Predicting the Immunologic Constant of Rejection

(1) Genelux Corporation, San Diego, CA, USA
(2) Virchow Center for Experimental Biomedicine, University of Würzburg, Am Hubland, Würzburg, Germany
(3) Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD, USA
(4) Department of Molecular Microbiology and Immunology, Saint Louis University School of Medicine, St Louis, MO, USA

Based on hypothesis-generating clinical studies, we postulated that immune-mediated cancer rejection is part of a broader phenomenon shared by autoimmunity, allograft rejection and clearance of pathogens that we called "Immunologic constant of rejection" (ICR). ICR includes the combined expression of Interferon-stimulated genes (ISGs) and Immune effector functions (IEFs).

Here, we tested the predictive value of genes associated with the ICR using GLV-1h68, an attenuated recombinant Vaccinia Virus (VACV) that selectively colonizes established human xenografts inducing their complete regression. We explored human cancer cell/VACV interactions in vitro and xenograft/VACV/host interactions in vivo adopting organism-specific expression arrays. Indeed, tumor rejection was associated in vivo with activation of ISGs and IEFs as predicted in the ICR theory. As expected, the expression of CXCL9-11, CXCL12, CCL5 chemokines, Irf1, granzyme A and B, perforin and FAS which compose the ICR was highly predictive of tumor rejection in this xenograft model.

This study provides the first prospective validation of a universal mechanism associated with tissue-specific destruction observable across species that may represent a tissue-specific target of immune enhancement for the therapy of cancer and chronic viral infections or immune suppression in the context of allograft rejection or autoimmunity.