Claims

1. An isolated monoclonal antibody or fragment thereof, containing variable domains of the heavy (VH) and light (VL) chains, wherein said antibody or fragment thereof comprises:

HCDR1 comprising the amino acid sequence of F-T-F-S-N-Y-A-M-S (SEQ ID NO: 7);

HCDR2 comprising the amino acid sequence of R-I-E-G-G-I-S-S-T-Y (SEQ ID NO: 8);

HCDR3 comprising the amino acid sequence of C-A-V-N-Y-Y-G-M-Y-Y (SEQ ID NO: 9);

LCDR1 comprising the amino acid sequence of T-G-T-S-E-D-V-G-F-G-N-Y (SEQ ID NO: 10);

LCDR2 comprising the amino acid sequence of R-V-N-T-R-P-S (SEQ ID NO: 11)

LCDR3 comprising the amino acid sequence of C-S-S-Y-K-A-G-G-T-Y
(SEQ ID NO: 12).

2. An isolated monoclonal antibody or fragment thereof specifically binding to human IL-17A and comprising variable domains of the heavy (VH) and light (VL) chains, wherein the said variable domain of the heavy chain (VH) comprises at least one of the amino acid sequence of SEQ ID NO: 13; the said variable domain of the light chain (VL) comprises at least one of the amino acid sequence of SEQ ID NO: 14.

3. An antibody fragment comprising variable domains according to Claims 1-2, wherein said fragment is selected from F(ab')2, F(ab)2, Fab' and Fab.

4. An antibody fragment comprising variable domains according to Claims 1-2, wherein said fragment is selected from Fv and scFv.

5. An isolated antibody of fragment thereof according to Claims 1-2, wherein said antibody is a humanized antibody or a human antibody.

6. An isolated antibody according to Claims 1-2, wherein said antibody is an IgG1, or IgG2, or IgG3, or IgG4, or IgA or IgD, or IgY.

7. An isolated antibody according to Claims 1-2, wherein said antibody has the binding affinity to human IL-17A characterized with $K_D \leq 10^{-10}$ M.

8. An isolated antibody according to Claims 1-2, wherein the kinetic association constant kon(1/Ms) for human IL-17A is at least 10^5 1/Msec and more.

9. An isolated antibody according to Claims 1-2, wherein said antibody inhibits the activity of human IL-17A by no less than 50%.

10. An isolated antibody according to Claims 1-2, wherein said antibody is produced by mammalian, yeast or bacterial cells.

11. An isolated antibody according to Claims 1-2, wherein said antibody contains additional M252Y/S254T/T256E modifications (amino acid substitution) in Fc-region.

12. An isolated antibody according to Claims 1-2, wherein said antibody contains an additional N434W modification in Fc-region.

13. An isolated antibody according to Claims 1-2, wherein said antibody contains an additional N434A modification in Fc-region.

14. An isolated antibody according to Claims 1-2, wherein said antibody contains an additional N434F modification in Fc-region.

15. An isolated antibody according to Claims 1-2, wherein said antibody contains additional H433K/N434F/Y436H modifications in Fc-region.

16. An isolated antibody according to Claims 1-2, wherein said antibody contains additional H433K/N434F/Y436H+M252Y/S254T/T256E modifications in Fc-region.

17. An isolated antibody according to Claims 1-2, wherein said antibody contains additional T307A/E380A/N434A modifications in Fc-region.

18. An isolated antibody according to Claims 1-2, wherein said antibody contains additional T250Q/M428L modifications in Fc-region.

19. An isolated antibody according to Claims 1-2, wherein said antibody is characterized by the full heavy chain sequence of SEQ ID NO: 15.

20. An isolated antibody according to Claims 1-2, wherein said antibody is characterized by the full light chain sequence of SEQ ID NO: 16.

21. Fab fragment of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

22. Fab’ fragment of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

23. Fv fragment (variable fragment) of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

24. F(ab')2 fragment of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

25. F(ab)2 fragment of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

26. scFv fragment (a single-chain Fv-fragment) of an antibody according to Claims 1-2 produced by mammalian, yeast or bacterial cells.

27. A DNA construct encoding an antibody according to any of Claims 1 – 2 and 5-20 or an antibody fragment according to any of Claims 21 – 26.

28. An expression vector comprising one or several DNAs (DNA constructs, DNA sequences) encoding an antibody according to any of Claims 1 – 2 and 5-20 or an antibody fragment according to any of Claims 21 – 26.

29. A cell line comprising a vector according to Claim 28 for the expression of an antibody according to any of Claims 1 – 2 and 2-20 or an antibody fragment according to any of Claims 21 – 26.

30. Method for the production of a monoclonal antibody according to Claims 1 – 2 and 5-20 or an antibody fragment according to Claims 21 – 26, characterized by culturing host cells according to Claim 29 in a culture medium under conditions suitable to obtain said antibody or fragment thereof, and further isolation and purification of said antibody or fragment thereof.

31. A pharmaceutical composition comprising an antibody according to any of Claims 1 – 2 and 5-20 or fragments thereof according to Claims 21 – 26, in combination with one or several pharmaceutically suitable carriers, vehicles or diluents.

32. A pharmaceutical composition according to Claim 31, to be used in the therapy of IL-17A-mediated disease or disorder, selected from rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, inflammatory bowel disease, asthma, allergic disorders, psoriasis, dermatitis, systemic sclerosis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, atherosclerosis, chronic fatigue syndrome, Wegener's disease, Henoch-Schonlein purpura, microscopic polyangiitis with renal involvement, chronic active hepatitis, uveitis, acute transverse myelitis, primary biliary cirrhosis, malignancies, polyglandular autoimmune syndrome type I and type II, Schmidt's syndrome, seronegative arthropathy, arthropathy, Reiter's syndrome, psoriatic arthropathy, arthropathy

associated with ulcerative colitis, enteropathic synovitis, spondyloarthropathy, atheromatosis disease/coronary sclerosis, atopic allergy, autoimmune bullous disease, pemphigus, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, Coombs positive hemolytic anemia, Myalgic encephalomyelitis/chronic fatigue syndrome, chronic active hepatic inflammation, cranial giant arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, pulmonary fibrosis, cryptogenic fibrosing alveolitis, mixed connective tissue disease associated with interstitial lung disease, systemic scleroderma associated with interstitial lung disease, rheumatoid arthrisit associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymuositis 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, osteoarthrosis, primary sclerosing cholangitis, 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, idiopathic thrombocytopenia, autoimmune thyroid disorders, hyperthyroid, autoimmune hypothyroidism (Hashimoto disease), atrophic autoimmune hypothyroidism, phacogenic uveitis, primary vasculitis, vitiligo, acute hepatic disease, chronic hepatic disease, cholestasis, idiosyncratic hepatic disease, allergies and asthma, Th1- and Th2-mediated disease, malignancies such as lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic malignancies (leukemia and lymphomas), abetalipoproteinaemia, acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, adenocarcinoma, allograft rejection, antiphospholipid syndrome, 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 gammapathy, multiple myeloma, myelodysplastic syndrome, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, neurodegenerative disorders, non-Hodgkin's lymphomas, osteoporosis, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, Raynaud's phenomenon and disease, Raynoud's disease, sarcoma, scleroderma disease, seronegative arthritis, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, a comprehensive systemic inflammatory response syndrome, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, thrombocytopenia, toxicity, grafting, urticaria, heterograft rejection for any organ or tissue, acute coronary syndrome, adult-onset Stills disease, alopecia areata, anaphylaxis, antiphospholipid antibody syndrome, aplastic anemia, coronary sclerosis, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, bullous pemphigoid, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis, cicatrical pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, dermatomyositis, erythema multiform, severe erythema multiform, gestational pemphigoid , inflammatory demyelinating disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, keratitis, Bechterew disease, motor neuron disease, mucosal pemphigoid, non-A, non-B hepatitis, optic neuritis, ovarian cancer, 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, hyperstosis and osteitis), sclerodermia, secondary amyloidosis, ankylosing spondylitis, systemic inflammation response syndrome, cranial arteritis, vasculitis.

33. The use of an isolated antibody according to Claims 1 – 2 and 5-20 or fragment thereof according to Claims 21 – 26 in the manufacture of a medicament for the treatment of IL-17A-mediated disease or

disorder, wherein the medicament comprising a therapeutically effective amount of isolated antibody or fragment thereof is to be adminstered to a patient who needs such a treatment; wherein the IL-17A-mediated disease or disorder is selected from rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, Crohn’s disease, ulcerative colitis, inflammatory bowel disease, asthma, allergic disorders, psoriasis, dermatitis, systemic sclerosis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, atherosclerosis, chronic fatigue syndrome, Wegener's disease, Henoch-Schonlein purpura, microscopic polyangiitis with renal involvement, chronic active hepatitis, uveitis, acute transverse myelitis, primary biliary cirrhosis, malignancies, polyglandular autoimmune syndrome type I and type II, Schmidt's syndrome, seronegative arthropathy, arthropathy, Reiter's syndrome, psoriatic arthropathy, arthropathy associated with ulcerative colitis, enteropathic synovitis, spondyloarthropathy, atheromatosis disease/coronary sclerosis, atopic allergy, autoimmune bullous disease, pemphigus, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, Coombs positive hemolytic anemia, Myalgic encephalomyelitis/chronic fatigue syndrome, chronic active hepatic inflammation, cranial giant arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, pulmonary fibrosis, cryptogenic fibrosing alveolitis, mixed connective tissue disease associated with interstitial lung disease, systemic scleroderma associated with interstitial lung disease, rheumatoid arthrisit associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymuositis 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, osteoarthrosis, primary sclerosing cholangitis, 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, idiopathic thrombocytopenia, autoimmune thyroid

disorders, hyperthyroid, autoimmune hypothyroidism (Hashimoto disease), atrophic autoimmune hypothyroidism, phacogenic uveitis, primary vasculitis, vitiligo, acute hepatic disease, chronic hepatic disease, cholestasis, idiosyncratic hepatic disease, allergies and asthma, Th1- and Th2-mediated disease, malignancies such as lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic malignancies (leukemia and lymphomas), abetalipoproteinaemia, acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, adenocarcinoma, allograft rejection, antiphospholipid syndrome, 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 gammapathy, multiple myeloma, myelodysplastic syndrome, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, neurodegenerative disorders, non-Hodgkin’s lymphomas, osteoporosis, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, Raynaud's phenomenon and disease, Raynoud's disease, sarcoma, scleroderma disease, seronegative arthritis, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, a comprehensive systemic inflammatory response syndrome, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, thrombocytopenia, toxicity, grafting, urticaria, heterograft rejection for any organ or tissue, acute coronary syndrome, adult-onset Stills disease, alopecia areata, anaphylaxis, antiphospholipid antibody syndrome, aplastic anemia, coronary sclerosis, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, bullous pemphigoid, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis, cicatrical pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, dermatomyositis,

erythema multiform, severe erythema multiform, gestational pemphigoid , inflammatory demyelinating disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, keratitis, Bechterew disease, motor neuron disease, mucosal pemphigoid, non-A, non-B hepatitis, optic neuritis, ovarian cancer, 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, hyperstosis and osteitis), sclerodermia, secondary amyloidosis, ankylosing spondylitis, systemic inflammation response syndrome, cranial arteritis, vasculitis.