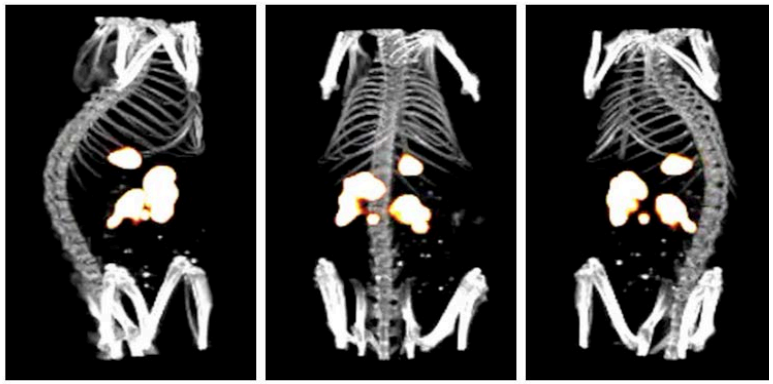

My research program uses a multidisciplinary approach consisting of chemical biology, screening technologies, proteomics, cell biology and molecular imaging to discover novel biomarkers of disease, interrogate the relationship of the tumor to its microenvironment, in order to develop targeted drug delivery systems, and to understand the signaling pathways involved in invasion and migration.

Imaging Research Group

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Development of Amplifiable Targeted Imaging Agents

A major research thrust has been the development of molecularly targeted imaging agents and their use in understanding disease biology. As an example, we were able to develop a plectin targeted SPECT based imaging agent that illuminated primary and metastatic (liver and peritoneal) PDAC. An exciting aspect of our work is the potential for it to have real clinical impact. We have since completed a phase O clinical trial to use the plectin targeted agent for imaging PDAC. The agent had ~2 fold tumor to background ratio however, kidney clearance was suboptimal. Screens are now being performed to develop an improved agent with improved kidney clearance.

Target Identification of Novel Imaging Agents and Determining their Importance in Pathologies

While the sequencing of the human genome holds out the hope for personalized medicine, analysis of DNA or RNA content alone may not be sufficient to understand most disease processes. Proteomic strategies that allow unbiased identification of proteins and their post-transcriptional and translational modifications are an essential complement to genomic strategies. However, the enormity of the proteome and limitations in proteomic methods make it difficult to determine the targets that are particularly relevant to human disease. We have developed a method to couple the power of combinatorial screening technologies such as phage display to identify those ligands. The result has been the identification of novel markers of PDAC and other cancers and diseases (atherosclerosis, myocardial infarction) as well as markers of PDAC mediated angiogenesis. Other examples include, the peptide sequence RPMC, which specifically targets colon cancer and subsequently demonstrated it to be a target for the alpha5-beta1 integrin. Similarly, we identified VCAM-1 targeted peptide sequences with homology to the protein SPARC or osteonectin, which has been shown to play an important role in tumorogenesis and metastasis. The interactions of VCAM-1 and SPARC provided important insights into the mechanisms of transendothelial leukocyte migration.

RECENT RESEARCH DEVELOPMENTS

- Completed a Phase 0 clinical trial.
- Developed functional proteomics methods to identify lead target molecules for imaging and drug delivery as well as identifying potential biomarkers of disease
- Identified new targets in cells of the remodeling heart after infarct.
- Developed targeted nanoparticles for improved efficacy and potency of small molecule drugs

RECENT GRANTS

- U.S. National Cancer Institute – Development of Molecularly Targeted Imaging Agents for Early Detection of PDAC
- ITI Health, Inc. – Development of a Targeted Reagent for Pancreatic Ductal Adenocarcinoma

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