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Using metabolism to differentiate aggressive versus indolent prostate cancer for diagnosis and treatment

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Many prostate cancers (PCa) detected by screening are indolent (will not leave the prostate) however, 90% of patients will receive immediate treatment. What is needed is a diagnostic tool that allows the whole prostate to be examined and is directly correlated to the metastatic behavior of the tumor. We are using a multi-prong approach to discover the metabolic changes in PCa. (1) We are metabolic profiling tumor and normal prostate tissue. (2) We are metabolic profiling both the intracellular and extracellular metabolites of four human prostate cancer cell lines with different degrees of metastatic behavior. (3) We are exploring the reduction of cell proliferation with metabolic inhibitors for therapeutic treatment. (4) We are following the progression of PCa with hyperpolarized magnetic resonance (MR) agents in PCa animal models. Hyperpolarization allows for over >10,000 fold sensitivity enhancement using MR. Polarization (signal enhancement) can be retained on the metabolites of the hyperpolarized molecule allowing for *in vivo* real time metabolic profiling.

Results: We observe significant differences in uptake of glutamine and the amount of intracellular glutamine, differences in phosphocholine and glycerophosphocholine, and differences in intracellular succinate levels between aggressive versus non-aggressive cell lines and in PCa tissue versus normal prostate tissue**.** In addition, in our hands we see no significant difference in the glycolytic rate (production of lactate) between the indolent and aggressive PCa cell lines in culture. Using dynamic nuclear polarization, we are designing new *in vivo* methods for interrogating metabolic pathways such as hyperpolarized choline and glutamine derivatives.

Conclusions: Metabolic profiling has revealed significant differences in metabolism between indolent and aggressive PCa. By using metabolic profiling, we can determine which specific metabolic inhibitors could be utilized to reduce tumor burden and with hyperpolarization this metabolic profiling can be performed *in vivo*.

Biography:

Dr. Niki Zacharias is an Assistant Professor in the Department of Cancer Systems Imaging at the University of Texas MD Anderson Cancer Center. She received her PhD in chemistry from California Institute of Technology in 2003. Prior to her faculty appointment, she was the James G. Boswell Fellow between Huntington Medical Research Institute and California Institute of Technology. As a chemical biologist, she is focused on utilizing chemical methods (imaging, magnetic resonance, hyperpolarization, fluorescence) to probe biological systems.