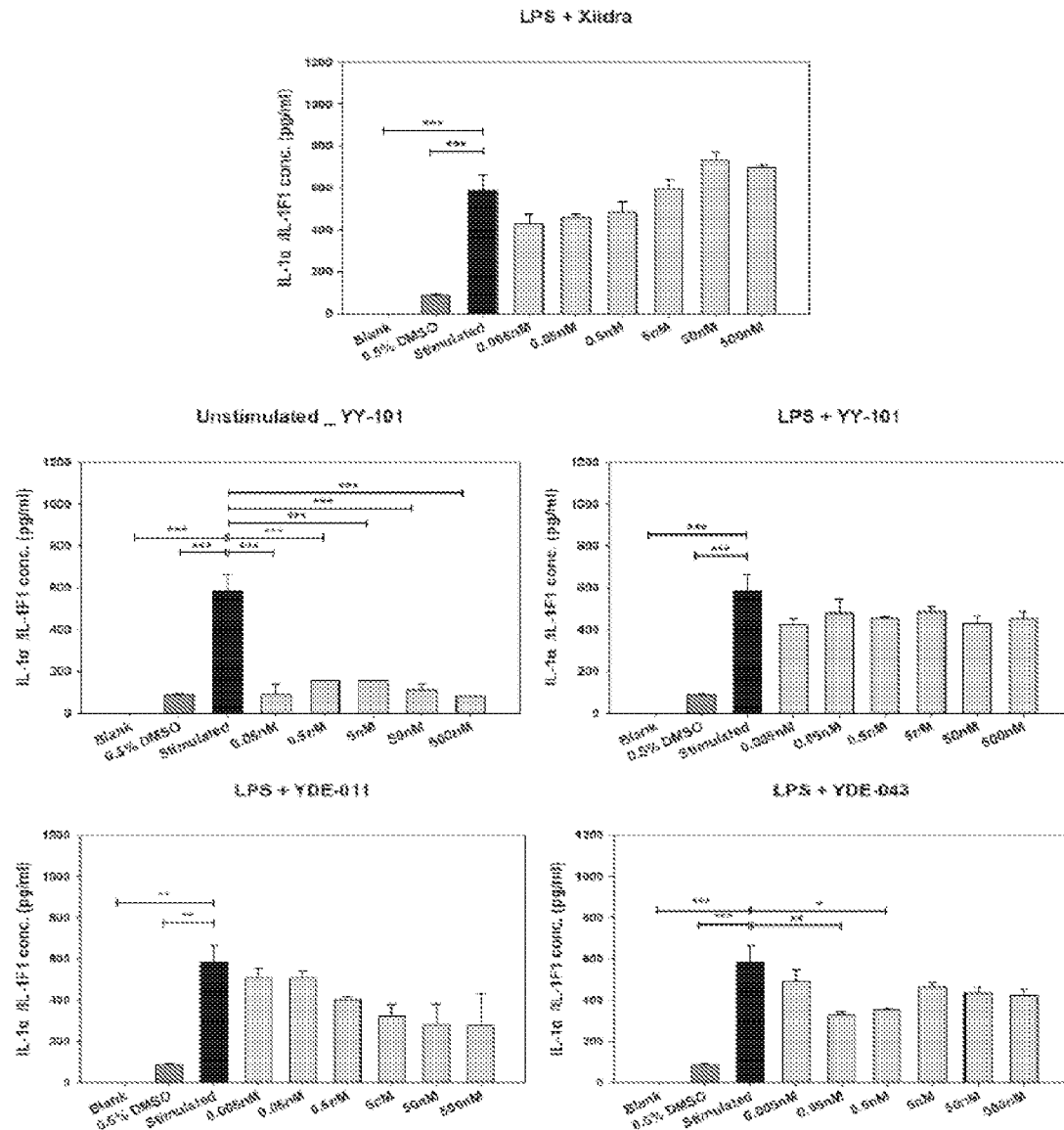


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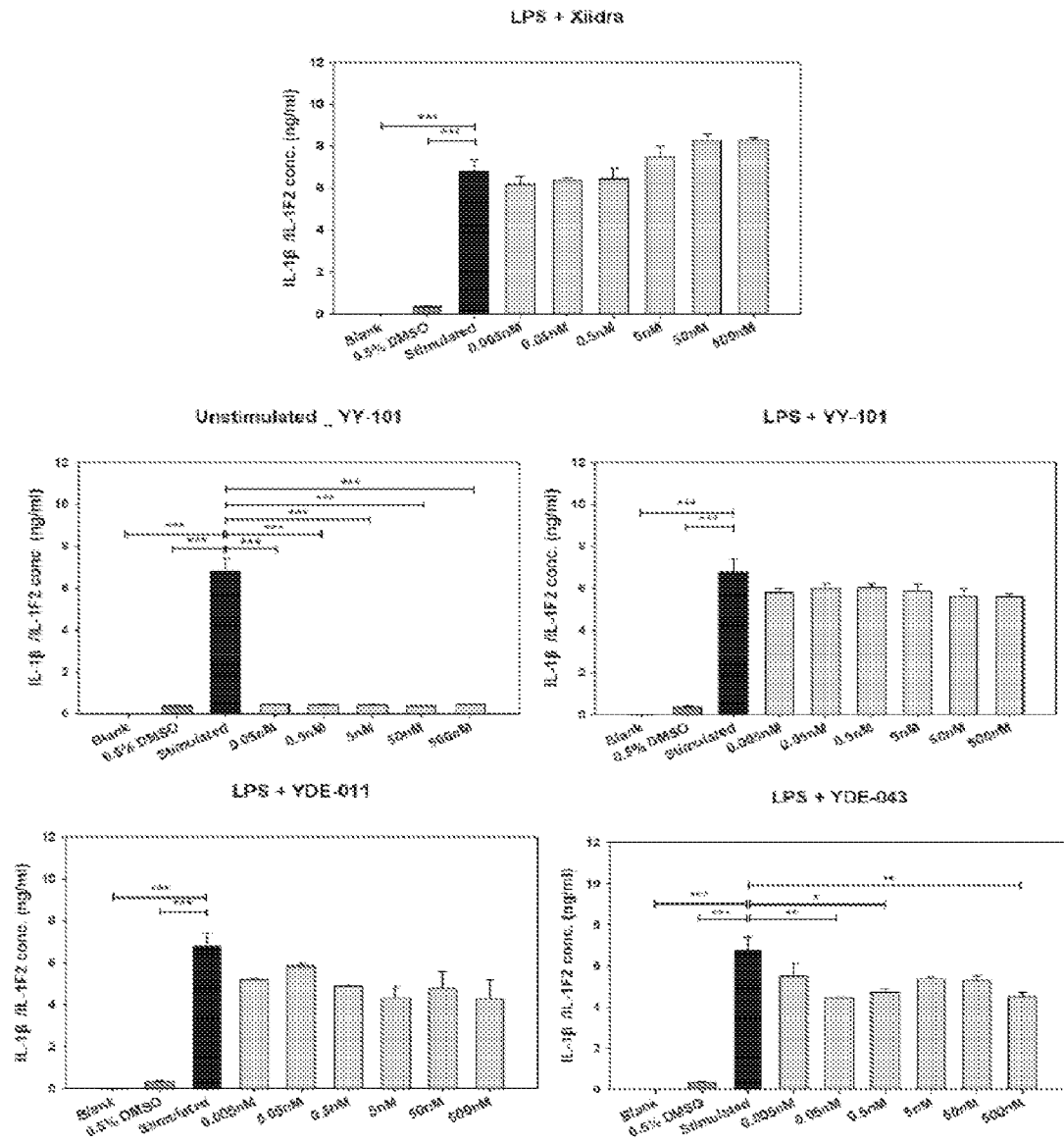


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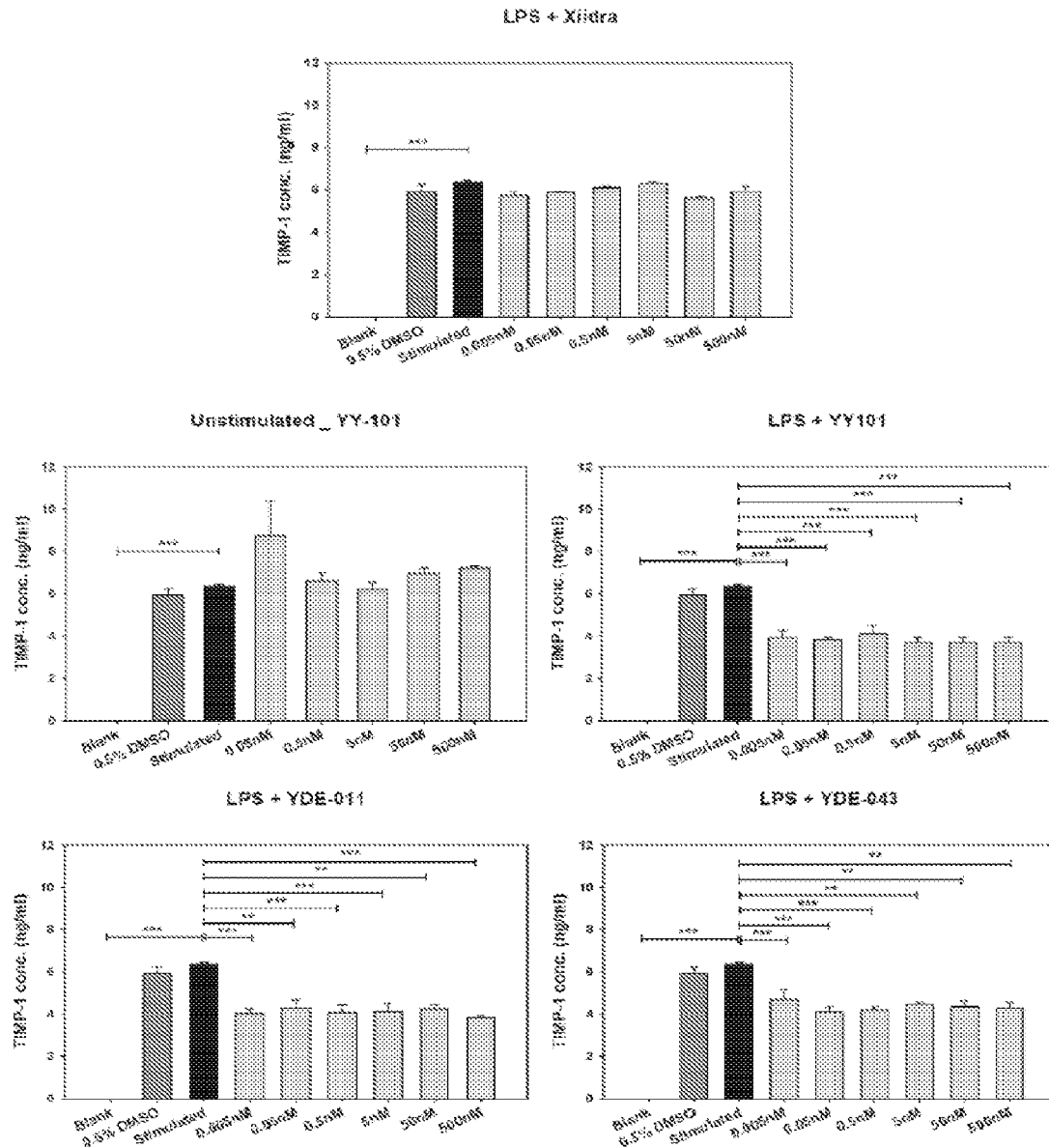


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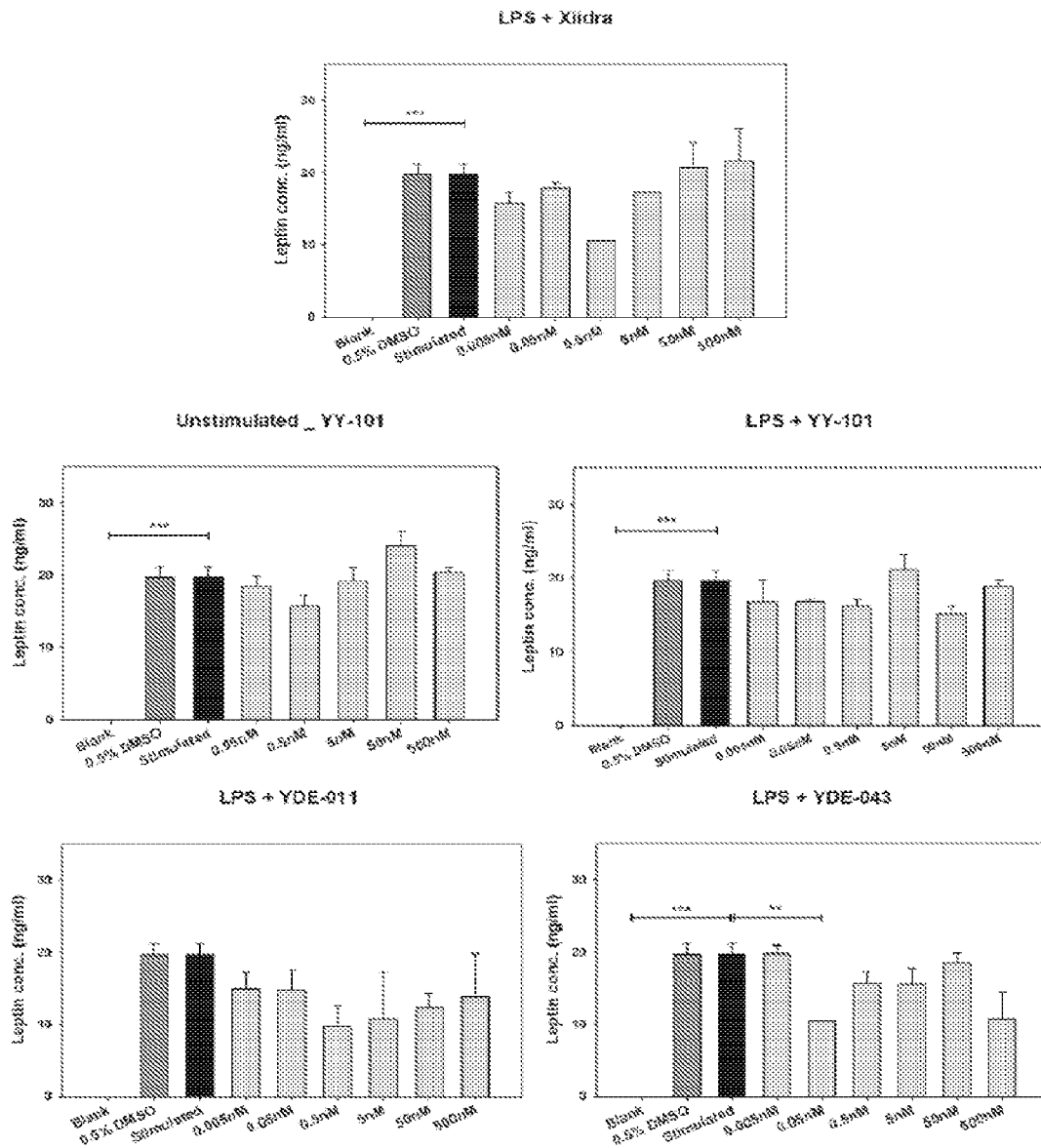


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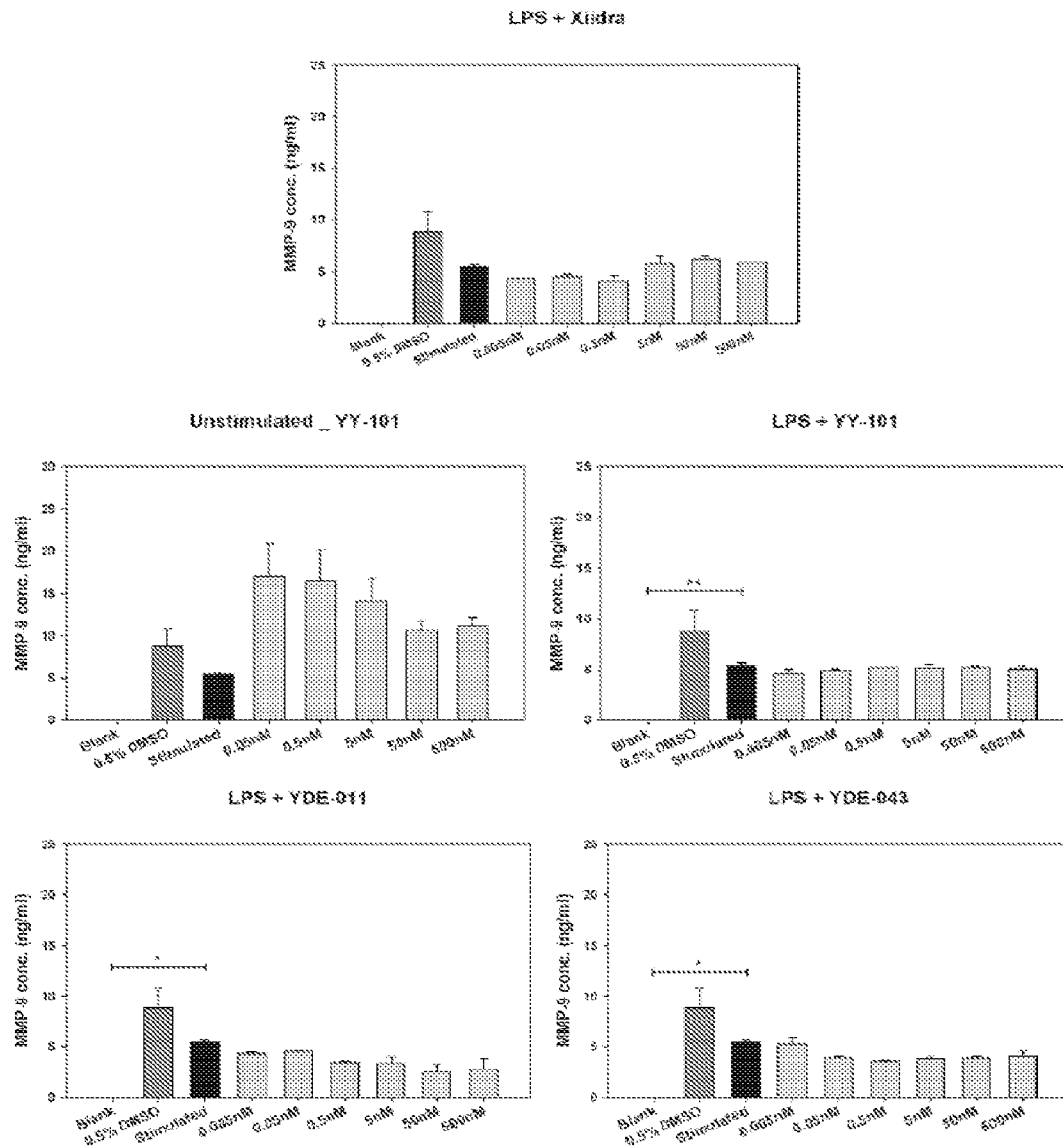


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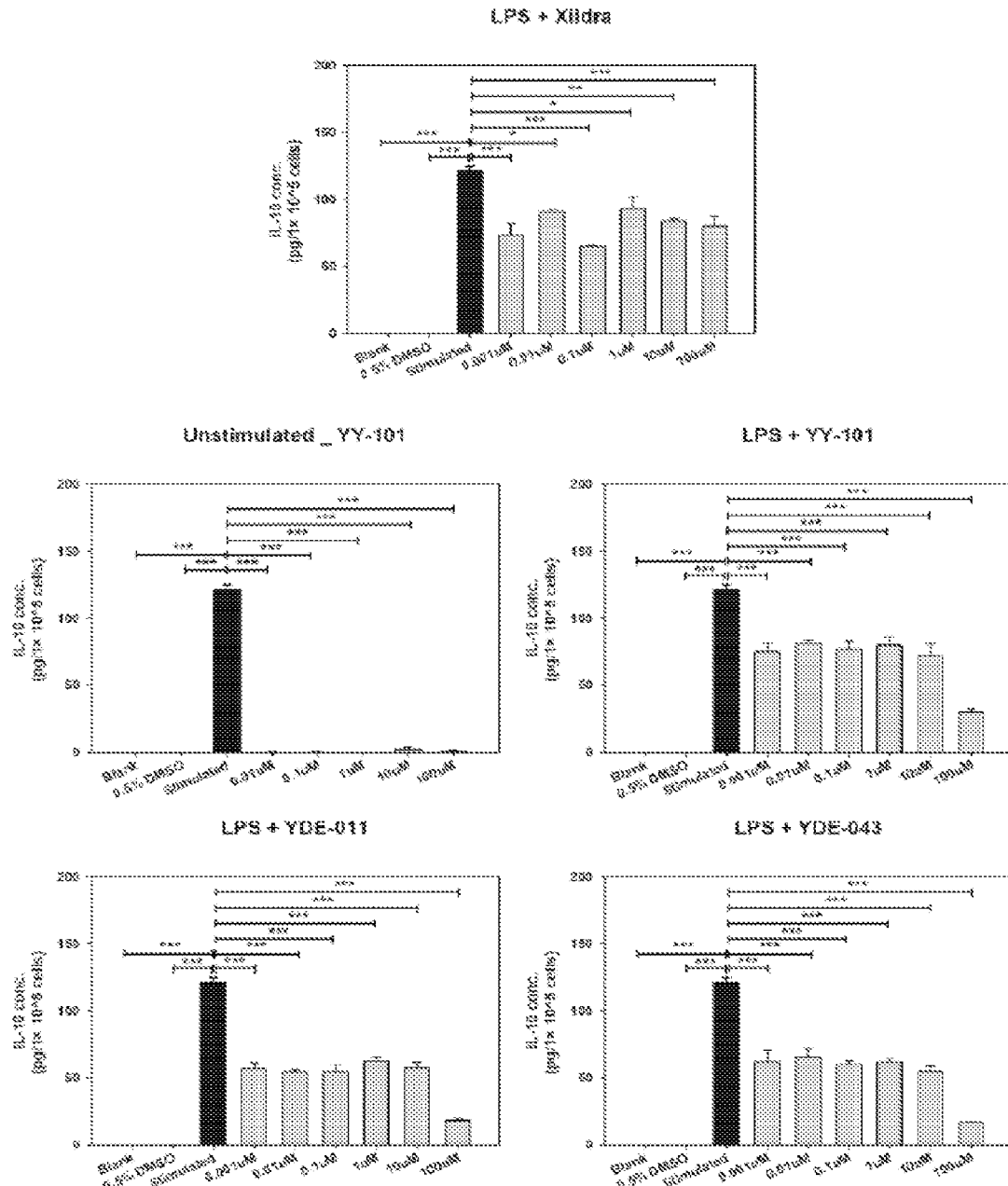


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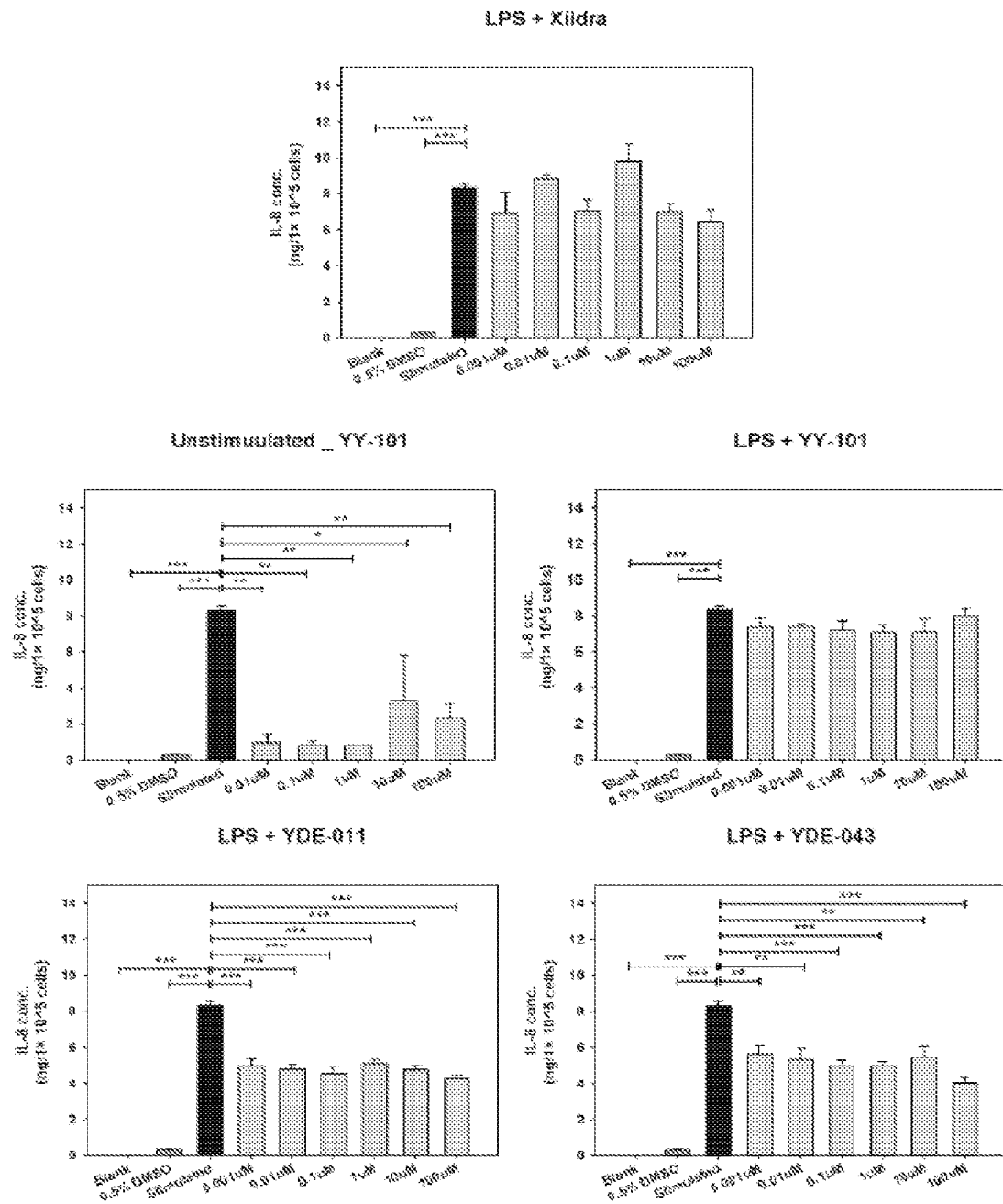


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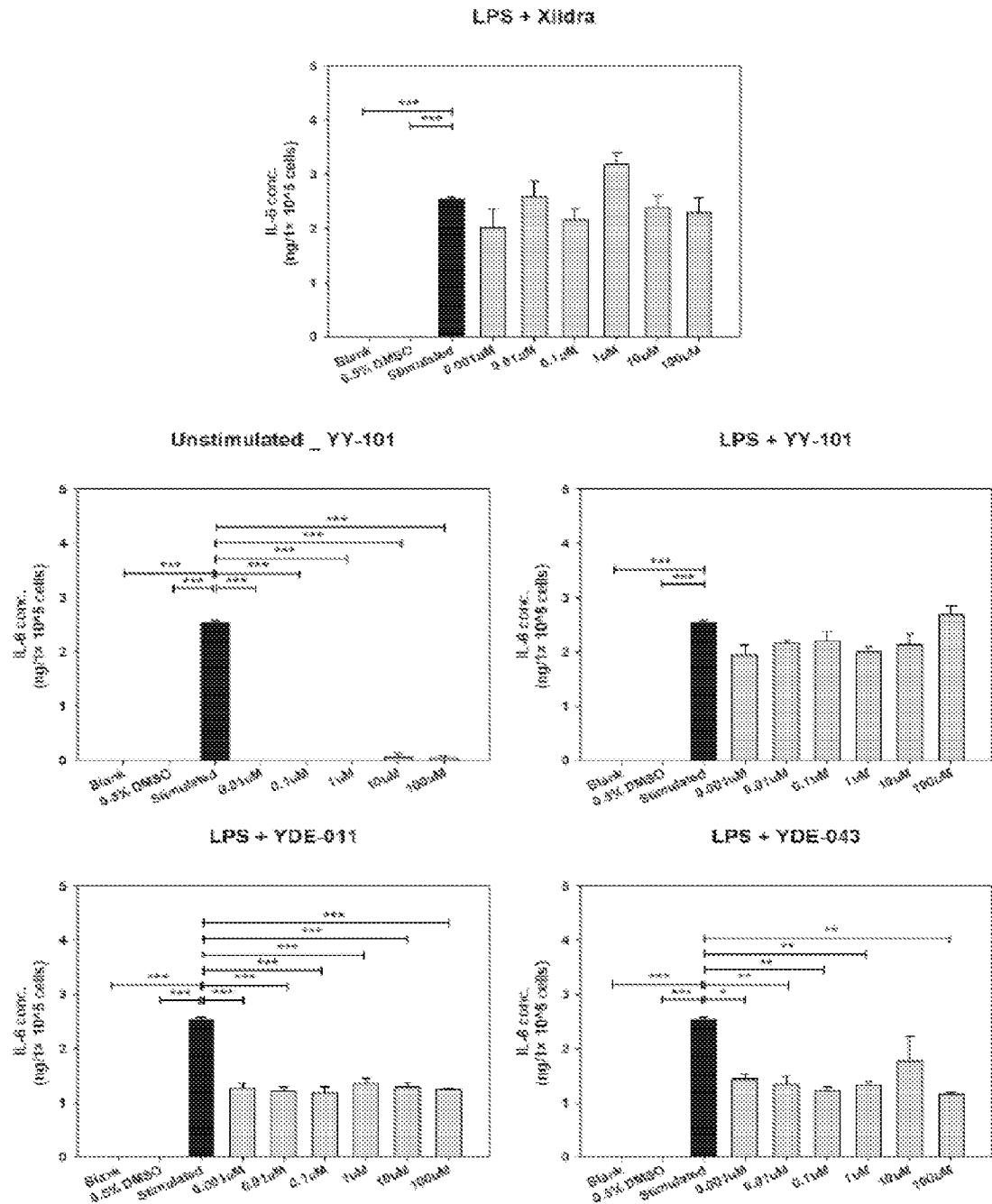


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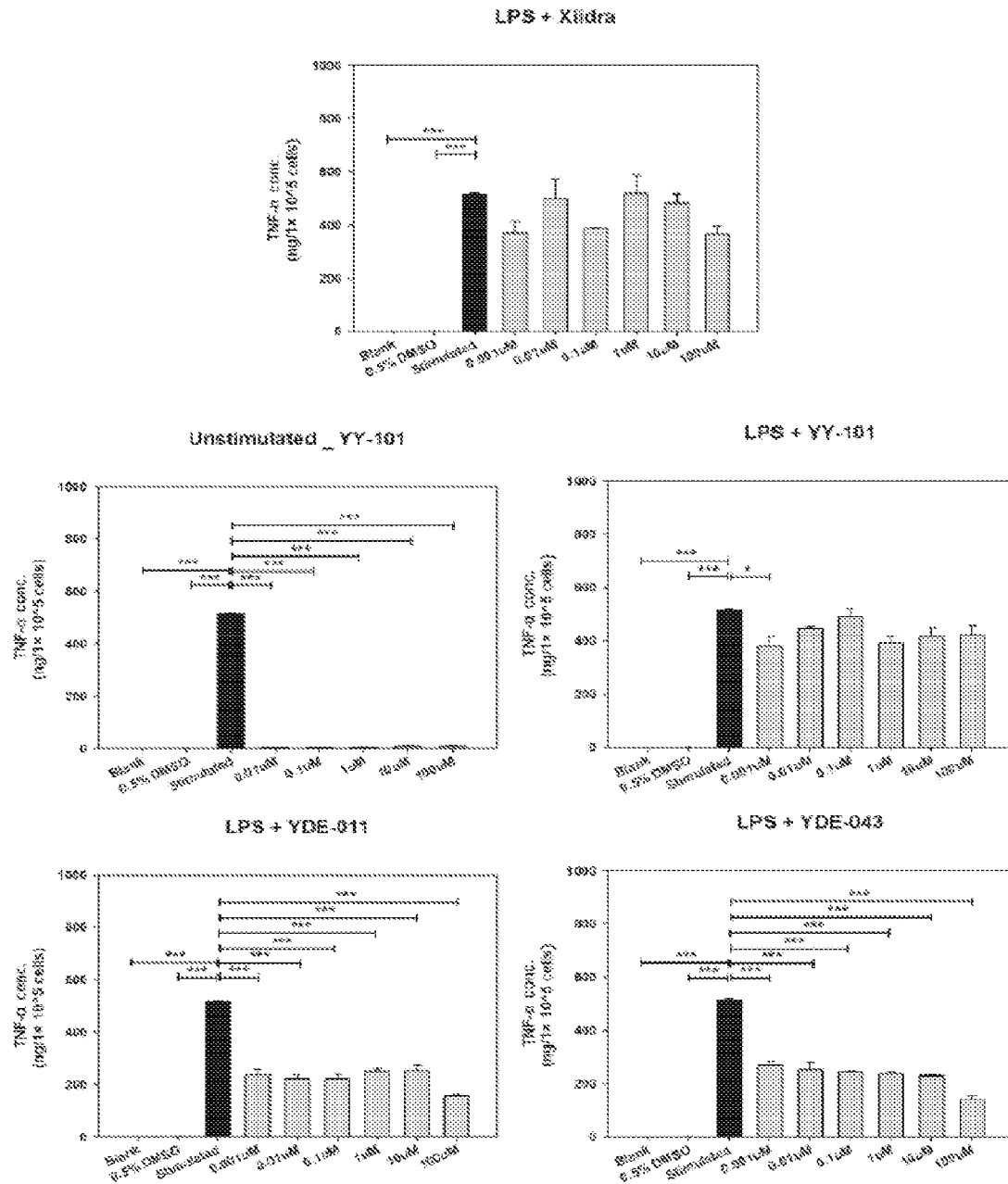


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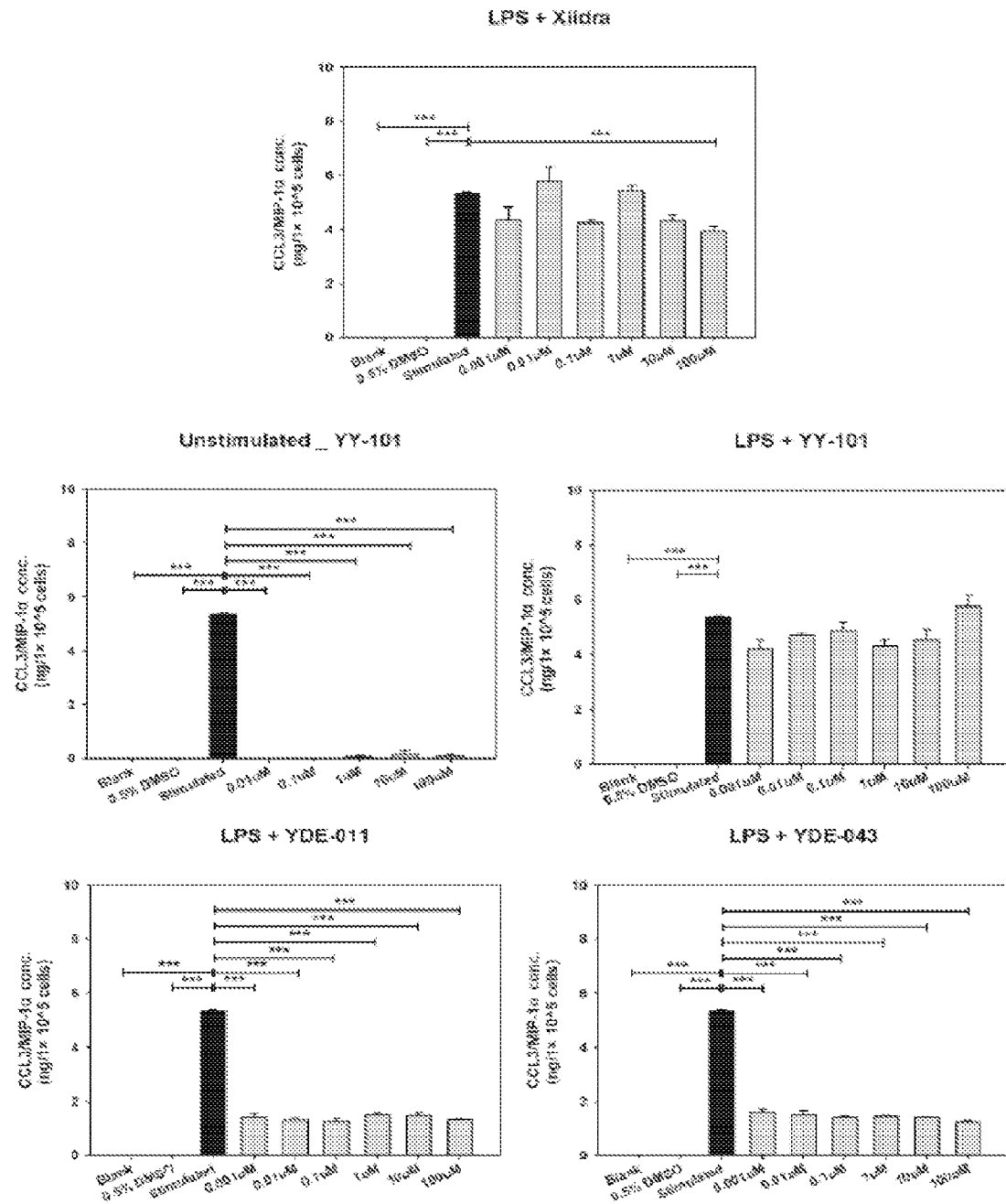


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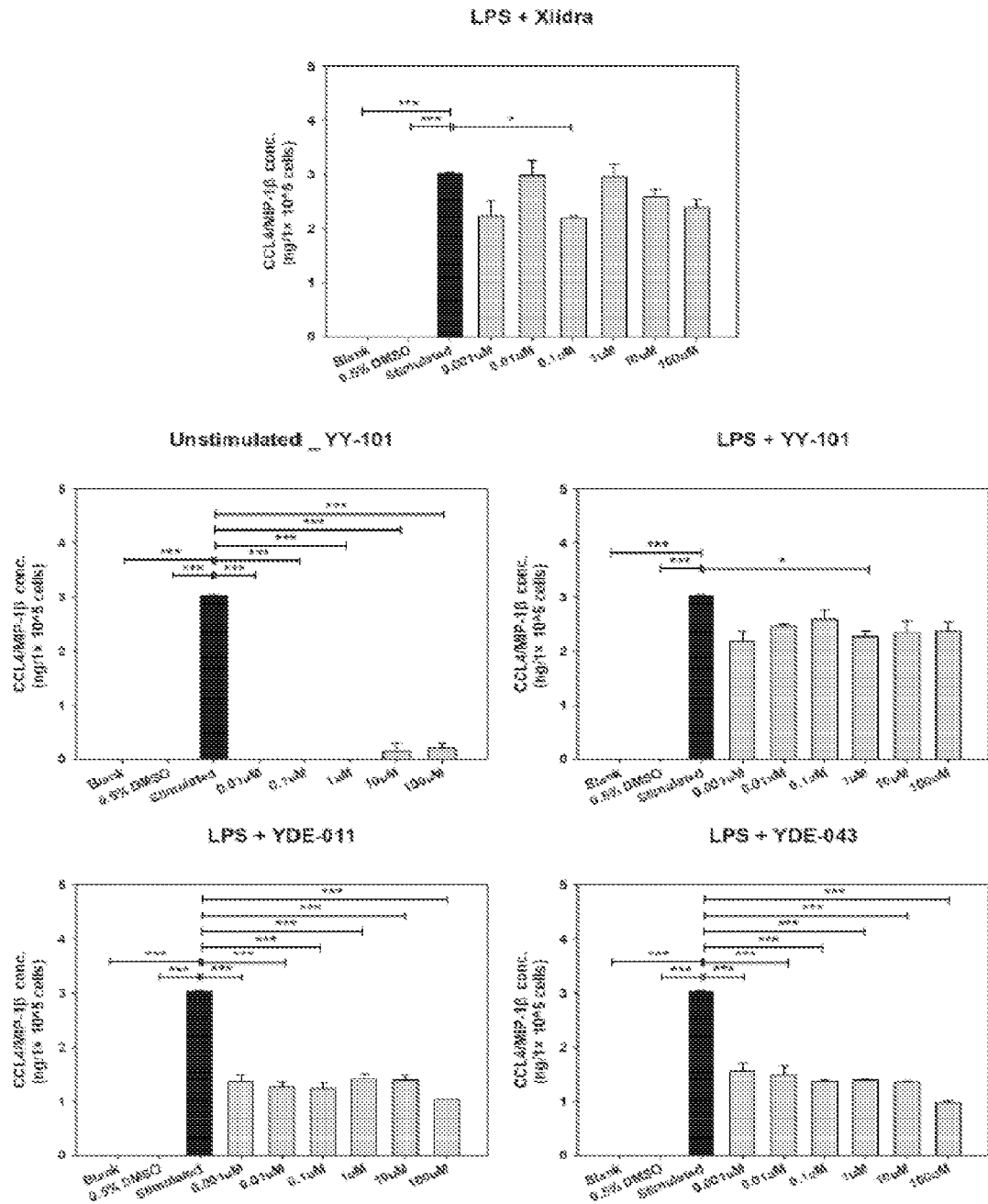


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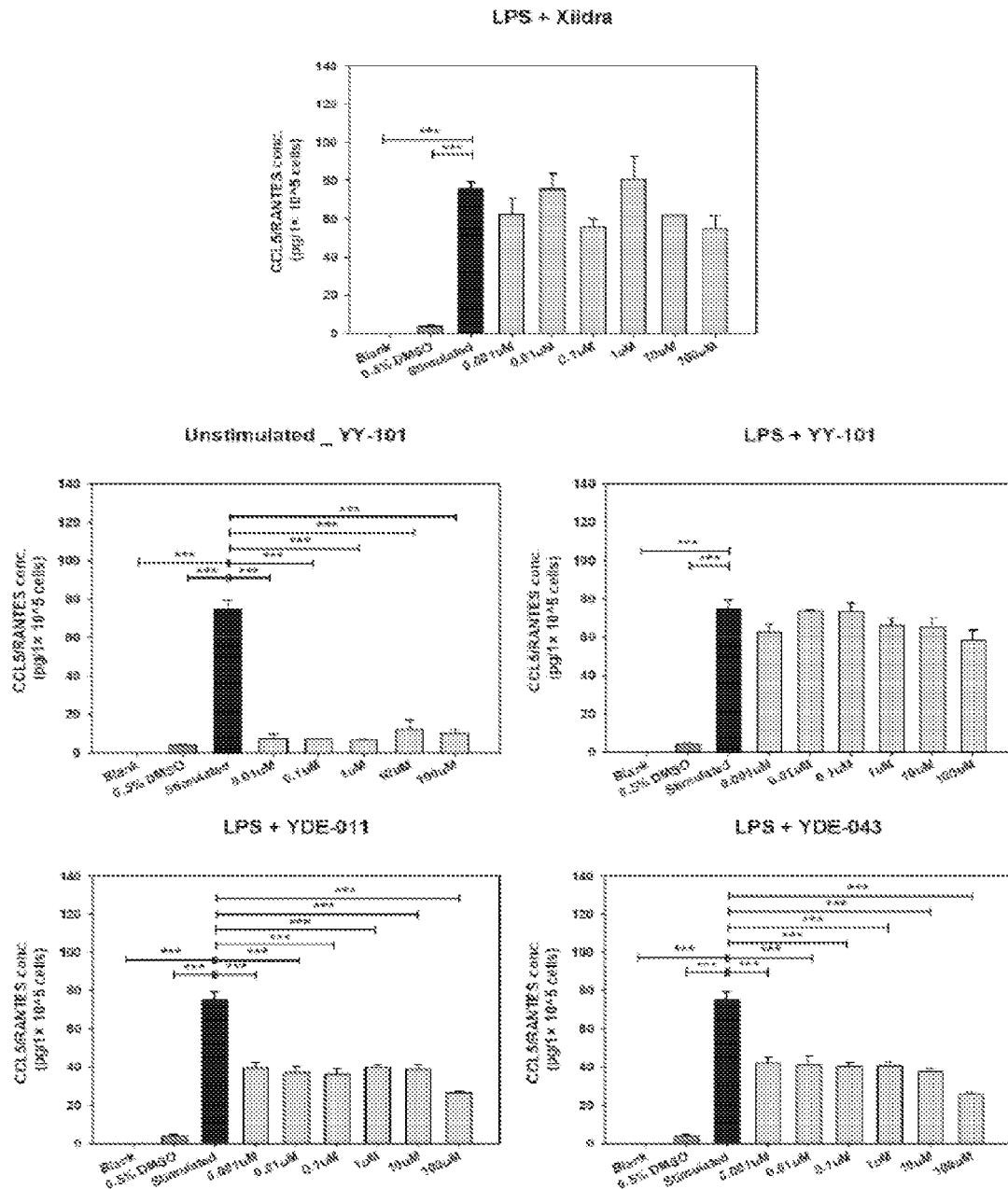


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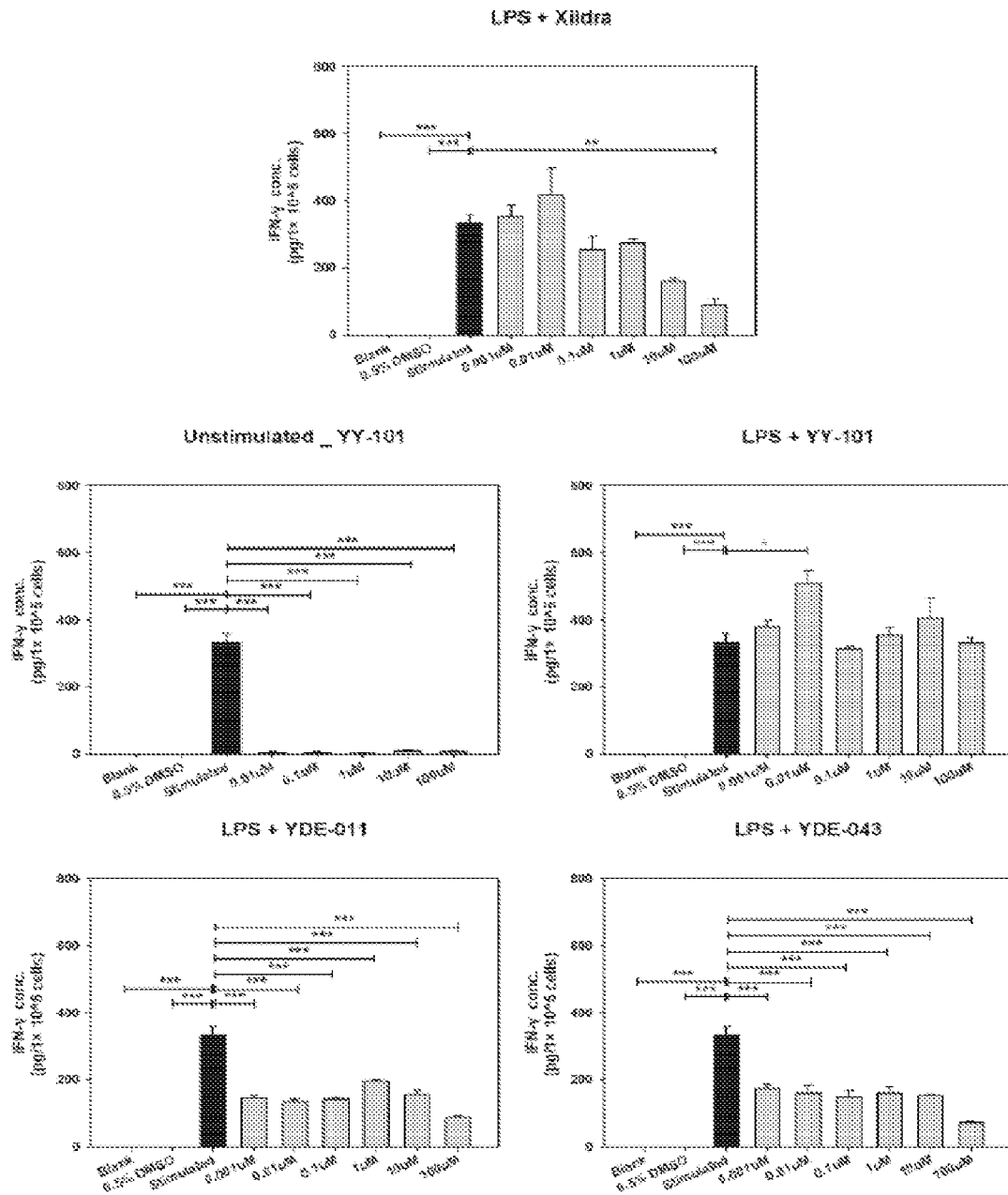


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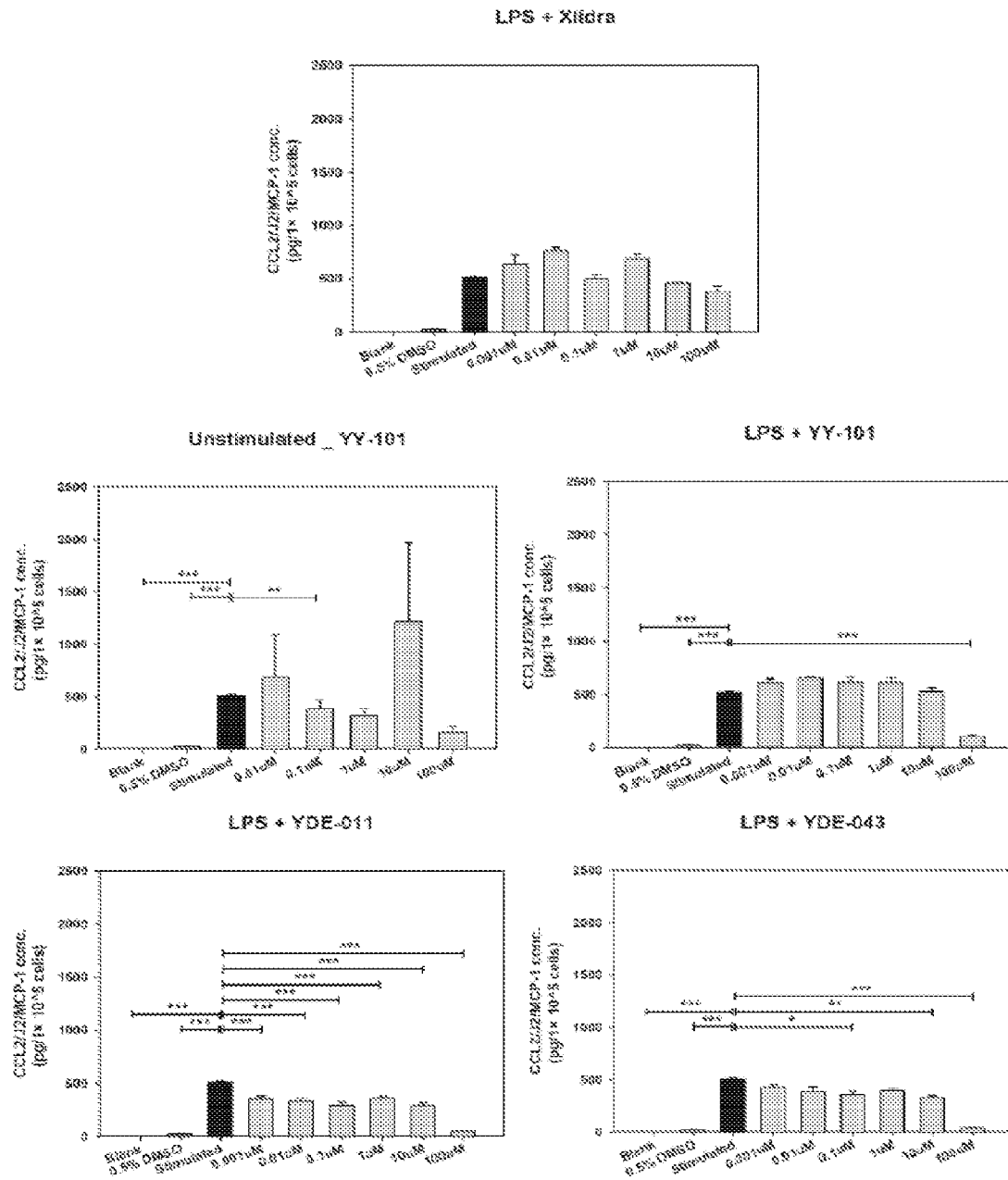


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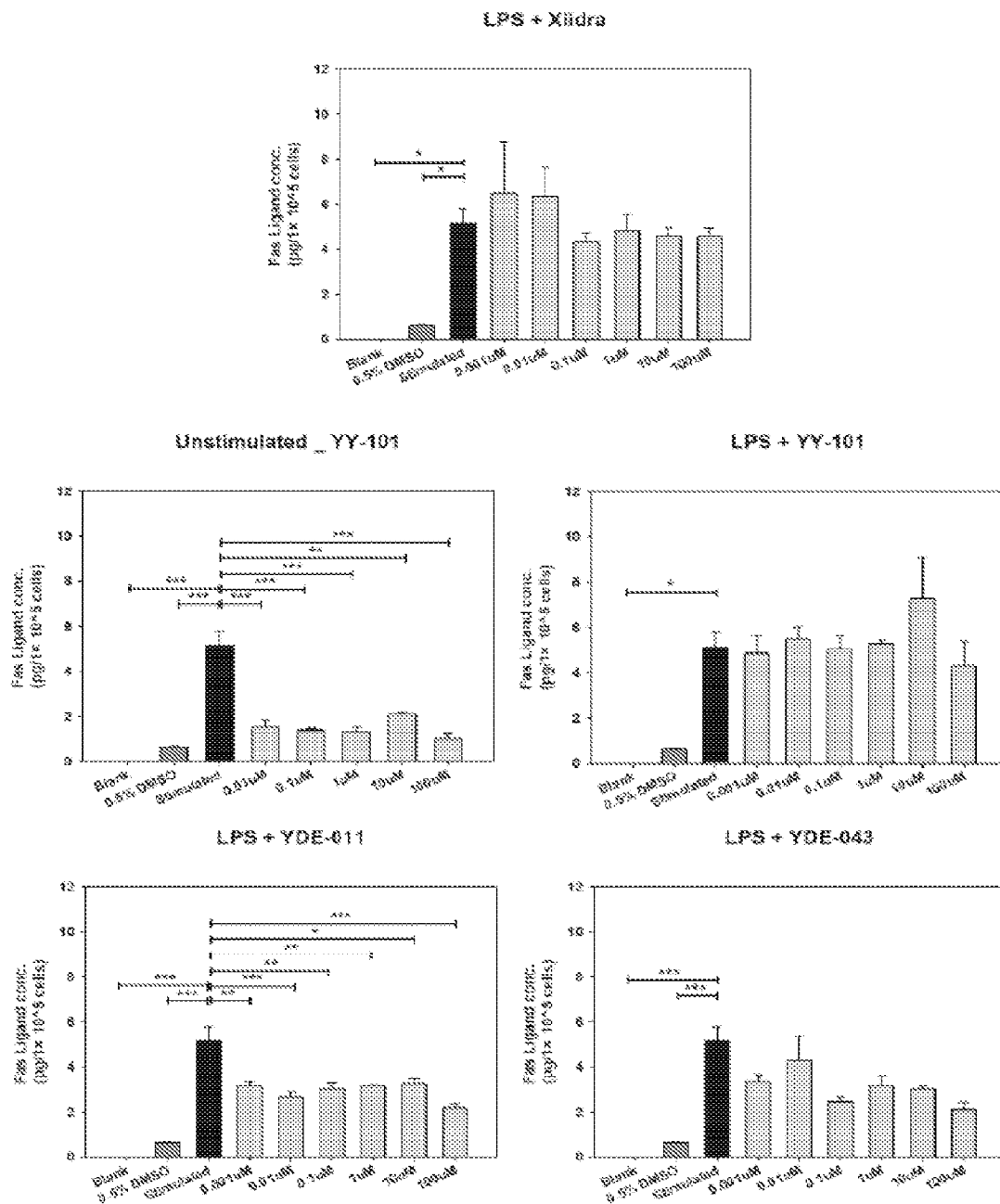


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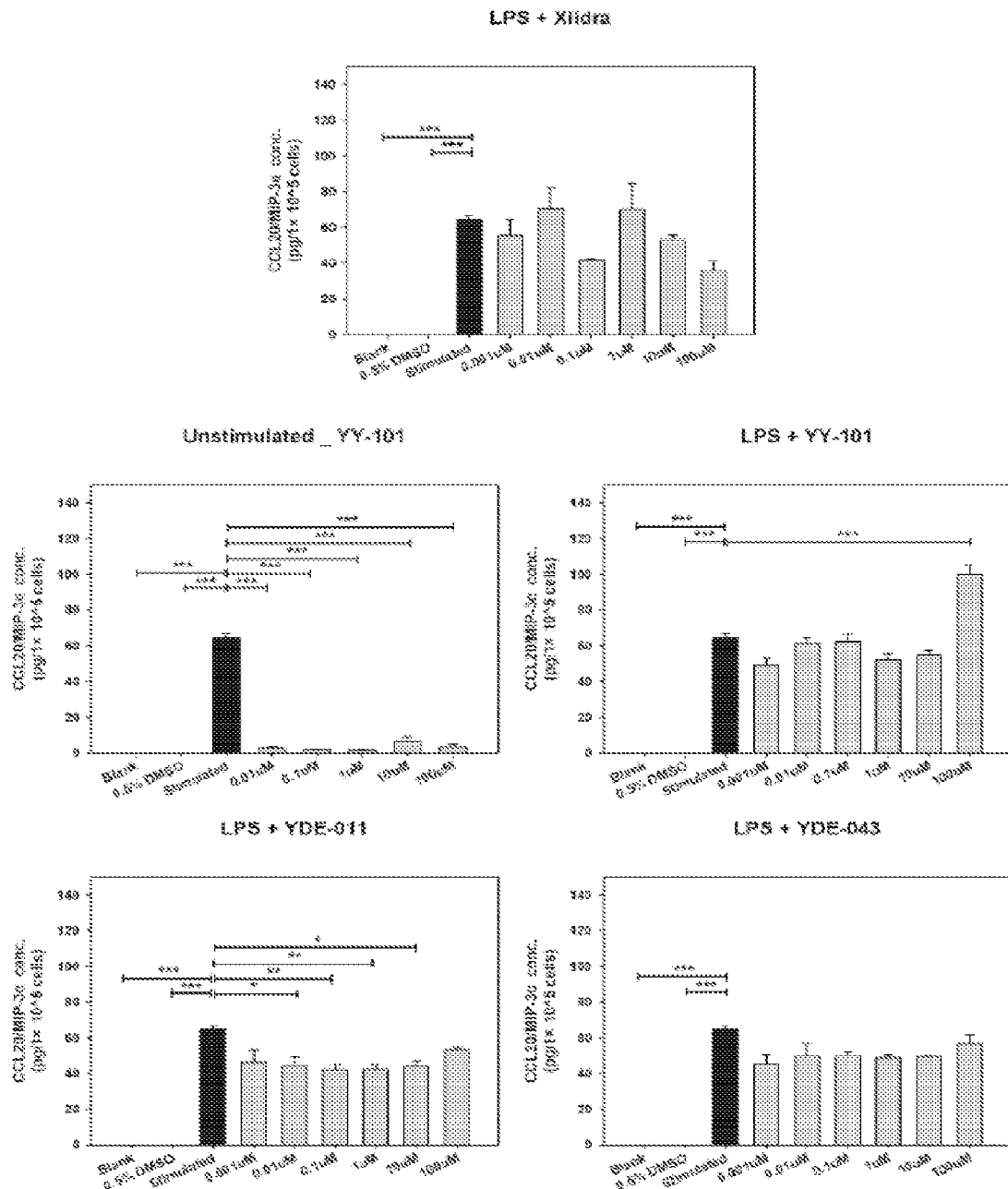


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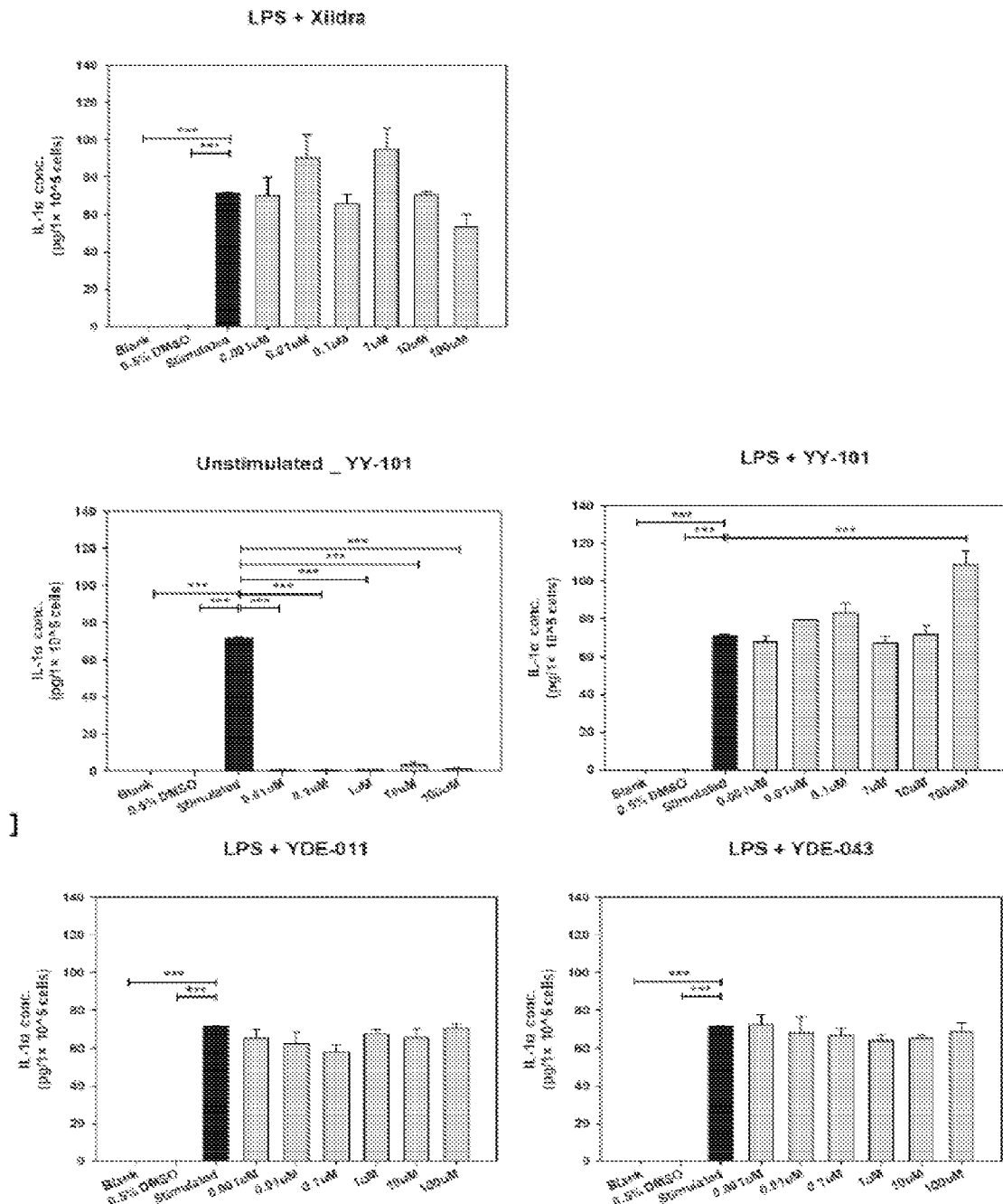


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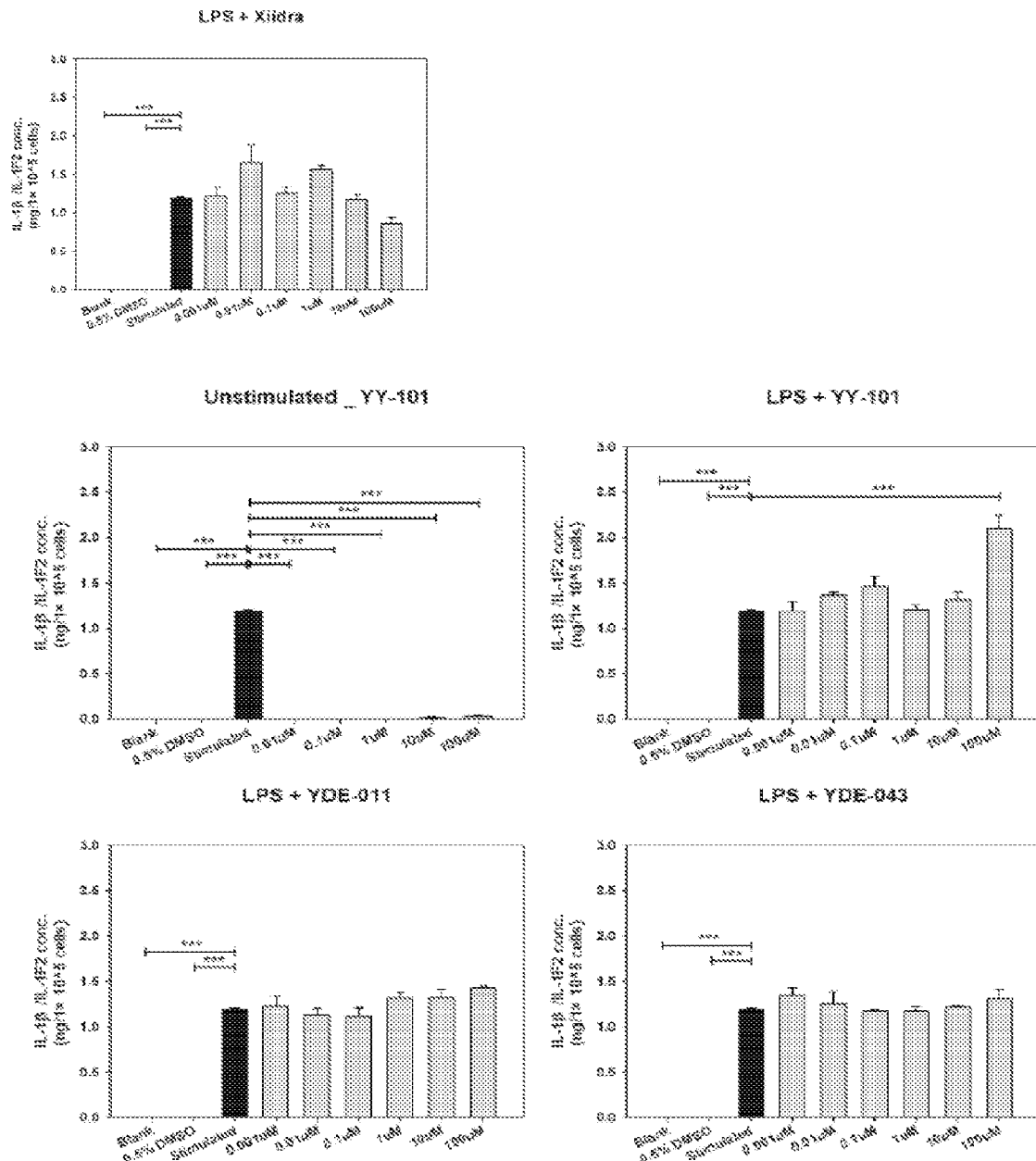


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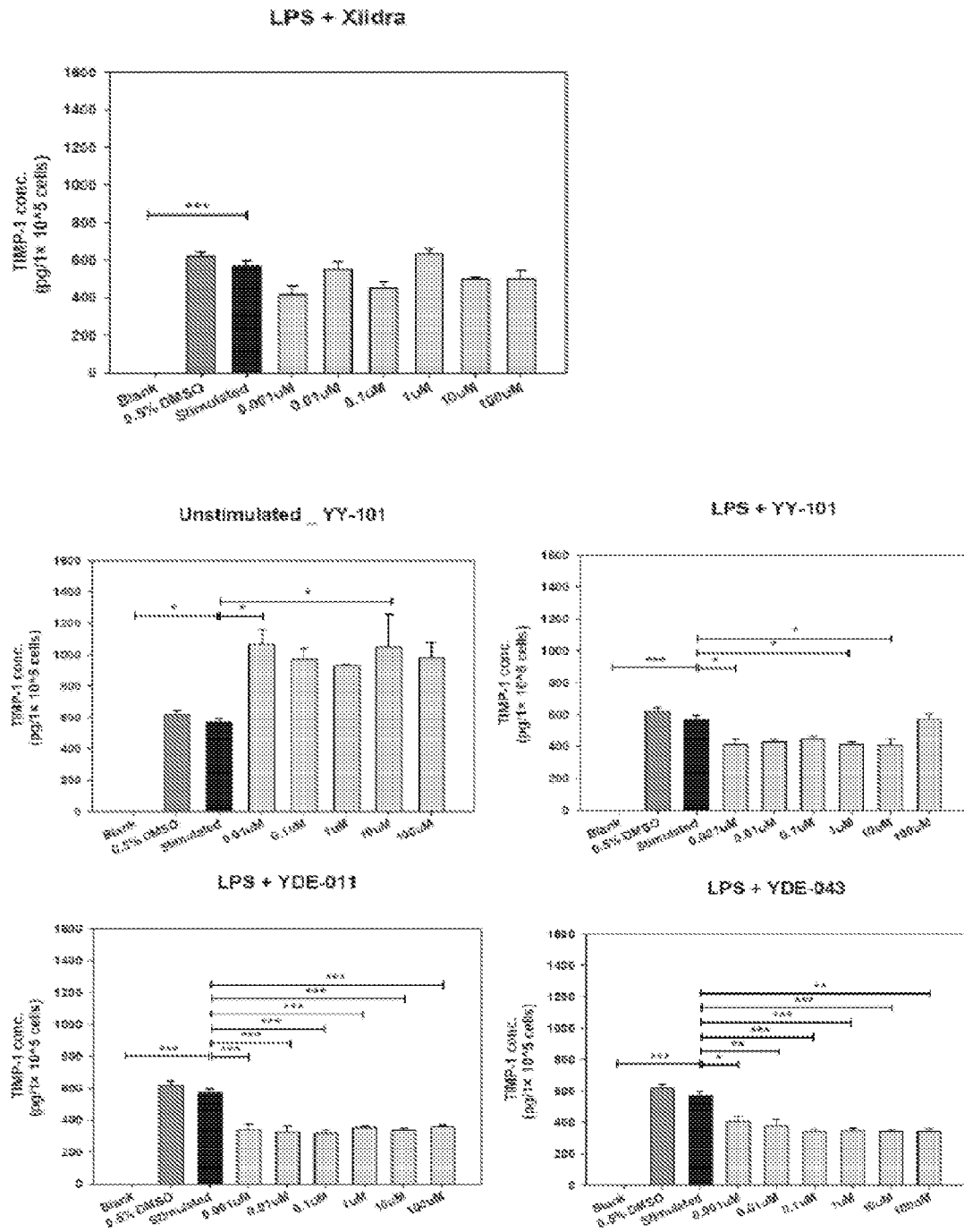


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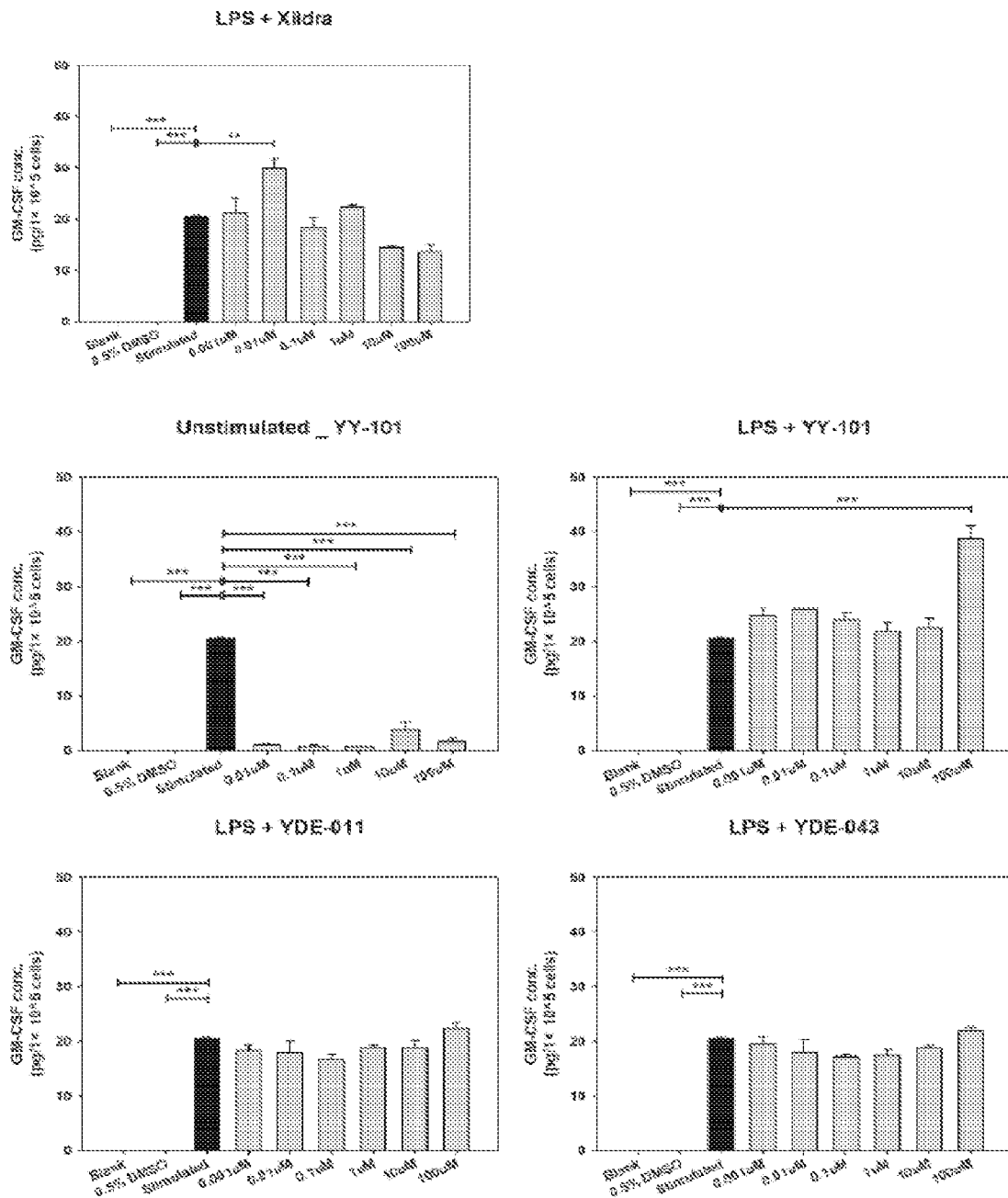


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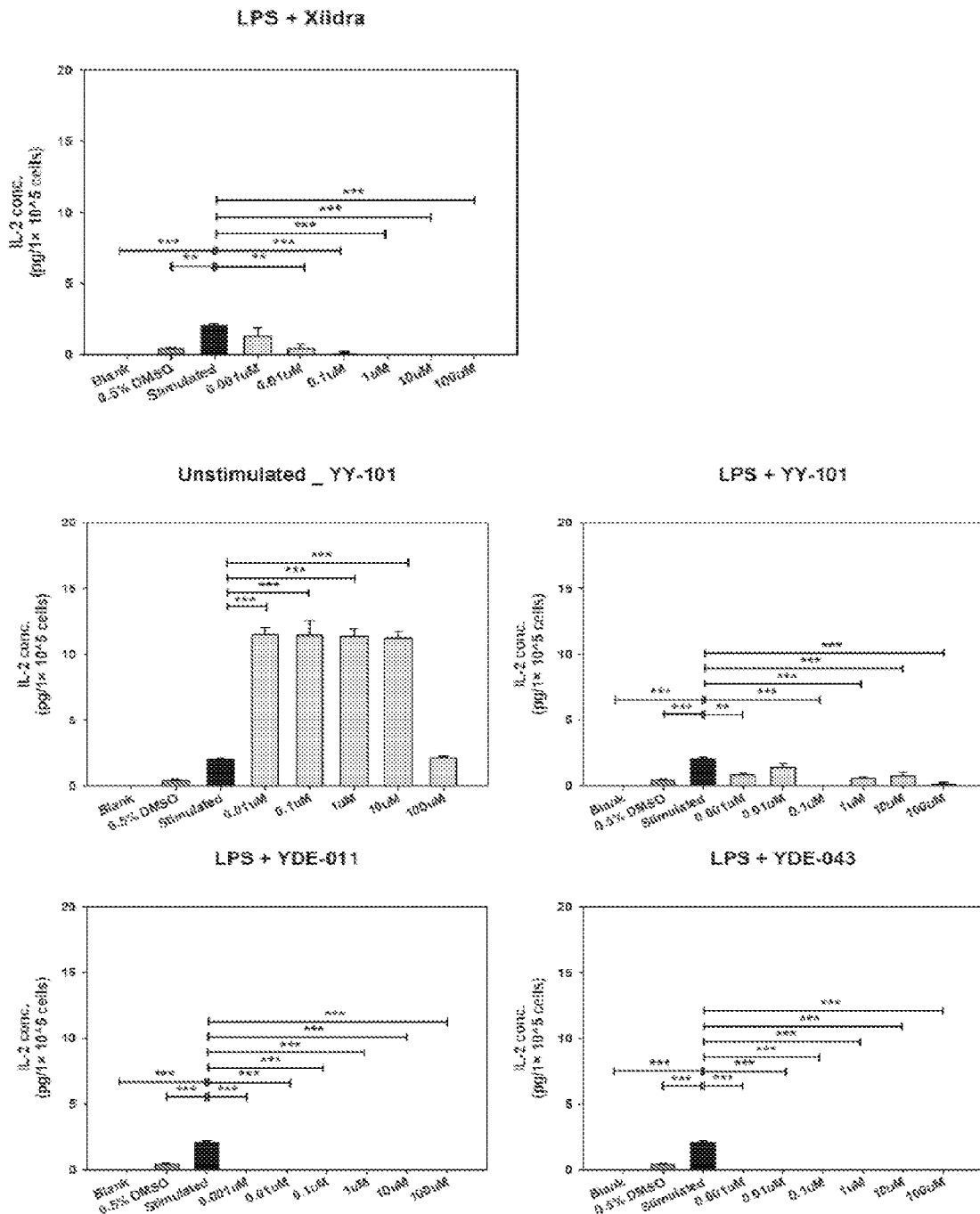


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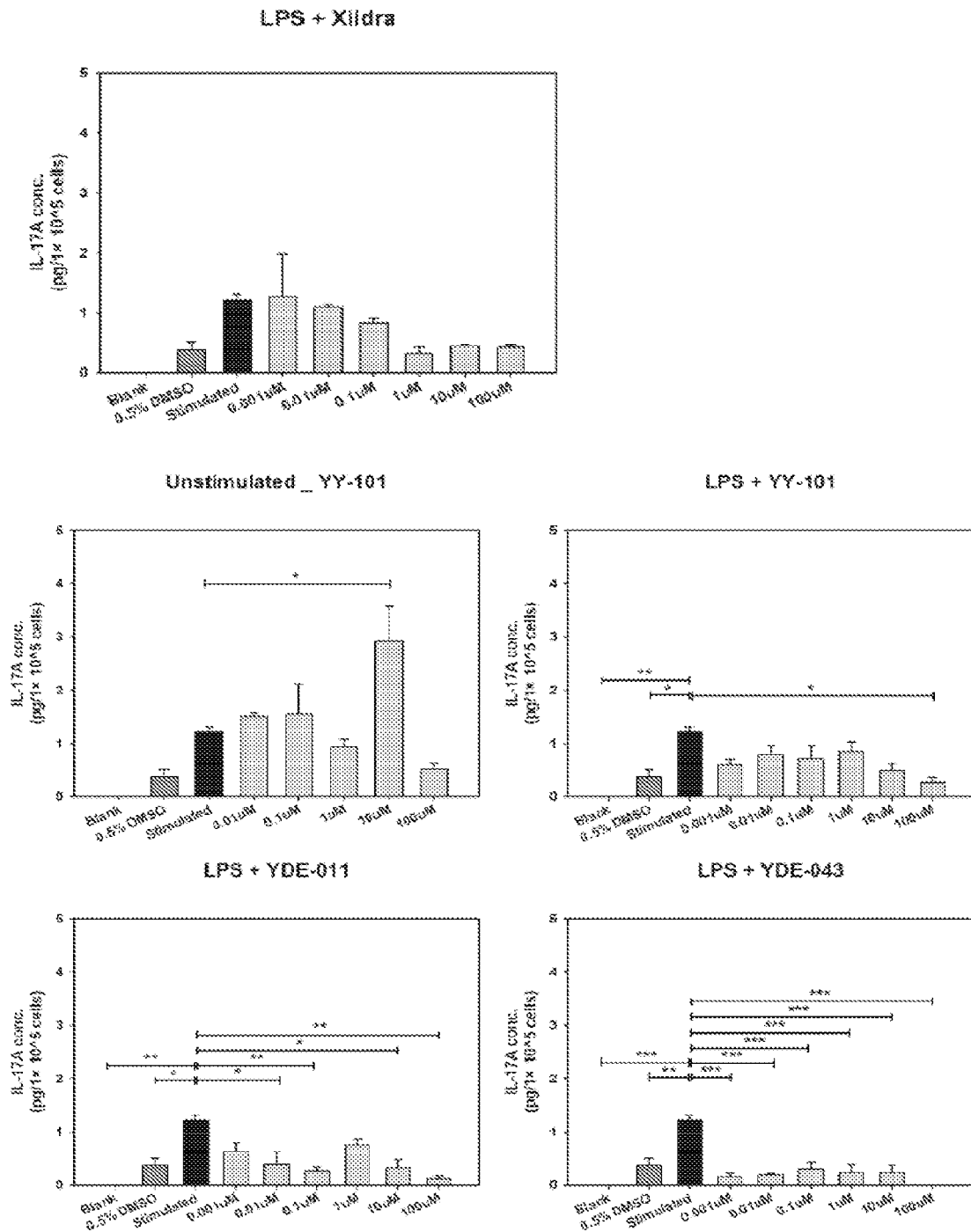


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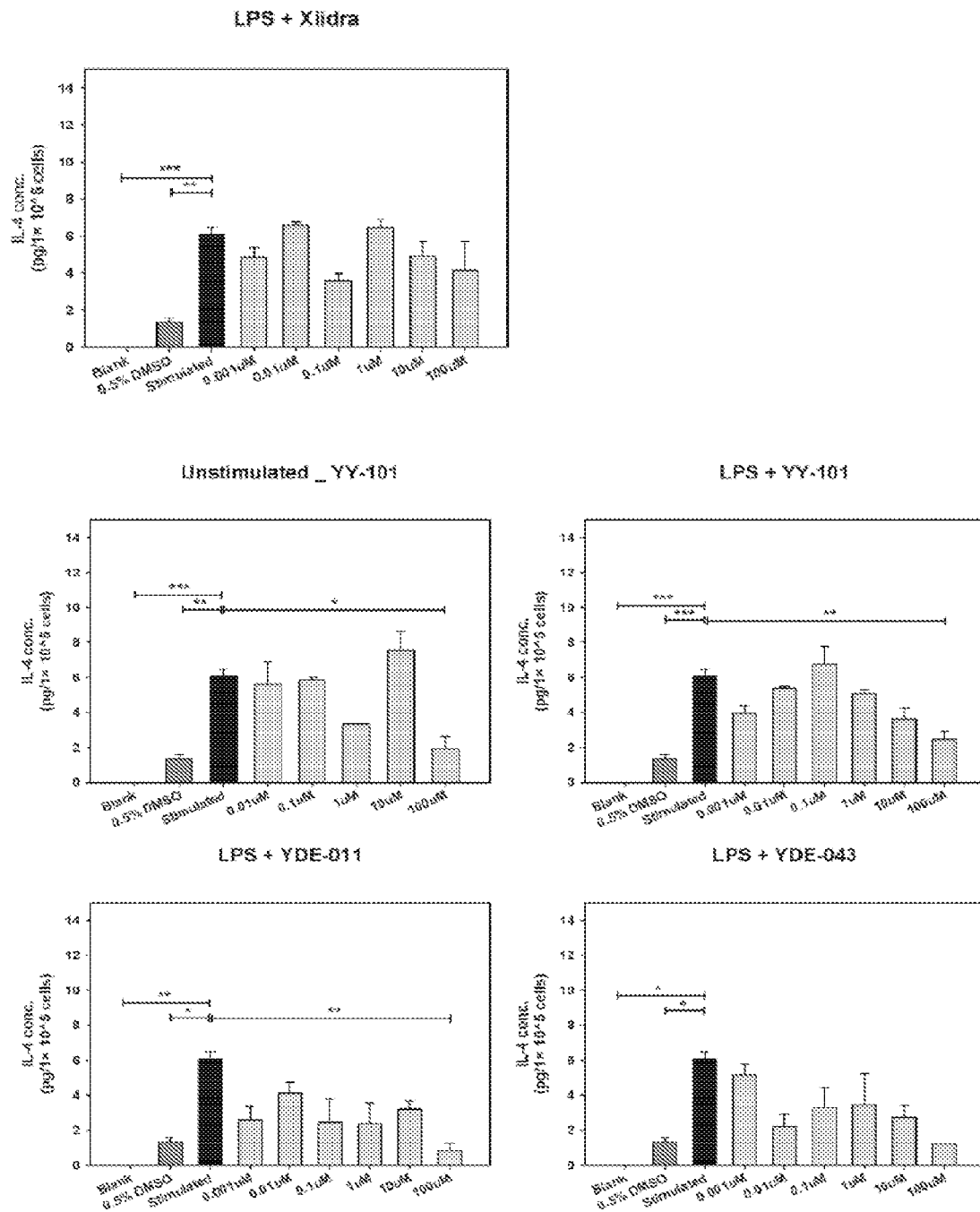


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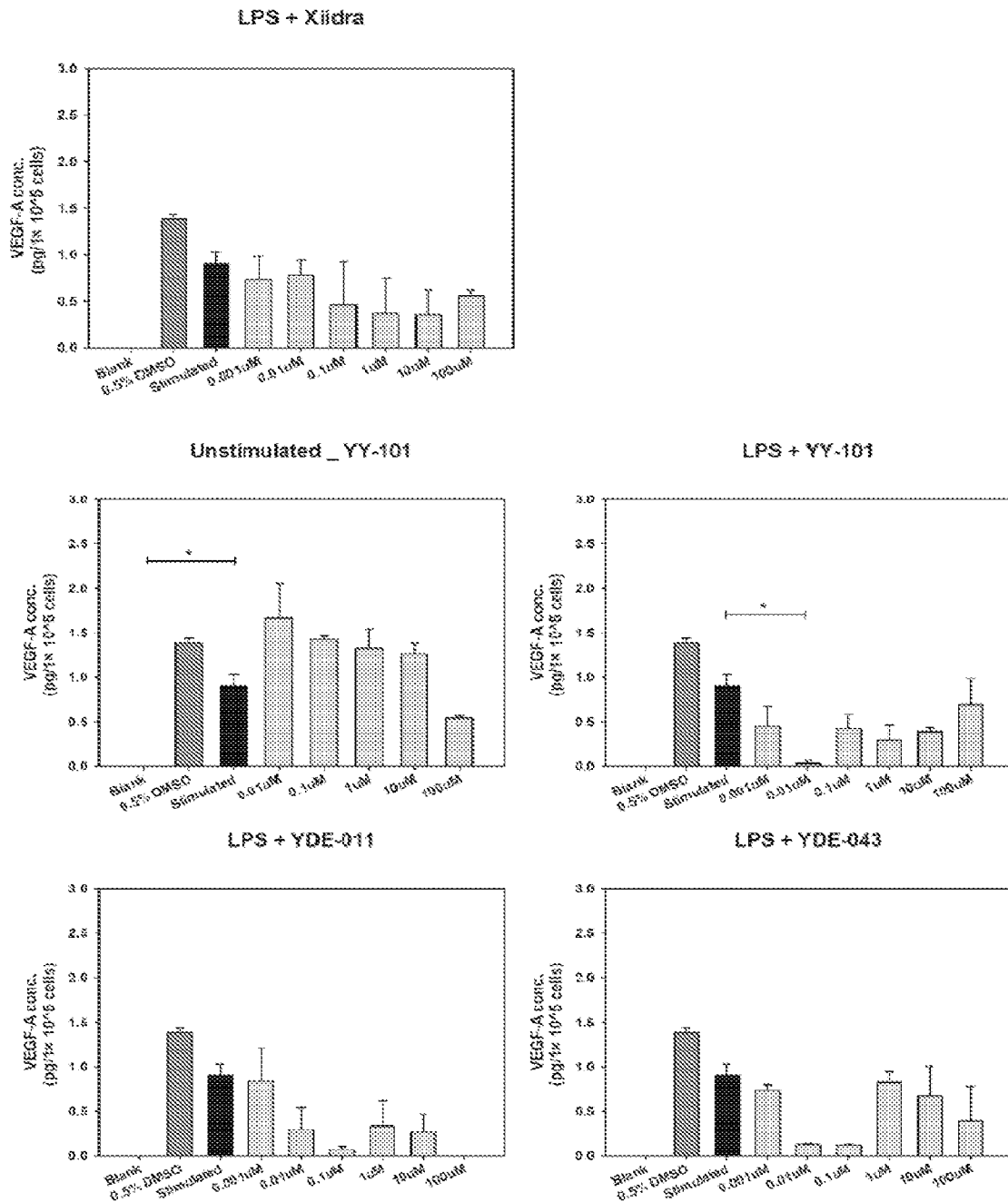


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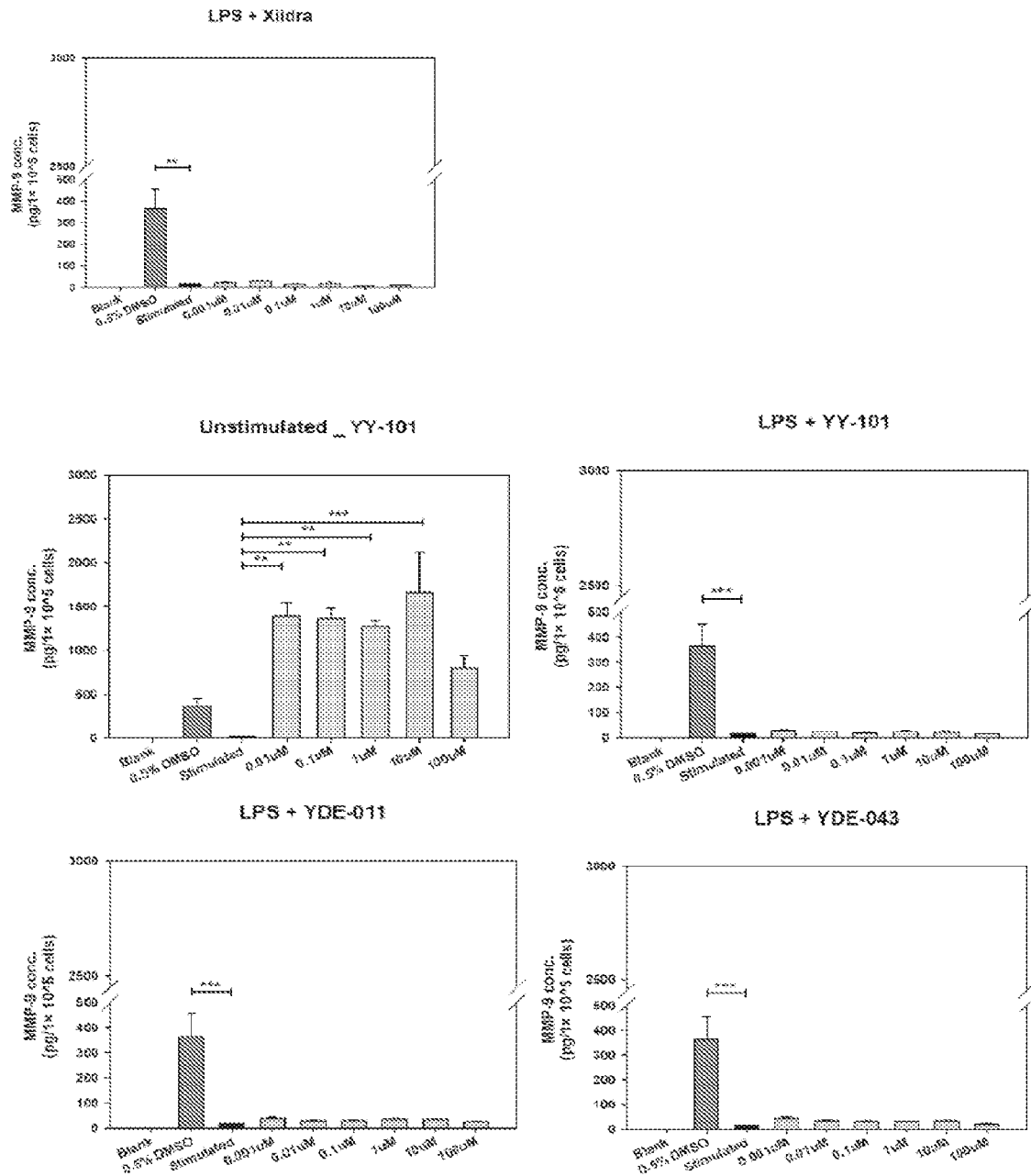


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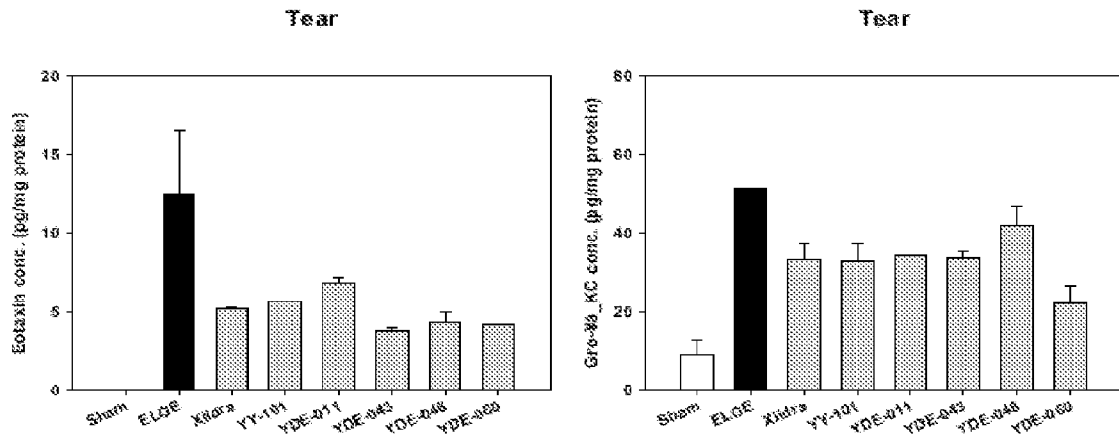


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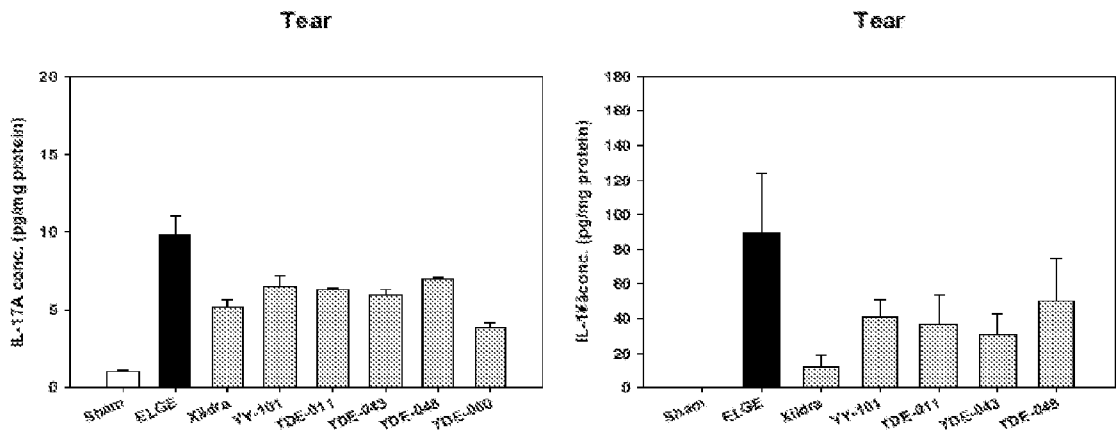


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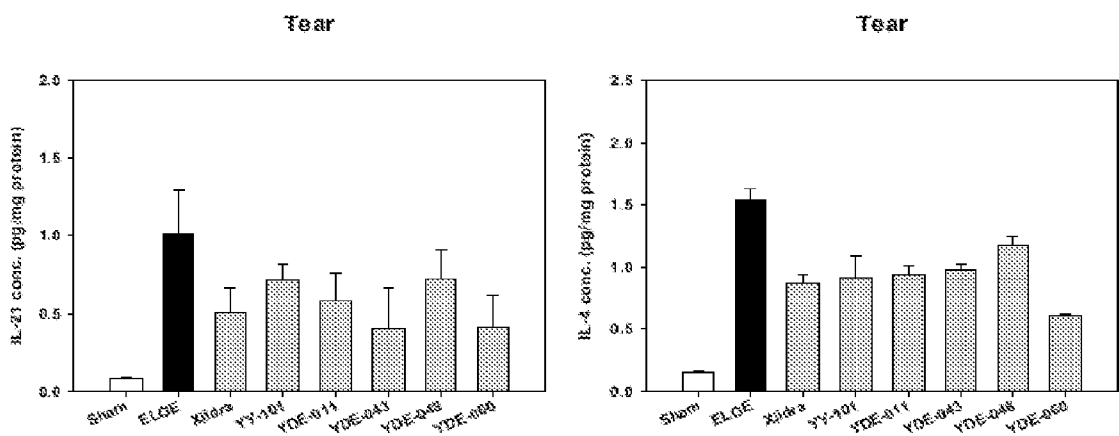


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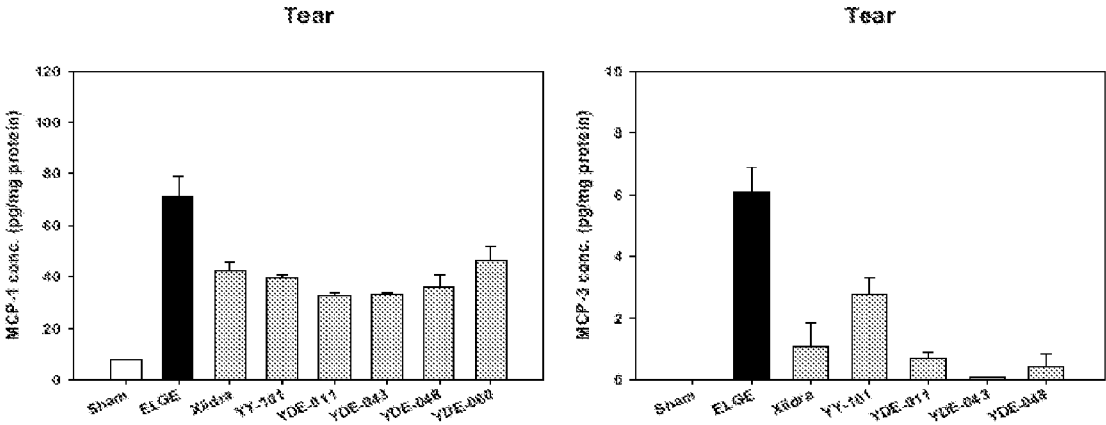


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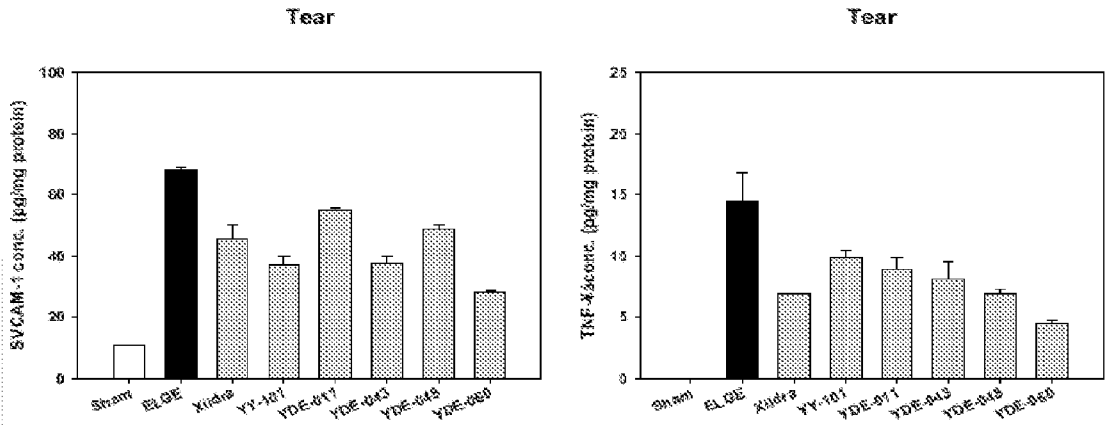


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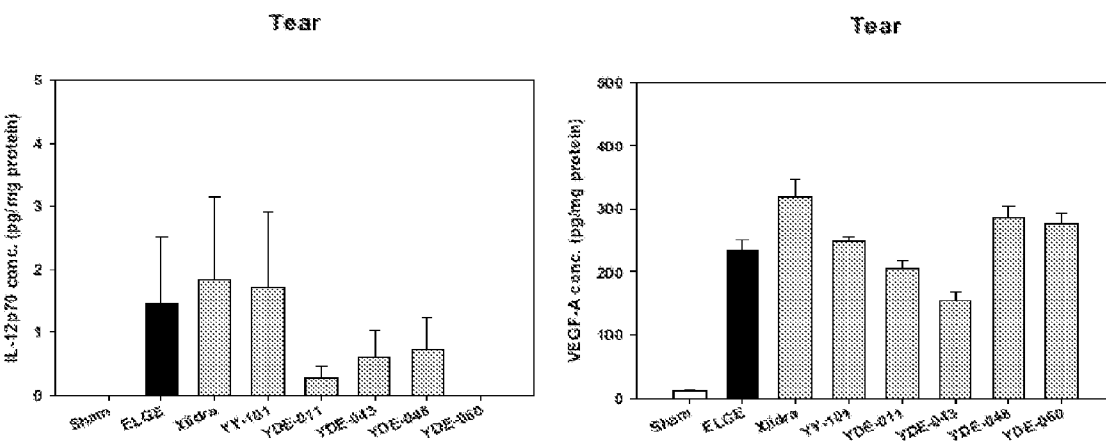


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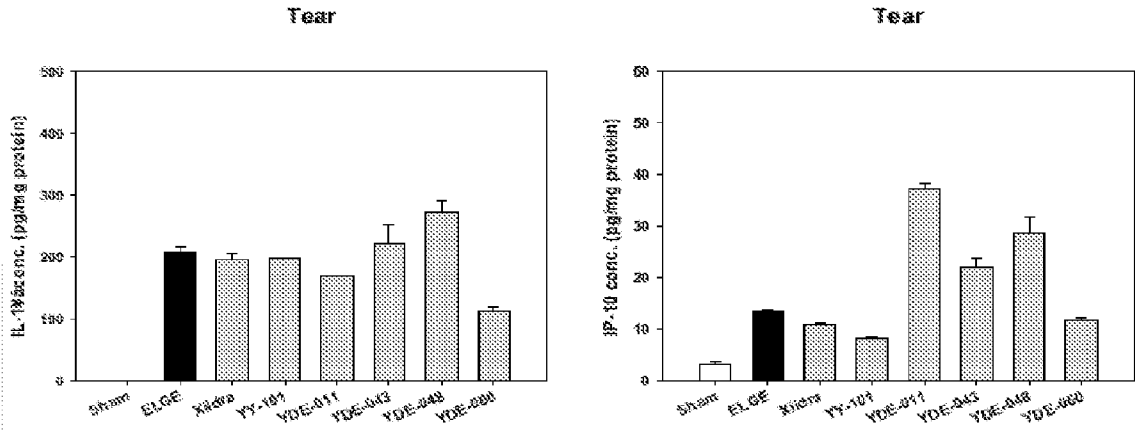


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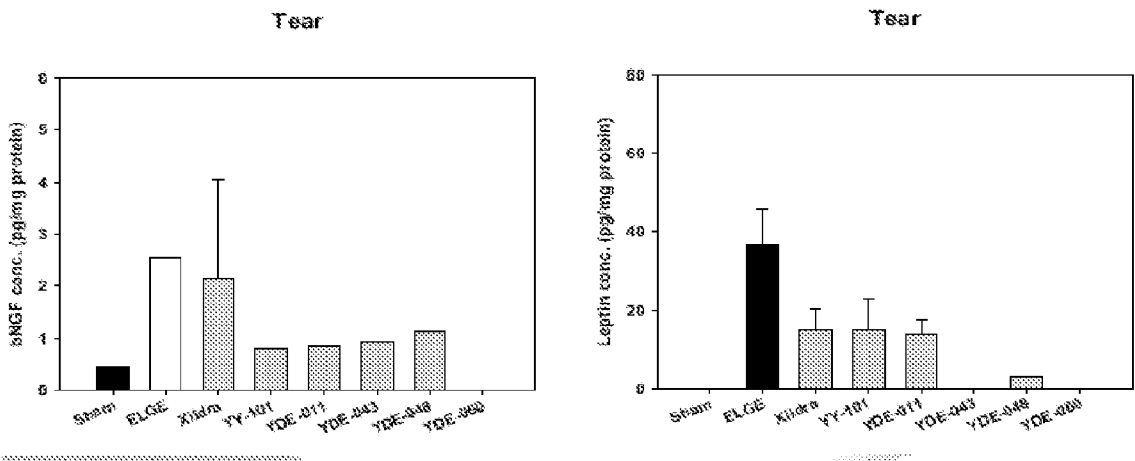


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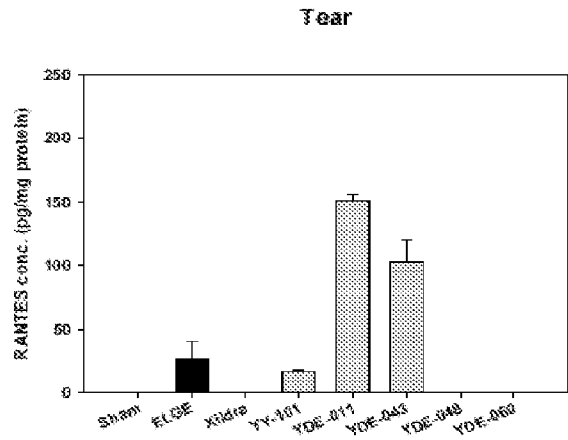


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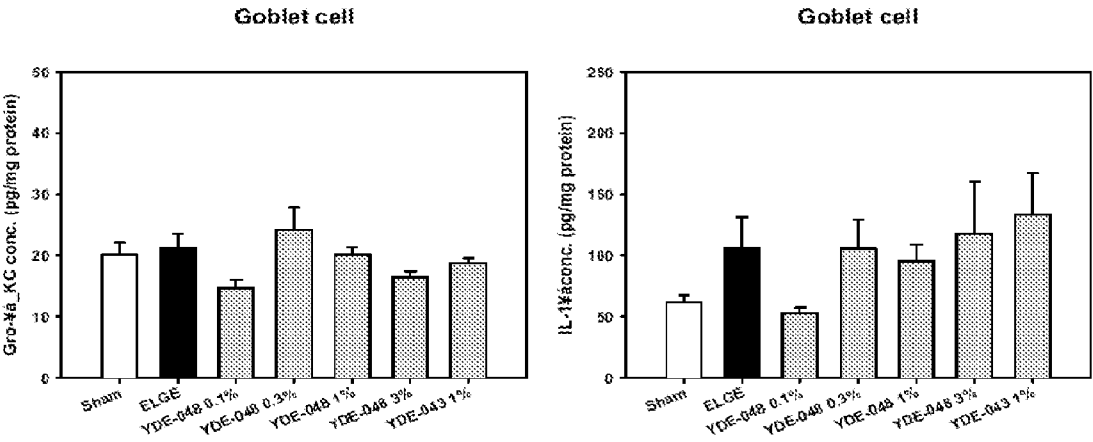


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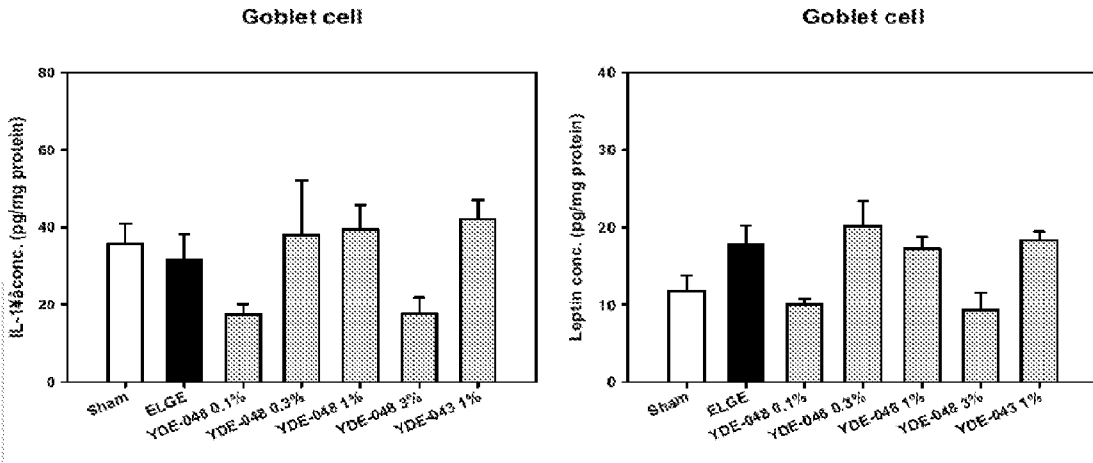


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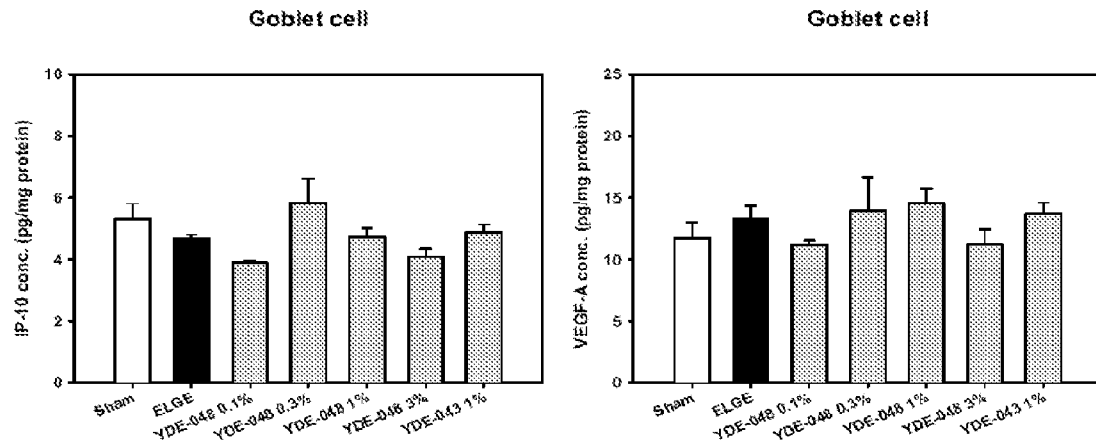


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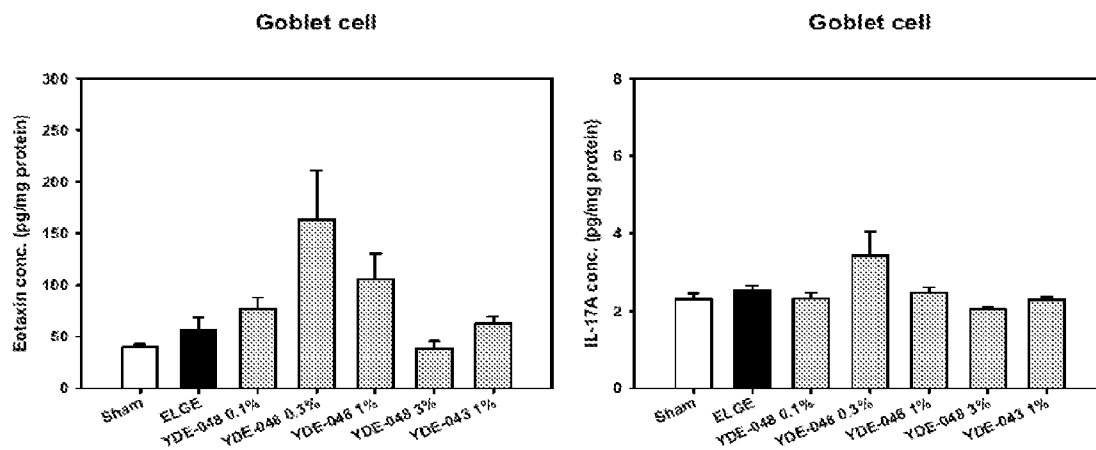


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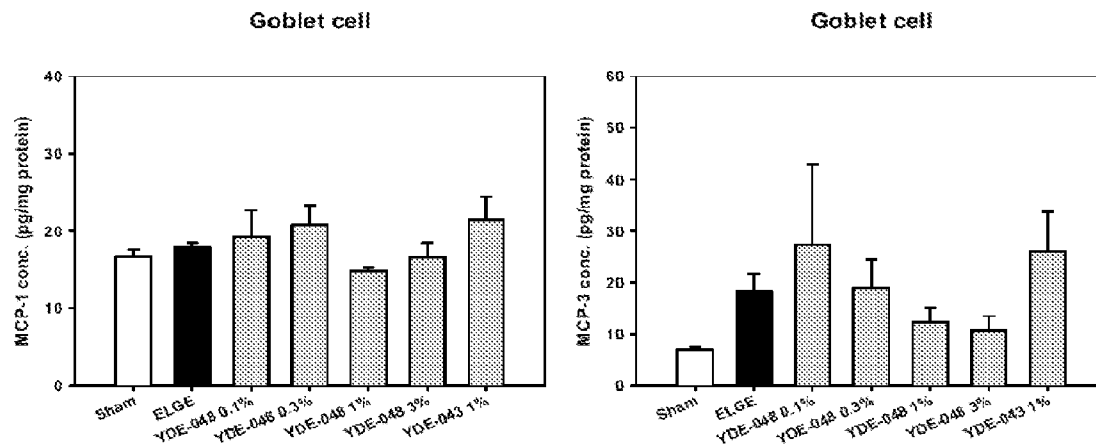


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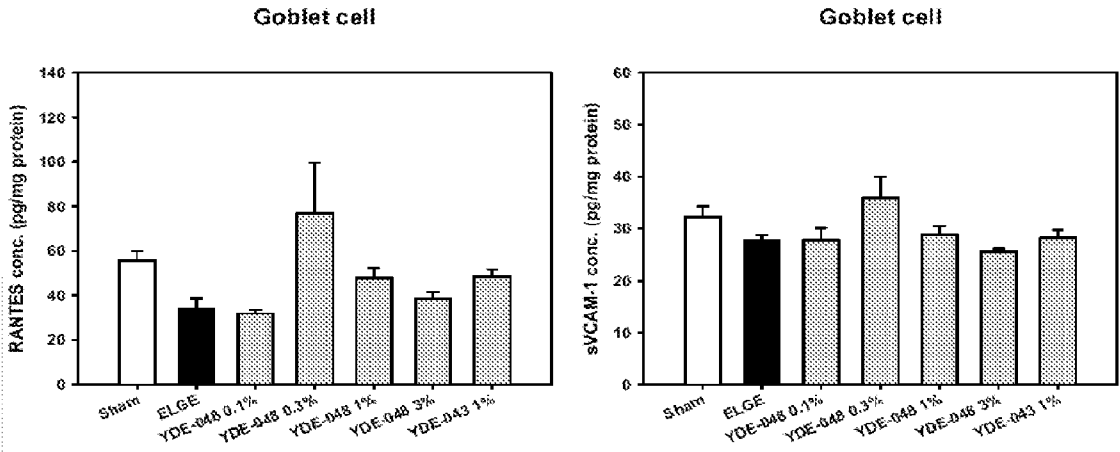


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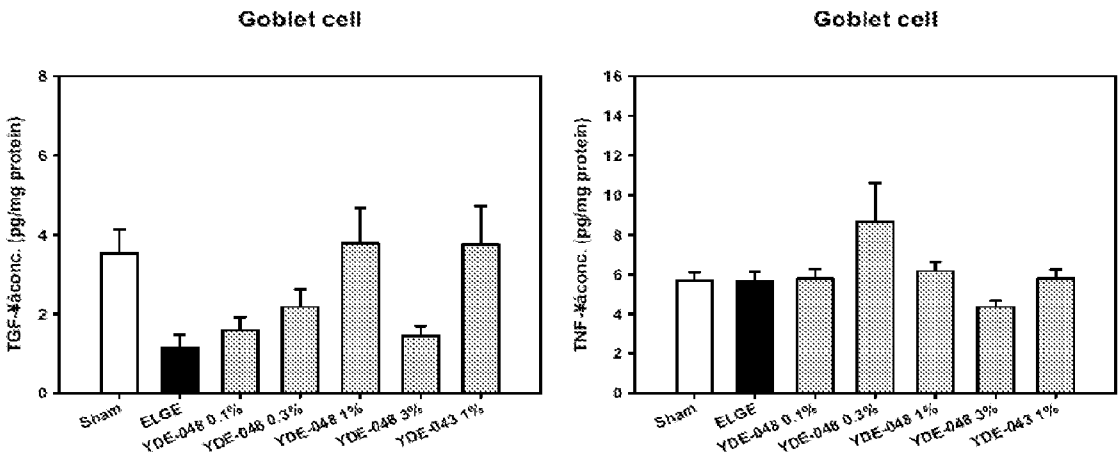


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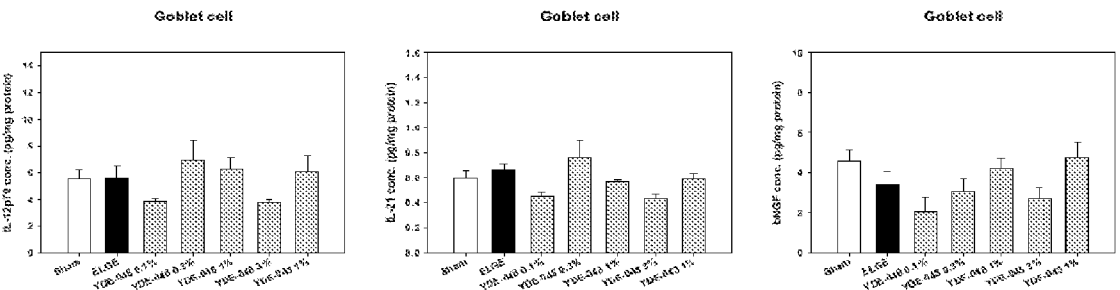


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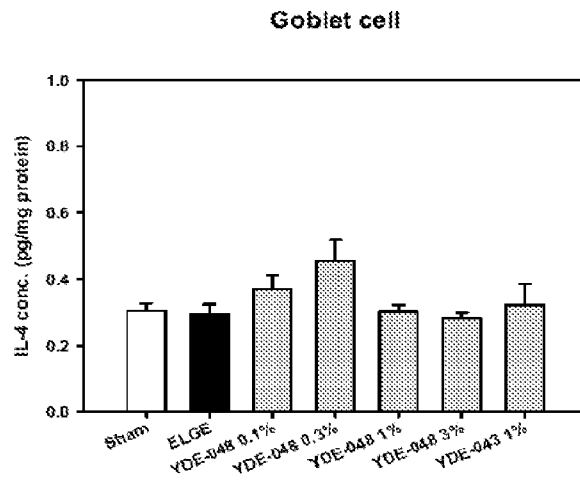


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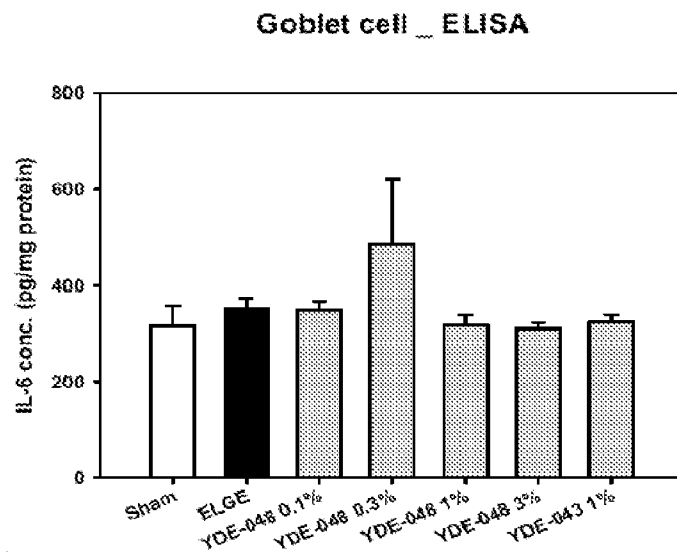


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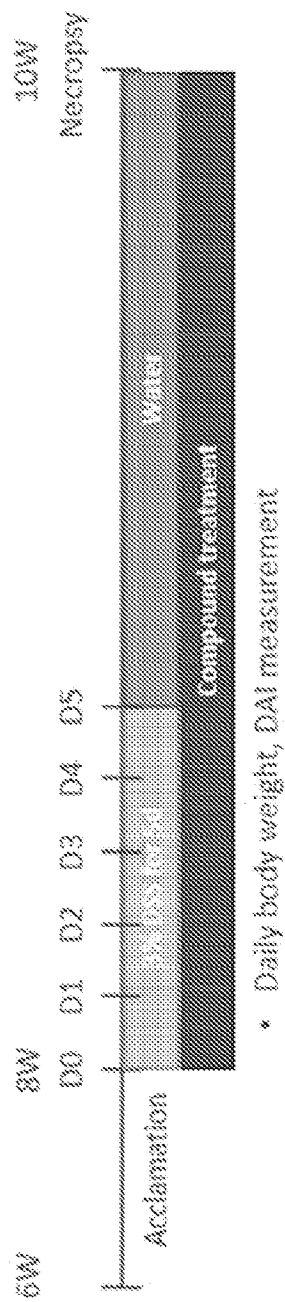


Figure 63

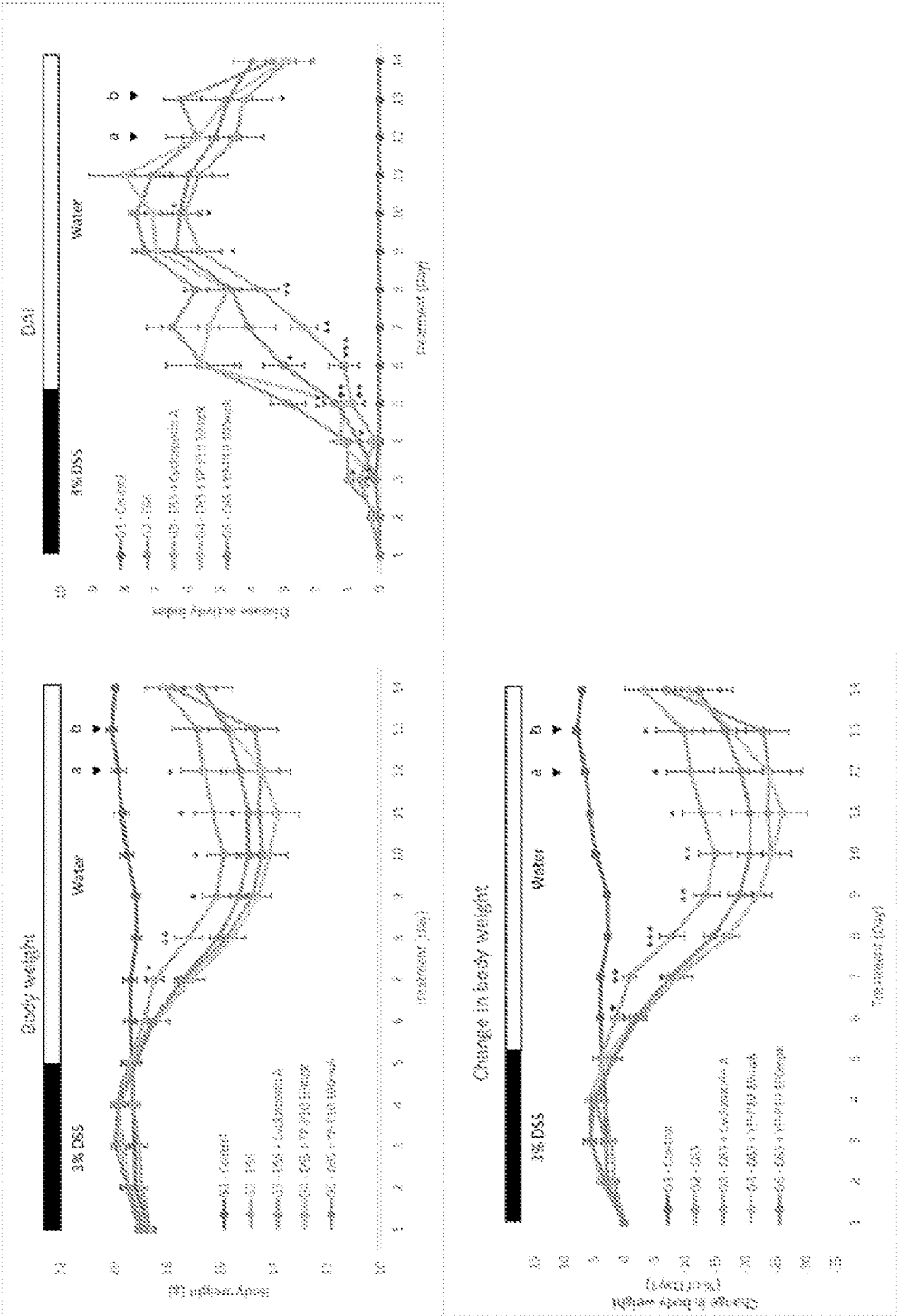
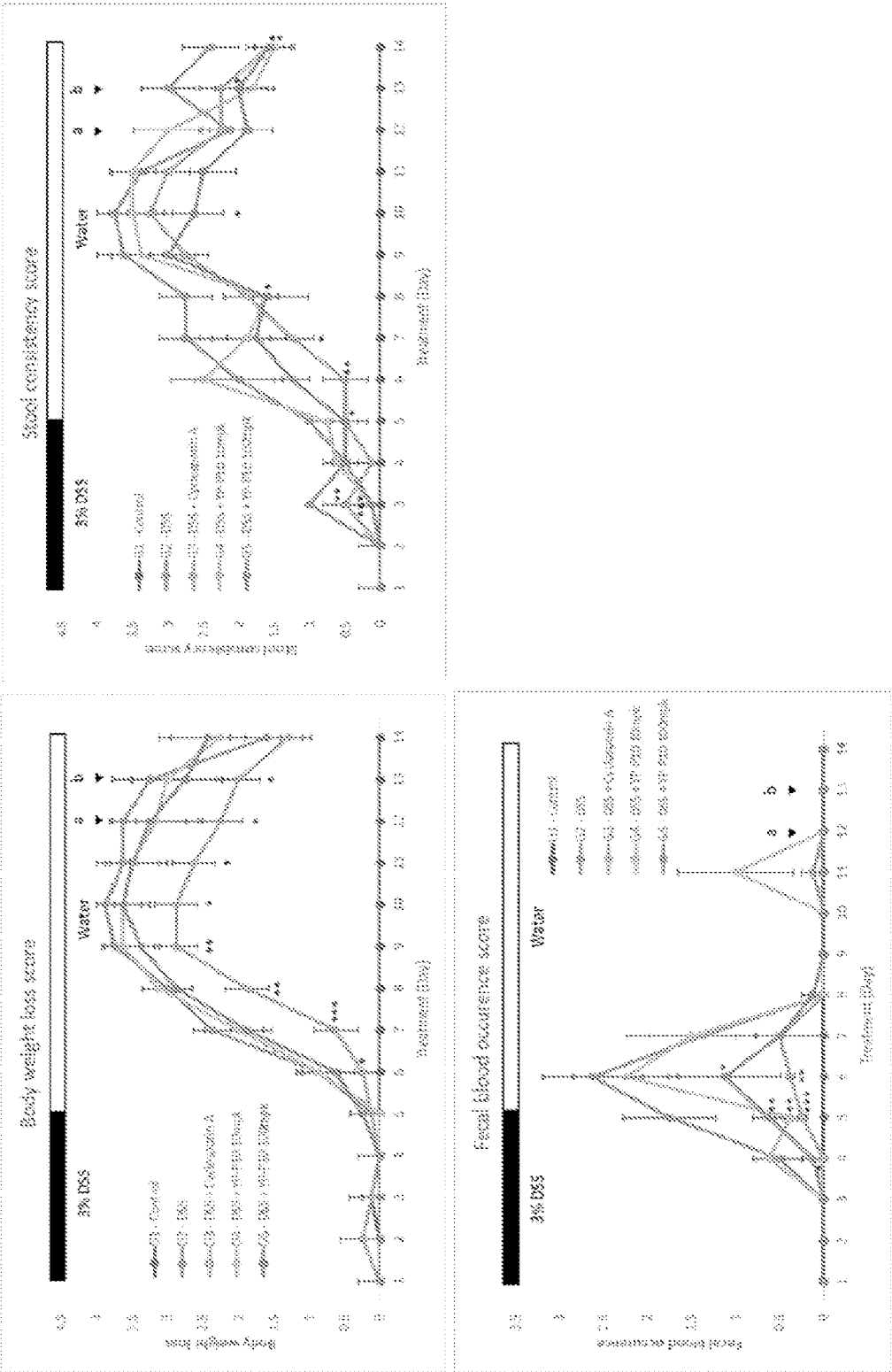


Figure 64



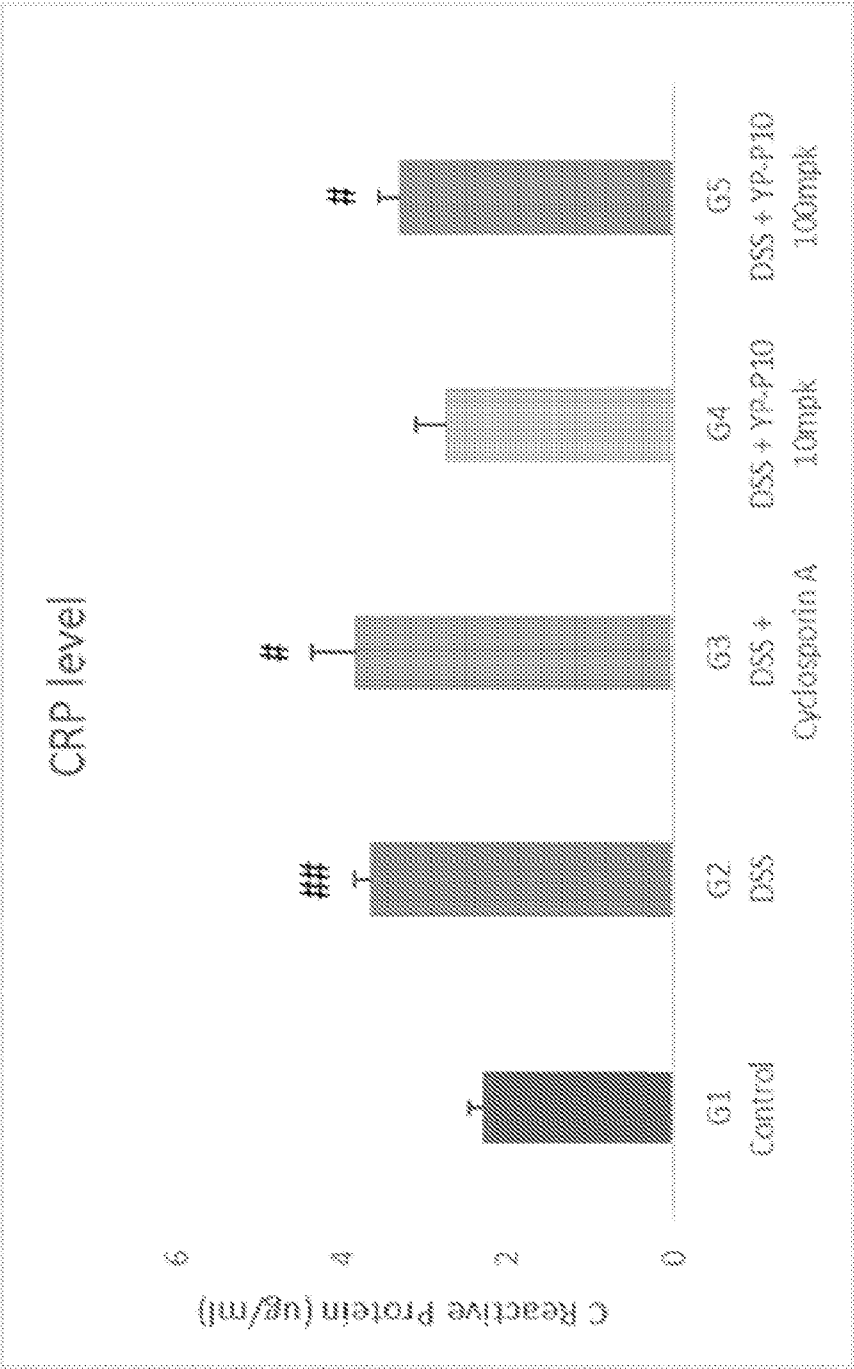


Figure 65

Figure 66

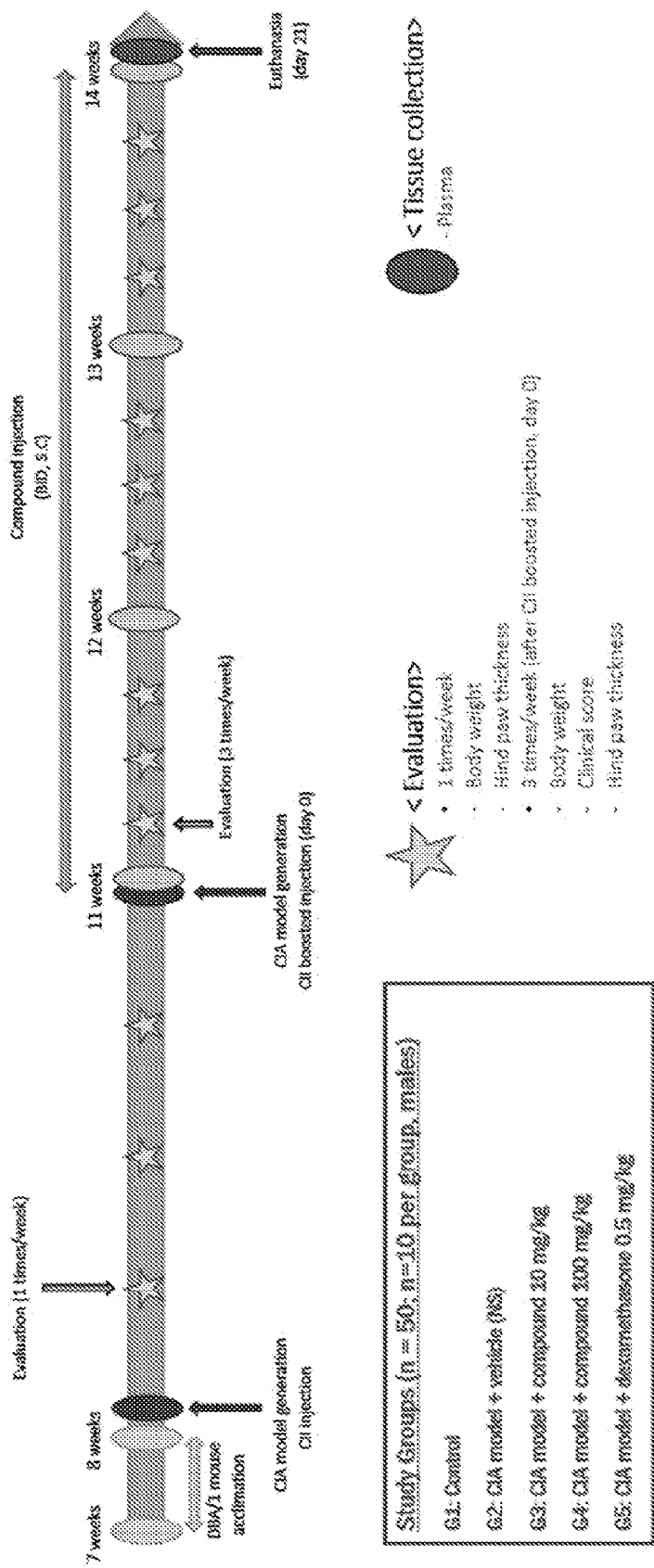


Figure 67

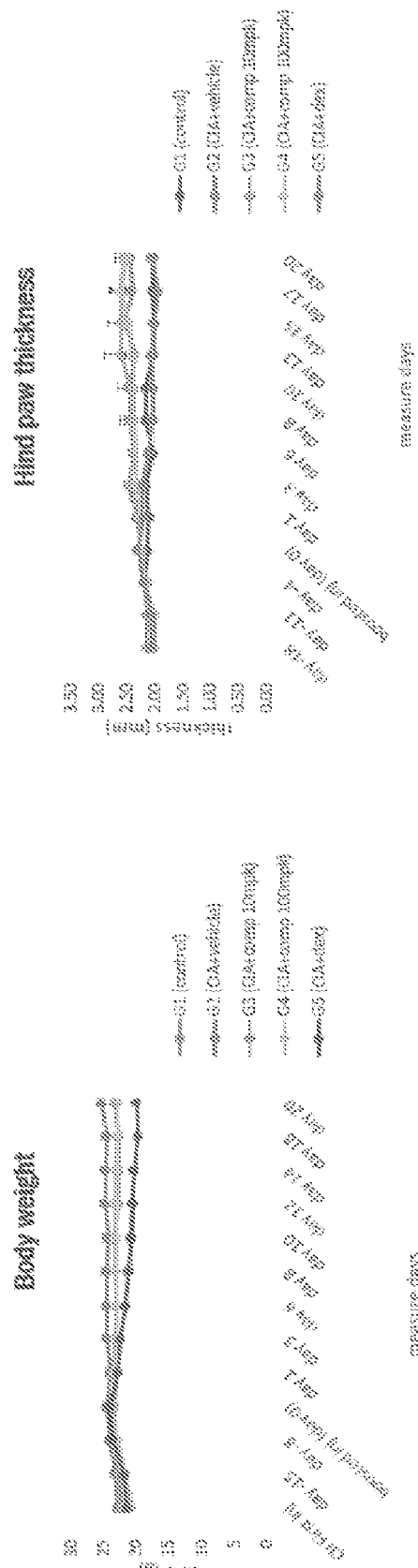


Figure 68

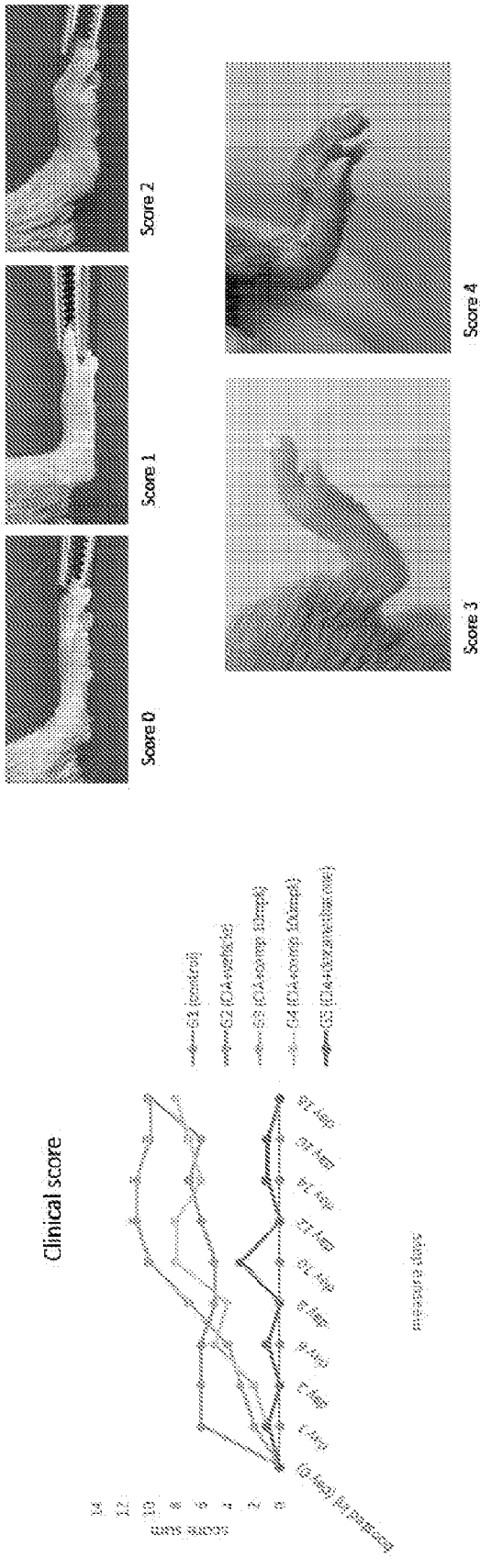


Figure 69

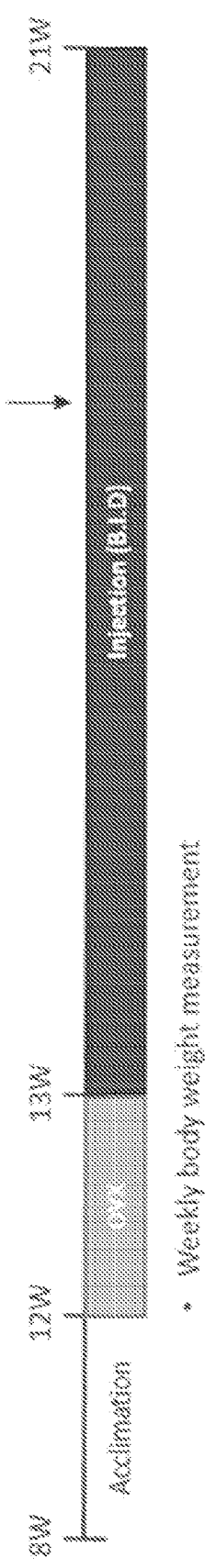
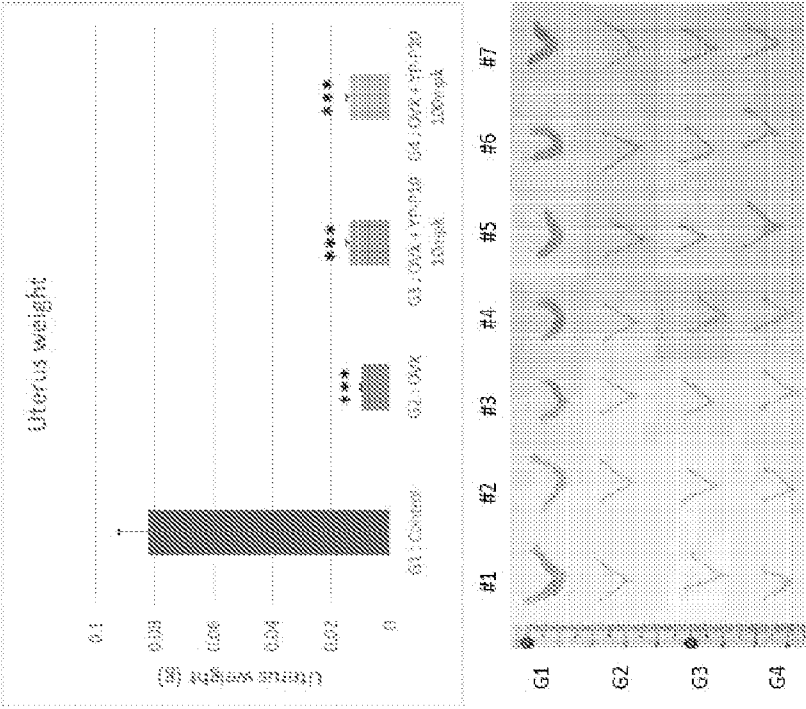
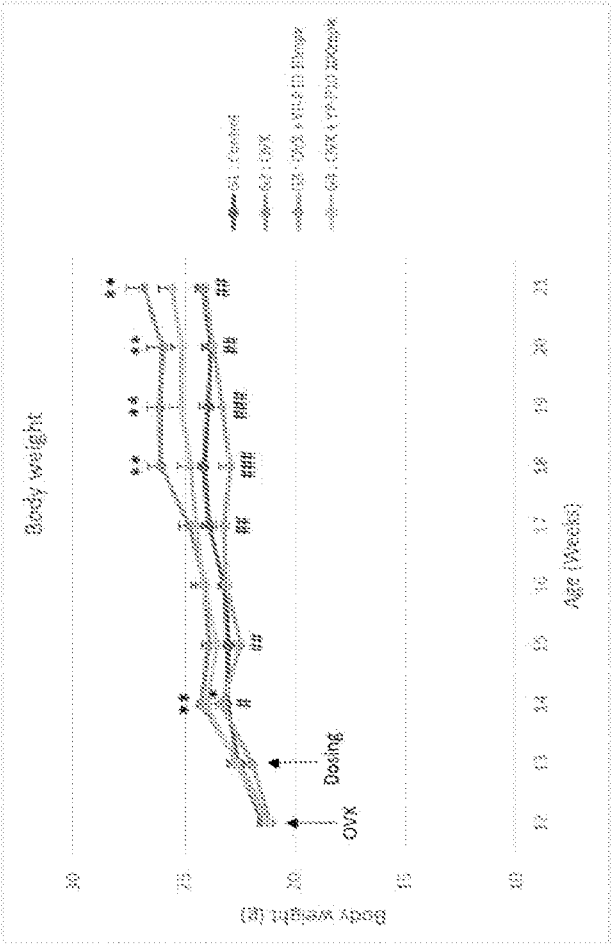


Figure 70



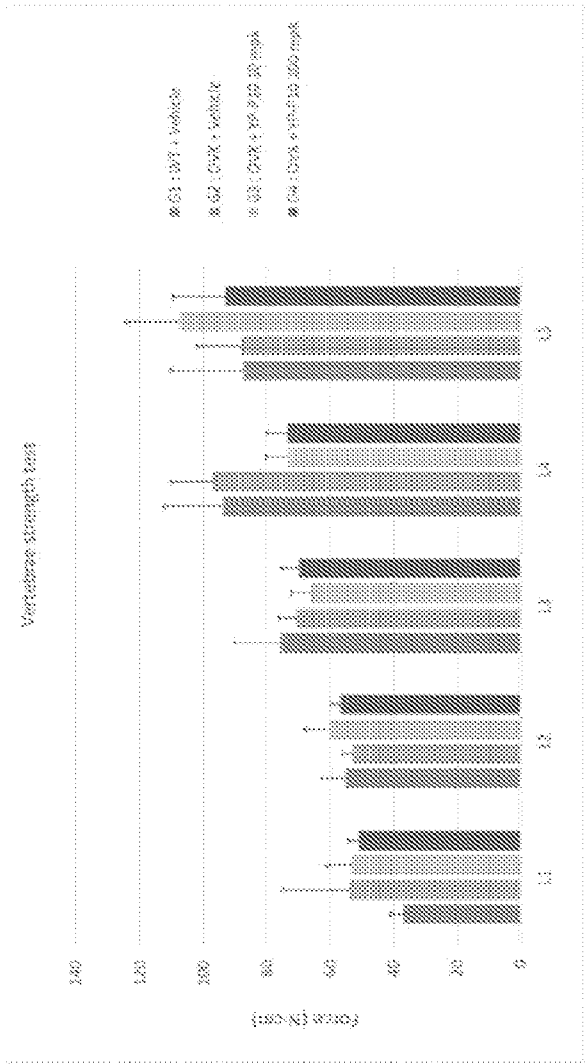
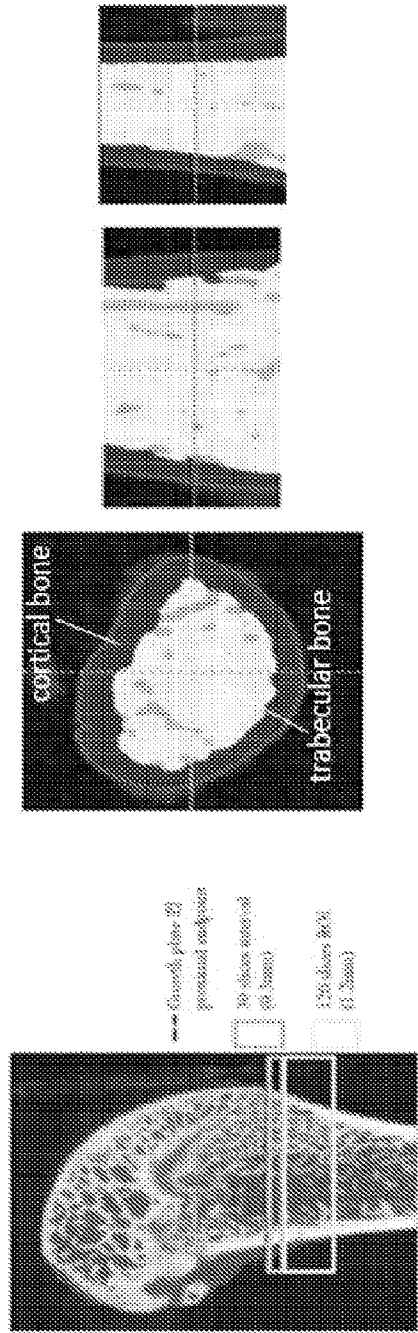


Figure 71

Figure 72



Trabecular dimension

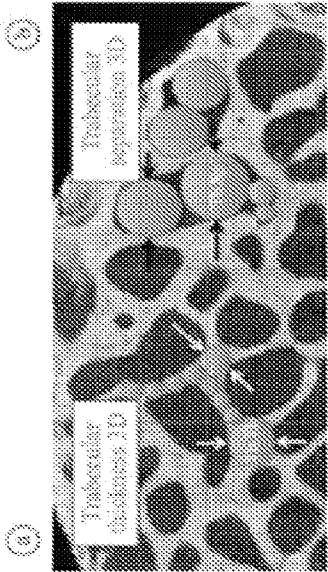
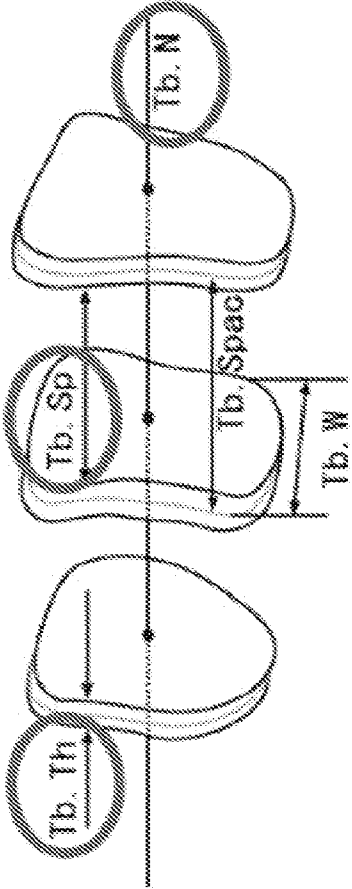


Figure 3. Schematic drawing of the principle of determination (Tb in A, and (Tb.Sp) in B, by 3D analysis.

Figure 73

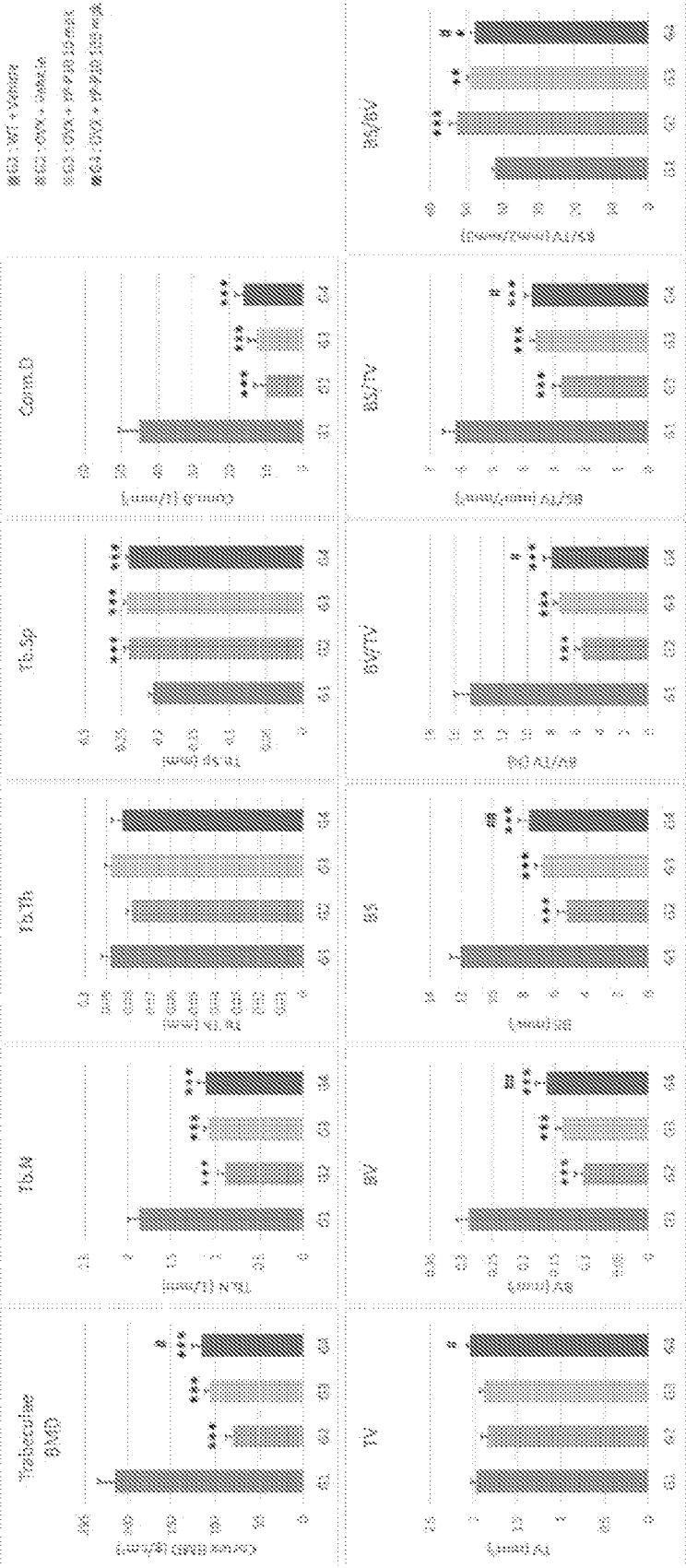


Figure 74

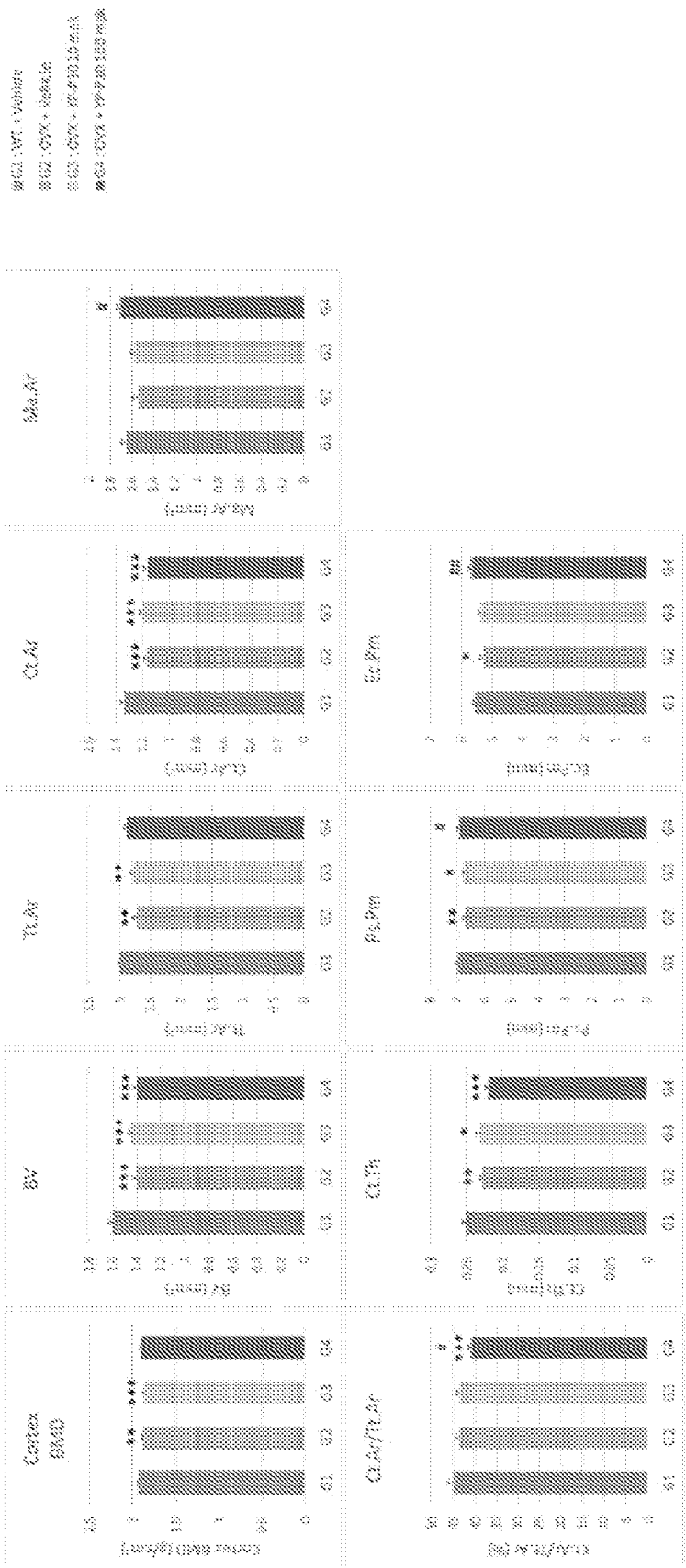


Figure 75

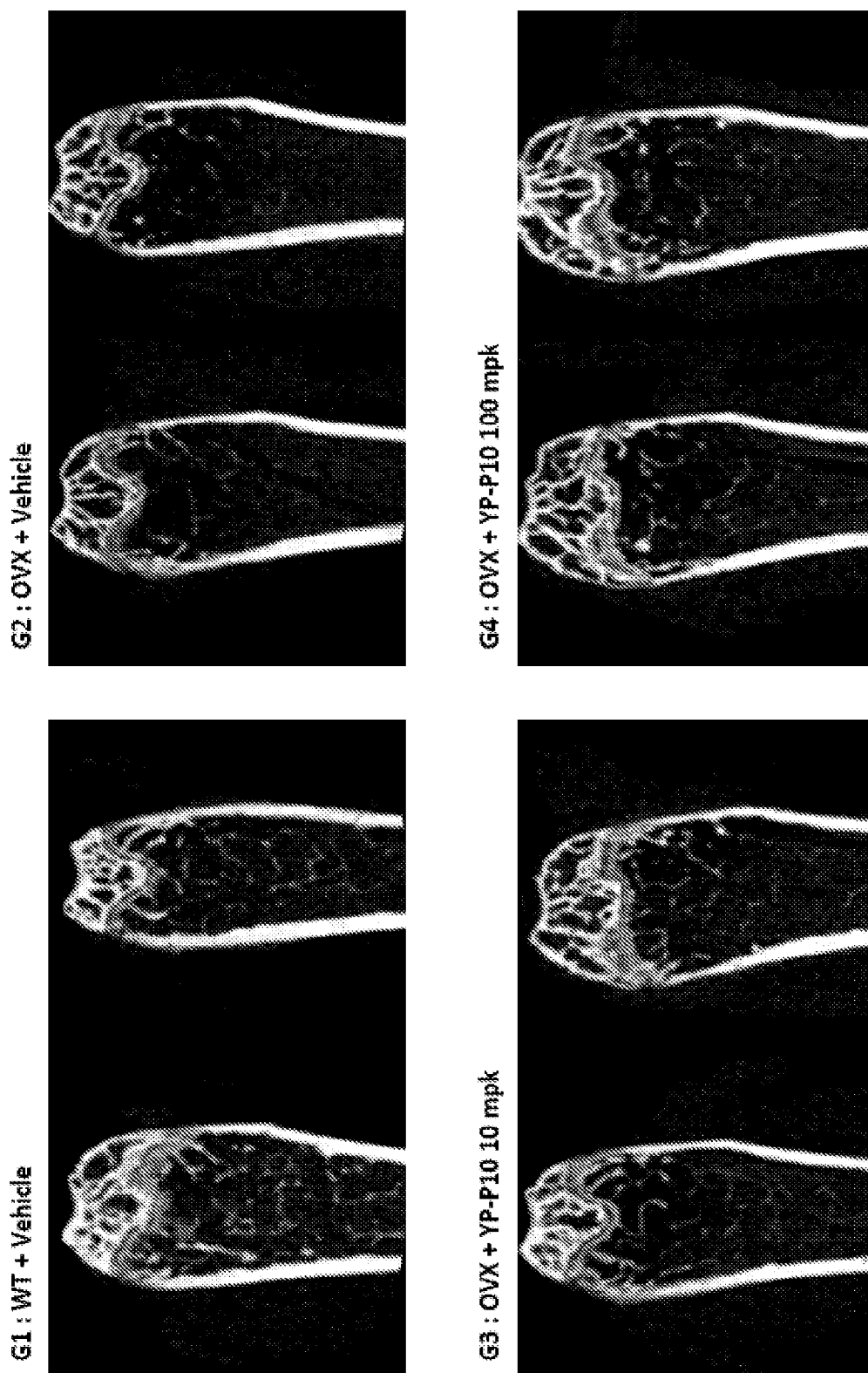


Figure 76

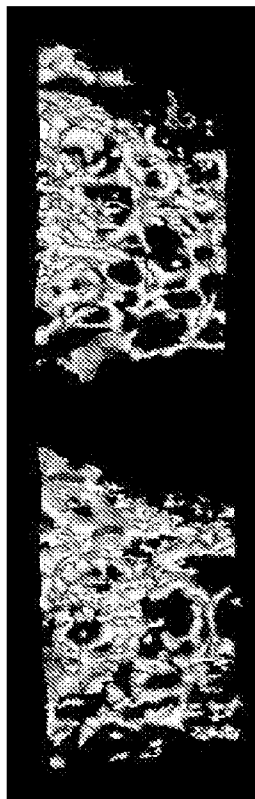
G1 : WT + Vehicle



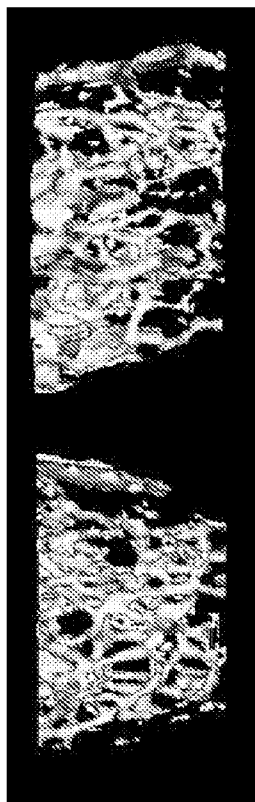
G2 : OVX + Vehicle



G3 : OVX + YP-P10 10 mpk



G4 : OVX + YP-P10 100 mpk



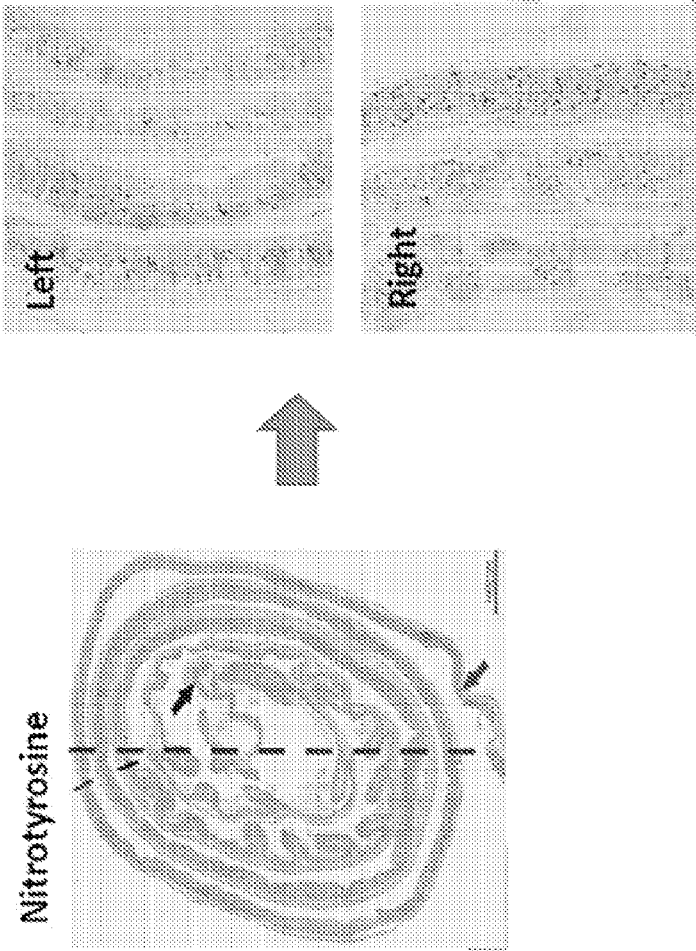
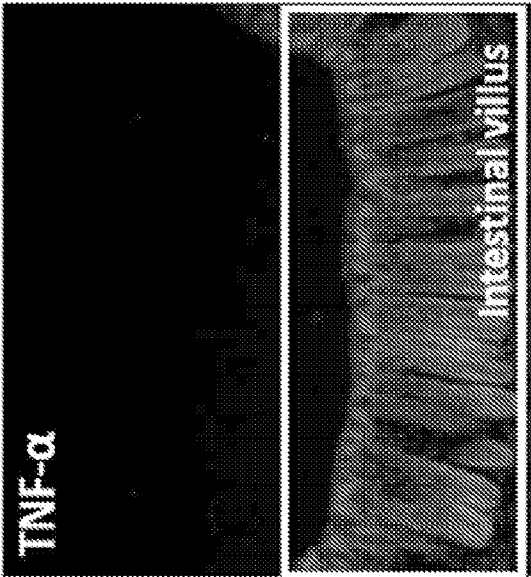


Figure 77



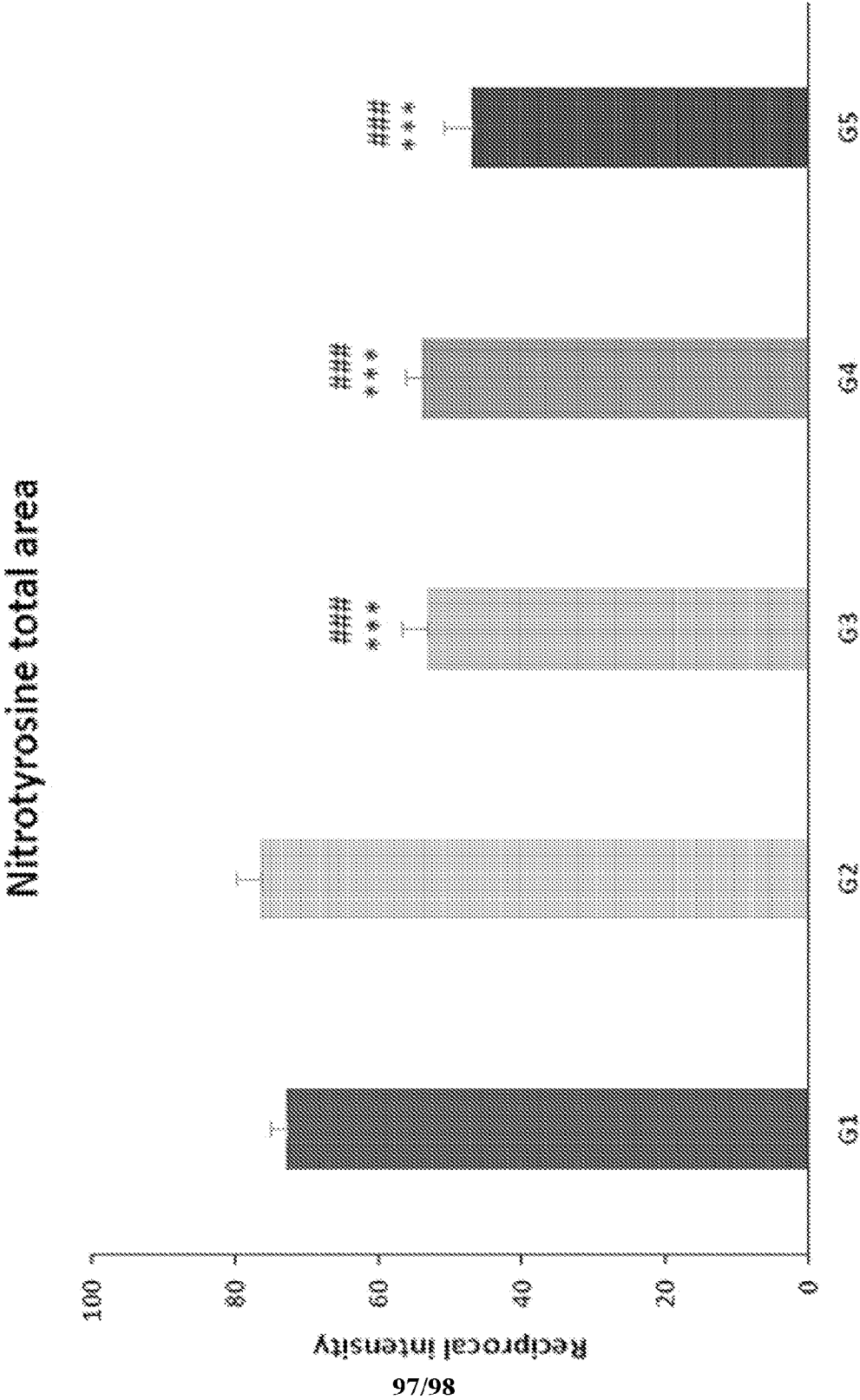


Figure 78

Figure 79

