

Poster presentation

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## Genetic resistance to GAHV-2 induced lymphoma in the chicken model

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from 11th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies (ICMAOI): Basic, Epidemiologic, and Clinical Research  
Bethesda, MD, USA. 6–7 October 2008

Published: 17 June 2009

*Infectious Agents and Cancer* 2009, **4**(Suppl 2):P28 doi:10.1186/1750-9378-4-S2-P28

This abstract is available from: <http://www.infectagentscancer.com/content/4/S2/P28>

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Oncogenic herpesvirus infections contribute to the occurrence of lymphomas in the human population. Genetic makeup has a role in susceptibility, but the basis of resistance and susceptibility is not well understood. To gain insight into how genetic resistance occurs in an animal model we have been studying the lymphomas that form in chickens following infection with gallus herpesvirus 2 (GaHV-2), the virus that causes Marek's disease. A significant association between MHC haplotype and the incidence of Marek's disease in chickens was recognized more than 30 years ago. Through mapping crossover break-points in two MHC recombinant haplotypes (*BR2* and *BR4*) that differ in the incidence of Marek's disease we have identified *BG1* as an MHC gene with a major influence in the occurrence of GaHV-2-associated lymphoma in the chicken. *BG1* is an Ig-family type I transmembrane protein containing an ITIM motif. The *BG1\*BR2* and *BG1\*BR4* alleles differ only in the 3'-untranslated region (3'-UTR) with the longer 3'-UTR of the susceptible *BR4* allele containing unique sequence. In dual firefly/renilla luciferase reporter assays we found that the 3'-UTR of the *BR4* suppresses translation of the firefly reporter gene in LMH cells activated with PMA. The 3'-UTR of *BR2* is far less inhibitory under the same conditions.

This experiment suggests that the 3'-UTR of the susceptible allele may have a negative influence on the expression of *BG1* protein in vivo. We are currently investigating the possibility that microRNA binding to the longer 3'-UTR

results in reduced *BG1* expression and increased tumors. *BG1* expression in cultured cells rapidly decreases in the presence of virus (avian poxvirus only tested so far). If *BG1* sends an inhibitory signal as the ITIM suggests, then down-regulation of *BG1* by viral infection may result in the availability of more activated cells for viral replication. With more cells infected the likelihood of transformation increases. (Supported by NIH/NCI R21 CA105426)