CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150030

Project Title:
Exploring molecular and immune mechanisms of response and resistance to combined BRAF/MEK inhibition in patients with high-risk resectable metastatic melanoma

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Melanoma is a major world health problem with an incidence that is rising rapidly. Tremendous progress has been made in the treatment of melanoma, including the discovery of the BRAF gene. Mutations in the BRAF gene occur in over half of melanomas, and result in a “short circuit” in melanoma cells, causing them to grow and spread. Treatment with BRAF inhibitors represents one of the most significant advances in decades, with tumors shrinking in up to 80% of patients. However tumors often grow back within 6 months. Our group has helped identify why tumors re-grow on therapy, and treatment strategies are now available to combat this. One way to do this is to give a BRAF inhibitor with a drug called a MEK inhibitor (thus cutting the short circuit at 2 points). This treatment prevents tumors from coming back for a much longer period of time. Because of this success, treatment with combined BRAF and MEK inhibitors (BRAFi/MEKi) is now being tested in patients with earlier stage melanoma. This includes patients with stage III disease, when melanoma has spread to lymph nodes. The standard treatment for this is surgery, however there is a high risk of relapse. We suspect that treatment with BRAFi/MEKi will be highly effective if given before surgery, making the tumors shrink and destroying small cancer cells elsewhere in the body. We are conducting a clinical trial to test this in patients, and will determine how safe and effective this strategy is. We will analyze tumors and blood during treatment to identify molecular and immune signatures predictive of response and resistance. Parallel studies will be performed in genetically engineered mice, with the ability to rapidly test insights gained. Together, these studies will help change the standard of chare for patients with high-risk melanoma and will give insight into which patients are most likely to benefit from this therapy. Overall, this will lead to more effective, personalized treatments for patients with melanoma.