Protein sequence identity between human thyroperoxidase region recognized by human autoantibodies and multiple vaccine antigens

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Background

Autoantibodies against human thyroperoxidase are associated with thyroid autoimmune disorders. Bresson et al.[1] determined the protein sequence recognized by human autoantibodies, to be KFPED.

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 KFPED and vaccine antigens or contaminants was examined to check if the autoantibodies could have been induced by vaccines.

Method

BLASTP methodology was used for protein sequence alignment.

As shown before[3], 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[4,5] and HPV vaccines[6] are produced using this technique. Such vaccines are however, contaminated with all Saccharomyces cerevisiae proteins.

Results

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

Autoantigen	KFPED
Vaccine Antigen	
Saccharomyces cerevisiae	20.2
Streptococcus pneumoniae	20.2
Corynebacterium diphtheriae	17.2
Bordetella pertussis	17.2
Neisseria meningitidis	17.2
Haemophilus influenzae	17.6
Salmonella typhi	20.2
Hepatitis B	~~16.8~~*
Clostridium tetani	17.6
Human Influenza A	17.6

*Hepatitis core protein match. Applicable to Hepatitis B infection, but not recombinant vaccines, as they do not contain core proteins.

Discussion

The results above show significant sequence alignment between the KFPED sequence and multiple vaccine antigens. The detailed results below, show 100% match in many cases. 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.[7] 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.[8]

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.[9]

Dr. François Verdier, an immunotoxicology expert with vaccine maker Aventis Pasteur (now Sanofi Pasteur) wrote in Biotechnology and Safety Assessment (2003)[10]:

“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[11], handling molecular mimicry and route of administration need to be revisited to avoid such off-target immune responses.

Detailed Results

Cft2p [Saccharomyces cerevisiae YJM1447]
AJV65893.1 859 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
20.2 bits(40)	199	5/5(100%)	5/5(100%)	0/5(0%)

```
Query  1    KFPED  5
           KFPED
Sbjct  393  KFPED  397
```

type I restriction-modification system endonuclease [Salmonella enterica subsp. enterica serovar Typhi]
OKK37939.1 1169 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
20.2 bits(40)	198	5/5(100%)	5/5(100%)	0/5(0%)

```
Query  1    KFPED  5
           KFPED
Sbjct  535  KFPED  539
```

ribonuclease J [Streptococcus pneumoniae]
WP_010976393.1 610 1

See 3 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
20.2 bits(40)	199	5/5(100%)	5/5(100%)	0/5(0%)

```
Query  1   KFPED  5
           KFPED
Sbjct  93  KFPED  97
```

core protein, partial [Hepatitis B virus]
AAM70066.1 130 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
16.8 bits(32)	3327	4/4(100%)	4/4(100%)	0/4(0%)

```
Query  1   KFPE  4
           KFPE
Sbjct  26  KFPE  29
```

trigger factor [Clostridium tetani E88]
AAO36849.1 438 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.6 bits(34)	1624	4/5(80%)	5/5(100%)	0/5(0%)

```
Query  1    KFPED  5
            KFPE+
Sbjct  226  KFPEE  230
```

excinuclease ABC subunit B [Corynebacterium diphtheriae bv. gravis]
OWN56144.1 698 1

See 3 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.2 bits(33)	2298	4/4(100%)	4/4(100%)	0/4(0%)

```
Query  2    FPED  5
            FPED
Sbjct  351  FPED  354
```

aminopeptidase N [Bordetella pertussis]
CFL96862.1 906 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.2 bits(33)	2296	4/4(100%)	4/4(100%)	0/4(0%)

```
Query  2    FPED  5
            FPED
Sbjct  368  FPED  371
```

DNA gyrase subunit A [Neisseria meningitidis]
WP_049343581.1 923 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.2 bits(33)	2295	4/4(100%)	4/4(100%)	0/4(0%)

```
Query  2    FPED  5
            FPED
Sbjct  651  FPED  654
```

hemagglutinin, partial [Influenza A virus (A/Texas/AF1703/2008(H3N2))]
ACD87457.1 347 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.6 bits(34)	1628	4/5(80%)	5/5(100%)	0/5(0%)

```
Query  1  KFPED  5
          KFPE+
Sbjct  2  KFPEN  6
```

30S ribosomal protein S17 [Haemophilus influenzae PittGG]
ABR00346.1 261 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
17.6 bits(34)	1634	4/5(80%)	5/5(100%)	0/5(0%)

```
Query  1   KFPED  5
           KFPE+
Sbjct  25  KFPEE  29
```

No matches to measles, mumps, rubella, polio, hepatitis A or human papilloma viruses, in the first 10000 results.

References

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