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Bioinformatics and epidemiological evidence link yeast protein containing HPV and Hepatitis B vaccines to numerous autoimmune disorders such as vitiligo, narcolepsy, hypothyroidism, systemic lupus erythematosus and rheumatoid arthritis

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Abstract

The human papillomavirus (HPV) vaccine and Hepatitis B vaccine (HBV) are recombinant vaccines produced by genetically modifying yeast (*Saccharomyces cerevisiae*). The vaccines therefore contain yeast proteins ranging from 7 mcg up to 5% of total protein content. The target proteins are weakly immunogenic. The human immune system has evolved sophisticated checks and balances to selectively attack danger associated proteins and pathogen associated proteins while tolerating self and harmless proteins. This mechanism is the reason why harmless target proteins in vaccines are weakly immunogenic. Vaccinologists defeat the immune system's checks and balances and force an immune response directed against these weakly immunogenic target proteins, by using immunological adjuvants. The result is a robust immune response directed against target proteins which makes the vaccines effective. However, this boosted immune response is not limited to the target proteins alone. The robust immune response is also directed at non-target proteins (yeast proteins in this case) thus resulting in numerous off-target immune responses. Numerous epidemiological studies and a meta analysis have linked yeast containing vaccines to autoimmune disorders. Here, bioinformatics analysis adds mechanistic evidence demonstrating that these vaccines can produce numerous autoimmune disorders due to molecular mimicry between yeast proteins and human self proteins. Pandemrix vaccine induced narcolepsy, an autoimmune disorder, due to molecular mimicry between H1N1 nucleoproteins in the vaccine and the human hypocretin receptor 2. This failure mechanism can affect all vaccines. The ultimate solution is to remove all non-target proteins from vaccines.

Background

The human papillomavirus (HPV) vaccine and Hepatitis B vaccine (HBV) are recombinant vaccines produced by genetically modifying yeast (*Saccharomyces cerevisiae*). The vaccines therefore contain yeast proteins ranging from 7 mcg (1) up to 5% of total protein content. (2,3) The vaccine target proteins (the HPV L1 protein and the Hepatitis B surface antigen) are weakly immunogenic. The human immune system has evolved sophisticated checks and balances to selectively attack danger associated proteins and pathogen associated proteins while tolerating self and harmless proteins. This mechanism is the reason why harmless target proteins in vaccines are weakly immunogenic. Vaccinologists defeat the immune system's checks and balances and force an immune response directed against these weakly immunogenic target proteins, by using immunological adjuvants. (4) The result is a robust immune response directed against target proteins which makes the vaccines effective. However, this boosted immune response is not limited to the target proteins alone. The robust immune response is also directed at non-target proteins (yeast proteins in this case) thus resulting in numerous off-target immune responses. Pandemrix vaccine induced narcolepsy, an autoimmune disorder, due to molecular mimicry between H1N1 nucleoproteins in the vaccine and the human hypocretin receptor 2. (5) This failure mechanism can affect all vaccines.

Epidemiological evidence

Frisch et al. (6) study shows high rate ratio (RR) for numerous autoimmune disorders following HPV vaccination. The disorders include hypothyroidism RR=1.77 (0.73-4.31) , ankylosing spondylitis RR=2.01 (0.49-8.16), rheumatoid arthritis RR=2.29 (0.73-7.24), vitiligo RR=4.70 (1.13-19.5), narcolepsy RR=3.44 (1.08-11.0), etc.

Szumilas(7) points out that, “In practice, the 95% CI is often used as a proxy for the presence of statistical significance if it does not overlap the null value (e.g. OR=1). Nevertheless, it would be inappropriate to interpret an OR with 95% CI that spans the null value as indicating evidence for lack of association between the exposure and outcome.”

Significance testing is often used to inappropriately dismiss many of these results as the 95% CI spans the null value, as Szumilas points out above. Thus introducing type 2 errors.

Wang et al.(8) also performed a meta analysis and concluded that HPV/HBV vaccines are associated with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Mechanistic evidence

As previously described, yeast proteins have strong protein sequence alignment to SLE related autoantigens (9)and to human thyroperoxidase (10), an autoantigen involved in hypothyroidism.

Cytotoxic T cells in vitiligo express the CCR4 skin-homing marker.(11) CD4+ T cells in SLE, RA and ankylosing spondylitis (AS) also express the CCR4 skin homing marker. As described before, this is evidence that the site of priming for these T cells were skin draining lymph nodes. This is consistent with subcutaneous (SC) or intramuscular (IM) administered antigens from vaccines.(12)

Here we add mechanistic evidence for vitiligo and narcolepsy as well.

Methods

BLASTP methodology was used for protein sequence alignment. As shown before (13), a BLASTP sequence alignment score of 19.3 was obtained comparing human hypocretin receptor 2 and H1N1 nucleoprotein contained in the Pandemrix vaccine. This level of sequence alignment was sufficient to cause a cross-reaction, thus autoimmunity that resulted in hypocretin dysregulation and narcolepsy. (5) Therefore any score equal to or higher than 19.3 suggests high probability of autoimmunity.

Results

H1N1 nucleoprotein vs. human hypocretin receptor 2, used as baseline.
For Pandemrix vaccine induced narcolepsy.

HCRT2 vs. X-179a

Score	Expect	Method	Identities	Positives	Gaps
19.6 bits(39)	0.018	Composition-based stats.	7/13(54%)	10/13(76%)	1/13(7%)

```
Query  34   YDDEEFLRYLWRE  46
            YD EE +R +WR+
Sbjct  111  YDKEE-MRRIWRQ  122
```

Human hypocretin receptor 2 vs. *S. cerevisiae*
For HPV/HBV induced narcolepsy.

Score	Expect	Method	Identities	Positives	Gaps
22.3 bits(46)	264	Composition-based stats.	11/23(48%)	12/23(52%)	0/23(0%)

```
Query  23   ETQEPFLNPTDYDDEEFLRYLWR  45
            ET   FLNP+    E   RY WR
Sbjct  116  ETNILFLNPSLNLLEHLHRYRWR  138
```

Human tyrosinase vs. *S.cerevisiae* (Tyrosinase is an autoantigen in vitiligo. (14))
For HPV/HBV induced vitiligo.

Score	Expect	Method	Identities	Positives	Gaps
27.7 bits(60)	123	Compositional matrix adjust.	16/70(23%)	30/70(42%)	2/70(2%)

```
Query  183  VSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIPYWDWRDAE  242
            V +  ++ G+ IWR     H      PW+R  LL        LT ++  ++   DW ++
Sbjct  93   VLLTQVVAGARIWRFPGKGHRKMN--PWYRRILLASLAIFSLLTVQFMYSNYWYDWHNSR  150

Query  243  KCDICTDEYM  252
                C + ++
Sbjct  151  TLAYCNNLFL  160
```

Score	Expect	Method	Identities	Positives	Gaps
26.6 bits(57)	390	Compositional matrix adjust.	12/22(55%)	14/22(63%)	4/22(18%)

```
Query  66    GPQFPFTGVDDRESWPSVFYNR  87
             GP+    G DD  SWPS+F NR
Sbjct  1026  GPE----GQDDDPSWPSIFENR  1043
```

GP100 vs. S.*cerevisiae* (GP100 is an autoantigen in vitiligo. (15))
For HPV/HBV induced vitiligo.

Score	Expect	Method	Identities	Positives	Gaps
21.9 bits(45)	9708	Compositional matrix adjust.	7/12(58%)	10/12(83%)	0/12(0%)

```
Query  627  VPQLPHSSSHWL  638
            VP+LP  ++HWL
Sbjct  128  VPRLPTFTTHWL  139
```

Score	Expect	Method	Identities	Positives	Gaps
29.3 bits(64)	63	Compositional matrix adjust.	19/71(27%)	31/71(43%)	1/71(1%)

```
Query  341  PTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLAEMSTPEATGM  400
            PT +PS    +  PTTEV+      +  A     T EKV + +V+     +    E   M
Sbjct  27   PTIDPSDPVQISFPTTEVVGHGSFGVVFATVIQETNEKVAIKKVLQDKRFKNRELEIMKM  86

Query  401  TPAEVSIVVLS  411
               + ++I+ L
Sbjct  87   L-SHINIIDLK  96
```

Discussion

Since all match scores are above the baseline value, there is high probability that yeast proteins in the HPV/HBV vaccine can induce vitiligo and narcolepsy. And these results are just a sample. There are numerous matches that exceed the baseline value.

Autoimmunity can result due to molecular mimicry between self proteins and any protein in the vaccine. Vaccines contain food proteins, animal proteins, viral, bacterial, fungal proteins used as growth media or excipients. Therefore any vaccine can cause autoimmune disorders. For this reason, the practice of using active comparators (that is other vaccines used as “placebo”) in control groups of clinical trials is dangerous as it underestimates risk of vaccine adverse events.(16)

Conclusion

Epidemiological and mechanistic evidence makes it clear that yeast proteins in HPV/HBV vaccines can cause numerous autoimmune disorders, including SLE, RA, AS, hypothyroidism, vitiligo and narcolepsy. Wraith et al.(17) have suggested bioinformatics analysis and autoimmune serology to check for autoimmunity during vaccine development. Vaccine makers have refused to perform such checks, resulting in devastating consequences. The ultimate solution is to remove all non-target proteins from all vaccines immediately.

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