Abstract:
The immune system plays an essential role in the elimination of tumor cells, a process known as immunosurveillence. Loss of this function leads to increased incidence of tumors and malignant transformation, however there is some ambiguity as to the specific roles of lymphocytes in tumor promotion or regression. In a mouse model of squamous tumor formation in which oncogenic Ras can be induced in basal/stem cells of the epidermis, we show that tumor formation on a *Rag1-/-* background is significantly enhanced. This contrasts with previous results showing that tumor formation with suprabasally expressed Ras is dependent on an intact adaptive immune system. In mice expressing Ras in the basal/stem cell compartment, the presence of lymphocytes does not simply delay tumor outgrowth, as tumor counts in *Rag +/+* mice stabilized over a 34-day time course, indicating a state of tumor equilibrium. Tumor numbers in *Rag1-/-* mice constantly increased. Lack of lymphocytes also resulted in increased mortality possibly due to abundant inflammation and tumor burden. This proposal is designed to distinguish between two hypotheses: that in mice expressing oncogenic Ras in the basal/stem cell compartment, rapid tumor growth in the absence of lymphocytes results from loss of CD8+ cytotoxic T lymphocytes (CTLs) that mediate immunosurveillance, and loss of Tregs which control tumor promoting skin inflammation.