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

Darja Kanduc[1]

[1] Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, Bari, Italy

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Address for correspondence Darja Kanduc, PhD, Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, 70126 Bari, Italy (e-mail: dkanduc@gmail.com).

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

Table 1 (*Continued*)

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

Abbreviation: fHbp, factor H-binding protein.
[a]Hexapeptides formed by overlapping pentapeptides have been underlined.
[b]Human protein names are given in italic.
[c]Further 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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Conflict of Interest
None declared.

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