Salmonella enterica induce an early pro-inflammatory response in chickens, but the response is short-lived, asymptomatic of clinical disease, and results in a persistent colonization of the cecum. The underlying mechanisms that control persistent colonization of chickens by Salmonella are unknown. We hypothesize that a tolerogenic response is induced by alterations of host signaling pathways that mediate the in vivo and functional activation of T regulatory (Treg) cells. Using chicken-specific c-kit immune arrays, cell isolations, and T cell suppression bioassays of infected cecal tissue, we evaluated the development of immunological tolerance in chickens infected with Salmonella enterica serovar Enteritidis in a persistent infection model.

The induction of a tolerogenic response in the cecum infected with S. Enteritidis began around 4 d post-infection. The response was induced by a series of phosphorylation-mediated changes in the cecae characterized by alterations in T cell signaling (depolarization of phospholipase c-1 (PLCG1)) and mTOR signaling pathways (increased phosphorylation of AMP-activated protein kinase (AMPK)) and blockage of IFN-g protection through the disruption of the JAK-STAT signaling pathway (dephosphorylation of JAK2, JAK3, and STAT4). Further, the response is characterized by a reduction in pro-inflammatory cytokine mRNA expression (P < 0.05) and an increase in anti-inflammatory cytokine mRNA expression (P < 0.05). Last, we found an expansion of the Treg population and subsequent immunosuppressive functions at the site of the Salmonella infection. These studies define a mechanism by which Salmonella infection influences the host responsiveness resulting in the establishment of a persistent colonization of the avian cecum. The identified tissue protein kinases also represent potential targets for future antimicrobial compounds for decreasing Salmonella loads from the intestines of food animals.

Key Words: Salmonella, kinome analysis, regulatory T cells, signaling pathways


Avian infectious bronchitis virus (IBV) causes a worldwide economically important disease in poultry. IBV replicates primarily at the tracheal mucosea, though virus pathology at local sites of IBV replication remains poorly elucidated. The present experiment aimed to evaluate the gene expression of in vivo mediators, and compare viral load and scores of lesions, in chickens challenged with 2 Brazilian IBV feld isolates (F3736 and F3715) previously identified as S1 analysis. Thirteen-day-old SPF chickens were housed in 3 isolators (G1, G2, and G3) with positive pressure. At 39 d of age, 3 chickens in G1 were mock infected with diluent media, while 5 chickens from G2 and G3 were infected with 10^9 EID50s/bird of F3736 and F3715 strains, respectively. At 5 d post-infection, birds were necropsied and tracheal samples collected from each group; a portion was processed for histopathology and the remaining part submitted to RNA extraction. RNA was processed by RT-qPCR using SYBR Green I for relative quantitation of inflammatory cytokines IL6, IL1β, and T-bet (Th1 lineage transcription factor), and for absolute quantitation of IBV S1 gene. Comparisons of the mean relative changes in gene expression were performed using the Mann Whitney test, probability level for signifcant cance was set as P ≤ 0.05. Our results showed that in both groups (F3736/G2 and F3715/G3) there was a signifcant increase of histopathology scores and viral load, compared with negative control group (G1), though no signifcant differences were observed between the challenged groups. IL6 and IL1β mRNA, pro-inflammatory cytokines precursors, were signifcantly upregulated only in the F3715 challenged group. TBET mRNA was upregulated in both challenged groups, with highest signifcantly increased for F3715 group. Although similar profiles of tracheal viral load and scores of lesions were observed for both challenged groups, we found an exacerbated immune response for F3715 group, indicating relevant differences in the pathology of the distinct IBV genotypes studied here.

Key Words: avian infectious bronchitis virus, IBV, RT-qPCR, immune response, Brazilian isolates.