

Herpes Virus Connection in Smyth Line Vitiligo

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Smyth line (SL) chickens develop a spontaneous vitiligo-like postnatal loss of pigment cells in the feather between 6 and 14 weeks of age. The early expression of the vitiligo-like syndrome, the easy access to the site of pigment cell destruction (feather), and the similarities regarding the spectrum of clinical and biological manifestations between Smyth line vitiligo and the human disease make the SL chicken an excellent animal model for vitiligo. Smyth line vitiligo is a multifactorial disorder involving an inherent pigment cell defect, an immune system component and environmental factors. One environmental factor reliably associated with the expression of vitiligo in vitiligo-susceptible SL chickens is turkey herpesvirus (HVT), which is routinely administered at hatch as a live virus vaccine to protect chickens from Marek's disease. The strong association between HVT vaccination and vitiligo was first noted when the incidence of vitiligo was only 10% to 20% in SL chickens not vaccinated compared to 70% to 95% in SL chickens vaccinated with HVT at hatch. Although this association between a virus and vitiligo does not necessarily constitute causation, nor does it exclude other environmental factors as triggers for expression of the disorder, these observations do however warrant further investigation into the mechanisms by which this herpesvirus influences the expression of autoimmune vitiligo in susceptible SL chickens.

At this time, we have completed a study examining the effect of HVT in SL and control BL chickens. Specifically, SL and BL chicks were either vaccinated at hatch with HVT (SL-HVT, BLHVT) or mock-injected (SL-Con, BL-Con). Immune organs (spleen, thymus, bursa), blood and feathers were collected when the chicks were 3, 6, 9, 14, 21, 28 and 42 days age.

For each time point, portions of thymus, spleen, bursa and feathers were snap-frozen for identification and localization of HVT and immune cells in these tissues. Staining and examination of tissue sections is currently ongoing. Once all tissue sections have been prepared and examined, we hope to gain insight into the interactions between the virus, immune cells and pigment cells. Moreover, differences between these interactions in BL-HVT and SL-HVT may provide insight into their role in triggering autoimmune vitiligo in SL chickens.

To address the question whether the extent or the distribution of the viral infection initiated by the HVT vaccination was different in SL-HVT compared to BL-HVT chicken, portions of thymus, spleen, bursa and blood were also used for virus reisolation. As expected, no HVT was isolated from mock injected chickens. In vaccinated SL and BL chickens, HVT could be isolated from spleen at all time points examined. Additionally, in both lines of chickens (SL-HVT and BL-HVT), HVT could be isolated from the thymus (3 and 9 days), bursa (6, 28 and 42 days) and blood (6 and 28 days). The amount of virus isolated from SL-HVT and BL-HVT chickens was comparable for each tissue. This finding suggested that the extent of HVT infection and distribution of HVT in these tissues does not appear to be a factor in the expression of SL vitiligo. It is however possible that SL-HVT and BL-HVT chickens differ with regard to the extent and type of HVT infection in the feather, the site of pigment cell loss. This aspect will be examined during the next six months of this project.

To address the question whether the immune system in SL chickens responds differently to HVT than that of BL controls, immune cell population analyses in thymus and spleen were also conducted. It was found that the effect of the HVT vaccination on the proportions of immune cells was different in SL-chickens than in BL-chickens. Specifically, vaccination with HVT resulted in altered immune cell profiles in the spleen of SL-HVT compared to SL-C on chickens, but not in BL chickens. The HVT associated alterations in SL-HVT compared to SL-C on chickens were suggestive of a different type and/or magnitude of immune response to the virus than in control BL chickens. Moreover, the types of alterations in immune cell profiles in the spleen were typical of those expected during a cell-mediated, rather than an antibody mediated, immune response.

To examine whether the appearance and amount of autoantibodies was affected by HVT vaccination, the presence and relative amount of pigment cell-specific autoantibodies in the blood were examined at all time points. Interestingly, examination of autoantibodies to pigment cells in the blood revealed the presence of autoantibodies in unvaccinated SL chickens (SL-Con) and not in HVT vaccinated chickens. No or very low levels of autoantibodies to pigment cells were detected in SL-HVT, BL-HVT and BL-C on chickens at all time points examined (342 days). This unexpected observation will be further investigated during the

next six months of this project. Overall, results from this project further support a role of HVT in the expression of vitiligo in vitiligo-susceptible Smyth line chickens.