Visualization and evaluation of immune responses to different HIV vaccines

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In 2009, a report was released describing the largest and most successful HIV vaccine trial to date showing 31.2% protection against HIV acquisition. More than 16,000 Thai volunteers in a high risk HIV area were vaccinated using the ALVAC and AIDSVAX vaccines or a placebo and later tested for HIV at the end of the trial. The results were promising with 31.2% protection, but need to be better. Using different formulations of the vaccine and studying their effects in animal models is the best way to evaluate their effectiveness and safety before continuing in human clinical trials. Using non-human primates (NHP) is key in HIV vaccine research since they can contract the virus and other animal models cannot. So if we are going to effectively evaluate how well a vaccine protects against HIV, NHPs are our only choice.

The AIDSVAX vaccine used in the study combined HIV protein and and a compound known as Alum. Alum is a type of adjuvant and adjuvants are used in vaccines that help stimulate the immune system without using a whole pathogen. Alum has been used in vaccines for over 70 years, but a stronger adjuvant called MF59 has been introduced in the recent years showing effectiveness in influenza vaccines. Researchers at the National Institutes of Health (NIH) decided to test if replacing Alum with MF59 in the AIDSVAX vaccine would provide better protection from HIV. They immunized Rhesus macaques with ALVAC and AIDSVAX with Alum or MF59 to compare the immune responses stimulated. In the end, when the animals were challenged with HIV, there was better protection in the Alum group than the MF59 group. To further understand the immune mechanisms behind this result, we helped by analyzing the animal's lymph nodes. We stained the lymph nodes for structures called germinal centers which is where specific immune cells develop to combat infections. Our analyses revealed no major differences between the germinal centers from the Alum and MF59 group except for one cell type, T follicular helper cells (Tfh). Tfh cells help other immune cells become better at recognizing pathogens allowing only the best cells to continue on to combat the infectious organism. There was a more intense stain for these cells in the Alum group suggesting they were better at choosing only the best immune cells to combat the infection.

Further investing these immune response as well as different vaccine and adjuvant formulations could help create a working HIV vaccine. A new human clinical trial in South Africa in November, 2016 will use the ALVAC and AIDSVAX formulated in MF59 in hopes of a more robust immune response and better protection from HIV.

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