serum or blood and evades innate host defenses. Recently, genetic variation in the human factor H gene cluster was found to affect susceptibility to developing meningococcal disease (Davila S et al. (2010) Nat Genetics doi:10.1038/ng.640). Binding of fH to fHbp is specific for human fH and could account for why *Neisseria meningitidis* is strictly a human pathogen.

[0005] There remains a need for a fHbp polypeptide that can elicit effective bactericidal antibody responses.

SUMMARY

[0006] Non-naturally occurring factor H binding proteins derived from variant 3 fHbp that can elicit antibodies that are bactericidal for at least one strain of *N. meningitidis*, and methods of use of such proteins, are provided.

[0006a] In one aspect of the present disclosure, there is provided a non-naturally occurring factor H binding protein (fHbp) comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of a variant 3 fHbp having an amino acid sequence set forth as SEQ ID NO: 13, the non-naturally fHbp comprising:

a substitution of the histidine at position 223 of the naturally occurring variant 3 fHbp with an amino acid selected from the group consisting of arginine, lysine, phenylalanine, tyrosine, and tryptophan, wherein the numbering of position 223 is based on the numbering of amino acid residues in the sequence of the mature fHbp ID 1 set forth in SEQ ID NO: 1; and

an epitope for the JAR 13 monoclonal antibody,

wherein the non-naturally occurring fHbp has lower affinity for human factor H (fH) than fHbp ID 79.

[0006b] In another aspect of the present disclosure, there is provided an immunogenic composition comprising:

a) the non-naturally occurring fHbp as disclosed herein; and

b) a pharmaceutically acceptable excipient.

[0006c] In a further aspect of the present disclosure, there is provided a use of the non-naturally occurring fHbp as disclosed herein, or the immunogenic composition as disclosed herein, in the manufacture of a medicament for eliciting an antibody response in a mammal.

[0006d] In another aspect of the present disclosure, there is provided a nucleic acid encoding the fHbp as disclosed herein.

[0006e] In a further aspect of the present disclosure, there is provided a recombinant expression vector comprising the nucleic acid as disclosed herein.

CLAIMS

WHAT IS CLAIMED IS:

1. A non-naturally occurring factor H binding protein (fHbp) comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of a variant 3 fHbp having an amino acid sequence set forth as SEQ ID NO: 13, the non-naturally fHbp comprising:

a substitution of the histidine at position 223 of the naturally occurring variant 3 fHbp with an amino acid selected from the group consisting of arginine, lysine, phenylalanine, tyrosine, and tryptophan, wherein the numbering of position 223 is based on the numbering of amino acid residues in the sequence of the mature fHbp ID 1set forth in SEQ ID NO: 1; and

an epitope for the JAR 13 monoclonal antibody,

wherein the non-naturally occurring fHbp has lower affinity for human factor H (fH) than fHbp ID 79.

2. The non-naturally occurring fHbp of claim 1, wherein the histidine is substituted with arginine.

3. The non-naturally occurring fHbp of any one of claims 1-2, wherein the variant 3 fHbp is a modular group V fHbp.

4. The non-naturally occurring fHbp of any one of claims 1-2, wherein the variant 3 fHbp is a modular group II fHbp.

5. The non-naturally occurring fHbp of any one of claims 1-3, wherein the non-naturally occurring fHbp comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of the fHbp ID 79 set forth in SEQ ID NO: 13.

6. The non-naturally occurring fHbp of any one of claims 1-5, wherein the non-naturally occurring fHbp comprises fHbp ID 28 comprising the amino acid substitution H223R.

7. The non-naturally occurring fHbp of any one of claims 1-5, wherein the non-naturally occurring fHbp comprises fHbp ID 67 or fHbp ID 175 comprising the amino acid substitution H223R.