

generally difficult to achieve sufficient concentrations of adsorptive treatment agents in the involved nail, nail bed or matrix by topical administration. (Wozel, Clin. Derm. 26:448-459, 2008), while the small amount of surface area affected may not qualify a patient for systemic or biologic treatment.

[0006] IL-17A is an inflammatory cytokine initially identified as a transcript selectively expressed by activated T cells. IL-17RA is a ubiquitously expressed and shown to bind IL-17A with an affinity of approximately 0.5 nM (Yao et al., 1995, Immunity 3:811-821). Five additional IL-17-like ligands (IL-17B-IL-17F) and four additional IL-17RA-like receptors (IL-17RB-IL-17RE) have been identified (Kolls and Linden, 2004, Immunity 21:467-476).

[0007] IL-17A and IL-17F bind and activate IL-17RA. IL-17RA has been shown to be important in regulating immune responses. Activation of the IL-17RA leads to production of cytokines, chemokines, growth factors, and other proteins that contribute to the symptoms and/or pathology of numerous diseases. IL-17A is an inflammatory cytokine that induces the production of cytokines and other mediators leading to diseases and physiological effects such as inflammation, cartilage degradation, and bone resorption. IL-17A also plays a role in a number of inflammatory conditions including arthritis (rheumatoid arthritis), psoriasis, inflammatory bowel disease, multiple sclerosis, and asthma. (Li et al., 2004, Huazhong Univ. Sci. Technolog. Med. Sci. 24:294-296; Fujino et al., 2003, Gut. 52:65-70; Kauffman et al., 2004, J. Invest. Dermatol. 123:1037-1044; Mannon et al., 2004, N. Engl. J Med. 351:2069-2079; Matusevicius et al., 1999, Mult Scler 5, 101-104; Linden et al., Eur Respir J. 2000 May;15(5):973-7; Molet et al., 2001, J. Allergy Clin. Immunol. 108:430-438). Recent studies have suggested that IL-17F plays a role in the induction of inflammatory responses (Oda et al., 2006, American J. Resp. Crit. Care Medicine, Jan. 15, 2006; Numasaki et al., 2004, Immunol Lett. 95:97-104).

[0008] There is currently a long-standing unmet need for safe and effective treatments for scalp and nail psoriasis. The invention contemplates treatments of scalp and nail psoriasis using IL-17 Receptor A (IL-17RA or IL-17R) antigen binding proteins, such as the monoclonal antibody brodalumab, as well as other agents that inhibit the IL-17 signaling axis.

SUMMARY OF INVENTION

[0009] The present invention provides the use of an antibody for the preparation of a medicament for the treatment of nail psoriasis, wherein the antibody specifically binds to IL-17 receptor A (IL-17RA) and has an antagonistic activity, wherein the antibody comprises the full length light chain amino acid sequence of SEQ ID NO: 9 and a full length heavy chain amino acid sequence of SEQ ID NO: 10, wherein the medicament comprises the antibody at a dose of 210 mg.

[0009a] In one embodiment, the invention provides methods of treating nail or scalp psoriasis or therapeutic agents for nail or scalp psoriasis comprising administering an IL-17RA antigen binding protein, such as a monoclonal antibody or fragment thereof that specifically binds to the IL-17RA. The

invention provides methods of treating nail or scalp psoriasis or therapeutic agents for nail or scalp psoriasis comprising administering monoclonal antibodies or fragment thereof that specifically bind to the IL-17RA and have antagonistic activities. Such antagonistic activities include inhibiting binding of IL-17A to the IL-17RA. An exemplary monoclonal antibody, known as AM-14 or brodalumab, comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:7 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:8. The full length light chain of brodalumab is set out as the amino acid sequence of SEQ ID NO: 9 and the full length heavy chain of brodalumab is set out as the amino acid sequence of SEQ ID NO: 10. The study described herein demonstrates that brodalumab is more efficacious than a placebo in treating scalp or nail psoriasis after 12 weeks of treatment.

[0010] In another embodiment, the invention also provides for use of an antibody or fragment thereof for the preparation of a medicament for the treatment of nail or scalp psoriasis, wherein the antibody or fragment thereof specifically binds to IL-17RA and has an antagonistic activity. The invention further provides for a composition for use in the treatment of nail or scalp psoriasis, wherein the composition comprises an antibody or fragment thereof that specifically binds to IL-17RA and has an antagonistic activity. Such antagonistic activity includes inhibiting binding of IL-17A to IL-17RA.

[0011] An aspect of the invention is methods of treating nail or scalp psoriasis, or therapeutic agents for nail or scalp psoriasis, comprising administering to a patient having nail or scalp psoriasis a composition comprising an antibody or fragment thereof selected from: an antibody, comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:7 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 8; an antibody comprising the full length light chain of SEQ ID NO: 9 and a full length heavy chain of SEQ ID NO: 10 and an antibody, comprising a light chain CDR1 comprising the amino acid sequence of SEQ ID NO:1, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO:2, a light chain CDR3 comprising the amino acid sequence of SEQ ID NO:3, a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:4, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:5, and a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO:6, wherein said antibody specifically binds to human IL-17RA. For example in the methods of treating nail or scalp psoriasis or therapeutic agents for nail and scalp psoriasis, the monoclonal antibody is a human monoclonal antibody that specifically binds to human IL-17RA and inhibits the binding of IL-17A to said IL-17RA.

What is Claimed:

1. Use of an antibody for the preparation of a medicament for the treatment of nail psoriasis, wherein the antibody specifically binds to IL-17 receptor A (IL-17RA) and has an antagonistic activity, wherein the antibody comprises the full length light chain amino acid sequence of SEQ ID NO: 9 and a full length heavy chain amino acid sequence of SEQ ID NO: 10, wherein the medicament comprises the antibody at a dose of 210 mg.
2. The use of claim 1, wherein the antibody inhibits binding of IL-17A to said IL-17RA.
3. The use of claim 1 or 2, wherein the medicament is to be administered to a patient suffering from psoriasis.
4. The use of any one of claims 1-3, wherein the medicament is to be administered to a patient suffering from plaque psoriasis, pustular psoriasis or psoriatic erythroderma.
5. The use of claim 3 or 4, wherein the patient has a Nail Psoriasis Severity Index (NAPSI) score of at least 6 or a modified NAPSI score of at least 2 or 3 on one or more nails.
6. The use of any one of claims 3-5, wherein the patient has a Psoriasis Scalp Severity Index (PSSI) score of at least 15.
7. The use of any one of claims 3-6, wherein the patient has a Scalp Surface Area (SSA) score of at least 30%.
8. The use of any one of claims 1-7, wherein the medicament is to be administered to a patient having 10% or greater body surface area affected by moderate to severe psoriasis and additionally having nail or scalp psoriasis.
9. The use of any one of claims 1-8, wherein the medicament is to be administered with a second treatment.
10. The use of claim 9, wherein said second treatment is to be administered prior to, concurrent with, or subsequent to administration of said medicament comprising said antibody.
11. The use of claim 9 or 10, wherein the second treatment is a topical treatment.

12. The use of claim 11, wherein the topical treatment is selected from the group consisting fluorouracil, dithranol, tazarotene, cyclosporine, calcineurin inhibitors, triamcinolone, fluocinonide, topical steroids, vitamin D₃, vitamin D₃ analogs, betamethasone dipropionate, betamethasone valerate, calcipotriol, clobetasol, XAMIOL, DAIVOBET, coal tar, urea, corticosteroids, retinoids, anthralin, topical methatrexate, keratolytics, salicylic acid, tofacitinab, apremilast, topical JAK inhibitors or a combination thereof.

13. The use of any one of claims 9-12, wherein the second treatment is selected from the group consisting of retinoids, acitretin cyclosporine, methotrexate, apremilast, tofacitinib, oral JAK inhibitors, oral PI3 kinase inhibitors, oral MAP kinase inhibitors, Fumaderm, fumarates, dimethyl fumarate, sulfasalazine, leflunomide, calcineurin inhibitors, azathioprine, thioguanine, hydroxyurea, hydroxychloroquine, antifungals or a combination thereof.

14. The use of any one of claims 9-13, wherein the second treatment is an antibody or chimeric protein specific for TNF, IL-17, IL-12/23 or IL-23.

15. The use of claim 14, wherein the antibody or chimeric protein is infliximab, adalimumab, etanercept, alefacept, ustekinumab, secukinumab, ixekizumab, guselkumab or a combination thereof.

16. The use of any one of claims 9-15, wherein the second treatment is selected from the group consisting of is triamcinolone acetonide photochemotherapy, laser therapy, Excimer laser, oral/topical psoralen shaving with UVA (PUVA), pulsed dye laser, radiation therapy, superficial radiotherapy, electron beam therapy, Grenz ray therapy, dermatome shaving, aloe vera extract, narrow band UV therapy, UV therapy or a combination thereof.

17. The use of any one of claims 1-16, wherein said medicament further comprises a pharmaceutically acceptable diluent.

18. The use of any one of claims 1-17, wherein said medicament comprises an aqueous solution of a glutamic acid buffer comprising a) said glutamic acid buffer comprises a glutamic acid concentration of 5-30 mM ($\pm$ 0.2 mM); b) said glutamic acid buffer comprises a pH of 4.5-5.2 ($\pm$ 0.2); c) said formulation further comprises 2-4% proline (w/v) and 0.005-0.02% (w/v) polysorbate 20 and d) the antibody or fragment thereof at a concentration of 100 to 150 mg/ml.

19. The use of claim 18, wherein the medicament has an osmolarity of 275 to 325 osm.

20. The use of claim 18 or 19, wherein the medicament has a viscosity of 5 to 7 cP at 25°C.