

## Study immune correlates of vaccine-induced protective immunity against rotavirus infection and diarrhea using B cell deficient neonatal gnotobiotic pigs

Lijuan Yuan<sup>1</sup>, Ke Wen<sup>1</sup>, Tammy Bui<sup>1</sup>, Mariah Weiss<sup>1</sup>, Guohua Li<sup>1</sup>, Jacob Kocher<sup>1</sup>, Xingdong Yang<sup>1</sup>, Sherrie Clark-Deener<sup>1</sup> and David Ayares<sup>2</sup>

<sup>1</sup>Virginia Polytechnic Institute and State University, USA

<sup>2</sup>Revivacor Inc., USA

Determinates of protective immunity induced by human rotavirus vaccines have not been clearly identified. Our previous studies have demonstrated a significant correlation between virus-specific intestinal IgA antibody secreting cell responses and serum IgA titers and protective immunity against rotavirus shedding and diarrhea. In this study we used cloned gnotobiotic pigs with homozygous (-/-) disruption in the gene encoding immunoglobulin heavy chain (HCKO) to discriminate the function of effector T-cells from B-cells and antibodies in protective immunity conferred by an attenuated human rotavirus (AttHRV) vaccine. HCKO pigs are confirmed incapable of producing antibodies. Similar as in wild type (WT) pigs, 2 oral doses of AttHRV vaccine significantly reduced the duration and severity of diarrhea and fecal virus shedding upon virulent rotavirus challenge in HCKO pigs. Importantly, there were significantly higher frequencies of IFN- $\gamma$  producing CD8<sup>+</sup> T cells and NK cells in HCKO pigs compared to WT pigs at post-inoculation day 28 and post-challenge day 7. Consistent with the greater effector T-cell responses, the HCKO pigs had significantly lower frequencies of total Tregs and IL-10 producing Tregs compared to WT pigs. Increased virus-specific IFN- $\gamma$  producing CD8<sup>+</sup> T cells and NK cells in the HCKO pigs may have functioned in a compensatory manner to reduce diarrhea and virus shedding titer, but did not affect the onset and duration of virus shedding, suggesting that prevention of initial virus infection requires B-cell mediated immunity. Depletion of CD8<sup>+</sup> T cells in HCKO pigs further discriminated the function of cytotoxic CD4<sup>+</sup> T cells from CD8<sup>+</sup> T cells.

### Biography

Lijuan Yuan completed her PhD at The Ohio State University and Post-doctoral training at NIAID, NIH. She is an Associate Professor at Virginia Tech. She has published 67 peer-reviewed publications, including 48 research papers, 13 invited reviews and 7 book chapters. She serves as ad-hoc reviewer for Journal of Virology, Virology, Vaccine, and many other journals (33 different journals), serves on special review panels for NIH from 2009-2014 (5 study sections); for NSF in 2013 and 2014; and for Wellcome Trust and several other international funding agencies. She is the recipient of Pfizer Award for Research Excellence in 2011.

[lyuan@vt.edu](mailto:lyuan@vt.edu)