Correlates of protection and HIV vaccine development

When used consistently, condoms can prevent almost 100% of HIV infections, but the many challenges associated with condom use mean they cannot be relied on for 100% prevention. For HIV prevention, an effective vaccine remains the “holy grail”, according to Barton Haynes (Duke Human Vaccine Institute, Durham, NC, USA) as he addressed the AIDS Vaccine Conference, Bangkok, Thailand, Sept 12–15, 2011.

Understanding which immune responses correlate with protection against HIV has remained an elusive impediment to vaccine development, and vaccines have largely been designed as best guesses. At the conference, Haynes presented the finding of antibody correlates of protection from the RV144 vaccine trial. Increasing titres of IgG antibodies and decreasing titres of IgA antibodies were correlated with protection; but Haynes says he “was surprised that the avidity didn’t correlate because it has correlated in other vaccine trials”. Jerome Kim (Walter Reed Army Institute of Research, Silver Spring, MD, USA) as he addressed the AIDS Vaccine Conference, Bangkok, Thailand, Sept 12–15, 2011.

A broadly active cellular response after HIV infection can slow progression to disease, and HIV vaccine design has focused on such responses to vaccines. For RV144, says Haynes, “there weren’t any real CD8 responses…induced by this vaccine, in contrast to the STEP trial where it was mostly CD8. This trial induced mostly CD4”. Reflecting on a possible change in focus from cellular to humoral responses for vaccine design, Haynes adds, “the immune system has evolved to work together. [An effective vaccine is] probably going to include cellular as well as antibodies as well as [an innate] immune response. I think we need all of that.” Although targets for vaccine design might swing between predominantly cellular, humoral, or innate responses, for the moment, antibodies could hold the best clues to protective vaccine-induced immune responses—at least for RV144 vaccine development. Considering the future for vaccine design, Kim adds “it’s definitely gotten more complex, but the pathway to our vaccine is a little simpler”.

The success of several HIV vaccine trials before RV144 have led to international collaboration, reflects Punnee Pitisuttithum (Mahidol University, Bangkok, Thailand), an RV144 trial collaborator. Reflecting on her own experience of the varied moods of optimism and failure in HIV research, Pitisuttithum adds that the similar experiences of other HIV researchers have led to the current trend for collaboration. Where previously the competitive atmosphere in HIV vaccine research meant that “everyone wanted to be a champion”, says Pitisuttithum, the challenges of achieving an efficacious HIV vaccine are now much better appreciated.

Significant progress in interventions and research to protect against new HIV infections, to slow progression to AIDS, and to reduce HIV transmission have been made in recent years. The promotion of male circumcision as a preventive measure in 14 sub-Saharan African countries preceded the success of the RV144 vaccine trial. As a result, WHO and UNAIDS have adopted male circumcision into the HIV prevention toolbox for sub-Saharan Africa. Other prevention trial successes have followed with early treatment for HIV-positive individuals in HIV-serodiscordant couples, HIV-preventive treatment for non-infected, high-risk individuals and the promise of microbicide gels in the CAPRISA study. Reflecting on possible benefits of RV144 for HSV-2, Kim adds “the CAPRISA study also showed a beneficial effect on HSV…Interaction between the two viruses could also be important and that’s something we need to look at.”

The HIV/AIDS pandemic peaked in 1996. That today fewer people annually are newly HIV infected, increasing numbers of people are living with the virus, and fewer people are dying from AIDS are encouraging momentum. However, 2·6 million people are infected annually, 1·8 million die each year, and 33 million people are living with the virus. Condoms and combination
antiretroviral drugs have also been instrumental in these changing trends. An effective vaccine could be a game changer.

Two main types of HIV vaccine are in development: those that prevent infection and those that slow or stop progression to AIDS. Communicating the different goals will be important as studies progress. Engagement with multiple stakeholders in vaccine design and implementation cannot be neglected, to which end lessons can be learned from circumcision trials, according to Helen Weiss (London School of Hygiene and Tropical Medicine, UK). Preparedness for implementation and understanding health infrastructure for a successful HIV vaccine will require broad engagement and the circumcision experience could provide implementation lessons for HIV vaccines, reflects Weiss. “Different models of providing circumcision either using mobile short-term camps or by integrating more horizontal programmes within the existing infrastructure”, could also be relevant for vaccines.

Reflecting on the existing and developing HIV intervention toolbox, Haynes comments “we’d love to add to that a vaccine that’s at least 50% effective”. However, implementing a partly protective vaccine equitably will prove challenging, as will effectively communicating the benefits of multiple partly protective interventions. Lessons from circumcision could also provide useful guidance on how to work with communities and “how to communicate what a partially protective strategy means”, adds Weiss. Additionally, the circumcision experience has provided evidence “that it’s very possible for a community to understand…partial protection, so...that they continue to practice safe sex”, reflects Weiss. With an expanding number of HIV interventions becoming available, and vaccines in development that target different stages of disease, important lessons about communicating the benefits of interventions alone, and in combination, can be learnt from the circumcision experience.

“A lot has been learnt about how that process is managed, and relationships with countries and policymakers within countries”, adds Weiss, “and about getting the different countries together to discuss their progress.” As with male circumcision, a viable vaccine will require partnership and collaborations, and according to Weiss the “importance of political leadership, partnership between organisations and coordination between providers is key”.

Onome Akpogheneta

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**Infectious disease surveillance update**

**Listeria in USA**

Officials from the US Centers for Disease Control and Prevention (CDC) continue to advise people not to eat cantaloupe melons produced by Jensen Farms in Colorado, USA, as the death toll from an outbreak of listeriosis linked to the fruits had risen to 23 by Oct 10. Four outbreak-associated strains of Listeria monocytogenes have been the cause of 109 reported infections in 24 states, with the CDC expecting more cases in coming weeks due to the incubation period before symptoms present. Meanwhile the US Food and Drug Administration (FDA) has issued a recall notice on romaine lettuce produced by True Leaf Farms of Salinas, CA, due to potential L monocytogenes contamination discovered during an FDA research programme.

**Cholera in central Africa**

An outbreak of *Vibrio cholerae* infection in the Central African Republic has claimed 16 lives, with a total of 57 cases reported so far. The disease has spread to the capital city of Bangui, where four recent cases were reported, the rest occurring in the surrounding prefectures of Ombella-Mpoko and Lobaye. Health minister Jean-Michel Mandaba has requested financial and technical aid from the country’s bilateral and multilateral partners to help deal with the situation, which comes after major outbreaks of the disease in several other countries in the region, including Burundi, Chad, the Democratic Republic of the Congo, and Nigeria.

**Encephalitis in India**

More than 400 people in northern India have died from viral encephalitis in a 1 month period up to Oct 5, 2011, with more than 2000 cases reported in the states of Uttar Pradesh and Bihar over 3 months. Both mosquito-borne Japanese encephalitis virus and enterovirus infection from contaminated water are thought to be the cause of the outbreak, which occurs annually after the monsoon season.

**Escherichia coli O157 in UK**

An outbreak of *Escherichia coli* O157 in England, Scotland, and Wales, was the cause of 250 infections and one death from December, 2010, to July, 2011. Although most of the cases were mild to moderate, 74 people attended hospital, and four developed haemolytic uraemic syndrome. The one death was in a patient with underlying health problems. The outbreak was not actively publicised at the time because the origin was unknown, though an investigation by the Health Protection Agency has since suggested a link to people handling loose leeks and potatoes at home.

Neil Bennet