Searching for an HIV vaccine: A heterologous prime-boost system using replicating vaccinia virus and plant-produced virus-like particles

The HIV-1 pandemic continues to cause millions of new infections and AIDS-related deaths each year, and a majority of these occur in regions of the world with limited access to antiretroviral therapy. Therefore, an HIV-1 vaccine is still desperately needed. The most successful HIV-1 clinical trial to date used a non-replicating canarypox viral vector and protein boosting, yet its modest efficacy left room for improvement. Efforts to derive novel vectors which can be both safe and immunogenic, have spawned a new era of live, viral vectors. One such vaccinia virus vector, NYVAC-KC, was specifically designed to replicate in humans and had several immune modulators deleted to improve immunogenicity and reduce pathogenicity. Two NYVAC-KC vectors were generated: one expressing the Gag capsid, and one with deconstructed-gp41 (dgp41), which contains an important neutralizing antibody target, the membrane proximal external region (MPER). These vectors were combined with HIV-1 Gag/dgp41 virus-like particles (VLPs) produced in the tobacco-relative *Nicotiana benthamiana*. Different plant expression vectors were compared in an effort to improve yield. A Geminivirus-based vector was shown to increase the amount of MPER present in VLPs, thus potentially enhancing immunogenicity. Furthermore, these VLPs were shown to interact with the innate immune system through Toll-like receptor (TLR) signaling, which activated antigen presenting cells to induce a Th2-biased response in a TLR-dependent manner. Furthermore, expression of Gag and dgp41 in NYVAC-KC vectors resulted in activation of antiviral signaling pathways reliant on TBK1/IRF3, which necessitated the use of higher doses in mice to match the immunogenicity of wild-type viral vectors. VLPs and NYVAC-KC vectors were tested in mice, ultimately showing that the best antibody and Gag-specific T cell responses were generated when both components were administered simultaneously. Thus, plant-produced VLPs and poxviral vectors represent a highly immunogenic HIV-1 vaccine candidate which warrants further study.

Bio-Sketch

Lydia Meador is the daughter of Greg and Judy Meador and the oldest of three girls. She is originally from Ponca City, OK but her love of science from a young age drove her to pursue higher education. Lydia graduated in 2011 from Oklahoma State University as a first-generation college student with two Bachelor’s degrees in Botany and Microbiology/Molecular Genetics. During her time at OSU, her participation in research activities earned her multiple prestigious national awards, including the Young Botanist Award from the Botanical Society of America, and the Barry M. Goldwater Scholar Award. She also received the National Science Foundation Graduate Research Fellowship to fund her doctoral studies at Arizona State University. For her graduate studies, Lydia desired to combine her two degrees in Botany and Microbiology by joining a plant biotechnology group at ASU which uses plants to produce pharmaceuticals, including vaccines. She was able to achieve this goal by joining a collaborative HIV vaccine project with the labs of Tsafrir Mor and Bert Jacobs for her PhD work. Lydia has presented at multiple national and international conferences and mentored over a dozen undergraduate students during her time at ASU. During her PhD, Lydia also received two dissertation fellowships: the ASU Dissertation Fellowship and the Philanthropic Education Organization Scholar Award for women completing their PhD. After successfully defending her thesis, Lydia will be joining the lab of Karen Hastings at the University of Arizona College of Medicine in downtown Phoenix where she will expand her virology and plant biotechnology knowledge by studying T cell cancer immunology in melanoma. Eventually, Lydia hopes to pursue a career in vaccinology/immunology for emerging infectious diseases.