

Role of NMDA receptor autoimmunity induced by food protein containing vaccines, in the etiology of autism, type 1 diabetes, neuropsychiatric and neurodegenerative disorders

Vinu Arumugham

Oct 2018

vinucubeacc@gmail.com

Abstract

Vaccines contain numerous animal and plant proteins (soy, peanut, sesame, maize, wheat, etc.). Vaccine excipients are derived from plant or animal sources. The mechanism of animal protein induced autoimmunity was previously described. Following a report associating maternal gluten intake to type 1 diabetes in the offspring, plant proteins were investigated.

The Pandemrix vaccine induced narcolepsy due to molecular mimicry between a H1N1 nucleoprotein peptide in the vaccine and the human hypocretin receptor 2. The BLASTP match score for this peptide was used as a baseline. BLASTP showed strong sequence alignment between gliadin, a wheat protein, and the human ionotropic N-methyl-D-aspartate receptor (NMDAR).

Analyzing further, strong sequence alignment was found between soy, peanut, sesame, maize, wheat and human glutamate receptors (GR), both ionotropic and metabotropic. There are reports of boosted wheat allergy and de novo synthesis of NMDAR antibodies following immunization. Once immunized with plant derived antigens, antibody levels will be increased by dietary exposure to these antigens.

GR are expressed in the brain, heart, pancreas and the T cells of the immune system. Vaccine induced GR antibodies (GRA) disrupt or destroy GR thus precipitating numerous disorders. This explains the epidemic of food intolerances and food associated immune mediated disorders.

Intestinal barrier disruption has been proposed as a cause for food associated autoimmune disorders. However, intestinal barrier disruption may itself be the result of GRA. GRA also disrupt the blood-brain barrier. This allows other anti-brain antibodies access to their targets. Vaccine-induced GRA can therefore explain a wide variety of disorders including autism, type 1 diabetes, attention deficit hyperactivity, epilepsy, schizophrenia, autoimmune encephalitis, Huntington's, Parkinson's, dementia, cancer and allergies.

The ultimate solution is to immediately remove all non-target proteins from all vaccines.

Background

Vaccines contain numerous animal and plant proteins (soy, peanut, sesame, maize, wheat, etc.). There are no labeling laws or regulations.(1) There are no safety specifications that regulate the quantity of these proteins contained in vaccines.(2) Vaccine excipients and growth media can be derived from plant and animal sources.(1,3) As an example, the appendix at the end of the document shows Polysorbate 80, a vaccine excipient, that is derived from maize and wheat. This is a source of maize and wheat protein contamination of vaccines. Manufacturers do not perform any testing on allergens in these products. Hydrolyzed gelatin used in vaccines was assumed to be safe. However, after numerous cases of IgE mediated gelatin allergy development following vaccination with gelatin containing vaccines, it was determined that the gelatin was "poorly hydrolyzed".(4)

The mechanism of animal proteins in vaccines inducing autoimmunity was previously described.

(5) Following a report associating maternal gluten intake to type 1 diabetes (T1D) in the offspring(6), the role of plant proteins in autoimmunity was investigated. Maternal gluten intake affecting the

offspring is similar to the problem of maternal milk intake causing autism in the offspring.(7,8) Milk related autism is mediated by folate receptor alpha antibodies (FRAA). These FRAA have been demonstrated to have higher affinity to bovine folate receptor proteins than human folate receptor proteins. So these FRAA were synthesized directed against bovine FR. Bovine FR has 90% homology to human FR.(9) So FRAA directed against bovine FR, cross-react, bind/block human folate receptors in the choroid plexus, block folate uptake to the brain thus resulting in autism spectrum disorders.(10) FRAA levels are increased by dietary intake of bovine milk as bovine milk contains the bovine folate receptor protein.(9) Therefore milk intake during pregnancy can affect the risk of autism in the offspring when the mother is producing FRAA. The role of bovine milk protein containing vaccines in the induction of FRAA was previously described.(11) Therefore the role of wheat protein (including gluten) containing vaccines, in T1D was investigated.

Methods

Protein sequences were obtained from Uniprot(12). BLASTP(13) was used to perform protein sequence alignment. The Pandemrix vaccine induced narcolepsy due to molecular mimicry between an influenza virus H1N1 nucleoprotein peptide (a non-target protein) in the vaccine and the human hypocretin receptor 2.(14) The BLASTP match score for this peptide (19.3) from a previous analysis(15) was used as a baseline. Any match score greater than 19.3 indicates high risk of autoimmunity.

Results and Discussion

BLASTP shows strong sequence alignment between gliadin and the human ionotropic N-methyl-D-aspartate receptor (NMDAR). Below are BLASTP results of sequence alignment between Alpha/beta-gliadin MM1 and human self proteins.

P18573 (GDA9_WHEAT) vs. homo sapiens

glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding), isoform CRA_c [Homo sapiens]

Score	Expect	Method	Identities	Positives	Gaps
33.9 bits(76)	1.1	Compositional matrix adjust.	44/98(45%)	46/98(46%)	23/98(23%)

```
Query 62 PYPQP--QPFPSQQPYLQLQPFQPLPYQP-----PQLPYPQ---PQLPYPQPQPF 108
      PYPQP QP P QP P P PQ YPQ PQ PYPQ PQ PYPQ
Sbjct 41 PYPQPPFQPSYQPGYPHGPSPYPQGGYPQGGYPQGGYPQGGYPQGGYPQGGYPQGG-- 98
```

```
Query 109 RPQQYPYQS-----QPQYSQPQQPISQQQQQQQQ 138
      PQ PYPQS QPQ Q P S Q Q++
Sbjct 99 YPQGPYPQSPFPPNPYQGPQVFPQDPPSPQHGNVQEE 136
```

The match score (33.9) is higher than the match score of 19.3 between H1N1 nucleoproteins and the human hypocretin receptor 2, which resulted in Pandemrix vaccine induced narcolepsy.(14)

This is a sample result. There are numerous peptide matches with scores above the baseline value of 19.3. So there is a high probability of wheat protein containing vaccines inducing antibodies that cross-react and bind to human NMDAR.

Similar to the above result, a 33-mer gliadin peptide binding to the glutamate receptor GRINA protein was previously reported as an explanation for extraintestinal manifestations of celiac disease.(16)

Analyzing further, strong sequence alignment was found between soy, peanut, sesame, maize, wheat and human glutamate receptors (GR), both ionotropic and metabotropic.

GRM1_HUMAN Metabotropic glutamate receptor 1 vs. plant proteins

glutamate receptor 3.1-like protein [*Triticum aestivum*] (wheat)

Score	Expect	Method	Identities	Positives	Gaps
65.5 bits(158)	9e-11	Compositional matrix adjust.	93/432(22%)	177/432(40%)	107/432(24%)
Query 81	AMFHTLDKINADPVLLPNITLGSEIRDS-CWHSSVALEQSIIEFIRDLSLIRDEKGINR				139
	A+ L+ IN+DP +L TL +++D+ C+ + + Q ++F+ +I++				
Sbjct 50	AIHTALEDINSDPVTLNGTTLKVQMKDTCNCFDGLGMVQ-LQFMETDVIAL-----				99
Query 140	CLPDGQSLPPGRTKKPIAGVIGPGSSSVAIQVQNLLQLFDIPQIAYSATSIDLSDKTL--				197
	IGP S+++ + + +P ++++ SD TL				
Sbjct 100	-----IGPQCSTISHMISYVANELQVPLMSFA-----SDATLSS				133
Query 198	--YKYFLRVVPSDTLQARAMLDIVKRYNWTYVSAVHTEGNYGESGMDAFKELAAQEGLCI				255
	+ +F+R PSD Q A+ ++V +W V+A+++ + YG +G+ A + + I				
Sbjct 134	IQFPFFVRTGPSDLYQMAVAEVDYHMKIVTAIYIDNVYGRNGIAALDDALTLKRCKI				193
Query 256	AHSDKIYSNAGEKSFDRLLRKLRLRERLPKARVVVCFCEGEMTVRGLLSAMRRLGVVGE-FSL				314
	++ SNA LL + P RV+V L S +L ++G +				
Sbjct 194	SYKVGFPNSAKRSDLINLLVSVSYMPE--RVIVLHTGAEPGLKLFVANQLNMMGNGYVW				251
Query 315	IGSD---GWADRDEVIIEGYEVEA-NGGITIKLQSPVRSFDDYFLKLRDLTNRNPWFPE				370
	I +D + D + + + G +T+++ P + + +N + W				
Sbjct 252	IATDWLSAYLDANSSVPAETISGLQGVLTLRPHIPNSK-----MKSNLVSKW---				298
Query 371	FWQHRFQCRLPGHLLLENPNFKRICTGNESLEENY--VQDSKMGF-VINAIYAMAHL---				424
	G +S + NY ++ + GF V ++++A+A L				
Sbjct 299	-----GTQSKKYNYSDLRVNTYGFVYVDSVAVARALDAF				333
Query 425	-----QNMHHALCPGHVGLCDAMKPID-GSKLLDFLIKSSFIVSGEEVWFDEKG				473
	++H + G +AM D GSKLL+ + K +F G+SG +V FD G				
Sbjct 334	FDDGGRISFNSDLHDGI--GGTLHLEAMSIFDMGSKLLEKIRKVNFSGISG-QVQFDAVG				390
Query 474	DAPG-RYDIMNL 484				
	+ YDI+N+				
Sbjct 391	NLIHPAYDIINV 402				

Glutamate receptor 2.7 [*Zea mays*] (maize or corn)

Score	Expect	Method	Identities	Positives	Gaps
78.2 bits(191)	3e-13	Compositional matrix adjust.	79/333(24%)	144/333(43%)	35/333(10%)

glutamate receptor 3.4 [*Glycine max*] (soy)

Score	Expect	Method	Identities	Positives	Gaps
68.9 bits(167)	2e-10	Compositional matrix adjust.	81/420(19%)	166/420(39%)	63/420(15%)

LOW QUALITY PROTEIN: glutamate receptor 3.5-like [*Sesamum indicum*] (sesame)

Score	Expect	Method	Identities	Positives	Gaps
68.6 bits(166)	3e-10	Compositional matrix adjust.	44/167(26%)	80/167(47%)	4/167(2%)

glutamate receptor 3.7-like [Arachis hypogaea] (peanut)

Score Expect Method Identities Positives Gaps
 66.2 bits(160) 1e-09 Compositional matrix adjust. 52/177(29%) 78/177(44%) 30/177(16%)

Human ionotropic NMDA vs. plant proteins

glutamate receptor 3.1-like protein [Triticum aestivum] (wheat)

Score Expect Method Identities Positives Gaps
 153 bits(386) 4e-38 Compositional matrix adjust. 202/930(22%) 377/930(40%) 157/930(16%)

Query	21	ACDPKIVNIGAVLS-TRKHEQMFREAVNQANKRHGWSKIQLNATSVTHKPNAIQMALSVC	79
Sbjct	25	ATGPPVNVNIGSILQFDSTTGGVAAVAIHTALEDINSPTVLNGTTL-----KVQMKDTNC	79
Query	80	ED----LISSQVYAILVSHPPPTPNDFHTPTVPSYTAGFYRIPVLGLTTRMSIYSDKSIHL	135
Sbjct	80	FDGFLGMVQLQFMETDVIALIGPQCSTISHMISYVANELQVPLMSFASDATL---SSIQF	136
Query	136	SF-LRTVPPYSHQSSVWFEMMRVYSWNHIIILLVSDHEGRAAQKRETLLEERESKAEKV	194
Sbjct	137	PFVVRTGPSLDYQMAAAVAEVDYVNHVKIVTAIYIDNVYGRNGIAALDDALTLKRCKISYK	196
Query	195	LQFDPGK--NVTALLMEAKELEARVILSASEDDAATVYRAAAMNMTGSGYVWLVE-	251
Sbjct	197	VGFPSNAKRSDLINLLVSVSYMEPRVIVLHTGAEPGLKLFVSVANQLNMMGNGYVWIATDW	256
Query	252	--REISGNALRYAPDGILGLQLI-----NGKNESAHS-----	282
Sbjct	257	LSAYLDANS-SVPAETISGLQGVTLRPHIPNSKMKSNLVSKWGTQSKKYNYSDLRVNTY	315
Query	283	-----DAVGVAQAVHELLE---KENITDPPRGCVGNTNIWKTGPLFKRVLMSKYAD--	332
Sbjct	316	GFYVYDSVWAVARALDAFFDDGGRISFSNDLHDGIGGTLHLEAMSIFD---MGSKLEKI	372
Query	333	-----GVTGRVEFNEDGDRKFANYSIMNLQNRKLVQVGIYNGTHVI-----	373
Sbjct	373	RKVNFSGISGQVQFDVAVGNLIHPAYDIINVIGMRTIGFWSNYSGLLSTVSPEALYSKP	432
Query	374	PN----DR---KIIWPGGETEKPRGYQMST---RLKIVTIHQEPFVYVKPTLSDGTCKEE	423
Sbjct	433	PNISLADQHLVDYIWPGETAQRPRGWVFPVSNKQLKIGVFNRFSSF-----KEI	480
Query	424	FTVNGDPVKKVICTGPNDTSPGSPRHTVPQCCYGFIDLLIKLARTMNFYEVHLVADGK	483
Sbjct	481	VTV-----DNATGSMK-----GYCIDVFTQALALLPYPVSYKFPVPG-	517
Query	484	FGTQERVNNSNKKKEWNGMMGELLSGQADMIVAPLTINNERAQYIEFSKPFKYQGLTIL--	541
Sbjct	518	-----NGTENPNYDKLVQMIESNEFDAAIGDIAITMRRTVTFDFTQPFIIETGLVILAP	570
Query	542	VKKEIPRSTLDSFMQPFQSTLWLLVGLSVHVAVMLYLLDRFSPFGRFKVNSEEEEEEDAL	601
Sbjct	571	VKEHITSSW--AFLQPFSELMWCVTGLFLLIVGVVIVWLEH-----RINDDFRGSVCQ	621
Query	602	TLSSAMWFSWGVLLNSGIGEGAPRSFSARILGMVWAGFAMIIVASYTANLAAFLVDRPE	661
Sbjct	622	QIIT-IFFSFSTLF---FAHENTMSALGRGVLIWLFVVLIIIVSSYTASLTSILTVQQLD	677
Query	662	ERITGINDPRLRNPSDKFIYATVKQSSVDIYFRRQVELSTMYRHMEKHNYESAAEAIQ-A	720
Sbjct	678	TSIKGIDDLKNSNDPIGFQVGSFAQD---YMKELNISRS-RLRALGSPQEQYAEALKIG	732

```

Query 721 VRDNKLHAFIWDSSAVLEFEASQKCDLVTTGELFFRSGFGIGMRKDSPWKQNVLSILKSH 780
      ++ + A + + +E S C + G F G+G +DSP + ++S +IL
Sbjct 733 PKEGGVMAIVDERPYVELFLSTYCKIAVAGTDFTSRGWGFAFPRDSPLQVDLSTAILLSLS 792

Query 781 ENGFMEDLDKTWVRYQECDSRSNA---PATLTFENMAGVFMLVAGGIVAGIFLIF--IEI 835
      ENG ++ + W+ EC + ++ L E+ G+F++ V + L F +
Sbjct 793 ENGELQRIHSHKWLNTGECTTDNSEFVDSNQLRLESFLGLFLICGVACVLALLLYFGIMLC 852

Query 836 AYKRHKDARRKQMLAFAAVNVWRKNLQDR 865
      Y RH+ + + ++F KN++ R
Sbjct 853 KYLRHEPRKSLRRFISFVHGKEPPKNMERR 882

```

Glutamate receptor 3.4 [Zea mays] (corn or maize)

Score	Expect	Method	Identities	Positives	Gaps
169 bits(429)	5e-42	Compositional matrix adjust.	176/780(23%)	311/780(39%)	126/780(16%)

glutamate receptor 3.4-like isoform X2 [Arachis hypogaea] (peanut)

Score	Expect	Method	Identities	Positives	Gaps
169 bits(427)	6e-42	Compositional matrix adjust.	174/805(22%)	339/805(42%)	141/805(17%)

glutamate receptor 3.4 isoform X2 [Sesamum indicum] (sesame)

Score	Expect	Method	Identities	Positives	Gaps
164 bits(414)	2e-40	Compositional matrix adjust.	177/810(22%)	330/810(40%)	139/810(17%)

glutamate receptor 3.4 isoform X1 [Glycine max] (soy)

Score	Expect	Method	Identities	Positives	Gaps
163 bits(412)	6e-40	Compositional matrix adjust.	177/799(22%)	324/799(40%)	155/799(19%)

Human GABA-A (epilepsy associated self antigen(17)) vs. plant proteins

ATP-citrate synthase beta chain protein 2 [Glycine max] (soy)

Score	Expect	Method	Identities	Positives	Gaps
32.0 bits(71)	11	Compositional matrix adjust.	19/74(26%)	39/74(52%)	5/74(6%)

cytochrome P450 78A7 [Sesamum indicum] (sesame)

Score	Expect	Method	Identities	Positives	Gaps
29.3 bits(64)	80	Compositional matrix adjust.	16/41(39%)	24/41(58%)	2/41(4%)

cytochrome P450 78A7-like [Arachis hypogaea] (peanut)

Score	Expect	Method	Identities	Positives	Gaps
28.5 bits(62)	135	Compositional matrix adjust.	12/34(35%)	21/34(61%)	0/34(0%)

agmatine coumaroyltransferase-2 [Zea mays] (corn or maize)

Score	Expect	Method	Identities	Positives	Gaps
27.7 bits(60)	274	Compositional matrix adjust.	12/43(28%)	20/43(46%)	0/43(0%)

IRE1 [Triticum aestivum] (wheat)

Score	Expect	Method	Identities	Positives	Gaps
26.6 bits(57)	670	Compositional matrix adjust.	9/35(26%)	19/35(54%)	0/35(0%)

Human LGI1 (an autoimmune encephalitis (AE) associated self antigen(17)) vs. plant proteins

unnamed protein product [Triticum aestivum] (wheat)

Score	Expect	Method	Identities	Positives	Gaps
48.1 bits(113)	1e-04	Compositional matrix adjust.	29/84(35%)	38/84(45%)	0/84(0%)

protein NSP-INTERACTING KINASE 3-like isoform X2 [Arachis hypogaea] (peanut)

Score	Expect	Method	Identities	Positives	Gaps
42.4 bits(98)	0.010	Compositional matrix adjust.	31/81(38%)	40/81(49%)	5/81(6%)

receptor protein kinase TMK1 [Sesamum indicum] (sesame)

Score	Expect	Method	Identities	Positives	Gaps
39.3 bits(90)	0.091	Compositional matrix adjust.	24/64(38%)	35/64(54%)	1/64(1%)

probably inactive leucine-rich repeat receptor-like protein kinase At3g28040 [Glycine max] (soy)

Score	Expect	Method	Identities	Positives	Gaps
38.5 bits(88)	0.17	Compositional matrix adjust.	25/62(40%)	34/62(54%)	2/62(3%)

putative leucine-rich repeat receptor-like serine/threonine-protein kinase [Zea mays] (corn or maize)

Score	Expect	Method	Identities	Positives	Gaps
37.0 bits(84)	0.55	Compositional matrix adjust.	42/155(27%)	63/155(40%)	18/155(11%)

Human CASPR2 (An AE associated self antigen(17)) vs. plant proteins

Pectin lyase-like superfamily protein [Zea mays] (corn or maize)

Score	Expect	Method	Identities	Positives	Gaps
33.1 bits(74)	14	Compositional matrix adjust.	28/103(27%)	44/103(42%)	10/103(9%)

wall-associated receptor kinase 2-like [Arachis hypogaea] (peanut)

Score	Expect	Method	Identities	Positives	Gaps
32.3 bits(72)	31	Compositional matrix adjust.	16/34(47%)	18/34(52%)	2/34(5%)

putative E3 ubiquitin-protein ligase UBR7 [Sesamum indicum] (sesame)

Score	Expect	Method	Identities	Positives	Gaps
31.6 bits(70)	56	Compositional matrix adjust.	14/42(33%)	25/42(59%)	2/42(4%)

histone-lysine N-methyltransferase EZA1 isoform X3 [Glycine max] (soy)

Score	Expect	Method	Identities	Positives	Gaps
31.2 bits(69)	71	Compositional matrix adjust.	18/42(43%)	20/42(47%)	2/42(4%)

unnamed protein product [Triticum aestivum] (wheat)

Score	Expect	Method	Identities	Positives	Gaps
30.4 bits(67)	144	Compositional matrix adjust.	14/53(26%)	22/53(41%)	0/53(0%)

There are reports of boosted peanut, almond, milk, eggs, soy, wheat specific IgE(18,19) following vaccination. Bovine serum albumin (BSA) in equine vaccines boosted BSA IgE in horses. Repeated BSA containing vaccine injections boosted IgE resulting in severe allergy and anaphylaxis. (20) Mammalian immune systems may be the most sensitive protein detectors. Post vaccine IgE antibody synthesis can be directed against target and non-target proteins in the vaccine.(21–27) De novo synthesis of NMDAR antibodies following immunization have also been reported.(28) Given the strong sequence alignment results above, antibodies directed against plant proteins in vaccines, have a high probability of cross-reacting with human self antigens thus inducing autoimmune disorders.

Role of immunological adjuvants

The target viral/bacterial proteins (e.g.: tetanus toxoid, diphtheria toxoid, hepatitis B surface antigen, etc.) in modern vaccines 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 vaccine 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 (plant proteins in this case) thus resulting in numerous off-target immune responses.

Once immunized with food derived antigens, antigen specific IgG1 and IgG4 antibody levels can be increased by dietary exposure to those antigens thus increasing autoimmune disease severity.(9,29–33)

GR are expressed in the brain, heart, pancreas(34) and the T cells(35,36) of the immune system. Antibodies binding to a receptor could have different effects, including (i) inhibition of receptor signaling, (ii) stimulation of receptor signaling, (iii) triggering of programmed cell death, (iv) cellular cytotoxicity, (v) cell clearance by complement-mediated pathways, and (vi) receptor internalization. (37) Vaccine induced GR antibodies (GRA) therefore can disrupt GR function or destroy GR thus precipitating numerous disorders. This explains the epidemic of food intolerances and food associated immune mediated disorders.

Intestinal barrier disruption – cause or effect of autoimmunity?

Intestinal barrier disruption has been proposed as a cause for food associated autoimmune disorders. However, intestinal barrier disruption may itself be the result of vaccine-induced GRA.(38,39)

Blood brain barrier disruption

GRA can also disrupt the blood-brain barrier (BBB).(40) This provides GRA and other anti-brain antibodies access to their targets in the brain. Vaccine induced anti-GAD65 antibodies(5,41) which can cause T1D (that may be subclinical) can now also attack the brain(17) due to BBB disruption.

Neuropsychiatric disorders

Vaccine-induced GRA mediated GR dysfunction can explain a wide variety of disorders including autism(42), attention deficit hyperactivity(43,44), epilepsy(45,46), schizophrenia (47,48), autoimmune encephalitis(17,49–52), and psychosis(17,47,48,52,53).

Immune system dysregulation

NMDAR antibodies binding to T cells can result in immune system dysregulation.(54) With such fundamental impairment, increased risk of allergies, cancer (54,55), infection and autoimmune disorders can be expected.

Type 1 diabetes

Numerous antibodies are associated with T1D.(41,56,57) The islet cells of the pancreas express GR. (34,58) GRA can also therefore mediate destruction of islet cells and cause type 1 diabetes. These off-target immune responses can be both cell mediated and humoral. In the case of cell mediated responses, since the non-target proteins are injected via the skin, cytotoxic T cells produced as a result express the skin-homing marker (CCR4). Since the pancreas secrete the ligand for CCR4, these cytotoxic T cells home to the pancreas, causing type 1 diabetes.(5)

Neurodegenerative disorders

NMDA dysregulation has a role in many neurodegenerative disorders. It contributes to Parkinson's(59,60), Alzheimer's(61) dementia(52,62) and Huntington's disease(63).

Cardiac disorders

NMDAR autoimmunity can result in cardiac dysrhythmias.(64,65)

Gluten-free diet

Eosinophilic esophagitis (EoE) is an IgG4 mediated disease. The IgG4 is commonly directed against cow's milk proteins like casein. A milk-free diet reduces IgG4 level and therefore helps in EoE(66). Similarly, a milk-free diet helps in IgG4 mediated FRAA related autism.(9) By the same mechanism, a gluten-free diet can help in IgG4 mediated anti-NMDAR antibody related autism. This explains the origin of the gluten-free, casein-free (GFCF) diet in autism and ADHD treatment.

IgE and IgG4 are naturally involved in helminth defense. Injection of any protein results in IgE antibody mediated sensitization against that protein.(67)

Once sensitized, dietary exposure to the protein causes the synthesis of IgG4 antibodies directed against the same protein. The immune system is treating the protein as a worm protein.(8)
The immune system can also treat the injected protein as a virus or bacteria and begin synthesis of IgG1 antibodies directed against the protein. Dietary exposure in this case will cause an increase in IgG1 synthesis.(29)

Results above show that various elimination diets such as soy-free, sesame-free, peanut-free, corn-free may also help in these vaccine-induced illnesses. Similar to FRAA associated autism and EoE, IgG4 responses predominate in LIG1 and CASPR2 associated encephalitis.(17) Therefore, elimination diets may help.

Conclusion

Japan had an outbreak of gelatin allergy about 20 years ago. Gelatin, a non-target protein contained in vaccines caused the development of these allergies.(22) Japan removed gelatin from all vaccines around 2000, as the ultimate solution to vaccine-induced gelatin allergy.(68) We have not learned anything from the Pandemrix vaccine induced narcolepsy disaster either.(14,69,70)
The ultimate solution to avoid these numerous vaccine-induced disorders is to avoid using proteins (plant, animal, non-target viral/bacterial, fungal proteins etc.) in vaccine production. If that is not possible, all non-target proteins from all vaccines should be removed during final steps of production by using processes like affinity chromatography.(71)

References

1. National Academies of Sciences and Medicine E. Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management, and Public Policy. Stallings VA, Oria MP, editors. Washington, DC: The National Academies Press; 2017.
2. Arumugham V. Evidence that Food Proteins in Vaccines Cause the Development of Food Allergies and Its Implications for Vaccine Policy. *J Dev Drugs*. 2015;4(137):2.
3. Vaccine Excipient & Media Summary [Internet]. 2015 [cited 2016 Jan 16]. Available from: <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf>
4. Nakayama T, Kumagai T. Gelatin allergy. *Pediatrics*. United States; 2004. p. 170–1.
5. Arumugham V, Trushin M V. 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*. 2018;10(8):2106.
6. Antvorskov JC, Halldorsson TI, Josefsen K, Svensson J, Granström C, Roep BO, et al. Association between maternal gluten intake and type 1 diabetes in offspring: national prospective cohort study in Denmark. *BMJ*. BMJ Publishing Group Ltd; 2018;362.
7. Frye RE, Sequeira JM, Quadros E, Rossignol DA. Folate Receptor Alpha Autoantibodies Modulate Thyroid Function in Autism Spectrum Disorder. *North Am J Med Sci*. 2014;7(1):1–7.

8. Arumugham V. Autism Spectrum Disorders: A special case of vaccine-induced cow's milk allergy? [Internet]. 2017. Available from: <https://www.zenodo.org/record/1034557>
9. Ramaekers VT, Sequeira JM, Blau N, Quadros E V. A milk-free diet downregulates folate receptor autoimmunity in cerebral folate deficiency syndrome. *Dev Med Child Neurol*. 2008;50(5):346–52.
10. Frye RE, Sequeira JM, Quadros E V, James SJ, Rossignol D a. Cerebral folate receptor autoantibodies in autism spectrum disorder. *Mol Psychiatry*. 2012;18(3):369–81.
11. Arumugham V. Epidemiological studies that ignore mechanism of disease causation are flawed and mechanistic evidence demonstrates that vaccines cause autism [Internet]. 2017. Available from: <https://doi.org/10.5281/zenodo.1041905>
12. UniProt: the universal protein knowledgebase. *Nucleic Acids Res*. 2017 Jan 4;45(D1):D158–69.
13. Altschul SF, Madden TL, Schäffer AA, Zhang J, Zhang Z, Miller W, et al. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. *Nucleic Acids Res*. 1997;25(17):3389–402.
14. Ahmed SS, Volkmuth W, Duca J, Corti L, Pallaoro M, Pezzicoli A, et al. Antibodies to influenza nucleoprotein cross-react with human hypocretin receptor 2 (ABSTRACT ONLY). *Sci Transl Med*. 2015;7(294):294ra105–294ra105.
15. Arumugham V. Significant protein sequence alignment between peanut allergen epitopes and vaccine antigens [Internet]. 2016. Available from: <https://www.zenodo.org/record/1034555>
16. Garcia-Quintanilla A, Miranzo-Navarro D. Extraintestinal manifestations of celiac disease: 33-mer gliadin binding to glutamate receptor GRINA as a new explanation. *Bioessays*. United States; 2016 May;38(5):427–39.
17. Lancaster E. The Diagnosis and Treatment of Autoimmune Encephalitis. *J Clin Neurol*. Korean Neurological Association; 2016 Jan 23;12(1):1–13.
18. Alice Hoyt, Peter Heymann, Alexander Schuyler, Scott Commins TAEP-M. Changes in IgE Levels Following One-Year Immunizations in Two Children with Food Allergy [Internet]. 2015. Available from: <https://wao.confex.com/wao/2015symp/webprogram/Paper9336.html>
19. Arumugham V. Vaccines and the development of food allergies: the latest evidence [Internet]. *BMJ*. 2016. Available from: <https://www.bmj.com/content/355/bmj.i5225/rr-0>
20. Gershwin LJ, Netherwood KA, Norris MS, Behrens NE, Shao MX. Equine IgE responses to non-viral vaccine components. *Vaccine*. Netherlands; 2012 Dec;30(52):7615–20.
21. Yamane H. N. U. Serological examination of IgE- and IgG-specific antibodies to egg protein during influenza virus immunization. *Epidemiol Infect*. 1988;100(2):291–9.
22. Nakayama T, Aizawa C, Kuno Sakai H. A clinical analysis of gelatin allergy and determination of its causal relationship to the previous administration of gelatin-containing acellular pertussis

- vaccine combined with diphtheria and tetanus toxoids [see comments]. *J Allergy Clin Immunol.* Elsevier; 1999 Jan 9;103(2 Pt 1):321–5.
23. Nakayama T, Kumagai T, Nishimura N, Ozaki T, Okafuji T, Suzuki E, et al. Seasonal split influenza vaccine induced IgE sensitization against influenza vaccine. *Vaccine.* 2015 Nov 9;33(45):6099–105.
 24. Davidsson A, Eriksson JC, Rudblad S, Brokstad KA. Influenza specific serum IgE is present in non-allergic subjects. *Scand J Immunol.* 2005 Dec;62(6):560–1.
 25. Smith-Norowitz T a, Wong D, Kusunruksa M, Norowitz KB, Joks R, Durkin HG, et al. Long term persistence of IgE anti-influenza virus antibodies in pediatric and adult serum post vaccination with influenza virus vaccine. *Int J Med Sci.* 2011;8(3):239–44.
 26. Smith-Norowitz TA, Tam E, Norowitz KB, Chotikanatis K, Weaver D, Durkin HG, et al. IgE anti Hepatitis B virus surface antigen antibodies detected in serum from inner city asthmatic and non asthmatic children. *Hum Immunol. United States;* 2014 Apr;75(4):378–82.
 27. Nagao M, Fujisawa T, Ihara T, Kino Y. Highly increased levels of IgE antibodies to vaccine components in children with influenza vaccine-associated anaphylaxis. *J Allergy Clin Immunol. United States;* 2016 Mar;137(3):861–7.
 28. Wang H. Anti-NMDA Receptor Encephalitis and Vaccination. Ciccodicola A, editor. *Int J Mol Sci. MDPI;* 2017 Jan 18;18(1):193.
 29. Husby S, Foged N, Oxelius VA, Svehag SE. Serum IgG subclass antibodies to gliadin and other dietary antigens in children with coeliac disease. *Clin Exp Immunol. England;* 1986 Jun;64(3):526–35.
 30. Savilahti EM, Rantanen V, Lin JS, Karinen S, Saarinen KM, Goldis M, et al. Early recovery from cow's milk allergy is associated with decreasing IgE and increasing IgG4 binding to cow's milk epitopes. *J Allergy Clin Immunol.* 2010;125.
 31. Piconi S, Trabattoni D, Rainone V, Borgonovo L, Passerini S, Rizzardini G, et al. Immunological effects of sublingual immunotherapy: clinical efficacy is associated with modulation of programmed cell death ligand 1, IL-10, and IgG4. *J Immunol. United States;* 2010 Dec;185(12):7723–30.
 32. Hoyt AEW, Schuyler AJ, Heymann PW, Platts-Mills TAE, Commins SP. Alum-Containing Vaccines Increase Total and Food Allergen-Specific IgE, and Cow's Milk Oral Desensitization Increases Bosd4 IgG4 While Peanut Avoidance Increases Arah2 IgE: The Complexity of Today's Child with Food Allergy. *J Allergy Clin Immunol. Elsevier;* 2017 Jul 7;137(2):AB151.
 33. Vickery BP, Lin J, Kulis M, Fu Z, Steele PH, Jones SM, et al. Peanut oral immunotherapy modifies IgE and IgG4 responses to major peanut allergens. *J Allergy Clin Immunol.* 2013;131(1).

34. Inagaki N, Kuromi H, Gono T, Okamoto Y, Ishida H, Seino Y, et al. Expression and role of ionotropic glutamate receptors in pancreatic islet cells. *FASEB J Off Publ Fed Am Soc Exp Biol. United States*; 1995 May;9(8):686–91.
35. Orihara K, Odemuyiwa SO, Dil N, Anaparti V, Moqbel R. Expression and roles of glutamate (NMDA) receptors on T cell subsets. *Allergy Asthma Clin Immunol. BioMed Central*; 2010 Nov 4;6(Suppl 2):P24–P24.
36. Ganor Y, Levite M. The neurotransmitter glutamate and human T cells: glutamate receptors and glutamate-induced direct and potent effects on normal human T cells, cancerous human leukemia and lymphoma T cells, and autoimmune human T cells. *J Neural Transm.* 2014;121(8):983–1006.
37. Ahmed SS, Montomoli E, Pasini FL, Steinman L. The Safety of Adjuvanted Vaccines Revisited: Vaccine-Induced Narcolepsy. *Isr Med Assoc J. Israel*; 2016;18(3-4):216–20.
38. Dumitra\cscu DL, Drug V. Functional and Motility Disorders of the Gastrointestinal Tract: Proceedings of the Humboldt Kolleg Neurogastro 2011 3rd International Symposium of Neurogastroenterology : Ia{\c{s}}i, Romania, November 2011. Editura Medical{\u{a}} Universitar{\u{a}} “Iuliu Ha{\c{t}}ieganu”; 2011.
39. Rao R, Samak G. Role of Glutamine in Protection of Intestinal Epithelial Tight Junctions. *J Epithel Biol Pharmacol.* 2012 Jan 22;5(Suppl 1-M7):47–54.
40. Xhima K, Weber-Adrian D, Silburt J. Glutamate Induces Blood{\textendash}Brain Barrier Permeability through Activation of N-Methyl-D-Aspartate Receptors. *J Neurosci. Society for Neuroscience*; 2016;36(49):12296–8.
41. Arumugham V. Role of MMR II vaccine contamination with GAD65 containing chick embryo cell culture in the etiology of type 1 diabetes [Internet]. 2017. Available from: <https://www.zenodo.org/record/1034771>
42. Rojas DC. The role of glutamate and its receptors in autism and the use of glutamate receptor antagonists in treatment. *J Neural Transm.* 2014 Aug 22;121(8):891–905.
43. Chang JP-C, Lane H-Y, Tsai GE. Attention deficit hyperactivity disorder and N-methyl-D-aspartate (NMDA) dysregulation. *Curr Pharm Des. United Arab Emirates*; 2014;20(32):5180–5.
44. Niederhofer H. Association of Attention-Deficit/Hyperactivity Disorder and Celiac Disease: A Brief Report. *Prim Care Companion CNS Disord. Physicians Postgraduate Press, Inc.*; 2011 Oct 28;13(3):PCC.10br01104.
45. Ghasemi M, Schachter SC. The NMDA receptor complex as a therapeutic target in epilepsy: a review. *Epilepsy Behav. United States*; 2011 Dec;22(4):617–40.
46. Bashiri H, Afshari D, Babaei N, Ghadami MR. Celiac Disease and Epilepsy: The Effect of Gluten-Free Diet on Seizure Control. *Adv Clin Exp Med. Poland*; 2016;25(4):751–4.

47. Kannan G, Gressitt KL, Yang S, Stallings CR, Katsafanas E, Schweinfurth LA, et al. Pathogen-mediated NMDA receptor autoimmunity and cellular barrier dysfunction in schizophrenia. *Transl Psychiatry*. Nature Publishing Group; 2017 Aug 1;7(8):e1186.
48. Lionetti E, Leonardi S, Franzonello C, Mancardi M, Ruggieri M, Catassi C. Gluten Psychosis: Confirmation of a New Clinical Entity. *Nutrients*. MDPI; 2015 Jul 8;7(7):5532–9.
49. Tüzün E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. *Acta Neuropathol*. 2009 Dec;118(6):737–43.
50. Gleichman AJ, Spruce LA, Dalmau J, Seeholzer SH, Lynch DR. Anti-NMDA Receptor Encephalitis Antibody Binding Is Dependent on Amino Acid Identity of a Small Region Within the GluN1 Amino Terminal Domain. *J Neurosci*. 2012 Aug 8;32(32):11082–94.
51. Shin Y-W, Lee S-T, Park K-I, Jung K-H, Jung K-Y, Lee SK, et al. Treatment strategies for autoimmune encephalitis. *Ther Adv Neurol Disord*. Sage UK: London, England: SAGE Publications; 2018 Aug 16;11:1756285617722347.
52. Poloni N, Vender S, Bolla E, Bortolaso P, Costantini C, Callegari C. Gluten encephalopathy with psychiatric onset: case report. *Clin Pract Epidemiol Ment Health*. Bentham Science Publishers; 2009 Jun 26;5:16.
53. Ellul P, Groc L, Tamouza R, Leboyer M. The Clinical Challenge of Autoimmune Psychosis: Learning from Anti-NMDA Receptor Autoantibodies. *Front Psychiatry*. Frontiers Media S.A.; 2017 Apr 19;8:54.
54. Kahlfuß S, Simma N, Mankiewicz J, Bose T, Lowinus T, Klein-Hessling S, et al. Immunosuppression by N-Methyl-d-Aspartate Receptor Antagonists Is Mediated through Inhibition of K(v)1.3 and K(Ca)3.1 Channels in T Cells. *Mol Cell Biol*. 1752 N St., N.W., Washington, DC: American Society for Microbiology; 2014 Mar 25;34(5):820–31.
55. Robinson HPC, Li L. Autocrine, paracrine and necrotic NMDA receptor signalling in mouse pancreatic neuroendocrine tumour cells. *Open Biol*. The Royal Society; 2017 Dec 20;7(12):170221.
56. Arumugham V. Bioinformatics analysis links type 1 diabetes to vaccines contaminated with animal proteins and autoreactive T cells express skin homing receptors consistent with injected vaccines as causal agent [Internet]. 2017. Available from: <https://www.zenodo.org/record/1034775>
57. Arumugham V. Milk containing vaccines cause milk allergies, EoE, autism and type 1 diabetes [Internet]. *The BMJ*. 2018. Available from: <https://www.bmj.com/content/361/bmj.k2396/rr>
58. Weaver CD, Yao TL, Powers AC, Verdoorn TA. Differential expression of glutamate receptor subtypes in rat pancreatic islets. *J Biol Chem*. United States; 1996 May;271(22):12977–84.

59. Di Lazzaro V, Capone F, Cammarota G, Di Giuda D, Ranieri F. Dramatic improvement of parkinsonian symptoms after gluten-free diet introduction in a patient with silent celiac disease. *Journal of neurology*. Germany; 2014. p. 443–5.
60. Ahmed I, Bose SK, Pavese N, Ramlackhansingh A, Turkheimer F, Hotton G, et al. Glutamate NMDA receptor dysregulation in Parkinson's disease with dyskinesias. *Brain*. England; 2011 Apr;134(Pt 4):979–86.
61. Zhang Y, Li P, Feng J, Wu M. Dysfunction of NMDA receptors in Alzheimer's disease. *Neurol Sci*. Milan: Springer Milan; 2016 Mar 12;37:1039–47.
62. Doss S, Wandinger K-P, Hyman BT, Panzer JA, Synofzik M, Dickerson B, et al. High prevalence of NMDA receptor IgA/IgM antibodies in different dementia types. *Ann Clin Transl Neurol*. Oxford, UK: BlackWell Publishing Ltd; 2014 Oct 18;1(10):822–32.
63. Fan MMY, Raymond LA. N-methyl-D-aspartate (NMDA) receptor function and excitotoxicity in Huntington's disease. *Prog Neurobiol*. England; 2007 Apr;81(5-6):272–93.
64. Ziaieian B, Shamsa K. Dazed, Confused, and Asystolic: Possible Signs of Anti-N-Methyl-D-Aspartate Receptor Encephalitis. *Texas Hear Inst J. Texas Heart® Institute, Houston*; 2015 Apr 1;42(2):175–7.
65. Liu C, Zhu J, Zheng X-Y, Ma C, Wang X. Anti-N-Methyl-D-aspartate Receptor Encephalitis: A Severe, Potentially Reversible Autoimmune Encephalitis. *Mediators Inflamm*. Hindawi; 2017 Jun 18;2017:6361479.
66. Kagalwalla AF, Amsden K, Shah A, Ritz S, Manuel-Rubio M, Dunne K, et al. Cow's milk elimination: a novel dietary approach to treat eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr*. 2012;55(6):711–6.
67. Arumugham V. Professional Misconduct by NAM Committee on Food Allergy [Internet]. 2016. Available from: <https://www.zenodo.org/record/1034559>
68. Kuno-Sakai H, Kimura M. Removal of gelatin from live vaccines and DTaP—an ultimate solution for vaccine-related gelatin allergy. *Biologicals*. 2003;31(4):245–9.
69. Arumugham V. Pandemrix and Arepanrix vaccine safety analysis and scrutiny fell short [Internet]. *The BMJ*. 2018. Available from: <https://www.bmj.com/content/363/bmj.k4152/rr-14>
70. Arumugham V. Pharmacovigilance is no substitute for good vaccine design [Internet]. *The BMJ*. 2018. Available from: <https://www.bmj.com/content/362/bmj.k3948/rr-11>
71. Zhao M, Vandersluis M, Stout J, Haupts U, Sanders M, Jacquemart R. Affinity chromatography for vaccines manufacturing: Finally ready for prime time? *Vaccine*. Netherlands; 2018 Apr;

Appendix

Allergen - Certificate

817061 Tween® 80 (Polysorbate) EMPROVE® ESSENTIAL Ph Eur,JP,NF

List of Allergens

Milk and products thereof (including lactose)	Lactose
Chicken	Eggs and products thereof
Beef	Pork
Fish and products thereof	Molluscs and products thereof
Crustaceans and products thereof	Yeast
Rye	Gluten
Soybeans and products thereof	Soy oil
Nuts and products thereof	Nut oil
Peanuts and products thereof	Peanut oil
Sesame seeds and products thereof	Sesame oil
Legumes/pulses	Lupines and products thereof
Cinnamon	Vanillin
Coriander	Celery and products thereof
Umbelliferae	Cocoa
Mustard and products thereof	Glutamate
Azo dyes	Tartrazine (E102)
Sulfur dioxide, Sulphites	Benzoic Acid (E210)
Parabenes (E211-E219)	Natural Rubber Latex

Because of the used raw materials and/or the manufacturing procedure we do not expect the listed allergens in the final product.

The following materials are used as raw material but are not present in the final product:

Maize, Wheat

We point out that Merck KGaA does not perform any testing on allergens in the above-mentioned product.

Dr. Jörg Schröder
Quality Services

file:///home/vinu/vinu/Health/vaccines/Aluminum/EMD_MILLIPORE_Allergen%20-%20Certificate.html

1/2

10/5/2018

Allergen - Certificate

This document has been produced electronically and is valid without a signature.
Date: 05-Dec-2014

Merck KGaA, Darmstadt, Germany

Corporation with General Partners
Frankfurter Str. 250
64293 Darmstadt, Germany
Phone +49 6151 72-0

Sigma-Aldrich Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
3050 Spruce Street
St. Louis, MO 63103, USA
Phone +1 (800) 521-8956 +1 (314) 771-5765

EMD Millipore Corporation

A subsidiary of Merck KGaA, Darmstadt, Germany
400 Summit Drive
Burlington, MA 01803, USA
Phone +1 (781) 533-6000

Page : 1 of 1