

Review of: "The COVID 19 vaccine patent race"

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Referee report on "The COVID 19 vaccine patent race"

This manuscript adds insights to how firms and laboratories positioned themselves before and during the race for the vaccine. We have seen numerous genealogies of this fight for resources, yet what makes this paper interesting is the focus on patents. In view of this here are some comments from someone who reads patents but has only a minor understanding of biology. My comments will focus in trying to understand who controls what.

To start with, despite numerous little typos (too many to record), I liked reading this and found that it enhanced my understanding of what went on. There are few parts of the paper that need improvement.

Page 2 firsts para: *"A variant thereof, 1-methyl pseudouridine ("m1Ψ") was later developed by Jason Schrum (but already anticipated in Kariko's and Weissmann's respective patent US8278036)"* I glanced through the patent, but lacking a background in biology I was not certain what is meant by "anticipated in the patent". It seems to me the patent was too broad referring in most claims to pseudouridine. If this is true and the patent is indeed broad it is worth mentioning. Next para talks about Pieter Cullis and the invention of LLPs. A quick patent search finds two patents on this, one filed in Japan and one in Australia. The 2014 patent from Japan seems to be the most relevant here. Yet, a patent filed just in Japan means that the inventors did not consider this idea to be of value, or, most likely, that they did not patent the core idea. Again, this has implications over who owns what.

Page 3 first para: "The group applied this approach to different coronavirus which were known at that time, including SARS, where the two substitutions are K968P and V969P, and filed a patent application on 25.10.2016 (US2020061185A1 and family members)." Looking at the legal events of this patent the owner seems to be THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES, MARYLAND. So it seems the US government is a key patent holder.

Page 3 third para: *"NIH received granted patents inter alia in the US and Europe, with claims related to a recombinant coronavirus protein comprising one or two proline substitutions near a junction between HRI and a central helix. Hence, even though the underlying application was filed before SARS CoV 2 entered the stage, the claims encompass also a SARS CoV 2 vaccines having the 2P mutation in that region."* It is not clear from this statement that the said patents refer to US2020061185A1 and family members.

Page 4 second para: *"Next to Moderna and BioNTech, also CureVac started to develop an mRNA vaccine. What then happened is quite unique: A patent search[12] using the 1273 amino acid long spike protein, plus the substitutions K986P and V987P (the latter derived by analogy from the corresponding 2P mutant of the SARS CoV spike protein as disclosed by the NIH group), revealed that within weeks after the publication of the SARS CoV 2 genome, companies filed patent applications disclosing or claiming said SARS CoV2 spike protein 2P mutant. Obviously, all applicants, – like the author of this article –had gone through the same exercise of combining the sequence of the SARS CoV 2 spike protein with the findings of the NIH group."* It would be nice to have a list of the companies and various actors who filed for a patent. I suspect they are more than the ones included in the remaining of the paper.

Page 5 is where the main add on of the paper rests. This discussion is very interesting indeed. Yet, unless one understands both patent drafting and biology it is impossible to fully understand the issues involved. I think that the paper would significantly benefit if this page was rewritten having a layman in mind.

Page 6 last para: *"This could lead to something that no one would have expected – namely, that, as a consequence of the seemingly simple modular technology for making new mRNA vaccines, industry will refrain from investing money therein - and that might lead to a decrease in numbers of new vaccines."* The technology is not only protected by patents. The main knowhow is protected by trade secrets. It would be lovely if there was some mention about what goes on in terms of such know how. In terms of production that is where the juice is. The same maybe true regarding data bases. Are there any key data bases that agents control?