concentration of the antigen (or a fragment thereof) in the test sample to a signal generated as a direct or indirect indication of the presence, amount or concentration of the antigen (or a fragment thereof) in a control or a calibrator. The calibrator is optionally part of a series of calibrators in which each of the calibrators differs from the other calibrators in the series by the concentration of the antigen (or a fragment thereof). One of the at least one binding protein comprises the binding porotein, such as the DVD-binding protein, disclosed herein.

If the test sample is from a patient, the methods disclosed herein can further comprise diagnosing, prognosticating, or assessing the efficacy of therapeutic/prophylactic treatment of the patient. If the methods further comprises assessing the efficacy of therapeutic/prophylactic treatment of the patient, the methods optionally further comprises modifying the therapeutic/prophylactic treatment of the patient as needed to improve efficacy. The methods disclosed herein can be adapted for use in an automated system or a semi-automated system.

Also provided is a kit for assaying a test sample for an antigen (or a fragment thereof). The kit comprises at least one component for assaying the test sample for an antigen (or a fragment thereof) and instructions for assaying the test sample for an antigen (or a fragment thereof), wherein the at least one component includes at least one composition comprising a binding protein disclosed herein.

The present disclosure provides use of an effective amount of the pharmaceutical composition of claim 77, in the manufacture of a medicament for treating a mammal.

The present disclosure provides use of the binding protein of claim 62, in the manufacture of a medicament for reducing human IL-17 activity, wherein IL-17 is to be contacted with such binding protein.

The present disclosure provides use of the binding protein of claim 62, in the manufacture of a medicament for reducing human IL-17 activity in a human subject suffering from a disorder in which IL-17 activity is detrimental.

The present disclosure provides Use of the binding protein of claim 62 in the manufacture of a medicament for treating a patient suffering from a disorder in which IL-17 is detrimental wherein said binding protein is to be administered either before, concurrent, or after the administration to the patient of a second agent, wherein the second agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1□ mAbs, anti-IL-6 or IL-6 receptor mAbs, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6,

IL-7, IL-8, IL-12, IL-13, IL-15, IL-16, IL-18, IL-23, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD-19, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1□ converting enzyme inhibitors, TNF□-converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, and TGF□□

Brief Description of the Drawings

Figure 1A is a schematic representation of Dual Variable Domain (DVD) constructs and shows the strategy for generation of a DVD-binding protein from two parent antibodies.

Figure 1B is a schematic representation of constructs DVD1-Ig, DVD2-Ig, and two chimeric mono-specific antibody clones.

Detailed Description of the Invention

Multivalent and/or multispecific binding proteins capable of binding two or more antigens are provided. Dual variable domain binding proteins (DVD-binding proteins), and pharmaceutical compositions thereof, as well as nucleic acids, recombinant expression vectors and host cells for making such DVD-binding proteins. Methods of using the DVD-binding proteins to detect specific antigens, either in vitro or in vivo are also provided.

Unless otherwise defined herein, scientific and technical terms used herein have the meanings that are commonly understood by those of ordinary skill in the art. In the event of any latent ambiguity, definitions provided herein take precedent over any dictionary or extrinsic definition. Unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. The use of "or" means "and/or" unless stated otherwise. The use of the term "including", as well as other forms, such as "includes" and "included", is

71. The binding protein of claim 63, wherein the binding protein is conjugated to an imaging agent selected from the group consisting of a radiolabel, an enzyme, a fluorescent label, a luminescent label, a bioluminescent label, a magnetic label, and biotin.

72. The binding protein of claim 63, wherein the binding protein further comprises a therapeutic or cytotoxic agent selected from the group consisting of an anti-metabolite, an alkylating agent, an antibiotic, a growth factor, a cytokine, an anti-angiogenic agent, an anti-mitotic agent, an anthracycline, toxin, and an apoptotic agent.

73. An isolated nucleic acid encoding a binding protein comprising the amino acid sequence of claim 62.

74. A vector comprising the isolated nucleic acid of claim 73.

75. A host cell comprising the vector of claim 74.

76. A method for producing a protein that binds IL-17, the method comprising the steps of culturing the host cell of claim 75 in a culture medium under conditions sufficient to produce a binding protein that binds IL-17.

77. A pharmaceutical composition comprising the binding protein of claim 62, and a pharmaceutically acceptable carrier.

78. ~~A method for treating a mammal comprising administering to the mammal~~ Use of an effective amount of the pharmaceutical composition of claim 77, in the manufacture of a medicament for treating a mammal.

79. ~~A method for reducing human IL-17 activity, the method comprising contacting human IL-17 with~~ Use of the binding protein of claim 62, in the manufacture of a medicament for reducing human IL-17 activity, wherein IL-17 is to be contacted with such binding protein~~such that human IL-17 activity is reduced~~.

80. ~~A method for reducing human IL-17 activity in a human subject suffering from a disorder in which IL-17 activity is detrimental, the method comprising administering to the human subject~~ Use of the binding protein of claim 62, in the manufacture of a medicament for reducing human IL-17 activity in a human subject suffering from a disorder in which IL-17 activity is detrimental~~such that human IL-17 activity in the human subject is reduced and/or treatment is achieved~~.

81. ~~A method for treating a patient suffering from a disorder in which IL-17 is detrimental comprising administering to the patient~~ Use of the binding protein of claim 62 in the manufacture of a medicament for treating a patient suffering from a disorder in which IL-17 is detrimental wherein said binding protein is to be administered either before,

concurrent, or after the administration to the patient of a second agent, wherein the second agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β mAbs, anti-IL-6 or IL-6 receptor mAbs, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-12, IL-13, IL-15, IL-16, IL-18, IL-23, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD-19, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adensosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1β converting enzyme inhibitors, TNFα-converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, and TGFβ.

82. The ~~method~~ use of claim 80 or 81, wherein the disorder is an autoimmune and/or inflammatory disorder.

83. The ~~method~~ use of claims 82, wherein the disorder is selected from the group consisting of autoimmune and inflammatory disorders, asthma, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, spondylosing arthropathy, psoriasis, gastrointestinal disorders, inflammatory bowel disease, ulcerative cholitis, Chrohn's disease, uveitis, and systemic lupus erythematosis.

84. The ~~method~~ use of claim 82, wherein the disorder is selected from the group consisting of immune and inflammatory diseases, autoimmune diseases, inflammation, Crohn's disease, psoriasis (including plaque psoriasis), arthritis (including rheumatoid arthritis, psoratic arthritis, osteoarthritis, or juvenile idiopathic arthritis), multiple sclerosis, ankylosing spondylitis, spondylosing arthropathy, systemic lupus erythematosus, uveitis, multiple sclerosis, sepsis, neurodegenerative diseases, neuronal regeneration, spinal cord injury, primary and metastatic cancers, a respiratory disorder; asthma; allergic and nonallergic asthma; asthma due to infection; asthma due to infection with respiratory syncytial virus (RSV); chronic obstructive pulmonary disease (COPD); a condition involving airway inflammation; eosinophilia; fibrosis and excess mucus production; cystic fibrosis; pulmonary fibrosis; an atopic disorder; atopic dermatitis; urticaria; eczema; allergic rhinitis; allergic enterogastritis; an inflammatory and/or autoimmune