The impact of robust memory T cell responses against respiratory syncytial virus

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Friday, April 17, 2015
2:30 p.m.
283 Eckstein Medical Research Building (EMRB)
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Respiratory syncytial virus (RSV) is the leading cause of infant hospitalizations due to bronchiolitis. Natural infection with RSV does not elicit long-lasting immunity and there is currently no licensed vaccine. A failed formalin-inactivated RSV (FI-RSV) vaccine resulted in increased morbidity and mortality observed in vaccinated children following natural RSV infection. The enhanced disease associated with the inactivated vaccine indicated that the memory immune response induced following immunization mediated increased pathogenesis upon an RSV infection. A lack of knowledge of the specific underlying immunological mediators of the enhanced disease symptoms associated with FI-RSV immunization has hindered current RSV vaccine development. In addition, FI-RSV immunization does not induce a memory CD8 T cell response, which is critical for mediating protection against most viral infections. While CD8 T cells are crucial for mediating RSV clearance, they also contribute to subsequent immunopathology. Therefore, it is unknown if a robust memory CD8 T cell response can mediate protection against RSV infection.

The research of my thesis primarily focuses on two goals: Determining the immunological factors that mediate the multiple distinct disease manifestations associated with FI-RSV vaccine-enhanced disease and evaluation of the protective capacity afforded by robust memory CD8 T cell responses. My work helps establish that distinct subsets of CD4 T cells mediate individual disease manifestations following RSV infection of FI-RSV-immunized mice. Specifically, a T helper 2 response was responsible for mediating the increased pulmonary pathology, mucus hypersecretion, and airway hyperresponsiveness associated with FI-RSV immunization. In contrast, TNF-α contributed to both the pulmonary dysfunction and weight loss in FI-RSV-immunized mice following RSV infection. While memory CD8 T cells have previously been shown to inhibit pathogenic memory CD4 T cell responses following RSV infection, I demonstrate that induction of robust memory CD8 T cell responses also mediate significant pulmonary dysfunction, weight loss, and mortality in mice following RSV infection. My work helps to identify a pathogenic role for robust memory T cell responses following RSV infection, but also provides a framework to appropriately assess the multiple disease parameters and immune responses in the murine model for future vaccine development.

Cory Knudson
Biographical Sketch

Cory Knudson was a small, but plump, baby upon his arrival to America from Seoul, South Korea. While his early childhood years took place in Rochester, Minnesota his family soon moved 30 minutes away to the small rural city Chatfield, MN. Here, this quiet and timid child learned about responsibility and developed hard work ethic by spending many days helping to take care of the farm animals. While Cory enjoyed the calm serenity of the country life, this experience also helped Cory decide to not pursue a career in agriculture or husbandry. In high school, Cory enjoyed science classes the most and choose to continue by studying biology at Winona State University, MN. At Winona State, Cory developed an interest in Immunology in the general Immunology course. Eventually, Cory had his first research experience by collecting ticks from deer during hunting season to evaluate the prevalence of *Borrelia burgdorferi*, the causative agent of Lyme disease. Cory’s first foray into scientific research was a very positive experience.

After a couple years, Cory enjoyed his time so much that he decided to pursue a career in research. Through advice from his advisor and undergraduate research mentor, Cory applied to and was fortunate to be accepted into the Graduate Program in Immunology at the University of Iowa. At Iowa, Cory developed a keen interest in Dr. Steven Varga’s research of T cell responses following RSV infection and would subsequently do his thesis work in Dr. Varga’s laboratory. In this quiet and peaceful work environment, Cory has spent the last several years studying T cell responses following RSV infection and would one day hopes to run his own laboratory to help uncover the mysteries of the world.