Award ID:
RP150590

Project Title:
Identifying Inhibitors of Ascl1 to Block Growth of Malignant Neuroendocrine and Neural Tumors

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Tumors with neuroendocrine features arise from a variety of anatomic sites. Because of their diverse tissues of origin, these tumors can have distinct biology. Nevertheless, they can also share properties such as a shared requirement for a specific protein for tumor growth. At least one of these neuroendocrine cancers, small cell lung carcinoma is a focus of the Recalcitrant Cancer Research Act of 2012 because it has a 5-year survival rate of < 20% and is estimated to cause the death of over 30,000 individuals in the US each year. The problem addressed in this proposal is the need for effective treatments for this recalcitrant tumor, and for other tumors with neural and neuroendocrine phenotypes that currently have no cure. One solution to this problem is to identify inhibitors of tumor-specific factors required for survival of the tumor cells. The transcription regulatory protein called Ascl1 is a factor present in multiple neural and neuroendocrine tumors. It is required for survival of tumor cells in small cell lung carcinoma, and possibly other tumors where it is present. Importantly, although Ascl1 is present in specific types of tumors, it is not present in normal adult tissues because its function in normal development is largely restricted to embryonic stages. This feature makes Ascl1 an attractive target for therapeutic intervention in cancer. This high impact/high risk project will develop assays to screen small molecules and natural products for their ability to inhibit Ascl1 function. The identification of novel inhibitors of a tissue and stage-restricted protein crucial in tumor growth in multiple malignant tumor types, such as neuroendocrine tumors where there are no effective long-term treatments available, provides unexplored therapeutic opportunities. Furthermore, this paradigm may be expanded to identify inhibitors of other Ascl1 related proteins crucial for growth of other cancers such as medulloblastoma and colon cancer.