human TNF-α, mature-human TNF-α, or truncated-human TNF-α to bind to its receptor. In yet another embodiment, the binding protein reduces one or more TNF-α biological activities selected from: TNF-dependent cytokine production; TNF-dependent cell killing; TNF-dependent inflammation; TNF-dependent bone erosion; and TNF-dependent cartilage damage.

In an embodiment , the binding protein has an on rate constant (K_{on}) selected from: at least about $10^2M^{-1}s^{-1}$; at least about $10^3M^{-1}s^{-1}$; at least about $10^4M^{-1}s^{-1}$; at least about $10^5M^{-1}s^{-1}$; and at least about $10^6M^{-1}s^{-1}$; as measured by surface plasmon resonance. In another embodiment, the binding protein has an off rate constant (K_{off}) selected from: at most about $10^{-3}s^{-1}$; at most about $10^{-4}s^{-1}$; at most about $10^{-5}s^{-1}$; and at most about $10^{-6}s^{-1}$, as measured by surface plasmon resonance. In yet another embodiment, the binding protein has a dissociation constant (K_D) selected from: at most about 10^{-7} M; at most about 10^{-8} M; at most about 10^{-9} M; at most about 10^{-10} M; at most about 10^{-11} M; at most about 10^{-12} M; and at most 10^{-13} M.

In another aspect, a method for treating a mammal is provided comprising administering to the mammal an effective amount of the pharmaceutical composition disclosed herein. In another embodiment, a method for reducing human TNF-α activity is provided, the method comprising: contacting human TNF-α with the binding protein disclosed herein such that human TNF-α activity is reduced. In another embodiment, provided is a method for reducing human TNF-α activity in a human subject suffering from a disorder in which TNF-α activity is detrimental, the method comprising administering to the human subject the binding protein disclosed herein such that human TNF-α activity in the human subject is reduced. In another embodiment, provided is a method for treating a subject for a disease or a disorder in which TNF-α activity is detrimental, the method comprising administering to the subject the binding protein disclosed herein such that treatment is achieved.

In one embodiment, the method treats diseases involving immune and inflammatory elements, such as autoimmune diseases, particularly those assocated with inflammation, including Crohn's disease, psoriasis (including plaque psoriasis), arthritis (including rheumatoid arthritis, psoratic arthritis, osteoarthritis, or juvenile idiopathic arthritis), multiple sclerosis, and ankylosing spondylitis. Therefore, the binding proteins herein may be used to treat these disorders.

In one embodiment there is provided use of an effective amount of the pharmaceutical composition of claim 18, in the manufacture of a medicament for treating a mammal.

In one embodiment there is provided use of the binding protein of claim 3 in the manufacture of a medicament for reducing human TNF-α activity in a human activity.

In one embodiment there is provided use of the binding protein of claim 3 in the manufacture of a medicament for reducing human TNF-α activity in a human subject suffering from a disorder in which TNF-α activity is detrimental.

In one embodiment there is provided use binding protein of claim 3 in the manufacture of a medicament for treating a patient suffering from a disorder in which TNF-α is detrimental wherein said medicament is to be administered either before, concurrent or after administration to the patient of a second agent, wherein the second agent is selected from the group consisting of an antibody, or fragment thereof, capable of binding human IL-12; PGEA; LPA; NGF, CGRP, SubP, RAGE; histamine; a histamine receptor blocker; bradykinin; IL-1aplha, IL-1beta, VEGF; PLGF; methotrexate; a corticosteroid, a glucocorticoid receptor modular; cyclosporine, rapamycin, FK506, and a non-steroidal anti-inflammatory agent.

Detailed Description of the Invention

Provided are TNF-α binding proteins, or antigen-binding portions thereof, that bind TNF-α, pharmaceutical compositions thereof, as well as nucleic acids, recombinant expression vectors and host cells for making such binding proteins and fragments. Also provided are methods of using the binding proteins disclosed herein to detect human TNF-α, to inhibit human TNF-α either in vitro or in vivo, and to regulate gene expression or TNF-α related functions.

19. ~~A method for treating a mammal comprising administering to the mammal~~ Use of an effective amount of the pharmaceutical composition of claim 18, in the manufacture of a medicament for treating a mammal.

20. ~~A method for reducing human TNF-α activity, the method comprising contacting human TNF-α with~~ Use of the binding protein of claim 3 in the manufacture of a medicament for reducing human TNF-α activity ~~such that human TNF-α activity is reduced~~.

21. ~~A method for reducing human TNF-α activity in a human subject suffering from a disorder in which TNF-α activity is detrimental, the method comprising administering to the human subject~~ Use of the binding protein of claim 3 in the manufacture of a medicament for reducing human TNF-α activity in a human subject suffering from a disorder in which TNF-α activity is detrimental such that human TNF-α activity in the human subject is reduced and/or treatment is achieved.

22. ~~A method for treating a patient suffering from a disorder in which TNF-α is detrimental comprising administering to the patient~~ Use of the binding protein of claim 3in the manufacture of a medicament for treating a patient suffering from a disorder in which TNF-α is detrimental wherein said medicament 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 an antibody, or fragment thereof, capable of binding human IL-12; PGE2; LPA; NGF; CGRP; SubP; RAGE; histamine; a histamine receptor blocker; bradykinin; IL-1alpha; IL-1beta; VEGF; PLGF; methotrexate; a corticosteroid, a glucocorticoid receptor modulator; cyclosporin, rapamycin, FK506, and a non-steroidal anti-inflammatory agent.

23. The ~~method~~ use of claim 21 or 22, wherein the disorder is an autoimmune and/or inflammatory disorder.

24. The ~~method~~ use of claims 23, wherein the disorder is selected from the group consisting of Crohn's disease, psoriasis, plaque psoriasis, arthritis, rheumatoid arthritis, psoratic arthritis, osteoarthritis, or juvenile idiopathic arthritis, multiple sclerosis, and ankylosing spondylitis.

25. The ~~method~~ use of claim 23, wherein the disorder is selected from the group consisting of 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 condition of the skin; an inflammatory and/or autoimmune condition of gastrointestinal organs; inflammatory bowel diseases (IBD); ulcerative colitis; Crohn's disease; an inflammatory and/or autoimmune condition of the liver; liver cirrhosis; liver fibrosis; liver fibrosis caused by hepatitis B and/or C virus; scleroderma; tumors or cancers; hepatocellular carcinoma;