Vaccinating against Covid-19: the quest for the Grail?

Press release of the French National Academy of Medicine

June 10, 2020

The first coronavirus pandemic, Covid-19 is a reminder to the international scientific community that it has never, to date, been able to develop vaccines against human Coronaviridae infections despite two recent alerts: the emergence of SARS-CoV-1 in 2002 and that of MERS-CoV in 2010. The only existing coronavirus vaccines have been developed in the veterinary field, mostly in the form of live attenuated vaccines, and have a limited effectiveness. The catastrophic effects of the current pandemic on global health and the world economy, the lack of any available antiviral treatment and the prospect of the likely persistence of MERS-CoV-2 in the future years make it more necessary than ever to develop an effective human vaccine, the only way to prevent infection and control its spread.

To date, more than 120 candidate vaccines are being developed by research teams from pharmaceutical companies and universities around the world, many of which having already reached clinical trials.

Even by shortening as much as possible the time required to develop a vaccine, generally estimated to be between 8 and 12 years, the most optimistic forecasts envisage a minimum time frame of 12 to 18 months for the development of a first vaccine against Covid-19, which will most likely exceed the end of the epidemic.

However, this optimism should be tempered in light of the many obstacles to overcome in developing such a vaccine:

- While the elimination of CoV-2-SARS appears to require a cellular and humoral response, the correlates of immune protection are not yet well established and the duration of protective immunity conferred by natural infection is not known;

- Animal models are quantitatively limited, both transgenic mice carrying the ACE2 receptor as ferrets and monkeys (rhesus and cynomolgus);

- The risk of initiating an immunopathological response by production of facilitating antibodies, observed in preclinical SARS and MERS vaccine trials using the whole S (spike) protein, should not be overlooked.

A good SARS-CoV-2 vaccine should ideally stimulate both cellular immunity for local protection (mucosal IgA) and humoral immunity for general protection (neutralizing IgM and IgG), while avoiding the appearance of facilitating antibodies.

The current preferred strategy is to obtain neutralizing antibodies by different processes: (i) attenuated or inactivated whole viruses; (ii) genetically modified non-replicative viral vectors (adenovirus, vaccinia) or replicative (amaril virus, attenuated influenza virus, measles vaccine) viral vectors; (iii) vaccine subunits obtained by genetic recombination; (iv) nucleic acids, DNA and messenger RNA.

Given the uncertainties about the forthcoming availability of a Covid-19 vaccine, the National Academy of Medicine recommends:

- to promote international coordination of vaccine research by encouraging teams involved in the development of a Covid-19 vaccine to share information on protective correlates, preclinical models, in order to reduce preclinical delays, and to plan collaborative vaccine trials;
- to facilitate early and frequent “contacts” with regulatory authorities in order to develop a harmonized consensus on vaccine design and the prerequisites for vaccine development and registration;
- to ensure that global funding for the development of a Covid-19 vaccine focuses on the goal of equitable global access to the vaccine;
- to master communication on the development and implementation of candidate vaccines by avoiding any premature statements that could raise false hopes in the general public;
- to maintain and strengthen barrier measures, currently the only available and proven effective means, as long as the circulation of SARS-CoV-2 in the population is not interrupted.