The Ideal SARS-CoV-2 Vaccine

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Abstract

It is of concern that major vaccine developers are targeting spike (S)—the most mutation-prone region of SARS-CoV-2. By the end of April 2020, at least 14 circulating mutations had been identified, with all of them occurring in S. Variants of Concern (VOC) including B.1.1.7 (United Kingdom), B.1.351 (South Africa), P.1 (Brazil), and B.1.617 (India) have concurrently arisen during vaccine development and roll out. While some may affect infectivity, preliminary evidence suggests that some may affect vaccine efficacy as the VOCs involve mutations within S. Indeed, there is already work being conducted on so-called "boosters" to provide additional immunization to these variants. It is of great concern that a VOC with a high level of resistance to vaccination-induced immunity will arise before a "booster" can be developed and distributed to counter it. It is felt that the only logical way to solve the SARS-CoV-2 problem via vaccination without risking an escape mutation is via a multiepitope approach. Sera from recovered patients demonstrates that there are other logical targets to utilize. Bioinformatics approaches have predicted B- and T-cell epitopes of interest and suggest potential concomitant sequences for vaccination targets. A comparison of sequences yielded by bioinformatics approaches and those occurring in recovered patients can help in finding the correct targets. The suggested ideal vaccine would be a mixture of several peptides chosen from these approaches which have been modified such as by fusion to TAT sequence. The positive charge would allow for fused protein antigen to improve cell penetration or polymers for endolysosomal or cytosolic delivery—like polyprolyl acrylic acid for instance. To render the mixture immunogenic, older adjuvants such as alum would have to be waived and rather specific toll-like-receptor (TLR) recognition would be utilized. One such way would be triggering of TLR3 since SARS-CoV-2 is an RNA virus and it is also the natural mode of activation. One possible way to achieve this is to couple poly(I:C) to the other end of the peptide or formulating the mixture with poly(I:C). The mucosal immune system would be the ideal target rather than intramuscularly or subcutaneously. Lastly, it is felt that nasal administration would be most advantageous.

Biography:

After obtaining his Ph.D. in Cancer Biology, Scott conducted a Postdoctoral Fellowship at the Moffitt Cancer Center and was subsequently accepted into the highly competitive FDA Commissioner's Fellowship Program where he worked in the Office of Orphan Products Development (OOPD) and published a paper in Cell Stem Cell. During the Fellowship, Scott was hired into OOPD at the FDA where he remained until relocation to the Boston area. After relocation, Scott has served various roles in regulatory affairs, intelligence, and research in both consulting and the biopharmaceutical industry. He has multiple peer-reviewed publications including a book chapter on orphan drug development in FDA Regulatory Affairs, 3rd Ed. His interest in SARS-CoV-2 was piqued upon reconnecting with a friend who is an immunologist from his days as a Postdoctoral Fellow who he has co-authored a manuscript with entitled "A new vaccine approach and convalescent plasma until its development."

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