Salmonella Immunity: Development of a Neutrophil Phagocytosis Assay and Stress Model in Swine

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Our laboratory is interested in the immunomodulation of porcine defense mechanisms against bacterial intracellular pathogens such as Salmonella typhimurium and S. choleraesuis. Past studies indicate that levels of serum tumor necrosis factor-α (TNF-α) increase after intranasal challenge with S. typhimurium but not after oral inoculation. Challenge with S. choleraesuis has no effect on serum TNF-α concentration in the blood, regardless of route. Route of inoculation with S. choleraesuis has been shown to affect levels of lymphocyte proliferation. Both oral and intranasal routes of inoculation stimulate peripheral blood B-cells while the intranasal route is more effective at stimulating peripheral blood T-cells. The inoculum dose of S. typhimurium or S. choleraesuis can also play an important role in the host immune response. TNF-α concentrations in the blood are much greater after a 10^6 S. typhimurium challenge than after a 10^4 S. typhimurium challenge. At high doses (≥10^9 CFU) S. choleraesuis causes signs of lymphocyte suppression, which may affect the ability of the immune system to eliminate the bacteria. Pigs administered an intranasal dose of 10^8 CFU S. choleraesuis have similar immune responses as naturally infected animals.

As a means to identify immune dysfunctions associated with salmonellosis in swine, flow cytometry was used to measure the rate of ingestion of S. choleraesuis by neutrophils from swine inoculated with homologous organism. Theoretically, infection could cause a change or defect in the rate of uptake by neutrophils without necessarily changing their capacity for ingestion. The rate of ingestion by neutrophils does not increase until 2 days post inoculation (PI) and remains elevated at least 4 days PI. The decreased rate of uptake, or early lag period, after S. choleraesuis exposure may provide an opportunity for the pathogen to colonize and/or replicate to levels that facilitate establishment of a carrier-state or clinical infection.

The production and marketing of pigs presents a number of stressful situations which can lead to production losses and disease. We are developing a porcine stress model to study the effect of marketing stress on porcine immunity and bacterial shedding at time of slaughter. This model utilizes 2-deoxy-D-glucose (2DG), a sugar analog, to induce many of the hallmark responses associated with physiological stress. 2DG remains in the blood stream for ≥ 2 hours which should allow for proper induction of a stress response. Intravenous and subcutaneous routes of injection look most promising based on release of endogenous blood glucose and cortisol, respectively. An understanding of the interaction between stress and immunity will provide important direction for future research into ways to reduce or eliminate Salmonella spp. and other diseases from pigs.