



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP160501

Project Title:  
De-Orphanizing TLX: Implications for Glioblastomas

Award Mechanism:  
Individual Investigator

Principal Investigator:  
Pownall, Henry

Entity:  
The Methodist Hospital Research Institute

### Lay Summary:

Glioblastoma brain tumors are deadly. Surgery and chemotherapy are used to combat disease but do not work well. Current survival after diagnosis is about one year and has not improved. New innovative strategies are needed. Two recent discoveries offer hope. First, brain tumor stem cells (BTSC) are responsible for glioblastoma growth. These cells reproduce indefinitely and their continued growth feeds the tumor. Thus, strategies to combat tumor cells often fail in long term treatments because they do not target BTSC and strategies to block BTSC growth should attack the cancer at its root. Second, scientists are focusing on proteins that regulate BTSC division. Knowledge of function of such proteins allows development of new drugs called targeted therapies which efficiently inhibit the specific cancer of interest in particular patients and do not act as systemic poisons. We work on a protein called tailless that is required for BTSC growth and is found at high levels in glioblastoma and other brain tumors of adults and children. It is now known that genetic knockout of tailless in mice effectively cures brain tumors. Thus, drugs that interfere with tailless could form the basis of novel and effective brain tumor treatments. While tailless was considered undruggable, we identified the first compounds that bind and modulate its activity in cells. We have worked with chemists to identify even better compounds that bind tightly to tailless and exert desirable effects on its activity. Our group is expert to develop new drugs and we have already taken therapeutics into human trials. We now plan to apply expertise to tailless and expect to create chemical probes which bind tailless with high affinity and block its activity in BTSC. These probes will be used to prove that tailless is a useful target in human cancer and to move to identification of clinical candidate drugs based on our compounds.