Ovarian Cancer Research Projects Update: December 2013
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Project Title:	**Project 1: Photoacoustic microscopy for early detection of ovarian cancer**	**Project 2: shRNA screen for ovarian cancer cell attachment**	**Project 3: Genomic and transcriptome profiling with clinical prognosis**	**Project 4: AXL in platinum-resistant tumors**
Goal:	To use a non-invasive imaging technique, photoacoustic microscopy (PAM) probe, to detect early ovarian cancer.	To identify new genes involved in attachment of ovarian cancer cells to omentum or other normal sites which begins the process of metastasis	To identify new genes involved in recurrent ovarian cancer using known clinical outcomes of patients	To identify whether AXL, a receptor tyrosine kinase, is involved in platinum-resistant ovarian cancer
Method:	PAM uses laser excitation of hemoglobin to determine neovascular architecture at capillary level resolution without exogenous contrast.	Using short-hairpin loop RNA (shRNA) technology, genes can be silenced. A shRNA screen can be performed using a 3D assay with human cells derived from the omentum to provide a realistic model of cancer cell attachment in patient abdominal surfaces.	Using DNA and RNA sequencing, genes of patients with recurrent cancer who had both good prognosis and poor prognosis will be identified.	Using platinum-resistant ovarian cancer cell lines, experiments will be performed to test this.
Progress:	-Met with bioengineer on Danforth Campus for collaboration on this project -Currently writing animal protocol to perform initial experiments in mice	-Learned the process of culturing human cells from omentum to derive fibroblasts and mesothelial cells which are involved in metastasis in patients -Currently growing cells from the omentum on a large scale in order to culture millions of cells for this experiment -Currently meeting with industry to purchase the shRNA library that contains 15,000 genes: we can then use this library with the 3D assay of tumor cells attaching to human omentum in a petri dish.	-Met with Elaine Mardis of the Genome Institute for collaboration on this project - Institutional Review Board (IRB) protocol has been approved and we are able to proceed with this project - Have identified patients with good prognosis	-Have acquired platinum-resistant cell lines -Have the AXL antibody to confirm AXL expression in platinum-resistant but not in platinum-sensitive cell lines
Future experiments:	( ) Develop an early stage ovarian cancer model by injecting cells into the ovarian bursa to simulate localized cancer ( )Validate the probe can detect this early stage cancer ( )Use longitudinal PAM imaging to determine how microvessel function, angiogenesis and signaling pathways involved during tumor growth. ( )Translational development to detection in patients – will require extensive discussions of best method for initial validation studies	( ) Optimize the ovarian cancer cells to accept the shRNA library ( ) Perform the screen for new genes by layering the ovarian cancer cells on top of the omentum (simulating how cancer cells invade the omentum in patients) ( ) Capture the cells that do not attach as the genes of interest for attachment ( ) Analyze the data and identify the gene ( ) Validate this gene or genes of interest through multiple experiments to ensure these genes should be pursued for therapeutic targeting to prevent attachment (earliest step of metastasis)	( ) Extract DNA and RNA of patients with the above criteria ( ) Work with the Genome Institute to perform the DNA and RNA sequencing ( ) Analyze the data ( ) Identify genes or genes of interest ( ) Validate this gene or genes of interest through multiple experiment to ensure these genes should be pursued for therapeutic targeting to prevent recurrent ovarian cancer	( ) Perform cell viability and chemosensitivity assays to confirm the role of AXL ( ) Administer an AXL inhibitor to these platinum-resistant cell lines to determine whether ovarian cancer cells will respond and can induce death of these platinum-resistant cell lines with AXL inhibition