CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170686

Project Title:
A Novel Chemical Strategy to Target EGFR for Destruction

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Resistance arises when tumors often adapt to the drug and manage to find alternate routes to resume cell growth. Selective proteolysis of a key regulator allows for rapid adjustments of its concentration and has emerged as a promising therapeutic means for cancer. The goal of this work is to develop a novel approach to modulate protein stability that would eliminate, rather than simply inhibit, the target protein, which would overcome drug resistance, a common shortcoming of targeted therapies.

Specifically, we will design and evaluate novel cell permeable compounds that exploit the cell's own proteasome-mediated degradation pathway to specifically eliminate the epidermal growth factor receptor (EGFR), a key regulator involved in cancers including lung, thyroid and breast. Small molecules designed will shuttle EGFR to the proteasome for destruction selectively. The advantage of this approach lies in smaller molecular size, potent degradation activity and modulatable speed of proteolysis. Our approach overcomes limitations of existing methods and will significantly improve the drug efficiency and bring broader applicability. Since this strategy is highly selective and may have wide therapeutic utility with the potential to subdue drug resistance and manipulate previously undruggable cancer regulators, the work proposed here may lead to a novel, effective strategy for cancer therapy in general and could have a major impact on existing drug therapies.