CLAIMS

1. A binding protein comprising an antigen binding domain capable of binding human sclerostin, the antigen binding domain comprising three CDRs in a heavy chain and three CDRs in a light chain,

wherein the heavy chain comprises a CDR-H1, a CDR-H2 and a CDR-H3;

wherein the CDR-H1 comprises the amino acid sequence of X_1-L-S-X_2-H (residues 31-35 of SEQ ID NO: 1);

wherein X_1 is E or G; and

wherein X_2 is M, V or L;

wherein the CDR-H2 comprises the amino acid sequence of G-X_3-X_4-P-E-X_5-G-E-X_6-I-Y-A-Q-K-F-Q-G (residues 50-66 of SEQ ID NO: 1);

wherein X_3 is F or S;

wherein X_4 is D or N;

wherein X_5 is D, E, V, Y, N, G, A, R, Q, H, F or I; and

wherein X_6 is T, I, L, M or N;

and

the CDR-H3 comprises the amino acid sequence of X_7-X_8-X_9-X_{10}-X_{11}-W-X_{12}-X_{13}-X_{14}-F-Q-H (residues 99-110 of SEQ ID NO: 1);

wherein X_7 is D or E;

wherein X_8 is S, T or A;

wherein X_9 is E, D, V, A, L, Y, W, Q, N, M or G;

wherein X_{10} is G or S;

wherein X_{11} is Y, F, R, N, V, S, P or I;

wherein X_{12} is E, Y, F or V;

wherein X_{13} is K, Q or I; and

wherein X_{14} is Y or F,

and

wherein the light chain comprises a CDR-L1, a CDR-L2 and a CDR-L3

wherein the CDR-L1 comprises an amino acid sequence of G-S-S-T-G-X_{15}-V-T- X_{16}- X_{17}-H-Y- X_{18}-Y (residues 23-36 of SEQ ID NO: 2),

wherein $X_{15}$is A, D, P, G, S, N, E, T or H;

wherein X_{16} is S, I, V, T, G or M;

wherein X_{17} is G, E, D, W, Y or N; and

wherein X_{18} is P or T;

wherein the CDR-L2 comprises the amino acid sequence of D-T- X_{19}- X_{20}-K- X_{21}-S (residues 52-58 of SEQ ID NO: 2),

wherein X_{19} is N, D, I, R, V or T;

wherein X_{20} is D or E; and

wherein X_{21} is H, Q, N or D;

and

wherein the CDR-L3 comprises the amino acid sequence of L-L- X_{22}- X_{23}- X_{24}- X_{25}- X_{26}- X_{27}-V (residues 91-99 of SEQ ID NO: 2);

wherein X_{22} is F or D;

wherein X_{23} is Y, D, F or N;

wherein X_{24} is G or R;

wherein X_{25} is G or S;

wherein X_{26} is T, S, N or R; and

wherein X_{27} is V, L, M or F.

2. The binding protein of claim 1, wherein the at least one CDR comprises an amino acid sequence selected from the group consisting of residues 31 - 35 of SEQ ID NO:1998; Residues 50 - 66 of SEQ ID NO:1998; Residues 99 - 110 of SEQ ID NO:1998; Residues 31 - 35 of SEQ ID NO:1999; Residues 50-66 of SEQ ID NO:1999; Residues 99 - 110 of SEQ ID NO:1999; Residues 31 - 35 of SEQ ID NO:2000; Residues 50 - 66 of SEQ ID NO:2000; Residues 99 - 110 of SEQ ID NO:2000; Residues 31 - 35 of SEQ ID NO:2001; Residues 50 - 66 of SEQ ID NO:2001; Residues 99 - 110 of SEQ ID NO:2001; Residues 31 - 35 of SEQ ID NO:2002; Residues 50 - 66 of SEQ ID NO:2002; Residues 99 - 110 of SEQ ID NO:2002; Residues 31 - 35 of SEQ ID NO:2003; Residues 50 - 66 of SEQ ID NO:2003; Residues 99 - 110 of SEQ ID NO:2003; Residues 31 - 35 of SEQ ID NO:2004; Residues 50 - 66 of SEQ ID NO:2004; Residues 99 - 110 of SEQ ID NO:2004; Residues 31 - 35 of SEQ ID NO:2005; Residues 50 - 66 of SEQ ID NO:2005; Residues 99 - 110 of SEQ ID NO:2005; Residues 31 - 35 of SEQ ID NO:2006; Residues 50 - 66 of SEQ ID NO:2006; Residues 99 - 110 of SEQ ID NO:2006; Residues 31 - 35 of SEQ ID NO:2007; Residues 50 - 66 of SEQ ID NO:2007; Residues 99 - 110 of SEQ ID NO:2007; Residues 23 - 36 of SEQ ID NO:2008; Residues 52 – 58 of SEQ ID NO:2008; Residues 91-99 of SEQ ID

NO:2008; Residues 23 - 36 of SEQ ID NO:2009; Residues 52 – 58 of SEQ ID NO:2009; Residues 91-99 of SEQ ID NO:2009; Residues 23 - 36 of SEQ ID NO. 2010; Residues 52 – 58 of SEQ ID NO:2010; Residues 91-99 of SEQ ID NO:2010; Residues 23 - 36 of SEQ ID NO:2011; Residues 52 – 58 of SEQ ID NO:2011; Residues 91-99 of SEQ ID NO:2011; Residues 23 - 36 of SEQ ID NO:2012; Residues 52 – 58 of SEQ ID NO:2012; Residues 91-99 of SEQ ID NO:2012; Residues 23 - 36 of SEQ ID NO:2013; Residues 52 – 58 of SEQ ID NO:2013; Residues 91-99 of SEQ ID NO:2013; Residues 23 - 36 of SEQ ID NO:2014; Residues 52 – 58 of SEQ ID NO:2014; Residues 91-99 of SEQ ID NO:2014; Residues 23 - 36 of SEQ ID NO:2015; Residues 52 – 58 of SEQ ID NO:2015; Residues 91-99 of SEQ ID NO:2015; Residues 23 - 36 of SEQ ID NO:2016; Residues 52 – 58 of SEQ ID NO:2016; Residues 91-99 of SEQ ID NO:2016; Residues 23 - 36 of SEQ ID NO:2017; Residues 52 – 58 of SEQ ID NO:2017; Residues 91-99 of SEQ ID NO:2017.

3. The binding protein of claim 1, wherein the antigen binding domain comprises a variable domain CDR set selected from the group consisting of:

VH AE10-6 AM1 CDR Set

VH AE10-6 AM1 CDR-H1	Residues 31-37 of SEQ ID NO:1998
VH AE10-6 AM1 CDR-H2	Residues 52-69 of SEQ ID NO:1998
VH AE10-6 AM1 CDR-H3	Residue 99-110 of SEQ ID NO:1998

VL AE10-6 AM1 Set

VL AE10-6 AM1 CDR-L1	Residues 24-34 of SEQ ID NO:2008
VL AE10-6 AM1 CDR-L2	Residues 50-56 of SEQ ID NO:2008
VL AE10-6 AM1 CDR-L3	Residues 91-99 of SEQ ID NO:2008

VH AE10-6 AM2 CDR Set

VH AE10-6 AM2 CDR-H1	Residues 31-37 of SEQ ID NO:1999
VH AE10-6 AM2 CDR-H2	Residues 52-69 of SEQ ID NO:1999
VH AE10-6 AM2 CDR-H3	Residue 99-110 of SEQ ID NO:1999

VL AE10-6 AM2 Set

VL AE10-6 AM2 CDR-L1	Residues 24-34 of SEQ ID NO:2009
VL AE10-6 AM2 CDR-L2	Residues 50-56 of SEQ ID NO:2009
VL AE10-6 AM2 CDR-L3	Residues 91-99 of SEQ ID NO:2009

VH AE10-6 AM3 CDR Set

VH AE10-6 AM3 CDR-H1	Residues 31-37 of SEQ ID NO:2000
VH AE10-6 AM3 CDR-H2	Residues 52-69 of SEQ ID NO:2000
VH AE10-6 AM3 CDR-H3	Residue 99-110 of SEQ ID NO:2000

VL AE10-6 AM3 Set

VL AE10-6 AM3 CDR-L1	Residues 24-34 of SEQ ID NO:2010
VL AE10-6 AM3 CDR-L2	Residues 50-56 of SEQ ID NO:2010
VL AE10-6 AM3 CDR-L3	Residues 91-99 of SEQ ID NO:2010

VH AE10-6 AM4 CDR Set

VH AE10-6 AM4 CDR-H1	Residues 31-37 of SEQ ID NO:2001
VH AE10-6 AM4 CDR-H2	Residues 52-69 of SEQ ID NO:2001
VH AE10-6 AM4 CDR-H3	Residue 99-110 of SEQ ID NO:2001

VL AE10-6 AM4 Set

VL AE10-6 AM4 CDR-L1	Residues 24-34 of SEQ ID NO:2011
VL AE10-6 AM4 CDR-L2	Residues 50-56 of SEQ ID NO:2011
VL AE10-6 AM4 CDR-L3	Residues 91-99 of SEQ ID NO:2011

VH AE10-6 AM5 CDR Set

VH AE10-6 AM5 CDR-H1	Residues 31-37 of SEQ ID NO:2002
VH AE10-6 AM5 CDR-H2	Residues 52-69 of SEQ ID NO:2002
VH AE10-6 AM5 CDR-H3	Residue 99-110 of SEQ ID NO:2002

VL AE10-6 AM5 Set

VL AE10-6 AM5 CDR-L1	Residues 24-34 of SEQ ID NO:2012
VL AE10-6 AM5 CDR-L2	Residues 50-56 of SEQ ID NO:2012
VL AE10-6 AM5 CDR-L3	Residues 91-99 of SEQ ID NO:2012

VH AE10-6 AM6 CDR Set

VH AE10-6 AM6 CDR-H1	Residues 31-37 of SEQ ID NO:2003
VH AE10-6 AM6 CDR-H2	Residues 52-69 of SEQ ID NO:2003
VH AE10-6 AM6 CDR-H3	Residue 99-110 of SEQ ID NO:2003

VL AE10-6 AM6 Set

VL AE10-6 AM6 CDR-L1	Residues 24-34 of SEQ ID NO:2013
VL AE10-6 AM6 CDR-L2	Residues 50-56 of SEQ ID NO:2013
VL AE10-6 AM6 CDR-L3	Residues 91-99 of SEQ ID NO:2013

VH AE10-6 AM7 CDR Set

VH AE10-6 AM7 CDR-H1	Residues 31-37 of SEQ ID NO:2004
VH AE10-6 AM7 CDR-H2	Residues 52-69 of SEQ ID NO:2004
VH AE10-6 AM7 CDR-H3	Residue 99-110 of SEQ ID NO:2004

VL AE10-6 AM7 Set

VL AE10-6 AM7 CDR-L1	Residues 24-34 of SEQ ID NO:2014
VL AE10-6 AM7 CDR-L2	Residues 50-56 of SEQ ID NO:2014
VL AE10-6 AM7 CDR-L3	Residues 91-99 of SEQ ID NO:2014

VH AE10-6 AM8 CDR Set

VH AE10-6 AM8 CDR-H1	Residues 31-37 of SEQ ID

	NO:2005
VH AE10-6 AM8 CDR-H2	Residues 52-69 of SEQ ID NO:2005
VH AE10-6 AM8 CDR-H3	Residue 99-110 of SEQ ID NO:2005

VL AE10-6 AM8 Set

VL AE10-6 AM8 CDR-L1	Residues 24-34 of SEQ ID NO:2015
VL AE10-6 AM8 CDR-L2	Residues 50-56 of SEQ ID NO:2015
VL AE10-6 AM8 CDR-L3	Residues 91-99 of SEQ ID NO:2015

VH AE10-6 AM9 CDR Set

VH AE10-6 AM9 CDR-H1	Residues 31-37 of SEQ ID NO:2006
VH AE10-6 AM9 CDR-H2	Residues 52-69 of SEQ ID NO:2006
VH AE10-6 AM9 CDR-H3	Residue 99-110 of SEQ ID NO:2006

VL AE10-6 AM9 Set

VL AE10-6 AM9 CDR-L1	Residues 24-34 of SEQ ID NO:2016
VL AE10-6 AM9 CDR-L2	Residues 50-56 of SEQ ID NO:2016
VL AE10-6 AM9 CDR-L3	Residues 91-99 of SEQ ID NO:2016

VH AE10-6 AM10 CDR Set

VH AE10-6 AM10 CDR-H1	Residues 31-37 of SEQ ID

	NO:2007
VH AE10-6 AM10 CDR-H2	Residues 52-69 of SEQ ID NO:2007
VH AE10-6 AM10 CDR-H3	Residue 99-110 of SEQ ID NO:2007

VL AE10-6 AM10 Set

VL AE10-6 AM10 CDR-L1	Residues 24-34 of SEQ ID NO:2017
VL AE10-6 AM10 CDR-L2	Residues 50-56 of SEQ ID NO:2017
VL AE10-6 AM10 CDR-L3	Residues 91-99 of SEQ ID NO:2017

4. The binding protein of claim 3, comprising at least two variable domain CDR sets.

5. The binding protein of claim 4, wherein the at least two variable domain CDR sets are selected from the group consisting of VH AE10-6 AM1 CDR Set and VL AE10-6 AM1 CDR Set; VH AE10-6 AM2 CDR Set and VL AE10-6 AM2 CDR Set; VH AE10-6 AM3 CDR Set and VL AE10-6 AM3 CDR Set; VH AE10-6 AM4 CDR Set and VL AE10-6 AM4 CDR Set; VH AE10-6 AM5 CDR Set and VL AE10-6 AM5 CDR Set; VH AE10-6 AM6 CDR Set and VL AE10-6 AM6 CDR Set; VH AE10-6 AM7 CDR Set and VL AE10-6 AM7 CDR Set; VH AE10-6 AM8 CDR Set and VL AE10-6 AM8_CDR Set; VH AE10-6 AM9_CDR Set and VL AE10-6 AM9_CDR Set; VH AE10-6 AM10_CDR Set and VL AE10-6 AM10 CDR Set.

6. The binding protein of claim 1, wherein the binding protein comprises at least one variable domain having an amino acid sequence selected from the group consisting of SEQ ID NOs 1719-1866; SEQ ID NOs1867-1997; SEQ ID NOs 1998-2007; and SEQ ID NOs 2008-2017.

7. The binding protein of claim 1, wherein the binding protein comprises two variable domains, wherein the first variable domain comprises a sequence selected from the

group consisting of SEQ ID NOs 1719-1866,and 1998-2007 and wherein the second variable domain comprises a sequence selected from the group consisting of SEQ ID NOs 1867-1997, and 2007-2017.

8. The binding protein of claim 1, wherein the binding protein:
(a) is capable of modulating a biological function of sclerostin;
(b) is capable of neutralizing sclerostin;
(c) wherein the sclerostin is pro-human sclerostin; mature-human sclerostin, or truncated-human sclerostin;
(d) wherein the binding protein diminishes the ability of sclerostin to bind to its receptor; and/or
(e) wherein the neutralizing binding protein is capable of reducing one or more of Th1 modulation; Th2 modulation; NK modulation; neutrophil modulation; monocyte-macrophage lineage modulation; neutrophil modulation; eosinophil modulation; B-cells modulation; cytokine modulation; chemokine modulation; adhesion molecule modulation; and cell recruitment modulation.

9. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising three CDRs of SEQ ID NO:2004.

10. The binding protein of claim 1, wherein the antigen binding domain comprises a light chain variable region (VL) comprising three CDRs of SEQ ID NO:2014.

11. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising three CDRs from SEQ ID NO:2004; and wherein the antigen binding domain comprises a light chain variable region (VL) comprising three CDRs of SEQ ID NO:2014.

12. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:2004.

13. The binding protein of claim 1, wherein the antigen binding domain comprises a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:2014.

14. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:2004; and wherein the antigen binding domain comprises a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:2014.

15. A pharmaceutical composition comprising the binding protein of claim 1, and a pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15, further comprising at least one additional agent for treating a disorder in which sclerostin activity is detrimental.

17. The pharmaceutical composition of claim 16, wherein the additional agent is selected from the group consisting of a therapeutic agent, imaging agent, cytotoxic agent, angiogenesis inhibitors; kinase inhibitors; co-stimulation molecule blockers; adhesion molecule blockers; anti-cytokine antibody or functional fragment thereof; methotrexate; cyclosporin; rapamycin; FK506; detectable label or reporter; a TNF antagonist; an anti-rheumatic; a muscle relaxant, a narcotic, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anesthetic, a neuromuscular blocker, an antimicrobial, an antipsoriatic, a corticosteroid, an anabolic steroid, an erythropoietin, an immunization, an immunoglobulin, an immunosuppressive, a growth hormone, a hormone replacement drug, a radiopharmaceutical, an antidepressant, an antipsychotic, a stimulant, an asthma medication, a beta agonist, an inhaled steroid, an oral steroid, an epinephrine or analog, a cytokine, and a cytokine antagonist.

Claims

What is claimed is:

1. A binding protein comprising an antigen binding domain capable of binding human sclerostin, the antigen binding domain comprising three CDRs in a heavy chain and three CDRs in a light chain,

wherein the heavy chain comprises a CDR-H1, a CDR-H2 and a CDR-H3;
wherein the CDR-H1 comprises the amino acid sequence of X_1-L-S-X_2-H (residues 31-35 of SEQ ID NO: 1);
wherein X_1 is E or G; and
wherein X_2 is M, V or L;
wherein the CDR-H2 comprises the amino acid sequence of G-X_3-X_4-P-E-X_5-G-E-X_6-I-Y-A-Q-K-F-Q-G (residues 50-66 of SEQ ID NO: 1);
wherein X_3 is F or S;
wherein X_4 is D or N;
wherein X_5 is D, E, V, Y, N, G, A, R, Q, H, F or I; and
wherein X_6 is T, I, L, M or N;
and
the CDR-H3 comprises the amino acid sequence of X_7-X_8-X_9-X_{10}-X_{11}-W-X_{12}-X_{13}-X_{14}-F-Q-H (residues 99-110 of SEQ ID NO: 1);
wherein X_7 is D or E;
wherein X_8 is S, T or A;
wherein X_9 is E, D, V, A, L, Y, W, Q, N, M or G;
wherein X_{10} is G or S;
wherein X_{11} is Y, F, R, N, V, S, P or I;
wherein X_{12} is E, Y, F or V;
wherein X_{13} is K, Q or I; and
wherein X_{14} is Y or F,
and
wherein the light chain comprises a CDR-L1, a CDR-L2 and a CDR-L3
wherein the CDR-L1 comprises an amino acid sequence of G-S-S-T-G-X_{15}-V-T- X_{16}- X_{17}-H-Y- X_{18}-Y (residues 23-36 of SEQ ID NO: 2),
wherein $X_{15}$is A, D, P, G, S, N, E, T or H;
wherein X_{16} is S, I, V, T, G or M;
wherein X_{17} is G, E, D, W, Y or N; and
wherein X_{18} is P or T;
wherein the CDR-L2 comprises the amino acid sequence of D-T- X_{19}-X_{20}-K- X_{21}-S (residues 52-58 of SEQ ID NO: 2),
wherein X_{19} is N, D, I, R, V or T;
wherein X_{20} is D or E; and
wherein X_{21} is H, Q, N or D;
and
wherein the CDR-L3 comprises the amino acid sequence of L-L- X_{22}- X_{23}-X_{24}- X_{25}- X_{26}- X_{27}-V (residues 91-99 of SEQ ID NO: 2);
wherein X_{22} is F or D;
wherein X_{23} is Y, D, F or N;

wherein X_{24} is G or R;
wherein X_{25} is G or S;
wherein X_{26} is T, S, N or R; and
wherein X_{27} is V, L, M or F.

2. The binding protein of claim 1, wherein the at least one CDR comprises an amino acid sequence selected from the group consisting of residues 31 - 35 of SEQ ID NO:1998; Residues 50 - 66 of SEQ ID NO:1998; Residues 99 - 110 of SEQ ID NO:1998; Residues 31 - 35 of SEQ ID NO:1999; Residues 50-66 of SEQ ID NO:1999; Residues 99 - 110 of SEQ ID NO:1999; Residues 31 - 35 of SEQ ID NO:2000; Residues 50 - 66 of SEQ ID NO:2000; Residues 99 - 110 of SEQ ID NO:2000; Residues 31 - 35 of SEQ ID NO:2001; Residues 50 - 66 of SEQ ID NO:2001; Residues 99 - 110 of SEQ ID NO:2001; Residues 31 - 35 of SEQ ID NO:2002; Residues 50 - 66 of SEQ ID NO:2002; Residues 99 - 110 of SEQ ID NO:2002; Residues 31 - 35 of SEQ ID NO:2003; Residues 50 - 66 of SEQ ID NO:2003; Residues 99 - 110 of SEQ ID NO:2003; Residues 31 - 35 of SEQ ID NO:2004; Residues 50 - 66 of SEQ ID NO:2004; Residues 99 - 110 of SEQ ID NO:2004; Residues 31 - 35 of SEQ ID NO:2005; Residues 50 - 66 of SEQ ID NO:2005; Residues 99 - 110 of SEQ ID NO:2005; Residues 31 - 35 of SEQ ID NO:2006; Residues 50 - 66 of SEQ ID NO:2006; Residues 99 - 110 of SEQ ID NO:2006; Residues 31 - 35 of SEQ ID NO:2007; Residues 50 - 66 of SEQ ID NO:2007; Residues 99 - 110 of SEQ ID NO:2007; Residues 23 - 36 of SEQ ID NO:2008; Residues 52 – 58 of SEQ ID NO:2008; Residues 91-99 of SEQ ID NO:2008; Residues 23 - 36 of SEQ ID NO:2009; Residues 52 – 58 of SEQ ID NO:2009; Residues 91-99 of SEQ ID NO:2009; Residues 23 - 36 of SEQ ID NO. 2010; Residues 52 – 58 of SEQ ID NO:2010; Residues 91-99 of SEQ ID NO:2010; Residues 23 - 36 of SEQ ID NO:2011; Residues 52 – 58 of SEQ ID NO:2011; Residues 91-99 of SEQ ID NO:2011; Residues 23 - 36 of SEQ ID NO:2012; Residues 52 – 58 of SEQ ID NO:2012; Residues 91-99 of SEQ ID NO:2012; Residues 23 - 36 of SEQ ID NO:2013; Residues 52 – 58 of SEQ ID NO:2013; Residues 91-99 of SEQ ID NO:2013; Residues 23 - 36 of SEQ ID NO:2014; Residues 52 – 58 of SEQ ID NO:2014; Residues 91-99 of SEQ ID NO:2014; Residues 23 - 36 of SEQ ID NO:2015; Residues 52 – 58 of SEQ ID NO:2015; Residues 91-99 of SEQ ID NO:2015; Residues 23 - 36 of SEQ ID NO:2016; Residues 52 – 58 of SEQ ID NO:2016; Residues 91-99 of SEQ ID NO:2016; Residues 23 - 36 of SEQ ID NO:2017; Residues 52 – 58 of SEQ ID NO:2017; Residues 91-99 of SEQ ID NO:2017.

3. The binding protein of claim 1, wherein the antigen binding domain comprises a variable domain CDR set selected from the group consisting of:

VH AE10-6 AM1 CDR Set

VH AE10-6 AM1 CDR-H1	Residues 31-37 of SEQ ID NO:1998
VH AE10-6 AM1 CDR-H2	Residues 52-69 of SEQ ID NO:1998
VH AE10-6 AM1 CDR-H3	Residue 99-110 of SEQ ID NO:1998

VL AE10-6 AM1 Set

VL AE10-6 AM1 CDR-L1	Residues 24-34 of SEQ ID NO:2008
VL AE10-6 AM1 CDR-L2	Residues 50-56 of SEQ ID NO:2008
VL AE10-6 AM1 CDR-L3	Residues 91-99 of SEQ ID NO:2008

VH AE10-6 AM2 CDR Set

VH AE10-6 AM2 CDR-H1	Residues 31-37 of SEQ ID NO:1999
VH AE10-6 AM2 CDR-H2	Residues 52-69 of SEQ ID NO:1999
VH AE10-6 AM2 CDR-H3	Residue 99-110 of SEQ ID NO:1999

VL AE10-6 AM2 Set

VL AE10-6 AM2 CDR-L1	Residues 24-34 of SEQ ID NO:2009
VL AE10-6 AM2 CDR-L2	Residues 50-56 of SEQ ID NO:2009
VL AE10-6 AM2 CDR-L3	Residues 91-99 of SEQ ID NO:2009

VH AE10-6 AM3 CDR Set

VH AE10-6 AM3 CDR-H1	Residues 31-37 of SEQ ID NO:2000
VH AE10-6 AM3 CDR-H2	Residues 52-69 of SEQ ID NO:2000
VH AE10-6 AM3 CDR-H3	Residue 99-110 of SEQ ID NO:2000

VL AE10-6 AM3 Set

VL AE10-6 AM3 CDR-L1	Residues 24-34 of SEQ ID NO:2010
VL AE10-6 AM3 CDR-L2	Residues 50-56 of SEQ ID NO:2010
VL AE10-6 AM3 CDR-L3	Residues 91-99 of SEQ ID NO:2010

VH AE10-6 AM4 CDR Set

VH AE10-6 AM4 CDR-H1	Residues 31-37 of SEQ ID NO:2001
VH AE10-6 AM4 CDR-H2	Residues 52-69 of SEQ ID NO:2001
VH AE10-6 AM4 CDR-H3	Residue 99-110 of SEQ ID NO:2001

VL AE10-6 AM4 Set

VL AE10-6 AM4 CDR-L1	Residues 24-34 of SEQ ID NO:2011
VL AE10-6 AM4 CDR-L2	Residues 50-56 of SEQ ID NO:2011
VL AE10-6 AM4 CDR-L3	Residues 91-99 of SEQ ID NO:2011

VH AE10-6 AM5 CDR Set

VH AE10-6 AM5 CDR-H1	Residues 31-37 of SEQ ID NO:2002
VH AE10-6 AM5 CDR-H2	Residues 52-69 of SEQ ID NO:2002
VH AE10-6 AM5 CDR-H3	Residue 99-110 of SEQ ID NO:2002

VL AE10-6 AM5 Set

VL AE10-6 AM5 CDR-L1	Residues 24-34 of SEQ ID NO:2012
VL AE10-6 AM5 CDR-L2	Residues 50-56 of SEQ ID NO:2012
VL AE10-6 AM5 CDR-L3	Residues 91-99 of SEQ ID NO:2012

VH AE10-6 AM6 CDR Set

VH AE10-6 AM6 CDR-H1	Residues 31-37 of SEQ ID NO:2003
VH AE10-6 AM6 CDR-H2	Residues 52-69 of SEQ ID NO:2003
VH AE10-6 AM6 CDR-H3	Residue 99-110 of SEQ ID NO:2003

VL AE10-6 AM6 Set

VL AE10-6 AM6 CDR-L1	Residues 24-34 of SEQ ID NO:2013
VL AE10-6 AM6 CDR-L2	Residues 50-56 of SEQ ID NO:2013
VL AE10-6 AM6 CDR-L3	Residues 91-99 of SEQ ID NO:2013

VH AE10-6 AM7 CDR Set	
VH AE10-6 AM7 CDR-H1	Residues 31-37 of SEQ ID NO:2004
VH AE10-6 AM7 CDR-H2	Residues 52-69 of SEQ ID NO:2004
VH AE10-6 AM7 CDR-H3	Residue 99-110 of SEQ ID NO:2004
VL AE10-6 AM7 Set	
VL AE10-6 AM7 CDR-L1	Residues 24-34 of SEQ ID NO:2014
VL AE10-6 AM7 CDR-L2	Residues 50-56 of SEQ ID NO:2014
VL AE10-6 AM7 CDR-L3	Residues 91-99 of SEQ ID NO:2014
VH AE10-6 AM8 CDR Set	
VH AE10-6 AM8 CDR-H1	Residues 31-37 of SEQ ID NO:2005
VH AE10-6 AM8 CDR-H2	Residues 52-69 of SEQ ID NO:2005
VH AE10-6 AM8 CDR-H3	Residue 99-110 of SEQ ID NO:2005
VL AE10-6 AM8 Set	
VL AE10-6 AM8 CDR-L1	Residues 24-34 of SEQ ID NO:2015
VL AE10-6 AM8 CDR-L2	Residues 50-56 of SEQ ID NO:2015
VL AE10-6 AM8 CDR-L3	Residues 91-99 of SEQ ID NO:2015
VH AE10-6 AM9 CDR Set	
VH AE10-6 AM9 CDR-H1	Residues 31-37 of SEQ ID NO:2006
VH AE10-6 AM9 CDR-H2	Residues 52-69 of SEQ ID NO:2006
VH AE10-6 AM9 CDR-H3	Residue 99-110 of SEQ ID NO:2006
VL AE10-6 AM9 Set	
VL AE10-6 AM9 CDR-L1	Residues 24-34 of SEQ ID NO:2016
VL AE10-6 AM9 CDR-L2	Residues 50-56 of SEQ ID NO:2016
VL AE10-6 AM9 CDR-L3	Residues 91-99 of SEQ ID NO:2016
VH AE10-6 AM10 CDR Set	
VH AE10-6 AM10 CDR-H1	Residues 31-37 of SEQ ID NO:2007
VH AE10-6 AM10 CDR-H2	Residues 52-69 of SEQ ID NO:2007
VH AE10-6 AM10 CDR-H3	Residue 99-110 of SEQ ID NO:2007
VL AE10-6 AM10 Set	
VL AE10-6 AM10 CDR-L1	Residues 24-34 of SEQ ID NO:2017
VL AE10-6 AM10 CDR-L2	Residues 50-56 of SEQ ID NO:2017
VL AE10-6 AM10 CDR-L3	Residues 91-99 of SEQ ID NO:2017

4. The binding protein of claim 3, comprising at least two variable domain CDR sets.

5. The binding protein of claim 4, wherein the at least two variable domain CDR sets are selected from the group consisting of VH AE10-6 AM1 CDR Set and VL AE10-6 AM1 CDR Set; VH AE10-6 AM2 CDR Set and VL AE10-6 AM2 CDR Set; VH AE10-6 AM3 CDR Set and VL AE10-6 AM3 CDR Set; VH AE10-6 AM4 CDR Set and VL AE10-6 AM4 CDR Set; VH AE10-6 AM5 CDR Set and VL AE10-6 AM5 CDR Set; VH AE10-6 AM6 CDR Set and VL AE10-6 AM6 CDR Set; VH AE10-6 AM7 CDR Set and VL AE10-6 AM7 CDR Set; VH AE10-6 AM8 CDR Set and VL AE10-6 AM8_CDR Set; VH AE10-6 AM9_CDR Set and VL AE10-6 AM9_CDR Set; VH AE10-6 AM10_CDR Set and VL AE10-6 AM10 CDR Set.

6. The binding protein of claim 1, wherein the binding protein comprises at least one variable domain having an amino acid sequence selected from the group consisting of SEQ ID NOs 1719-1866; SEQ ID NOs1867-1997; SEQ ID NOs 1998-2007; and SEQ ID NOs 2008-2017.

7. The binding protein of claim 1, wherein the binding protein comprises two variable domains, wherein the first variable domain comprises a sequence selected from the group consisting of SEQ ID NOs 1719-1866,and 1998-2007 and wherein the second variable domain comprises a sequence selected from the group consisting of SEQ ID NOs 1867-1997, and 2007-2017.

8. The binding protein of claim 1, wherein the binding protein:
(a) is capable of modulating a biological function of sclerostin;
(b) is capable of neutralizing sclerostin;
(c) wherein the sclerostin is pro-human sclerostin; mature-human sclerostin, or truncated-human sclerostin;
(d) wherein the binding protein diminishes the ability of sclerostin to bind to its receptor; and/or
(e) wherein the neutralizing binding protein is capable of reducing one or more of Th1 modulation; Th2 modulation; Nk modulation; neutrophil modulation; monocyte-macrophage lineage modulation; neutrophil modulation; eosinophil modulation; B-cells modulation; cytokine modulation; chemokine modulation; adhesion molecule modulation; and cell recruitment modulation.

9. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising three CDRs of SEQ ID NO:2004.

10. The binding protein of claim 1, wherein the antigen binding domain comprises a light chain variable region (VL) comprising three CDRs of SEQ ID NO:2014.

11. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising three CDRs from SEQ ID NO:2004; and wherein the antigen binding domain comprises a light chain variable region (VL) comprising three CDRs of SEQ ID NO:2014.

12. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:2004.

13. The binding protein of claim 1, wherein the antigen binding domain comprises a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:2014.

14. The binding protein of claim 1, wherein the antigen binding domain comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO:2004; and wherein the antigen binding domain comprises a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO:2014.

15. An isolated nucleic acid encoding the binding protein amino acid sequence of claim 1.

16. A vector comprising the isolated nucleic acid of claim 15.

17. A host cell comprising the vector of claim 16.

18. A method of producing a protein capable of binding sclerostin, comprising culturing the host cell of claim 17 in culture medium under conditions sufficient to produce a binding protein capable of binding sclerostin.

19. A protein of claim 1produced by the method of claim 18.

20. Use of an effective amount of the protein of claim 19, in the manufacture of a medicament for treating a mammal.

21. A pharmaceutical composition comprising the binding protein of claim 1, and a pharmaceutically acceptable carrier.

22. The pharmaceutical composition of claim 21, further comprising at least one additional agent for treating a disorder in which sclerostin activity is detrimental.

23. The pharmaceutical composition of claim 22, wherein the additional agent is selected from the group consisting of a therapeutic agent, imaging agent, cytotoxic agent, angiogenesis inhibitors; kinase inhibitors; co-stimulation molecule blockers; adhesion molecule blockers; anti-cytokine antibody or functional fragment thereof; methotrexate; cyclosporin; rapamycin; FK506; detectable label or reporter; a TNF antagonist; an anti-rheumatic; a muscle relaxant, a narcotic, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anesthetic, a neuromuscular blocker, an antimicrobial, an antipsoriatic, a corticosteroid, an anabolic steroid, an erythropoietin, an immunization, an immunoglobulin, an immunosuppressive, a growth hormone, a hormone replacement drug, a radiopharmaceutical, an antidepressant, an antipsychotic, a stimulant, an asthma medication, a beta agonist, an inhaled steroid, an oral steroid, an epinephrine or analog, a cytokine, and a cytokine antagonist.

24. Use of the binding protein of claim 1, in the manufacture of a medicament for reducing human sclerostin activity.

25. Use of the binding protein of claim 1, in the manufacture of a medicament for reducing human sclerostin activity in a human subject suffering from a disorder in which sclerostin activity is detrimental.

26. Use of the binding protein of claim 1, in the manufacture of a medicament for treating a subject for a disease or a disorder in which sclerostin activity is detrimental.

27. The use of claim 26, wherein the disorder is selected from the group consisting of a respiratory disorder; asthma; allergic and nonallergic asthma; asthma due to infection; asthma due to infection with respiratory syncytial virus (RSV); chronic obstructive pulmonary disease (COPD); a condition involving airway inflammation; eosinophilia; fibrosis and /or excess mucus production; cystic fibrosis; pulmonary fibrosis; an atopic disorder; atopic dermatitis; urticaria; eczema; allergic rhinitis; allergic enterogastritis; an inflammatory and/or autoimmune condition of the skin; an inflammatory and/or

autoimmune condition of gastrointestinal organs; inflammatory bowel disease (IBD); ulcerative colitis; Crohn's disease; an inflammatory and/or autoimmune condition of the liver; liver cirrhosis; liver fibrosis; liver fibrosis caused by hepatitis B and/or C virus; scleroderma; a tumors; a cancer; hepatocellular carcinoma; glioblastoma; lymphoma; Hodgkin's lymphoma; a viral infection; HTLV-1 infection; a suppression of expression of protective type 1 immune response, and a suppression of expression of protective type 1 immune responses during vaccination.

28. Use of the binding protein of claim 1 in the manufacture of a medicament for treating a patient suffering from a disorder in which sclerostin is detrimental before, concurrent, or after the administration of a second agent, wherein the second agent is selected from the group consisting of an inhaled steroid; a beta-agonist; a short-acting or long-acting beta-agonist; an antagonist of leukotrienes or leukotriene receptors; ADVAIR; an IgE inhibitor; an anti-IgE antibody; XOLAIR; a phosphodiesterase inhibitor; a PDE4 inhibitor; a xanthine; an anticholinergic drug; a mast cell-stabilizing agent; Cromolyn; an IL-4 inhibitor; an IL-5 inhibitor; an eotaxin/CCR3 inhibitor; an antagonist of histamine or its receptors including H1, H2, H3, and H4; an antagonist of prostaglandin D or its receptors DP1 and CRTH2; a TNF antagonist; a soluble fragment of a TNF receptor; ENBREL; a TNF enzyme antagonist; a TNF converting enzyme (TACE) inhibitor; a muscarinic receptor antagonist; a TGF-beta antagonist; an interferon gamma; perfenidone; a chemotherapeutic agent, methotrexate; leflunomide; sirolimus (rapamycin) or an analog thereof, CCI-779; a COX2 or cPLA2 inhibitors; an NSAIDs; an immunomodulator; a p38 inhibitor; TPL-2, MK-2 and NFkB inhibitors; budenoside; epidermal growth factor; a corticosteroid; cyclosporine; sulfasalazine; an aminosalicylate; 6-mercaptopurine; azathioprine; metronidazole; a lipoxygenase inhibitor; mesalamine; olsalazine; balsalazide; an antioxidant; a thromboxane inhibitor; an IL-1 receptor antagonist; an anti-IL-1β antibody; an anti-IL-6 antibody; a growth factor; an elastase inhibitor; a pyridinyl-imidazole compound; an antibody or agonists of TNF, LT, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-28, IL-29, IL-30, IL-31, IL-32, IL-33, EMAP-II, GM-CSF, FGF, or PDGF; an antibody of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands; FK506; rapamycin; mycophenolate mofetil; ibuprofen; prednisolone; a phosphodiesterase inhibitor; an adenosine agonist; an antithrombotic agent; a complement inhibitor; an adrenergic agent; IRAK, NIK, IKK, p38, or a MAP kinase inhibitor; an IL-1β converting enzyme inhibitor; a TNF-α converting enzyme inhibitor; a T-cell signaling inhibitor; a metalloproteinase inhibitor; a 6-mercaptopurine; an angiotensin converting enzyme inhibitor; a soluble cytokine receptor; a soluble p55 TNF receptor; a soluble p75 TNF receptor; sIL-1RI; sIL-1RII; sIL-6R; an anti-inflammatory cytokine; IL-4; IL-10; IL-11; SOST; and TGF-β.