UC San Diego
MOORES CANCER CENTER
An NCI-designated Comprehensive Cancer Center

Cancer Center Support Grant – CCSG 2016

"Monitoring the Dynamics of Early Tumor Response to Therapy by Detecting Circulating Tumor DNA in Blood and Urine"

Hatim Husain, MD

The emergence of drug resistance ultimately limits the success of virtually all targeted cancer therapies, and strategies to understand how this process arises and how it might be reversed represents an important topic in oncology. This is eminently important in the example of epidermal growth factor receptor (EGFR) mutated lung cancer for which we have FDA approved tyrosine kinase inhibitors for those patients who have activating mutations. We have preliminarily shown that early disease monitoring within the first week of therapy can predict therapeutic responsiveness to anti-EGFR inhibitors.

Resistance to targeted therapies in lung cancer involves the outgrowth of resistant clones, and conceptually it is plausible that early intervention strategies that target the resistance subclones may lead to longer term response. Our study focuses on the early identification of resistance during the first week of therapy to inform which patients will have a response, which patients may have a suboptimal response, and which patients may not have a response. Furthermore we will qualitatively assess the clonal dynamics that are important that define resistance. We hypothesize that signatures as early as one week into therapy will be important for defining specific resistance patterns. Our work will extend our efforts to create a sample size of patients to test the hypothesis.

Circulating tumor DNA monitoring in blood and urine has potential utility to act as an early pharmacodynamic biomarker for proof of concept studies of targeted therapies in development. Specifically, this approach could be used to determine whether an investigational drug is inducing apoptosis of the targeted tumor cells by quantitating daily changes in urine ctDNA levels of the targeted tumor DNA mutation(s). In addition, for chemotherapies and immunotherapies that do not target a specific tumorgenomic alteration, tumor response could be determined by quantitating levels of tumor DNA mutation(s) prevalent for the tumor type under investigation.