methods of detecting IL-1α and IL-1β in a sample or in methods of treating or preventing a disorder in an individual that is associated with or suspected to be associated with IL-1 activity.

In one aspect, there is provided a binding protein comprising first and second polypeptide chains, wherein said first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region; and

n is independently 0 or 1; and

wherein said second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region; and

n is independently 0 or 1;

wherein, in said first polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 204; and VD2 comprises the amino acid sequence of SEQ ID NO: 213;

wherein, in said second polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 238; and

VD2 comprises the amino acid sequence of SEQ ID NO: 216; and

wherein the binding protein binds human IL-1β and human IL-1α.

In one aspect, there is provided a binding protein comprising first and second polypeptide chains, wherein said first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region; and

n is independently 0 or 1; and

wherein said second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region; and

n is independently 0 or 1;

wherein, in said first polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 213; and

VD2 comprises the amino acid sequence of SEQ ID NO: 204;

wherein, in said second polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 216; and

VD2 comprises the amino acid sequence of SEQ ID NO: 238; and

wherein the binding protein binds human IL-1β and human IL-1α.

In one aspect, there is provided a binding protein conjugate comprising a binding protein as described above, said binding protein conjugate further comprising an agent selected from the group consisting of: an immunoadhesion molecule, an imaging agent, a therapeutic agent, and a cytotoxic agent.

In one aspect, there is provided a pharmaceutical composition comprising a binding protein as described above, and a pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition comprising a binding protein conjugate as described above, and a pharmaceutically acceptable carrier.

In one aspect, there is provided a binding protein conjugate comprising a binding protein as described above, said binding protein conjugate further comprising an agent selected from the group consisting of: an immunoadhesion molecule, an imaging agent, a therapeutic agent, and a cytotoxic agent.

In one aspect, there is provided a pharmaceutical composition comprising a binding protein as described above, and a pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition comprising a binding protein conjugate as described above, and a pharmaceutically acceptable carrier.

In one aspect, there is provided a binding protein comprising first and second polypeptide chains, wherein said first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region; and

n is independently 0 or 1; and

wherein said second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region; and

n is independently 0 or 1;

wherein, in said first polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 204; and

VD2 comprises the amino acid sequence of SEQ ID NO: 213;

wherein, in said second polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 238; and

VD2 comprises the amino acid sequence of SEQ ID NO: 216; and

wherein said first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 212, and said second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 215; and

wherein the binding protein binds human IL-1β and human IL-1α.

In one aspect, there is provided a binding protein comprising first and second polypeptide chains, wherein said first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first heavy chain variable domain;

VD2 is a second heavy chain variable domain;

C is a heavy chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region; and n is independently 0 or 1; and

wherein said second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region; and n is independently 0 or 1;

wherein, in said first polypeptide chain,

VD1 comprises the amino acid sequence of SEQ ID NO: 213; and
VD2 comprises the amino acid sequence of SEQ ID NO: 204;
wherein, in said second polypeptide chain,
VD1 comprises the amino acid sequence of SEQ ID NO: 216; and
VD2 comprises the amino acid sequence of SEQ ID NO: 238; and
wherein said first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 219, and said second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 220; and
wherein the binding protein binds human IL-1β and human IL-1α.

In one aspect, there is provided an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide chain amino acid sequence of a binding protein described above.

In one aspect, there is provided a vector comprising one or more isolated nucleic acid molecules as defined above.

In one aspect, there is provided a host cell comprising a vector as defined above.

In one aspect, there is provided a method of producing a binding protein, comprising culturing the host cell described above in culture medium under conditions sufficient to produce the binding protein.

In one aspect, there is provided the use of the binding protein as described above in the manufacture of a medicament for reducing human IL-1α activity such that human IL-1 protein activity is reduced.

In one aspect, there is provided the use of the binding protein as described above or a crystal thereof, in the manufacture of a medicament for reducing human IL-1 activity in a human subject suffering from a disorder in which IL-1 activity is detrimental, such that human IL-1 activity in the human subject is reduced.

In one aspect, there is provided the use of the binding protein as described above or a crystal thereof in the manufacture of a medicament for treating a disorder in which IL-1 activity is detrimental, such that treatment is achieved in a human subject.

In an embodiment, the invention provides a binding protein comprising first and second polypeptide chains, wherein said first polypeptide chain comprises a first VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first heavy chain variable domain;
VD2 is a second heavy chain variable domain;
C is a heavy chain constant domain;
X1 is a linker with the proviso that it is not CH1;

X2 is an Fc region; and

n is independently 0 or 1; and

wherein said second polypeptide chain comprises a second VD1-(X1)n-VD2-C-(X2)n, wherein:

VD1 is a first light chain variable domain;

VD2 is a second light chain variable domain;

C is a light chain constant domain;

X1 is a linker with the proviso that it is not CH1;

X2 does not comprise an Fc region; and

n is independently 0 or 1;

wherein, in said first polypeptide chain, VD1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 60-148, 196, 198, 200, 202, 204, 206, 208 and 210; and VD2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 213 and 227;

wherein, in said second polypeptide chain, VD1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 149-189, 197, 199, 201, 203, 205, 207, 209 and 211; and VD2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 216 and 229; and

wherein the binding protein binds human IL-1β and human IL-1α.

In an embodiment, a binding protein described above comprises a first polypeptide chain that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 212, 217, 226, 230, 232, 234, and 236.

In another embodiment, a binding protein described above comprises a second polypeptide chain that comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 215, 218, 228, 231, 233, 235, and 237.