CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170180

Project Title:
Mechanistic Roles of Long Non-Coding RNA in Glioblastoma Development and Treatment

Award Mechanism:
Individual Investigator

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

Lay Summary:

Glioblastomas (GBMs) are the most common and fatal brain tumors. Glioblastomas are largely refractory to surgical therapy, radiotherapy, chemotherapy, and adjuvant therapy. Consequently, the prognosis for patients with glioblastoma is very poor. Texas has the second highest rate of death from brain tumor in the US. Little is known about the mechanisms underlying oncogenesis of glioblastoma. Studies outlined in this proposal will test the biology functions of EGFR induced long non-coding RNAs (lncRNAs) and underlying mechanisms in glioblastoma development and progression. The lncRNAs are long RNAs which do not encode proteins. lncRNAs have been strongly implicated in cell fate decisions and in cancer development. We propose to identify and characterize a novel cancer-causing lncRNA, EGFR-ILncR. We predict that EGFR-ILncR (1) is an important regulator of glioblastoma cell growth and invasion, (2) indicates grade of glioma and informs patient survival, and (3) is a potentially useful therapeutic target for treating glioblastoma. We will use new methodology in conjunction with a variety of molecular and cell-based assays, and animal model, to determine 1) whether the aberrant EGFR activation causes EGFR-ILncR overexpression in glioblastoma; 2) whether EGFR-ILncR enhances cell growth and invasion, through H2A ubiquitination- and Bmi1-mediated mechanisms, and, thus contributing to tumor formation; 3) the clinical significance of our findings using human tumor specimens.

We predict that completion of these studies will contribute to a better understanding of the molecular mechanisms for glioblastoma development through expression of abnormal lncRNA. Furthermore, accomplishing our goals is highly relevant to the development of novel therapeutic agents that inhibit EGFR-ILncR for better combating glioblastoma. Thus, our studies may revolutionize our understanding and treating glioblastoma.