

was measured at 450 nm using an appropriate Tecan-Sunrise plate reader (Tecan). The antibody binding was proportional to the color signal produced.

Those clones that demonstrated suppression at the level corresponding to that of control Fab antibody AIN457 were marked as positive and used in further tests. Genes of the variable domains of positive clones were subject to sequencing in accordance with standard protocols on *Applied Biosystems 3130 Genetic Analyzer (Applied Biosystems)* followed by the appropriate analysis. Clones comprising 3 VHHPab variable domains were selected for further studies (Figure 7). In addition, it was found that 3VHHPab clone is represented in combination with 23 light chain domains of various sequences, three of which are shown at Figure 8. This indicates its relative structural resistance and the fact that this is VHH domain and not the light chain that contributes to IL-17A binding.

Example 7

Comparative k_{off} (k_{diss})-screening of anti-IL-17A VHHPab candidates

The comparative k_{off} screening for anti-IL-17A Fab-candidates was performed using Pall Forte Bio Octet Red 96 system. Anti-FABCH1 biosensors were rehydrated for 30 min in a working buffer comprising 10 mM PBS (pH 7.2-7.4), 0.1% Tween-20 and 0.1% BSA. 10x working buffer was added to test the samples of *E.coli* supernatants up to 1x of the final concentration. Then anti-FABCH1 biosensors were steeped into *E.coli* supernatants containing Fab-fragments of candidate antibodies and incubated for 12 hours at a temperature of 4°C. Sensors coated with Fab-fragments were transferred to wells with working buffer, and a baseline was registered (60 sec). Then sensors were transferred to wells with analyte solution (IL-17A, 30 µg/ml) to achieve the antigen-antibody association (300 sec). After that, sensors were returned into wells with working buffer for further dissociation (300 sec). The used sensors were subject to regeneration after each test: they were placed three times into regenerating buffer (Gly-HCl, pH 1.7) and then were applicable for use in further experiments. The

curves obtained were analyzed with Octet Data Analysis (version 7.0) according to the standard procedure with 1:1 interaction model.

The results obtained for k_{off} -screening of anti-IL-17A Fab candidates are presented at Figure 9 and Table 1. Specific and high-affine binding of all unique VHHFab with human IL-17A was demonstrated, wherein 3VHHFab showed very fast k_{on} and very slow k_{dis} (1/c) that was beyond the detection limit of the device.

Table 1. VHHFab affinity to human IL-17A

	K_D (M)	k_{on} (1/Mc)	k_{dis} (1/c)
1VHH	2.485E-08	2.498E04	6.206E-04
2VHH	1.352E-08	1.628E05	2.201E-03
3VHHVK4B11	-	-	<2.272E-06

Thus, 3VHHVK4B11 candidate was selected for further investigation based on the analytical results obtained.

Example 8

Generation of VHHIgG1 antibodies with mutations in FR1 and FR2 of VHH variable domain

Genes of the variable domain of the light and heavy VHH chains of 3VHHVK4B11 candidate were cloned in pEE-HcnpEE-Lc plasmid for joint transient expression in CHO-EBNA cells as described in Example 3. Further, substitutes at positions 44 and 45 (Kabat numbering scheme) were introduced by means of oligonucleotide-directed mutagenesis using PfuUltraHS polymerase (Stratagene) in accordance with Protocol [Q5® Site-Directed Mutagenesis Kit (NEB)] and procedure described in [34]. Plasmid pEE-3VHH was used as a matrix. PCR products were fractioned on low-melting agarose and purified on appropriate columns. After ligation, DNA was transformed into *E.coli*. Upon selection of mutant clones with correct sequences, plasmids with mutations in 3VHH were co-transfected with pEE-LcVK4B11(refer to Figure 9 and Table 2).

CLAIMS:

1. A humanized monoclonal IgG antibody that specifically binds to human IL-17A comprising a heavy chain variable domain represented by a V_{HH} -derivative and a light chain variable domain V_L , wherein:

a) the V_{HH} -derivative comprises 3 hypervariable regions HCDR1, HCDR2 and HCDR3, wherein:

HCDR1 comprises the amino acid sequence of SEQ ID NO: 1:

G-T-F-A-T-X32-X33-X34-X35, wherein

X32 is an amino acid selected from the group comprising S, N, K, R, E, W, Q, D, A, V and F;

X33 is an amino acid selected from the group comprising P or S;

X34 is an amino acid selected from the group comprising M and I;

X35 is an amino acid selected from the group comprising G, N, S, A, L, I, R, V and Q;

HCDR2 comprises the amino acid sequence of SEQ ID NO: 2:

X50-I -X52a-S-G-X55-D-R-I-Y-A-D-S-V-K-G, wherein

X50 is an amino acid selected from the group comprising A, G and L;

X52a is an amino acid selected from the group comprising P and A;

X55 is an amino acid selected from the group comprising G, S, T, L, R, D, E, K, A, I and P;

HCDR3 comprises the amino acid sequence of SEQ ID NO: 3:

C-A- X94-X95- X96- X97-F-X99-X100-X100a- X100b - X100c - X100d - X100e - X100f – D- Y – D-S, wherein

X94 is an amino acid selected from the group comprising K, S, T, V, D and G;

X95 is an amino acid selected from the group comprising R and K;

X96 is an amino acid selected from the group comprising G, R, Y, H, D, W and K;

X97 is an amino acid selected from the group comprising R, A, V, S, L and H;
 X99 is an amino acid selected from the group comprising D, E, G, A, R, V, K and Q;
 X100 is an amino acid selected from the group comprising G, S and N;
 X100a is an amino acid selected from the group comprising G, T, P, V, R, N and K;
 X100b is an amino acid selected from the group comprising V, S, T, L, A, H, G, M, C and I;
 X100c is an amino acid selected from the group comprising Y, W and S;
 X100d is an amino acid selected from the group comprising R, V, L, Y, A, W, K, G, Q and I;
 X100e is an amino acid selected from the group comprising T, L, A and S;
 X100f is an amino acid selected from the group comprising T, L, G, P, N, A, Q, F, I and D;

b) the light chain variable domain V_L comprises a variable domain of the light chain of a human antibody or a variable domain of the light chain of a humanized antibody.

2. The antibody according to Claim 1, characterized by increased aggregation stability of V_{HH} -derivative compared to the native VHH antibody isolated from an immunized animal from Camelidae family.

3. The antibody according to Claim 1, wherein the light chain variable domain V_L is the human antibody derivative.

4. The antibody according to Claim 1, wherein the light chain variable domain V_L is the humanized fragment of an antibody, preferably mammalian.
5. The antibody according to Claim 1, wherein said antibody is one of any of the following isotypes: IgG1, IgG2, IgG3 or IgG4.
6. The antibody according to Claim 5, comprising a non-native modified Fc as a part of IgG.
7. The antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >6 months at a temperature of 4°C the content of aggregates increases by not more than 5% of their initial content in the solution.
8. The antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >2 weeks at a temperature of 37°C the content of aggregates increases by not more than 5% of their initial content in the solution.
9. The antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >48h at a temperature of 42°C the content of aggregates increases by not more than 5% of their initial content in the solution.
10. The antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for > 6 h at a temperature of 50°C the content of aggregates increases by not more than 5% of their initial content in the solution.

11. The antibody according to Claims 1-10 that specifically binds to human IL-17A, wherein:

HCDR1 comprises the amino acid sequence of G-T-F-A-T-S-P-M-G (SEQ ID NO: 4);

HCDR2 comprises the amino acid sequence of A-I-S-P-S-G-G- D-R-I-Y- A-D-S-V-K-G (SEQ ID NO: 5);

HCDR3 comprises the amino acid sequence of C-A-V-R-R-R-F-D-G-T-S-Y-Y-T-G-D-Y-D-S (SEQ ID NO: 6).

12. The antibody according to Claim 11 that specifically binds to human IL-17A, wherein the V_{HH} -derivative comprises an amino acid sequence

QVQLVQSGGGLVQAGGSLRLSCAASGGTFATSPMGWLRQAPGKG
TEFVA AISPSGGDRIYADSVKGRFTISRDNAGYFIYLMNSLKPEDTAVYY
C AVR RRF DGTSYYTGDYDSWGQGTLVTVSS (SEQ ID NO: 7).

13. The antibody according to Claim 12 that specifically binds to human IL- 17A, wherein the variable domain of the light chain of the human antibody comprises the amino acid sequence of

EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLL
IYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYSYSPVTFG
Q GTKVEIKR (SEQ ID NO: 8).

14. The antibody according to Claims 1-10 that specifically binds human IL- 17A, wherein:

a) the V_{HH} -derivative comprises the following amino acid sequence:

QVQLVQSGGGLVQAGGSLRLSCAASGGTFATSPMGWLRQAPGKGT
EFVAAISPSGGDRIYADSVKGRFTISRDNAGYFIYLMNSLKPEDTAVYYC
AVRRRFDGTSYYTGDYDSWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG

QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSL
SLSPGK (SEQ ID NO: 9).

b) the variable domain of the light chain of the human antibody comprises the following amino acid sequence:

EIVLTQSPGTL SLSPGERATL SCRASQSVSSSYLAWYQQKPGQAPRL
LIYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYSYSPVTFG
QGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV
DNALQSGNSQESVTEQDSKSTYSLSTLTLSKADYEKHKVYACEVTHQG
LSSPVTKSFNRGEC (SEQ ID NO: 10).

15. The antibody according to Claim 1, wherein said antibody has the binding affinity to human IL-17A characterized with K_D of 10^{-10} M and lower.

16. The antibody according to Claim 1, wherein the kinetic association constant $k_{on}(1/Mc)$ for human IL-17A is not less than 10^5 1/Msec.

17. The antibody according to Claim 1, wherein the kinetic dissociation constant $dis(1/s)$ for human IL-17A is not more than 10^{-5} 1/sec.

18. The antibody according to Claim 1, wherein said antibody inhibits the activity of human IL-17A by no less than 50 %.

19. The antibody according to Claim 1, wherein said antibody is produced by mammalian, yeast or bacterial cells.

20. Fragment of an antibody according to Claims 1- 19, wherein the fragment of an antibody comprises V_{HH} -derivative comprising:

a V_{HH} -derivative comprises 3 hypervariable regions HCDR1, HCDR2 and HCDR3, wherein:

HCDR1 comprises the amino acid sequence of SEQ ID NO: 1:

G-T-F-A-T-X32-X33-X34 - X35, wherein

X32 is an amino acid selected from the group comprising S, N, K, R, E, W, Q, D, A, V and F;

X33 is an amino acid selected from the group comprising P or S;

X34 is an amino acid selected from the group comprising M and I;

X35 is an amino acid selected from the group comprising G, N, S, A, L, I, R, V and Q;

HCDR2 comprises the amino acid sequence of SEQ ID NO: 2:

X50-I-X52a-S-G-X55-D-R-I-Y-A-D-S-V-K-G, wherein

X50 is an amino acid selected from the group comprising A, G and L;

X52a is an amino acid selected from the group comprising P and A;

X55 is an amino acid selected from the group comprising G, S, T, L, R, D, E, K, A, I and P;

HCDR3 comprises the amino acid sequence of SEQ ID NO: 3:

C-A- X94-X95- X96- X97-F-X99-X100-X100a- X100b - X100c - X100d - X100e - X100f – D- Y – D-S, wherein

X94 is an amino acid selected from the group comprising K, S, T, V, D and G;

X95 is an amino acid selected from the group comprising R and K;

X96 is an amino acid selected from the group comprising G, R, Y, H, D, W and K;

X97 is an amino acid selected from the group comprising R, A, V, S, L and H;

X99 is an amino acid selected from the group comprising D, E, G, A, R, V, K and Q;

X100 is an amino acid selected from the group comprising G, S and N;

X100a is an amino acid selected from the group comprising G, T, P, V, R, N and K;

X100b is an amino acid selected from the group comprising V, S, T, L, A, H, G, M, C and I;

X100c is an amino acid selected from the group comprising Y, W and S;
X100d is an amino acid selected from the group comprising R, V, L, Y, A, W, K, G, Q and I;
X100e is an amino acid selected from the group comprising T, L, A and S;
X100f is an amino acid selected from the group comprising T, L, G, P, N, A, Q, F, I and D.

21. Fragment of an antibody according to Claim 20, wherein said fragment is represented by a light chain, heavy chain, and variable domains of the light and/or heavy chain that are a part of an antibody sequence, wherein the heavy chain comprises a first V_{HH} -derivative and the variable domain of the heavy chain is a second V_{HH} -derivative.

22. Fragment of an antibody according to Claim 21, wherein said fragment is represented by a light chain, heavy chain, and variable domains of the light and/or heavy chain that are parts of Fab.

23. Fragment of an antibody according to Claim 21, wherein said fragment is represented by variable domain of the light chain and/or V_{HH} -derivative that are parts of scFv.

24. Methods of production of antibodies according to any of Claims 1 - 19 or fragments thereof according to Claims 20-23, involving phases selected from the following: directed mutagenesis, display methods, genetic engineering, methods for directed mutagenesis at different positions of the VHH domain of Camelidae antibodies.

25. A DNA construct encoding an antibody according to any of Claims 1 - 19 or an antibody fragment according to any of Claims 20-23.

26. An expression vector comprising one or several DNA constructs according to

Claim 25.

27. A cell line comprising the expression vector according to Claim 26 or DNA construct according to Claim 25.

28. Method of production of a humanized monoclonal antibody according to Claims 1- 19 or an antibody fragment according to Claims 20-23, which involves incubation of a cell line according to Claim 27 in a culture medium under the conditions sufficient to obtain said antibody or fragment thereof, followed by the isolation and purification of obtained antibody or its fragment.

29. A host cell comprising the vector according to Claim 26.

30. Method of production of an antibody according to any of Claims 1-19 or an antibody fragment according to Claims 20-23, which involves incubation of a cell line according to Claim 29 in a culture medium under the conditions sufficient to obtain said antibody or fragment thereof, followed by isolation and purification of obtained antibody or its fragment.

31. A pharmaceutical composition comprising an antibody according to any of Claims 1-19 or fragments thereof according to Claims 20-23, in combination with one or several pharmaceutically suitable excipients, diluents or carriers.

32. A pharmaceutical composition according to Claim 31, further comprising TNF- α inhibitors.

33. A pharmaceutical composition according to Claim 31, to be used in the therapy of IL-17A-mediated disease or disorder.

34. A pharmaceutical composition according to Claim 33, wherein an IL-17A-mediated disease or disorder is selected from: rheumatoid arthritis, juvenile chronic

arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, asthma, allergic disorders, psoriasis, dermatitis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, Wegener's disease, uveitis, Schmidt's syndrome, acute respiratory distress syndrome, seronegative arthropathy, arthropathy, psoriatic arthropathy, enteropathic synovitis, atopic allergy, autoimmune bullous disease, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, cranial giant arteritis, cryptogenic autoimmune hepatitis, pulmonary fibrosis, cryptogenic fibrosing alveolitis, systemic scleroderma associated with interstitial lung disease, rheumatoid arthritis associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymyositis associated with lung disease, Sjogren disease associated with lung disease, ankylosing spondylitis associated with lung disease, diffuse pulmonary vasculitis, fibrosis, lung disease with lymphocyte infiltration, autoimmune hepatitis, autoimmune hepatitis type I (classic autoimmune or lupoid hepatitis), autoimmune hepatitis type II (associated with anti-LKM antibody), autoimmune hypoglycemia, acute graft-associated immune disease, chronic graft-associated immune disease, type I psoriasis, type II psoriasis, discoid lupus erythematosus, multiple sclerosis (all types), sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture syndrome, pulmonary manifestations of polyarteritis nodosa, acute rheumatic fever, rheumatoid spondylitis, Still's disease, systemic scleroderma, Sjogren's Syndrome, Takayasu disease/arthritis, autoimmune thrombocytopenia, autoimmune thyroid disorders, vitiligo, acute hepatic disease, idiosyncratic hepatic disease, allergies and asthma, Th1-and Th2-mediated disease, malignancies comprising lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic malignancies (leukemia and lymphomas), acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, adenocarcinoma, allograft rejection, B-cell lymphoma, bone graft rejection, bone marrow transplant (BMT) rejection, Burkitt lymphoma,

inflammatory response to bypass, cartilage graft rejection, chronic myelocytic leukemia (CML), chronic inflammatory pathologies, chronic lymphatic leukemia (CLL), rectocolic carcinoma, cystic fibrosis, cytokine therapy-induced disorders, demyelinating disease, dermatitis, dermatological conditions, any organ or tissue graft rejection, hairy-cell leukemia, heart transplant rejection, Hodgkin disease, idiopathic pulmonary fibrosis, antibody-mediated cytotoxicity, iridocyclitis /uveitis/optic neuritis, juvenile rheumatoid arthritis, renal transplant rejection, liver transplant rejection, lymphoedema, malignant lymphoma, malignant histiocytosis, malignant melanoma, mixed connective-tissue disease, monoclonal gammopathy, multiple myeloma, myelodysplastic syndrome, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, non-Hodgkin's lymphomas, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, Raynaud's phenomenon and disease, sarcoma, scleroderma disease, seronegative arthritis, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, heterograft rejection for any organ or tissue, adult-onset Stills disease, anaphylaxis, antiphospholipid antibody syndrome, aplastic anemia, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus infection, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, bullous pemphigoid, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis, cicatricial pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, erythema multiform, severe erythema multiform, gestational pemphigoid , inflammatory demyelinating disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, keratitis, motor neuron disease, mucosal pemphigoid, non-A, non-B hepatitis, oligoarticular JIA, polyarteritis nodosa, polychondritis, polymyalgia rheumatica, poliosis, polyarticular juvenile idiopathic arthritis, polymyositis, polymyalgia rheumatica (PMR), prostate and rectal cancer and hematopoietic malignancies (leukemia and lymphoma), relapsing

neuromyelitis optica, rheumatic heart disease, SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis), scleroderma, secondary amyloidosis, ankylosing spondylitis, urticaria, vasculitis.

35. Use of a compound comprising an isolated antibody according to Claims 1-19 or fragment thereof according to Claims 20-23 for the treatment of IL-17A-mediated disease or disorder, characterized by its administration of a therapeutically effective amount to a patient who needs such a treatment.

36. Use of a compound comprising an isolated antibody according to Claims 1-19 or fragment thereof according to Claims 20-23 for the treatment of IL-17A-mediated disease or disorder according to Claim 35, wherein an IL-17A-mediated disease or disorder is selected from: rheumatoid arthritis, juvenile chronic arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, asthma, allergic disorders, psoriasis, dermatitis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, Wegener's disease, uveitis, Schmidt's syndrome, acute respiratory distress syndrome, seronegative arthropathy, arthropathy, psoriatic arthropathy, enteropathic synovitis, atopic allergy, autoimmune bullous disease, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, cranial giant arteritis, cryptogenic autoimmune hepatitis, pulmonary fibrosis, cryptogenic fibrosing alveolitis, systemic scleroderma associated with interstitial lung disease, rheumatoid arthritis associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymyositis associated with lung disease, Sjogren disease associated with lung disease, ankylosing spondylitis associated with lung disease, diffuse pulmonary vasculitis, fibrosis, lung disease with lymphocyte infiltration, autoimmune hepatitis, autoimmune hepatitis type I (classic autoimmune or lupoid hepatitis), autoimmune hepatitis type II (associated with anti-LKM antibody), autoimmune hypoglycemia, acute graft-associated immune disease, chronic graft-

associated immune disease, type I psoriasis, type II psoriasis, discoid lupus erythematosus, multiple sclerosis (all types), sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture syndrome, pulmonary manifestations of polyarteritis nodosa, acute rheumatic fever, rheumatoid spondylitis, Still's disease, systemic scleroderma, Sjogren's Syndrome, Takayasu disease/arthritis, autoimmune thrombocytopenia, autoimmune thyroid disorders, vitiligo, acute hepatic disease, idiosyncratic hepatic disease, allergies and asthma, Th1-and Th2-mediated disease, malignancies comprising lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic malignancies (leukemia and lymphomas), acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, adenocarcinoma, allograft rejection, B-cell lymphoma, bone graft rejection, bone marrow transplant (BMT) rejection, Burkitt lymphoma, inflammatory response to bypass, cartilage graft rejection, chronic myelocytic leukemia (CML), chronic inflammatory pathologies, chronic lymphatic leukemia (CLL), rectocolic carcinoma, cystic fibrosis, cytokine therapy-induced disorders, demyelinating disease, dermatitis, dermatological conditions, any organ or tissue graft rejection, hairy-cell leukemia, heart transplant rejection, Hodgkin disease, idiopathic pulmonary fibrosis, antibody-mediated cytotoxicity, iridocyclitis /uveitis/optic neuritis, juvenile rheumatoid arthritis, renal transplant rejection, liver transplant rejection, lymphoedema, malignant lymphoma, malignant histiocytosis, malignant melanoma, mixed connective-tissue disease, monoclonal gammopathy, multiple myeloma, myelodysplastic syndrome, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, non-Hodgkin's lymphomas, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, Raynaud's phenomenon and disease, sarcoma, scleroderma disease, seronegative arthritis, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, heterograft rejection for any organ or tissue, adult-onset Stills disease, anaphylaxis, antiphospholipid antibody syndrome,

aplastic anemia, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus infection, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, bullous pemphigoid, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis, cicatricial pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, erythema multiform, severe erythema multiform, gestational pemphigoid, inflammatory demyelinating disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, keratitis, motor neuron disease, mucosal pemphigoid, non-A, non-B hepatitis, oligoarticular JIA, polyarteritis nodosa, polychondritis, polymyalgia rheumatica, poliosis, polyarticular juvenile idiopathic arthritis, polymyositis, polymyalgia rheumatica (PMR), prostate and rectal cancer and hematopoietic malignancies (leukemia and lymphoma), relapsing neuromyelitis optica, rheumatic heart disease, SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis), scleroderma, secondary amyloidosis, ankylosing spondylitis, urticaria, vasculitis.

37. Use of a compound comprising an isolated antibody according to Claims 1-19 or fragment thereof according to Claims 20-23 for the treatment of IL-17A-mediated disease or disorder according to 36, further comprising the administration of TNF- α inhibitors.