Cancer immunology, bioinformatics and chemokine evidence link vaccines contaminated with animal proteins to autoimmune disease: a detailed look at Crohn's disease and Vitiligo

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Background

Catalase is an autoantigen in Crohn's disease (CD) and other inflammatory bowel diseases (IBD). Vaccines are contaminated with catalase and can be a cause of CD as previously described.[1]

Glycoprotein 2 (GP2) is another autoantigen linked to CD.[2,3]

Tyrosinase and GP100 are autoantigens linked to vitiligo.[4,5]

Vaccines are contaminated with numerous animal proteins.[6] The role of animal protein contaminated vaccines in the etiology of type 1 diabetes (T1D) and neuromyelitis optica spectrum disorders (NMOSD), were previously described.[7–9]

Methods

Uniprot[10] and BLASTP[11] are used to determine homology between human proteins and animal proteins that contaminate vaccines.

Results

Homology to human GP2
Bos taurus 77%
Sus scrofa 76%
Cavia porcellus 72%
Gallus gallus 43%

Homology to human tyrosinase
Bos taurus 87%
Sus scrofa 90%
Cavia porcellus 85%
Gallus gallus 73%

Homology to human GP100
Bos taurus 77%
Sus scrofa 81%
Cavia porcellus 77%
Gallus gallus 42%

Discussion

LASR T cells

As previously described for T1D, low affinity self reactive (LASR) T cells that barely qualify to be positively selected in the thymus, can have high enough affinity to self peptides to be functional and cause autoimmune disease upon activation.[7] T cells with T cell receptors (TCR) that recognize peptides that differ by as little as one amino acid from a self peptide, can be positively selected and migrate to the periphery.[12]
If homology is 100%, animal derived peptides being identical to self peptides, have a low probability of causing autoimmune disease. This is because T cells that bind self peptides with high affinity would be negatively selected in the thymus. With 42%-90% homology between human and animal proteins shown above, there are many regions where protein sequence is identical except for one to two amino acid difference. Sample sequence results are shown below highlighting autoepitopes aligning to near-identical regions. These peptides from near-identical regions can be expected to activate LASR T cells, resulting in autoimmune disease. Live viruses or aluminum adjuvants in subunit vaccines provide the necessary innate immune system derived costimulation[13] required for LASR T cell activation.[14] It was previously shown in the case of T1D, that autoepitopes are indeed located at near-identical regions of the proteins.[7]

Therefore, as in T1D, these animal proteins can be expected to cause the development of autoimmune diseases such as Crohn's and vitiligo.

Evidence from cancer research on LASR T cell mediated autoimmunity

Cancer research has demonstrated that immunization with homologous xenogeneic proteins (such as vaccines contaminated with animal proteins that resemble human proteins) results in autoimmunity.[15]
As Naftzger et al.[15] describe, tolerance can be broken by introducing altered antigens. Animal proteins are an ideal source of altered antigens. As shown before[7] and in sections below, animal proteins contain numerous regions that are altered compared to human proteins. Yu et al.[16] describe another mechanism of altered antigens breaking self-tolerance, that involves MHC binding stability. Exposure to peptide sequence IMDQVPFSV caused autoimmunity to ITDQVPFSV.
Engelhorn et al.[17] describe generation of immune responses to self as a result of presenting numerous antigen variants. This is exactly the case with vaccines contaminated with animal cell cultures containing thousands of animal proteins that are variants of human proteins.
Skipper et al.[18] describe a strong T cell response to YMDGTMSQV on melanoma cells which is a single amino acid change from the normal tyrosinase sequence YMNGTMSQV.

The natural purpose of LASR T cells is likely to be cancer defense. With animal protein contaminated vaccines, we trigger the cancer response. A cancer related mutation can cause a single amino acid alteration in a self peptide. Numerous animal peptides naturally have single amino acid alterations compared to human peptides. With thousands of animal proteins contaminating vaccines, a widespread cancer response results following vaccination. Thus increasing the probability of autoimmunity as described by Engelhorn et al.[17]

Skin homing receptors - the smoking gun

As described in the case of T1D[7], autoreactive CD8+ T cells in vitiligo, also express CCR4 skin homing chemokine receptors.[19] CD4+ T cells in Crohn's disease also express CCR4 skin homing receptors.[20]

The role of yeast (*Saccharomyces cerevisiae*) contaminated vaccines in the etiology of Systemic Lupus Erythematosus (SLE) was previously described.[21] Wang et al.[22] provide epidemiological evidence of vaccines causing SLE and rheumatoid arthritis. Yang et al.[23] describe increased expression of CCR4 skin homing receptors on CD4+ T cells in ankylosing spondylitis, rheumatoid arthritis and SLE as well.

Dendritic cells that capture antigens, imprint T cells with homing receptors corresponding to the location where the antigens were captured.[24,25] This is evidence that the antigens involved in the above diseases were all captured in skin tissue, as would be expected with intramuscular or subcutaneous administration of animal protein contaminated vaccines.

Animals don't like our proteins being injected into them either …

Immunizing mice with human proteins caused the development of vitiligo in mice.[15] So, immunizing humans with animal proteins resulting in vitiligo (or any number of other autoimmune diseases) comes as no surprise at all.

Conclusion

The above findings add to the growing evidence of vaccines inducing autoimmune diseases.[22,26–29] Autoantibody and autoreactive T cell levels can vary from person to person. Not everyone will develop overt disease. For every case of diagnosed autoimmune disease, there are numerous subclinical cases. Balaji et al.[30] describe long term persistent inflammation following typhoid vaccine and decreased adiponectin levels in asymptomatic children. A likely case of autoimmunity against adiponectin as previously described.[31] These subclinical diseases could shave decades off your life. So "rare" diagnosed vaccine adverse events are the tip of the iceberg.

It is quite obvious that there are fundamental problems with vaccine design and safety. Vaccine designers need to go back to the drawing board. We need vaccines that are safe by design.[29,32]

Detailed sample BLASTP results

Human GP2 vs. bovine GP2

pancreatic secretory granule membrane major glycoprotein GP2 precursor [Bos taurus]
NP_001069418.2 534 1

See 1 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
1214 bits(2856)	0.0	415/540(77%)	431/540(79%)	9/540(1%)

```
Query  1    MPHLMERMVGSGLLWLALVSCILTQASAVQRGYGNPIEASSYGLDLDCGAPGTPEAHVCF  60
            M +L+ERM     LWLAL S ILT  S  Q GY N     SY  DLDCGAPGTPEA+ CF
Sbjct  1    MSQLLERM--TSVLWLALASYILTLSSTEQQGYRNSTNTGSYEKDLDCGAPGTPEAQLCF  58

Query  61   DPCQNYTLLDEPFRSTENSAGSQGCDKNMSGWYRFVGEGGVRMSETCVQVHRCQTDAPMW  120
            DPCQNYTLL+EPFRSTEN    QGCD +  GWYRFVG+GGVRM E CV   RCQT AP+W
Sbjct  59   DPCQNYTLLNEPFRSTENTEDIQGCDSDKHGWYRFVGDGGVRMPEDCVPTFRCQTSAPLW  118

Query  121  LNGTHPALGDGITNHTACAHWSGNCCFWKTEVLVKACPGGYHVYRLEGTPWCNLRYCTVP  180
            LNGTHP LG+GI N TACAHWSGNCC WKTEVLVKACPG Y VYRLEGTP C LRYCT
Sbjct  119  LNGTHPGLGEGIVNRTACAHWSGNCCLWKTEVLVKACPGPYYVYRLEGTPQCSLRYCT--  176

Query  181  RDPSTVEDKCEKACRPEEEC-LALNSTWGCFCRQDLNSSDVHSLQPQLDCGPREIKVKVD  239
             DP T EDKC+  CRPEEEC L    TWGCFCRQDLN SDVHSLQPQLDCG  EIKV  D
Sbjct  177  -DPATAEDKCDRTCRPEEECRLV-SGTWGCFCRQDLNVSDVHSLQPQLDCGDTEIKVSLD  234

Query  240  KCLLGGLGLGEEVIAYLRDPN--CSSILQTEERNWVSVTSPVQASACRNILERNQTHAIY  297
            KCLLG LG G+EV AYLRD N  CSS  Q EE NW+SVT P QA AC NILERNQTHAIY
Sbjct  235  KCLLGSLGFGDEVHAYLRDGNWNCSSLRQSEEENWISVTNPTQAGACGNILERNQTHAIY  294

Query  298  KNTLSLVNDFIIRDTILNINFQCAYPLDMKVSLQAALQPIVSSLNVSVDGNGEFIVRMAL  357
             NTLSLVNDFIIRDTIL INFQCAYPLDMKVSLQ ALQPIVSSLN+ VDG GEF VRMAL
Sbjct  295  INTLSLVNDFIIRDTILSINFQCAYPLDMKVSLQMALQPIVSSLNITVDGEGEFTVRMAL  354

Query  358  FQDQNYTNPYEGDAVELSVESVLYVGAILEQGDTSRFNLVLRNCYATPTEDKADLVKYFI  417
            FQDQ+YT PYEG AV LSVES LYVG ILE GDTSRFNLVL NCYATPTEDK D VKYFI
Sbjct  355  FQDQDYTSPYEGTAVMLSVESMLYVGTILERGDTSRFNLVLKNCYATPTEDKTDPVKYFI  414

Query  418  IRNSCSNQRDSTIHVEENGQSSESRFSVQMFMFAGHYDLVFLHCEIHLCDSLNEQCQPSC  477
             IRNSC NQRDSTI VEENG S ESRFSVQMF FAG YDLVFLHCE+ LCD   E+CQPSC
Sbjct  415  IRNSCPNQRDSTISVEENGVSAESRFSVQMFKFAGNYDLVFLHCEVSLCDFIKEECQPSC  474

Query  478  SRSQVRSEVPAIDLARVLDLGPITRRGAQSPGVMNGTPSTAGFLVAWPMVLLTVLLAWLF  537
            SRSQ RSE  AID ARVLDLGPITR GAQS GVM GTP TAGFLVAWP+VLL VLLA LF
Sbjct  475  SRSQLRSEGVAIDPARVLDLGPITRKGAQSLGVMSGTPNTAGFLVAWPLVLLPVLLAGLF  534
```

Human tyrosinase vs. bovine tyrosinase

Autoepitopes identified by Kemp et al.[4] are highlighted below showing that 3 out of 4 epitopes align to near-identical regions, exactly as would be expected for LASR T cell mediated autoimmunity.

TPA: tyrosinase precursor [Bos taurus]
DAA14054.1 530 1

See 2 more title(s)

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Method	Identities	Positives	Gaps
983 bits(2541)	0.0	Compositional matrix adjust.	461/530(87%)	493/530(93%)	1/530(0%)

```
Query  1    MLLAVLYCLLWSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILL  60
            MLLA LYCLLWSF+TSAGHFPRAC SSK+L EKECCPPW+GD SPCG+LSGRGSCQ+++L
Sbjct  1    MLLAALYCLLWSFRTSAGHFPRACASSKSLTEKECCPPWAGDGSPCGRLSGRGSCQDVIL  60

Query  61   SNAPLGPQFPFTGVDDRESWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERRLLVR  120
            S APLGPQFPFTGVDDRESWPS+FYNRTCQC  NFMGFNCG+CKFGF GP CTERRLLVR
Sbjct  61   STAPLGPQFPFTGVDDRESWPSIFYNRTCQCFSNFMGFNCGSCKFGFRGPRCTERRLLVR  120

Query  121  RNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTYGQMKNGSTPMFNDINIYDLFVWMH  180
            RNIFDLS PEK+KF AYLTLAKHT S DYVIP GTYGQM +G+TP+FND+++YDLFVWMH
Sbjct  121  RNIFDLSVPEKNKFLAYLTLAKHTTSPDYVIPTGTYGQMNHGTTPLFNDVSVYDLFVWMH  180

Query  181  YYVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIPYWDWRD  240
             YYVS D LLG   SE+WRDIDFAHEAP  FLPWHRLFLL WEQEIQKLTGDENFTIPYWDWRD
Sbjct  181  YYVSRDTLLGDSEVWRDIDFAHEAPGFLPWHRLFLLLWEQEIQKLTGDENFTIPYWDWRD  240

Query  241  AEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRN  300
            AE CD+CTDEYMGG++P   NPNLLSPASFFSSWQIVCSRLEEYNS  Q+LCNGT EGPL  RN
Sbjct  241  AENCDVCTDEYMGGRNPANPNLLSPASFFSSWQIVCSRLEEYNSRQALCNGTSEGPLLRN  300

Query  301  PGNHDKSRTPRLPSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFASPLTGIADASQS  360
            PGNHDK+RTPRLPSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFA P+TGIADASQS
Sbjct  301  PGNHDKARTPRLPSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFADPVTGIADASQS  360

Query  361  SMHNALHIYMNGTMSQVQGSANDPIFLLHHAFVDSIFEQWLRRHRPLQEVYPEANAPIGH  420
            SMHNALHIYMNGTMSQV GSANDPIFLLHHAFVDSIFEQWLR++ PLQ+VYPEANAPIGH
Sbjct  361  SMHNALHIYMNGTMSQVPGSANDPIFLLHHAFVDSIFEQWLRKYHPLQDVYPEANAPIGH  420

Query  421  NRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYLEQASRIWSWLLG  480
             NRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDS+PD  FQDYIK YLEQA RIW  WL+G
Sbjct  421  NRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSEPDI FQDYIKPYLEQAQRIWPWLIG  480

Query  481  AAMVGAVLTALLAGLVSLLCRHKRKQLPEEKQPLLMEKEDYHSL-YQSHL  529
            AA+VG+VLTA+L GL SLLCR KR QLPEEKQPLLMEKEDYH+L YQSHL
Sbjct  481  AAVVGSVLTAVLGGLTSLLCRRKRNQLPEEKQPLLMEKEDYHNLMYQSHL  530
```

Human gp100 vs. pig gp100

melanocyte protein PMEL [Sus scrofa]
XP_020947439.1 663 1

GenPeptGraphics Next Match Previous Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
1561 bits(3673)	0.0	537/667(81%)	544/667(81%)	36/667(5%)

```
Query  1    MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTE--AQRL  58
            MDLVL  CLLH AV GA LAVGAT  PR  DWLGVSRQLRTKAWN QLYPEWTE  A
Sbjct  27   MDLVLRKCLLHVAVMGAFLAVGATEGPRGRDWLGVSRQLRTKAWNSQLYPEWTEIRAP--  84

Query  59   DCWRGGQVSLKVSNDGPTLIGANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGG  118
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            DCWRGG VSLKVSNDGPTLIGANASFSIAL FP SQKVLPDGQVIW NNTIINGSQVWGG
Sbjct  85   DCWRGGRVSLKVSNDGPTLIGANASFSIALHFPKSQKVLPDGQVIWANNTIINGSQVWGG  144

Query  119  QPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTWGQYWQVLGGPVSGLSIGTGRAM  178
             QPVYPQE +  CIFPDG  CP G  SQ RSFVYVWK WGQYWQVLGGPVSGLSIGTG A
Sbjct  145  QPVYPQEPNATCIFPDGAACPPGPSSQRRSFVYVWKAWGQYWQVLGGPVSGLSIGTGKAV  204

Query  179  LGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLRNQPL  238
             LGTHTMEVTVYHRRGS SYVPLAHS SAFT+TDQVPFSVSVSQL ALD GNK FLR QPL
Sbjct  205  LGTHTMEVTVYHRRGSQSYVPLAHSRSAFTVTDQVPFSVSVSQLQALDRGNKRFLRKQPL  264

Query  239  TFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPL  298
             TFALQLHDPSGYLA ADLSYTWDFGD  GTLISRALVVTHTYLE GPVTAQVVLQAAIPL
Sbjct  265  TFALQLHDPSGYLAGADLSYTWDFGDNTGTLISRALVVTHTYLESGPVTAQVVLQAAIPL  324

Query  299  TSCGSSPVPGTTDGHRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEV  358
             TSCGSSPVPGTTDG  PTAE P TTA QVPTTEVVGTTPGQ PTAEPSGTT VQVPT E
Sbjct  325  TSCGSSPVPGTTDGPVPTAETPGTTAKQVPTTEVVGTTPGQMPTAEPSGTTAVQVPTAE-  383

Query  359  ISTAPVQMPTAESTGM--TPEKVPVSEVMGTTLAEMSTPEATGMTPAEVSIVVLSGTTAA  416
                          GM  TP+  P SEV GTT A M T E     P        SGTT A
Sbjct  384  --------------GMGTTPDQAPTSEVRGTTPAVMPTVE-----P--------SGTTVA  416

Query  417  QVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVKRQVPLDCV  476
             QVTTTE VETTA E P PEPE PD S  M TE  TGS  PLLDGTATL LVKRQVPLDCV
Sbjct  417  QVTTTELVETTAGEVPTPEPESPDVSPFMPTEGLTGSQSPLLDGTATLILVKRQVPLDCV  476

Query  477  LYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPP  536
             LYRYGSFS TLDIVQGIESAEILQAVPS EGDAFELTVSCQGGLPKEACM+ISSPGCQPP
Sbjct  477  LYRYGSFSLTLDIVQGIESAEILQAVPSSEGDAFELTVSCQGGLPKEACMDISSPGCQPP  536

Query  537  AQRLCQPVLPSPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQV  596
              AQRLCQPV PSPACQLVLHQ+LKGGSGTYCLNVSLADTNSLA VSTQL+MPGQE GLGQ
Sbjct  537  AQRLCQPVSPSPACQLVLHQVLKGGSGTYCLNVSLADTNSLAMVSTQLVMPGQESGLGQA  596

Query  597  PLIVGILLVLMAVVLASLIYRRRLMKQD--FSVPQLPHSSSHWLRLPRIFCSCPIGENSP  654
             PL VGILLVL A  LASLIYRRRLMKQD     PQLPH  S WLRLP  F SCP+GENSP
Sbjct  597  PLFVGILLVLIALLLASLIYRRRLMKQDSALPLPQLPHGRSPWLRLPWGFRSCPVGENSP  656

Query  655  LLSGQQV  661
             LLSGQQV
Sbjct  657  LLSGQQV  663
```

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