

Animal Model for Autoimmune Vitiligo: the Smyth Line Chicken

**Gisela F. Erf, Ph.D.; Professor,
Immunology
University of Arkansas,
Poultry Science Center**

The mutant Smyth line (SL) chicken developed by Dr. J. Robert Smyth, Jr. at the University of Massachusetts, Amherst, MA, is the only animal model for autoimmune vitiligo that recapitulates the entire spectrum of clinical and biological manifestations of the human disease. The onset and incidence of SL vitiligo is predictable, the lesion is easily accessible and the target tissue (feather) regenerates, thus providing opportunity to study the evolving lesion prior to and throughout the development of SL vitiligo in the same individual. The incidence of vitiligo in this line ranges from 70 to 95% and visible signs of pigment loss in the feathers are evident when the chickens are between 6 and 20 weeks of age. Previous studies by J. Robert Smyth, Jr. and co-workers describe the presence of a competent pigment system at hatch. Prior to visible signs of vitiligo, the earliest abnormality detected within SL melanocytes are irregularly shaped melanosomes containing pigmented membrane extensions, hyperactive melanization, and selective autophagocytosis of melanosomes. These aberrant processes precede the degeneration of SL melanocytes, but are not sufficient to cause vitiligo without a functioning immune system. They do, however, appear to be involved in provoking an immune response resulting in autoimmune destruction of melanocytes. Our research has further defined the immune system involvement in SL vitiligo: 1) immunohistochemistry and cell population analyses conducted throughout the development of



vitiligo point strongly to an important role of cell-mediated immune activity in the destruction of melanocytes; 2) *in vivo* studies demonstrated the presence of feather melanocyte-specific cell-mediated immunity in SL chickens with vitiligo; 3) *in situ* studies provided evidence that melanocytes in SL vitiligo die by apoptosis, which appeared to be initiated by cytotoxic T cells; and 4) examination of the target tissue revealed interferon gamma production, altered antioxidant capacity, and heightened oxidative stress in feathers during active vitiligo. Additionally, our research uncovered a strong association between administration of live (but not dead) turkey herpesvirus (HVT) at hatch and the expression of vitiligo in vitiligo-susceptible SL chickens. Hence, the expression of SL vitiligo requires an environmental component (e.g., HVT, which translocates to the feather) in addition to a genetic and immune

system component, a phenomenon typically observed in autoimmune disorders. Considering the accessibility of the target tissue (the feather), the ability of the target tissue to regenerate, and the predictability of the development of SL vitiligo, this animal model offers unique opportunities to study the etiopathology of autoimmune vitiligo. Moreover, there are two MHC-matched lines of chickens that serve as controls. These are the parental Brown line of chickens, which has a < 2% incidence of vitiligo, and the Light Brown Leghorn chickens, which are vitiligo-resistant. Together, the SL and control lines of chickens allow for various comparisons between different phenotypes and provide opportunity to explore treatment approaches through *in vivo* and *in vitro* studies.

AVIAN MODEL FOR HUMAN AUTOIMMUNE VITILIGO



The Smyth line chickens

SMYTH LINE CHICKEN

The bird on the left is normally pigmented, the middle one has the "erratic" form of vitiligo (partially depigmented) and the one right is completely amelanotic. The vitiligo typically appears when the chicks are between 8 and 20 weeks of age. These birds are adult roosters - and are stable at this time with no new feather growth .