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Profile

Sarah Gilbert: carving a path towards a COVID-19 vaccine

It was the news from Wuhan, China, in the first days of 2020 that made Sarah Gilbert sit up and think. As Professor of Vaccinology at the University of Oxford in the UK, and a leading scientist at the university's Jenner Institute, her research team wasted no time in getting involved. "We had recently started thinking about an appropriate response to Disease X; how could we mobilise and focus our resources to go more quickly than we had ever gone before. And then Disease X arrived", she says. Once the genome sequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became available in mid-January, Gilbert's team set to work to design a vaccine, using recombinant DNA techniques to create a SARS-CoV-2 antigen and embedding it within a primate adenovirus vector. "At this point it all felt quite theoretical, our goal then being to design a vaccine and to have a paper published showing what was possible in terms of a rapid response to an unknown outbreak, using our adenoviral vectored vaccine technology", she says.

Gilbert's team was awarded a £2.2 million grant from the UK's National Institute for Health Research and the UK Research and Innovation in March, 2020, to scale up her team's efforts to move into coronavirus disease 2019 (COVID-19) vaccine preclinical and clinical trials. "The way various grants have been awarded to different strategic aspects of the project is important, as much of the work can go on in parallel—for example, my colleague Sandy Douglas has received funding for work on scaling up vaccine manufacturing processes at the same time as we are progressing work in developing trials", she says. Preclinical work at Public Health England's Porton Down facility is the immediate priority, complementing parallel initiatives taking place at the US National Institutes of Health and at the Commonwealth Scientific and Industrial Research Organisation in Australia, among others. Gilbert's team has received ethical approval for a clinical trial, and conditional approval from the UK Medicines and Healthcare products Regulatory Agency to screen volunteers for trial enrolment. Another reason for speed is for her team to assess the efficacy of a vaccine in volunteers who have not yet been infected. "Ideally, we need the clinical trial to be taking place when the majority of volunteers have not been exposed to the virus. We will exclude volunteers who have a positive PCR test for SARS-CoV-2, or who have had fever or cough in the past month. Some will inevitably have been exposed, and that is useful too, as we want to know what the vaccine means for people who have been exposed to the coronavirus", she says.

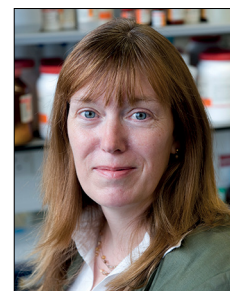
Gilbert's early vaccine work at the University of Oxford started in 1994 with Adrian Hill, who today is Director of the Jenner Institute, with a focus on malaria vaccine research, and, given her particular interest in cellular immunology, the importance of T-cell responses to parasite infection.

"From what we were seeing in malaria endemic regions, individuals with a specific HLA type did much better after becoming infected with malaria than others with different HLA profiles. This led us to look at creating vaccine candidates that could trigger favourable T-cell responses, rather than relying solely on antibody responses, the prevailing vaccine model at that time", she explains. This approach coincided with advancements in recombinant DNA techniques, with vaccinologists being able to generate specific antigens that could be safely incorporated in a host virus, as an alternative to the risks associated with using live attenuated vaccines. The ability to create recombinant viral vector vaccines is a core function of Gilbert's research group at the Jenner Institute, which over the past few years has progressed work on many vaccines, including those for influenza and Zika virus and early stage trials for Middle East respiratory syndrome coronavirus vaccine, a helpful template for the work on a COVID-19 vaccine. As Chair of the management committee that oversees initial vaccine production within the University of Oxford, Gilbert and colleagues have suspended all other concurrent vaccine research to prioritise efforts on COVID-19.

Gilbert is understandably cautious when asked to map out a timetable for the trial, but hopes to have vaccinated 500 volunteers by mid-May; this will be followed by an extension of the maximum age of trial volunteers from 55 to 70 years, later moving on to the over-70 age group. Phase 3 expansion is expected to involve 5000 volunteers; results from the earlier trials will be included in the efficacy follow-up. "The best-case scenario is that by the autumn of 2020, we have an efficacy result from phase 3 and the ability to manufacture large amounts of the vaccine, but these best-case timeframes are highly ambitious and subject to change", Gilbert says. "Our ability to determine vaccine efficacy will be affected by the amount of virus transmission in the local population over the summer, and we are also beginning to think about initiating trials with partners in other countries to increase our ability to determine vaccine efficacy", she says.

Sharing knowledge with parallel COVID-19 vaccine efforts worldwide is crucial. "WHO is in the process of creating a forum for everyone who is developing COVID-19 vaccines to come together and present their plans and initial findings. It is essential that we all measure immunological responses to the various vaccines in the same way, to ensure comparability and generalisability of our collective findings. Work is continuing at a very fast pace, and I am in no doubt that we will see an unprecedented spirit of collaboration and cooperation, convened by WHO, as we move towards a shared global goal of COVID-19 prevention through vaccination", Gilbert says.

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