anti–IL-36R antibody, arguing that the IL-36 axis is required to maintain the lesional phenotype in human psoriatic skin. Taken together, these data indicate that IL-36R ligands, including IL-36α, IL-36β, and IL-36γ, exert proinflammatory effects *in vitro* and *in vivo* and that IL-36Ra acts as a natural antagonist, thus mimicking the IL-1/IL-1Ra system.

There is therefore evidence that IL-36R ligands are involved in a number of disease conditions, and there is a need for new therapeutic agents targeting this pathway, in particular for use in the treatment of inflammatory diseases.

Summary ~~of the invention~~

The present ~~invention~~ disclosure addresses the above need by providing biotherapeutics, in particular antibodies, which bind to IL-36R. ~~In one aspect, t~~The antibodies of the present ~~invention~~ disclosure block IL36 ligand-mediated signaling (α, β and/or γ). ~~In one aspect t~~The antibodies of the present ~~invention~~ disclosure are useful, for example for the treatment of epithelial-mediated inflammation/fibrosis in diseases such as psoriasis, inflammatory bowel disease, scleroderma, COPD, and chronic kidney disease.

~~In one aspect, t~~The present disclosure ~~invention~~ provides an anti-IL-36R antibody having one or more of the properties below.

~~In one aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ has high molecular/cellular binding potency. ~~In one aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ binds to human IL-36R at a $K_D < 0.1$ nM. ~~In a f~~Further ~~aspect~~, an anti-IL-36R antibody of the present disclosure~~invention~~, in particular a humanized anti-IL-36R antibody, binds to human IL-36R at a $K_D < 50$ pM. ~~In one aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ binds to IL-36R expressing cells at an EC_{90} <5 nM.

~~In another aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ has high cell-based functional blocking potency. ~~In one aspect, an~~The anti-IL-36R antibody of the present

disclosure ~~invention~~ blocks all three IL-36R agonistic ligands (α, β, γ) at an IC_{90} ≤5 nM, in disease-relevant cell lines and primary cells.

~~In one aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ has the molecular/cellular binding potency and the cell-based functional blocking potency set forth above.

~~In a further aspect, an~~The anti-IL-36R antibody of the present disclosure ~~invention~~ has high selectivity for example greater than 1000-fold selectivity against human IL-1R1 or IL-36R negative cell lines. ~~In a f~~Further ~~aspect~~, ~~an~~ the anti-IL-36R antibody of the present disclosure ~~invention~~ does not bind to human IL-1R1 or IL-36R negative cell lines.

In one aspect, there is provided an "anti-interleukin-36 receptor" (anti-IL-36R) antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 35, 102, 103, 104, 105 106 or 140 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

In another aspect, there is provided an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

In another aspect, there is provided an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 103 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In another aspect, there is provided an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 104(L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In another aspect, there is provided an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87.

In another aspect, there is provided an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88.

In another aspect, there is provided an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

In another aspect, there is provided a pharmaceutical composition comprising an antibody or antigen-binding fragment described herein and a pharmaceutically acceptable carrier.

In embodiment one, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof, which binds to human IL-36R at a K_D equal to or < 0.1 nM.

In embodiment two, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the said antibody or antigen-binding fragment is a monoclonal antibody or antigen-binding fragment thereof.

In embodiment three, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one or two, wherein the said antibody or antigen-binding fragment is a humanized antibody or antigen-binding fragment thereof.

In embodiment four, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment three, which binds to human IL-36R at a K_D equal to or < 50 pM.

In embodiment five, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to any one of embodiment one to four, which does not bind to human IL-1R1.

In embodiment six, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 35, 102, 103, 104, 105 106 or 140 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment seven, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 102 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment eight, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 103 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment nine, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 104 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment ten, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 105 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment eleven, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 106 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment twelve, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment six, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 140 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment thirteen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 76, 77, 78, 79, 80, 81, 82 or 83; and a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 87, 88, 89, 90, 91, 92, 93, 94 or 95.
In embodiment fourteen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment thirteen, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87;or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88; or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

In embodiment fifteen, the present disclosure ~~invention~~ provides an in the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising

the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87;or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88; or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

In embodiment sixteen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); **or**
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); or **or**
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 54 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 or 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).

In embodiment seventeen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 84, 85 or 86; and a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 96, 97, 98, 99, 100 or 101.

In embodiment eighteen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodim~~n~~ent seventeen, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 85; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 100; or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 85; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:101.

In embodiment nineteen, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment seventeen, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 86; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 100; or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 86; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:101.

In embodiment twenty, the present disclosure ~~invention~~ provides an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of any one of SEQ ID NO: 114, 115, 116, 117, 118, 119, 120 or 121; and a heavy chain comprising the amino acid sequence of any one of SEQ ID NO: 125, 126, 127, 128, 129, 130, 131, 132 or 133.

In embodiment twenty one, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

In embodiment twenty two, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

In embodiment twenty three, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

In embodiment twenty four, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

In embodiment twenty five, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

In embodiment twenty six, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

In embodiment twenty seven, the present disclosure ~~invention~~ provides an anti-IL-36R antibody, wherein the antibody comprises a light chain comprising the amino acid sequence of any one of SEQ ID NO: 122, 123 or 124; and a heavy chain comprising the amino acid sequence of any one of SEQ ID NO: 134, 135, 136, 137, 138 or 139.

In embodiment twenty eight, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty seven, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 123; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 138.

In embodiment twenty nine, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to embodiment twenty seven, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 123; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 139.

In embodiment thirty, the present disclosure ~~invention~~ provides an anti-IL-36R antibody according to twenty seven, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 124; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 138.

In embodiment thirty one, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 103 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment thirty two, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 104(L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

In embodiment thirty three, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36(L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).

In embodiment thirty four, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof according to embodiment one, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36(L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).

In one embodiment, an antibody or antigen-binding fragment thereof according to any one of embodiments one to thirty-four is a monoclonal antibody. In one embodiment, an antibody or antigen-binding fragment thereof according to any one of embodiments one to thirty-four is a humanized antibody. In one embodiment, an antibody or antigen-binding fragment thereof according to any one of embodiments one to thirty-four is a monoclonal humanized antibody.

In embodiment thirty five, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 21 (L-CDR1); the amino acid sequence of SEQ ID NO: 30 (L-CDR2); the amino acid sequence of SEQ ID NO: 39 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 48 (H-CDR1); the amino acid sequence of SEQ ID NO: 57 (H-CDR2); the amino acid sequence of SEQ ID NO: 67 (H-CDR3); **or**
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 22 (L-CDR1); the amino acid sequence of SEQ ID NO: 31 (L-CDR2); the amino acid sequence of SEQ ID NO: 40 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 49 (H-CDR1); the amino acid sequence of SEQ ID NO: 58 (H-CDR2); the amino acid sequence of SEQ ID NO: 68 (H-CDR3); **or**
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23 (L-CDR1); the amino acid sequence of SEQ ID NO: 32 (L-CDR2); the amino acid sequence of SEQ ID NO: 41 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 50 (H-CDR1); the amino acid sequence of SEQ ID NO: 59 (H-CDR2); the amino acid sequence of SEQ ID NO: 69 (H-CDR3); **or**
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 24 (L-CDR1); the amino acid sequence of SEQ ID NO: 33 (L-CDR2); the amino acid sequence of SEQ ID NO: 42 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 51 (H-CDR1); the amino acid sequence of SEQ ID NO: 60 (H-CDR2); the amino acid sequence of SEQ ID NO: 70 (H-CDR3); **or**

In embodiment thirty six, the present disclosure ~~invention~~ provides an anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 11; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 2; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 12; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 3; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 13; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 4; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 14; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 5; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 15; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 16; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 7; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 17; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 18; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 9; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 19; **or**

a light chain variable region comprising the amino acid sequence of SEQ ID NO: 10; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 20.

In a further embodiment thirty seven, the present disclosure ~~invention~~ provides a pharmaceutical composition comprising an antibody or antigen-binding fragment according to any one of the previous embodiments and a pharmaceutically acceptable carrier.

In a further embodiment thirty eight, the present disclosure ~~invention~~ provides an antibody or antigen-binding fragment or pharmaceutical composition according to any one of the previous embodiments, for use in medicine.

In a further embodiment thirty nine, the present disclosure ~~invention~~ provides an antibody or antigen-binding fragment or pharmaceutical composition according to any one of the embodiments 1-37, wherein the use is the treatment of an inflammatory disease, of an autoimmune disease, of a respiratory disease, of a metabolic disorder, of an epithelial mediated inflammatory disorder, fibrosis or of cancer.

In a further embodiment forty~~-~~, the present disclosure ~~invention~~ provides an antibody or antigen-binding fragment or pharmaceutical composition according to any one of the embodiments 1-37, wherein the use is for the treatment of psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma or ankylosing spondylitis.

In a further embodiment forty one, the present disclosure ~~invention~~ provides an antibody or antigen-binding fragment or pharmaceutical composition according to any one of the embodiments 1-37, wherein the use is for the treatment of inflammatory bowel disease.

In a still further embodiment forty two, the present disclosure ~~invention~~ provides an antibody or antigen-binding fragment or pharmaceutical composition according to embodiment 41, wherein the ~~the~~ disease is Crohns disease.

In another embodiment forty three, the present disclosure ~~invention~~ provides a method of treating a disease comprising administering the antibody or antigen-binding fragment or pharmaceutical composition according to any one of the embodiments 1-37, to a patient in need thereof, wherein the disease is selected from an inflammatory disease, an autoimmune disease, a respiratory disease, a metabolic disorder, an epithelial mediated inflammatory disorder, fibrosis and cancer.

In another embodiment forty four, the present disclosure ~~invention~~ provides a method according to embodiment 43 wherein the disease is selected from psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma and ankylosing spondylitis.

In a still further embodiment forty five, the present disclosure ~~invention~~ provides a method for treating Crohns disease.

Further embodiments of the disclosure ~~invention~~ encompass:

- An isolated polynucleotide comprising a sequence encoding an anti-IL-36R antibody or antigen-binding fragment according to the disclosure~~invention~~, preferably a DNA or RNA sequence;
- an isolated polynucleotide according to the disclosure~~invention~~, encoding a sequence as defined by one or more of SEQ ID NOs. 1 to 140;
- a vector comprising a polynucleotide according to the disclosure~~invention~~, preferably an expression vector, more preferred a vector comprising the polynucleotide according to the disclosure ~~invention~~ in functional association with an expression control sequence;
- a host cell comprising a polynucleotide according to the disclosure ~~invention~~ and/or a vector according to the disclosure~~invention~~;
- a method for the production of an anti-IL-36R antibody or antigen-binding fragment according to the disclosure~~invention~~, preferably a recombinant production method comprising the use of a polynucleotide according to the disclosure~~invention~~, and/or of a vector according to the disclosure ~~invention~~ and/or of a host cell according to the disclosure~~invention~~;

- such a method preferably comprises the steps (a) cultivating the host cell under conditions allowing the expression of the anti-IL-36R antibody or antigen-binding fragment and (b) recovering the anti-IL-36R antibody or antigen-binding fragment;
- a diagnostic kit or diagnostic method comprising an anti-IL-36R antibody or antigen-binding fragment according to the disclosure~~invention~~, or the use thereof;
- a Diagnostic kit or diagnostic method according the disclosure~~invention~~, for the diagnosis of an inflammatory disease, an autoimmune disease, a respiratory disease, a metabolic disorder, an epithelial mediated inflammatory disorder, fibrosis, cancer, psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma, ankylosing spondylitis, or Crohns disease.

Brief Description of the Figures

Figure 1: IL-36 antagonist ligands (IL-36RA/IL1F5 , IL-38/ILF10) inhibit the signaling cascade.

Figure 2: Gene chip analyses demonstrate IL-36R ligands are upregulated in psoriatic skin (IL-36 RA, IL-36 α and IL-36 γ).

Figure 3: Expression profile using human skin sections.
Formalin-fixed paraffin embedded with antibody titrations using antibody 33D10

Figure 4: Method to Evaluate Epidermal thickness of human skin sections

Description of the invention

This invention relates to anti-IL-36R antibodies. In one aspect, the antibodies of the present invention are for diagnostic and therapeutic use, for example in humans.

Claims

~~1. An anti-IL-36R antibody or antigen-binding fragment thereof, which binds to human IL-36R at a K_D equal to or < 0.1 nM.~~

~~2. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim 1, wherein the said antibody or antigen-binding fragment is a monoclonal antibody or antigen-binding fragment thereof.~~

~~3. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim 1 and/or 2, wherein the said antibody or antigen-binding fragment is a humanized antibody or antigen-binding fragment thereof.~~

~~4. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 3, which binds to human IL-36R at a K_D equal to or < 50 pM.~~

~~5. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 4, which does not bind to human IL-1R1.~~

~~6~~1. An "anti-interleukin-36 receptor" (anti-IL-36R) antibody or antigen-binding fragment thereof ~~according to one or more of claims 1 to 5~~, wherein the antibody or antigen-binding fragment thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 35, 102, 103, 104, 105 106 or 140 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~7~~2. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~6~~1, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 102 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~83~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~61~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 103 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~94~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~61~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 104 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~105~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~61~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 105 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~116~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~61~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 106 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~127~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~61~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:
a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 140 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62, 108, 109, 110 or 111 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

~~138~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to ~~one or more of~~ claim~~s~~ 1 ~~to 5~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 76, 77, 78, 79, 80, 81, 82 or 83; and a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 87, 88, 89, 90, 91, 92, 93, 94 or 95.

9. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 8 and a pharmaceutically acceptable carrier.

~~1410~~. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~138~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light

chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87;or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88; or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 77; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

~~15~~11. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim ~~13~~8, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87;or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88; or
a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

12. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 1 and a pharmaceutically acceptable carrier.

~~16. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises:~~
~~a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); or~~

~~a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising~~

~~20~~13. An anti-IL-36R antibody according to ~~one or more of~~ claim~~s~~ 1 ~~to 5~~, wherein the antibody comprises a light chain comprising the amino acid sequence of any one of SEQ ID NO: 114, 115, 116, 117, 118, 119, 120 or 121; and a heavy chain comprising the amino acid sequence of any one of SEQ ID NO: 125, 126, 127, 128, 129, 130, 131, 132 or 133.

14. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 13 and a pharmaceutically acceptable carrier.

~~21~~15. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

16. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 15 and a pharmaceutically acceptable carrier.

~~22~~17. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

18. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 17 and a pharmaceutically acceptable carrier.

~~23~~19. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 115; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

20. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 19 and a pharmaceutically acceptable carrier.

~~24~~21. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 125.

22. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 21 and a pharmaceutically acceptable carrier.

~~25~~23. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 126.

24. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 23 and a pharmaceutically acceptable carrier.

~~26~~25. An anti-IL-36R antibody ~~according to claim 20~~, wherein the antibody ~~thereof~~ comprises a light chain comprising the amino acid sequence of SEQ ID NO: 118; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 127.

26. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 25 and a pharmaceutically acceptable carrier.

~~27. An anti-IL-36R antibody according to one or more of claims 1 to 5, wherein the antibody comprises a light chain comprising the amino acid sequence of any one of SEQ ID NO: 122, 123 or 124; and a heavy chain comprising the amino acid sequence of any one of SEQ ID NO: 134, 135, 136, 137, 138 or 139.~~

~~28. An anti-IL-36R antibody according to claim 27, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 123; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 138.~~

~~29. An anti-IL-36R antibody according to claim 27, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 123; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 139.~~

~~30. An anti-IL-36R antibody according to claim 27, wherein the antibodycomprises a light chain comprising the amino acid sequence of SEQ ID NO: 124; and a heavy chain comprising the amino acid sequence of SEQ ID NO: 138.~~

~~31~~27. An anti-IL-36R antibody or antigen-binding fragment thereof ~~according to one or more of claims 1 to 5~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 103 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

28. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 27 and a pharmaceutically acceptable carrier.

~~32~~29. An anti-IL-36R antibody or antigen-binding fragment thereof ~~according to one or more of claims 1 to 5~~, wherein the antibody or antigen-binding fragment ~~fragment~~ thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 104(L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and
b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3).

30. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 29 and a pharmaceutically acceptable carrier.

31. An anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87.

32. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 31 and a pharmaceutically acceptable carrier.

33. An anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88.

34. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 33 and a pharmaceutically acceptable carrier.

35. An anti-IL-36R antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89.

36. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to claim 35 and a pharmaceutically acceptable carrier.

~~33. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises:~~

~~a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36(L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and~~

~~b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).~~

~~34. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises:~~

~~a) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36(L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and~~

~~b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).~~

~~35. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises:~~

~~the amino acid sequence of SEQ ID NO: 107 (H-CDR1); the amino acid sequence of SEQ ID NO: 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 54 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 or 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3).~~

~~17. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises a light chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 84, 85 or 86; and a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NO: 96, 97, 98, 99, 100 or 101.~~

~~18. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim 17, wherein the antibody or antigen-binding fragment fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 85; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 100; or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 85; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:101.~~

~~19. An anti-IL-36R antibody or antigen-binding fragment thereof according to claim 17, wherein the antibody or antigen-binding fragment fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 86; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 100; or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 86; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:101.~~

~~a light chain variable region comprising the amino acid sequence of SEQ ID NO: 21 (L-CDR1); the amino acid sequence of SEQ ID NO: 30 (L-CDR2); the amino acid sequence of SEQ ID NO: 39 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 48 (H-CDR1); the amino acid sequence of SEQ ID NO: 57 (H-CDR2); the amino acid sequence of SEQ ID NO: 67 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 22 (L-CDR1); the amino acid sequence of SEQ ID NO: 31 (L-CDR2); the amino acid sequence of SEQ ID NO: 40 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 49 (H-CDR1); the amino acid sequence of SEQ ID NO: 58 (H-CDR2); the amino acid sequence of SEQ ID NO: 68 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23 (L-CDR1); the amino acid sequence of SEQ ID NO: 32 (L-CDR2); the amino acid sequence of SEQ ID NO: 41 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 50 (H-CDR1); the amino acid sequence of SEQ ID NO: 59 (H-CDR2); the amino acid sequence of SEQ ID NO: 69 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 24 (L-CDR1); the amino acid sequence of SEQ ID NO: 33 (L-CDR2); the amino acid sequence of SEQ ID NO: 42 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 51 (H-CDR1); the amino acid sequence of SEQ ID NO: 60 (H-CDR2); the amino acid sequence of SEQ ID NO: 70 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 25 (L-CDR1); the amino acid sequence of SEQ ID NO: 34 (L-CDR2); the amino acid sequence of SEQ ID NO: 43 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 52 (H-CDR1); the amino acid sequence of SEQ ID NO: 61 (H-CDR2); the amino acid sequence of SEQ ID NO: 71 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26 (L-CDR1); the amino acid sequence of SEQ ID NO: 35 (L-CDR2); the amino acid sequence of SEQ ID NO: 44 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 (H-CDR1); the amino acid sequence of SEQ ID NO: 62 (H-CDR2); the amino acid sequence of SEQ ID NO: 72 (H-CDR3); or~~

~~a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 54 (H-CDR1); the amino acid sequence of SEQ ID NO: 63 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27 (L-CDR1); the amino acid sequence of SEQ ID NO: 36 (L-CDR2); the amino acid sequence of SEQ ID NO: 45 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 54 (H-CDR1); the amino acid sequence of SEQ ID NO: 64 (H-CDR2); the amino acid sequence of SEQ ID NO: 73 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28 (L-CDR1); the amino acid sequence of SEQ ID NO: 37 (L-CDR2); the amino acid sequence of SEQ ID NO: 46 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 55 (H-CDR1); the amino acid sequence of SEQ ID NO: 65 (H-CDR2); the amino acid sequence of SEQ ID NO: 74 (H-CDR3); or a light chain variable region comprising the amino acid sequence of SEQ ID NO: 29 (L-CDR1); the amino acid sequence of SEQ ID NO: 38 (L-CDR2); the amino acid sequence of SEQ ID NO: 47 (L-CDR3); and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 56 (H-CDR1); the amino acid sequence of SEQ ID NO: 66 (H-CDR2); the amino acid sequence of SEQ ID NO: 75 (H-CDR3).~~

~~36. An anti-IL-36R antibody or antigen-binding fragment thereof according to one or more of claims 1 to 5, wherein the antibody or antigen-binding fragment fragment thereof comprises a light chain protein comprising the amino acid sequence of SEQ ID NO: 1; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 11; or~~

~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 2; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 12; or~~

~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 3; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 13; or~~

~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 4; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 14; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 5; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 15; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 6; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 16; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 7; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 17; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 8; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 18; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 9; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 19; or~~
~~a light chain protein comprising the amino acid sequence of SEQ ID NO: 10; and a heavy chain protein comprising the amino acid sequence of SEQ ID NO: 20.~~

~~37. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to one or more of claims 1 to 36 and a pharmaceutically acceptable carrier.~~

~~38. An antibody or antigen-binding fragment according to one or more of claims 1 to 36 or pharmaceutical composition according to claim 37, for use in medicine.~~

~~39. An antibody or antigen-binding fragment or pharmaceutical composition according to claim 38, wherein the use in medicine is the use in a method for the treatment of an inflammatory disease, of an autoimmune disease, of a respiratory disease, of a metabolic disorder, of an epithelial mediated inflammatory disorder, fibrosis or of cancer.~~

~~40. An antibody or antigen-binding fragment or pharmaceutical composition according to one or more of claims 38 or 39, wherein the use in medicine is the use in a~~

~~method for the treatment of psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma or ankylosing spondylitis.~~

~~41. An antibody or antigen-binding fragment or pharmaceutical composition according to one or more of claims 38 to 40, wherein the use in medicine is the use in a method for the treatment of inflammatory bowel disease.~~

~~42. An antibody or antigen-binding fragment or pharmaceutical composition according to one or more of claims 38 to 41, wherein the the use in medicine is the use in a method for the treatment of Crohn's disease.~~

~~43. A method of treating a disease comprising administering the antibody or antigen-binding fragment according to one or more of claims 1 to 36 or a pharmaceutical composition according to claim 38, to a patient in need thereof, wherein the disease is selected from an inflammatory disease, an autoimmune disease, a respiratory disease, a metabolic disorder, an epithelial mediated inflammatory disorder, fibrosis and cancer.~~

~~44. A method according to claim 43, wherein the disease is selected from psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma and ankylosing spondylitis.~~

~~45. A method according to claim 43 and/or 44, wherein the disease is Crohn's disease.~~

~~46. An isolated polynucleotide comprising a sequence encoding an anti-IL-36R antibody or antigen-binding fragment according to one or more of claims 1 to 36, preferably a DNA or RNA sequence.~~

~~47. An isolated polynucleotide according to claim 46, encoding a sequence as defined by one or more of SEQ ID NOs. 1 to 140.~~

48. A vector comprising a polynucleotide according to claim 46 and/or 47, preferably an expression vector, more preferred a vector comprising the polynucleotide according to the invention in functional association with an expression control sequence.

49. A host cell comprising a polynucleotide according to claim 46 and/or 47, and/or a vector according to claim 48.

50. Method for the production of an anti-IL-36R antibody or antigen-binding fragment according to one or more of claims 1 to 36, preferably a recombinant production method comprising the use of a polynucleotide according to claim 46 and/or 47, and/or of a vector according to claim 48 and/or of a host cell according to claim 49.

51. Method according to claim 50, comprising the steps (a) cultivating the host cell under conditions allowing the expression of the anti-IL-36R antibody or antigen-binding fragment and (b) recovering the anti-IL-36R antibody or antigen-binding fragment.

52. Diagnostic kit or diagnostic method comprising an anti-IL-36R antibody or antigen-binding fragment according to one or more of claims 1 to 36, or the use thereof.

53. Diagnostic kit or diagnostic method according to claim 52, for the diagnosis of an inflammatory disease, an autoimmune disease, a respiratory disease, a metabolic disorder, an epithelial mediated inflammatory disorder, fibrosis, cancer, psoriasis, inflammatory bowel disease, psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, COPD, chronic asthma, ankylosing spondylitis, or Crohn's disease.