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Low dose antigen exposure in extreme early life promotes adaptive immune response in lambs and piglets

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Mucosal tolerance is defined as a state of antigen-specific non-responsiveness to oral antigens that prevents local and peripheral overreaction to oral antigens. In newborn lambs, the gut-wall is semi-permeable for up to 36 hours after birth allowing maternal antibodies from the colostrum to enter the suckling neonate's circulation. We propose antigen introduced in extreme early life can readily access the gut-associated lymphoid tissues (GALT) and circumvent induction of mucosal tolerance. To test this hypothesis, newborn lambs were fed low doses of ovalbumin (OVA) starting immediately after birth for either a single day, for 3 consecutive days, or 9 consecutive days. At 4 weeks of age, lambs were immunized with OVA in Incomplete Freund's Adjuvant (IFA) via intraperitoneal (i.p.) injection. Lambs gavaged with low dose OVA for 9 days developed significant serum anti-OVA IgG titres (prior to i.p. injection), but low IgA titres, and these titres were augmented after i.p. immunization (day 50). These lambs showed significant anti-OVA IgA titres in lung washes indicating induction of mucosal immunity. When splenocytes were re-stimulated with OVA ex vivo, the group of newborn lambs administered OVA for 3 days produced significantly higher IFN-γ expression relative to media-stimulated cells suggesting induction of antigen-specific, Th-1 biased cell-mediated immunity. Thus, perinatal antigen exposure primes local and distal mucosal antibody production as well as cell-mediated immunity in newborn lambs. To establish if one dose prior to 'gut-closure' was sufficient to induce an immune response, piglets were drenched with OVA the day after birth and then boosted at 4 weeks of age with OVA with IFA via i.p. route. We observed a significant induction of OVA-specific serosal IgG and IgA antibody production, modest induction of IgG antibody production in the lungs, but low induction of cell-mediated immunity from restimulated lamina propria lymphocytes. Thus, while a single oral dose exposure of OVA was sufficient to prime the serosal immune response, it was not sufficient to induce robust mucosal or cell-mediated immunity. Thus, we observed that adaptive immunity can be induced in lambs and pigs to a soluble antigen (even in the absence of adjuvants) if oral exposure occurs very early in life.

Biography

Heather L Wilson completed her PhD from the University of Saskatchewan, Canada and her Postdoctoral studies from Vaccine & Infectious Disease Organization (VIDO). She is currently a Research Scientist at VIDO focusing of oral vaccination in neonates using pigs as an animal model. She has published more than 30 journal articles and reviews. Her projects are currently funded by Saskatchewan Agriculture Development Fund, Ontario Pork, and Alberta Livestock and Meat Agency.

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