Strong protein sequence alignment between vaccine antigens and adiponectin: an autoantigen involved in atherosclerosis-related coronary artery disease, cerebral infarction, diabetes mellitus and obesity

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Background

Autoantibodies against adiponectin have been associated with atherosclerosis-related coronary artery disease, cerebral infarction, diabetes mellitus and obesity [1]. The origin of these autoantibodies is unknown. We know from Pandemrix vaccine induced narcolepsy,[2] that vaccine antigens can induce autoimmunity due to molecular mimicry. Protein sequence alignment between adiponectin and vaccine antigens or contaminants was examined to check if the autoantibodies could have been induced by vaccines. Balaji et al.[3] report long term persistence of inflammation and decreased serum adiponectin levels in children vaccinated with Salmonella typhi conjugate vaccine. Potentially, another case of autoantibodies induced against adiponectin and autoimmune disease related inflammation.

Method

Protein sequence for adiponectin was obtained from Uniprot.[4]

BLASTP methodology was used for protein sequence alignment.

As shown before[5], a BLASTP sequence alignment score of 19.3 was obtained comparing human hypocretin receptor and H1N1 nucleoprotein contained in the Pandemrix vaccine. This level of sequence alignment was sufficient to cause autoimmunity that resulted in hypocretin dysregulation and narcolepsy.[2] Therefore any score equal to or higher than 19.3 suggests high probability of autoimmunity.

While vaccines target one or a few particular viral, bacterial proteins, most vaccines are contaminated with all proteins from that virus or bacteria. Example: the Pandemrix vaccine contained both H1N1 hemagglutinin (target) and H1N1 nucleoproteins (contaminant). The exceptions are recombinant vaccines. In recombinant vaccines, the vaccine contains only the target protein from the target organism. The target protein is produced usually by genetically modifying yeast (Saccharomyces cerevisiae). Hepatitis B[6,7] and HPV vaccines[8] are produced using this technique. Such vaccines are however, contaminated with all Saccharomyces cerevisiae proteins.

Results

The table below shows sequence alignment scores between adiponectin and vaccine antigens. A score equal to or greater than 19.3 indicates high probability of inducing cross-reacting autoantibodies following vaccination.

Autoantigen	Adiponectin
Vaccine Antigen	
Saccharomyces cerevisiae	30.3
Streptococcus pneumoniae	47.3
Corynebacterium diphtheriae	41.4
Bordetella pertussis	32.5
Neisseria meningitidis	50.3
Haemophilus influenzae	35.4
Salmonella typhi	27.8

Discussion

The results above show strong sequence alignment between adiponectin and vaccine antigens. Therefore there is a high probability that these autoantibodies were induced as a result of vaccination.

Most vaccines involve injecting viral or bacterial proteins as an intramuscular injection. The route of exposure during natural infection by these viruses and bacteria is usually through the eyes, nose or mouth and not intramuscular injection. We have evolved immune mechanisms specific to routes of exposure and specific to pathogens. Examples include skin-homing versus gut-homing immune cells produced by different lymph nodes.[9] Pathogen Associated Molecular Patterns (PAMP) or Danger Associated Molecular Patterns (DAMP) recognized by pattern recognition receptors (PRR) expressed on dendritic cells (DC). Aluminum adjuvanted vaccines artificially boost and induce immune responses to viral, bacterial antigens introduced through an artificial route of exposure. This completely disrupts the natural immune response to the vaccine antigens by activating immune pathways quite different from the pathways involved during natural infection. Therefore, protections against autoimmunity during natural infection which have evolved over millions of years, are bypassed in the case of vaccine induced immune responses.

One can therefore logically expect a skewed immune response which could include autoimmunity as was demonstrated in the case of Pandemrix vaccine induced narcolepsy. Pandemrix vaccine contained H1N1 viral proteins along with squalene as an adjuvant.

Similarly, with aluminum adjuvanted vaccines that artificially boost immune response to weakly immunogenic vaccine antigens, the natural protection against autoimmunity can be disrupted.[10]

Dr. François Verdier, an immunotoxicology expert with vaccine maker Aventis Pasteur (now Sanofi Pasteur) wrote in Biotechnology and Safety Assessment (2003)[11]:

“Advances in computer software such as LifeSeq from Incyte and the availability of the human genome sequence allow rapid comparison between the protein sequence alignment of a vaccine antigen and a host protein.”

He also explains that this can catch primary structure mimicry but may miss conformational mimicry. He recommends, “From these hypothesises (sic), a recommended strategy would be to avoid any vaccine antigen presenting a mimicry with a host antigen involved in an autoimmune disease.”

A recommendation the vaccine industry has mostly ignored, resulting in devastating consequences.

Genetic susceptibility

The efficiency of producing autoimmunity in the presence of molecular mimicry could of course be influenced by genetic variations. So it may be possible to identify genetic markers for such susceptibility. While such identification would be interesting, the root cause, vaccines, need to be fixed.

Action

All vaccine design aspects including removal of contaminating proteins[12], handling molecular mimicry and route of administration need to be revisited to avoid such off-target immune responses.

Detailed Results

hypothetical protein [Neisseria meningitidis]
WP_079453994.1 421 3

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
50.3 bits(111)	7e-05	36/75(48%)	39/75(52%)	14/75(18%)

```
Query  42   GIPGH------PGHNGAPGRDGRDGTPGEKGEKG-DPGLIGPKGDIGETG--VP-GAEGP  91
            GIPG       PG  G  G  G DG PGE GE G D    G KGD G+TG   P G +GP
Sbjct  58   GIPGERGLDGLPGAKGDAGPKGADGLPGERGERGAD----GAKGDKGDTGERGPIGPQGP  113

Query  92   RGFPGIQGRKGEPGE  106
            G  G QG  GE G+
Sbjct  114  QGLTGPQGQRGETGQ  128
```

peptidase [Streptococcus pneumoniae]
WP_050203256.1 2228 21

See 1 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
47.3 bits(104)	6e-04	29/63(46%)	33/63(52%)	15/63(23%)

```
Query  59   DGTPGEKGEKGDPGLIGP------KGDIGE---TGVP------GAEGPRGFPGIQGRKGE  103
            DG  GEKG+ G+ GL G      KGD GE   TG       GA+G RG  G QG KG+
Sbjct  590  DGAKGEKGDRGERGLTGAQGAKGEKGDRGERGLTGAQGAKGEKGAQGERGLTGAQGEKGD  649

Query  104  PGE  106
             GE
Sbjct  650  QGE  652
```

hypothetical protein BU167_11350 [Corynebacterium diphtheriae]
OWM52181.1 262 5

See 3 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
41.4 bits(90)	0.032	31/60(52%)	32/60(53%)	6/60(10%)

```
Query  47   PGHNGAPGRDGRDGTPGEKGEKGDPGLIGPKGDIGETGVPGAEGPRGFPGIQGRKGEPGE  106
             PG  G PG  G  G  GE G  G PG  GPKG  GETG P  +GP   PG  G KG  GE
Sbjct  93   PGPQGPPGPAGPKGATGETGPQGPPGPAGPKGATGETG-P--QGP---PGPAGPKGATGE  146
```

Uncharacterised protein [Bordetella pertussis]
CPO53678.1 403 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
32.5 bits(69)	18	15/31(48%)	15/31(48%)	11/31(35%)

```
Query  27   VL----LPLPKGACTGWMAGIPGHPGHNGAP  53
            VL    LPL         AGIP H GH GAP
Sbjct  128  VLRRQGLPL-------RQAGIPAHSGHHGAP  151
```

Eaf1p [Saccharomyces cerevisiae YJM1615]
AJV21135.1 982 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
30.3 bits(64)	81	11/17(65%)	12/17(70%)	1/17(5%)

```
Query  187  DQYQENNVDQASGSVLL  203
            D+Y ENNVD AS  V L
Sbjct  256  DHYNENNVD-ASETVFL  271
```

hypothetical protein [Haemophilus influenzae]
WP_041175161.1 784 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
35.4 bits(76)	2.3	22/47(47%)	25/47(53%)	9/47(19%)

```
Query  63   GEKGEKGDPGLIGPKGDIGETGVPGAEGPRGFPGIQGRKGEPGEGAY  109
            GEKGE G+ GL    G+ GE G  G +G R   G Q   GE G  AY
Sbjct  608  GEKGERGERGL---QGERGERGLQGEQGER---GLQ---GEKGKSAY  645
```

virulence effector SrfC [Salmonella enterica subsp. enterica serovar Typhi]
OKK36092.1 714 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
27.8 bits(58)	494	9/14(64%)	10/14(71%)	1/14(7%)

```
Query  127  NMPIRFTK-IFYNQ  139
            NM IRFT  IF N+
Sbjct  104  NMAIRFTRDIFSNE  117
```

No matches for measles, mumps, rubella, human polio, human papilloma, hepatitis A, hepatitis B, human influenza A viruses or *C. tetani*, in the first 10000 results.

References

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