CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180147

Project Title:
Prevalence of Rare Passenger Mutations in Biopsy Tissue as Cancer Stratification Markers

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Rice University

Lay Summary:

Cancer is caused by acquired mutations in DNA, and different patients' cancer cells and tumors will possess different mutation rates. Only a small proportion of mutations are actually the drive" mutations that cause cancer, and thus far research efforts have focused on understanding and detecting these driver mutations. In contrast, non-pathogenic passenger mutations, considered the incidental by-products of cancer, have received relatively little study as potential markers for cancer diagnostic or prognostic tests.

The PI hypothesizes that the prevalence of passenger mutations in a tissue biopsy sample may be correlated with the mutability of a patient's tumor. In other words, patients whose biopsy samples exhibit a high number of acquired passenger mutations are likely to have an instance of cancer that more likely acquires drug resistance mutations in the future, and thus may require more aggressive treatment. Should the hypothesis be validated through studies on retrospective samples, passenger mutations may take on an expanded role as predictive or prognostic markers.

Use of passenger mutation prevalence in biopsy tissue samples has not been economically feasible until now, due to the rarity of somatic mutations, the high depth of sequencing required, and the intrinsic error rate of sequencing. The PI's research group has recently developed technologies to simultaneously enrich hundreds of rare mutations, allowing sequencing cost required for profiling passenger mutations to be reduced 1000-fold. This technology thus uniquely enables the proposed evaluation of passenger mutations. Patient stratification tests based on the results of this research could significantly improve the outcomes of cancer care by providing individualized therapy guidance.