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(Must hold a primary appointment in Pathology)
Appointment Category: _____House Staff _____Clin Fellow _____Research Fellow
____Medical Student  __V__Graduate Student (Program:_Pathobiology )
Register for: _____ Clinical Research _____Translational Research  _____Basic Research
Full Poster Title *  _Amplification of Notch3 and identification of Notch3 target
gene in ovarian cancer___________________________
Where has the work been presented?
Meeting Name ____________________________________________________
Meeting Date ____________________________________________________
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In Preparation (Y/N) - Where? __Cancer research___________________________
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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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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)
Amplification of Notch3 and identification of Notch3 target gene in ovarian cancer
Joon T Park, Ie-Ming Shih, Tian-Li Wang

Abstract
Gene amplification is one of the common mechanisms that activate oncogenes. In this study, we used SNP array to analyze genome-wide DNA copy number alterations in 31 high-grade ovarian serous carcinomas, the most lethal gynecologic neoplastic disease in women. We identified an amplicon at 19p13.12 in 6 (19.5%) of 31 ovarian high-grade serous carcinomas. This amplification was validated by digital karyotyping, quantitative real-time PCR, and dual-color fluorescence in situ hybridization (FISH). Furthermore, Notch3 DNA copy number is positively correlated with Notch3 protein expression based on parallel immunohistochemistry and FISH studies in 111 high-grade tumors. Although several Notch3 downstream genes have been reported, the predominant Notch3-regulated gene(s) in ovarian cancer remains elusive. Based on expression-profiling analysis, we have identified Pbx1, a proto-oncogene in hematopoietic malignancy, as a main Notch3 target gene. Pbx1 expression is transcriptionally regulated by Notch3 activation and Notch3/CSL protein complex directly binds to Pbx1 promoter segment harboring the CSL binding sequence. The growth-inhibitory effect of gamma-secretase inhibitor could be partially reversed by ectopic Pbx1 expression. Furthermore, functional studies by Pbx1 shRNA knockdown demonstrate that Pbx1 mediates cell proliferation and tumorigenicity. Taken together, the above findings indicate that Notch3 is amplified in ovarian cancer and Pbx1 is a direct target gene of Notch3. Inactivation of Notch3 and Pbx1 can be a potential therapeutic approach for ovarian carcinomas.