CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120343

Project Title:
Gli Transcriptional Activity in Basal Cell Carcinomas

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas at Austin

Lay Summary:

Basal cell carcinomas (a form of skin cancer) are the most common form of cancer in humans and are primarily, if not exclusively driven by activating mutations in the Hedgehog signaling pathway. Mutations in the Hedgehog signaling pathway also drive the formation of a spectrum of different cancers, including brain, muscle and bone. All of these organs require Hedgehog signaling for their initial formation during embryogenesis, and the inappropriate activation of the pathway after embryonic development causes the formation of tumors that are reminiscent of the less differentiated cell types found during embryogenesis. By studying how Hedgehog signaling regulates cell activity during embryonic development we can understand how it mis-regulates cell function in tumors. Hedgehog signaling exerts its effect on cell function by regulating the activity of Gli proteins. Gli proteins function by regulating gene activity by binding to DNA through poorly understood mechanisms. Here we describe a series of experiments that will significantly enhance our understanding of how Gli proteins control gene activation and thereby cell function in Basal cell carcinoma. We will perform these experiments in the developing mouse limb, a well described system for understanding Hedgehog signaling and in adult mice genetically modified to form inducible basal cell carcinoma at a high rate. A better understanding of how Hedgehog signaling, through the Gli proteins, controls gene expression will aid in understanding the consequence of aberrant Hedgehog signaling in Basal cell carcinoma and other Hedgehog-dependent tumors. This, in turn, will aid in the rational design of more precisely targeted anti-Hedgehog cancer therapies.