CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110390

Project Title:
A functional genetic approach to identify new potential therapeutic targets for medulloblastoma.

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

With more than 300 new cases diagnosed in the US every year, medulloblastoma is the most common brain tumor in children. Although 75% of cases can be treated combining surgery, radiotherapy and chemiotherapy, 25% of affected children fail to respond to the therapy. Moreover, many patients that have been cured show severe neurological side effects, including psychiatric disorders, growth retardation, and cognitive impairment. Better therapies are thus required for the treatment of this highly malignant cancer. If we understood the basic mechanisms of medulloblastoma formation and progression, we could use this knowledge to design new therapies. If we figured out, for example, what regulates specifically the proliferation of medulloblastoma cells, we could design a therapeutic strategy to target exclusively tumor cells. Such a strategy would be at the same time effective and cause little side effects. One of the best-studied mechanisms that cause the formation of medulloblastoma is dysregulation of the signaling pathway activated by the extracellular factor Sonic Hedgehog (Shh). Importantly, mutations in genes that code for components of the Shh signaling pathway cause more than a fourth of human medulloblastomas. We have recently shown that the transcription factor Atoh1 regulates Shh signaling during medulloblastoma formation. Our recent data suggest that the role of Atoh1 in the regulation of medulloblastoma cell proliferation might be broader than expected. If we could clarify the role of Atoh1 in tumor progression and how its function is regulated, we could identify new directions for the development of better therapies. In this proposal, we describe a strategy to identify both genes regulated by Atoh1 and genes that regulate the activity of Atoh1 in medulloblastoma cells. These experiments will shed light on the regulation medulloblastoma proliferation and pave the way for the development of much needed new treatment for this devastating disease.