GEORGE MASON UNIVERSITY
COLLEGE OF SCIENCE
BIOLOGY DEPARTMENT SEMINAR
Fall 2015

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"Identification of Aggressive Prostate Cancer Susceptibility Genes Using Mouse Models"

Neuroendocrine (NE) differentiation has gained increased attention as a prostate cancer (PC) prognostic marker. The aim of this study is to determine whether host germline genetic variation influences tumor progression and metastasis in C57BL/6-Tg(TRAMP)8247Ng/J (TRAMP) mouse model of aggressive NEPC. TRAMP mice were crossed to the eight progenitor strains of the Collaborative Cross recombinant inbred panel to address this. Tumor growth and metastasis burden were quantified in heterozygous transgene positive F1 male mice at 30 weeks of age. Compared to wild-type C57BL/6J-Tg(TRAMP)824Ng/J males, TRAMP x CAST/EiJ, TRAMP x NOD/ShiLtJ and TRAMP x NZO/HlLtJ F1 males displayed significant increases in tumor growth. Conversely, TRAMP x WSB/EiJ and TRAMP x PWK/PhJ F1 males displayed significant reductions in tumor growth. Interestingly, despite reduced tumor burden, TRAMP x WSB/EiJ males had an increased nodal metastasis burden. Patterns of distant pulmonary metastasis tended to follow the same patterns as that of local dissemination in each of the strains. All tumors and metastases displayed positive staining for NE markers, synaptophysin, and FOXA2. These experiments conclusively demonstrate that the introduction of germline variation by breeding modulates tumor growth, local metastasis burden, and distant metastasis frequency in this model of NEPC. These strains will be useful as model systems to facilitate the identification of germline modifier genes that promote the development of aggressive forms of PC.

TUESDAY October 6, 2015
3:00-4:15 PM
Johnson Center Room Meeting Room F