CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100900

Project Title:
Relating drug resistance and tumor microenvironment to cancer cell heterogeneity

Award Mechanism:
Individual Investigator

Principal Investigator:
Wu, Lani F

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Phenotypic heterogeneity among cancer cells, observed even within single tumors, presents enormous challenges for developing optimized and targeted treatment plans. In practical terms, heterogeneity can translate into varying degrees of tumorigenicity and drug response among tumor cells. This phenotypic heterogeneity has been an impediment to diagnosing and treating cancer. Promising approaches for profiling cancer are being developed based on genomic, mRNA, or miRNAs analysis. However, these approaches require pooling many cancer cells, and ensemble measurements may miss the presence and behaviors of clinically important subpopulations. Importantly, cellular heterogeneity–influenced by many non-genetic factors–is likely to be an important factor in determining overall drug responses in cancer treatment. A key paradigm shift of our work is to investigate whether measurements of cellular heterogeneity can provide informative and quantitative readouts of cancer population pathophysiology, and potentially serve as predictors for therapeutic outcome. In preliminary studies, we developed an image-based platform that can measure the phenotypes of large numbers of individual cells, extract phenotypic signatures from cellular heterogeneity, and test whether these signatures can be used to predict the drug sensitivities of cancer cell lines. Here, we propose to apply our platform to screen for biomarkers that can identify drug-resistant subpopulations, and to characterize the evolution of their phenotypes in time. This work will develop an analytical and experimental framework for associating functional significance to identified cancer subpopulations and help to establish a new paradigm in which tumor heterogeneity can be used to predict patient clinical outcome.