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Vaccine testing using humanized mice

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The ability to assess human immune responses for the development of new vaccines is critical because responses shown in animal models frequently do not reliably translate to humans. We have developed a humanized mouse that utilizes the immunodeficient Nod scid IL-2R γ c^{-/-} mouse background engrafted with human peripheral blood lymphocytes (PBLs) and supplemented with human BLyS (B lymphocyte stimulator, BAFF) to use for vaccine testing. Both human B and T lymphocytes readily engraft in this mouse and form follicular-like structures in the spleen. We have used model antigens and have shown that both T-cell dependent (peptide plus protein adjuvant) and T-cell independent (Pneumovax23 polysaccharides) antigens generate antibody responses. Recently, we have been testing virus-like particles (VLPs) as a method of presenting antigens in a more native form to the humanized mouse immune system. In collaboration with other investigators, we have engineered VLPs on a Newcastle Disease Virus background that contain surface antigens for Respiratory Syncytial Virus (RSV) or HIV. Humanized mice, immunized with these VLPs, have mounted serum antibody responses by day 14 post-priming. Secondary immunization results in even higher antibody titers. Upon takedown of the mice at 21-28 days post-immunization, we can readily detect antigen specific antibody secreting cells in the spleen and bone marrow by Elispot analysis. Because PBLs are used to reconstitute these mice, the responses of multiple donors can be used to assess the immunogenicity of new vaccine formulations providing a good basis for clinical testing.

Biography

Madelyn Schmidt completed her B.S. at Northeastern University in Boston, MA and her Ph.D. degree at the University of Massachusetts Medical School, Graduate School of Biomedical Sciences, Worcester, MA. She is currently an assistant professor in the Department of Microbiology and Physiological Systems and a member of the Program in Immunology and Virology at the University of Massachusetts Medical School. She has published numerous papers in reputed journals and served on scientific review committees.