

Activation of G-protein Estrogen Receptor and Tumor Progression in a Melanoma Prone Transgenic Mouse Model

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Increased estrogen levels have previously been linked to decreased proliferation and metastasis in melanoma. G-1, a selective agonist of G-protein-coupled estrogen receptor (GPER) was shown to promote long-lasting protective phenotype alterations in melanocytes from transforming into melanoma, including an increase in cell differentiation. G-1 only activates the estrogen signaling pathway associated with GPER in melanocytes without activating any other classical estrogen pathways. We initiated an in vivo study to assess the efficacy of LNS8801, the active isomer of G-1, in a transgenic mouse model that develops spontaneous metastatic melanoma. Exposure to ultraviolet (UV) light has been associated with enhanced skin cancer incidence, we set up two cohorts of mice with or without UV exposure in the presence or absence of LNS8801. Possible alterations in pigmented lesion in these different groups were monitored using a small animal imaging system, IVIS. The images of the lesions were quantified using ImageJ software to measure the progression of the tumors. Potential therapeutic effectiveness by LNS8801 in the presence of UV, the most prevalent environmental toxicant associated with skin cancer, will be evaluated. Tumor tissue specimens and blood samples were collected at various timepoints to examine changes in gene expression that have been linked with melanoma progression and melanocyte differentiation. Our preliminary results show that there were no differential responses to LNS8801 in the absence of UV however, inclusion of UV appears to provide the female transgenic mice with a reduction in tumor progression. Funded by R25ES020721 and the ASPET Fellow Program.

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