The overarching goals of research in the Sgroi laboratory are to develop better ways to identify patients who are at risk for the development of breast cancer and to identify those breast cancer patients who are likely to benefit from targeted drug therapies. We are taking several different approaches to achieving these goals. First, we are deciphering specific molecular events that occur during the earliest stages of tumor development and using this knowledge to develop biomarkers that will predict for increased risk of progression to cancer. Second, using DNA microarray technologies, we are searching for novel breast cancer biomarkers to identify patients with hormone-receptor-positive breast cancer who are most likely to benefit from extended hormonal therapy. Finally, we are taking a combined approach—based on analysis of tissue from breast cancer patients and various laboratory studies—to identifying biomarkers that will predict how individual breast cancer patients will respond to novel targeted therapeutics.
The comparative analysis of the transcriptome and proteome of normal breast epithelium and malignant breast epithelium (left) combined with a proteome network analysis has led to the discovery of a novel robust network-based biomarker (center) with clinical relevance (right).

Presently, my laboratory is focused on applying high-throughput DNA microarray and proteomic technologies as a means to predict the clinical behavior of human breast cancer in the setting of specific hormonal and chemotherapeutic regimens. We have independently developed two complementary biomarkers—the HOXB13/IL17BR (H/I) index and the molecular Grade Index (MGI)—that predict endocrine responsiveness (to both tamoxifen and letrozole) and risk of recurrence, respectively, in early stage ER+ breast cancer. This novel biomarker outperforms existing biomarkers in predicting outcome, and comparative analysis to assess the clinical significance of this biomarker is currently underway in several prospective clinical trials including the Trans-ATAC and BIG 1-98.

Most recently, using a prospective-retrospective study design, we have demonstrated in the MA.17 clinical trial that the HOXB13:IL17BR biomarker predicts therapeutic benefit from extended adjuvant letrozole. As a result of these data, we anticipate assessing the HOXB13:IL17BR biomarker in additional clinical trials of extended adjuvant hormonal therapy.

Given that HOXB13 expression in clinical breast cancers is associated with poor clinical outcome, we are currently investigating the functional activity of HOXB13 and assessing its possible role as a surrogate marker for a nonclassical estrogen receptor signaling pathway.

Lastly, using an artificial zinc-finger transcription factors combinatorial library technology, we developed an in vitro breast cancer model of drug resistance to a clinically important antiendocrine therapeutic agent. Our results demonstrate that this approach can be used successfully to induce stable drug resistance in human cancer cell lines and to identify a gene expression signature that is associated with a clinically relevant drug-resistance phenotype. These experiments provide an important proof of principle for the use of combinatorial zinc-finger transcription factor libraries to induce and to study important cellular phenotypes, including human cancer drug resistance. We are currently using this approach to identify potential biomarkers for HER2-directed and PARP1-directed therapies.

Selected Publications:


* denotes co-senior authorship