



Molecular Mimicry between Meningococcal B Factor H-Binding Protein and Human Proteins

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Abstract

This study calls attention on molecular mimicry and the consequent autoimmune cross reactivity as the molecular mechanism that can cause adverse events following meningococcal B vaccination and warns against active immunizations based on entire antigen.

Keywords

- molecular mimicry
- Trumenba vaccine
- factor H-binding protein
- human proteome
- adverse events

Introduction

The bacterium *Neisseria meningitidis* (aka meningococcus) can cause a multitude of severe illnesses, collectively termed meningococcal disease.¹ Numerous vaccines are available and, among them, a meningococcal B vaccine (namely, Trumenba) has been approved for children and contains the lipoprotein factor H-binding protein (fHbp).² Indeed, as described by Seib et al,³ preclinical studies demonstrated that fHbp elicits a robust bactericidal antibody response that correlates with the amount of fHbp expressed on the bacterial surface. However, according to the vaccine-prescribing informations,⁴ numerous adverse events occur following fHbp vaccine administration. That is, verbatim:

- Immune system disorders.
- Hypersensitivity reactions, including anaphylactic reactions.
- Nervous system disorders.
- Syncope.

Currently, at the best of the author's knowledge, no investigation/hypothesis has been proposed to define the molecular mechanism that triggers the adverse events following the Trumenba vaccine administration. In analyzing the issue,

this study posed the question of whether molecular mimicry between the vaccine antigen and the human proteins might play a role as already found in analogous research models.^{5,6}

Materials and Methods

Molecular mimicry between the bacterial fHbp antigen and human proteins was analyzed according to published methodology.^{5,6} In brief, the fHbp antigen, 274 amino acids (aa) as described at <https://www.uniprot.org/uniprotkb/Q9JXV4/>, was dissected into pentapeptides offset each other by one aa residue (i.e., MNRTA, NRTAF, RTAFC, and so forth) and the resulting bacterial pentapeptides were analyzed for occurrences within the human proteome.

Pentapeptides were used since a peptide grouping composed of 5 aa defines a minimal immune unit that can (1) induce highly specific antibodies and (2) determine antigen–antibody specific interaction.^{7–10} Peptide match and peptide search programs available at www.uniprot.org¹¹ were used.

Results

Following molecular mimicry analyses, it was found that fHbp pentapeptides repeatedly occur for a total of 2,809

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multiple occurrences in human protein alterations which can lead to severe diseases. The bacterial versus human pentapeptide overlap is of such a dimension that obviously it cannot be reported in the context of an article. Consequently, data are reported as ► **Supplementary Table S1** that is a fundamental part of this report.

In parallel, the severe diseases^{12–45} that could derive from the massive molecular mimicry and consequent cross-reactivity and autoimmunity are numerous. Here, only a short synopsis that gives an overview of such diseases is given in ► **Table 1**, thus confirming the vaccine-induced injuries listed in the Trumenba vaccine-prescribing informations.⁴

Conclusion

The vast sharing of immune peptide determinants between the bacterial fHbp antigen and the human proteins warns against Trumenba utilization to prevent meningococcal diseases. Indeed, the present data speak for themselves and clearly predict a very high incidence of autoimmune pathologies in the vaccinees as a result of molecular mimicry and the consequent potential cross-reactivity, thus factually confirming what had already been stated in the prescribing information of the Trumenba vaccine.⁴

In synthesis, this report adds to numerous previous studies,^{5–10} and further references therein, that explicated

Table 1 Peptides shared between fHbp protein and human proteins that—when altered—are associated with myelination, neuropathy, myopathy, ataxia, etc.

Peptides ^a	Human proteins: name and associated diseases ^{b,c}
KNEKL	<i>Chondroitin sulfate N-acetylgalactosaminyltransferase 1</i> Neuropathy ¹²
IGAVL	<i>Claudin-11. Oligodendrocyte-specific protein.</i> Autoantigen of autoimmune-demyelinating disease ¹³
SPELN	<i>Complex I intermediate-associated protein 30, mitochondrial</i> Deficiency may be associated with leukodystrophy ¹⁴
HAVIS, VDGQL	<i>Contactin-associated protein 1</i> Alterations associated with hypomyelinating neuropathy ¹⁵
GSDDA	<i>Delta-1-pyrroline-5-carboxylate synthase</i> Spastic paraplegia; progressive weakness, and spasticity of the lower limbs. Bladder incontinence, gait difficulties, neuropathy ¹⁶
AAKQG	<i>DNA polymerase subunit gamma-1</i> Neuronal loss, spongiform degeneration, demyelination ¹⁷
KLKND, LADAL	<i>DnaJ homolog subfamily C member 3</i> Neurodegeneration, ataxia, peripheral neuropathy, hearing loss ¹⁸
SAEVE, VQDSE	<i>Dystonin</i> Hypotonia, respiratory, and feeding difficulties ¹⁹
LTALQ	<i>E3 ubiquitin-protein ligase LRSAM1</i> Disorder of the peripheral nervous system ²⁰
LKLAA, RIGDI	<i>FYVE, RhoGEF, and PH domain-containing protein 4</i> Peripheral nerve demyelination ²¹
LPEGG	<i>Gelsolin</i> Required for normal myelin wrapping ²²
GSDDA	<i>Guanine nucleotide-binding protein subunit beta-4</i> Disorder of the peripheral nervous system ²³
TGKLK	<i>Laminin subunit alpha-2</i> Muscular dystrophy ²⁴
KSPEL	<i>Lysophosphatidylserine lipase ABHD12</i> Hearing loss, ataxia, retinitis pigmentosa, early-onset cataract ²⁵
GKMVA	<i>Myelin P2 protein</i> Neuropathy with progressive weakness and atrophy ²⁶
PEGGR	<i>Myelin protein P0</i> Dysmyelinating neuropathy ²⁷
VSRFD	<i>Neurofibromin</i> Neuropathy with progressive weakness and atrophy ²⁸
KLPEG	<i>Patatin-like phospholipase domain-containing protein 6</i> Mental retardation, spastic paraplegia, ataxia, blindness ²⁹

Table 1 (Continued)

Peptides ^a	Human proteins: name and associated diseases ^{b,c}
AEKGS	<i>Potassium voltage-gated channel subfamily D member 3</i> Spinocerebellar ataxia, incoordination of gait ³⁰
LADAL	<i>Prelamin-A/C</i> Disorder of the peripheral nervous system ³¹
SGEFQ	<i>Probable helicase senataxin</i> Spinocerebellar ataxia, neuropathy, dexterity difficulties ³²
SGGGG	<i>Ribose-5-phosphate isomerase</i> Leukoencephalopathy, psychomotor retardation ³³
NTGKL	<i>RNA polymerase II subunit A C-terminal domain phosphatase</i> Cataracts, facial dysmorphism, neuropathy ³⁴
DFAAK GGVA SAEVE	<i>Sacsin</i> Cerebellar ataxia, hypermyelination, mitral valve prolapse ³⁵
SDDAS TGKLK	<i>Serine/threonine-protein kinase DCLK2</i> Disorders of neuronal structure ³⁶
AAKQG KSLQS	<i>Voltage-gated sodium channel subunit alpha Nav1.8</i> Detrimental to motor axons ³⁷
TSFDK	<i>Sodium/potassium-transporting ATPase subunit alpha-3</i> Related to neurological disorders, epilepsy ³⁷
LQSLT, QGAEK	<i>Solute carrier family 12 member 6</i> Sensorimotor neuropathy, mental retardation ³⁸
<u>SSGGGG</u>	<i>Solute carrier family 25 member 46</i> Peripheral sensorimotor neuropathy ³⁹
KMVAK	<i>Thioredoxin, mitochondrial</i> Severe cerebellar atrophy, epilepsy, dystonia, optic atrophy ⁴⁰
LAAQG	<i>Thymidine phosphorylase</i> Leukoencephalopathy, cachexia, neuropathy, myopathy ⁴¹
DIGAV	<i>Trifunctional enzyme subunit alpha, mitochondrial</i> Hypoglycemia, cardiomyopathy, axonopathy, weakness, hepatic dysfunction, respiratory failure ⁴²
<u>LAAKQG</u>	<i>Wolframin</i> Diabetes, sensorineural deafness, dementia ⁴³
<u>SSGGGG</u>	<i>Zinc finger SWIM domain-containing protein 6</i> Abnormal gait, autistic features ⁴⁴
SSGGG	<i>Beta-1,4 N-acetylgalactosaminyltransferase 1</i> Axonal degeneration ⁴⁵

Abbreviation: fHbp, factor H-binding protein.

^aHexapeptides formed by overlapping pentapeptides have been underlined.

^bHuman protein names are given in italic.

^cFurther disease details are available in OMIM, PubMed, and UniProt databases.

how only vaccinal protocols based on peptide sequences uniquely present in the pathogenic antigens can provide therapeutic vaccines free of adverse events.

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None.

Conflict of Interest

None declared.

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