# COMPOSITIONS INCLUDING SBI ADJUVANTS AND METHODS OF USE THEREOF

## CROSS-REFERENCE TO RELATED APPLICATIONS

**[0001]** This application claims priority to U.S. Provisional Patent Application 63/156,860 filed on March 4, 2021, the entire contents of which is hereby incorporated by reference.

## BACKGROUND

**[0002]** In recent years, progress has been made in the development of vaccines for a variety of diseases and conditions. However, these efforts have not been able to generate broadly neutralizing vaccines.

## SUMMARY

**[0003]** The present disclosure provides compositions for stimulating an immune response against an antigen and/or for enhancing immunogenicity of an antigen. In some examples, compositions disclosed herein comprise immunogenic compositions comprising: (1) an antigen fragment or an antigen variant, fused to (2) an adjuvant comprising a complement C3d-binding region. In some examples, an immunogenic composition disclosed herein can enhance the titers of the resulting antibody response and/or result in a measurable T cell response. In some examples, the adjuvant is or comprises a complement C3d-binding region of a Sbi protein from Staphylococcus aureus (e.g., Sbi III and/or Sbi IV). Also provided herein are pharmaceutical compositions and methods of using said pharmaceutical compositions to stimulate an immune response against an antigen and/or to enhance immunogenicity of an antigen.

**[0004]** The present disclosure provides a polypeptide comprising a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus. In some examples, a polypeptide is a fusion polypeptide comprising: (i) a fragment antigen that comprises an epitope of a target protein antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0005]** In some examples, a complement C3d-binding polypeptide is or comprises one or both of domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain III of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof.

**[0006]** In some examples, a fragment antigen has an amino acid sequence length of at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% compared to the amino acid sequence length of the target protein antigen. In some examples, a fragment antigen has an amino acid sequence length of no more than 50% of the amino acid sequence length of the target protein antigen. In some examples, a fragment antigen has an amino acid sequence length of no more than 40%, 30%, 20%, 10% or 5% of the amino acid sequence length of the target protein antigen.

**[0007]** In some examples, a fragment antigen has about 10-300 amino acid residues in length. In some examples, a fragment antigen has at least 10 amino acid residues in length. In some examples, a fragment antigen has less than about 300 amino acid residues in length. In some examples, a fragment antigen has about 10-300, 10-250, 10-200, 10-150, 10-100, 10-90, 10-80, 10-70, 10-60, 10-50, 10-40, 10-30, 10-20, 20-300, 30-300, 40-300, 50-300, 60-300, 70-300, 80-300, 90-100, 100-300, 150-300, 200-300, 250-300, 20-250, 30-200, 40-150, 50-100, 60-90, or 70-80 amino acids residues in length. In some examples, a fragment antigen has about 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, or 300 amino acids residues in length.

**[0008]** Also provided herein is a fusion polypeptide comprising: (i) an antigen variant or a fragment antigen variant that comprises an epitope of a target protein antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0009]** In some examples, a complement C3d-binding polypeptide is or comprises one or both of domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional

fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain III of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide is or comprises domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof.

**[0010]** In some examples, an antigen variant or fragment antigen variant amino acid sequence length is identical to the amino acid sequence length of the target protein antigen.

**[0011]** In some examples, an antigen variant or fragment antigen variant comprises at least one modified amino acid compared to the target protein antigen. In some examples, a modified amino acid comprises N-linked glycosylation. In some examples, an antigen variant or fragment antigen variant comprises at least one amino acid mutation compared to the target protein antigen. In some examples, an antigen variant or fragment antigen variant comprises 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40 or 50 amino acid mutations compared to the target protein antigen. In some examples, the mutation introduces a Serine, a Threonine, an Alanine, or an amino acid at a particular position which is different from the amino acid present at that position in the target protein antigen. In some examples, the mutation prevents formation of a disulfide bond.

**[0012]** In some examples, a fragment antigen is characterized in that when expressed in vivo, it binds to a Major Histocompatibility Complex (MHC) molecule. In some examples, a MHC molecule is or comprises a MHC I molecule or a MHC II molecule.

**[0013]** In some examples, a fragment antigen is characterized in that when expressed in vivo, it does not bind to a MHC molecule.

**[0014]** In some examples, a fragment antigen is characterized in that when expressed in vivo, it folds into a three-dimensional conformation that is substantially identical to the three-dimensional conformation of the fragment antigen as it is in its native position in the target protein antigen.

**[0015]** In some examples, a fragment antigen, antigen variant or fragment antigen variant further comprises an amino acid sequence from a second target protein antigen.

**[0016]** In some examples, a target protein antigen is or comprises an infectious disease antigen. In some examples, an infectious disease antigen is or comprises a viral antigen, a bacterial antigen, a fungal antigen, or combinations thereof. In some examples, a viral antigen is or comprises an influenza antigen. In some examples, a viral antigen is or comprises a coronavirus polypeptide. In some examples, a coronavirus polypeptide is or comprises a SARS-CoV-2 protein. In some examples, a SARS-CoV-2 protein is or comprises a Spike protein (SARS-CoV-2 S) or fragment thereof; an Envelope protein (SARS-CoV-2 E) or fragment thereof; a Membrane protein (SARS-CoV-2 M) or fragment thereof; a nucleocapsid protein (SARS-CoV-2 N) or fragment thereof; an accessory factor polypeptide or fragment thereof; or any combination thereof. In some examples, a SARS-CoV-2 protein comprises a Spike protein or a fragment thereof (e.g., RBD).

**[0017]** In some examples, a target protein antigen is or comprises a cancer antigen.

**[0018]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has an amino acid sequence at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 3.

**[0019]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 4.

**[0020]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 5.

**[0021]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 6.

**[0022]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 7.

**[0023]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 20.

**[0024]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 21.

**[0025]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 22.

**[0026]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 23.

**[0027]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 24.

**[0028]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 25.

**[0029]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO:26.

**[0030]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 27.

**[0031]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 28.

**[0032]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 29.

**[0033]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 30.

**[0034]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 31.

**[0035]** In some examples, a fragment antigen, antigen variant or fragment antigen variant has at least 80%, 85%, 90%, or 100% identity to the amino acid sequence of SEQ ID NO: 8.

**[0036]** In some examples, a complement C3d-binding polypeptide comprises an Sbi domain III having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 9.

**[0037]** In some examples, a complement C3d-binding polypeptide comprises an Sbi domain IV having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 10.

**[0038]** In some examples, a Sbi domain III and a Sbi domain IV are contiguous.

**[0039]** In some examples, a Sbi domain III and a Sbi domain IV are separated by a linker.

**[0040]** In some examples, (a) and (b) are encoded by a nucleotide sequence and are disposed in the same nucleotide sequence or in different nucleotide sequences. In some examples, (a) is disposed N-terminus of (b). In some examples, (a) is disposed C-terminus of (b).

**[0041]** In some examples, (a) and (b) are contiguous or separated by a linker. In some examples, the linker is a peptidyl linker. In some examples, the peptidyl linker comprises at least 60% glycine and/or serine. In some examples, the linker is chosen from a Gly-Gly-

Gly-Gly-Ser (Gly4-Ser) linker, or a Histidine linker. In some examples, the linker is a Gly4-Ser linker. In some examples, the linker comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 repeats of the Gly4-Ser linker. In some examples, the linker comprises 3 repeats of the Gly4-Ser linker. In some examples, the linker comprises the sequence of SEQ ID NO: 11.

**[0042]** In some examples, a fusion polypeptide further comprises a secretion peptide. In some examples, the secretion peptide is about 10-30 amino acids in length. In some examples, a secretion peptide is about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 amino acids in length. In some examples, a secretion peptide comprises an amino acid having at least 80%, 85%, 90%, or 100% identity to the amino acid sequence of SEQ ID NO: 1. In some examples, a secretion peptide comprises an amino acid having at least 80%, 85%, 90%, or 100% identity to the amino acid sequence of SEQ ID NO: 2.

**[0043]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 12.

**[0044]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 13.

**[0045]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 14.

**[0046]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 15.

**[0047]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 16.

**[0048]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 17.

**[0049]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 18.

**[0050]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 19.

**[0051]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 32.

**[0052]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 33.

**[0053]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 34.

**[0054]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:35.

**[0055]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:36.

**[0056]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:37.

**[0057]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:38.

**[0058]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:39.

**[0059]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:40.

**[0060]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:41.

**[0061]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:42.

**[0062]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 43.

**[0063]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO: 44.

**[0064]** In some examples, a fusion polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the amino acid sequence of SEQ ID NO:45.

**[0065]** In some examples, a fusion polypeptide is encoded by a polynucleotide which is or comprises RNA. In some examples, a fusion polynucleotide is or comprises messenger RNA.

**[0066]** In some examples, a fusion polypeptide is encoded by a polynucleotide which is or comprises DNA.

**[0067]** Disclosed herein is a fusion polynucleotide encoding any one of the fusion polypeptides disclosed herein.

**[0068]** Also disclosed herein is a fusion polynucleotide comprising a nucleotide sequence encoding: (i) a fragment antigen that comprises an epitope of a target protein antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus. In one aspect, the present disclosure refers to a fusion polynucleotide comprising a nucleotide sequence encoding: (i) a fragment antigen, an antigen variant, or a fragment antigen variant, that comprises an epitope of a target protein antigen, wherein the target protein antigen is or comprises: (a) an infectious antigen chosen from a viral antigen or a fungal antigen or combinations thereof; or (b) a cancer antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of *Staphylococcus aureus*, wherein the fusion polynucleotide is RNA. In another aspect, the present disclosure refers to a fusion polynucleotide comprising a nucleotide sequence encoding: (i) a fragment antigen, an antigen variant, or a fragment antigen variant, that comprises an epitope of a target protein antigen, wherein the target protein antigen is or comprises: (a) an infectious antigen chosen from a viral antigen or a fungal antigen or combinations thereof; or (b) a cancer antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of *Staphylococcus aureus,* wherein the polynucleotide has at least 80% identity to the nucleotide sequence of any one of SEQ ID NOs: 46, 47, 48, 49, 50, 51, 52, 53, or 54.

**[0069]** Disclosed herein is a polynucleotide comprising a nucleotide sequence encoding: (i) an antigen variant or a fragment antigen variant that comprises an epitope of a target protein antigen; and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0070]** In some examples, a fusion polynucleotide is or comprises RNA. In some examples, a polynucleotide is or comprises messenger RNA.

**[0071]** In some examples, a fusion polynucleotide is or comprises DNA.

**[0072]** In some examples, a complement C3d-binding polypeptide encoded by the polynucleotide is or comprises one or both of domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide encoded by the polynucleotide is or comprises domain III of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide encoded

by the polynucleotide is or comprises domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof. In some examples, a complement C3d-binding polypeptide encoded by the polynucleotide is or comprises domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof.

**[0073]** In some examples, a fusion polynucleotide encodes a fragment antigen that has an amino acid sequence length of at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% compared to the amino acid sequence length of the target protein antigen. In some examples, a fusion polynucleotide encodes a fragment antigen that has an amino acid sequence length of no more than 50% of the amino acid sequence length of the target protein antigen. In some examples, a fusion polynucleotide encodes a fragment antigen has an amino acid sequence length of no more than 40%, 30%, 20%, 10% or 5% of the amino acid sequence length of the target protein antigen.

**[0074]** In some examples, a fusion polynucleotide encodes an antigen variant or fragment antigen variant having an amino acid sequence length that is identical to the amino acid sequence length of the target protein antigen.

**[0075]** In some examples, a fusion polynucleotide encodes an antigen variant or fragment antigen variant which comprises at least one modified amino acid compared to the target protein antigen.

**[0076]** In some examples, a fusion polynucleotide encodes a fragment antigen which is characterized in that when expressed in vivo, it binds to a Major Histocompatibility Complex (MHC) molecule. In some examples, a MHC molecule is or comprises a MHC I molecule or a MHC II molecule.

**[0077]** In some examples, a fusion polynucleotide encodes a fragment antigen which is characterized in that when expressed in vivo, it does not bind to a MHC molecule.

**[0078]** In some examples, a fusion polynucleotide encodes a fragment antigen which is characterized in that when expressed in vivo, it folds into a three-dimensional conformation that is substantially identical to the three-dimensional conformation of the fragment antigen as it is in its native position in the target protein antigen.

**[0079]** In some examples, a fusion polynucleotide encodes a fragment antigen, antigen variant or fragment antigen variant which further comprises an amino acid sequence from a second target protein antigen.

**[0080]** In some examples, a target protein antigen is or comprises an infectious disease antigen. In some examples, an infectious disease antigen is or comprises a viral antigen, a bacterial antigen, a fungal antigen, or combinations thereof. In some examples, an antigen is or comprises a viral antigen. In some examples, a viral antigen is or comprises an influenza antigen. In some examples, a viral antigen is or comprises a coronavirus polypeptide. In some examples, a coronavirus polypeptide is or comprises a SARS-CoV-2 protein. In some examples, a SARS-CoV-2 protein is or comprises a Spike protein (SARS-CoV-2 S) or fragment thereof; an Envelope protein (SARS-CoV-2 E) or fragment thereof; a Membrane protein (SARS-CoV-2 M) or fragment thereof; a nucleocapsid protein (SARS-CoV-2 N) or fragment thereof; an accessory factor polypeptide or fragment thereof; or any combination

thereof. In some examples, the SARS-CoV-2 protein comprises a Spike protein or a fragment thereof (e.g., RBD).

**[0081]** In some examples, a target protein antigen is or comprises a cancer antigen.

**[0082]** In some examples, (a) is disposed C-terminus of (b). In some examples, (a) and (b) are contiguous or separated by a nucleotide sequence encoding a linker. In some examples, the linker is a peptidyl linker. In some examples, the peptidyl linker comprises at least 60% glycine and/or serine. In some examples, the linker is chosen from a Gly-Gly-Gly-Gly-Ser (Gly4-Ser) linker, or a Histidine linker.

**[0083]** In some examples, a fusion polynucleotide further comprises a nucleotide sequence encoding a secretion peptide.

**[0084]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 46.

**[0085]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 47.

**[0086]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 48.

**[0087]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 49.

**[0088]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 50.

**[0089]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 51.

**[0090]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 52.

**[0091]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 53.

**[0092]** In some examples, a fusion polynucleotide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 54.

**[0093]** Disclosed herein is an expression vector comprising any one of the fusion polynucleotides disclosed herein.

**[0094]** In some examples, an expression vector comprises a viral vector. In some examples, a viral vector comprises a retrovirus vector, an adenovirus vector, an adeno-associated virus vector or a lentivirus vector or an RNA vector.

**[0095]** Also disclosed herein is a composition for delivering any one of the fusion polypeptides disclosed herein.

**[0096]** Disclosed herein is a composition for delivering any one of the fusion polynucleotides disclosed herein.

**[0097]** This disclosure provides a pharmaceutical composition that delivers a fusion polypeptide disclosed herein, a fusion polynucleotide disclosed herein, or an expression vector comprising a fusion polynucleotide disclosed herein.

**[0098]** In some examples, a pharmaceutical composition further comprises a pharmaceutically acceptable excipient, a diluent, or a combination thereof.

**[0099]** Disclosed herein is a method of making comprising: recombinantly joining a first nucleotide sequence that encodes a fragment antigen comprising an epitope of a target protein antigen, and a second nucleotide sequence that encodes a complement C3d-binding polypeptide from a immunoglobulin-binding protein (Sbi) of Staphylococcus aureus to form a polynucleotide comprising the first nucleotide sequence and the second nucleotide sequence.

**[0100]** In some examples, the method further comprises expressing the polynucleotide in a cell to produce a fusion polypeptide encoded by the polynucleotide.

**[0101]** Disclosed herein is a cell comprising a fusion polypeptide disclosed herein, a fusion polynucleotide disclosed herein, or an expression vector comprising a fusion polynucleotide disclosed herein.

**[0102]** In some examples, the cell is contacted with the fusion polynucleotide, fusion polypeptide or expression vector. In some examples, contacting occurs in vivo, in vitro or ex vivo.

**[0103]** Disclosed herein is a kit comprising a fusion polypeptide disclosed herein, a fusion polynucleotide disclosed herein, or an expression vector comprising a fusion polynucleotide disclosed herein, and instructions for use.

**[0104]** In some examples, the kit further comprises: a polynucleotide comprising a nucleotide sequence that encodes a target protein antigen; or a target protein antigen encoded by the polynucleotide.

**[0105]** The disclosure provides, a method comprising administering to a subject in need thereof at least one dose of a pharmaceutical composition comprising a fusion polypeptide disclosed herein, a fusion polynucleotide disclosed herein, or an expression vector comprising a fusion polynucleotide disclosed herein.

**[0106]** In some examples, the at least one dose is administered in an effective amount to induce an immune response against the fragment antigen in the subject.

**[0107]** In some examples, the immune response comprises generation of a neutralizing antibody titer against the fragment antigen.

**[0108]** In some examples, a neutralizing antibody titer is increased by at least 50%, as compared to a neutralizing antibody titer induced by a fragment antigen in the absence of the complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0109]** In some examples, the generation of a neutralizing antibody titer has been established in a mouse model using a dose of at least 0.1 μg.

**[0110]** In some examples, the at least one dose is administered in an effective amount to stimulate B cells while reducing induction of T cell response.

**[0111]** Disclosed herein is a method comprising administering to a subject: a first dose of a pharmaceutical composition disclosed herein; and a second dose of a pharmaceutical composition disclosed herein. In some examples, a pharmaceutical composition comprises a fusion polypeptide disclosed herein, a fusion polynucleotide disclosed herein, or an expression vector comprising a fusion polynucleotide disclosed herein.

**[0112]** In some examples, a first dose and a second dose are administered by at least 3 days, 4 days, 5 days, 6 days, 7 days, 2 weeks, 3 weeks, or 4 weeks apart.

**[0113]** In some examples, a first dose and a second dose are in the same amount.

**[0114]** In some examples, a first dose and a second dose are in different amounts.

**[0115]** Further disclosed herein is a method comprising: administering to a subject in need thereof a dose of a pharmaceutical composition disclosed herein, such that the subject receives: a first dose of a pharmaceutical composition that delivers a polynucleotide comprising a nucleotide sequence that encodes a target protein antigen or a target protein antigen encoded by the polynucleotide; and a second dose of a pharmaceutical composition disclosed herein.

**[0116]** In some examples, (a) the polynucleotide comprising a nucleotide sequence that encodes a target protein antigen further comprises a nucleotide sequence encoding a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or (b) the target protein antigen encoded by the polynucleotide further comprises a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0117]** In some examples, the method further comprises, prior to the administering step, administering to the subject the first dose of the pharmaceutical composition that delivers a polynucleotide comprising a nucleotide sequence that encodes a target protein antigen or a target protein antigen encoded by the polynucleotide.

**[0118]** This disclosure provides, a method comprising: administering to a subject in need thereof a dose of a pharmaceutical composition disclosed herein, such that the subject receives: a first dose of the pharmaceutical composition of claim disclosed herein, and a second dose of a

pharmaceutical composition that delivers a polynucleotide comprising a nucleotide sequence that encodes a target protein antigen or a target protein antigen encoded by the polynucleotide.

**[0119]** In some examples, (a) the polynucleotide comprising a nucleotide sequence that encodes a target protein antigen further comprises a nucleotide sequence encoding a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or (b) the target protein antigen encoded by the polynucleotide further comprises a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0120]** Disclosed herein is a method comprising: administering to a subject in need thereof a dose of a pharmaceutical composition disclosed herein, such that the subject receives: a first dose of a pharmaceutical composition that delivers a polynucleotide comprising a nucleotide sequence that encodes a fusion polypeptide comprising (i) a target protein antigen and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or a fusion polypeptide encoded by the polynucleotide; and a second dose of the pharmaceutical composition disclosed herein.

**[0121]** In some examples, the method further comprises, prior to the administering step, administering to the subject the first dose of the pharmaceutical composition that delivers a polynucleotide comprising a nucleotide sequence that encodes a fusion polypeptide comprising (i) a target protein antigen and (ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or a fusion polypeptide encoded by the polynucleotide.

**[0122]** In some examples, a first dose and a second dose are administered by at least 3 days, 4 days, 5 days, 6 days, 7 days, 2 weeks, 3 weeks, or 4 weeks apart.

**[0123]** In some examples of any of the methods disclosed herein, the subject in need thereof is a subject who is suffering from or is susceptible to a disease, disorder, or condition induced by the target protein antigen.

**[0124]** In some examples, a subject is a mammalian subject.

**[0125]** In some examples, a subject is a human subject.

**[0126]** In some examples, administration can be performed by intramuscular administration, intradermal administration, intravenous administration, subcutaneous administration, or combinations thereof.

**[0127]** Disclosed herein is a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for use in enhancing the immunogenicity of an antigen.

**[0128]** Also disclosed herein is a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for use in stimulating an immune response against an antigen.

**[0129]** Further disclosed herein is a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for use in method of treating a disease or ameliorating a symptom of a disease.

**[0130]** This disclosure provides, a method for enhancing the immunogenicity of an antigen, comprising administering to a subject in need thereof, a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein.

**[0131]** This disclosure also provides a method for stimulating an immune response against an antigen, comprising administering to a subject in need thereof, a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein.

**[0132]** Additionally provided herein is a method of treating a disease or ameliorating a symptom of a disease comprising administering to a subject in need thereof, a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein.

**[0133]** This disclosure provides use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein in the preparation of a medicament for enhancing the immunogenicity of a fragment antigen.

**[0134]** This disclosure also provides, use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, in the preparation of a medicament for stimulating an immune response against a antigen.

**[0135]** Further provided herein is use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, in the preparation of a medicament for treating a disease or ameliorating a symptom of a disease.

**[0136]** Provided herein is the use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for enhancing the immunogenicity of a fragment antigen.

**[0137]** Further provided herein is the use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for stimulating an immune response against a antigen.

**[0138]** This disclosure provides use of a composition comprising a fusion polypeptide disclosed herein, or a fusion polynucleotide disclosed herein, or a pharmaceutical composition disclosed herein, for treating a disease or ameliorating a symptom of a disease.

**[0139]** In some examples of any of the methods or uses disclosed herein, the subject is a mammal.

**[0140]** In some examples of any of the methods or uses disclosed herein, the subject is a human.

**[0141]** In some examples of any of the methods or uses disclosed herein, a single dose of the fusion polypeptide, fusion polynucleotide or pharmaceutical composition is administered.

**[0142]** In some examples of any of the methods or uses disclosed herein, a plurality of doses of the fusion polypeptide, fusion polynucleotide or pharmaceutical composition is administered.

**[0143]** In some examples of any of the methods or uses disclosed herein, the fusion polypeptide, fusion polynucleotide or pharmaceutical composition is administered at a dose of about 0.5 micrograms to 10 micrograms.

**[0144]** In some examples of any of the methods or uses disclosed herein, administration of the fusion polynucleotide, fusion polypeptide or pharmaceutical composition results in a humoral response. In some examples, the humoral response is an antibody response.

**[0145]** In some examples of any of the methods or uses disclosed herein, administration of the fusion polynucleotide, fusion polypeptide or pharmaceutical composition results in an increased titer of an antibody response. In some examples, the increase in titer is an increase of about 10 fold to about 500 fold. In some examples, the increased titer of the antibody response is compared to administration of an otherwise similar fusion polynucleotide that does not comprise an Sbi domain III, or a fragment or variant thereof; and Sbi domain IV, or a fragment or a variant thereof. In some examples, the increased titer of the antibody response is compared to administration of an otherwise similar fusion polypeptide that does not comprise an Sbi domain III, or a fragment or variant thereof; and an Sbi domain IV, or a fragment or a variant thereof. In some examples, the increased titer of the antibody response is compared to administration of an otherwise similar pharmaceutical composition that does not comprise a nucleotide sequence encoding Sbi domain III, or a fragment or variant thereof; and Sbi domain IV, or a fragment or a variant thereof.

**[0146]** In some examples of any of the methods or uses disclosed herein, the composition is administered via any one of the following routes of administration: intramuscular, intravenous, subcutaneous, intrathecal, intradermal, ocular, intranasal, sublingual, or oral.

**[0147]** This disclosure provides, an in vitro method of selecting a fragment antigen by identifying a polypeptide fragment that folds into a three-dimensional conformation that is substantially identical to the three-dimensional conformation as in a target protein antigen from which the fragment is derived.

**[0148]** In some examples, the method comprises the steps of: providing a mammalian cell display system that displays a library of fragment antigen candidates on cell surface; exposing the mammalian cell display system to a composition comprising antibodies that bind to

a target protein antigen from which the fragment antigen candidates are derived; detecting fragment antigen candidates that bind to the target protein antigen-binding antibodies, wherein the binding of a fragment antigen candidate that binds to at least one of the target protein antigen-binding antibodies is indicative of its likelihood to fold into a three-dimensional conformation that is substantially identical to the three-dimensional conformation as in the target protein antigen.

**[0149]** In some examples, the method further comprises a step of generating antibodies that bind to the target protein antigen.

**[0150]** In some examples, the generation of the antibodies comprises (i) immunizing animals with a target protein antigen or a polynucleotide encoding the same from which the fragment antigen candidates are derived; and (ii) identifying antibodies that bind to the target protein antigen.

**[0151]** In some examples, the mammalian cell display system comprises HEK293T cells, HeLa cells, or CHO cells.

**[0152]** In some examples, the polypeptide fragment is identified based on binding affinity to the antibody in a serum binding assay or a similar assay.

**[0153]** Also provided herein is a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof.

**[0154]** In some examples, the polynucleotide comprises a sequence encoding a complement C3d-binding polypeptide from Sbi.

**[0155]** In some examples, the complement C3d-binding polypeptide is or comprises one or both of domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof.

**[0156]** In some examples, the polynucleotide is or comprises RNA. In some examples, the polynucleotide is or comprises messenger RNA.

**[0157]** In some examples, the polynucleotide is or comprises DNA.

**[0158]** In some examples, the polynucleotide encodes a polypeptide which has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 9.

**[0159]** In some examples, the polynucleotide encodes a polypeptide which has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleotide sequence of SEQ ID NO: 10.

**[0160]** This disclosure provides an isolated polypeptide comprising an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0161]** In some examples, the polypeptide comprises a complement C3d-binding polypeptide from Sbi.

**[0162]** In some examples, the complement C3d-binding polypeptide is or comprises one or both of domain III and domain IV of the Sbi of Staphylococcus aureus, or a functional fragment or a variant thereof.

**[0163]** In some examples, the polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 9.

**[0164]** In some examples, the polypeptide has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 100% identity to the amino acid sequence of SEQ ID NO: 10.

**[0165]** Also provided herein is an expression vector comprising a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof.

**[0166]** Further provided herein is a composition for delivering an isolated polypeptide comprising an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus.

**[0167]** This disclosure also provides a composition for delivering a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof.

**[0168]** Provided herein is a pharmaceutical composition that delivers a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof; an isolated polypeptide comprising an

immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or an expression vector comprising a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof.

**[0169]** In some examples, the pharmaceutical composition further comprises a pharmaceutically acceptable excipient, a diluent, or a combination thereof.

**[0170]** This disclosure provides a method comprising administering to a subject in need thereof at least one dose of a pharmaceutical composition comprising: a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof; an isolated polypeptide comprising an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus; or an expression vector comprising a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof.

**[0171]** Further disclosed herein is a method for enhancing the immunogenicity of an antigen, comprising administering to a subject in need thereof, a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof; an isolated polypeptide comprising an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a pharmaceutical composition comprising the same.

**[0172]** This disclosure also provides a method for stimulating an immune response against an antigen, comprising administering to a subject in need thereof, a recombinant polynucleotide comprising a nucleotide sequence encoding an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a fragment thereof; an isolated polypeptide comprising an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus, or a pharmaceutical composition comprising the same.

**[0173]** Also provided herein is the use of an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus as an adjuvant in an immunogenic composition.

**[0174]** This disclosure provides an immunoglobulin-binding protein (Sbi) of Staphylococcus aureus for use as an adjuvant in an immunogenic composition.

## CLAIMS

*What is claimed is:*

1. A fusion polynucleotide comprising a nucleotide sequence encoding:

(i) a fragment antigen, an antigen variant, or a fragment antigen variant, that comprises an epitope of a target protein antigen, wherein the target protein antigen is or comprises:

(a) an infectious antigen chosen from a viral antigen or a fungal antigen or combinations thereof; or

(b) a cancer antigen; and

(ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of *Staphylococcus aureus*,

wherein the fusion polynucleotide is RNA.

2. The fusion polynucleotide of claim 1, wherein the complement C3d-binding polypeptide is or comprises domain III and domain IV of the Sbi of *Staphylococcus aureus*, or a functional fragment or a variant thereof.

3. The fusion polynucleotide of claim 1, wherein the viral antigen is or comprises an influenza antigen or a coronavirus polypeptide.

4. The fusion polynucleotide of claim 3, wherein the coronavirus polypeptide is or comprises a SARS-CoV 2 protein chosen from: a Spike protein (SARS-CoV-2 S) or fragment thereof; an Envelope protein (SARS-CoV-2 E) or fragment thereof; a Membrane protein (SARS-CoV-2 M) or fragment thereof; a nucleocapsid protein (SARS-CoV-2 N) or fragment thereof; an accessory factor polypeptide or fragment thereof; or any combination thereof.

5. The fusion polynucleotide of claim 1, wherein (i) and (ii) are contiguous.

6. The fusion polynucleotide of claim 1, wherein the polynucleotide further comprises a nucleotide sequence encoding a secretion peptide.

7. A fusion polynucleotide comprising a nucleotide sequence encoding:

(i) a fragment antigen, an antigen variant, or a fragment antigen variant, that comprises an epitope of a target protein antigen, wherein the target protein antigen is or comprises:

(a) an infectious antigen chosen from a viral antigen or a fungal antigen or combinations thereof; or

(b) a cancer antigen; and

(ii) a complement C3d-binding polypeptide from an immunoglobulin-binding protein (Sbi) of *Staphylococcus aureus,*

wherein the polynucleotide has at least 80% identity to the nucleotide sequence of any one of SEQ ID NOs: 46, 47, 48, 49, 50, 51, 52, 53, or 54.

8. An expression vector comprising the fusion polynucleotide of claim 1.

9. The fusion polynucleotide of claim 1, wherein the polynucleotide encodes an antigen variant or fragment antigen variant which comprises at least one modified amino acid compared to the target protein antigen.

10. The fusion polynucleotide of claim 1, wherein the polynucleotide encodes a fragment antigen which is characterized in that when expressed in vivo, it binds to a Major Histocompatibility Complex (MHC) molecule.

11. The fusion polynucleotide of claim 10, wherein the MHC molecule is or comprises a MHC I molecule.

12. The fusion polynucleotide of claim 1, wherein the fragment antigen is characterized in that when expressed in vivo, it folds into a three-dimensional conformation that is substantially identical to the three-dimensional conformation of the fragment antigen as it is in its native position in the target protein antigen.

13. The fusion polynucleotide of claim 1, wherein the fragment antigen encoded by the polynucleotide has an amino acid sequence length of:

(i) at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% compared to the amino acid sequence length of the target protein antigen;

(ii) no more than 50% of the amino acid sequence length of the target protein antigen;

(iii) about 10-300 amino acid residues; or

(iv) a combination thereof.

14. The fusion polynucleotide of claim 1, wherein (i) is positioned N-terminus of (ii).

15. The fusion polynucleotide of claim 7, wherein the polynucleotide is or comprises RNA.

16. A pharmaceutical composition comprising the fusion polynucleotide of claim 1.

17. A cell comprising the fusion polynucleotide of claim 1.

18. The fusion polynucleotide of claim 4, wherein the SARS-CoV-2 protein comprises a RBD domain or a portion thereof.

19. The fusion polynucleotide of claim 18, wherein the SARS-CoV-2 protein encoded by the fusion polynucleotide has at least 80% identity to the sequence of any one of SEQ ID NOs: 3, 4, 5, 6, 7, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or 31.

20. The fusion polynucleotide of claim 1, wherein the complement C3d-binding polypeptide encoded by the fusion polynucleotide has at least 80% identity to the sequence of SEQ ID NO: 9 or SEQ ID NO: 10.

21. The fusion polynucleotide of claim 1, wherein the fragment antigen, antigen variant or fragment antigen variant further comprises an amino acid sequence from a second target protein antigen.

22. The fusion polynucleotide of claim 1, wherein (i) is positioned C-terminus of (ii).

23. The fusion polynucleotide of claim 1, wherein (i) and (ii) are separated by a nucleotide sequence encoding a linker.

24. The fusion polynucleotide of claim 10, wherein the MHC molecule is or comprises a MHC II molecule.

25. The fusion polynucleotide of claim 1, wherein the polynucleotide has at least 80% identity to the nucleotide sequence of any one of SEQ ID NOs: 46, 47, 48, 49, 50, 51, 52, 53, or 54.

26. The fusion polynucleotide of claim 1, wherein the complement C3d-binding polypeptide is or comprises domain III of the Sbi of *Staphylococcus aureus*, or a functional fragment or a variant thereof.

27. The fusion polynucleotide of claim 1, wherein the complement C3d-binding polypeptide is or comprises domain IV of the Sbi of *Staphylococcus aureus*, or a functional fragment or a variant thereof.