# A major boost for HIV vaccine identification and development

Failure to develop an HIV vaccine so far calls for a change of tune. EAVI2020 aims to accelerate development thanks to a platform dedicated to the discovery of new vaccine candidates. In its efforts, it even brought nine promising candidates to clinical evaluation.

HEALTH

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The worldwide push for a COVID-19 vaccine can't make us forget about 30 years of efforts to identify one for HIV. Since 2015, some of the most competitive research groups in Europe have been working together to speed up the process and increase the chances of success.

Robin Shattock, chair in Mucosal Infection and Immunity at Imperial College London, leads one of these research groups under the EAVI2020 (European AIDS Vaccine Initiative 2020) project. The project's prototype RNA vaccines not only show promise for HIV treatment: they also have had a positive impact on vaccine development for COVID-19.

We spoke with Shattock to discuss the project's continued importance and achievements so far.

## A vaccine for HIV-1 has yet to be discovered, despite decades of research. How would you explain this?

Robin Shattock: There is no shortcut to an effective HIV vaccine, and it would be easy to underestimate what needs to be achieved to get there. We are talking about

one of the biggest biological challenges of a generation. It is predicated on international cooperation and real commitment.

The biggest hurdle is the development of a single vaccine that can prevent infection from the wide range of circulating HIV strains. To make things worse, HIV can persist in infected individuals and nobody has ever been cured through a natural immune response. This contrasts greatly with COVID-19, which is currently driven by a single viral isolate showing minimal diversity and where the majority of individuals naturally recover from infection and eliminate the virus. In short, an HIV vaccine would be unlike any vaccine previously developed against infectious threats.

## How can the EAVI2020 approach facilitate a breakthrough?

We have been actively developing a portfolio of vaccine candidates. These can be used both to understand human response to a diversity of HIV immunogens, and to maximise immune response to the widest range of viral isolates. Besides, we are developing a combination-vaccine approach. It can generate neutralising antibodies able to inactivate a virus before it invades target cells, along with cellular responses able to eliminate infected cells where the virus may have evaded destruction by antibodies.

This double line of defence not only offers the best potential to prevent infection, but it may also be effective in treating patients already infected. Our goal is to test both concepts through human clinical evaluation.

## What are the most important outcomes of the project so far?

At the outset of the project, we were highly ambitious. We planned to bring up to 10 new stabilised envelope trimers through preclinical development, and up to eight to good manufacturing practices (GMPs). This had never been attempted in other programmes of this size and scope.

We are now happy to report that we have exceeded expectations. We have nine envelope products destined for the clinic. In parallel, we have brought two complex T-cell vaccines to the point where they are ready for clinical evaluation in HIV-positive and -negative subjects. This provides us with a unique and unprecedented portfolio of vaccine candidates. This is simply unrivalled in an international setting.

## What would you consider as the most promising candidate you identified and why?

One of the major challenges in developing an effective HIV vaccine is to provide protection against the enormous diversity of circulating strains. In this context, we are not anticipating a single vaccine candidate as being appropriate to move forward. Our approach is rather to develop a combination vaccine. The latter would contain a minimal set of HIV envelope proteins to provide a diverse antibody response, as well as T-cell immunogens to engage both antibody and cellular arms of the immune response. We are still at an early stage of clinical assessment, but we are encouraged by data generated in our preclinical models.

## What were the main difficulties you faced and how did you overcome them?

The major difficulty has been the COVID-19 pandemic. A number of our clinical trials were put on hold as countries and clinical centres prioritised their response to COVID-19. In addition, all research centres were closed to all non-essential work and most research staff were reassigned to support COVID-related efforts in laboratory diagnosis and vaccine development.

Many of the technologies developed within the EAVI2020 project have actually been applied to vaccine development and isolation of therapeutic antibodies. The EAVI2020 HIV vaccine clinical trials are now being reinitiated, and all supporting research laboratories are back to working at full capacity. Project delays have been factored into the project and timelines adjusted, and approvals for no-cost extensions to complete the work have been favourably received by the Commission. We will continue to monitor the impact of COVID-19 on the programme along with the impact of a potential second wave.

## What do you still need to achieve before the end of the project?

As we move into the final phase of the project, we are well-positioned to provide a unique set of clinical trials that will generate critical information. We need to ensure that investment in the development of our novel vaccine candidates is maximised by completing the wide range of clinical trials and associated immunological assessments. With these, we can select clinical candidates for efficacy studies. We can also feed back into the evaluation of preclinical assessment, to understand how to better use these models in the future.

## Based on project outcomes, how close would you say we are to seeing a working vaccine?

The EAVI2020 project continues to provide a unique and key contribution to international HIV vaccine efforts. We are trailblazing the rapid testing of novel vaccines in humans.

During the course of the project, it has become increasingly clear that the study of human responses to vaccination may prove critical, whereas animal studies have not proved predictive. The EAVI2020 project is setting a new international benchmark for what can be achieved. Our hope and vision is that clinical evaluation of the vaccine candidates in our portfolio will drive and inform large-scale efficacy testing through international agencies including the European and Developing Countries Clinical Trials Partnership.

## Keywords

EAVI2020, HIV, COVID-19, coronavirus, AIDS

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