Protein Marker Changes as a Result of Glutamatergic Signaling and Immune Checkpoint Inhibition in Melanoma-Prone Transgenic Mice

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Melanoma, while the least common form of skin cancer, is the deadliest and accounts for the majority of skin cancer mortality. The American Cancer Society estimates that in 2022, approximately 100,000 new cases of invasive melanoma will be diagnosed and 7,650 will result in death. Metastatic melanoma is refractory to many therapies and improvements in therapeutic strategies are essential. The availability of an experimental animal model that recapitulates many of the characteristics in human disorder is a valuable tool in translational research. Our lab has shown that when melanocytes, the pigment-forming cells of the skin, ectopically express a normal neuronal receptor, metabotropic glutamate receptor 1, and activated by its natural ligand, glutamate, leads to cell transformation in vitro and metastatic melanoma formation in vivo. In this study, we have taken excised tumor specimens after the mice have been on treatment for 6, 12, and 18 weeks. Expression of several protein markers were assessed by Western immunoblots to consider for the application as biomarkers to predict treatment outcomes. The protein markers we have selected have been shown by others to be associated with immune evasion, cell metabolism, and DNA damage. At the end of our 18-week longitudinal study the mice were stratified into responders or non-responders based on the RECIST criteria used in human clinical trials. Our preliminary results suggest differential expression profiles between responder and non-responder mice in some treatment modalities and time courses. Complementary assays may further delineate the most suitable biomarkers in therapy prediction. Supported by R25ES020721.