

CLAIMS

1. ~~An isolated polypeptide comprising a Desmoglein 2 (DSG2) fusion polypeptide, wherein the DSG2 fusion polypeptide comprises:
 - a. a whole or a portion of a DSG2 protein (SEQ ID NO: 1); and
 - b. a whole or a portion of an immunoglobulin protein.~~
2. ~~The isolated polypeptide of claim 1, wherein the DSG2 fusion polypeptide comprises a portion of the DSG2 protein.~~
3. ~~The isolated polypeptide of claim 2, wherein the portion of the DSG2 protein is a whole or a portion of an extracellular region of the DSG2 protein.~~
4. ~~The isolated polypeptide of claim 3, wherein the portion of DSG2 protein is the whole extracellular region of DSG2 protein.~~
5. ~~The isolated polypeptide of claim 4, wherein the whole extracellular region of DSG2 protein comprises the amino acid sequence of SEQ ID NO: 3.~~
6. ~~The isolated polypeptide of claim 3, wherein the portion of the DSG2 protein is a portion of an extracellular region of the DSG2 protein.~~
7. ~~The isolated polypeptide of claim 6, wherein the portion of an extracellular region of the DSG2 protein comprises at least one domain, wherein the at least one domain is an extracellular cadherin domain 1 (EC1), an extracellular cadherin domain 2 (EC2), an extracellular cadherin domain 3 (EC3), an extracellular cadherin domain 4 (EC4), or an extracellular anchor domain (EA).~~
8. ~~The isolated polypeptide of claim 7, wherein the portion of an extracellular region of the DSG2 protein comprises two domains.~~

9. The isolated polypeptide of claim 8, wherein the portion of the extracellular region of the DSG2 protein is EC4EA, EC1EC2, EC2EC3, EC3EC4, EC1EA, EC1EC3, EC2EC4, or EC3EA.
10. The isolated polypeptide of claim 7, wherein the portion of an extracellular region of the DSG2 protein comprises three domains.
11. The isolated polypeptide of claim 10, wherein the portion of the extracellular region of the DSG2 protein is EC1EC3EA, EC1EC4EA, EC1EC3EA, EC3EC4EA, EC1EC2EC3, EC2EC3EC4, or EC2EC4EA.
12. The isolated polypeptide of claim 7, wherein the portion of an extracellular region of the DSG2 protein comprises four domains.
13. The isolated polypeptide of claim 12, wherein the portion of the extracellular region of the DSG2 protein is EC1EC2EC4EA, EC2EC3EC4EA, EC1EC2EC3EC4EA, EC1EC2EC3EC4, or EC1EC2EC3EA.
14. The isolated polypeptide of claim 1, wherein the DSG2 fusion polypeptide comprises a portion of an immunoglobulin protein.
15. The isolated polypeptide of claim 1 or claim 14, wherein the immunoglobulin protein is an IgG, an IgM, an IgA, an IgD or, an IgE.
16. The isolated polypeptide of claim 15, wherein the immunoglobulin is an IgG.
17. The isolated polypeptide of claim 16, wherein the IgG is an IgG1, an IgG2, an IgG3, and an IgG4.
18. The isolated polypeptide of claim 14, wherein the portion of the immunoglobulin protein is an Fc region, an Fab region, a heavy chain variable (VH) domain, a heavy chain constant domain, a light chain variable (VL) domain, or a light chain constant domain.

~~19. The isolated polypeptide of claim 18, wherein the portion of the immunoglobulin protein is an Fc region.~~

~~20. The isolated polypeptide of claim 19, wherein the Fc region is an IgG1 Fc region (SEQ ID NO: 5), an IgG2 Fc region (SEQ ID NO: 7), an IgG3 Fc region (SEQ ID NO: 9), or an IgG4 Fc region (SEQ ID NO: 11).~~

~~21. The isolated polypeptide of claim 18, wherein the portion of the immunoglobulin protein is a heavy chain constant domain.~~

~~22. The isolated polypeptide of claim 21, wherein the heavy chain constant is an IgG1 heavy chain constant domain (SEQ ID NO: 4), an IgG2 heavy chain constant domain (SEQ ID NO: 6), an IgG3 heavy chain constant domain (SEQ ID NO: 8), or an IgG4 heavy chain constant domain (SEQ ID NO: 10).~~

~~23. The isolated polypeptide of any one of claims 1-22, wherein the DSG2 fusion polypeptide further comprises a linker.~~

~~24. The isolated polypeptide of claim 23, wherein the linker is from about 5 amino acids to about 50 amino acids in length.~~

~~25. The isolated polypeptide of claim 24, wherein the linker is GGGGS (SEQ ID NO: 12).~~

~~26. The isolated polypeptide of claim 24, wherein the linker is EAAAK (SEQ ID NO: 13).~~

~~27. The isolated polypeptide of any one of claims 1-26, wherein the DSG2 fusion polypeptide further comprises a signal sequence.~~

~~28. A cell expressing the isolated polypeptide of any one of claims 1-27.~~

~~29. A method of treating a condition associated with serum anti-DSG2 autoantibodies, the method comprising contacting the subject with the isolated polypeptide of any one of claims 1-27, or a cell of claim 28.~~

~~30. The method of claim 29, wherein the condition is a cardiomyopathy.~~

~~31. The method of any one of claims 29 or 30, wherein the condition is an autoimmune disorder.~~

~~32. 1. A method of treating~~ Use of a desmoglein 2 (DSG2) fusion polypeptide in the manufacture of a pharmaceutical composition for treating post-COVID-19 syndrome in a subject, the method fusion polypeptide comprising:
(i) ~~contacting the subject with the isolated polypeptide of any one of claims 1-27, or a cell of claim 28; and~~
(ii) ~~evaluating one or more symptoms associated with post COVID-19 syndrome selected from the group consisting of arrhythmia, myocarditis, heart failure, shortness of breath, fatigue, edema, orthopnea, limitations to exertion, impaired cognitive abilities, palpitations, dizziness, syncope, and lightheadedness,~~
~~wherein the treatment is effective in ameliorating the one or more symptoms associated with post COVID-19 syndrome~~
a. a whole or a portion of a DSG2 protein (SEQ ID NO: 1); and
b. a protein or a fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* or used for purification of the DSG2 fusion polypeptide.

~~33. 2. The method of claim 32~~ use of claim 1, wherein serum of the subject comprises anti-DSG2 antibodies.

~~34. 3. The method of claim 32~~ use of claim 1, wherein the subject was previously diagnosed with COVID-19.

~~35. The method of claim 34, wherein serum of the subject comprises anti SARS-CoV-2 antibodies.~~

4. The use of any one of claims 1 to 3, wherein the protein or the fragment of a protein is a sequence tag.

5. The use of any one of claims 1 to 3, wherein the portion of the DSG2 protein comprises the whole extracellular region of DSG2 protein comprising the amino acid sequence of SEQ ID NO: 3.

6. The use of any one of claims 1 to 3, wherein the portion of the DSG2 protein is a portion of an extracellular region of the DSG2 protein.

7. The use of claim 6, wherein the portion of the extracellular region of the DSG2 protein comprises at least one domain, wherein the at least one domain is an extracellular cadherin domain 1 (EC1), an extracellular cadherin domain 2 (EC2), an extracellular cadherin domain 3 (EC3), an extracellular cadherin domain 4 (EC4), or an extracellular anchor domain (EA).

8. The use of any one of claims 1 to 3 and 5 to 7, wherein the protein or the fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* is a whole or a portion of an immunoglobulin protein.

9. The use of claim 8, wherein the immunoglobulin is an IgG.

10. The use of claim 8 or 9, wherein the portion of the immunoglobulin protein is an Fc region.

~~36. The method of claim 34, wherein the serum of the subject does not comprise anti SARS-CoV-2 antibodies.~~

~~37. 11. A method of~~ Use of a desmoglein 2 (DSG2) fusion polypeptide in the manufacture of a pharmaceutical composition for treating COVID-19 in a subject, the method-fusion polypeptide comprising:

(i) ~~contacting the subject with the isolated polypeptide of any one of claims 1-27, or a cell of claim 28; and~~

(ii) ~~evaluating one or more symptoms associated with COVID-19 selected from the group consisting of fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea, trouble breathing, persistent pain or pressure in the chest, wherein the treatment is effective in ameliorating the one or more symptoms associated with COVID-19~~

a. a whole or a portion of a DSG2 protein (SEQ ID NO: 1); and

b. a protein or a fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* or used for purification of the DSG2 fusion polypeptide.

~~38. A method of treating cardiomyopathy in a subject, the method comprising:~~

(i) ~~contacting the subject with the isolated polypeptide of any one of claims 1-27, or a cell of claim 28, and~~

(ii) ~~measuring one or more symptoms associated with cardiomyopathy selected from the group consisting of arrhythmia, palpitations, myocarditis, heart failure, poor cardiac output, and reduced ejection fraction.~~

~~39. The method of claim 38, wherein the cardiomyopathy is arrhythmogenic right ventricular cardiomyopathy.~~

~~40. The method of claim 38, wherein the cardiomyopathy is caused by a virus, a bacterium, a parasite or a fungus.~~

~~41. The method of claim 40, wherein the cardiomyopathy is caused by a virus and wherein the virus is a SARS-CoV2, an adenovirus, a hepatitis virus, a parvovirus, a herpes simplex virus, an echovirus, an Epstein Barr virus, a rubella virus, a cytomegalovirus, or an HIV.~~

~~42. The method of claim 40, wherein the cardiomyopathy is caused by a bacterium and wherein the bacterium is a Staphylococcus, a Streptococcus, or a Borrelia.~~

~~43. The method of claim 40, wherein the cardiomyopathy is caused by a parasite and wherein the parasite is a Trypanosoma or a Toxoplasma.~~

~~44. The method of claim 40, wherein the cardiomyopathy is caused by a fungus and wherein the fungus is a Candida, an Aspergillus, or a Histoplasma.~~

~~45.~~ 12. The method of claim 38 use of claim 11, wherein the serum of the subject comprises anti-DSG2 antibodies.

13. The use of claim 11 or 12, wherein the protein or the fragment of a protein is a sequence tag.

14. The use of any one of claims 11 to 13, wherein the portion of the DSG2 protein comprises the whole extracellular region of DSG2 protein comprising the amino acid sequence of SEQ ID NO: 3.

15. The use of any one of claims 11 to 13, wherein the portion of the DSG2 protein is a portion of an extracellular region of the DSG2 protein.

16. The use of claim 15, wherein the portion of the extracellular region of the DSG2 protein comprises at least one domain, wherein the at least one domain is an extracellular cadherin domain 1 (EC1), an extracellular cadherin domain 2 (EC2), an extracellular cadherin domain 3 (EC3), an extracellular cadherin domain 4 (EC4), or an extracellular anchor domain (EA).

17. The use of any one of claims 11, 12, and 14 to 16, wherein the protein or the fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* is a whole or a portion of an immunoglobulin protein.

18. The use of claim 17, wherein the immunoglobulin is an IgG.

19. The use of claim 17 or 18, wherein the portion of the immunoglobulin protein is an Fc region.

20. A desmoglein 2 (DSG2) fusion polypeptide for use in the treatment of post-COVID-19 syndrome, the fusion polypeptide comprising:
a. a whole or a portion of a DSG2 protein (SEQ ID NO: 1); and
b. a protein or a fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* or used for purification of the DSG2 fusion polypeptide.

21. A desmoglein 2 (DSG2) fusion polypeptide for use in the treatment of COVID-19, the fusion polypeptide comprising:
a. a whole or a portion of a DSG2 protein (SEQ ID NO: 1); and
b. a protein or a fragment of a protein which is capable of improving the expression and/or stability of the DSG2 protein *in vitro* or *in vivo* or used for purification of the DSG2 fusion polypeptide.