AN AUDIENCE WITH…

Wayne Koff

The success rate for vaccines is even lower than for biopharmaceutical drugs, by some accounts. In an attempt to turn things around and address long-standing vaccinology problems, Wayne Koff, Chief Scientific Officer at the International AIDS Vaccine Initiative (IAVI), and colleagues proposed a Human Vaccines Project in 2013. Top vaccinologists met to outline a scientific approach and business strategy in 2014, and the Human Vaccines Project could now launch by this summer, Koff tells **Asher Mullard**.

When and why did you start thinking about the Human Vaccines Project?

In 2009, we began to get a series of data that created a renaissance around the development of an HIV vaccine, mainly around the identification of broadly neutralizing antibodies in HIV-infected individuals. That was the good news. The bad news was that as we began to make immunogens to elicit these neutralizing antibodies we learned that we didn't quite understand their evolution in people.

When we started looking across the vaccine field, we noted a number of common scientific impediments to vaccine development. We don't understand how to elicit specific immune responses in humans, whether it be the generation of broadly neutralizing antibodies, epitope-specific cellular immune responses, or site-specific responses. Or, why do some vaccines such as the small-pox vaccine provide long-term protection, while others provide only weeks of durability of antibody response? Another commonality was the large number of vaccines for infectious diseases and cancers that had failed in efficacy trials during the past decade. That got a number of us thinking: is there a better way of doing this?

Many of these questions have been plaguing the field for years. Why only address them now?

We couldn't have done this a decade ago. The reason we proposed this now is really because we've had a series of technological advances in antigen discovery, adjuvant discovery, vector delivery, genomics and other 'omics, and in monitoring systems immunology. We now have a tool-kit at our disposal that we can use to really probe the human immune system.

The other reason why a concept like this had never been undertaken is that we haven't had the immunogens that we've needed to test different hypotheses in humans. When we brought 35 leading vaccinologists together last February, we had universal endorsement that, if the resources were available to make the reagents that are needed to approach these 'transvaccinology' questions, this project had the potential to now greatly accelerate vaccine development.

What are your scientific priorities?

Our scientific plan is based on two interrelated issues. One, we need to decipher the human immunome just like the Human Genome Project deciphered the human genome. We don't have a catalogue right now of the naive immunological repertoire. Related to this, we don't have a catalogue of the human peptidome. What are the peptides that are expressed on the outside of infected or neoplastic cells that could be targets for our immune system? These catalogues will greatly facilitate rational vaccine discovery.

The other piece of the puzzle is the large numbers of small iterative clinical trials that need to be done to pose and answer transvaccinology questions. So, for example, the pertussis vaccine has a durability problem. Small trials of the licensed pertussis vaccine with different novel adjuvants or delivery systems will help us to improve and understand the durability of the response. Alternatively, the rotavirus vaccine is only moderately effective in the developing world, where it is needed, but is wonderful in Scandinavia, where it is needed less. There are some ongoing studies of this already, but the project would aim to bring considerably greater resources to accelerate solutions to this and related transvaccinology problems. Iterative trials could also help us to understand why influenza vaccines are pretty weak in the elderly.

If successful, the project aims to: improve the efficacy rates of licensed vaccines; accelerate the development of new and improved vaccines; and, this is really longer-term, redefine the whole licensure of vaccines by identifying novel markers for safety and efficacy. We want to get away from the 100,000-person efficacy trials that follow a couple of safety and efficacy markers, and maybe move towards a future where you could run a 1,000-person trial that follows 1,000 markers.

How much will this cost?

The minimum estimate was US$1 billion over a decade. It will probably need even more, but a billion is a good start. To give you a sense of what this means, at IAVI we've raised about $850 million in the HIV-vaccine space in about 15 years. The money will come from across the board on the spectrum of donors, including research agencies, development agencies, companies and corporate partners, and high net-worth individuals. I am great believer that if the scientific plan is clear enough and endorsed by the key stakeholders, then the money will be raised.

Also, we'll soon be announcing support from the first of what we think will be a number of the vaccine companies who will support the project. We've reached out to all of the vaccine companies. To me, the Human Vaccines Project will not be successful unless the vaccine companies are sitting around the table and are actively engaged. They have a large number of immunogens already available for human testing, and other key reagents to help address the key problems impeding vaccine development. At the end of the day, these are the companies that are going to make the vaccines.