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(54) **ANTIBODIES FOR IL-17C**

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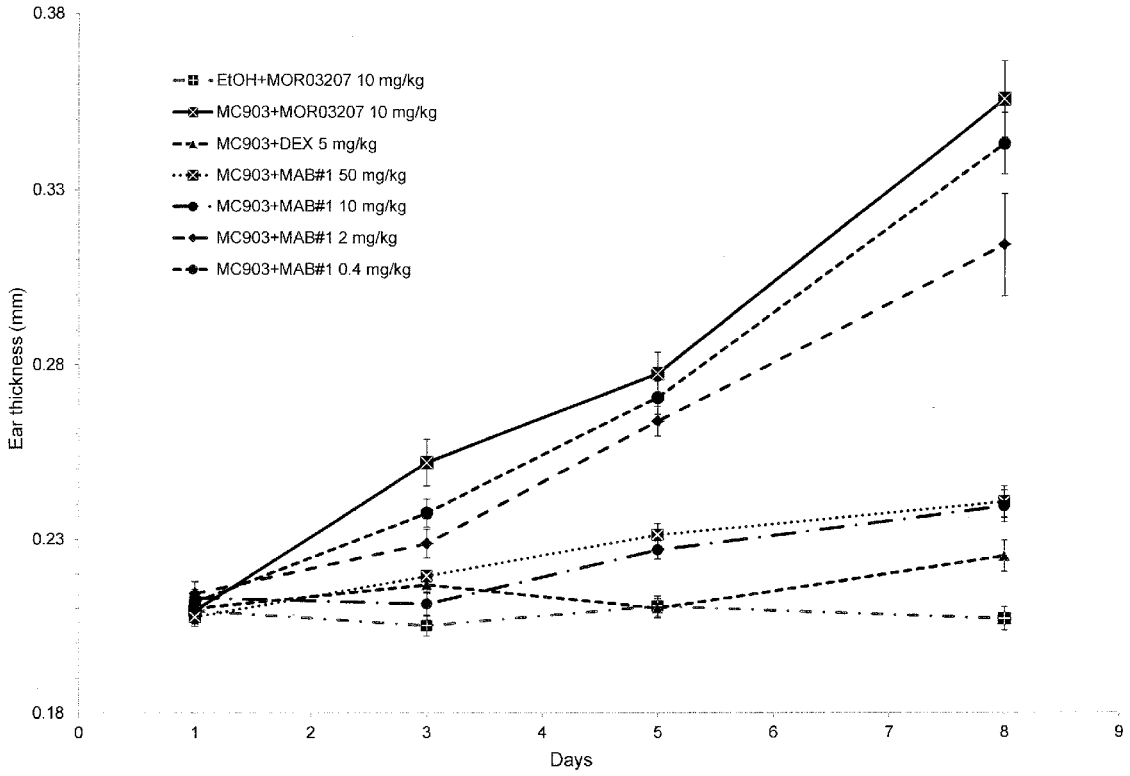
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(57) **ABSTRACT**

The present invention provides antibodies or antibody fragments binding to human IL-17C. In particular, it relates to antibodies or antibody fragments that have combined beneficial properties and are therefore useful for the treatment of humans having, for example, atopic dermatitis or psoriasis.

Specification includes a Sequence Listing.



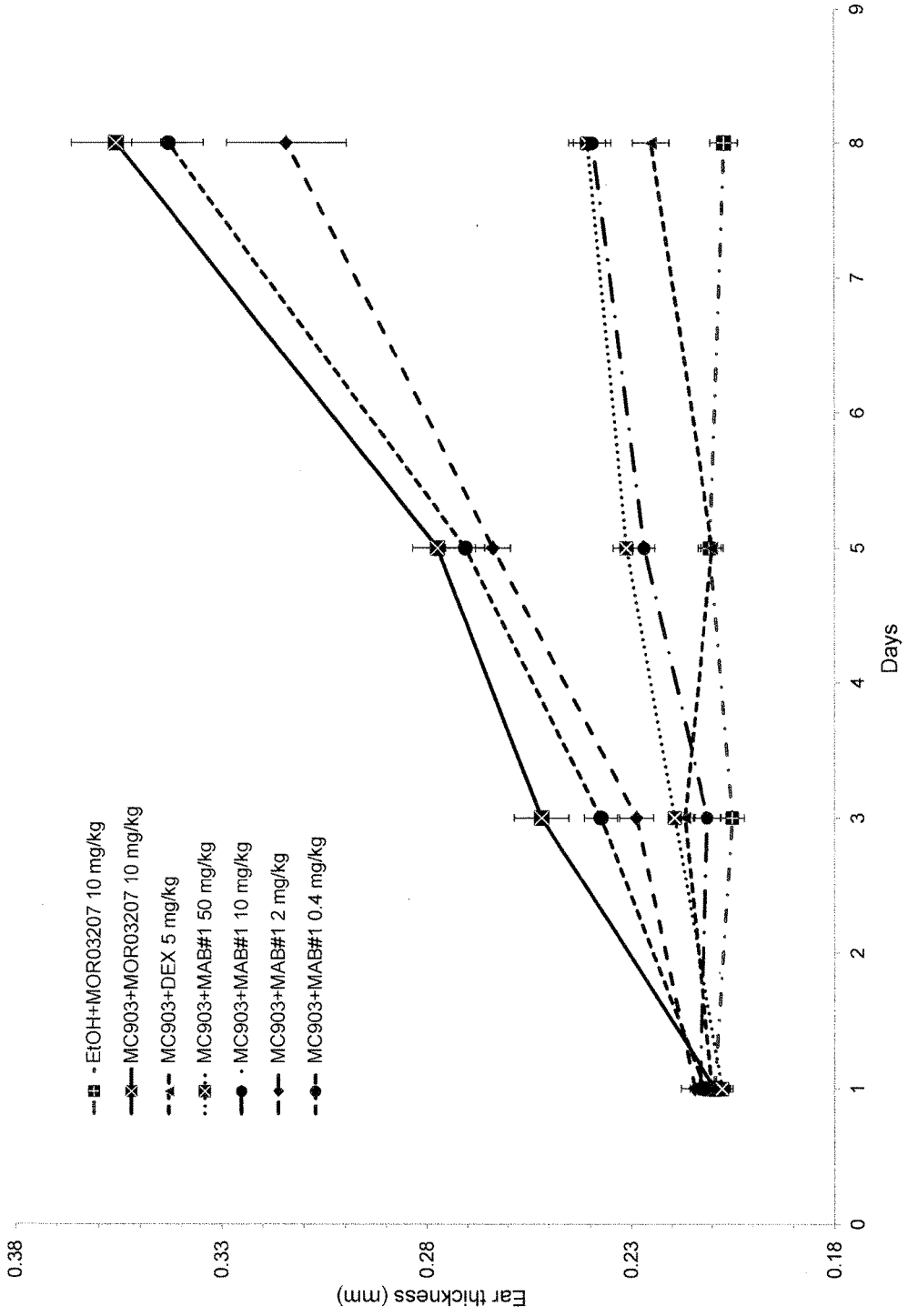

EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 5 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg
Ear thickness (mm)
0.38
0.33
0.28
0.23
0.18
Days
0
1
2
3
4
5
6
7
8
9

Figure 1

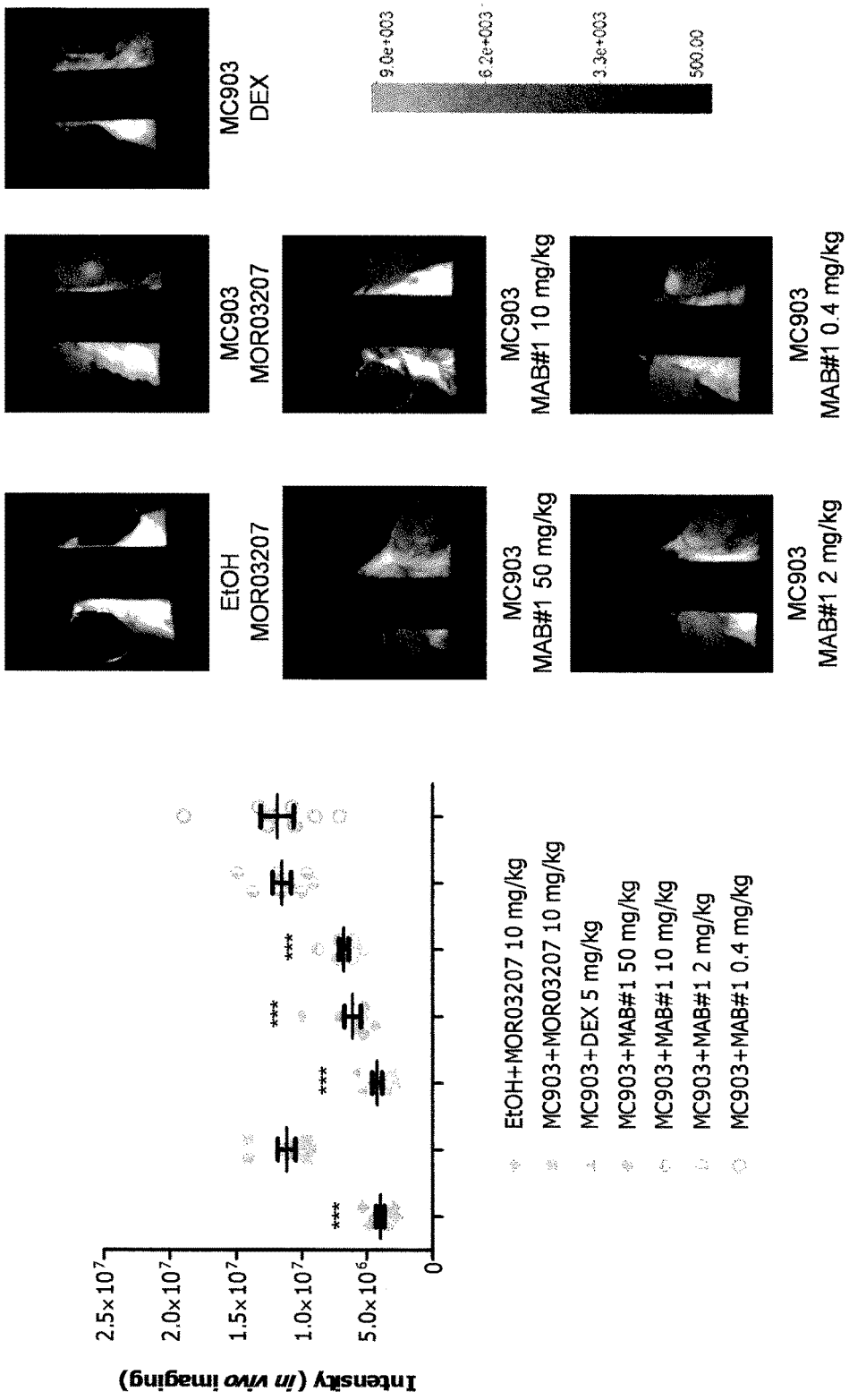

MC903
DEX
9.0e+003
6.2e+003
3.3e+003
500.00
EtOH
MOR03207
MC903
MOR03207
MC903
MAB#1 50 mg/kg
MC903
MAB#1 10 mg/kg
MC903
MAB#1 2 mg/kg
MC903
MAB#1 0.4 mg/kg
Intensity (in vivo imaging)
2.5x10^7
2.0x10^7
1.5x10^7
1.0x10^7
5.0x10^6
0
***
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 5 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg

Figure 2

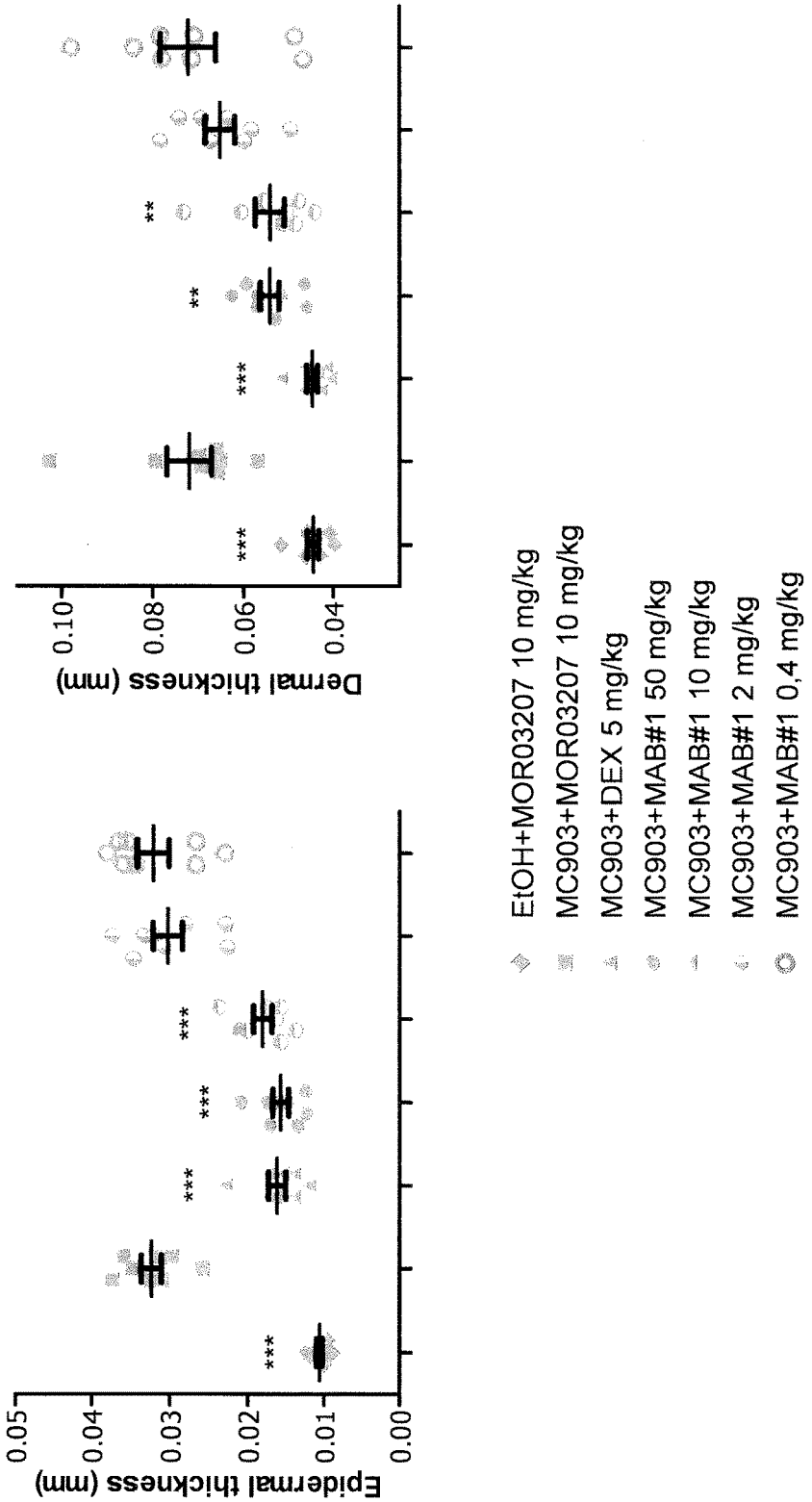

Dermal thickness (mm)
0.10
0.08
0.06
0.04
Epidermal thickness (mm)
0.05
0.04
0.03
0.02
0.01
0.00
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 5 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0,4 mg/kg

Figure 3

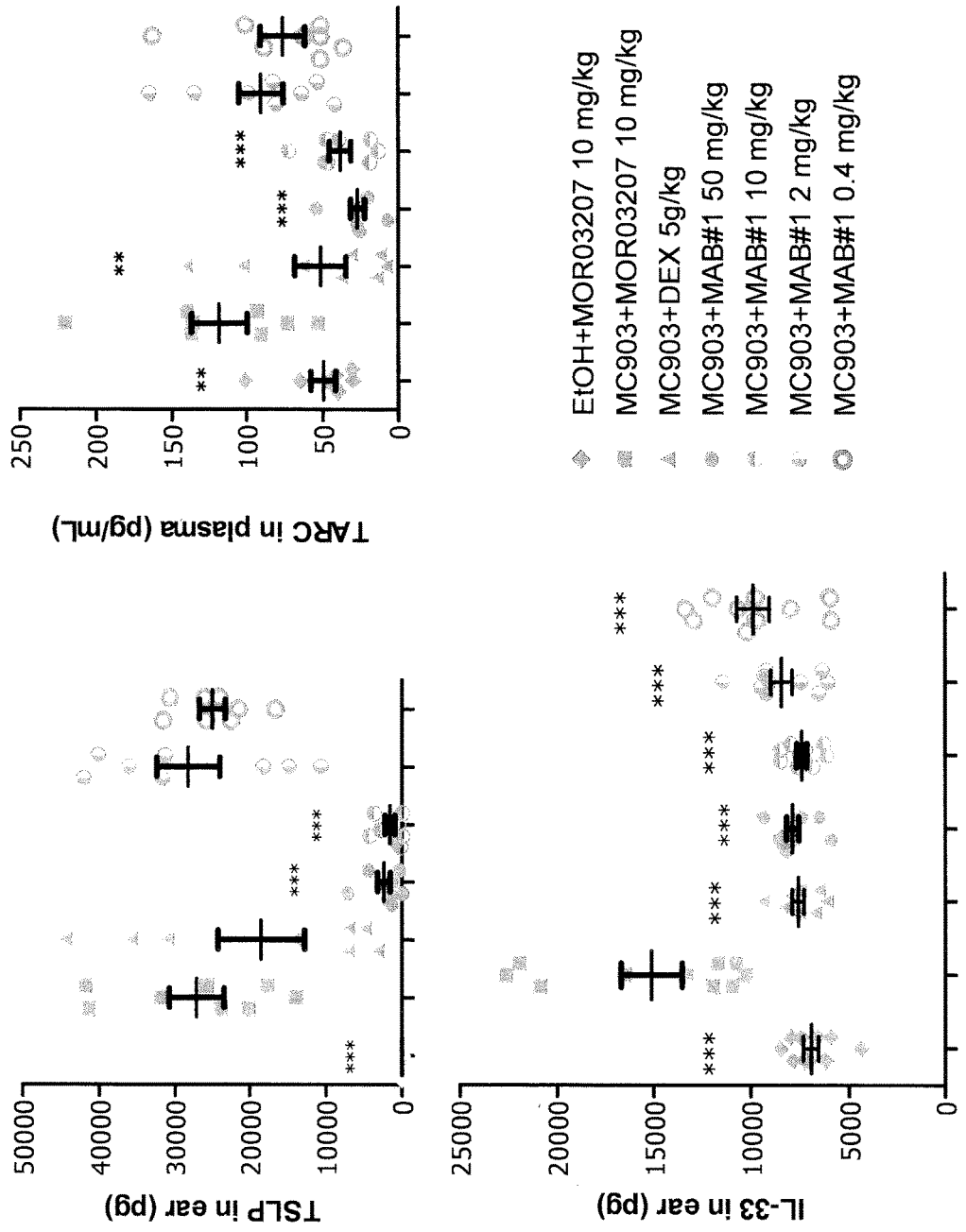

TARC in plasma (pg/mL)
250
200
150
100
50
0
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 5g/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg
TSLP in ear (pg)
50000
40000
30000
20000
10000
0
IL-33 in ear (pg)
25000
20000
15000
10000
5000
0

Figure 4

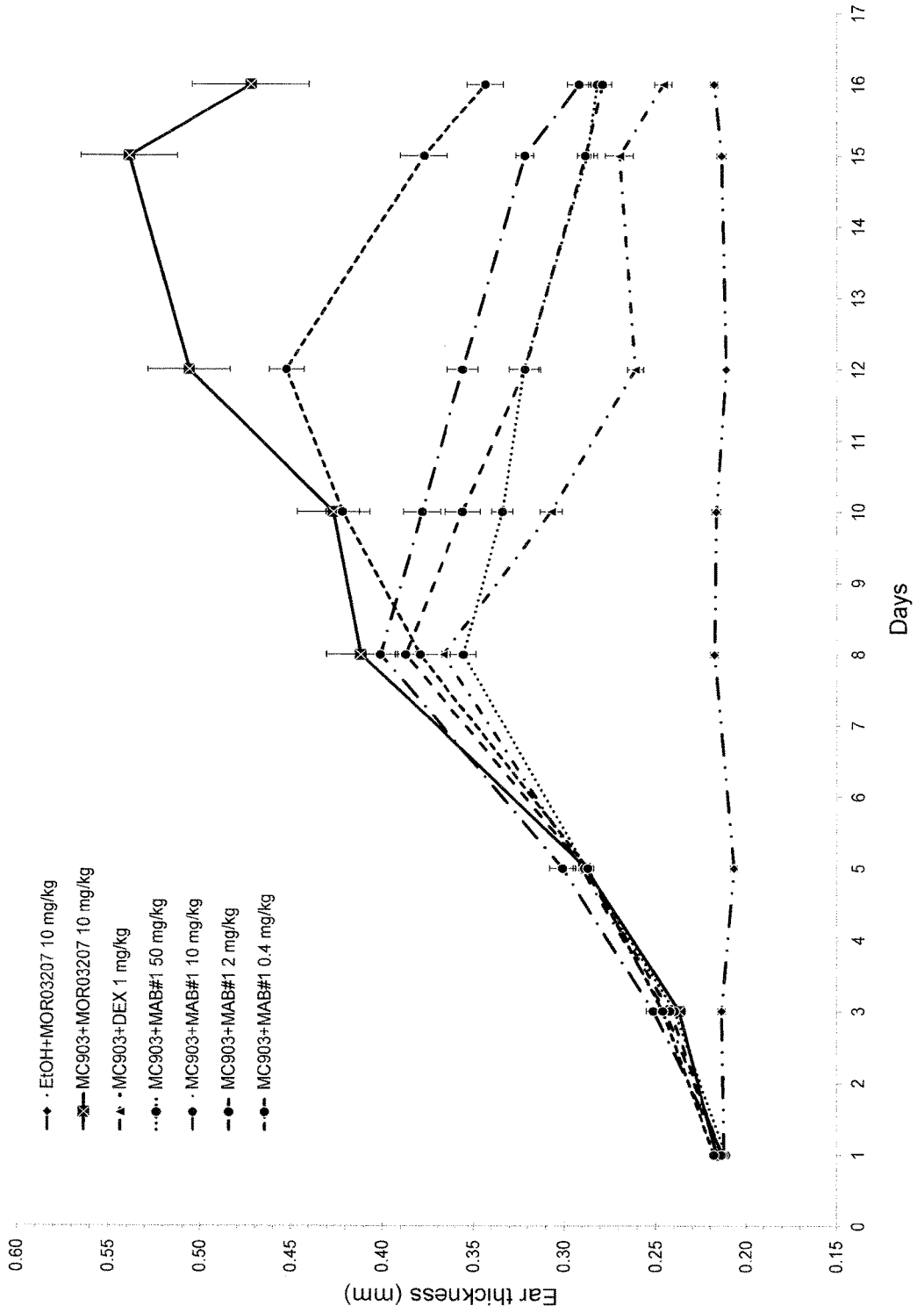

EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 1 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg
Ear thickness (mm)
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
Days
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17

Figure 5

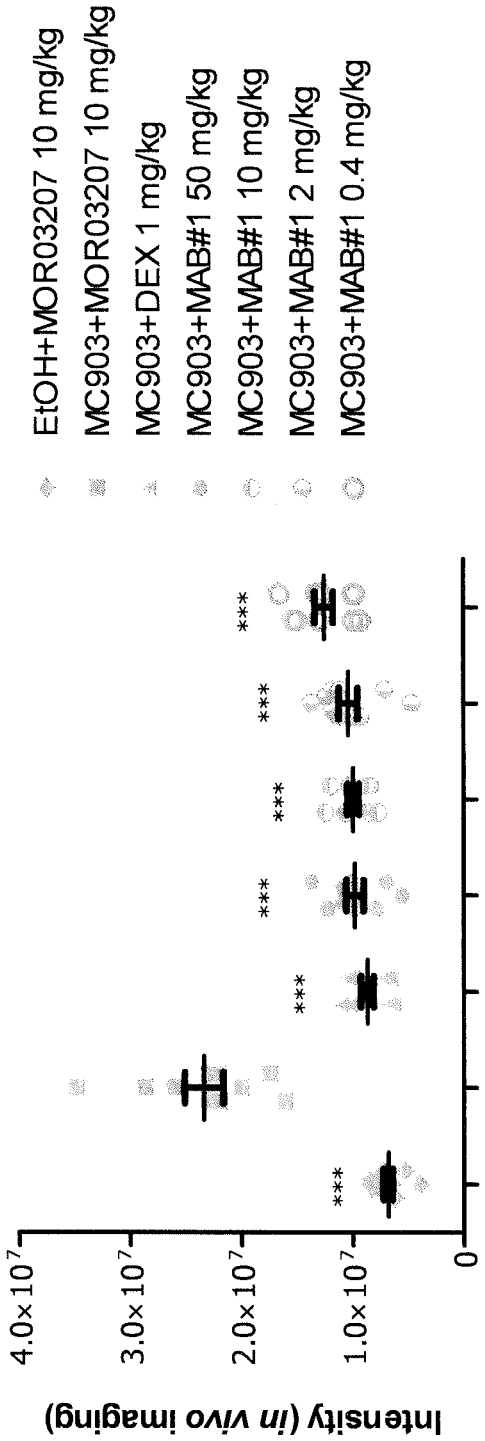

EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 1 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg
***
4.0×10^7
3.0×10^7
2.0×10^7
1.0×10^7
0
Intensity (in vivo imaging)

Figure 6

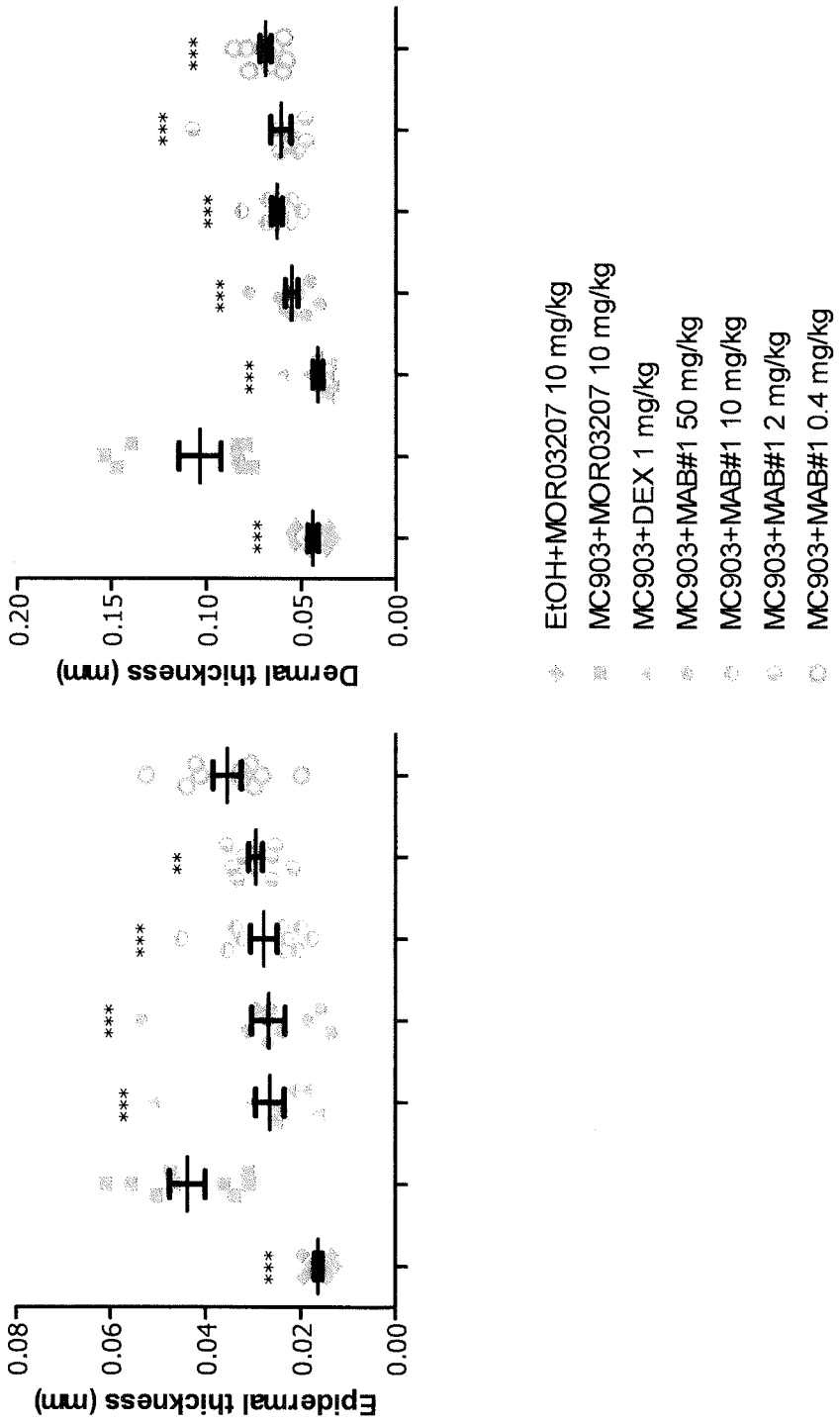

Dermal thickness (mm)
0.20
0.15
0.10
0.05
0.00
Epidermal thickness (mm)
0.08
0.06
0.04
0.02
0.00
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 1 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg

Figure 7

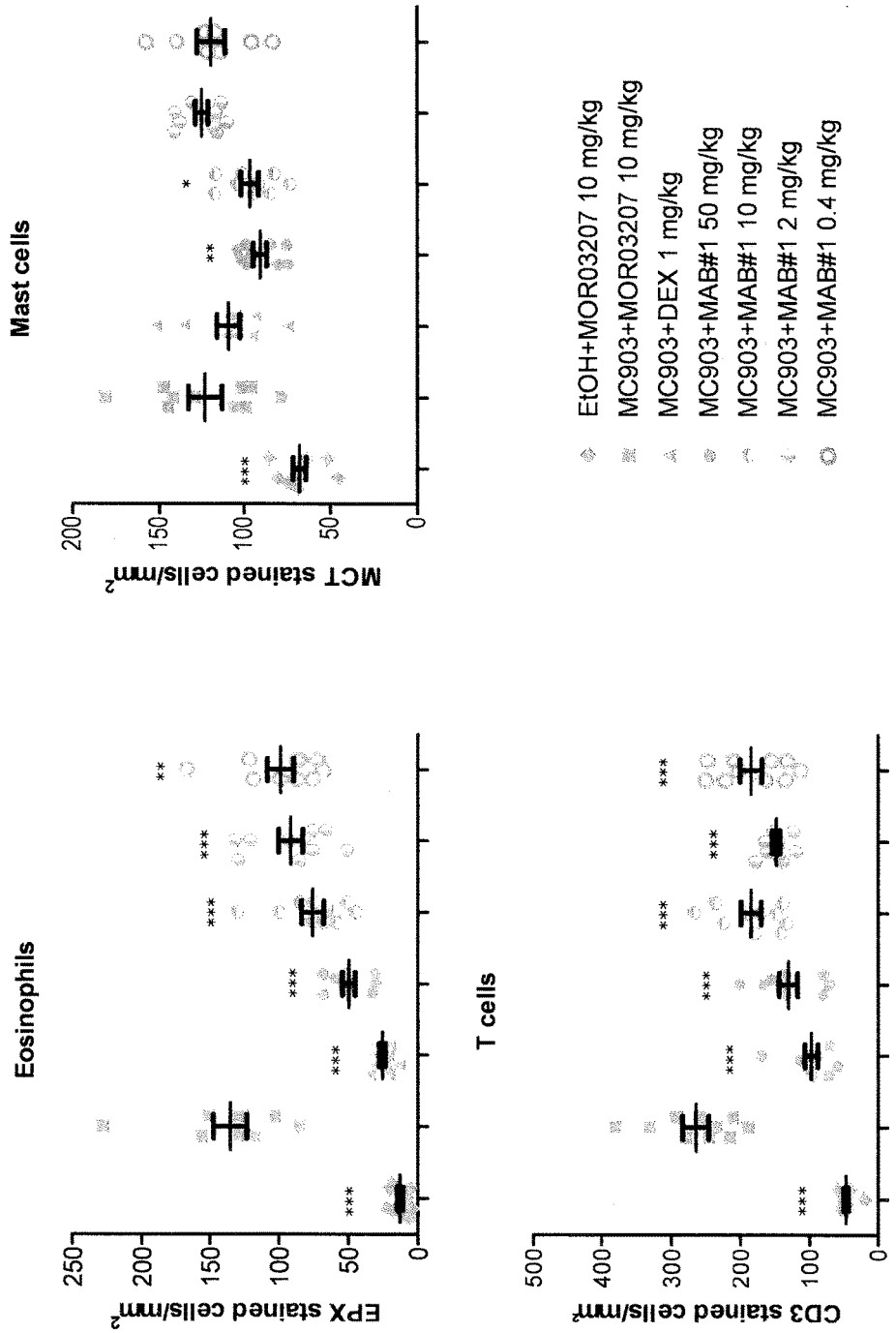

Mast cells
MCT stained cells/mm²
Eosinophils
EPX stained cells/mm²
T cells
CD3 stained cells/mm²
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 1 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg

Figure 8

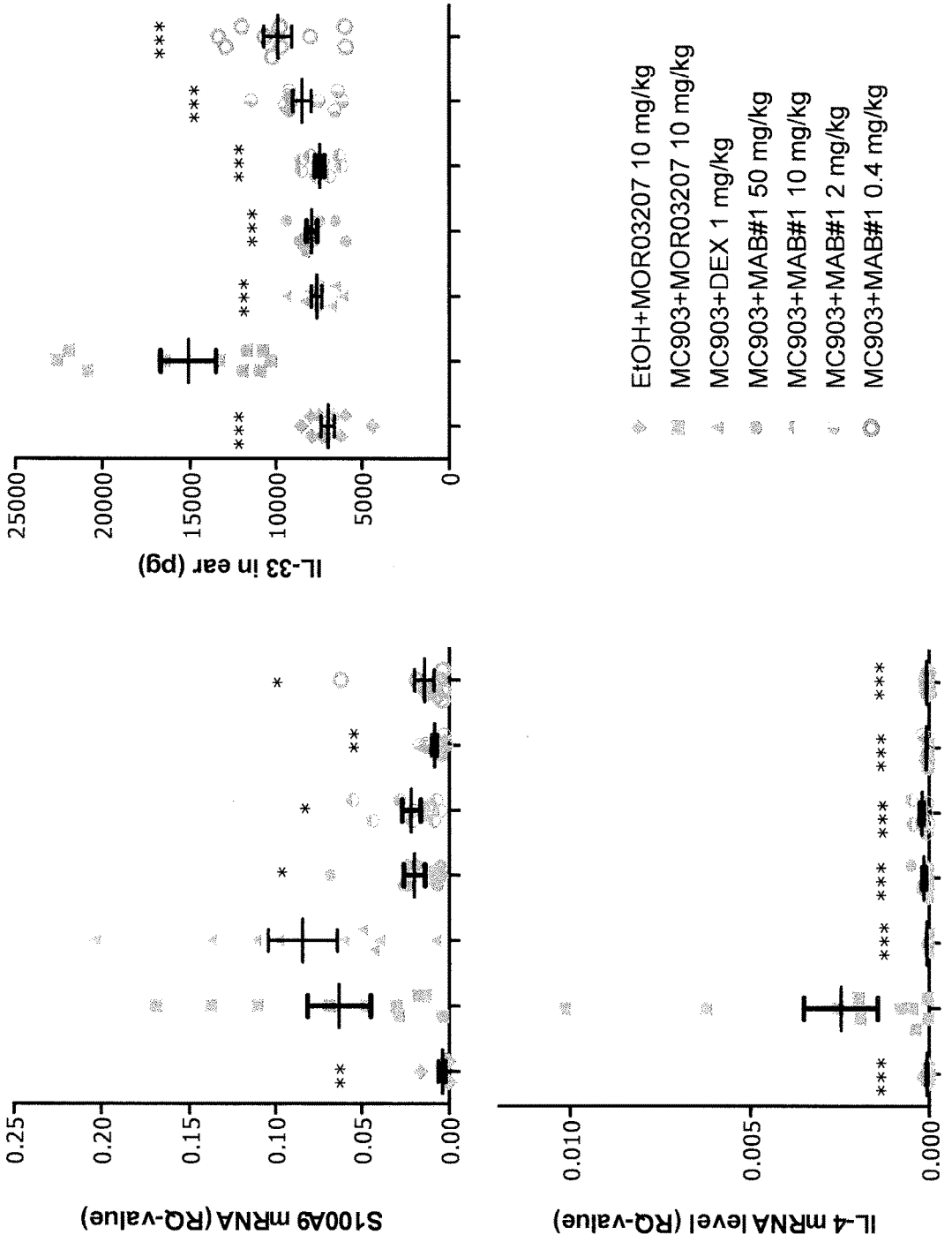

IL-33 in ear (pg)
25000
20000
15000
10000
5000
0
S100A9 mRNA (RQ-value)
0.25
0.20
0.15
0.10
0.05
0.00
IL-4 mRNA level (RQ-value)
0.010
0.005
0.000
EtOH+MOR03207 10 mg/kg
MC903+MOR03207 10 mg/kg
MC903+DEX 1 mg/kg
MC903+MAB#1 50 mg/kg
MC903+MAB#1 10 mg/kg
MC903+MAB#1 2 mg/kg
MC903+MAB#1 0.4 mg/kg

Figure 9

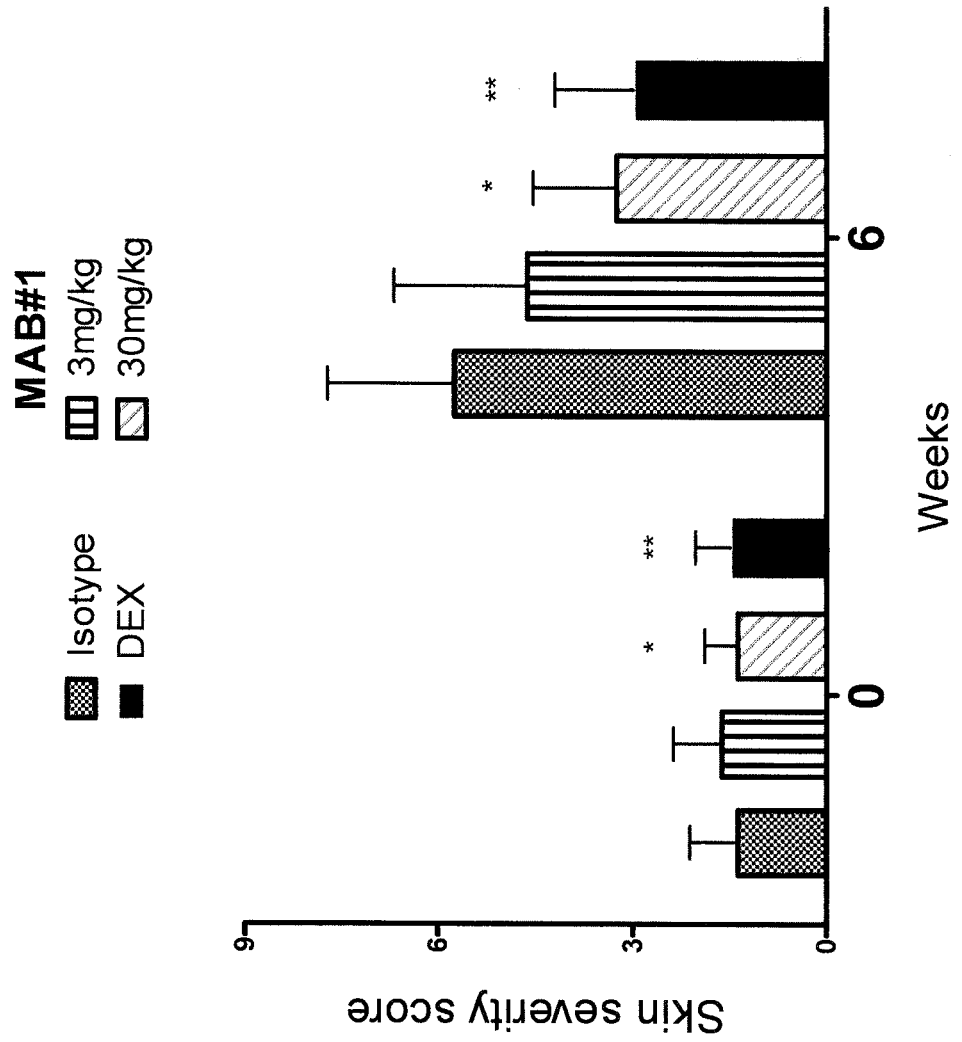

MAB#1
Isotype
DEX
3mg/kg
30mg/kg
Skin severity score
0
3
6
9
0
6
Weeks
*
**
*
**

Figure 10

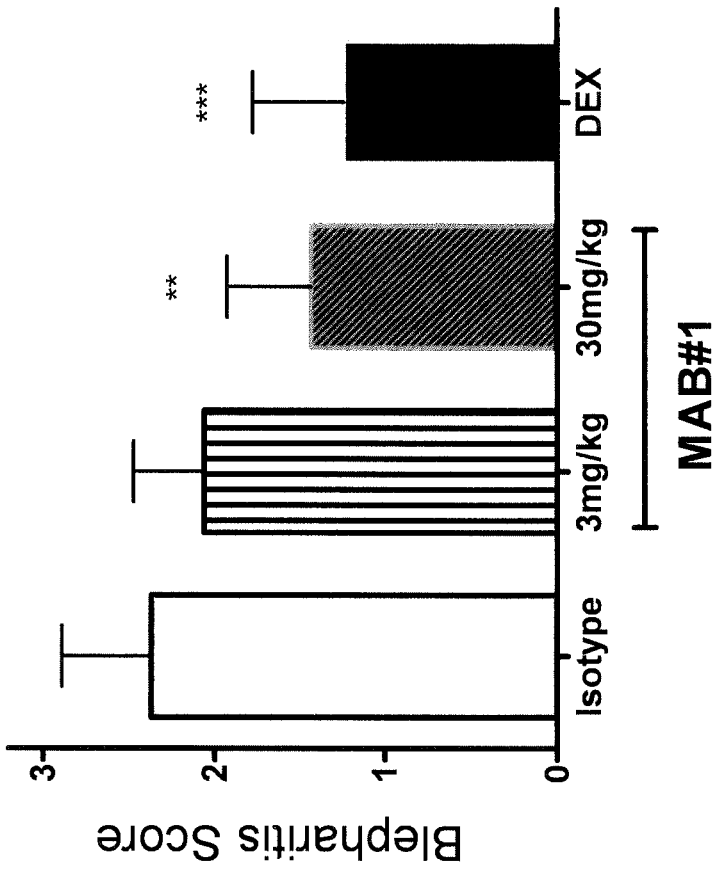


Figure 11

ANTIBODIES FOR IL-17C

FIELD OF THE INVENTION

[0001] The present application relates to antibodies or antibody fragments which interact with human IL-17C. The invention also relates to nucleic acids, vectors and host cells capable of expressing said antibodies or fragments thereof, pharmaceutical compositions comprising said antibodies or fragments thereof and uses of said antibodies or fragments thereof for the treatment of specific diseases.

BACKGROUND

[0002] IL-17C is a secreted homodimer of the IL17 protein family. In vitro it has been shown that IL-17C stimulates the release of TNF-α and IL-1β from the monocytic cell line THP-1 (Li et al. (2000) Proc. Natl. Acad. Sci. U.S.A. 97, 773-8). IL-17C can induce the mRNA expression of inflammatory cytokines such as IL-1β, IL-6 and IL-23 in peritoneal exudates cells (PECS) and the 3T3 cell line (Yamaguchi et al. (2007) J. Immunol 179, 7128-36).

[0003] The role of IL-17C as a proinflammatory cytokine relevant for host defense was postulated in several studies (Chang et al. (2011) Immunity 35, 611-621, Song et al. (2011) Nature Immunology 12, 12, Ramirez-Carrozzi et al. (2011) Nature Immunology 12, 12). Also a potential role in the progression of specific tumours and cancerous tissues was recently shown (Xinyang Song (2014) Immunity 40, 140-152).

[0004] Recently in WO 2013/057241 it was experimentally evaluated that inhibition of IL-17C is a promising approach to treat inflammatory disorders. However, respective antibodies used in WO 2013/057241 were surrogate antibodies specific for mouse IL-17C, but were shown not to be reactive to human IL-17C at all. In addition, further antibodies that antagonize IL-17C were already suggested (e.g. in WO 1999/060127), but are either polyclonal sera or surrogate antibodies which specifically bind to mouse IL-17C only.

[0005] Accordingly, a need exists to study and identify antibodies that bind to human IL-17C to ameliorate IL-17C related diseases or disorders in human.

SUMMARY OF THE INVENTION

[0006] The present disclosure provides novel antibodies and antibody fragments. The antibodies and antibody fragments disclosed herein bind to human IL-17C and also cross-react with IL-17C from the cynomolgus monkey and the mouse. In addition the disclosed antibodies inhibit binding of IL-17C to its receptor throughout the relevant species—human, mouse and cynomolgus monkey—with an IC_{50} concentration of 80 pM or less. As disclosed and exemplified herein, said antibodies proved to be effective in various in vivo mouse models for atopic dermatitis and psoriasis.

[0007] Thus, the disclosed antibodies or antibody fragments are superior in terms of effectiveness and provide well suited and promising compounds for the treatment of humans having, for example; atopic dermatitis or psoriasis.

[0008] The present disclosure provides antibodies or antibody fragments that bind to human IL-17C having CDR regions according to Table 1 of the present specification. The present disclosure also provides specific antibodies or antibody fragments having a variable heavy chain region and a variable light chain CDR regions comprising the amino acid sequences according to Table 1 of the present specification.

[0009] The present disclosure also provides specific antibodies or antibody fragments which compete with the specific antibodies or antibody fragments disclosed herein. The present disclosure also provides specific antibodies or antibody fragments which bind to the same epitope as the specific antibodies or antibody fragments disclosed herein.

[0010] The present disclosure also provides the isolated antibodies or antibody fragments of the present disclosure for use in medicine.

[0011] The present disclosure also provides also provides methods for treating a subject suffering from a disorder, such as an inflammatory disorder, by administering to said subject an effective amount of the antibodies or antibody fragments of the present disclosure. Preferably said subject is a human.

[0012] The present disclosure also provides pharmaceutical compositions comprising the isolated antibodies or antibody fragments of the present disclosure, and a pharmaceutically acceptable carrier.

[0013] The present disclosure also provides nucleic acids encoding the antibodies or antibody fragments of the present disclosure.

[0014] The present disclosure also provides vectors comprising nucleic acids encoding the antibodies or antibody fragment antibodies of the present disclosure.

[0015] The present disclosure also provides host cell comprising vector or nucleic acids encoding the antibodies or antibody fragments of the present disclosure.

[0016] There is utility in the claimed antibodies or antibody fragments. Furthermore, there is utility in the claimed method to identify such antibodies or fragments.

[0017] Utilization of the claimed antibodies or antibody fragments is to alter the biological activity of human IL-17C. In particular the claimed antibodies or antibody fragments are for therapeutic use, such as the treatment of inflammatory disorders like e.g. rheumatoid arthritis, psoriasis, pulmonary inflammation, COPD and/or the treatment of atopic dermatitis (AD), including moderate-to-severe AD.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] FIG. **1**: MAB#1 dose-dependently prevents the ear thickening induced by topical application of MC903 on ear skin.

[0019] Data are expressed as mean values±standard error of the mean (SEM) (n=8 per group). Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. (DEX: dexamethasone; EtOH: ethanol)

[0020] FIG. **2**: MAB#1 dose-dependently reduces the ear inflammation induced by topical application of MC903 on ear skin.

[0021] Ear inflammation was assessed at Day 5 using in vivo imaging. Left panel: quantification of signal intensity in ears. Individual data points (n=8 per group) represent the average intensity of both ears; data are also shown as mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Right panel: representative images of mouse ears from animals from different treatment groups were acquired on the Bruker in-vivo Xtreme Imager 24 h after injection of the Prosense 680 probe. (DEX: dexamethasone; EtOH: ethanol)

[0022] FIG. **3**: MAB#1 dose-dependently reduces the thickening of epidermal and dermal skin layer induced by topical application of MC903 on ear skin.

[0023] Data are presented as individual data points (n=8 per group) and mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Left panel: data for epidermal thickness; Right panel: data for dermal thickness.

[0024] FIG. **4**: MAB#1 dose-dependently inhibits the MC903-mediated increase in TSLP and IL-33 expression in ear and TARC levels in plasma.

[0025] Data are presented as individual data points (n=8 per group) and mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 group was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Top left panel: data for TSLP protein expression in ear; Bottom left panel: data for IL-33 protein expression in ear; Top right panel: data for TARC protein levels in plasma.

[0026] FIG. **5**: Therapeutic administration of MAB#1 dose-dependently reduces the ear thickening induced by topical application of MC903 on ear skin.

[0027] Data are expressed as mean values±SEM (n=10 per group). Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. DEX: dexamethasone; EtOH: ethanol.

[0028] FIG. **6**: Therapeutic administration of MAB#1 dose-dependently reduces the ear inflammation induced by topical application of MC903 on ear skin.

[0029] Ear inflammation was assessed at Day 12 using in vivo imaging and the signal intensity in ears is graphically represented. Individual data points (n=10 per group) represent the average intensity of both ears; data are also shown as mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. DEX: dexamethasone; EtOH: ethanol.

[0030] FIG. **7**: Therapeutic administration of MAB#1 dose-dependently reduces the thickening of epidermal and dermal skin layer induced by topical administration of MC903 on ear skin.

[0031] Data are presented as individual data points (n=10 per group) and mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Left panel: data for epidermal thickness; Right panel: data for dermal thickness. DEX: dexamethasone; EtOH: ethanol.

[0032] FIG. **8**: Therapeutic administration of MAB#1 dose-dependently reduces the dermal infiltration of eosinophils, T cells and mast cells.

[0033] Data are presented as individual data points (n=10 per group) and mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Top left panel: data for eosinophils; Top right panel: data for mast cells; Bottom left panel: data for T cells. DEX: dexamethasone; EtOH: ethanol.

[0034] FIG. **9**: Therapeutic administration of MAB#1 reduces expression of IL-33, IL-4 and S100A9, which were still increased at Day 16 (11 days after stopping MC903 application).

[0035] Data are presented as individual data points (n=10 per group) and mean values (horizontal lines)±SEM. Statistical significance versus MC903+MOR03207 group was calculated using ANOVA and Dunnett's multiple comparison test: *p<0.05; **p<0.01; ***p<0.001. Top left panel: data for S100A9 mRNA expression in ear; Bottom left panel: data for IL-4 mRNA expression in ear; Top right panel: data for IL-33 protein levels in ear.

[0036] FIG. **10**: MAB#1 reduces macroscopic clinical signs of AD-like inflammation in the spontaneous & chronic Flaky Tail model

[0037] Clinical scoring of cutaneous inflammation for each mouse was done at start (week 0) and at end (week 6) of treatment. Data are the mean±SD for each treatment group (n=8 per group). Statistical significance versus the isotype antibody treated group was calculated using ANOVA and Dunnett's multiple comparison test (*p<0.05; **p<0.01; ***p<0.001).

[0038] FIG. **11**: MAB#1 reduces eczematous-like eyelid inflammation in the spontaneous & chronic Flaky Tail model.

[0039] Skin eyelid inflammation was scored at end of the treatment (week 6). Data are the mean t SD for each treatment group (n=8 per group). Statistical significance versus the isotype antibody treated group was calculated using ANOVA and Dunnett's multiple comparison test (*p<0.05; **p<0.01; ***p<0.001).

DETAILED DESCRIPTION OF THE INVENTION

[0040] The disclosure pertains to a number of antibodies or antibody fragments that recognize human IL-17C.

Definitions

[0041] The term "IL-17C" refers to a protein known as interleukin 17C,

Human IL-17C has the amino acid sequence of (UniProt Q9P0M4):

(SEQ ID No.: 1)

MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLA

RGAKWGQALPVALVSSLEAASHRGRHERPSATTQCPVLRPEEVLEADTHQR

SISPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTGRETAALNSVRLLQSLLV

LRRRPCSRDGSGLPTPGAFAFHTEFIHVPVGCTCVLPRSV

-continued

Mouse IL-17C has the amino acid sequence of (UniProt Q8K4C5):

(SEQ ID No.: 2)

MSLLLLGWLPTGMTHQDPPSWGKPRSHRTLRCYSAEELSHGQAPPHLLTRS

ARWEQALPVALVASLEATGHRRQHEGPLAGTQCPVLRPEEVLEADTHERSIS

PWRYRIDTDENRYPQKLAVAECLCRGCINAKTGRETAALNSVQLLQSLLVLRR

QPCSRDGTADPTPGSFAFHTEFIRVPVGCTCVLPRSTQ

Cynomolgus monkey IL-17C has the amino acid sequence of (XP_005592825.1):

(SEQ ID No.: 3)

MTLLPGLLFLTWLHACLAHQDPFLRGHPHTHGTPRCYSAEELPLGQAPPHLLA

RGAKWGQALPVALVSSLEAAGHRRRHDRPSAATQCPVLRPEEVLEADTHQR

SISPWRYRVDTDEDRYPQKLAFAECLCRGCIDPRTGRETAALNSVRLLQSLLV

LRRRPCSRDGSGLPTPGAFAFHTEFIRVPVGCTCVLPRSV

The term "IL17RA" refers to a protein known as interleukin 17 receptor A. Human IL17RA has the amino acid sequence of (UniProt Q96F46):

(SEQ ID No.: 4)

MGAARSPPSAVPGPLLGLLLLLLGVLAPGGASLRLLDHRALVCSQPGLNCTVKNSTC

LDDSWIHPRNLTPSSPKDLQIQLHFAHTQQGDLFPVAHIEVVTLQTDASILYLEGAELS

VLQLNTNERLCVRFEFLSKLRHHHRRWRFTFSHFWDPDQEYEVTVHHLPKPIPDG

DPNHQSKNFLVPDCEHARMKVTTPCMSSGSLWDPNITVETLEAHQLRVSFTLWNES

THYQILLTSFPHMENHSCFEHMHHIPAPRPEEFHQRSNVTLTLRNLKGCCRHQVQ1Q

PFFSSCLNDCLRHSATVSCPEMPDTPEPIPDYMPLWVYWFITGISILLVGSVILLIVCM

TWRLAGPGSEKYSDDTKYTDGLPAADLIPPPLKPRKVINIIYSADHPLYVDVVLKFAQ

FLLTACGTEVALDLLEEQAISEAGVMTWVGRQKQEMVESNSKIIVLCSRGTRAKWQ

ALLGRGAPVRLRCDHGKPVGDLFTAAMNMILPDFKRPACFGTYVVCYFSEVSCDGD

VPDLFGAAPRYPLMDRFEEVYFRIQDLEMFQPGRMHRVGELSGDNYLRSPGGRQL

RAALDRFRDWQVRCPDWFECENLYSADDQDAPSLDEEVFEEPLLPPGTGIVKRAPL

VREPGSQACLAIDPLVGEEGGAAVAKLEPHLQPRGQPAPQPLHTLVLAAEEGALVA

AVEPGPLADGAAVRLALAGEGEACPLLGSPGAGRNSVLFLPVDPEDSPLGSSTPMA

SPDLLPEDVREHLEGLMLSLFEQSLSCQAQGGCSRPAMVLTDPHTPYEEEQRQSV

QSDQGYISRSSPQPPEGLTEMEEEEEEEQDPGKPALPLSPEDLESLRSLQRQLLFR

QLQKNSGWDTMGSESEGPSA

The term "IL17RE" refers to a protein known as interleukin 17 receptor E. Human IL17RE has the amino acid sequence of (UniProt Q8NFR9):

(SEQ ID No.: 5)

MGSSRLAALLLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFTGSSAYIPCRT

WWALFSTKPWCVRVWHCSRCLCQHLLSGGSGLQRGLFHLLVQKSKKSSTFKFYRR

HKMPAPAQRKLLPRRHLSEKSHHISIPSPDISHKGLRSKRTQPSDPETWESLPRLDS

QRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECEELSSPYDVQKIVSGG

HTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQH

TQMVMALTLRCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQL

CFKFSFGNSSHVECPHQTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPG

LGQDTLVPPVYTVSQARGSSPVSLDLIIPFLRPGCCVLVWRSDVQFAWKHLLCPDVS

YRHLGLLILALLALLTLLGVVLALTCRRPQSGPGPARPVLLLHAADSEAQRRLVGALA

ELLRAALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLWSGADL

-continued

RPVSGPDPRAAPLLALLHAAPRPLLLLAYFSRLCAKGDIPPPLRALPRYRLLRDLPRL

LRALDARPFAEATSWGRLGARQRRQSRLELCSRLEREAARLADLG

Murine IL17RE has the amino acid sequence of (UniProt Q8BH06):

(SEQ ID No.: 6)

MGSPRLAALLLSLPLLLIGLAVSARVACPCLRSWISHCLLAYRVDKRFAGLQWGWF

PLLVRKSKSPPKFEDYWRHRTPASFQRKLLGSPSLSEESHRISIPSSAISHRGQRTK

RAQPSAAEGREHLPEAGSQKCGGPEFSFDLLPEVQAVRVTIPAGPKASVRLCYQW

ALECEDLSSPFDTQKIVSGGHTVDLPYEFLLPCMCIEASYLQEDIVRRKKCPFQSWP

EAYGSDFWQSIRFTDYSQHNQMVMALTLRCPLKLEASLCWRQDPLTPCETLPNATA

QESEGWYILENVDLHPQLCFKFSFENSSHVECPHQSGSLPSWTVSMDTQAQQLTL

HFSSRTYATFSAAWSDPGLGPDTPMPPVYSISQTQGSVPVTLDLIIPFLRQENCILVW

RSDVHFAWKHVLCPDVSHRHLGLLILALLALTALVGVVLVLLGRRLLPGSGRTRPVLL

LHAADSEAQRRLVGALAELLRTALGGGRDVIVDLWEGTHVARIGPLPWLWAARERV

AREQGTVLLLWNCAGPSTACSGDPQAASLRTLLCAAPRPLLLAYFSRLCAKGDIPRP

LRALPRYRLLRDLPRLLRALDAQPATLASSWSHLGAKRCLKNRLEQCHLLELEAAKD

DYQGSTNSPCGFSCL

[0042] The terms "antagonist of IL-17C" and an "IL-17C antagonist", are used interchangeably herein and refer to any molecule which inhibits the activity or function of IL-17C. The term "IL-17C antagonist" includes, but is not limited to, antibodies or antibody fragments specifically binding to IL-17C. Preferably, an IL-17C antagonist in the present disclosure is an antibody specific for human IL-17C. Such an antibody may be of any type, such as a murine, a rat, a chimeric, a humanized or a human antibody.

[0043] The term "antibody" as used herein refers to a protein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds which interacts with an antigen. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FR's arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (Clq) of the classical complement system. The term "antibody" includes for example, monoclonal antibodies, human antibodies, humanized antibodies, camelised antibodies and chimeric antibodies. The antibodies can be of any isotype (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass. Both the light and heavy chains are divided into regions of structural and functional homology.

[0044] The phrase "antibody fragment", as used herein, refers to one or more portions of an antibody that retain the ability to specifically interact with (e.g., by binding, steric hindrance, stabilizing spatial distribution) an antigen. Examples of binding fragments include, but are not limited to, a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a F(ab)2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the VH and CH1 domains; a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; a dAb fragment (Ward et al., (1989) Nature 341:544-546), which consists of a VH domain; and an isolated complementarity determining region (CDR). Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al., (1988) Science 242:423-426; and Huston et al., (1988) Proc. Natl. Acad. Sci. 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term "antibody fragment". These antibody fragments are obtained using conventional techniques known to those of skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies. Antibody fragments can also be incorporated into single domain antibodies, maxibodies, minibodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, (2005) Nature Biotechnology 23:1126-1136). Antibody fragments can be grafted into scaffolds based on polypeptides such as Fibronectin type III (Fn3) (see U.S. Pat. No. 6,703,199, which describes fibronectin polypeptide monobodies). Antibody fragments can be incorporated into single chain molecules comprising a pair of tandem Fv segments

(VH-CH1-VH-CH1) which, together with complementary light chain polypeptides, form a pair of antigen-binding sites (Zapata et al., (1995) Protein Eng. 8:1057-1062; and U.S. Pat. No. 5,641,870).

[0045] A "human antibody" or "human antibody fragment", as used herein, includes antibodies and antibody fragments having variable regions in which both the framework and CDR regions are derived from sequences of human origin. Furthermore, if the antibody contains a constant region, the constant region also is derived from such sequences. Human origin includes, e.g., human germline sequences, or mutated versions of human germline sequences or antibody containing consensus framework sequences derived from human framework sequences analysis, for example, as described in Knappik et al., (2000) J Mol Biol 296:57-86).

[0046] The structures and locations of immunoglobulin variable domains, e.g., CDRs, may be defined using well known numbering schemes, e.g., the Kabat numbering scheme, the Chothia numbering scheme, or a combination of Kabat and Chothia (see, e.g., Sequences of Proteins of Immunological Interest, U.S. Department of Health and Human Services (1991), eds. Kabat et al.; Lazikani et al., (1997) J. Mol. Bio. 273:927-948); Kabat et al., (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services; Chothia et al., (1987) J. Mol. Biol. 196: 901-917; Chothia et al., (1989) Nature 342:877-883; and Al-Lazikani et al., (1997) J. Mol. Biol. 273:927-948.

[0047] A "humanized antibody" or "humanized antibody fragment" is defined herein as an antibody molecule which has constant antibody regions derived from sequences of human origin and the variable antibody regions or parts thereof or only the CDRs are derived from another species. For example a humanized antibody can be CDR-grafted, wherein the CDRs of the variable domain are from a non-human origin, while one or more frameworks of the variable domain are of human origin and the constant domain (if any) is of human origin.

[0048] The term "chimeric antibody" or "chimeric antibody fragment" is defined herein as an antibody molecule which has constant antibody regions derived from, or corresponding to, sequences found in one species and variable antibody regions derived from another species. Preferably, the constant antibody regions are derived from, or corresponding to, sequences found in humans, and the variable antibody regions (e.g. VH, VL, CDR or FR regions) are derived from sequences found in a non-human animal, e.g. a mouse, rat, rabbit or hamster.

[0049] The term "isolated" refers to a compound, which can be e.g. an antibody or antibody fragment, that is substantially free of other antibodies or antibody fragments having different antigenic specificities. Moreover, an isolated antibody or antibody fragment may be substantially free of other cellular material and/or chemicals. Thus, in some aspects, antibodies provided are isolated antibodies which have been separated from antibodies with a different specificity. An isolated antibody may be a monoclonal antibody. An isolated antibody may be a recombinant monoclonal antibody. An isolated antibody that specifically binds to an epitope, isoform or variant of a target may, however, have cross-reactivity to other related antigens, e.g., from other species (e.g., species homologs).

[0050] The term "recombinant antibody", as used herein, includes all antibodies that are prepared, expressed, created or segregated by means not existing in nature. For example antibodies isolated from a host cell transformed to express the antibody, antibodies selected and isolated from a recombinant, combinatorial human antibody library, and antibodies prepared, expressed, created or isolated by any other means that involve splicing of all or a portion of a human immunoglobulin gene, sequences to other DNA sequences or antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom. Preferably, such recombinant antibodies have variable regions in which the framework and CDR regions are derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies can be subjected to in vitro mutagenesis (or, when an animal transgenic for human Ig sequences is used, in vivo somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline VH and VL sequences, may not naturally exist within the human antibody germline repertoire in vivo. A recombinant antibody may be a monoclonal antibody. In an embodiment, the antibodies and antibody fragment disclosed herein are isolated from the Ylanthia® antibody library as disclosed in U.S. Ser. No. 13/321,564 or U.S. Ser. No. 13/299,367, which both herein are incorporated by reference.

[0051] The term "monoclonal antibody" as used herein refers to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a unique binding site having a unique binding specificity and affinity for particular epitopes.

[0052] As used herein the term "binds specifically to", "specifically binds to", is "specific to/for" or "specifically recognizes", or the like, refers to measurable and reproducible interactions such as binding between a target and an antibody or antibody fragment, which is determinative of the presence of the target in the presence of a heterogeneous population of molecules including biological molecules. For example, an antibody or antibody fragment that specifically binds to a target (which can be an antigen or an epitope of an antigen) is an antibody or antibody fragment that binds this target with greater affinity, avidity, more readily, and/or with greater duration than it binds to other targets. In certain embodiments, an antibody or antibody fragment specifically binds to an epitope on a protein that is conserved among the protein from different species. In another embodiment, specific binding can include, but does not require exclusive binding. The antibodies or antibody fragments disclosed herein specifically bind to human IL-17C. Preferably, the disclosed antibodies or antibody fragments specific for human IL-17C specifically bind to IL-17C of another species, such as IL-17C from mouse, rat, rhesus monkey and/or cynomolgus monkey. Even more preferred the antibodies or antibody fragments disclosed herein are specific for human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C. Methods for determining whether two molecules specifically bind are well known in the art and include, for example, a standard ELISA assay. The scoring may be carried out by standard color development (e.g. secondary antibody with horseradish peroxide and tetramethyl benzidine with hydrogen peroxide). The reaction in certain wells is scored by the optical density, for example, at 450 nm.

Typical background (=negative reaction) may be 0.1 OD; typical positive reaction may be 1 OD. This means the difference positive/negative can be more than 5-fold. Typically, determination of binding specificity is performed by using not a single reference antigen, but a set of about three to five unrelated antigens, such as milk powder, BSA, transferrin or the like.

[0053] The term "avidity" is used to describe the combined strength of multiple bond interactions between proteins. Avidity is distinct from affinity which describes the strength of a single bond. As such, avidity is the combined synergistic strength of bond affinities (functional affinity) rather than the sum of bonds. With the antibodies of the present disclosure, both antigen-binding sites from the VH/VL pairs simultaneously interact with IL-17C. Whilst each single binding interaction may be readily broken (depending on the relative affinity), because many binding interactions are present at the same time, transient unbinding of a single site does not allow the molecule to diffuse away, and binding of that site is likely to be reinstated. The overall effect is synergistic, strong binding of antigen to antibody.

[0054] As used herein, the term "affinity" refers to the strength of interaction between the polypeptide and its target at a single site. Within each site, the binding region of the polypeptide interacts through weak non-covalent forces with its target at numerous sites; the more interactions, the stronger the affinity.

[0055] The term "K_D", as used herein, refers to the dissociation constant, which is obtained from the ratio of K_d to K_a (i.e. K_d/K_a) and is expressed as a molar concentration (M). K_D values for antigen binding moieties like e.g. monoclonal antibodies can be determined using methods well established in the art. Methods for determining the K_D of an antigen binding moiety like e.g. a monoclonal antibody are SET (soluble equilibrium titration) or surface plasmon resonance using a biosensor system such as a Biacore® system. In the present disclosure an antibody specific to IL-17C typically has a dissociation rate constant (K_D) (k_{off}/k_{on}) of less than 5×10^{-2}M, less than 10^{-2}M, less than 5×10^{-3}M, less than 10^{-3}M, less than 5×10^{-4}M, less than 10^{-4}M, less than 5×10^{-5}M, less than 10^{-5}M, less than 5×10^{-6}M, less than 10^{-6}M, less than 5×10^{-7}M, less than 10^{-7}M, less than 5×10^{-8}M, less than 10^{-8}M, less than 5×10^{-9}M, less than 10^{-9}M, less than 5×10^{-10}M, less than 10^{-10}M, less than 5×10^{-11}M, less than 10-11M, less than 5×10^{-12}M, less than 10^{-12}M, less than 5×10^{-13}M, less than 10^{-13}M, less than 5×10^{-14}M, less than 10^{-14}M, less than 5×10^{-15}M, or less than 10^{-15}M or lower.

[0056] "Cross competes" means the ability of an antibody, antibody fragment or other antigen-binding moieties to interfere with the binding of other antibodies, antibody fragments or antigen-binding moieties to a specific antigen in a standard competitive binding assay. The ability or extent to which an antibody, antibody fragment or other antigen-binding moieties is able to interfere with the binding of another antibody, antibody fragment or antigen-binding moieties to a specific antigen, and, therefore whether it can be said to cross-compete according to the invention, can be determined using standard competition binding assays. One suitable assay involves the use of the Biacore technology (e.g. by using the BIAcore 3000 instrument (Biacore, Uppsala, Sweden)), which can measure the extent of interactions using surface plasmon resonance technology. Another assay for measuring cross-competing uses an ELISA-based approach. A high throughput process for "epitope binning" antibodies based upon their cross-competition is described in International Patent Application No. WO 2003/48731. Cross-competition is present if the antibody or antibody fragment under investigation reduces the binding of one of the antibodies described in Table 1 to IL-17C by 60% or more, specifically by 70% or more and more specifically by 80% or more and if one of the antibodies described in Table 1 reduces the binding of said antibody or antibody fragment to IL-17C by 60% or more, specifically by 70% or more and more specifically by 80% or more.

[0057] The term "epitope" includes any proteinacious region which is specifically recognized by an antibody or fragment thereof or a T-cell receptor or otherwise interacts with a molecule. Generally epitopes are of chemically active surface groupings of molecules such as amino acids or carbohydrate or sugar side chains and generally may have specific three-dimensional structural characteristics, as well as specific charge characteristics. As will be appreciated by one of skill in the art, practically anything to which an antibody can specifically bind could be an epitope.

[0058] "Binds the same epitope as" means the ability of an antibody, antibody fragment or other antigen-binding moiety to bind to a specific antigen and binding to the same epitope as the exemplified antibody when using the same epitope mapping technique for comparing the antibodies. The epitopes of the exemplified antibody and other antibodies can be determined using epitope mapping techniques. Epitope mapping techniques are well known in the art. For example, conformational epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., hydrogen/deuterium exchange, x-ray crystallography and two-dimensional nuclear magnetic resonance.

[0059] Compositions of the present disclosure may be used for therapeutic or prophylactic applications. The present disclosure, therefore, includes a pharmaceutical composition containing an antibody (or functional antibody fragment) as disclosed herein and a pharmaceutically acceptable carrier or excipient therefor. In a related aspect, the present disclosure provides a method for treating an inflammatory disorder. Such method contains the steps of administering to a subject in need thereof an effective amount of the pharmaceutical composition that contains an antibody (or functional antibody fragment) as described or contemplated herein.

[0060] The present disclosure provides therapeutic methods comprising the administration of a therapeutically effective amount of an IL-17C antibody as disclosed to a subject in need of such treatment. A "therapeutically effective amount" or "effective amount", as used herein, refers to the amount of an IL-17C antibody necessary to elicit the desired biological response. In accordance with the subject invention, the therapeutic effective amount is the amount of an IL-17C antibody necessary to treat and/or prevent a disease.

[0061] "Subject" or "species", as used in this context refers to any mammal, including rodents, such as mouse or rat, and primates, such as cynomolgus monkey (*Macaca fascicularis*), rhesus monkey (*Macaca mulatta*) or humans (*Homo sapiens*). Preferably the subject is a primate, most preferably a human.

Embodiments

[0062] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment comprises

[0063] (a) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 7, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 8, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 9, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 13, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 14 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 15, or

[0064] (b) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 20, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 21, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 22, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 26, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 27 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 28.

[0065] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises

[0066] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0067] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0068] In another embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment comprises

[0069] (a) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 10, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 11, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 12, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 13, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 14 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 15, or

[0070] (b) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 23, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 24, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 25, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 26, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 27 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 28.

[0071] In a further embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises

[0072] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0073] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0074] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment comprises

[0075] (a) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 7, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 8, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 9, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 13, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 14 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 15, or

[0076] (b) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 10, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 11, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 12, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 13, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 14 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 15, or

[0077] (c) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 20, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 21, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 22, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 26, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 27 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 28.

[0078] (d) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 23, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 24, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 25, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 26, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 27 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 28.

[0079] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises

[0080] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0081] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0082] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID

No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0083] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0084] In another embodiment of the present disclosure the antibody or antibody fragment specifically binds to human IL-17C.

[0085] In another embodiment of the present disclosure the antibody or antibody fragment is a monoclonal antibody or antibody fragment.

[0086] In another embodiment of the present disclosure the antibody or antibody fragment is a human, humanized or chimeric antibody or antibody fragment. In another embodiment of the present disclosure the antibody or antibody fragment is of the IgG isotype. In another embodiment the antibody or antibody fragment is IgG1.

[0087] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises

[0088] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, and further comprises a heavy chain of SEQ ID No.: 17 or a light chain of SEQ ID No.: 16, or

[0089] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15 and further comprises a heavy chain of SEQ ID No.: 17 or a light chain of SEQ ID No.: 16, or

[0090] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28 and further comprises a heavy chain of SEQ ID No.: 30 or a light chain of SEQ ID No.: 29, or

[0091] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, and further comprises a heavy chain of SEQ ID No.: 30 or a light chain of SEQ ID No.: 29.

[0092] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16.

[0093] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29.

[0094] In a further embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 43 and a light chain of SEQ ID No.: 42.

[0095] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 56 and a light chain of SEQ ID No.: 55.

[0096] In another embodiment of the present disclosure the antibody or antibody fragment is an isolated antibody or antibody fragment.

[0097] In another embodiment of the present disclosure the antibody or antibody fragment is a recombinant antibody or antibody fragment.

[0098] In one embodiment, the present disclosure refers to an antibody or antibody fragment specific for IL-17C for use in the treatment of a disorder or condition associated with the undesired presence of IL-17C.

[0099] In one embodiment, the present disclosure refers to a nucleic acid composition comprising a nucleic acid sequence or a plurality of nucleic acid sequences encoding an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment comprises

[0100] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0101] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0102] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0103] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0104] In another embodiment, the present disclosure refers to a vector composition comprising a vector or a plurality of vectors comprising the nucleic acid sequence or plurality of nucleic acid sequences encoding an antibody or antibody fragment as disclosed in Table 1.

[0105] In one embodiment, the present disclosure refers to a cell comprising a vector composition comprising a vector or a plurality of vectors comprising the nucleic acid sequence or plurality of nucleic acid sequences encoding an antibody or antibody fragment as disclosed in Table 1.

[0106] In another embodiment, the present disclosure refers to a pharmaceutical composition comprising an antibody or antibody fragment as disclosed in Table 1 and a pharmaceutically acceptable carrier or excipient.

[0107] In one embodiment, said antibody or antibody fragment specific for IL-17C blocks the binding of IL-17C to the receptor of IL-17C. In a further embodiment, said antibody or antibody fragment specific for IL-17C blocks the binding of IL-17C to the receptor of IL-17C, wherein said receptor is IL17RE. In another embodiment the present disclosure refers to an antibody or antibody fragment specific for IL-17C, wherein said antibody or antibody fragment blocks the binding of IL-17C to IL17RE. In another embodiment said antibody or antibody fragment comprises the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the

LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0108] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0109] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0110] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0111] In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the a heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29.

[0112] In another embodiment the present disclosure refers to an antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment bivalently binds to an IL-17C homodimer and forms a complex consisting of said antibody or antibody fragment and one IL-17C homodimer and wherein said antibody or antibody fragment blocks the binding of IL-17C to IL17RE.

[0113] In certain embodiments, said antibody or antibody fragment specific for IL-17C blocks the binding of IL-17C to one or more receptors of IL-17C. In another embodiment said antibody or antibody fragment comprises the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0114] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0115] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0116] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

[0117] In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the a heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29.

[0118] In alternative embodiments, said antibody or antibody fragment specific for the receptor of IL-17C blocks the binding of IL-17C to receptors of IL-17C, wherein the receptors of IL-17C include IL17RE and IL17RA. In alternative embodiments, said antibody or antibody fragment specific for the receptor of IL-17C blocks the binding of IL-17C to IL17RE and IL17RA. In certain embodiments, said antibody or antibody fragment specific for IL-17C blocks the binding of IL-17C to IL17RE with an IC_{50} concentration of less than 100 nM, 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 20 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In certain aspects the IC_{50} concentration can be determined by ELISA; SET, FACS or MSD (Meso Scale Discovery). In another aspect the IC_{50} concentration can be determined by the method as described herein in Example 3. In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the a heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29.

[0119] In one embodiment the disclosed antibody or antibody fragment is specific for human IL-17C. In a further embodiment the disclosed antibody or antibody fragment specific for IL-17C is cross-reactive with IL-17C of another species, such as IL-17C from mouse, rat, rhesus monkey and/or cynomolgus monkey. In another embodiment the antibody or antibody fragment is specific for human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C. In a further embodiment the antibody or antibody fragment is specific for human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C. In another embodiment the antibody or antibody fragment is specific for human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C, wherein said antibody or antibody fragment comprises

[0120] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0121] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0122] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0123] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28. In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least

80%, at least 90% or at least 95% identity to the a heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29.

[0124] In yet another embodiment the disclosed antibody or antibody fragment specifically binds to human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C and blocks the binding of human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C to its specific receptor IL17RE with an IC_{50} concentration of less than 100 nM, 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 20 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In another aspect said antibody is in IgG1 format. In another embodiment said IC_{50} concentration is determined in a Receptor Inhibition Assay as described herein in Example 3.

[0125] In yet another embodiment the disclosed antibody or antibody fragment specifically binds to human IL-17C and blocks the binding of human IL-17C to human IL17RE with an IC_{50} concentration of less than 100 nM, 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 20 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In another aspect said antibody is in IgG1 format. In another embodiments said IC_{50} concentration is determined in a Receptor Inhibition Assay as described herein in Example 3.

[0126] In yet another embodiment the disclosed antibody or antibody fragment specifically binds to cynomolgus monkey IL-17C and blocks the binding of cynomolgus monkey IL-17C to cynomolgus monkey IL17RE with an IC_{50} concentration of less than 100 nM, 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 20 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In another aspect said antibody is in IgG1 format. In another embodiments said IC_{50} concentration is determined in a Receptor Inhibition Assay as described herein in Example 3.

[0127] In yet another embodiment the disclosed antibody or antibody fragment specifically binds to human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C, and blocks the binding of human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C, to human IL17RE, cynomolgus monkey IL17RE and mouse IL17RE, respectively, each with an IC_{50} concentration of less than 100 nM, 90 nM, 80 nM, 70 nM, 60 nM, 50 nM, 40 nM, 30 nM, 20 nM, 10 nM, 9 nM, 8 nM, 7 nM, 6 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In a preferred embodiment said antibody or antibody fragment comprises

[0128] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0129] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0130] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0131] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28. In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29. In another aspect said antibody is in IgG1 format. In another embodiments said IC_{50} concentration is determined in a Receptor Inhibition Assay as described herein in Example 3.

[0132] In yet another embodiment the disclosed antibody or antibody fragment inhibits human IL-17C, cynomolgus monkey IL-17C and mouse IL-17C driven activation of a NF-κB reporter gene in NIH3T3 cells with an IC_{50} concentration of less than 100 pM, 90 pM, 80 pM, 70 pM, 60 pM, 50 pM, 40 pM, 30 pM, 20 pM, 10 pM, 9 pM, 8 pM, 7 pM, 6 pM, 5 pM, 4 pM, 3 pM, 2 pM or 1 pM. In a preferred embodiment said antibody or antibody fragment comprises

[0133] the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0134] the HCDR1 region of SEQ ID No.: 10, the HCDR2 region of SEQ ID No.: 11, the HCDR3 region of SEQ ID No.: 12, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

[0135] the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28, or

[0136] the HCDR1 region of SEQ ID No.: 23, the HCDR2 region of SEQ ID No.: 24, the HCDR3 region of SEQ ID No.: 25, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28. In another embodiment said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29. In another aspect said antibody is in IgG1 format. In another embodiments said IC_{50} concentration is determined in a IL-17C-driven NF-κB reporter assay as described herein in Example 4.

[0137] In one embodiment the disclosed antibody or antibody fragment is specific for human IL-17C encoded by the amino acid sequence of SEQ ID No.: 1. In one embodiment

the disclosed antibody or antibody fragment is specific for a polypeptide comprising the amino acid sequence of SEQ ID No.: 1. In a further embodiment said monoclonal antibody or antibody fragment is a monoclonal antibody specific for a polypeptide consisting of the amino acid sequence of SEQ ID No.: 1. In another embodiment the disclosed antibody or antibody fragment is specific for human IL-17C encoded by the amino acid sequence of SEQ ID No.: 1 and is a monoclonal antibody or antibody fragment.

[0138] In one embodiment the disclosed antibody or antibody fragment specific for IL-17C is a monoclonal antibody or antibody fragment.

[0139] In one embodiment the disclosed antibody or antibody fragment specific for IL-17C is a human, humanized or chimeric antibody. In certain embodiments, said antibody or antibody fragment specific for IL-17C is an isolated antibody or antibody fragment. In another embodiment said antibody or antibody fragment is a recombinant antibody or antibody fragment. In a further embodiment said antibody or antibody fragment is a recombinant human antibody or antibody fragment. In a further embodiment said recombinant human antibody or antibody fragment is an isolated recombinant human antibody or antibody fragment. In a further embodiment said recombinant human antibody or antibody fragment or isolated recombinant human antibody or antibody fragment is monoclonal.

[0140] In another embodiment the disclosed antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16 or a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29 or a heavy chain and a light chain that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the a heavy chain of SEQ ID No.: 17 or 30 and to the light chain of SEQ ID No.: 16 or 29.

[0141] In one embodiment the disclosed antibody or antibody fragment comprises a human heavy chain constant region and a human light chain constant region. In a further embodiment said human heavy chain constant region comprises the amino acid sequences of SEQ ID No.: 17 and the human light chain constant region comprises the amino acid sequences of SEQ ID No.: 16 or said human heavy chain constant region comprises the amino acid sequences of SEQ ID No.: 30 and the human light chain constant region comprises the amino acid sequences of SEQ ID No.: 29.

[0142] In one embodiment the disclosed antibody or antibody fragment is of the IgG isotype. In another embodiment said antibody is IgG1.

[0143] In one embodiment said antibody fragment is a bivalent antibody fragment.

[0144] In another embodiment, the present disclosure refers to an antibody or antibody fragment that cross-competes with an antibody described in Table 1. In one embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs defined by Kabat of one of the antibodies in Table 1. In another embodiment the present disclosure refers to an antibody or antibody fragment specific for human IL-17C wherein said antibody or antibody fragment bivalently binds to an IL-17C homodimer and forms a complex consisting of said antibody or antibody fragment and one IL-17C homodimer and wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs defined by Kabat of one of the antibodies in Table 1.

[0145] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 7, the HCDR2 is the amino acid sequence of SEQ ID No.: 8, the HCDR3 is the amino acid sequence of SEQ ID No.: 9, the LCDR1 is the amino acid sequence of SEQ ID No.: 13, the LCDR2 is the amino acid sequence of SEQ ID No.: 14 and the LCDR3 is the amino acid sequence of SEQ ID No.: 15. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising the VH according to SEQ ID No.: 17 and the VL according to SEQ ID No.: 16.

[0146] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 20, the HCDR2 is the amino acid sequence of SEQ ID No.: 21, the HCDR3 is the amino acid sequence of SEQ ID No.: 22, the LCDR1 is the amino acid sequence of SEQ ID No.: 26, the LCDR2 is the amino acid sequence of SEQ ID No.: 27 and the LCDR3 is the amino acid sequence of SEQ ID No.: 28. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising the VH according to SEQ ID No.: 30 and the VL according to SEQ ID No.: 29.

[0147] In another embodiment, the present disclosure refers to an antibody or antibody fragment that cross-competes with an antibody described in Table 1. In one embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs defined by Chothia of one of the antibodies in Table 1. In another embodiment the present disclosure refers to an antibody or antibody fragment specific for human IL-17C wherein said antibody or antibody fragment bivalently binds to an IL-17C homodimer and forms a complex consisting of said antibody or antibody fragment and one IL-17C homodimer and wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs defined by Chothia of one of the antibodies in Table 1.

[0148] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 10, the HCDR2 is the amino acid sequence of SEQ ID No.: 11, the HCDR3 is the amino acid sequence of SEQ ID No.: 12, the LCDR1 is the amino acid sequence of SEQ ID No.: 13, the LCDR2 is the amino acid sequence of SEQ ID No.: 14 and the LCDR3 is the amino acid sequence of SEQ ID No.: 15. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising the VH according to SEQ ID No.: 17 and the VL according to SEQ ID No.: 18.

[0149] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 23, the HCDR2 is the amino acid sequence of SEQ ID No.: 24, the HCDR3 is the amino acid sequence of SEQ ID No.: 25, the LCDR1 is the amino acid sequence of SEQ ID No.: 26, the LCDR2 is the amino acid sequence of SEQ ID No.: 27 and the LCDR3 is the amino acid sequence of SEQ ID No.: 28. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment cross-competes with an antibody or antibody fragment comprising the VH according to SEQ ID No.: 30 and the VL according to SEQ ID No.: 29.

[0150] In a certain embodiment, the disclosure refers to an antibody or antibody fragment that cross-competes with an antibody described in Table 1 and reduces the specific binding of one of the antibodies described in Table 1 by at least 70%, 80% or 90% in an ELISA-based cross-competition assay. In a certain embodiment, the present disclosure refers to an monoclonal antibody or antibody fragment that cross-competes with an antibody described in Table 1 and reduces the specific binding of one of the antibodies described in Table 1 to IL-17C by at least 70%, 80% or 90% in an ELISA-based cross-competition assay. A representative assay set-up is illustrated in Example 6 in the present disclosure.

[0151] In another embodiment, the present disclosure refers to an antibody or antibody fragment that binds to (e.g., by binding, stabilizing, spatial distribution) the same epitope as one of the antibodies in Table 1. In a further embodiment said antibody or antibody fragment binds to (e.g., by binding, stabilizing, spatial distribution) the same epitope as an antibody or antibody fragment comprising 6 CDRs defined by Kabat of one of the antibodies in Table 1. In yet another embodiment said antibody or antibody fragment binds to (e.g., by binding, stabilizing, spatial distribution) the same epitope of IL-17C as an antibody or antibody fragment comprising 6 CDRs defined by Kabat of one of the antibodies in Table 1. In yet another embodiment said antibody or antibody fragment binds to (e.g., by binding, stabilizing, spatial distribution) the same epitope of polypeptide comprising the amino acid sequence of SEQ ID No.: 1 as an antibody or antibody fragment comprising 6 CDRs defined by Kabat of one of the antibodies in Table 1.

[0152] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment binds to the same epitope as an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 10, the HCDR2 is the amino acid sequence of SEQ ID No.: 11, the HCDR3 is the amino acid sequence of SEQ ID No.: 12, the LCDR1 is the amino acid sequence of SEQ ID No.: 13, the LCDR2 is the amino acid sequence of SEQ ID No.: 14 and the LCDR3 is the amino acid sequence of SEQ ID No.: 15. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment binds to the same epitope as an antibody or antibody fragment comprising the VH according to SEQ ID No.: 17 and the VL according to SEQ ID No.: 18.

[0153] In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment binds to the same epitope as an antibody or antibody fragment comprising 6 CDRs, wherein the HCDR1 is the amino acid sequence of SEQ ID No.: 23, the HCDR2 is the amino acid sequence of SEQ ID No.: 24, the HCDR3 is the amino acid sequence of SEQ ID No.: 25, the LCDR1 is the amino acid sequence of SEQ ID No.: 26, the LCDR2 is the amino acid sequence of SEQ ID No.: 27 and the LCDR3 is the amino acid sequence of SEQ ID No.: 28. In another embodiment the present disclosure refers to an antibody or antibody fragment, wherein said antibody or antibody fragment binds to the same epitope as an antibody or antibody fragment comprising the VH according to SEQ ID No.: 30 and the VL according to SEQ ID No.: 29.

[0154] Regions of a given polypeptide that include an epitope can be identified using any number of epitope mapping techniques, well known in the art. See, e.g., Epitope Mapping Protocols in Methods in Molecular Biology, Vol. 66 (Glenn E. Morris, Ed., 1996) Humana Press, Totowa, N.J. For example, epitopes may be determined by e.g., concurrently synthesizing large numbers of peptides on solid supports, the peptides corresponding to portions of the protein molecule, and reacting the peptides with antibodies while the peptides are still attached to the supports. Such techniques are known in the art and described in, e.g., U.S. Pat. No. 4,708,871; Geysen et al., (1984) Proc. Natl. Acad. Sci. USA 8:3998-4002; Geysen et al., (1985) Proc. Natl. Acad. Sci. USA 82:78-182; Geysen et al., (1986) Mol. Immunol. 23:709-715. Similarly, epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., hydrogen/deuterium exchange, x-ray crystallography and two-dimensional nuclear magnetic resonance. See, e.g., Epitope Mapping Protocols, supra. Antigenic regions of proteins can also be identified using standard antigenicity and hydropathy plots, such as those calculated using, e.g., the Omiga version 1.0 software program available from the Oxford Molecular Group. This computer program employs the Hopp/Woods method, Hopp et al., (1981) Proc. Natl. Acad. Sci USA 78:3824-3828; for determining antigenicity profiles, and the Kyte-Doolittle technique, Kyte et al., (1982) J. Mol. Biol. 157:105-132; for hydropathy plots.

[0155] In one embodiment, the present disclosure refers to an antibody or antibody fragment comprising 6 CDRs defined by Kabat of any of the antibodies in Table 1. In another aspect, the disclosure pertains to an isolated monoclonal antibody or fragment thereof comprising 6 CDRs defined by Kabat of each of the antibodies in Table 1.

[0156] In another embodiment, the present disclosure refers to an antibody or antibody fragment comprising 6 CDRs defined by Chotia of any of the antibodies in Table 1. In another aspect, the disclosure pertains to an isolated monoclonal antibody or fragment thereof comprising 6 CDRs defined by Chotia of each of the antibodies in Table 1.

[0157] In certain embodiments, the present disclosure refers to the antibodies or antibody fragments disclosed in in Table 1, wherein said antibodies or antibody fragments can bind to IL-17C with an affinity of about less than 100 nM, more preferably less than about 60 nM, and still more preferably less than about 30 nM. Further preferred are antibodies or antibody fragments that bind to IL-17C with an affinity of less than about 10 nM, and more preferably less than about 3 nM.

[0158] In certain embodiments, the present disclosure refers to the antibodies or antibody fragments disclosed in Table 1, wherein said antibodies or antibody fragments can bind to IL-17C with a monovalent affinity of about less than 100 nM, more preferably less than about 60 nM, and still more preferably less than about 30 nM. Further preferred are antibodies or antibody fragments that bind to IL-17C with a monovalent affinity of less than about 10 nM, and more preferably less than about 3 nM.

[0159] In another embodiment, the present disclosure refers to antibodies or antibody fragments specific for IL-17C, wherein said antibodies or antibody fragments have a monovalent affinity to IL-17C with a dissociation rate constant (K_D) of less than 5×10^{-2}M, less than 10^{-2}M, less than 5×10^{-3}M, less than 10^{-3}M, less than 5×10^{-4}M, less than 10^{-4}M, less than 5×10^{-5}M, less than 10^{-5}M, less than 5×10^{-6}M, less than 10^{-6}M, less than 5×10^{-7}M, less than 10^{-7}M, less than 5×10^{-8}M, less than 10^{-8}M, less than 5×10^{-9}M, less than 10^{-9}M, less than 5×10^{-10}M, less than 10^{-10}M, less than 5×10^{-11}M, less than 10^{-11}M, less than 5×10^{-12}M, less than 10^{-12}M, less than 5×10^{-13}M, less than 10^{-13}M, less than 5×10^{-14}M, less than 10^{-14}M, less than 5×10^{-15}M, or less than 10^{-15}M and wherein said antibodies or antibody fragments in a bivalent format have an affinity to IL-17C with a dissociation rate constant (K_D) which is at least 2-fold, 5-fold, 10-fold, 100-fold, 1000-fold, 10000-fold, 100000-fold lower than the dissociation rate constant (KD) in a monovalent format. In a further embodiment the bivalent affinity of said antibodies or antibody fragments is determined in IgG-format, wherein the monovalent affinity of said antibodies or antibody fragments is determined in Fab-format.

[0160] The compositions of the present disclosure are preferably pharmaceutical compositions comprising an antibody or antibody fragment specific for IL-17C as disclosed herein and a pharmaceutically acceptable carrier, diluent or excipient, for the treatment of an inflammatory disorder or cancer. Such carriers, diluents and excipients are well known in the art, and the skilled artisan will find a formulation and a route of administration best suited to treat a subject with the IL-17C antibodies or antibody fragments of the present disclosure.

[0161] In another embodiment the present disclosure refers to pharmaceutical compositions comprising an antibody or antibody fragment specific for IL-17C as disclosed herein for the use in the treatment of a disorder or condition associated with the undesired presence of IL-17C. In another embodiment said condition associated with the undesired presence of IL-17C is an inflammatory disorder or cancer. In another embodiment said inflammatory disorder is rheumatoid arthritis, psoriasis, pulmonary inflammation, COPD and/or atopic dermatitis (AD), including moderate-to-severe AD. In a preferred embodiment said inflammatory disorder is atopic dermatitis (AD) and/or moderate-to-severe AD.

[0162] In another embodiment the present disclosure refers to the use of said pharmaceutical compositions comprising an antibody or antibody fragment specific for IL-17C as disclosed herein in the preparation of a medicament for the treatment of a disorder or condition associated with the undesired presence of IL-17C. In another embodiment said condition associated with the undesired presence of IL-17C is an inflammatory disorder or cancer. In another embodiment said inflammatory disorder is rheumatoid arthritis, psoriasis, pulmonary inflammation, COPD and/or atopic dermatitis (AD), including moderate-to-severe AD. In a preferred embodiment said inflammatory disorder is atopic dermatitis (AD) and/or moderate-to-severe AD.

[0163] In another embodiment the present disclosure refers to the use of said pharmaceutical composition for the treatment of a disorder or condition associated with the undesired presence of IL-17C. In another embodiment said condition associated with the undesired presence of IL-17C is an inflammatory disorder or cancer. In another embodiment said inflammatory disorder is rheumatoid arthritis, psoriasis, pulmonary inflammation, COPD and/or atopic dermatitis (AD), including moderate-to-severe AD. In a preferred embodiment said inflammatory disorder is atopic dermatitis (AD) and/or moderate-to-severe AD.

[0164] In another aspect, provided herein is a method of treating atopic dermatitis (AD) and/or moderate-to-severe atopic dermatitis (AD) in a subject, the method comprising administering a pharmaceutical composition comprising a therapeutically effective amount of the IL-17C antibodies or antibody fragments of the present disclosure. In one embodiment said subject is resistant, non-responsive or inadequately responsive to treatment by either a topical corticosteroid (TCS) or a calcineurin inhibitor. In another embodiment the subject is a subject in need thereof. In a preferred embodiment said subject is a human. In alternative aspects said subject is a rodent, such as a rat or a mouse.

[0165] In another embodiment, the present disclosure refers to a method for the prophylaxis of an inflammatory disorder in a subject, said method comprising administering an IL-17C antagonist to said subject. "Prophylaxis" as used in this context refers to methods which aim to prevent the onset of a disease or which delay the onset of a disease. In some embodiments said subject is a human. In alternative aspects said subject is a rodent, such as a rat or a mouse.

[0166] In some embodiments, the antibodies or antibody fragments specific for IL-17C of the present disclosure are administered subcutaneously. In other aspects the antibodies or antibody fragments specific for IL-17C of the present disclosure are administered intra-venously, intra-articularly or intra-spinally.

[0167] In one embodiment, the disclosure pertains to an isolated monoclonal antibody or fragment thereof comprising a VH and a VL of any of the antibodies in Table 1.

[0168] In another embodiment, the disclosure pertains to an isolated monoclonal antibody or fragment thereof comprising a Heavy chain (IgG1) and a Light chain of any of the antibodies in Table 1.

[0169] In another embodiment, the disclosure refers to an isolated nucleic acid encoding a heavy chain sequence and/or light chain sequence of an antibody that binds to IL-17C the nucleic acid comprising

[0170] a HCDR1 region of SEQ ID No.: 58, the HCDR2 region of SEQ ID No.: 59, the HCDR3 region of SEQ ID No.: 60, the LCDR1 region of SEQ ID No.: 64, the LCDR2 region of SEQ ID No.: 65 and the LCDR3 region of SEQ ID No.: 66, or

[0171] a HCDR1 region of SEQ ID No.: 61, the HCDR2 region of SEQ ID No.: 62, the HCDR3 region of SEQ ID No.: 63, the LCDR1 region of SEQ ID No.: 64, the LCDR2 region of SEQ ID No.: 65 and the LCDR3 region of SEQ ID No.: 66, or

[0172] a HCDR1 region of SEQ ID No.: 33, the HCDR2 region of SEQ ID No.: 34, the HCDR3 region of SEQ ID

No.: 35, the LCDR1 region of SEQ ID No.: 39, the LCDR2 region of SEQ ID No.: 40 and the LCDR3 region of SEQ ID No.: 41, or

[0173] a HCDR1 region of SEQ ID No.: 36, the HCDR2 region of SEQ ID No.: 37, the HCDR3 region of SEQ ID No.: 38, the LCDR1 region of SEQ ID No.: 39, the LCDR2 region of SEQ ID No.: 40 and the LCDR3 region of SEQ ID No.: 41, or

[0174] a HCDR1 region of SEQ ID No.: 46, the HCDR2 region of SEQ ID No.: 47, the HCDR3 region of SEQ ID No.: 48, the LCDR1 region of SEQ ID No.: 52, the LCDR2 region of SEQ ID No.: 53 and the LCDR3 region of SEQ ID No.: 54, or

[0175] a HCDR1 region of SEQ ID No.: 49, the HCDR2 region of SEQ ID No.: 50, the HCDR3 region of SEQ ID No.: 51, the LCDR1 region of SEQ ID No.: 52, the LCDR2 region of SEQ ID No.: 53 and the LCDR3 region of SEQ ID No.: 54.

[0176] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a VH region of SEQ ID No.: 19 and a VL region of SEQ ID No.: 18, or a VH region and a VL region that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the VH region of SEQ ID No.: 19 and/or the VL region of SEQ ID No.: 18.

[0177] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a VH region of SEQ ID No.: 68 and a VL region of SEQ ID No.: 67, or a VH region and a VL region that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the VH region of SEQ ID No.: 68 and/or the VL region of SEQ ID No.: 67.

[0178] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a VH region of SEQ ID No.: 32 and a VL region of SEQ ID No.: 31, or a VH region and a VL region that has at least 60%, at least 70%, at least 80%, at least 90% or at least 95% identity to the VH region of SEQ ID No.: 32 and/or the VL region of SEQ ID No.: 31.

[0179] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a Heavy chain (IgG1) of SEQ ID No.: 45 and a Light chain of SEQ ID No.: 44.

[0180] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a Heavy chain (IgG1) of SEQ ID No.: 70 and a Light chain of SEQ ID No.: 69.

[0181] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a Heavy chain (IgG1) of SEQ ID No.: 71 and a Light chain of SEQ ID No.: 57.

[0182] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a VH and a VL of any of the antibodies in Table 1.

[0183] In another embodiment, the disclosure refers to a nucleic acid encoding an isolated monoclonal antibody or fragment thereof wherein the nucleic acid comprises a Heavy chain (IgG1) and a Light chain of any of the antibodies in Table 1.

[0184] In another embodiment, the disclosure refers to a method of producing an isolated monoclonal antibody or fragment thereof of any of the antibodies in Table 1.

TABLE 1

Antibody		Antibody sequences SEQ ID No.:	[aa]/DNA
MAB#1	HCDR (Kabat)	SEQ ID No.: 7	DYAMH
	HCDR2 (Kabat)	SEQ ID No.: 8	YIGGVGEGTQYAESVKG
	HCDR3 (Kabat)	SEQ ID No.: 9	GFAIRYYGFDY
	HCDR1 (Chothia)	SEQ ID No.: 10	GFTVSDY
	HCDR2 (Chothia)	SEQ ID No.: 11	GGVGEG
	HCDR3 (Chothia)	SEQ ID No.: 12	GFAIRYYGFDY
	LCDR1 (Kabat & Chothia)	SEQ ID No.: 13	SGDKLGDKYAY
	LCDR2 (Kabat & Chothia)	SEQ ID No.: 14	QDSKRPS
	LCDR3 (Kabat & Chothia)	SEQ ID No.: 15	QVFTFPLVTT
	VL	SEQ ID No.: 16	SYELTQPPSVSVSPGQTASITCSGDKLGDKYAYW YQQKPGQSPVLVIYQDSKRPSGIPERFSGSNSGN TATLTISGTQAEDEADYYCQVFTFPLVTTVFGGT KLTVLGQ
	VH	SEQ ID No.: 17	EVQLLESGGGLVQPGGSLRLSCAASGFTVSDYAM HWVRQAPGKGLEWVSYIGGVGEGTQYAESVKGR FTISRDNSKNTLYLQMNSLRAEDTAVYYCARGFAI RYYGFDYWGQGTLVTVSS
	VL (DNA)	SEQ ID No.: 18	agctatgaactgacccagccgccgagcgttagcgttagcccaggcca gaccgccagcattacctgtagcggcgacaaactgggcgacaaatac gcctactggtatcagcagaaaccgggccagagcccggtgctggttatc tatcaggatagcaaacgcccgagcggcattccagaacgctttagcgg cagcaacagcggcaacaccgccaccctgaccattagcggcaccca ggccgaagacgaagccgattattactgccaggttttcactttcccgctgg ttactactgtgtttggcggcggtaccaagctgaccgtgctgggccag
	VH (DNA)	SEQ ID No.: 19	gaagtgcagctgctggaaagcggtggcggtctggtgcagccaggtgg tagcctgcgcctgagctgtgccgcaagcggcttcacagtgtccgacta cgcaatgcattgggtgcgccaagcaccaggcaaaggcctggaatgg

TABLE 1-continued

Antibody		Antibody sequences SEQ ID No.:	[aa]/DNA
			gtgagttcataggtggcgtgggtgaggggacacaatatgcagagag
			cgtgaaaggtcgctttaccattagtcgcgataacagcaaaaacaccct
			gtatctgcaaatgaacagcctgcgggcagaagataccgcagtttattat
			tgcgcgcgtggtttcgcaatccgttattatggatttgattattggggccagg
			gcaccctggttactgtctcgagc
	HCDR1 (Kabat)	SEQ ID No.: 33	gactacgcaatgcat
	HCDR2 (Kabat)	SEQ ID No.: 34	tacataggtggcgtgggtgaggggacacaatatgcagagagcgtga
			aaggt
	HCDR3 (Kabat)	SEQ ID No.: 35	ggtttcgcaatccgttattatggatttgattat
	HCDR1 (Chothia)	SEQ ID No.: 36	ggcttcacagtgtccgactac
	HCDR2 (Chothia)	SEQ ID No.: 37	ggtggcgtgggtgagggg
	HCDR3 (Chothia)	SEQ ID No.: 38	ggtttcgcaatccgttattatggatttgattat
	LCDR1 (Kabat & Chothia)	SEQ ID No.: 39	agcggcgacaaactgggcgacaaatacgcctac
	LCDR2 (Kabat & Chothia)	SEQ ID No.: 40	caggatagcaaacgcccgagc
	LCDR3 (Kabat & Chothia	SEQ ID No.: 41	caggttttcactttcccgctggttactact
	Light chain	SEQ ID No.: 42	SYELTQPPSVSVSPGQTASITCSGDKLGDKYAYW
			YQQKPGQSPVLVIYQDSKRPSGIPERFSGSNSGN
			TATLTISGTQAEDEADYYCQVFTFPLVTTVFGGGT
			KLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLIS
			DFYPGAVTVAWMDSSPVKAGVETTTPSKQSNNK
			YAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKT
			VAPTECS
	Heavy chain (IgG1)	SEQ ID No.: 43	EVQLLESGGGLVQPGGSLRLSCAASGFTVSDYAM
			HWVRQAPGKGLEWVSYIGGVGEGTQYAESVKGR
			FTISRDNSKNTLYLQMNSLRAEDTAVYYCARGFAI
			RYYGFDYWGQGTLVTVSSASTKGPSVFPLAPSSK
			STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV
			HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV
			NHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLG
			GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
			EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
			LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK
			GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP
			SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS
			KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
			SLSPGK
	Light chain (DNA)	SEQ ID No.: 44	agctatgaactgacccagccgccgagcgttagcgttagcccaggcca
			gaccgccagcattacctgtagcggcgacaaactgggcgacaaatac
			gcctactggtatcagcagaaaccgggccagagcccggtgctggttatc
			tatcaggatagcaaacgcccgagcggcattccagaacgctttagcgg
			cagcaacagcggcaacaccgccaccctgaccattagcggcaccca
			ggccgaagacgaagccgattattactgccaggttttcactttcccgctgg
			ttactactgtgtttggcggcggtaccaagctgaccgtgctgggccagcc
			caaagccgcccctagcgtgaccctgttcccccaagcagcgaggaa
			ctccaggccaacaaggccaccctcgtgtgcctgatcagcgacttctac
			cctggcgccgtgaccgtggcctggaaggccgatagcagccctgtgaa
			ggccggcgtggaaaccaccaccccagcaagcagagcaacaaca
			aatacgccgccagcagctacctgagcctgaccccgagcagtggaa
			gtcccacagatcctacagctgccaggtcacacacgagggcagcacc
			gtggaaaagaccgtggcccccaccatcagc
	Heavy chain (IgG1, DNA)	SEQ ID No.: 45	gaagtgcagctgctggaaagcggtggcggtctggtgcagccaggtgg
			tagcctgcgcctgagctgtgccgcaagcggcttcacagtgtccgacta
			cgcaatgcattgggtgcgccaagcaccaggcaaaggcctggaatgg
			gtgagttacataggtggcgtgggtgaggggacacaatatgcagagag
			cgtgaaaggtcgctttaccattagtcgcgataacagcaaaaacaccct
			gtatctgcaaatgaacagcctgcgggcagaagataccgcagtttattat
			tgcgcgcgtggtttcgcaatccgttattatggatttgattattggggccagg
			gcaccctggttactgtctcgagcgcgtcgaccaaaggccccagcgtgt
			tccctctggcccccagcagcaagagcacctctggcggaacagccgc
			cctgggctgcctggtcaaggactacttccccgagcccgtgaccgtgtcc
			tggaactctggcgccctgaccagcggcgtgcacacctttccagccgtg
			ctccagagcagcggcctgtacagcctgagcagcgtcgtgaccgtgcc
			cagcagcagcctgggcacccagacctacatctgcaacgtgaaccac
			aagcccagcaacacaaaggtggacaagcgggtggaacccaagag
			ctgcgacaagacccacacctgtccccctgccctgcccctgaactgct
			gggaggcccctccgtgttcctgttcccccaaagcctaaggacaccct
			gatgatcagccggaccccgaagtgacctgcgtggtggtggacgtgt
			cccacgaggaccctgaagtgaagtttaattggtacgtggacggcgtgg
			aagtgcacaacgccaagaccaagcccagagaggaacagtacaac
			agcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactgg
			ctgaacggcaaagagtacaagtgcaaggtgtccaacaaggccctgc

TABLE 1-continued

Antibody		Antibody sequences SEQ ID No.:	[aa]/DNA
			ctgcccccatcgagaaaaccatcagcaaggccaaaggccagcccc
			gcgagccccaggtgtacacactgccccctagccgggaagagatgac
			caagaaccaggtgtccctgacctgcctcgtgaagggcttctaccccag
			cgacattgccgtggaatgggagagcaacggccagcccgagaacaa
			ctacaagaccacccccccctgtgctggacagcgacggctcattcttcctg
			tacagcaagctgaccgtggacaagagccggtggcagcagggcaac
			gtgttcagctgctccgtgatgcacgaggccctgcacaaccactacacc
			cagaagtccctgagcctgagccccggcaag
DNA (optimized)	HCDR1 (Kabat)	SEQ ID No.: 58	gactacgctatgcac
	HCDR2 (Kabat)	SEQ ID No.: 59	tatatcggcggcgtgggcgagggcacccagtacgctgagtctgtgaa gggc
	HCDR3 (Kabat)	SEQ ID No.: 60	ggcttcgccatccggtactacggcttcgactac
	HCDR1 (Chothia)	SEQ ID No.: 61	ggcttcaccgtgtccgactac
	HCDR2 (Chothia)	SEQ ID No.: 62	ggcggcgtgggcgagggc
	HCDR3 (Chothia)	SEQ ID No.: 63	ggcttcgccatccggtactacggcttcgactac
	LCDR1 (Kabat & Chothia	SEQ ID No.: 64	tccggcgacaagctgggcgataagtacgcctac
	LCDR2 (Kabat & Chothia)	SEQ ID No.: 65	caggactccaagcggccctcc
	LCDR3 (Kabat & Chothia	SEQ ID No.: 66	caggtgttcaccttccccctggtcaccacc
	VL (DNA)	SEQ ID No.: 67	tcctacgagctgacccagccccctccgtgtccgtgtctcctggccaga
			ccgcctccatcacctgttccggcgacaagctgggcgataagtacgcct
			actggtatcagcagaagcccggccagtccccctgctggtcatctacc
			aggactccaagcggccctccggcatccctgagcggttctccggctcca
			actccggcaacaccgccaccctgaccatctccggcacccaggccga
			ggacgaggccgactactactgccaggtgttcaccttcccccctggtcacc
			accgtgttcggcggaggcaccaagctgaccgtgctgggccag
	VH (DNA)	SEQ ID No.: 68	gaggtgcagctgctggaatccggcggaggactggtgcagcctggcg
			gctccctgagactgtcttgcgccgcctccggcttcaccgtgtccgactac
			gctatgcactgggtccgacaggcccctggcaagggcctggaatgggt
			gtcctatatcggcggcgtgggcgagggcacccagtacgctgagtctgt
			gaagggccggttcaccatctcccgggacaactccaagaacaccctgt
			acctgcagatgaactccctgcgggccgaggacaccgccgtgtactac
			tgtgccagaggcttcgccatccggtactacggcttcgactactggggcc
			agggcaccccttcaccttctac
	Light chain (DNA)	SEQ ID No.: 69	tcctacgagctgacccagccccctccgtgtccgtgtctcctggccaga
			ccgcctccatcacctgttccggcgacaagctgggcgataagtacgcct
			actggtatcagcagaagcccggccagtccccctgctggtcatctacc
			aggactccaagcggccctccggcatccctgagcggttctccggctcca
			actccggcaacaccgccaccctgaccatctccggcacccaggccga
			ggacgaggccgactactactgccaggtgttcaccttcccccctggtcacc
			accgtgttcggcggaggcaccaagctgaccgtgctgggccagcctaa
			ggccgctccctccgtgaccctgttcccccccatcctccgaggaactgca
			ggccaacaaggccaccctggtctgcctgatctccgacttctaccctggc
			gccgtgaccgtggcctggaaggccgacagctctcctgtgaaggccgg
			cgtggaaaccaccacccccctccaagcagtccaacaacaaatacgcc
			gcctcctcctacctgtccctgaccccgagcagtggaagtcccaccgg
			tcctacagctgccaggtcacacacgagggctccaccgtggaaaaga
			ccgtggcccctaccgagtgctcc
	Heavy chain (IgG1, DNA)	SEQ ID No.: 70	gaggtgcagctgctggaatccggcggaggactggtgcagcctggcg
			gctccctgagactgtcttgcgccgcctccggcttcaccgtgtccgactac
			gctatgcactgggtccgacaggcccctggcaagggcctggaatgggt
			gtcctatatcggcggcgtgggcgagggcacccagtacgctgagtctgt
			gaagggccggttcaccatctcccgggacaactccaagaacaccctgt
			acctgcagatgaactccctgcgggccgaggacaccgccgtgtactac
			tgtgccagaggcttcgccatccggtactacggcttcgactactggggcc
			agggcaccctggtcaccgtgtctagcgcctccaccaagggcccctcc
			gtgttccctctggcccctccagcaagtccacctctggcggcaccgctg
			ccctgggctgcctggtcaaggactacttccccgagcccgtgaccgtgtc
			ctggaactctggcgccctgacctccggcgtgcacaccttccctgccgtg
			ctgcagtcctccggcctgtactccctgtcctccgtcgtgaccgtgccctcc
			agctctctgggcacccagacctacatctgcaacgtgaaccacaagcc
			ctccaacaccaaggtggacaagcgggtggaacccaagtcctgcgac
			aagacccacacctgtccccctgccctgcccctgaactgctgggcgg
			accttccgtgttcctgttccccccaaagcccaaggacaccctgatgatct
			cccggacccccgaagtgacctgcgtggtggtggacgtgtcccacgag
			gaccctgaagtgaagttcaattggtacgtggacggcgtggaagtgcac
			aacgccaagaccaagcccagagaggaacagtacaactccacctac
			cgggtggtgtccgtgctgaccgtgctgcaccaggactggctgaacggc
			aaagagtacaagtgcaaggtgtccaacaaggccctgcctgcccccat
			cgaaaagaccatctccaaggccaagggccagccccgcgagcccca

TABLE 1-continued

Antibody		Antibody sequences SEQ ID No.:	[aa]/DNA
			ggtgtacacactgccccctagccgggaagagatgaccaagaaccag
			gtgtccctgacctgtctggtcaagggcttctacccctccgacattgccgt
			ggaatgggagtccaacggccagcccgagaacaactacaagaccac
			ccccccctgtgctggactccgacggctcattcttcctgtactccaagctga
			ccgtggacaagtcccggtggcagcagggcaacgtgttctcctgctccg
			tgatgcacgaggccctgcacaaccactacacccagaagtccctgtcc
			ctgagccccggcaag
MAB#2	HCDR1 (Kabat)	SEQ ID No.: 20	SDHYIS
	HCDR2 (Kabat)	SEQ ID No.: 21	YISSSGSTTYYAESVKG
	HCDR3 (Kabat)	SEQ ID No.: 22	QSYYFLPYFDV
	HCDR1 (Chothia)	SEQ ID No.: 23	GFTFSDH
	HCDR2 (Chothia)	SEQ ID No.: 24	SSSGST
	HCDR3 (Chothia)	SEQ ID No.: 25	QSYYFLPYFDV
	LCDR1 (Kabat & Chothia)	SEQ ID No.: 26	TGTSSDVGSYNLVS
	LCDR2 (Kabat & Chothia)	SEQ ID No.: 27	EGSKRPS
	LCDR3 (Kabat& Chothia)	SEQ ID No.: 28	ASRGSRRVLYV
	VL	SEQ ID No.: 29	QSALTQPASVSGSPGQSITISCTGTSSDVGSYNLV
			SWYQQHPGKAPKLMIYEGSKRPSGVSNRFSGSK
			SGNTASLTISGLQAEDEADYYCASRGSRRVLYVFG
			GGTKLTVLGQ
	VH	SEQ ID NO.: 30	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDHYI
			SWIRQAPGKGLEWVSYISSSGSTTYYAESVKGRF
			TISRDNAKNSLYLQMNSLRAEDTAVYYCARQSYYF
			LPYFDVWGQGTLVTVSS
	VL (DNA)	SEQ ID No.: 31	cagagcgccctgacccagccagccagcgttagcggtagcccaggcc
			agagcattaccattagctgcaccggcaccagcagcgacgtgggcag
			ctataacctggttagctggtatcagcagcatccgggcaaagccccgaa
			actgatgatctatgaaggcagcaaacgcccgagcggcgttagcaac
			cgctttagtggcagcaaaagcggcaacaccgccagcctgaccattag
			cggcctgcaagccgaagacgaagccgattattactgcgcaagtcgg
			ggaagccgtcgtgtgctgtatgtttttggcggcggtaccaagctgaccgt
			gctgggccag
	VH (DNA)	SEQ ID No.: 32	caggtgcagctggtggaaagcggcggtggcctggtgaaaccaggcg
			gtagcctgcgcctgagctgcgccgccagcggctttacctttagcgatca
			ttacattagctggattcgccaggccccaggcaaaggcctggaatgggt
			tagctatattagcagcagtggcagcaccacctattacgccgagagcgt
			gaaaggccgctttaccattagccgcgataacgccaaaaacagcctgt
			atctgcaaatgaacagcctgcgggccgaagatacccgccgtgtattatt
			gcgcgcgacaatcctactatttcctgccttatttcgacgtttggggccagg
			gcaccctggttactgtctcgagc
	HCDR1 (Kabat)	SEQ ID No.: 46	agcgatcattacattagc
	HCDR2 (Kabat)	SEQ ID No.: 47	tatattagcagcagtggcagcaccacctattacgccgagagcgtgaa
			aggc
	HCDR3 (Kabat)	SEQ ID No.: 48	caatcctactatttcctgccttatttcgacgtt
	HCDR1 (Chothia)	SEQ ID No.: 49	ggctttacctttagcgatcat
	HCDR2 (Chothia)	SEQ ID No.: 50	agcagcagtggcagcacc
	HCDR3 (Chothia)	SEQ ID No.: 51	caatcctactatttcctgccttatttcgacgtt
	LCDR1 (Kabat & Chothia	SEQ ID No.	accggcaccagcagcgacgtgggcagctataacctggttagc
	LCDR2 (Kabat & Chothia)	SEQ ID No.: 53	gaaggcagcaaacgcccgagc
	LCDR3 (Kabat & Chothia)	SEQ ID No.: 54	gcaagtcggggaagccgtcgtgtgctgtatgtt
	Light chain	SEQ ID No.: 55	QSALTQPASVSGSPGQSITISCTGTSSDVGSYNLV
			SWYQQHPGKAPKLMIYEGSKRPSGVSNRFSGSK
			SGNTASLTISGLQAEDEADYYCASRGSRRVLYVFG
			GGTKLTVLGQPKAAPSVTLFPPSSEELQANKATLV
			CLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQS
			NNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTV
			EKTVAPTECS
	Heavy chain (IgG1)	SEQ ID No.: 56	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDHYI
			SWIRQAPGKGLEWVSYISSSGSTTYYAESVKGRF
			TISRDNAKNSLYLQMNSLRAEDTAVYYCARQSYYF
			LPYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKS
			TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH
			TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN
			HKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGG
			PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE
			VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
			TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG

TABLE 1-continued

Antibody		Antibody sequences SEQ ID No.:	[aa]/DNA
			QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK
	Light chain (DNA)	SEQ ID No.: 57	cagagcgccctgacccagccagccagcgttagcggtagcccaggcc agagcattaccattagctgcaccggcaccagcagcgacgtgggcag ctataacctggttagctggtatcagcagcatccgggcaaagccccgaa actgatgatctatgaaggcagcaaacgcccgagcggcgttagcaac cgctttagtggcagcaaaagcggcaacaccgccagcctgaccattag cggcctgcaagccgaagacgaagccgattattactgcgcaagtcgg ggaagccgtcgtgtgctgtatgtttttggcggcggtaccaagctgaccgt gctgggccagcccaaagccgcccctagcgtgaccctgttccccccaa gcagcgaggaactccaggccaacaaggccaccctcgtgtgcctgat cagcgacttctaccctggcgccgtgaccgtggcctggaaggccgata gcagccctgtgaaggccggcgtggaaaccaccaccccagcaagc agagcaacaacaaatacgccgccagcagctacctgagcctgaccc ccgagcagtggaagtcccacagatcctacagctgccaggtcacaca cgagggcagcaccgtggaaaagaccgtggccccccaccgagtgcag c
	Heavy chain (DNA, IgG1)	SEQ ID No.: 71	caggtgcagctggtggaaagcggcggtggcctggtgaaaccaggcg gtagcctgcgcctgagctgcgccgccagcggctttacctttagcgatca ttacattagctggattcgccaggccccaggcaaaggcctggaatgggt tagctatattagcagcagtggcagcaccacctattacgccgagagcgt gaaaggccgctttaccattagccgcgataacgccaaaaacagcctgt atctgcaaatgaacagcctgcgggccgaagataccgccgtgtattatt gcgcgcgacaatcctactatttcctgccttatttcgacgtttggggccagg gcaccctggttactgtctcgagcgcgtcgaccaaaggccccagcgtgt tccctctggccccagcagcaagagcacctctggcggaacagccgc cctgggctgcctggtcaaggactacttccccgagcccgtgaccgtgtcc tggaactctggcgccctgaccagcggcgtgcacacctttccagccgtg ctccagagcagcggcctgtacagcctgagcagcgtcgtgaccgtgcc cagcagcagcctgggcacccagacctacatctgcaacgtgaaccac aagcccagcaacacaaaggtggacaagcgggtggaacccaagag ctgcgacaagacccacacctgtccccctgccctgcccctgaactgct gggaggcccctccgtgttcctgttcccccaaagcctaaggacaccct gatgatcagccggaccccgaagtgacctgcgtggtggtggacgtgt cccacgaggaccctgaagtgaagtttaattggtacgtggacggcgtgg aagtgcacaacgccaagaccaagcccagagaggaacagtacaac agcacctaccgggtggtgtccgtgctgaccgtgctgcaccaggactgg ctgaacggcaaagagtacaagtgcaaggtgtccaacaaggccctgc ctgcccccatcgagaaaaccatcagcaaggccaaaggccagcccc gcgagccccaggtgtacacactgccccctagccgggaagagatgac caagaaccaggtgtccctgacctgcctcgtgaagggcttctaccccag cgacattgccgtggaatgggagagcaacggccagcccgagaacaa ctacaagaccacccccccctgtgctggacagcgacggctcattcttcctg tacagcaagctgaccgtggacaagagccggtggcagcagggcaac gtgttcagctgctccgtgatgcacgaggccctgcacaaccactacacc cagaagtccctgagcctgagccccggcaag

WORKING EXAMPLES

List of Abbreviations

[0185] ANOVA analysis of variance
BSA bovine serum albumin
BW body weight
CDR Complementarity determining region

DLS Dynamic Light Scattering

DMEM Dulbecco's Modified Eagle Medium

[0186] EC_{50} 50% effective concentration
ECD extracellular domain
ECL electrochemiluminescence
ELISA enzyme-linked immunosorbent assay

EtOH Ethanol

[0187] Fab antigen-binding fragment

FBS Foetal Bovine Serum

[0188] Fc constant fragment

HPLC High Performance Liquid Chromatography

[0189] i.p. intraperitoneal(ly)
i.v. intravenous(ly)
IC_{50} 50% inhibitory concentration

IFN-γ Interferon-gamma

[0190] Ig immunoglobulin
IHC immunohistochemistry
IL-17R interleukin 17 receptor
IL-xx interleukin xx
K_D dissociation constant
MC903 calcipotriol
MPEK mouse primary keratinocytes
mRNA messenger ribonucleic acid
NF-κB nuclear factor kappa B

p.o. per os, oral(ly)
PBS phosphate buffered saline
qPCR quantitative polymerase chain reaction
qRT-PCR quantitative real-time polymerase chain reaction
SEM standard error of the mean
Th2 Type 2 helper T cells

Example 1: Generation of Antien, Fab Fragments and Antibodies

[0191] 1.1 Antigen Generation and Quality control

[0192] Amino acid sequences of IL-17C from human, cynomolgus monkey and mouse, were aligned.

[0193] Without leader sequence, homology of 79% is shared among all three species.

	Human	Cynomolgus	Mouse
Human	100%	95%	79%
Cynomolgus		100%	79%
Mouse			100%

[0194] IL-17C form different species was purchased from different providers or produced in-house and solubilised, if necessary. Per 100 μg protein 4 μl biotinylation reagent of the ECL™ biotinylation module were added and incubated for 60 min at room temperature in the dark with gentle agitation. Subsequently biotinylated protein was purified using Zeba™ Desalt spin columns and OD280 nm was determined.

[0195] Antigens were biotinylated by using the ECL™ biotinylation module (GE Healthcare; #1061918). After biotinlyation the product was purified using Zeba™ Desalt spin columns (Pierce; #89889).

[0196] Biotinylated and non-biotinylated mouse, cynomolgus and human IL-17C were subjected to a quality control comprising analyses under denaturing, reducing and denaturing, non-reducing conditions in SDS-PAGE and in native state by High Pressure-Size Exclusion Chromatography (HP-SEC) and Dynamic Light Scattering (DLS).

[0197] HP-SEC was performed on a Dionex UltiMate 3000 Titanium HPLC system (Dionex Corporation, Germering, Germany) in combination with Wyatt miniDAWN Treos and Wyatt Optilab rEX (Wyatt Technology Europe, Dernbach, Germany). For separation a Tosoh TSK-Gel G3000SWxI column was used (Tosoh Bioscience, Stuttgart, Germany). For each sample 15 μg of protein was loaded onto the column, separation was performed at a flow rate of 0.5 ml/min and recorded analyzing the UV absorption at 280 nm. The running buffer was composed of 49 mM NaH_2PO_4, 51 mM Na_2HPO_4, 100 mM K_2SO_4, 0.0005% Tween-80 at pH 6.8.

[0198] All DLS experiments were performed using a DynaPro Titan cuvette system (Wyatt Technology Europe, Dernbach, Germany) with protein concentrations between 0.2 and 1.0 mg/ml. In case of precipitation or particle formation, the sample was centrifuged at 10.000 g for 5 minutes prior to the experiment.

[0199] The extracellular domain (ECD) of mouse IL-17 receptor E (UniProt Q8BH06, isoform 1) and human IL-17 receptor E (UniProt Q8NFR9) were cloned in the expression vector pMAX_vk_Fc2_His using KpnI and EcoRV resulting in C-terminal Fc2_H fusion constructs. Beside the natural leader (AG00158) a second construct with a VK-Leader was generated (AG00159).

[0200] Both constructs were transiently expressed in HKB11 cells. The cell suspension was scaled up three days post transfection and the cell culture supernatant was harvested 6 days post transfection. After sterile filtration, the solution was subjected to protein A affinity chromatography. Buffer exchange was performed to PBS and samples were sterile filtered (0.2 μm pore size). Protein concentrations were determined by UV-spectrophotometry. Purity of the products was analysed under denaturing, reducing and denaturing, non-reducing conditions in SDS-PAGE and in native state by HP-SEC and DLS.

1.2. Pannings and Fab/Antibody Generation

[0201] For the antibody generation the MorphoSys Ylanthia® library was used to select Fab fragments against human IL-17C. The MorphoSys Ylanthia® library (Tiller et al. mAbs 5:3, 1-26; May/June (2013) and U.S. Pat. No. 8,728,981) is a commercially available phagemid library and employs the CysDisplay® technology for displaying the Fab on the phage surface (Lohning et al., WO2001/05950).

[0202] To identify IL-17C-specific antibodies different panning strategies were used. Each panning strategy comprised at least 3 individual rounds of panning against the respective antigens including human IL-17C (SEQ ID NO.: 1) and mouse IL-17C.

[0203] The isolated clones identified were maturated, engineered and/or germlined in order to increase affinity and/or functionality. Thereafter several hundred clones were screened and functionality was rigorously tested in in vitro assays comprising e.g. the evaluation of binding to human, cynomolgus monkey and mouse IL-17C via SET, inhibition of binding of human, cynomolgus monkey and mouse IL-17C to its respective IL-17RE and functional inhibition of IL-17C (IL-17RE-driven NF-κB reporter assay in mouse NIH3T3 cells and IL-17C mediated CSF3 expression in mouse primary keratinocytes (MPEK)).

[0204] Finally two preferred lead molecules (MAB#1 and MAB#2) were selected and are further described in the working examples as outlined below.

Example 2: Affinity Determination in Monovalent Fab and Bivalent IgG Format

[0205] Monovalent Fab and bivalent IgG affinity was determined by SET. Therefore purified Fabs were titrated on human, cynomolgus or mouse IL-17C for determination of KD. Respectively purified IgGs were titrated on human, cynomolgus or mouse IL-17C for EC_{50} determination.

[0206] Solution equilibrium titration (SET) was basically performed as described in the literature (Friquet et al., (1985) J. Immunol. Meth. 77: 305-19). In order to improve the sensitivity and accuracy of the SET method, it was transferred from classical ELISA to ECL based technology (Haenel et al. (2005) Anal Biochem. 339.1: 182-84).

[0207] Respective results for MAB#1 and MAB#2 are shown in Table 2 and Table 3 respectively.

Example 3: Characterization of IL-17C Specific Fabs or IgGs for Receptor Inhibition Activity

[0208] Purified IL-17C specific Fabs or IgGs, respectively were tested for its capacity to inhibit the binding of IL-17C

to its specific receptor IL-17RE. Therefore MA6000 384-well plates (Meso Scale Discovery, MSD) were coated with 30 µl of mouse IL17RE/Fc chimeric protein at 75 ng/ml in PBS at 4° C. overnight. The next day a serial antibody dilution (concentrations from 0.001 to 100 nM) were pre-incubated for 30 min at RT with an equal volume of biotinylated human/cynomolgus or mouse IL-17C to determine an IC_{50} concentration for receptor binding inhibition. After blocking of plates for 1 h with 2.5% BSA in PBST, previously formed antibody-ligand complexes were added for 1 h to coated IL17RE/Fc and receptor binding was detected via Streptavidin-ECL using MSD Sector Imager.

[0209] Both antibodies (MAB#1 and MAB#2) equally inhibited interaction of human/cynomolgus or mouse IL-17C with IL-17RE in Fab and in IgG format. IC_{50} concentrations in the double-digit pM-range were observed for both antibodies in IgG format throughout all three clinically relevant species. Results are shown in rows 3 and 4 in Table 2 and Table 3 respectively.

Example 4: Functional Testing in IL-17C-Driven NF-κB Reporter Assay

[0210] Purified IL-17C specific IgGs were further tested for their ability to inhibit the biological activity of human, mouse and cynomolgus IL-17C in a functional cell based assay that monitors the IL-17C driven activation of a NF-κB reporter gene in NIH3T3 cells overexpressing the murine IL-17RE.

[0211] NIH3T3 cells were cultured in DMEM supplemented with 10% FBS and 1% Pen/Strep at 37° C., 5% CO_2. For the assay, NIH3T3 cells were transfected in suspension with total amount of 100 ng DNA (20 ng mouse IL-17RE expression construct, 50 ng NF-κB luciferase reporter construct and 30 ng pBluescript) using the Polyplus jet-PEI transfection agent. In brief, the DNA was diluted in 5 µl 150 mM NaCl (per well) and 0.2 µl jet-PEI in 8 µl 150 mM NaCl (per well) was prepared. After 5 minutes incubation at room temperature, the JetPEI® solution was added to the DNA solution and further incubated for 20-30 minutes at room temperature. NIH3T3 cells were diluted to have ~40,000 cells in 87 µl medium. The cells were added to the DNA-JetPEI I® mix (87 µl cells and 13 µl DNA-JetPEI I® mix/well) and the final volume was transferred into 96 well plates.

[0212] After an overnight incubation at 37° C. in a humidified 5% CO_2 incubator, the medium was removed and replaced jetPEI® with 90 µl medium containing 5% FBS and 1% Pen/Strep. 10 µl of a serial antibody dilution made in DPBS that was pre-incubated for 30 minutes at room temperature with an equal volume of purified recombinant IL-17C (either human IL-17C (Novus #NBP1-42910), mouse mIL-17C (R&D Systems #2306-ml-025) or cynomolgus IL-17C (produced in house)), was added to the cells. The final concentration of IL-17C was 0.5 ng/ml.

[0213] After incubating the plates at 37° C. in CO_2 incubator, 100 µl SteadyLite Plus (Perkin Elmer) is added followed by readout of the luminescence on the Envision (Perkin Elmer).

[0214] Both antibodies effectively reduced NF-κB reporter gene activation mediated by IL-17RE in the presence of human, mouse and cynomolgus IL-17C. Respective results can be found in row 5 of Table 2 and Table 3 respectively.

Example 5: IL-17C-Driven Gene Expression in Primary Human Keratinocytes

[0215] Keratinocytes endogenously express the IL-17RE and IL-17RA receptors, both of which are needed for functional signaling of IL-17C. Human primary keratinocytes derived from healthy individuals and mouse primary keratinocytes derived from C57BL/6 mice were therefore used to determine the capacity of MAB#1 IgG1 and MAB#2 IgG1 to inhibit the biological activity of respectively human and mouse IL-17C in a more physiological context.

[0216] NHEK (normal human epidermal keratinocytes) were obtained from Lonza and cultured in Keratinocyte Growth Medium with supplements (KGM-Gold™ Bullet kit, Lonza) following manufacturer's protocol. NHEKs that were sub-cultured to and cryopreserved at passage 3 were thawed and immediately seeded in KGM cell culture medium at 30,000 cells/well in a 96 well cell culture plate. After 2 days, the medium was removed and changed to KGM-Gold w/o hydrocortisone prior to addition of hIL-17C (Novus #NBP1-42910) and hTNFα (Peprotech #300-01A) to final concentrations of 10 ng/ml each.

[0217] For testing antibodies, the human IL-17C was first pre-incubated for 30 minutes at room temperature with an equal volume of a serial dilution of antibody made in DPBS. Cells were stimulated with recombinant IL-17C (pre-incubated with or without a dilution of antibody) in presence of TNFα. Co stimulation with IL-17C and TNFα is known to result in synergistic induction of various genes and was shown to be necessary as IL-17C alone has limited effect on the expression of investigated genes.

[0218] Cells were cultured for 48 hours and then total RNA was extracted using RNeasy 96 Kit (Qiagen), reverse transcribed using Taqman® Reverse Transcription Reagents (Applied Biosystems) and the expression of beta-defensin 2 DEFB4A (human) or CSF3 (mouse) genes was determined by quantitative polymerase chain reaction (qPCR). In brief, 10 µl PCR reactions were prepared using Taqman® universal PCR master mix/No AmpErase® UNG and predesigned Assay-on-demand Gene expression primer/probe sets for DEF4B or CSF3 (#Hs00823638_m1, all Applied Biosystems). qPCR was performed on the ViiA7™ Real-Time PCR instrument (Applied Biosystems). Gene expression was normalized to a housekeeping gene either R-actin (Taqman primer set #4310881E) or GAPDH (Taqman primer set #4310893E).

[0219] Both antibodies (MAB#1 and MAB#2) were shown to effectively reduce 2 DEFB4A (human) or CSF3 (mouse) gene expression respectively and confirmed their ability to neutralize the biological activity of human IL-17C and also mouse IL-17C (Table 2 and Table 3).

[0220] Overview of Functional In Vitro Characterization:

[0221] Respective results from in vitro testing are summarized in Table 2 for MAB#1 and in Table 3 for MAB#2. The amino acid and the nucleic acid sequences of the variable regions and the CDRs of those two antibodies are shown in Table 1. Both antibodies fulfilled respective criteria and were considered as potential molecules for clinical development.

TABLE 2

Summary in vitro characterization MAB#1

MAB#1	Human IL-17C	Mouse IL-17C	Cynomolgus IL-17C
SET monovalent affinity (Fab)	K_D = 3950 ± 50 pM (n = 2)	K_D = 28000 ± 4000 pM (n = 2)	K_D = 22000 ± 100 pM (n = 2)
SET apparent affinity (IgG)	EC_{50} = 19 ± 6.9 pM (n = 3)	EC_{50} = 387 ± 63 pM (n = 3)	EC_{50} = 257 ± 59 pM
Receptor inhibition assay - Fab format	IC_{50} = 2900 pM	IC_{50} = 6000 pM	IC_{50} = 2700 pM
Receptor inhibition assay - IgG format	IC_{50} = 59 pM	IC_{50} = 55 pM	IC_{50} = 44 pM
NF-κB reporter assay	IC_{50} = 31.3 ± 12.1 pM (n = 3)	IC_{50} = 47.6 ± 9.4 pM (n = 3)	IC_{50} = 12.8 ± 1.9 pM (n = 3)
Keratinocyte assay	IC_{50} = 319.2 ± 86.3 pM (n = 3)	IC_{50} = 112.1 ± 26.7 pM (n = 3)	n.d.

TABLE 3

Summary in vitro characterization MAB#2

MAB#2	Human IL-17C	Mouse IL-17C	Cynomolgus IL-17C
SET monovalent affinity (Fab)	K_D = 37 ± 17 pM (n = 2)	K_D = 460 ± 90 pM (n = 2)	K_D = 63 ± 20 pM (n = 2)
SET apparent affinity (IgG)	EC_{50} = 16 ± 4 pM (n = 3)	EC_{50} = 323 ± 12 pM (n = 3)	NT
Receptor inhibition assay - Fab format	IC_{50} = 76 pM	IC_{50} = 150 pM	IC_{50} = 50 pM
Receptor inhibition assay - IgG format	IC_{50} = 58 pM	IC_{50} = 48 pM	IC_{50} = 57 pM
NF-κB reporter assay	IC_{50} = 18.5 ± 2.2 pM (n = 3)	IC_{50} = 64.8 ± 8.6 pM (n = 3)	IC_{50} = 12.9 ± 4.5 pM (n = 3)
Keratinocyte assay	IC_{50} = 279.9 ± 161.7 pM (n = 3)	IC_{50} = 51.0 ± 9.0 pM (n = 3)	n.d.

Example 6: ELISA-Based Cross-Competition Assay

[0222] Cross-competition of an anti-IL-17C antibody or another IL-17C binding agent may be detected by using an ELISA assay according to the following standard procedure.

[0223] The general principle of the ELISA-assay involves coating of an anti-IL-17C antibody (such as MAB#1 or MAB#2) onto the wells of an ELISA plate. An excess amount of a second, potentially cross-competitive, anti-IL-17C antibody is then added in solution (i.e. not bound to the ELISA plate). Subsequently a limited amount of IL-17C-Fc is then added to the wells.

[0224] The antibody which is coated onto the wells and the antibody in solution will compete for binding of the limited number of IL-17C molecules. The plate is then washed to remove IL-17C molecules that has not bound to the coated antibody and to also remove the second, solution phase antibody as well as any complexes formed between the second, solution phase antibody and IL-17C. The amount of bound IL-17C is then measured using an appropriate IL-17C detection reagent. Therefore, IL-17C may be fused with a tag, e.g. Fc, Flag, etc. which can be detected via an appropriate tag-specific agent.

[0225] An antibody in solution that is cross-competitive to the coated antibody will be able to cause a decrease in the number of IL-17C molecules that the coated antibody can bind relative to the number of IL-17C molecules that the coated antibody can bind in the absence of the second, solution phase antibody.

[0226] This assay is described in more detail further below for two antibodies termed Ab-X and Ab-Y. In the instance where Ab-X is chosen to be the immobilized antibody, it is coated onto the wells of the ELISA plate, after which the plates are blocked with a suitable blocking solution to minimize non-specific binding of reagents that are subsequently added. An excess amount of Ab-Y is then added to the ELISA plate such that the moles of Ab-Y IL-17C binding sites per well are at least 10 fold higher than the moles of Ab-X IL-17C binding sites that are used, per well, during the coating of the ELISA plate. IL-17C is added such that the moles of IL-17C added per well were at least 25-fold lower than the moles of Ab-X IL-17C binding sites that are used for coating each well. Following a suitable incubation period, the ELISA plate is washed and a detection reagent specific for the IL-17C antigen is added to measure the amount of IL-17C molecules specifically bound by the coated anti-IL-17C antibody (in this case Ab-X). The background signal for the assay is defined as the signal obtained in wells with the coated antibody (in this case Ab-X), second solution phase antibody (in this case Ab-Y), buffer only (i.e. no IL-17C) and detection reagents. The positive control signal for the assay is defined as the signal obtained in wells with the coated antibody (in this case Ab-X), second solution phase antibody buffer only (i.e. no second solution phase antibody), IL-17C detection reagents. The ELISA assay needs to be run in such a manner so as to have the positive control signal be at least 6 times the background signal.

[0227] To avoid any artifacts (e.g. significantly different affinities between Ab-X and Ab-Y for IL-17C) resulting from the choice of which antibody to use as the coating antibody and which to use as the second (competitor) antibody, the cross-blocking assay needs to be run in two formats: 1) format 1 is where Ab-X is the antibody that is coated onto the ELISA plate and Ab-Y is the competitor antibody that is in solution and 2) format 2 is where Ab-Y is the antibody that is coated onto the ELISA plate and Ab-X is the competitor antibody that is in solution.

Example 7: IL-23 Induced Psoriasis-Model in Mice

[0228] To examine in vivo efficacy and therapeutic potential, both candidate antibodies were further evaluated in an IL-23 induced psoriasis-model in mice.

[0229] The IL-23 induced psoriasis-model in mice was essentially carried out as described by Rizzo H et al. J Immunol (2011) Vol. 186(3) pp. 1495-1502.

[0230] In brief, skin lesions were induced in Balb/C mice by intradermal injection of IL-23 into the ears (1 μg) for 4 consecutive days (day1 to day4). Measurement of gross ear thickness was done daily up to day 5 on which the mice were sacrificed. At sacrifice, the pinna ears were sampled and cut longitudinally in 2 halves. One half was fixed in formalin for in depth histological analysis of epidermal/dermal thickness of ear skin. The second half was immersed in RNAlater for quantitative reverse-transcription polymerase chain reaction (qRT-PCR) analysis of mRNA expression levels of disease-relevant IL-17A, IL-22 and IL-1β proinflammatory cytokines and LCN2, S100A8 and S100A9 anti-microbial pro-

teins. Groups (n=10) of IL-23 injected mice were treated with the MAB#1 or MAB#2 antibodies which were administered twice i.p. at a dose of 10 mg/kg (once 3 days before and once just before the first IL-23 intradermal injection).

[0231] Each antibody was tested in 2 independent experiments divided over 3 different studies. In each study the following control groups (each n=10) were included:

[0232] A control group of mice did not receive daily injections of IL-23 but instead received daily intradermal injection of the same volume of a BSA/PBS solution. This group was treated with a negative control isotype antibody MOR03207 (2×10 mg/kg, i.p.).

[0233] For each of the studies the gross ear thickness and epidermal thickness was followed over time and individual data points per animal were used to determine the % prevention of the IL-23 mediated thickening. qPCR expression data were expressed using the Rq (relative quantity) equation (Rq=2−ΔCt where ΔCt=Ct (gene of interest)−Ct (housekeeping gene)) after normalization to cyclophilin A expression levels used as housekeeping gene. For all measurements, mean±SEM data of groups were compared with a one-way analysis of variance (ANOVA) and Dunnett multiple comparison post hoc test using PRISM software. A "p" value of <0.05 was considered to be statistically significant (*: p<0.05; **: p<0.01; ***: p<0.001; ns: not significant) In summary, the administration of both candidates IgGs MAB#1 and MAB#2 (2×10 mg/kg) ameliorated the IL-23 induced skin inflammation, demonstrating the in vivo efficacy and therapeutic potential of both antibodies. Both antibodies had similar effects at level of IL-23 induced epidermal thickening and a similar impact at level of IL-23 induced gene expression. (see Table 4).

TABLE 4

Summary In vivo efficacy in IL-23 model

	MAB#1	MAB#2
% prevention of Gross ear thickness (mean and significance in 2-3 studies)	−34 Significant in 2 out of 2 studies	−6 Not significant in 2 out of 2 studies
% prevention of epidermal thickness (mean and significance in 2-3 studies)	−62 Significant in 2 out of 2 studies	−50 Significant in 2 out of 2 studies
Number of disease related genes significantly reduced (in each of the 3 studies performed)	nt/3/6	1/6/nt

Example 8: MC903 Mouse Model of Atopic Dermatitis

[0234] The efficacy of the MAB#1 antibody in atopic dermatitis was examined in a non-infectious cutaneous inflammation mouse model of atopic dermatitis where topical application of the low-calcemic vitamin D3 analogue MC903 (calcipotriol) induces atopic dermatitis like skin lesion characterized by a red and scaly skin, accompanied by an epidermal hyperplasia and dermal infiltration of various cell types as well as an increase of Th2 cytokine in skin and elevated serum IgE (Li M et al. Proc Natl Acad Sci USA (2006) Vol. 103(31) pp. 11736-11741; Li M et al. J Invest Dermatol. (2009) Vol. 129(2). pp. 498-502).

8.1 Animals

[0235] BALB/c mice (female, 8-week old) were obtained from Janvier Labs (France). Mice were kept on a 12 hours light/dark cycle (0700-1900). Temperature was maintained at 22° C., and food and water were provided ad libitum.

8.2. Experimental Procedures

[0236] In order to induce an AD-like response, 2 nmol MC903 (Tocris, dissolved in ethanol) was topical applied in a volume of 20 μL on both ears of mice for 5 consecutive days. A non-disease control group received the same quantity of ethanol (EtOH).

[0237] The severity of skin inflammation (erythema and thickening) was observed daily. Ear thickness was measured with an electronic caliper (Mitutoyo). Inflammation was further assessed using an in vivo imaging technique. To that end, Prosense 680 probe (1.6 nmol, Perkin Elmer) was administered by intraperitoneal route 24 hours before imaging. Imaging was performed with the Bruker In-vivo Xtreme Imaging System. Images were captured by a deeply cooled 4MP CCD camera (f-stop 1.1, binning 2×2, 5 sec acquisition time, Ex 630 nm, Em 700 nm). For anatomical co-registration, a reflectance image was taken (f-stop 2.8, 0.175 sec acquisition time). All images were taken with a 190×190 field of view and images were analysed using Molecular Imaging Software version 7.1 (Bruker Biospin, Billerica, Mass., USA). For each group, the mean values and standard error of mean (sem) was calculated using for each mouse the mean value of left and right ear.

[0238] At sacrifice, samples form ear skin were collected and fixed in 4% formaldehyde before embedding in paraffin. 4 μm-thick slices were stained with hematoxylin and eosin (H&E stain) for histomorphometric evaluation of epidermal thickness by image analysis with Sisn'Com software (France). Five fields per ear (high power field ×20) covering the whole ear from top to bottom were measured, and the 5 values were averaged per ear and per mice (left/right ear). An additional set of tissue slices were prepared for IHC staining of IL-17C using the anti-IL-17C biotinylated MAB antibody (and biotinylated MOR03207 isotype negative control antibody). Processing and staining was essentially done as described above.

[0239] Ear skin samples were also taken for analysis of cytokine expression using qPCR or ELISA. Ear tissue pieces for qPCR gene analysis were submerged in RNALater@ stabilisation solution (Ambion) and stored at −20° C. Ear skin samples for quantification at protein level were immediately snap frozen in liquid N2 and stored at −80° C. For gene expression analysis, tissue was disrupted and lysed in RNA lysis solution using Precellys homogenisator (microtubes filled with 1.4 mm ceramide beads, 3 times 3 cycles of 15 sec at 6000 rpm). Total RNA was further extracted using NucleoSpin® RNA Kit according to manufactures guidelines (Macherey-Nagel) and 300 ng was reverse-transcribed using Applied Biosystems™ High-Capacity cDNA Reverse Transcription Kit. 5 μL of 10-fold diluted cDNA was used in real-time quantitative PCR reactions using SYBR Green technology with gene-specific primers from Qiagen. qPCR was performed on the ViiA™ 7 Real-Time PCR System (Applied Biosystems). Gene expression was normalized to the expression of 3 different house-keeping genes (cyclophilin, b-actin and GAPDH) and expressed as relative mRNA level of specific gene expression as obtained using

the $2^{-\Delta Ct}$ method, with ΔCt=Ctgene−Geomean Ct-value (housekeeping genes). For quantification of expression at protein level, tissues were first disrupted and lysed in 250 μL lysis buffer (T-PER™ Tissue Protein Extraction Reagent (Pierce) supplemented with Protease Inhibitor Cocktail (Roche) and Halt™ Phosphatase Inhibitor Cocktail (Pierce)) using Precellys homogenisator (microtubes filled with 2.8 mm metal beads, 10 min 14000 rpm at 4° C.). The amount of TSLP in ears was determined using a TSLP mouse DuoSet ELISA kits from R&D System. The amount was normalized to total protein content in lysate which was determined using Coomassie Protein Assay Reagent (Thermo Fisher) in reference to BSA protein standard. Data were expressed as amount of cytokine in ear which was calculated using the formula: concentration cytokine in sample/concentration of protein in sample×total ear protein content.

[0240] The significance of effect of a treatment on each of the readouts was assessed with Prism® Software using one-way ANOVA followed by a Dunnett's multiple comparison post-hoc test versus the MC903+MOR03207 control group with *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$.

8.3. Efficacy of MAB#1 in a Mouse Model of Atopic Dermatitis (Prophylactic)

[0241] The efficacy of various doses of MAB#1 in the MC903 atopic dermatitis model was assessed in a prophylactic setting. In brief, skin lesions were induced in BALB/c mice by topical administration of 2 nmol MC903 (dissolved in ethanol) on both ears for 5 consecutive days; mice were sacrificed at Day 8. MAB#1 was administered i.p. 3 times, i.e. 3 days before, at start of and 4 days after the first MC903 application. Effects on ear swelling, ear inflammation, epidermal hyperplasia, dermal thickness and gene expression were evaluated. A group of mice which received an isotype negative control antibody (MOR03207) served as comparator. Dexamethasone (5 mg/kg in 0.5% methyl cellulose, administered daily by oral route (p.o.) as of the first day of MC903 application) was used as active comparator. Mice were randomly divided into equal groups (n=10).

[0242] The severity of skin inflammation (erythema and thickening) was followed during the course of the experiment. The gross ear thickness was measured using a Mitutoyo thickness gage during the course of the experiment. Inflammation was further assessed at Day 5 using an in vivo imaging technique as described in 8.2).

[0243] Ethanol (as vehicle control) had no effect on ears. In contrast, MC903-treated ears became red and swollen. Treatment with MAB#1 at doses of 2 mg/kg or higher significantly prevented ear thickening. The effect of MAB#1 was maximal at a dose of 10 mg/kg and was comparable to the effect of dexamethasone (FIG. **1**). In line with these observations, ear inflammation (assessed by in vivo imaging at Day 5) was clearly increased in MC903-treated animals and reduced by MAB#1 with significant and near maximal effect observed at a dose of 10 mg/kg (FIG. **2**).

[0244] To confirm the reduction of ear thickness by MAB#1, histological sections of ears collected at Day 8 were stained with hematoxylin and eosin for histomorphometric evaluation of epidermal and dermal thickness. Values of five fields per ear covering the whole ear from top to bottom were captured, and averaged per mouse. MAB#1 at doses of 10 mg/kg and higher significantly prevented the increase in thickness of both epidermal and dermal layer (FIG. **3**).

8.3.1 Effect of MAB#1 on Gene Expression

[0245] To further characterize the effect of MAB#1 in the MC903 atopic dermatitis-like skin inflammation model, the expression of various atopic dermatitis-relevant genes was analysed at mRNA level by qPCR or at protein level by enzyme-linked immunosorbent assay (ELISA). TSLP and IL-33 protein expression in ears and TARC level in plasma were increased by MC903 application and significantly inhibited upon treatment with MAB#1 at doses of 10 mg/kg or higher (FIG. **4**). A similar inhibitory effect was observed with MAB#1 on several other genes that were upregulated in MC903-treated ears, like IL-31 (a cytokine linked with itch in atopic dermatitis), the Th2-cytokine IL-4, and other genes that have been shown to be upregulated in human atopic dermatitis, like S100A8/9 and IFN-γ. Vice versa, MAB#1 was shown to prevent the downregulation of FLG2 in MC903-treated ears, which might suggest a potential role of MAB#1 in restoring barrier function.

8.4 Efficacy of MAB#1 in a Mouse Model of Atopic Dermatitis (Therapeutic)

[0246] The efficacy of various doses of MAB#1 in the MC903 atopic dermatitis model was assessed in a more disease-relevant therapeutic setting. In brief, skin lesions were induced in BALB/c mice before the start of any treatment by topical administration of 2 nmol MC903 (dissolved in ethanol) on both ears for 5 consecutive days. MAB#1 was administered i.p. 4 times, with the first administration at the last day of MC903 skin application (Day 5) and following ones at Day 8, 12 and 15. Mice were sacrificed at Day 16. Effects on ear swelling, ear inflammation, epidermal hyperplasia, dermal thickness and gene expression were evaluated. In addition, effect on influx of immune cells (eosinophils, T cells and mast cells) was also evaluated. A group of mice which received an isotype negative control antibody (MOR03207) served as comparator. Dexamethasone (1 mg/kg in 0.5% methyl cellulose, administered p.o. starting as of the last day of MC903 application at Day 5 and subsequently from Day 8 to 12 and from Day 15 to 16) was used as active comparator.

8.4.1 Effect of MAB#1 on Gross Ear Thickness and Inflammation

[0247] The gross ear thickness was measured using a Mitutoyo thickness gage during the course of the experiment. Topical application of MC903 on ears elicited a marked increase in ear thickness as of Day 3 as compared to ears treated with ethanol (as vehicle control for MC903). Disease activity was well induced at Day 5 (i.e. day of first treatment) and continued to evolve after (even though MC903 application was stopped) as evident from a continued increase in ear swelling in the group treated with the negative control antibody MOR03207 (FIG. **5**). Treatment with MAB#1 at doses of 0.4 mg/kg or higher significantly reduced ear thickening as of Day 12, with the higher doses of MAB#1 having a stronger effect and significantly reducing ear thickness even at earlier time points (as of Day 8 for MAB#1 at 50 mg/kg and as of Day 10 for doses of 10 and 2 mg/kg). In line with these observations, ear inflammation

as assessed by in vivo imaging (as described in 8.2) at Day 12, was still increased in animals treated with negative control antibody and significantly reduced by MAB#1 at all doses, with maximal effect observed at dose of 2 mg/kg (FIG. **6**).

8.4.2 Effect of MAB#1 on Ear Epidermal/Dermal Thickness

[0248] To confirm the reduction of ear thickness by MAB#1, histological sections of ears collected at Day 16 were stained with hematoxylin and eosin for histomorphometric evaluation of epidermal and dermal thickness. MAB#1 at doses of 2 mg/kg and higher strongly reduced the increase in thickness of both epidermal and dermal layer, in line with the measurements of gross ear thickness (FIG. **7**).

8.4.3 Effect of MAB#1 on Dermal Cell Infiltration

[0249] To further characterize the effect of MAB#1 on disease processes in the MC903 atopic dermatitis model, we evaluated the effect on cell infiltrations. More specifically, we assessed the effect on eosinophils, T-lymphocytes and mast cells by immunohistochemistry (IHC) and subsequent quantification of the area that stained with respectively antibodies detecting eosinophil peroxidase, T cell marker CD3 and mast cell tryptases (for details see (Marsais, 2016)). In line with the increased inflammation and ear thickness, infiltration of eosinophils, T cells and to lesser extent mast cells was still prominent at Day 16 in ears of mice in which disease activity was induced by MC903. Treatment of MAB#1 reduced the dermal infiltration of all three cell types examined (FIG. **8**). A significant reduction in number of infiltrated eosinophils and T cells was observed at all MAB#1 doses tested with the higher dose of 50 mg/kg having the more stronger effect reducing the influx of these cell types to levels comparable to the effect of dexamethasone. The effect on mast cell infiltration was in general weaker but still significant: influx was significantly reduced by MAB#1 at the higher doses of 50 and 10 mg/kg.

8.4.4 Effect of MAB#1 on Gene Expression

[0250] Expression was analysed on ear skin samples or plasma collected at Day 16 either by qPCR for eight disease-relevant genes or by ELISA for TSLP and IL-33 produced in ears and TARC in plasma as described in 8.2.

[0251] No significant differential expression could be observed for most of the analysed genes between EtOH-treated non-disease control mice and mice in which disease was induced by application of MC903 for the first 5 days. Only levels of IL-33 protein and IL-4, S100A9 and IFN-γ mRNA expression levels were still increased. Increased expression levels for those genes (except IFN-γ) were reduced by MAB#1 treatment as shown in FIG. **9** at all dose levels.

8.5. Results

[0252] MAB#1 prevented the generation of an atopic dermatitis-like skin inflammation in the MC903 model, with a significant impact on epidermal and dermal thickening, inflammation and type 2 T helper cell (Th2)-like gene expression when dosed prophylactically at 3×10 mg/kg intraperitoneally (i.p.). Significant effects on gross ear thickness were already observed in this model at doses of 3×2 mg/kg (i.p.). Also in the therapeutic MC903 model MAB#1 improved skin inflammation. Significant therapeutic effects on gross ear thickness, epidermal thickening, inflammation and influx of eosinophils and T cells were observed at doses of 4×0.4 mg/kg (i.p.), up to doses of 4×2 to 10 mg/kg (i.p.).

Example 9: Flaky Tail Mouse Model of Atopic Dermatitis

[0253] The efficacy of the MAB#1 antibody was evaluated in the Flaky Tail model. Flaky Tail mice have a mutation in the Flg and Matt ($Matt^{ma/ma}Flg^{ft/ft}$) genes resulting in skin barrier dysfunction. These mice spontaneously develop atopy and progressive dermatitis characterised by a mixed Th2/Th17 inflammatory phenotype and reproduce cardinal features of AD in man.

9.1. Animals & Experimental Procedures

[0254] Flaky tail ($Matt^{ma}/^{ma}Flg^{ft/ft}$) mice on a congenic C57BL/6J background were used as described in Fallon et al (2009) Nat Genet. 41(5): 602-608 and Saunders et al (2013) J Allergy Clin Immunol 132(5): 1121-1129. Female Flaky tail mice, 9-10 weeks old, were randomized into four groups (8 mice per group) and treated for 6 weeks as follows:

[0255] Group I: Isotype negative control antibody (MOR03207) (30 mg/kg, ip twice weekly×6 weeks)

[0256] Group II: MAB#1 (3 mg/kg, ip twice weekly×6 weeks)

[0257] Group III: MAB#1 (30 mg/kg, ip twice weekly×6 weeks)

[0258] Group IV: Dexamethasone 2 mg/kg (ip twice per week×6 weeks) as active comparator

[0259] The severity of AD-like skin inflammation was scored using the macroscopic diagnostic criteria adapted from assessment of skin inflammation in the NC/Nga mouse model as described in Saunders et al (2013) J Allergy Clin Immunol 132(5): 1121-1129. In brief, a scoring system (0: none; 1: mild; 2: moderate; 3: marked) was applied to the signs of erythema, excoriation and scaling. The total scores for each mouse (with the maximum of 9) were calculated from the sum of the individual scores for each of the three parameters.

[0260] The occurrence of eczematous lesions in eyelid skin was monitored at end of the study and blepharitis was scored separately for its severity (0: normal, 1: eyelid erythema and/or edema, 2: eyelid erythema, edema and scaling, 3: eyelid erythema, edema, scaling, erosion). The maximum blepharitis score (mean of both eyes) for each mouse is 3.

9.2. Efficacy of MAB#1 in Spontaneous & Chronic Flaky Tail Mouse Model of AD

[0261] Clinical scoring of skin inflammation shows that Flaky Tail mice had already signs of spontaneous eczematous-like dermatitis at start of treatment which further progressed during the 6-week follow up period into an overt dermatitis, in non-treated animals. Treatment with MAB#1 reduces progression with significant effect comparable to the effect of dexamethasone observed at the highest tested dose of 30 mg/kg (FIG. **10**). A similar effect of the MAB#1 antibody is observed at the level of blepharitis at the end of the treatment (FIG. **11**). .

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35 40 45

Pro His Leu Leu Ala Arg Gly Ala Lys Trp Gly Gln Ala Leu Pro Val
50 55 60

Ala Leu Val Ser Ser Leu Glu Ala Ala Ser His Arg Gly Arg His Glu
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Arg Pro Ser Ala Thr Thr Gln Cys Pro Val Leu Arg Pro Glu Glu Val
85 90 95

Leu Glu Ala Asp Thr His Gln Arg Ser Ile Ser Pro Trp Arg Tyr Arg
100 105 110

Val Asp Thr Asp Glu Asp Arg Tyr Pro Gln Lys Leu Ala Phe Ala Glu
115 120 125

Cys Leu Cys Arg Gly Cys Ile Asp Ala Arg Thr Gly Arg Glu Thr Ala
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Ala Leu Asn Ser Val Arg Leu Leu Gln Ser Leu Leu Val Leu Arg Arg
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Leu Pro Arg Ser Val
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Tyr Ser Ala Glu Glu Leu Ser His Gly Gln Ala Pro Pro His Leu Leu
35 40 45

Thr Arg Ser Ala Arg Trp Glu Gln Ala Leu Pro Val Ala Leu Val Ala
50 55 60

Ser Leu Glu Ala Thr Gly His Arg Arg Gln His Glu Gly Pro Leu Ala
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Gly Thr Gln Cys Pro Val Leu Arg Pro Glu Glu Val Leu Glu Ala Asp
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Thr His Glu Arg Ser Ile Ser Pro Trp Arg Tyr Arg Ile Asp Thr Asp

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Glu Asn Arg Tyr Pro Gln Lys Leu Ala Val Ala Glu Cys Leu Cys Arg
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Gly Cys Ile Asn Ala Lys Thr Gly Arg Glu Thr Ala Ala Leu Asn Ser
    130                 135                 140

Val Gln Leu Leu Gln Ser Leu Leu Val Leu Arg Arg Gln Pro Cys Ser
145                 150                 155                 160

Arg Asp Gly Thr Ala Asp Pro Thr Pro Gly Ser Phe Ala Phe His Thr
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Glu Phe Ile Arg Val Pro Val Gly Cys Thr Cys Val Leu Pro Arg Ser
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Thr Gln


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            20                  25                  30

Thr Pro Arg Cys Tyr Ser Ala Glu Glu Leu Pro Leu Gly Gln Ala Pro
        35                  40                  45

Pro His Leu Leu Ala Arg Gly Ala Lys Trp Gly Gln Ala Leu Pro Val
    50                  55                  60

Ala Leu Val Ser Ser Leu Glu Ala Ala Gly His Arg Arg Arg His Asp
65                  70                  75                  80

Arg Pro Ser Ala Ala Thr Gln Cys Pro Val Leu Arg Pro Glu Glu Val
                85                  90                  95

Leu Glu Ala Asp Thr His Gln Arg Ser Ile Ser Pro Trp Arg Tyr Arg
            100                 105                 110

Val Asp Thr Asp Glu Asp Arg Tyr Pro Gln Lys Leu Ala Phe Ala Glu
        115                 120                 125

Cys Leu Cys Arg Gly Cys Ile Asp Pro Arg Thr Gly Arg Glu Thr Ala
    130                 135                 140

Ala Leu Asn Ser Val Arg Leu Leu Gln Ser Leu Leu Val Leu Arg Arg
145                 150                 155                 160

Arg Pro Cys Ser Arg Asp Gly Ser Gly Leu Pro Thr Pro Gly Ala Phe
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Ala Phe His Thr Glu Phe Ile Arg Val Pro Val Gly Cys Thr Cys Val
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Leu Pro Arg Ser Val
        195


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Leu Arg Leu Leu Asp His Arg Ala Leu Val Cys Ser Gln Pro Gly Leu
        35                  40                  45

Asn Cys Thr Val Lys Asn Ser Thr Cys Leu Asp Asp Ser Trp Ile His
    50                  55                  60

Pro Arg Asn Leu Thr Pro Ser Ser Pro Lys Asp Leu Gln Ile Gln Leu
65                  70                  75                  80

His Phe Ala His Thr Gln Gln Gly Asp Leu Phe Pro Val Ala His Ile
                85                  90                  95

Glu Trp Thr Leu Gln Thr Asp Ala Ser Ile Leu Tyr Leu Glu Gly Ala
            100                 105                 110

Glu Leu Ser Val Leu Gln Leu Asn Thr Asn Glu Arg Leu Cys Val Arg
        115                 120                 125

Phe Glu Phe Leu Ser Lys Leu Arg His His His Arg Arg Trp Arg Phe
    130                 135                 140

Thr Phe Ser His Phe Val Val Asp Pro Asp Gln Glu Tyr Glu Val Thr
145                 150                 155                 160

Val His His Leu Pro Lys Pro Ile Pro Asp Gly Asp Pro Asn His Gln
                165                 170                 175

Ser Lys Asn Phe Leu Val Pro Asp Cys Glu His Ala Arg Met Lys Val
            180                 185                 190

Thr Thr Pro Cys Met Ser Ser Gly Ser Leu Trp Asp Pro Asn Ile Thr
        195                 200                 205

Val Glu Thr Leu Glu Ala His Gln Leu Arg Val Ser Phe Thr Leu Trp
    210                 215                 220

Asn Glu Ser Thr His Tyr Gln Ile Leu Leu Thr Ser Phe Pro His Met
225                 230                 235                 240

Glu Asn His Ser Cys Phe Glu His Met His His Ile Pro Ala Pro Arg
                245                 250                 255

Pro Glu Glu Phe His Gln Arg Ser Asn Val Thr Leu Thr Leu Arg Asn
            260                 265                 270

Leu Lys Gly Cys Cys Arg His Gln Val Gln Ile Gln Pro Phe Phe Ser
        275                 280                 285

Ser Cys Leu Asn Asp Cys Leu Arg His Ser Ala Thr Val Ser Cys Pro
    290                 295                 300

Glu Met Pro Asp Thr Pro Glu Pro Ile Pro Asp Tyr Met Pro Leu Trp
305                 310                 315                 320

Val Tyr Trp Phe Ile Thr Gly Ile Ser Ile Leu Leu Val Gly Ser Val
                325                 330                 335

Ile Leu Leu Ile Val Cys Met Thr Trp Arg Leu Ala Gly Pro Gly Ser
            340                 345                 350

Glu Lys Tyr Ser Asp Asp Thr Lys Tyr Thr Asp Gly Leu Pro Ala Ala
        355                 360                 365

Asp Leu Ile Pro Pro Pro Leu Lys Pro Arg Lys Val Trp Ile Ile Tyr
    370                 375                 380

Ser Ala Asp His Pro Leu Tyr Val Asp Val Val Leu Lys Phe Ala Gln
385                 390                 395                 400

Phe Leu Leu Thr Ala Cys Gly Thr Glu Val Ala Leu Asp Leu Leu Glu
                405                 410                 415
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Glu Gln Ala Ile Ser Glu Ala Gly Val Met Thr Trp Val Gly Arg Gln
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Lys Gln Glu Met Val Glu Ser Asn Ser Lys Ile Ile Val Leu Cys Ser
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Arg Gly Thr Arg Ala Lys Trp Gln Ala Leu Leu Gly Arg Gly Ala Pro
    450                 455                 460

Val Arg Leu Arg Cys Asp His Gly Lys Pro Val Gly Asp Leu Phe Thr
465                 470                 475                 480

Ala Ala Met Asn Met Ile Leu Pro Asp Phe Lys Arg Pro Ala Cys Phe
                485                 490                 495

Gly Thr Tyr Val Val Cys Tyr Phe Ser Glu Val Ser Cys Asp Gly Asp
            500                 505                 510

Val Pro Asp Leu Phe Gly Ala Ala Pro Arg Tyr Pro Leu Met Asp Arg
        515                 520                 525

Phe Glu Glu Val Tyr Phe Arg Ile Gln Asp Leu Glu Met Phe Gln Pro
    530                 535                 540

Gly Arg Met His Arg Val Gly Glu Leu Ser Gly Asp Asn Tyr Leu Arg
545                 550                 555                 560

Ser Pro Gly Gly Arg Gln Leu Arg Ala Ala Leu Asp Arg Phe Arg Asp
                565                 570                 575

Trp Gln Val Arg Cys Pro Asp Trp Phe Glu Cys Glu Asn Leu Tyr Ser
            580                 585                 590

Ala Asp Asp Gln Asp Ala Pro Ser Leu Asp Glu Glu Val Phe Glu Glu
        595                 600                 605

Pro Leu Leu Pro Pro Gly Thr Gly Ile Val Lys Arg Ala Pro Leu Val
    610                 615                 620

Arg Glu Pro Gly Ser Gln Ala Cys Leu Ala Ile Asp Pro Leu Val Gly
625                 630                 635                 640

Glu Glu Gly Gly Ala Ala Val Ala Lys Leu Glu Pro His Leu Gln Pro
                645                 650                 655

Arg Gly Gln Pro Ala Pro Gln Pro Leu His Thr Leu Val Leu Ala Ala
            660                 665                 670

Glu Glu Gly Ala Leu Val Ala Ala Val Glu Pro Gly Pro Leu Ala Asp
        675                 680                 685

Gly Ala Ala Val Arg Leu Ala Leu Ala Gly Glu Gly Glu Ala Cys Pro
    690                 695                 700

Leu Leu Gly Ser Pro Gly Ala Gly Arg Asn Ser Val Leu Phe Leu Pro
705                 710                 715                 720

Val Asp Pro Glu Asp Ser Pro Leu Gly Ser Ser Thr Pro Met Ala Ser
                725                 730                 735

Pro Asp Leu Leu Pro Glu Asp Val Arg Glu His Leu Glu Gly Leu Met
            740                 745                 750

Leu Ser Leu Phe Glu Gln Ser Leu Ser Cys Gln Ala Gln Gly Gly Cys
        755                 760                 765

Ser Arg Pro Ala Met Val Leu Thr Asp Pro His Thr Pro Tyr Glu Glu
    770                 775                 780

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785                 790                 795                 800

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Glu Glu Gln Asp Pro Gly Lys Pro Ala Leu Pro Leu Ser Pro Glu Asp
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Ser Ala
865


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            20                  25                  30

His Trp Asn Thr Arg Cys Pro Leu Ala Ser His Thr Asp Asp Ser Phe
        35                  40                  45

Thr Gly Ser Ser Ala Tyr Ile Pro Cys Arg Thr Trp Trp Ala Leu Phe
    50                  55                  60

Ser Thr Lys Pro Trp Cys Val Arg Val Trp His Cys Ser Arg Cys Leu
65                  70                  75                  80

Cys Gln His Leu Leu Ser Gly Gly Ser Gly Leu Gln Arg Gly Leu Phe
                85                  90                  95

His Leu Leu Val Gln Lys Ser Lys Lys Ser Ser Thr Phe Lys Phe Tyr
            100                 105                 110

Arg Arg His Lys Met Pro Ala Pro Ala Gln Arg Lys Leu Leu Pro Arg
        115                 120                 125

Arg His Leu Ser Glu Lys Ser His His Ile Ser Ile Pro Ser Pro Asp
    130                 135                 140

Ile Ser His Lys Gly Leu Arg Ser Lys Arg Thr Gln Pro Ser Asp Pro
145                 150                 155                 160

Glu Thr Trp Glu Ser Leu Pro Arg Leu Asp Ser Gln Arg His Gly Gly
                165                 170                 175

Pro Glu Phe Ser Phe Asp Leu Leu Pro Glu Ala Arg Ala Ile Arg Val
            180                 185                 190

Thr Ile Ser Ser Gly Pro Glu Val Ser Val Arg Leu Cys His Gln Trp
        195                 200                 205

Ala Leu Glu Cys Glu Glu Leu Ser Ser Pro Tyr Asp Val Gln Lys Ile
    210                 215                 220

Val Ser Gly Gly His Thr Val Glu Leu Pro Tyr Glu Phe Leu Leu Pro
225                 230                 235                 240

Cys Leu Cys Ile Glu Ala Ser Tyr Leu Gln Glu Asp Thr Val Arg Arg
                245                 250                 255

Lys Lys Cys Pro Phe Gln Ser Trp Pro Glu Ala Tyr Gly Ser Asp Phe
            260                 265                 270

Trp Lys Ser Val His Phe Thr Asp Tyr Ser Gln His Thr Gln Met Val
        275                 280                 285

Met Ala Leu Thr Leu Arg Cys Pro Leu Lys Leu Glu Ala Ala Leu Cys
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Pro Gln Leu Cys Phe Lys Phe Ser Phe Gly Asn Ser Ser His Val Glu
            340                 345                 350

Cys Pro His Gln Thr Gly Ser Leu Thr Ser Trp Asn Val Ser Met Asp
        355                 360                 365

Thr Gln Ala Gln Gln Leu Ile Leu His Phe Ser Ser Arg Met His Ala
    370                 375                 380

Thr Phe Ser Ala Ala Trp Ser Leu Pro Gly Leu Gly Gln Asp Thr Leu
385                 390                 395                 400

Val Pro Pro Val Tyr Thr Val Ser Gln Ala Arg Gly Ser Ser Pro Val
                405                 410                 415

Ser Leu Asp Leu Ile Ile Pro Phe Leu Arg Pro Gly Cys Cys Val Leu
            420                 425                 430

Val Trp Arg Ser Asp Val Gln Phe Ala Trp Lys His Leu Leu Cys Pro
        435                 440                 445

Asp Val Ser Tyr Arg His Leu Gly Leu Leu Ile Leu Ala Leu Leu Ala
    450                 455                 460

Leu Leu Thr Leu Leu Gly Val Val Leu Ala Leu Thr Cys Arg Arg Pro
465                 470                 475                 480

Gln Ser Gly Pro Gly Pro Ala Arg Pro Val Leu Leu Leu His Ala Ala
                485                 490                 495

Asp Ser Glu Ala Gln Arg Arg Leu Val Gly Ala Leu Ala Glu Leu Leu
            500                 505                 510

Arg Ala Ala Leu Gly Gly Gly Arg Asp Val Ile Val Asp Leu Trp Glu
        515                 520                 525

Gly Arg His Val Ala Arg Val Gly Pro Leu Pro Trp Leu Trp Ala Ala
    530                 535                 540

Arg Thr Arg Val Ala Arg Glu Gln Gly Thr Val Leu Leu Leu Trp Ser
545                 550                 555                 560

Gly Ala Asp Leu Arg Pro Val Ser Gly Pro Asp Pro Arg Ala Ala Pro
                565                 570                 575

Leu Leu Ala Leu Leu His Ala Ala Pro Arg Pro Leu Leu Leu Leu Ala
            580                 585                 590

Tyr Phe Ser Arg Leu Cys Ala Lys Gly Asp Ile Pro Pro Pro Leu Arg
        595                 600                 605

Ala Leu Pro Arg Tyr Arg Leu Leu Arg Asp Leu Pro Arg Leu Leu Arg
    610                 615                 620

Ala Leu Asp Ala Arg Pro Phe Ala Glu Ala Thr Ser Trp Gly Arg Leu
625                 630                 635                 640

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Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu Ser Leu Pro Leu Leu
1               5                  10                  15

Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg
            20                  25                  30

Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe
        35                  40                  45

Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys
    50                  55                  60

Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser
65                  70                  75                  80

Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His
                85                  90                  95

Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr
            100                 105                 110

Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu
        115                 120                 125

Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu
    130                 135                 140

Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala
145                 150                 155                 160

Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser
                165                 170                 175

Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp
            180                 185                 190

Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr
        195                 200                 205

Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp
    210                 215                 220

Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp
225                 230                 235                 240

Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro
                245                 250                 255

Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro
            260                 265                 270

Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr
        275                 280                 285

Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser
    290                 295                 300

Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu
305                 310                 315                 320

Pro Ser Trp Thr Val Ser Met Asp Thr Gln Ala Gln Gln Leu Thr Leu
                325                 330                 335

His Phe Ser Ser Arg Thr Tyr Ala Thr Phe Ser Ala Ala Trp Ser Asp
            340                 345                 350

Pro Gly Leu Gly Pro Asp Thr Pro Met Pro Pro Val Tyr Ser Ile Ser
        355                 360                 365

Gln Thr Gln Gly Ser Val Pro Val Thr Leu Asp Leu Ile Ile Pro Phe
    370                 375                 380

Leu Arg Gln Glu Asn Cys Ile Leu Val Trp Arg Ser Asp Val His Phe
385                 390                 395                 400
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Ala Trp Lys His Val Leu Cys Pro Asp Val Ser His Arg His Leu Gly
                405                 410                 415

Leu Leu Ile Leu Ala Leu Leu Ala Leu Thr Ala Leu Val Gly Val Val
            420                 425                 430

Leu Val Leu Leu Gly Arg Arg Leu Leu Pro Gly Ser Gly Arg Thr Arg
        435                 440                 445

Pro Val Leu Leu Leu His Ala Ala Asp Ser Glu Ala Gln Arg Arg Leu
    450                 455                 460

Val Gly Ala Leu Ala Glu Leu Leu Arg Thr Ala Leu Gly Gly Gly Arg
465                 470                 475                 480

Asp Val Ile Val Asp Leu Trp Glu Gly Thr His Val Ala Arg Ile Gly
                485                 490                 495

Pro Leu Pro Trp Leu Trp Ala Ala Arg Glu Arg Val Ala Arg Glu Gln
            500                 505                 510

Gly Thr Val Leu Leu Leu Trp Asn Cys Ala Gly Pro Ser Thr Ala Cys
        515                 520                 525

Ser Gly Asp Pro Gln Ala Ala Ser Leu Arg Thr Leu Leu Cys Ala Ala
    530                 535                 540

Pro Arg Pro Leu Leu Leu Ala Tyr Phe Ser Arg Leu Cys Ala Lys Gly
545                 550                 555                 560

Asp Ile Pro Arg Pro Leu Arg Ala Leu Pro Arg Tyr Arg Leu Leu Arg
                565                 570                 575

Asp Leu Pro Arg Leu Leu Arg Ala Leu Asp Ala Gln Pro Ala Thr Leu
            580                 585                 590

Ala Ser Ser Trp Ser His Leu Gly Ala Lys Arg Cys Leu Lys Asn Arg
        595                 600                 605

Leu Glu Gln Cys His Leu Leu Glu Leu Glu Ala Ala Lys Asp Asp Tyr
    610                 615                 620

Gln Gly Ser Thr Asn Ser Pro Cys Gly Phe Ser Cys Leu
625                 630                 635


<210> SEQ ID NO 7
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic peptide"

<400> SEQUENCE: 7

Asp Tyr Ala Met His
1               5


<210> SEQ ID NO 8
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic peptide"

<400> SEQUENCE: 8

Tyr Ile Gly Gly Val Gly Glu Gly Thr Gln Tyr Ala Glu Ser Val Lys
1               5                   10                  15

Gly
```

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<210> SEQ ID NO 9
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 9

Gly Phe Ala Ile Arg Tyr Tyr Gly Phe Asp Tyr
1 5 10

<210> SEQ ID NO 10
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 10

Gly Phe Thr Val Ser Asp Tyr
1 5

<210> SEQ ID NO 11
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 11

Gly Gly Val Gly Glu Gly
1 5

<210> SEQ ID NO 12
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 12

Gly Phe Ala Ile Arg Tyr Tyr Gly Phe Asp Tyr
1 5 10

<210> SEQ ID NO 13
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 13

Ser Gly Asp Lys Leu Gly Asp Lys Tyr Ala Tyr
1 5 10

-continued

<210> SEQ ID NO 14
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 14

Gln Asp Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 15
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 15

Gln Val Phe Thr Phe Pro Leu Val Thr Thr
1 5 10

<210> SEQ ID NO 16
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 16

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Asp Lys Tyr Ala
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Leu Val Ile Tyr
35 40 45

Gln Asp Ser Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Phe Thr Phe Pro Leu Val Thr
85 90 95

Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

<210> SEQ ID NO 17
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 17

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

-continued

```
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Gly Gly Val Gly Glu Gly Thr Gln Tyr Ala Glu Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Phe Ala Ile Arg Tyr Tyr Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> SEQ ID NO 18
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic polynucleotide"

<400> SEQUENCE: 18

agctatgaac tgacccagcc gccgagcgtt agcgttagcc caggccagac cgccagcatt     60

acctgtagcg gcgacaaact gggcgacaaa tacgcctact ggtatcagca gaaaccgggc    120

cagagcccgg tgctggttat ctatcaggat agcaaacgcc cgagcggcat tccagaacgc    180

tttagcggca gcaacagcgg caacaccgcc accctgacca ttagcggcac ccaggccgaa    240

gacgaagccg attattactg ccaggttttc actttcccgc tggttactac tgtgtttggc    300

ggcggtacca agctgaccgt gctgggccag                                     330


<210> SEQ ID NO 19
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic polynucleotide"

<400> SEQUENCE: 19

gaagtgcagc tgctggaaag cggtggcggt ctggtgcagc caggtggtag cctgcgcctg     60

agctgtgccg caagcggctt cacagtgtcc gactacgcaa tgcattgggt gcgccaagca    120

ccaggcaaag gcctggaatg ggtgagttac ataggtggcg tgggtgaggg gacacaatat    180

gcagagagcg tgaaaggtcg ctttaccatt agtcgcgata acagcaaaaa caccctgtat    240

ctgcaaatga acagcctgcg ggcagaagat accgcagttt attattgcgc gcgtggtttc    300

gcaatccgtt attatggatt tgattattgg ggccagggca ccctggttac tgtctcgagc    360


<210> SEQ ID NO 20
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 20

Ser Asp His Tyr Ile Ser
1 5

<210> SEQ ID NO 21
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 21

Tyr Ile Ser Ser Ser Gly Ser Thr Thr Tyr Tyr Ala Glu Ser Val Lys
1 5 10 15

Gly

<210> SEQ ID NO 22
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 22

Gln Ser Tyr Tyr Phe Leu Pro Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 23
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 23

Gly Phe Thr Phe Ser Asp His
1 5

<210> SEQ ID NO 24
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 24

Ser Ser Ser Gly Ser Thr
1 5

<210> SEQ ID NO 25
<211> LENGTH: 11
<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 25

Gln Ser Tyr Tyr Phe Leu Pro Tyr Phe Asp Val
1 5 10

<210> SEQ ID NO 26
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 26

Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr Asn Leu Val Ser
1 5 10

<210> SEQ ID NO 27
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 27

Glu Gly Ser Lys Arg Pro Ser
1 5

<210> SEQ ID NO 28
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic peptide"

<400> SEQUENCE: 28

Ala Ser Arg Gly Ser Arg Arg Val Leu Tyr Val
1 5 10

<210> SEQ ID NO 29
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 29

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
20 25 30

Asn Leu Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

-continued

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Arg Gly Ser Arg
85 90 95

Arg Val Leu Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

Gln

<210> SEQ ID NO 30
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 30

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
20 25 30

Tyr Ile Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Thr Tyr Tyr Ala Glu Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gln Ser Tyr Tyr Phe Leu Pro Tyr Phe Asp Val Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 31
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 31

cagagcgccc tgacccagcc agccagcgtt agcggtagcc caggccagag cattaccatt 60

agctgcaccg gcaccagcag cgacgtgggc agctataacc tggttagctg gtatcagcag 120

catccgggca aagccccgaa actgatgatc tatgaaggca gcaaacgccc gagcggcgtt 180

agcaaccgct ttagtggcag caaaagcggc aacaccgcca gcctgaccat tagcggcctg 240

caagccgaag acgaagccga ttattactgc gcaagtcggg gaagccgtcg tgtgctgtat 300

gtttttggcg gcggtaccaa gctgaccgtg ctgggccag 339

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<210> SEQ ID NO 32
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 32

caggtgcagc tggtggaaag cggcggtggc ctggtgaaac caggcggtag cctgcgcctg 60

agctgcgccg ccagcggctt tacctttagc gatcattaca ttagctggat tcgccaggcc 120

ccaggcaaag gcctggaatg ggttagctat attagcagca gtggcagcac cacctattac 180

gccgagagcg tgaaaggccg ctttaccatt agccgcgata acgccaaaaa cagcctgtat 240

ctgcaaatga acagcctgcg ggccgaagat accgccgtgt attattgcgc gcgacaatcc 300

tactatttcc tgccttattt cgacgtttgg ggccagggca ccctggttac tgtctcgagc 360

<210> SEQ ID NO 33
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 33

gactacgcaa tgcat 15

<210> SEQ ID NO 34
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 34

tacataggtg gcgtgggtga ggggacacaa tatgcagaga gcgtgaaagg t 51

<210> SEQ ID NO 35
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 35

ggtttcgcaa tccgttatta tggatttgat tat 33

<210> SEQ ID NO 36
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 36

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ggcttcacag tgtccgacta c 21

<210> SEQ ID NO 37
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 37

ggtggcgtgg gtgagggg 18

<210> SEQ ID NO 38
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 38

ggtttcgcaa tccgttatta tggatttgat tat 33

<210> SEQ ID NO 39
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 39

agcggcgaca aactgggcga caaatacgcc tac 33

<210> SEQ ID NO 40
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 40

caggatagca aacgcccgag c 21

<210> SEQ ID NO 41
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 41

caggttttca ctttcccgct ggttactact 30

<210> SEQ ID NO 42
<211> LENGTH: 214

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 42

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Asp Lys Tyr Ala
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Leu Val Ile Tyr
35 40 45

Gln Asp Ser Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Phe Thr Phe Pro Leu Val Thr
85 90 95

Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys
100 105 110

Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln
115 120 125

Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly
130 135 140

Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly
145 150 155 160

Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala
165 170 175

Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser
180 185 190

Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val
195 200 205

Ala Pro Thr Glu Cys Ser
210

<210> SEQ ID NO 43
<211> LENGTH: 450
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 43

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Gly Gly Val Gly Glu Gly Thr Gln Tyr Ala Glu Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

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65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Phe Ala Ile Arg Tyr Tyr Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450
```

<210> SEQ ID NO 44

-continued

<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 44

agctatgaac tgacccagcc gccgagcgtt agcgttagcc caggccagac cgccagcatt 60

acctgtagcg gcgacaaact gggcgacaaa tacgcctact ggtatcagca gaaaccgggc 120

cagagcccgg tgctggttat ctatcaggat agcaaacgcc cgagcggcat tccagaacgc 180

tttagcggca gcaacagcgg caacaccgcc accctgacca ttagcggcac ccaggccgaa 240

gacgaagccg attattactg ccaggttttc actttcccgc tggttactac tgtgtttggc 300

ggcggtacca agctgaccgt gctgggccag cccaaagccg cccctagcgt gaccctgttc 360

cccccaagca gcgaggaact ccaggccaac aaggccaccc tcgtgtgcct gatcagcgac 420

ttctaccctg gcgccgtgac cgtggcctgg aaggccgata gcagccctgt gaaggccggc 480

gtggaaacca ccacccccag caagcagagc aacaacaaat acgccgccag cagctacctg 540

agcctgaccc ccgagcagtg gaagtcccac agatcctaca gctgccaggt cacacacgag 600

ggcagcaccg tggaaaagac cgtggccccc accgagtgca gc 642

<210> SEQ ID NO 45
<211> LENGTH: 1350
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 45

gaagtgcagc tgctggaaag cggtggcggt ctggtgcagc caggtggtag cctgcgcctg 60

agctgtgccg caagcggctt cacagtgtcc gactacgcaa tgcattgggt gcgccaagca 120

ccaggcaaag gcctggaatg ggtgagttac ataggtggcg tgggtgaggg gacacaatat 180

gcagagagcg tgaaaggtcg ctttaccatt agtcgcgata acagcaaaaa caccctgtat 240

ctgcaaatga acagcctgcg ggcagaagat accgcagttt attattgcgc gcgtggtttc 300

gcaatccgtt attatggatt tgattattgg ggccagggca ccctggttac tgtctcgagc 360

gcgtcgacca aaggccccag cgtgttccct ctggccccca gcagcaagag cacctctggc 420

ggaacagccg ccctgggctg cctggtcaag gactacttcc ccgagcccgt gaccgtgtcc 480

tggaactctg gcgccctgac cagcggcgtg cacaccttc cagccgtgct ccagagcagc 540

ggcctgtaca gcctgagcag cgtcgtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacacaaagg tggacaagcg ggtggaaccc 660

aagagctgcg acaagaccca cacctgtccc ccctgccctg cccctgaact gctgggaggc 720

ccctccgtgt tcctgttccc cccaaagcct aaggacaccc tgatgatcag ccggacccc 780

gaagtgacct gcgtggtggt ggacgtgtcc cacgaggacc ctgaagtgaa gtttaattgg 840

tacgtggacg gcgtggaagt gcacaacgcc aagaccaagc ccagagagga acagtacaac 900

agcacctacc gggtggtgtc cgtgctgacc gtgctgcacc aggactggct gaacggcaaa 960

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gagtacaagt gcaaggtgtc caacaaggcc ctgcctgccc ccatcgagaa aaccatcagc 1020

aaggccaaag gccagccccg cgagccccag gtgtacacac tgcccctag ccgggaagag 1080

atgaccaaga accaggtgtc cctgacctgc ctcgtgaagg gcttctaccc cagcgacatt 1140

gccgtggaat gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggctcatt cttcctgtac agcaagctga ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgctccgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagtccc tgagcctgag ccccggcaag 1350

<210> SEQ ID NO 46
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 46

agcgatcatt acattagc 18

<210> SEQ ID NO 47
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 47

tatattagca gcagtggcag caccacctat tacgccgaga gcgtgaaagg c 51

<210> SEQ ID NO 48
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 48

caatcctact atttcctgcc ttatttcgac gtt 33

<210> SEQ ID NO 49
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 49

ggctttacct ttagcgatca t 21

<210> SEQ ID NO 50
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 50

agcagcagtg gcagcacc 18

<210> SEQ ID NO 51
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 51

caatcctact atttcctgcc ttatttcgac gtt 33

<210> SEQ ID NO 52
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 52

accggcacca gcagcgacgt gggcagctat aacctggtta gc 42

<210> SEQ ID NO 53
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 53

gaaggcagca aacgcccgag c 21

<210> SEQ ID NO 54
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 54

gcaagtcggg gaagccgtcg tgtgctgtat gtt 33

<210> SEQ ID NO 55
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polypeptide"

<400> SEQUENCE: 55

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Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
            20                  25                  30

Asn Leu Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Arg Gly Ser Arg
                85                  90                  95

Arg Val Leu Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
            100                 105                 110

Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu
        115                 120                 125

Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe
    130                 135                 140

Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val
145                 150                 155                 160

Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys
                165                 170                 175

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
            180                 185                 190

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu
        195                 200                 205

Lys Thr Val Ala Pro Thr Glu Cys Ser
    210                 215


<210> SEQ ID NO 56
<211> LENGTH: 450
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic polypeptide"

<400> SEQUENCE: 56

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp His
            20                  25                  30

Tyr Ile Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Thr Tyr Tyr Ala Glu Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gln Ser Tyr Tyr Phe Leu Pro Tyr Phe Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
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        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450


<210> SEQ ID NO 57
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Synthetic polynucleotide"

<400> SEQUENCE: 57
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cagagcgccc tgacccagcc agccagcgtt agcggtagcc caggccagag cattaccatt 60

agctgcaccg gcaccagcag cgacgtgggc agctataacc tggttagctg gtatcagcag 120

catccgggca aagccccgaa actgatgatc tatgaaggca gcaaacgccc gagcggcgtt 180

agcaaccgct ttagtggcag caaaagcggc aacaccgcca gcctgaccat tagcggcctg 240

caagccgaag acgaagccga ttattactgc gcaagtcggg gaagccgtcg tgtgctgtat 300

gtttttggcg gcggtaccaa gctgaccgtg ctgggccagc ccaaagccgc ccctagcgtg 360

accctgttcc ccccaagcag cgaggaactc caggccaaca aggccaccct cgtgtgcctg 420

atcagcgact tctaccctgg cgccgtgacc gtggcctgga aggccgatag cagccctgtg 480

aaggccggcg tggaaaccac cacccccagc aagcagagca acaacaaata cgccgccagc 540

agctacctga gcctgacccc cgagcagtgg aagtcccaca gatcctacag ctgccaggtc 600

acacacgagg gcagcaccgt ggaaaagacc gtggcccccа ccgagtgcag c 651

<210> SEQ ID NO 58
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 58

gactacgcta tgcac 15

<210> SEQ ID NO 59
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 59

tatatcggcg gcgtgggcga gggcacccag tacgctgagt ctgtgaaggg c 51

<210> SEQ ID NO 60
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 60

ggcttcgcca tccggtacta cggcttcgac tac 33

<210> SEQ ID NO 61
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 61

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ggcttcaccg tgtccgacta c 21

<210> SEQ ID NO 62
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 62

ggcggcgtgg gcgagggc 18

<210> SEQ ID NO 63
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 63

ggcttcgcca tccggtacta cggcttcgac tac 33

<210> SEQ ID NO 64
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 64

tccggcgaca agctgggcga taagtacgcc tac 33

<210> SEQ ID NO 65
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 65

caggactcca agcggccctc c 21

<210> SEQ ID NO 66
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic oligonucleotide"

<400> SEQUENCE: 66

caggtgttca ccttcccct ggtcaccacc 30

<210> SEQ ID NO 67
<211> LENGTH: 330

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 67

tcctacgagc tgacccagcc cccctccgtg tccgtgtctc ctggccagac cgcctccatc 60

acctgttccg gcgacaagct gggcgataag tacgcctact ggtatcagca gaagcccggc 120

cagtcccccg tgctggtcat ctaccaggac tccaagcggc cctccggcat ccctgagcgg 180

ttctccggct ccaactccgg caacaccgcc accctgacca tctccggcac ccaggccgag 240

gacgaggccg actactactg ccaggtgttc accttccccc tggtcaccac cgtgttcggc 300

ggaggcacca agctgaccgt gctgggccag 330

<210> SEQ ID NO 68
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 68

gaggtgcagc tgctggaatc cggcggagga ctggtgcagc ctggcggctc cctgagactg 60

tcttgcgccg cctccggctt caccgtgtcc gactacgcta tgcactgggt ccgacaggcc 120

cctggcaagg gcctggaatg ggtgtcctat atcggcggcg tgggcgaggg cacccagtac 180

gctgagtctg tgaagggccg gttcaccatc tcccgggaca actccaagaa caccctgtac 240

ctgcagatga actccctgcg ggccgaggac accgccgtgt actactgtgc cagaggcttc 300

gccatccggt actacggctt cgactactgg ggccagggca ccctggtcac cgtgtctagc 360

<210> SEQ ID NO 69
<211> LENGTH: 642
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 69

tcctacgagc tgacccagcc cccctccgtg tccgtgtctc ctggccagac cgcctccatc 60

acctgttccg gcgacaagct gggcgataag tacgcctact ggtatcagca gaagcccggc 120

cagtcccccg tgctggtcat ctaccaggac tccaagcggc cctccggcat ccctgagcgg 180

ttctccggct ccaactccgg caacaccgcc accctgacca tctccggcac ccaggccgag 240

gacgaggccg actactactg ccaggtgttc accttccccc tggtcaccac cgtgttcggc 300

ggaggcacca agctgaccgt gctgggccag cctaaggccg ctccctccgt gaccctgttc 360

cccccatcct ccgaggaact gcaggccaac aaggccaccc tggtctgcct gatctccgac 420

ttctaccctg gcgccgtgac cgtggcctgg aaggccgaca gctctcctgt gaaggccggc 480

gtggaaacca ccaccccctc caagcagtcc aacaacaaat acgccgcctc ctcctacctg 540

tccctgaccc ccgagcagtg gaagtcccac cggtcctaca gctgccaggt cacacacgag 600

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ggctccaccg tggaaaagac cgtggcccct accgagtgct cc 642

<210> SEQ ID NO 70
<211> LENGTH: 1350
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 70

gaggtgcagc tgctggaatc cggcggagga ctggtgcagc ctggcggctc cctgagactg 60

tcttgcgccg cctccggctt caccgtgtcc gactacgcta tgcactgggt ccgacaggcc 120

cctggcaagg gcctggaatg ggtgtcctat atcggcggcg tgggcgaggg cacccagtac 180

gctgagtctg tgaagggccg gttcaccatc tcccgggaca actccaagaa caccctgtac 240

ctgcagatga actccctgcg ggccgaggac accgccgtgt actactgtgc cagaggcttc 300

gccatccggt actacggctt cgactactgg ggccagggca ccctggtcac cgtgtctagc 360

gcctccacca agggcccctc cgtgttccct ctggcccccc ccagcaagtc cacctctggc 420

ggcaccgctg ccctgggctg cctggtcaag gactacttcc ccgagcccgt gaccgtgtcc 480

tggaactctg gcgccctgac ctccggcgtg cacaccttcc ctgccgtgct gcagtcctcc 540

ggcctgtact ccctgtcctc cgtcgtgacc gtgccctcca gctctctggg cacccagacc 600

tacatctgca acgtgaacca caagccctcc aacaccaagg tggacaagcg ggtggaaccc 660

aagtcctgcg acaagaccca cacctgtccc ccctgccctg cccctgaact gctgggcgga 720

ccttccgtgt tcctgttccc cccaaagccc aaggacaccc tgatgatctc ccggacccccc 780

gaagtgacct gcgtggtggt ggacgtgtcc cacgaggacc ctgaagtgaa gttcaattgg 840

tacgtggacg gcgtggaagt gcacaacgcc aagaccaagc ccagagagga acagtacaac 900

tccacctacc gggtggtgtc cgtgctgacc gtgctgcacc aggactggct gaacggcaaa 960

gagtacaagt gcaaggtgtc caacaaggcc ctgcctgccc ccatcgaaaa gaccatctcc 1020

aaggccaagg gccagccccg cgagccccag gtgtacacac tgcccccctag ccgggaagag 1080

atgaccaaga accaggtgtc cctgacctgt ctggtcaagg gcttctaccc ctccgacatt 1140

gccgtggaat gggagtccaa cggccagccc gagaacaact acaagaccac ccccccctgtg 1200

ctggactccg acggctcatt cttcctgtac tccaagctga ccgtggacaa gtcccggtgg 1260

cagcagggca acgtgttctc ctgctccgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagtccc tgtccctgag ccccggcaag 1350

<210> SEQ ID NO 71
<211> LENGTH: 1350
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic polynucleotide"

<400> SEQUENCE: 71

caggtgcagc tggtggaaag cggcggtggc ctggtgaaac caggcggtag cctgcgcctg 60

agctgcgccg ccagcggctt tacctttagc gatcattaca ttagctggat tcgccaggcc 120

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ccaggcaaag gcctggaatg ggttagctat attagcagca gtggcagcac cacctattac    180

gccgagagcg tgaaaggccg ctttaccatt agccgcgata acgccaaaaa cagcctgtat    240

ctgcaaatga acagcctgcg ggccgaagat accgccgtgt attattgcgc gcgacaatcc    300

tactatttcc tgccttattt cgacgtttgg ggccagggca ccctggttac tgtctcgagc    360

gcgtcgacca aaggccccag cgtgttccct ctggccccca gcagcaagag cacctctggc    420

ggaacagccg ccctgggctg cctggtcaag gactacttcc ccgagcccgt gaccgtgtcc    480

tggaactctg gcgccctgac cagcggcgtg cacacctttc cagccgtgct ccagagcagc    540

ggcctgtaca gcctgagcag cgtcgtgacc gtgcccagca gcagcctggg cacccagacc    600

tacatctgca acgtgaacca caagcccagc aacacaaagg tggacaagcg ggtggaaccc    660

aagagctgcg acaagaccca cacctgtccc ccctgccctg cccctgaact gctgggaggc    720

ccctccgtgt tcctgttccc cccaaagcct aaggacaccc tgatgatcag ccggaccccc    780

gaagtgacct gcgtggtggt ggacgtgtcc cacgaggacc ctgaagtgaa gtttaattgg    840

tacgtggacg gcgtggaagt gcacaacgcc aagaccaagc ccagagagga acagtacaac    900

agcacctacc gggtggtgtc cgtgctgacc gtgctgcacc aggactggct gaacggcaaa    960

gagtacaagt gcaaggtgtc caacaaggcc ctgcctgccc ccatcgagaa aaccatcagc   1020

aaggccaaag gccagccccg cgagccccag gtgtacacac tgcccccctag ccgggaagag   1080

atgaccaaga accaggtgtc cctgacctgc ctcgtgaagg gcttctaccc cagcgacatt   1140

gccgtggaat gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg   1200

ctggacagcg acggctcatt cttcctgtac agcaagctga ccgtggacaa gagccggtgg   1260

cagcagggca acgtgttcag ctgctccgtg atgcacgagg ccctgcacaa ccactacacc   1320

cagaagtccc tgagcctgag ccccggcaag                                    1350
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1: An antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment cross-competes with an antibody comprising

(a) the HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

(b) the HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

2: An antibody or antibody fragment specific for IL-17C wherein said antibody or antibody fragment comprises

(a) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 7, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 8, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 9, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 13, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 14 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 15, or

(b) a HCDR1 region comprising the amino acid sequence of SEQ ID No.: 20, a HCDR2 region comprising the amino acid sequence of SEQ ID No.: 21, a HCDR3 region comprising the amino acid sequence of SEQ ID No.: 22, a LCDR1 region comprising the amino acid sequence of SEQ ID No.: 26, a LCDR2 region comprising the amino acid sequence of SEQ ID No.: 27 and a LCDR3 region comprising the amino acid sequence of SEQ ID No.: 28.

3: An antibody or antibody fragment according to claim **2** wherein said antibody or antibody fragment comprises

(a) a HCDR1 region of SEQ ID No.: 7, the HCDR2 region of SEQ ID No.: 8, the HCDR3 region of SEQ ID No.: 9, the LCDR1 region of SEQ ID No.: 13, the LCDR2 region of SEQ ID No.: 14 and the LCDR3 region of SEQ ID No.: 15, or

(b) a HCDR1 region of SEQ ID No.: 20, the HCDR2 region of SEQ ID No.: 21, the HCDR3 region of SEQ ID No.: 22, the LCDR1 region of SEQ ID No.: 26, the LCDR2 region of SEQ ID No.: 27 and the LCDR3 region of SEQ ID No.: 28.

4: An antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment is specific for human IL-17C.

5: An isolated antibody or antibody fragment according to claim **4**, wherein said antibody or antibody fragment is specific for human IL-17C, cynomolgus IL-17C and mouse IL-17C.

6: The antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment is a human, humanized or chimeric antibody or antibody fragment.

7: An antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 17 and a light chain of SEQ ID No.: 16.

8: An antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment comprises a heavy chain of SEQ ID No.: 30 and a light chain of SEQ ID No.: 29.

9: An antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment is an isolated antibody or antibody fragment.

10: An antibody or antibody fragment according to claim **1**, wherein said antibody or antibody fragment is a recombinant antibody or antibody fragment.

11. (canceled)

12: A nucleic acid composition comprising a nucleic acid sequence or a plurality of nucleic acid sequences encoding the antibody or antibody fragment according to claim **1**.

13: A vector composition comprising a vector or a plurality of vectors comprising the nucleic acid sequence or plurality of nucleic acid sequences of claim **12**.

14: A cell comprising the vector composition of claim **13**.

15: A pharmaceutical composition comprising the antibody or antibody fragment according to claim **1** and a pharmaceutically acceptable carrier or excipient.

16: A method for treating a subject with an inflammatory disorder, said method comprising administering the antibody or antibody fragment of claim **1** to the subject.

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