9th ANNUAL DEPARTMENT OF PATHOLOGY YOUNG INVESTIGATORS’ DAY
POSTER SESSION

Thursday, April 5th, 2007
TURNER CONCOURSE

REGISTRATION FORM

E-mail COMPLETED Registration form and abstract to:
Stacey Morgan (smorgan9@jhmi.edu) on or before
Friday, March 16th, 2007

If you have questions or problems regarding your submission, please contact Stacey Morgan via e-mail (smorgan9@jhmi.edu)

Applicant’s Name:  ____Julie Michelle Wu_________   Degree:  _____MD______
Applicant’s Division:  ____Pathology__________________________
Faculty Preceptor:  ____Pedram Argani__________________________
(Must hold a primary appointment in Pathology)
Appointment Category:   __X__House Staff  _____Clin Fellow _____Research Fellow
                         _____Medical Student _____Graduate Student (Program:____________)
Register for:    __X__ Clinical Research  ____Translational Research _______Basic Research

Full Poster Title *  Heterogeneity of Breast Cancer Metastases: A Rapid Autopsy Study Using Matched Primary-Metastases Tissue Microarrays (TMAs)

Where has the work been presented?
Meeting Name   _USCAP 2007________________________________________
Meeting Date   _March 2007________________________________________
Not Previously Presented  _yes_____________________________________
Where is this work being published?  ______________________________________
Journal Name, Volume, Page, Date  ______________________________________
In Preparation  _X_________________________________________________
Author(s) (First & Last)  _Julie M. Wu, Pedram Argani_____________________

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INCLUDE A ONE-PAGE ABSTRACT (including title and all authors) OF THE WORK YOU WILL BE PRESENTING

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**Title:** HETEROGENEITY OF BREAST CANCER METASTASES: A RAPID AUTOPSY STUDY USING MATCHED PRIMARY-METASTASES TISSUE MICROARRAYS (TMAs)

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**Background:** Heterogeneity of biomarker expression among a patient's primary breast carcinoma (PBC) and their metastatic breast carcinomas (MBCs), as well as among different MBCs from different sites in the same patient, has not been well studied.

**Design:** We performed eight rapid autopsies (post-mortem intervals, 1-4 hours) on patients who died of MBC. Paraffin tissue blocks from the patients' archived PBC and multiple different MBCs were used to construct single patient TMAs. Eight TMA slides containing PBCs and in total 515 spots derived from 108 MBC sites were immunohistochemically labeled for the following: estrogen receptor (ER), progesterone receptor (PR), Her-2/neu, E-cadherin, Fascin, EGFR, C-Met, Cox-2, and Mesothelin. Methylation of the RASSF1a, HIN1, Cyclin D2, Twist, and RARβ gene promoters was assessed quantitatively on dissected PBC and MBC samples.

**Result:** Extensive heterogeneity was observed between PBC and their paired MBC, as well as among multiple MBC from the same patient. The patterns observed are summarized into three categories: 1. **Markers Downregulated Uniformly in All Metastases of a Case:** ER, PR. Three cases were ER-PR- and two cases were ER+PR+ in the PBC and all MBC. However, one ER+PR+ PBC was ER-PR- in all its MBC, one ER+PR- PBC was ER-PR- in all its MBC, and one ER+PR+ PBC was ER+PR- in all its MBC. 2. **Markers Consistently Expressed between Primary and Metastasis:** Fascin, implicated in the lung metastasis gene expression signature of PBC (Nature 2005;436: 518-524), was overexpressed in the PBC and all MBC in 1 of 8 cases. Interestingly, this was the only case with bulky lung metastasis. Promoter hypermethylation of RASSF1a, RARβ, Cyclin D2, Twist, and RARβ was very similar in the PBC and all MBC in all 7 evaluable cases. 3. **Markers Variably Expressed among Metastases:** E-cadherin was variably downregulated in the MBC of one case; the E-cadherin positive invasive ductal PBC gave rise to both E-cadherin positive ductal MBC and E-cadherin negative MBC with lobular morphology. Variable overexpression in MBC compared to the PBC was observed for Cox-2 (5 cases), EGFR (4 cases), C-met (2 cases), and Mesothelin (1 case). No case strongly overexpressed Her-2/neu, but 3 cases showed variable expression ranging from negative to weakly positive (2+) in different MBC.

**Conclusion:** Therapeutic targets identified in the PBC or even some MBC may not reflect targets present in all metastatic sites.