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Potent neutralizing antibodies against CMV infection of both fibroblast and epithelial cell infection induced using a multivalent eVLP vaccine candidate

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Abstract

Background
A prophylactic vaccine to prevent congenital transmission of Cytomegalovirus (CMV) is the highest public health vaccine priority for which a vaccine is currently lacking. Several lines of evidence demonstrate that neutralizing antibodies against CMV confer significant efficacy, of which gB is a major target. However, one shortcoming of past vaccines that targeted only the gB glycoprotein was a failure to induce high titer neutralizing antibody responses that could prevent infection of epithelial cells; live attenuated and adjuvanted recombinant gB vaccines tested in clinical trials induced titers approximately 20-fold below levels associated with natural immunity.

Methods
Using an enveloped virus-like-particle (eVLP) technology in which particles are produced *in vitro* after expression of MLV Gag protein, we have developed a multivalent vaccine that targets the gB protein as well as the gH protein, part of a pentameric complex associated with epithelial cell entry. The eVLPs can be produced in a variety of mammalian cell types, with current production in a GMP-suitable CHO cell line.

Results
Electron microscopy (negative staining and immunogold surface labeling) after tangential flow filtration and anion exchange chromatography has confirmed particle structure after purification and surface antigen localization, with antigen density quantified by ELISA. Immunization of balb/c mice with recombinant gB or the same dose of gB presented in eVLPs demonstrates much stronger (~10X) neutralizing antibody responses induced with the eVLPs, which is associated with a strong Th1 response. Immunization of rabbits with our clinical candidate, comprised of gB and gH eVLPs absorbed to alum, has demonstrated significant neutralizing antibody responses within 2 weeks of the first immunization; titers 2 weeks after the second immunization are greater or comparable to that of natural immunity in fibroblast and epithelial cells, respectively.

Conclusions
Combined use of eVLP delivery and CMV antigens in addition to gB represents a potent and safe approach to CMV vaccine development.

Biography

Dr. Anderson is a co-founder of VBI Vaccines, a vaccine development company dedicated to innovative formulation, development & delivery of vaccines that expand coverage and enhance protection in both established and emerging markets. He currently serves as Vice President, Research, and is actively involved in management of preclinical research efforts and for building and protecting VBI's intellectual property. Prior to joining VBI, Dr. Anderson served as a consultant to the Company while directing academic research as an Assistant Professor at Harvard Medical School. At Harvard, he developed a multi-disciplinary research program focused on elucidating mechanisms by which inflammation is regulated within the central nervous system, with relevance to a variety of human neurodegenerative diseases, including brain tumors, multiple sclerosis, and Alzheimer's disease. He is a highly published investigator, appearing as primary author on studies appearing in the most prestigious scientific journals, including *Nature* and *Science*. He has been invited to give lectures at international conferences in the United States and abroad. Dr. Anderson completed his undergraduate studies at the University of California, Davis and received a PhD in immunology from Harvard University.