ABSTRACT

Development of new vaccine technology has been plagued with problems in the past. The current RNA based SARS-CoV-2 vaccines were approved in the US using an emergency order without extensive long term safety testing. In this paper the Pfizer COVID-19 vaccine was evaluated for the potential to induce prion-based disease in vaccine recipients. The RNA sequence of the vaccine as well as the spike protein target interaction were analyzed for the potential to convert intracellular RNA binding proteins TAR DNA binding protein (TDP-43) and Fused in Sarcoma (FUS) into their pathologic prion conformations. The results indicate that the vaccine RNA has specific sequences that may induce TDP-43 and FUS to fold into their pathologic prion conformations. In the current analysis a total of sixteen UG tandem repeats (ΨGΨG) were identified and additional UG (ΨG) rich sequences were identified. Two GGΨA sequences were found. Potential G Quadruplex sequences are possibly present but a more sophisticated computer program is needed to verify these. Furthermore, the spike protein, created by the translation of the vaccine RNA, binds angiotensin converting enzyme 2 (ACE2), a zinc containing enzyme. This interaction has the potential to increase intracellular zinc. Zinc ions have been shown to cause the transformation of TDP-43 to its pathologic prion configuration. The folding of TDP-43 and FUS into their pathologic prion conformations is known to cause ALS, front temporal lobar degeneration, Alzheimer’s disease and other neurological degenerative diseases. The enclosed finding as well as additional potential risks leads the author to believe that regulatory approval of the RNA based vaccines for SARS-CoV-2 was premature and that the vaccine may cause much more harm than benefit.

Keywords
COVID-19, Vaccines, Diabetes, Immunity.

Introduction
Vaccines have been found to cause a host of chronic, late developing adverse events. Some adverse events like type 1 diabetes may not occur until 3-4 years after a vaccine is administered [1]. In the example of type 1 diabetes the frequency of cases of adverse events may surpass the frequency of cases of severe infectious disease the vaccine was designed to prevent. Given that type 1 diabetes is only one of many immune mediated diseases potentially caused by vaccines, chronic late occurring adverse events are a serious public health issue.

The advent of new vaccine technology creates new potential mechanisms of vaccine adverse events. For example, the first killed polio vaccine actually caused polio in recipients because the up scaled manufacturing process did not effectively kill the polio virus before it was injected into patients. RNA based vaccines offers special risks of inducing specific adverse events. One such potential adverse event is prion based diseases caused by activation of intrinsic proteins to form prions. A wealth of knowledge has been published on a class of RNA binding proteins shown to participating in causing a number of neurological diseases including Alzheimer’s disease and ALS. TDP-43 and FUS are among the best studied of these proteins [2].

The Pfizer RNA based COVID-19 vaccine was approved by the US FDA under an emergency use authorization without long term safety data. Because of concerns about the safety of this vaccine a study was performed to determine if the vaccine could potentially induce prion based disease.

Methods
Pfizer’s RNA based vaccine against COVID-19 was evaluated for the potential to convert TDP-43 and or FUS to their prion based
information pertaining to construction of nuclear bombs. In the past, for example, there were prohibitions for publishing without national/international oversight is also a concern. and Melinda Gates Foundation, and Ellison Medical Foundation The fact that this research, which could be used for bioweapons FUS and others can be activated to form disease causing prions. mechanisms by which certain RNA binding proteins like TDP-43, origins due to potential for misuse of research data on the disease, ALS and other neurodegenerative diseases. This concern originates due to potential for misuse of research data on the mechanisms by which certain RNA binding proteins like TDP-43, FUS and others can be activated to form disease causing prions. The fact that this research, which could be used for bioweapons development, is funded by private organizations including the Bill and Melinda Gates Foundation, and Ellison Medical Foundation [2] without national/international oversight is also a concern. In the past, for example, there were prohibitions for publishing information pertaining to construction of nuclear bombs.

Results

Analysis of the Pfizer vaccine against COVID-19 identified two potential risk factors for inducing prion disease is humans. The RNA sequence in the vaccine [3] contains sequences believed to induce TDP-43 and FUS to aggregate in their prion based conformation leading to the development of common neurodegenerative diseases. In particular it has been shown that RNA sequences GGUA [4], UG rich sequences [5], UG tandem repeats [6], and G Quadruplex sequences [7], have increased affinity to bind TDP-43 and or FUS and may cause TDP-43 or FUS to take their pathologic configurations in the cytoplasm. In the current analysis a total of sixteen UG tandem repeats (ΨGΨG) were identified and additional UG (ΨG) rich sequences were identified. Two GGΨA sequences were found. G Quadruplex sequences are possibly present but sophisticated computer programs are needed to verify these.

The spike protein encoded by the vaccine binds angiotensin converting enzyme 2 (ACE2), an enzyme which contains zinc molecules [8]. The binding of spike protein to ACE2 has the potential to release the zinc molecule, an ion that causes TDP-43 to assume its pathologic prion transformation [9].

Discussion

There is an old saying in medicine that “the cure may be worse than the disease.” The phrase can be applied to vaccines. In the current paper the concern is raised that the RNA based COVID-19 vaccines have the potential to cause more disease than the epidemic of COVID-19. This paper focuses on a novel potential adverse event mechanism causing prion disease which could be even more common and debilitating than the viral infection the vaccine is designed to prevent. While this paper focuses on one potential adverse event there are multiple other potential fatal adverse events as discussed below.

Over the last two decades there has been a concern among certain scientists that prions could be used as bioweapons. More recently there has been a concern that ubiquitous intracellular molecules could be activated to cause prion disease including Alzheimer’s disease, ALS and other neurodegenerative diseases. This concern originates due to potential for misuse of research data on the mechanisms by which certain RNA binding proteins like TDP-43, FUS and other RNA sequences capable of causing TDP-43 and FUS to assume toxic configurations. Published data has shown that there are several different factors that can contribute to the conversion of certain RNA binding proteins including TDP-43, FUS and related molecules to their pathologic states. These RNA binding proteins have many functions and are found in both the nucleus and the cytoplasm. These binding proteins have amino acid regions, binding motifs that bind specific RNA sequences. Binding to certain RNA sequences when the proteins are in the cytoplasm is believed to causes the molecules to fold in certain ways leading to pathologic aggregation and prion formation in the cytoplasm [2]. The current analysis indicates Pfizer's RNA based COVID-19 vaccine contains many of these RNA sequences that have been shown to have high affinity for TDP-43 or FUS and have the potential to induce chronic degenerative neurological diseases.

Zinc binding to the RNA recognition motif of TDP-43 is another mechanism leading to formation of amyloid like aggregations [9]. The viral spike protein, coded by the vaccine RNA sequence, binds ACE2 an enzyme containing zinc molecules [8]. This interaction has the potential to increase intracellular zinc levels leading to prion disease. The initial binding could be between spike proteins on the surface of the cell transfected by the vaccine and ACE2 on the surface of an adjacent cell. The resulting complex may become internalized. Alternatively, the interaction could initially take place in the cytoplasm of a cell that makes ACE2 and has been transfected with the vaccine RNA coding for the spike protein. The interaction is quite concerning given the belief that the virus causing COVID-19, SARS-CoV-2, is a bioweapon [10,11] and it is possible that the viral spike protein may have been designed to cause prion disease.

Another related concern is that the Pfizer vaccine uses a unique RNA nucleoside 1-methyl-3'-pseudouridylyl (Ψ). According to FDA briefing documents, this nucleoside was chosen to reduce activation of the innate immune system [12]. RNA molecules containing this nucleoside will undoubtedly have altered binding [13]. Unfortunately, the effect on TDP-43, FUS and other RNA binding proteins is not published. The use of this nucleoside in a vaccine can potentially enhance the binding affinity of RNA sequences capable of causing TDP-43 and FUS to assume toxic configurations.

There are many other potential adverse events that can be induced by the novel RNA based vaccines against COVID-19. The vaccine places a novel molecule, spike protein, in/on the surface of host cells. This spike protein is a potential receptor for another possibly novel infectious agent. If those who argue that the COVID-19 is actually a bioweapon are correct, then a second potentially more dangerous virus may be released that binds spike protein found on the host cells of vaccine recipients. Data is not publicly available to provide information on how long the vaccine RNA is translated in the vaccine recipient and how long after translation the spike protein will be present in the recipient’s cells. Such studies pertaining to in vivo expression will be complex and challenging. Genetic diversity protects species from mass casualties caused by infectious agents. One individual may be killed by a virus while
another may have no ill effects from the same virus. By placing the identical receptor, the spike protein, on cells of everyone in a population, the genetic diversity for at least one potential receptor disappears. Everyone in the population now becomes potentially susceptible to binding with the same infectious agent.

Autoimmunity and the opposing condition, metabolic syndrome, are well known adverse events caused by vaccines [14]. COVID-19 infections are associated with the induction of autoantibodies and autoimmune disease [15,16] making it more than plausible a vaccine could do the same. One author has found amino acid sequences coded by the spike protein to be identical to sequences in human proteins including proteins found in the CNS [17]. Autoimmunity can also be induced by epitope spreading when a foreign antigen, like the spike protein, is presented by an antigen presenting cell that also has self molecules attached to its MHC molecules.

Finally, others working in the field have published additional support that COVID-19 vaccines could potentially induce prion disease. Authors [18] found prion related sequences in the COVID-19 spike protein which were not found in related coronaviruses. Others [19] have reported a case of prion disease, Creutzfeldt-Jakob disease, initially occurring in a man with COVID-19.

Many have raised the warning that the current epidemic of COVID-19 is actually the result of an bioweapons attack released in part by individuals in the United States government [10,11]. Such a theory is not far fetched given that the 2001 anthrax attack in the US originated at Fort Detrick, a US army bioweapon facility. Because the FBI’s anthrax investigation was closed against the advice of the lead FBI agent in the case, there are likely conspirators still working in the US government. In such a scenario the primary focus of stopping a bioweapons attack must be to apprehend the conspirators or the attacks will never cease. Approving a vaccine, utilizing novel RNA technology without extensive testing is extremely dangerous. The vaccine could be a bioweapon and even more dangerous than the original infection.

References
1. Classen JB, Classen DC. Clustering of cases of insulin dependent diabetes (IDDM) occurring three years after Hemophilus influenza B (HiB) immunization support causal relationship between immunization and IDDM. Autoimmunity. 2002; 35: 247-253.
2. King OD, Gitler AD, Shorter J. The tip of the iceberg: RNA-binding proteins with prion-like domains in neurodegenerative disease. Brain Res. 2012; 1462: 61-80.
3. WHO, International Non Proprietary Names Program: 11889. 9/2020.
4. Kapeli K, Pratt GA, Vu AQ, et al. Distinct and shared functions of ALS-associated proteins TDP-43, FUS and TAF15 revealed by multisystem analyses. Nature Communications. 2016; 7: 12143.
5. Kuo P, Chiang C, Wang Y, et al. The crystal structure of TDP-43 RRM1-DNA complex reveals the specific recognition for UG- and TG-rich nucleic acids. Nucleic Acids Research. 2014; 42: 4712-4722.
6. Tollervey JR, Curt T, Rogelj B, et al. Characterizing the RNA targets and position-dependent splicing regulation by TDP-43; implications for neurodegenerative diseases. Nat Neurosci. 2011; 14: 452-458.
7. Imperatore JA, McAninch DS, Valdez-Simon AN, et al. FUS recognizes G quadruplex structures within neuronal mRNAs. Frontiers in Molecular Biosciences. 2020; 7: 6.
8. Shang J, Ye G, Shi K, et al. Structural basis of receptor recognition by SARS-CoV-2. Nature. 2020; 581: 221-225.
9. Garnier C, Devred F, Byrne D, et al. Zinc binding to RNA recognition motif of TDP-43 induces the formation of amyloid-like aggregates. Sci Rep. 2017; 7: 6812.
10. Classen JB. COVID-19, MMR vaccine, and bioweapons. Diabetes & its Complications.2020; 4: 1-8.
11. Classen JB. Evidence supporting the hypothesis that the 2019 epidemic of E-vaping acute lung injury (EVALI) was caused in part by COVID-19. Diabetes & Complications. 2020; 4: 1-2.
12. Pfizer-Biotech: COVID-19 Vaccine (BNT162, PF-07302048), Vaccines and Related Biological Products Advisory Committee Briefing Document. Meeting Date: 10 December 2020.
13. Roundtree IA, Evans ME, Pan, et al. Dynamic RNA modifications in gene expression regulation. Cell. 2017; 169: 1187-1200.
14. Classen JB. Review of Vaccine Induced Immune Overload and the Resulting Epidemics of Type 1 Diabetes and Metabolic Syndrome, Emphasis on Explaining the Recent accelerations in the Risk of Prediabetes and other Immune Mediated Diseases. J Mol Genet Med. 2014; S1: 025.
15. Amiral J. Can COVID-19 Induce an autoimmune disease associated with long- lasting symptoms and delayed complications? Ann Clin Immunol Microbiol. 2020; 2: 1014.
16. Wang YE, Mao T, Klein J, et al. Diverse functional autoantibodies in patients with COVID-19. medRxiv preprint. 2020.
17. Lyons-Weiler J. Pathogenic priming likely contributes to serious and critical illness and mortality in COVID-19 via autoimmunity. Journal of Translational Autoimmunity. 2020; 3: 100051.
18. Tetz G, Tetz V. SARS-CoV-2 prion-like domains in spike proteins enable higher affinity to ACE2. Preprint. 2020.
19. Young MJ, O’Hare M, Mattiello M, et al. Creutzfeldt-Jakob disease in a man with COVID-19: SARS-CoV-2-accelerated neuro degeneration? Brain, Behavior, and Immunity. 2020; 89: 601-603.