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Register for:  _____ Clinical Research  _____Translational Research  ___X_Basic Research

Full Poster Title *  ____KRAS2 Gene Mutations in Acinar-Ductal Metaplasia in the Pancreas: Pancreatic Neoplasia May Start Prior to Pancreatic Intraepithelial Neoplasia Lesions____

Where has the work been presented?

Meeting Name  ___USCAP________________________________________
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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:
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Friday, March 14th, 2008

If you have questions or problems regarding your submission, please
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KRAS2 Gene Mutations in Acinar-Ductal Metaplasia in the Pancreas: Pancreatic Neoplasia May Start Prior to Pancreatic Intraepithelial Neoplasia Lesions

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Background: Pancreatic intraepithelial neoplasm (PanIN) is a precursor to invasive ductal adenocarcinoma of the pancreas. Mutations in KRAS2 proto-oncogene are thought to be early events in the development of PanIN lesions. Observations made in genetically engineered mouse models suggest that the acinar/centroacinar compartment can give rise to ductal neoplasia. In order to integrate findings in mice and men, we examined human acinar cells, acinar-ductal metaplasia lesions and PanINs for KRAS2 gene mutations to determine if KRAS2 gene mutations occur before the development of PanINs in human pancreata. Methods: Surgically resected pancreata were screened for PanIN lesions associated with acinar to ductal metaplasia. PanIN lesions, acinar-ductal metaplasia, and acinar cells from the same lobule, as well as stromal cells were microdissected using laser capture microdissection. Genomic DNA from the microdissected tissues was subjected to nested PCR amplification of KRAS2 gene followed by PCR DNA sequencing. Results: Seventeen sets of lesions from 16 surgically resected pancreata were analyzed. KRAS2 gene mutations at codon 12 were present in 8 of 17 (47%) PanIN lesions. In 4 of these 8 cases (50%) with KRAS2 mutations in PanINs, the same KRAS2 mutation was present in the acinar-ductal metaplasia lesion associated with the PanIN. The remaining acinar-ductal metaplasia lesions, all of the adjacent acinar cells and all control stromal cell samples were KRAS2 wild type. Conclusion: Human pancreatic neoplasia may originate from foci of acinar-ductal metaplasia prior to pancreatic intraepithelial neoplasia lesions.