Plant proteins that contaminate SARS-CoV-2 vaccines, excipients have high protein sequence homology to IEDB listed thrombocytopenia related platelet factor 4 epitopes thus explaining induction of autoimmune bleeding disorders

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Abstract

SARS-CoV-2 mRNA vaccines and a viral vector based vaccine have been authorized for use in the US. AstraZeneca's viral vector based vaccines have been authorized for use in many European countries.

Numerous cases of bleeding disorders have been reported following SARS-CoV-2 vaccine administration. Vaccine Adverse Event Reporting System (VAERS) in the US shows 200 cases of platelet disorders following the vaccines. Such cases have also been investigated in Europe following AstraZeneca vaccine administration. Prof. Pål Andre Holme of the Oslo University Hospital and Prof. Andreas Greinacher at the University of Greifswald have independently found evidence for this being a vaccine induced autoimmune disorder. Greinacher and others identified platelet factor 4 (PF4) as the target of autoantibodies induced by the vaccine. Greinacher's team have named it vaccine-induced prothrombotic immune thrombocytopenia (VIPIT).

Animal/plant/fungal/viral protein contamination of vaccines and the risk of them inducing autoimmune diseases was predicted and world vaccine regulatory bodies were all repeatedly warned of the dangers. Safety engineering processes such as design Failure Modes and Effects Analysis (FMEA) are still being ignored in the vaccine industry ten years after the Pandemrix induced narcolepsy disaster.

We show plant proteins that contaminate the vaccines have high protein sequence homology to epitopes known to be involved in thrombocytopenia, using Immune Epitope Database (IEDB) data and BLASTP bioinformatics analysis. BLASTP match score range is 27.8-19.6. The score for the epitope involved in Pandemrix induced narcolepsy was 19.7, in comparison. The conditions required for inducing autoimmunity are immunization using homologous xeneogeneic antigens that are similar to self antigens (plant proteins in this case) and costimulation of the innate immune system either by the adenovirus, lipid-in-water emulsion or the mRNA in the vaccines acting as adjuvants.

Bleeding disorders are just the latest of numerous vaccine-induced diseases. For every individual diagnosed with VIPIT, thousands will develop subclinical disease. Of course, VIPIT is not the only autoimmune disorder induced by these contaminants.

Introduction

A novel coronavirus, now named SARS-CoV-2 was identified in hospitalized patients in Wuhan, China, in December 2019. The disease caused by the virus, now named COVID-19, can range in severity from asymptomatic to acute respiratory distress syndrome (ARDS) and death. mRNA based SARS-CoV-2 vaccines developed by Pfizer and Moderna have been authorized for use in the US. A viral vector based vaccine from Janssen has also been authorized for use in the US. AstraZeneca's viral vector based vaccine has been authorized for use in many European countries.

Numerous cases of bleeding and clotting disorders have been reported following SARS-CoV-2 vaccine administration, in the US and Europe. Vaccine Adverse Event Reporting System (VAERS) (Centers for Disease Control and Prevention 2021) in the US shows 200 cases of platelet disorders following the vaccines. Numerous cases of bleeding and clotting disorders have also been investigated in Europe following the AstraZeneca vaccine administration. Prof. Pål Andre Holme of the Oslo University Hospital and Prof. Andreas Greinacher at the University of Greifswald have independently found evidence for this being a vaccine induced autoimmune disorder (Beaubien 2021). Greinacher and others identified platelet factor 4 (PF4) as the target of autoantibodies induced by the vaccine (Vogel 2021). Greinacher's team have named it vaccine-induced prothrombotic immune thrombocytopenia (VIPIT).

Animal/plant/fungal/viral protein contamination of vaccines and the risk of them inducing autoimmune diseases was predicted (Arumugham and Trushin 2018; Arumugham 2019a, 2020a; Lyons-Weiler 2020; Arumugham 2020b) and world vaccine regulatory bodies were all repeatedly warned of the dangers.
These include public health authorities in the United States including the Food and Drug Administration (FDA), Centers for Disease Control (CDC), the National Institutes of Health (NIH), the European Medicines Agency (EMA), the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) and Joint Committee on Vaccination and Immunisation (JCVI), the German Robert Koch Institute, the Australian Technical Advisory Group on Immunisation (ATAGI), the World Health Organization (WHO), doctors/researchers at many universities, research centers, medical journals and news organizations. Any safety critical product must be designed for safety which requires a design Failure Modes and Effects Analysis (FMEA) (Arumugham 2019b). An FMEA would have immediately identified these risks during vaccine design. However regulators have learned nothing from the exact same failure mode ten years ago which caused the Pandemrix induced narcolepsy disaster (Ahmed et al. 2015; Arumugham 2018a, b).

Now once more, that prediction has come true. As we will show below, plant proteins that contaminate the vaccines have high protein sequence homology to epitopes known to be involved in thrombocytopenia. The two conditions required for inducing autoimmunity are immunization using homologous xeneogeneic antigens that are similar to self antigens (plant proteins in this case) and the simultaneous stimulation of the innate immune system (Arumugham and Trushin 2018). The chimpanzee adenovirus provides the innate immune system stimulation in the case of the AstraZeneca vaccine. The lipid-in-water emulsion and the mRNA act as adjuvants (Reichmuth et al. 2016) and provide the innate immune system stimulation in the case of lipid encapsulated mRNA vaccines.

Methods

Basic local alignment search tool for proteins (BLASTP) (Altschul et al. 1997), Universal Protein Resource (UniProt) (The UniProt Consortium 2017) and the Immune Epitope Database (IEDB) (Vita et al. 2019) were used for bioinformatics analysis. Specifically, the BLASTP sequence alignment of IEDB thrombocytopenia related epitopes was performed against maize, wheat proteomes and the SARS-CoV-2 spike protein. Vaccines contain residual proteins from these organisms due to media used to grow viruses or as contaminants of excipients. Lipids in the mRNA vaccines are derived from plant or animal sources. AstraZeneca vaccine contains Polysorbate 80 (CHMP 2021) which is derived from wheat and corn/maize (Arumugham and Trushin 2019).

Results summary

IEDB thrombocytopenia related epitopes	Vaccine antigens	BLASTP match score
CLDLQAPLYKKIIKKLLES (PF4)	*Triticum aestivum*	27.8
EAEEDGDLQ (PF4)	*Triticum aestivum*	25.2
KTTSQVRPRHITSLEVIKAG (PF4)	*Zea mays*	26.9
LLPDPSAPT (Thrombopoietin)	Vaccine-induced spike protein	19.6

Table 1

Discussion

Table 1 shows the BLASTP match scores comparing multiple vaccine antigens with IEDB thrombocytopenia related epitopes.

An influenza virus nucleoprotein contaminating the Pandemrix vaccine, induced antibodies that cross-reacted with the human hypocretin receptor to cause narcolepsy. That can be used as a baseline to assess cross-reactivity potential. Nucleocapsid protein [Influenza A virus (A/reassortant/NYMC X-179A(California/07/2009 x NYMC X-157)(H1N1))] ADE29096.1 vs. human hypocretin receptor 2 (HCRTR2) produces a BLASTP score of 19.7. This level of cross reactivity resulted in Pandemrix vaccine-induced narcolepsy (Ahmed et al. 2015). As seen in Table 1, the scores are much higher. And the entries listed are just the top vaccine antigen matches. There are of course numerous matches with a score greater than 19.7.

Autoimmunity induction following vaccine administration can take a couple of weeks. So in the case of VIPIT, symptoms can be expected two weeks after the first dose of the vaccine. Alternately, a person can develop subclinical disease following the first dose. The second dose will result in a recall response which can have an onset interval of just a few days following the vaccine. Greinacher reports 4-16 days as the observed interval between vaccine doses and VIPIT.

Low platelet count has been observed within 48 hours of the vaccine in many cases reported to the VAERS. These can be explained by IgE mediated mechanisms. COVID-19 severity itself in a majority of cases is due to IgE mediated sensitization to antigens with homology to SARS-CoV-2 proteins, which results in "slow rolling anaphylaxis" upon infection as previously described (Arumugham 2020c).
People making IgE that recognize SARS-CoV-2 spike protein due to cross-reaction will suffer "slow rolling anaphylaxis" upon infection or vaccination. One signature of this condition is low platelet count (A Kasperska-Zajaç 2006; Peppers et al. 2018). This is likely what is being observed following vaccination. The anaphylaxis after vaccination in these cases is delayed (not the usual <30 min. immediate reaction) because the mRNA translation to spike protein takes hours. Similarly, viral vector infection of cells using the AstraZeneca/Janssen vaccines that subsequently produce spike proteins, takes hours. So again we have delayed, "slow rolling anaphylaxis". So treatment to avoid this problem

with COVID-19 as well as post-vaccination may be the same - H1/H2 histamine blockers like famotidine/cetirizine (Arumugham 2020c).

Detailed BLASTP results

CLDLQAPLYKKIIKKLLES (IEDB) vs.

hypothetical protein CFC21_098147 [Triticum aestivum]
KAF7096153.1 643 1

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
27.8 bits(58)	1.5	9/13(69%)	10/13(76%)	2/13(15%)

```
Query  1    CLDLQAPLYKKII  13
            CL L  PLYKK+I
Sbjct  222  CLSL--PLYKKVI  232
```

EAEEDGDLQ (IEDB) vs.

hypothetical protein CFC21_072560 [Triticum aestivum]
KAF7066606.1 1203 3

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
25.2 bits(52)	2.0	7/7(100%)	7/7(100%)	0/7(0%)

```
Query  1    EAEEDGD  7
            EAEEDGD
Sbjct  197  EAEEDGD  203
```

KTTSQVRPRHITSLEVIKAG (IEDB) vs.

Galactokinase [Zea mays]
PWZ57176.1 568 1

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
26.9 bits(56)	20	8/8(100%)	8/8(100%)	0/8(0%)

```
Query  12   TSLEVIKA  19
            TSLEVIKA
Sbjct  434  TSLEVIKA  441
```

Platelet Factor 4 vs.

hypothetical protein CFC21_095713 [Triticum aestivum]
KAF7093294.1 725 1

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
34.1 bits(73)	2.9	19/39(49%)	20/39(51%)	7/39(17%)

```
Query  1   MSSAARSR-LTRATRQEML-FLALLLLPVVVAFARAEAE  37
           M  AA  R L R     +L  LALLL V  A AR E E
Sbjct  50  MAAAAAARGLSR-----LLPLLALLLLTVLAAAARDEGE  83
```

hypothetical protein CFC21_053104 [Triticum aestivum]
KAF7043793.1 384 1

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
32.9 bits(70)	7.0	12/18(67%)	13/18(72%)	1/18(5%)

```
Query  1   MSSAAR-SRLTRATRQEM  17
           MSS  R SRLTRA R E+
Sbjct  21  MSSSRRASRLTRASRPEL  38
```

hypothetical protein CFC21_016952 [Triticum aestivum]
KAF7001241.1 1018 1

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
30.8 bits(65)	33	10/12(83%)	10/12(83%)	2/12(16%)

```
Query  17  MLFLAL--LLLP  26
           MLFLAL  LLLP
Sbjct  11  MLFLALSALLLP  22
```

Autoimmunity induction is not limited to plant proteins. The spike protein peptides have homology to thrombocytopenia related epitopes. So spike proteins induced by the vaccines can also cause the development of autoimmunity directed at these epitopes, thus resulting in clotting disorders. LLPDPSAPT is a thrombocytopenia associated epitope in the IEDB. Below is BLASTP comparison to spike protein (QHD43416.1)

unnamed protein product
Query_30841 9 1

Alignment statistics for match #1

Score	Expect	Method	Identities	Positives	Gaps
19.6 bits(39)	0.002	Composition-based stats.	6/9(67%)	8/9(88%)	0/9(0%)

```
Query  805  ILPDPSKPS  813
            +LPDPS P+
Sbjct  1    LLPDPSAPT  9
```

Integrin beta is also listed as a thrombocytopenia target in IEDB.
Below is BLASTP comparison to spike protein (QHD43416.1)

tr|H3BM21|H3BM21_HUMAN Integrin beta (Fragment) OS=Homo sapiens OX=9606 PE=3 SV=1
Query_59343 787 91

Alignment statistics for match #1

Score	Expect	Method	Identities	Positives	Gaps
22.3 bits(46)	0.18	Compositional matrix adjust.	13/26(50%)	16/26(61%)	4/26(15%)

```
Query  197  IDGYFKIYSKHTPINL-VRDLPQGFS  221
            +D Y KI SK   + L VRDLP+  S
Sbjct  360  VDAYGKIRSK---VELEVRDLPEELS  382
```

Conclusion

Animal/plant/fungal/viral/bacterial protein contaminated vaccines can cause numerous autoimmune disorders. Specifically, we showed that wheat and corn proteins in the vaccines have high homology to thrombocytopenia related epitopes. Vaccine regulators have been warned about this repeatedly for years. They have repeatedly ignore these warnings, with devastating effect. SARS-CoV-2 vaccine-induced bleeding, clotting disorders are just the latest of numerous vaccine-induced diseases (Arumugham 2020d). VIPIT is just the tip of the iceberg. Autoimmune disorders are not binary, yes or no. They are a spectrum. For every individual diagnosed with VIPIT, thousands will develop subclinical disease. Their lives will be cut short due to bleeding, clotting complications arising in response to another unrelated health condition. And of course, VIPIT is not the only autoimmune disorder induced by these vaccines. Since the full risks of these vaccines have not been accounted, the claim often made that the benefits outweigh the risks, is not supported by evidence.

References

A Kasperska-Zajaç BR (2006) Platelet function in anaphylaxis - PubMed. J Investig Allergol Clin Immunol

Ahmed SS, Volkmuth W, Duca J, et al (2015) Antibodies to influenza nucleoprotein cross-react with human hypocretin receptor 2. Sci Transl Med 7:294ra105-294ra105. https://doi.org/10.1126/scitranslmed.aab2354

Altschul SF, Madden TL, Schäffer AA, et al (1997) Gapped BLAST and PSI- BLAST: a new generation of protein database search programs. Nucleic Acids Res 25:3389–3402. https://doi.org/10.1093/nar/25.17.3389

Arumugham V (2019a) Vaccination with bovine, chick, yeast antigens synthesizes cross-reactive antibodies targeting human acetylcholine receptor and MuSK protein to cause Myasthenia Gravis: Confirmed by natural experiment (VAERS data), bioinformatics, case reports, animal experiments and titer study. https://doi.org/10.5281/zenodo.3421558. Accessed 16 Sep 2019

Arumugham V (2020a) The Pfizer/BioNTech vaccine is unnecessary, unsafe and should not be authorized. Please see attached document for details. https://www.regulations.gov/document/FDA-2020-N-1898-0039. Accessed 24 Mar 2021

Arumugham V (2020b) Analyzing 23000+ epitopes covering 82 autoimmune diseases in the Immune Epitope Database, 57% have only one and 78% have up to two amino acid residue differences compared to animal, fungal or plant peptides present in vaccines; an unmistakable signature o. https://doi.org/10.5281/zenodo.3603480. Accessed 13 Jan 2020

Arumugham V (2019b) ERVEBO Ebola vaccine will create a rice allergy epidemic, add to numerous autoimmune diseases, cancer and make Ebola disease even more severe. Design for safety and vaccine safety regulation remain abject failures. Incompetence or indifference? https://doi.org/10.5281/zenodo.3595020. Accessed 17 Jan 2020

Arumugham V (2018a) Pandemrix and Arepanrix vaccine safety analysis and scrutiny fell short. In: BMJ. https://www.bmj.com/content/363/bmj.k4152/rr-14

Arumugham V (2018b) Pharmacovigilance is no substitute for good vaccine design. In: BMJ. https://www.bmj.com/content/362/bmj.k3948/rr-11

Arumugham V (2016) Significant protein sequence alignment between peanut allergen epitopes and vaccine antigens. https://www.zenodo.org/record/1034555

Arumugham V (2020c) Immunological Mechanisms Explaining the Role of Vaccines, IgE, Mast Cells, Histamine, Elevating Ferritin, IL-6, D-dimer, VEGF Levels in COVID-19 and Dengue, Potential Treatments Such as Mast Cell Stabilizers, Antihistamines: Predictions and Confirmations. SSRN Electron J. https://doi.org/10.2139/ssrn.3722710

Arumugham V (2020d) Vaccines and Biologics injury table based on mechanistic evidence – Feb 2020 Covering over 125 conditions. https://doi.org/10.5281/zenodo.2582634. Accessed 23 Apr 2020

Arumugham V, Trushin M V. (2019) Role of NMDA receptor autoimmunity induced by food protein containing vaccines, in the etiology of autism, type 1 diabetes, neuropsychiatric and

neurodegenerative disorders. In: Int. J. Pharm. Res. https://doi.org/10.5281/zenodo.1463600. Accessed 15 Apr 2019

Arumugham V, Trushin M V (2018) Cancer immunology, bioinformatics and chemokine evidence link vaccines contaminated with animal proteins to autoimmune disease: a detailed look at Crohn's disease and Vitiligo. J Pharm Sci Res 10:2106

Beaubien J (2021) European Scientists Zero In On AstraZeneca COVID-19 Vaccine Blood Clot Link : Coronavirus Updates : NPR. https://www.npr.org/sections/coronavirus-live-updates/2021/03/21/979781065/european-scientists-zero-in-on-astrazeneca-blood-clot-link. Accessed 24 Mar 2021

Centers for Disease Control and Prevention (2021) The Vaccine Adverse Event Reporting System (VAERS) Request Form. https://wonder.cdc.gov/controller/datarequest/D8;jsessionid=447B43486F1720811AF4BB727EE4F8DC. Accessed 4 Sep 2019

CHMP (2021) COVID-19 Vaccine AstraZeneca, COVID 19 Vaccine (ChAdOx1 S [recombinant]). https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement_en.pdf. Accessed 24 Mar 2021

Lyons-Weiler J (2020) Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. J Transl Autoimmun 3:100051. https://doi.org/10.1016/j.jtauto.2020.100051

Peppers BP, Vatsayan A, Dalal J, et al (2018) A case series: Association of anaphylaxis with a significant decrease in platelet levels and possible secondary risk of thrombosis. Immunity, Inflamm Dis 6:377–381. https://doi.org/10.1002/iid3.224

Reichmuth AM, Oberli MA, Jeklenec A, et al (2016) mRNA vaccine delivery using lipid nanoparticles. Ther Deliv 7:319–334. https://doi.org/10.4155/tde-2016-0006

The UniProt Consortium (2017) UniProt: the universal protein knowledgebase. Nucleic Acids Res 45:D158–D169

Vita R, Mahajan S, Overton JA, et al (2019) The Immune Epitope Database (IEDB): 2018 update. Nucleic Acids Res 47:D339–D343. https://doi.org/10.1093/nar/gky1006

Vogel G (2021) Data concerns and safety worries fuel crisis of confidence in AstraZeneca vaccine. Science (80-). https://doi.org/10.1126/science.abi6726