

10th ANNUAL DEPARTMENT OF PATHOLOGY YOUNG INVESTIGATORS' DAY
POSTER SESSION

POSTER #

44

(for Admin. use)

Thursday, April 17th, 2008
TURNER CONCOURSE
REGISTRATION FORM

Applicant's Name: Andrea Proctor Subhawong Degree: MD

Applicant's Division: Pathology

Faculty Preceptor: Pedram Argani
(Must hold a primary appointment in Pathology)

Appointment Category: House Staff Clin Fellow Research Fellow
 Medical Student Graduate Student (Program: _____)

Register for: Clinical Research Translational Research Basic Research

Full Poster Title **Most Basal-like Breast Carcinomas Demonstrate the Same Rb-/p16+ Immunophenotype as the HPV-related Poorly-Differentiated Squamous Carcinomas Which They Resemble Morphologically**

Where has the work been presented?

Meeting Name USCAP _____

Meeting Date 3/3/08 _____

In Preparation (Y/N) - Where? Yes, for AJSP, submission in March

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

**E-mail COMPLETED Registration form and abstract to:
Stacey Morgan (smorgan9@jhmi.edu) on or before
Friday, March 14th, 2008**

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

Most Basal-like Breast Carcinomas Demonstrate the Same Rb-/p16+ Immunophenotype as the HPV-related Poorly-Differentiated Squamous Carcinomas Which They Resemble Morphologically

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ABSTRACT

Background: Basal-like carcinomas (BLC) of the breast, as defined by gene expression profiling, are high grade malignancies with a poor prognosis. By immunohistochemistry (IHC), BLC are estrogen receptor (ER), progesterone receptor (PR) and HER-2 negative ("triple-negative"), and typically express high-molecular-weight cytokeratins CK5/6 and/or EGFR. BLC often have a pushing border, minimal desmoplasia, a ribbon-like growth pattern with central necrosis, and focal squamous features. This morphology resembles that of human papilloma virus (HPV)-related poorly-differentiated carcinomas of the oropharynx, vulva, and penis. Inactivation of the Retinoblastoma (Rb) tumor suppressor by high risk HPV in the latter cancers leads to diffuse p16 labeling by IHC, since Rb normally suppresses p16 expression. In addition, HPV E6 protein inactivates p53 in these cancers. The Rb/p16/p53 immunophenotype of BLC of the breast has not been studied.

Design: We created tissue microarrays (TMAs) from 71 breast cancers which by IHC corresponded to specific types defined by expression profiling. These were luminal (ER+), HER-2+ (3+ score by IHC or amplification ratio >4 by FISH), BLC (triple negative, strong CK5/6+ and/or EGFR+), or unclassified triple negative, CK5/6- and EGFR- cancers (UTNC). The TMAs were analyzed by IHC for expression of p16, Rb, p53, and Ki-67. HPV status was evaluated by in situ hybridization.

Results: The Rb negative/p16 diffuse positive immunophenotype (Rb-/p16+) was identified in 15 of 21 BLC and 9 of 12 TNC, but only 1 of 14 HER-2+ and none of the luminal cancers ($p < 0.01$). Elston Grade 3 BLC with the Rb-/p16+ phenotype had significantly higher Ki-67 indices (mean 72%) compared to Elston grade 3 HER-2+ cancers (mean 42%) ($p < 0.01$). Rb-/p16+/p53+ BLC had the highest proliferation indices of any BLC subset. None of these cancers contained HPV DNA.

Conclusion: Unlike other breast cancers, BLC frequently show an Rb-/p16+ phenotype, similar to the HPV-related cancers that they morphologically resemble, although BLC lack evidence of HPV infection. Inactivation of Rb and p53 likely promotes the high proliferative rate, and also may contribute to the histologic similarities between HPV-related cancers and BLC, though the inactivation occurs through different mechanisms. While BLC, as currently defined, are a heterogeneous group, the Rb-/p16+ phenotype may identify a more biologically homogeneous subset.