Can ChAdOx1, a replication-deficient adenoviral (Ad) vector used to deliver SARS-Cov2 spike protein as a vaccine, recombine with the homologous human Ad to generate a novel Ad+Spike virus?

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Letter

The development of a vaccine for Covid19 is being expedited [1]. The underlying technology for the vaccines are varied: 'nucleic acid (DNA and RNA), virus-like particle, peptide, viral vector (replicating and non-replicating), recombinant protein, live attenuated virus and inactivated virus' [2]. Among these, ChAdOx1, a genetically modified, weakened version of a common cold virus (adenovirus) is now in human clinical trials [3]. The ChAd vector (Chimpanzee adenovirus) was introduced in 2012 Chimpanzee adenovirus Y25 [4]. A large proportion of human adults possess significant titres of neutralising antibodies to human Adv, hence the requirement for a different adenovirus. The deletion of a single transcriptional unit, E1, ensures these viruses cant replicate. Other genes like the E3 region may also be deleted. Now, in the Covid19 vaccine ChAdOx1, the spike protein gene from MERS-CoV strain Camel/Qatar/2/2014 'was inserted into the E1 locus of a genomic clone of ChAdOx1 using site-specific recombination' [5].

One of the theories about the genesis of SARS-Cov2 is recombination with coronaviruses from pangolins [6]. Whether or not it happened in SARS-Cov2, there is no denying that such recombinations do happen.

How do we know that the spike protein wont be inserted into a human adenovirus using recombination?

Human adenovirus shares 95% homology to ChAd. The spike protein may be inserted after the E1 protein in a viable human virus. What will happen after that to the virus is anyone's guess. Note, that there is precedence for such recombinant adenoviruses - using 'ping-pong' zoonosis and anthroponosis', where the genome of a promiscuous pathogen is 'embedded with evidence of unprecedented multiple, multidirectional, stable, and reciprocal cross-species infections of hosts from three species (human, chimpanzee, and bonobo)' [7].

Another critique - co-stimulation in host cells

A spike protein from SARS-Cov2, which is supposed to bind to ACE2 and CD147 [8], has been inserted in an adenovirus. The adenovirus has its own host-cell receptor preferences [9] - what will be the consequences of co-stimulation in those cells in which both these receptors are expressed?

References

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