B10

Correlation between gene expression profile and tumor behavior of pancreatic neuroendocrine tumors and carcinoids

[1]**Yunguang Tong, PhD**; [2]Nicholas N. Nissen, MD; [2]Vijay Menon, MD; [3]Edward Wolin, MD; [3]Run Yu, MD, PhD

[1]Division of Endocrinology, [2]Department of Surgery, [3]Division of Oncology and Carcinoid and Neuroendocrine Tumor Center, Cedars-Sinai Medical Center, Los Angeles, CA 90048

Background: Clinical parameters are often inadequate to predict the behavior of common neuroendocrine tumors (NETs) such as non-functioning pancreatic NETs (NF PNETs) and mid-gut carcinoid tumors (carcinoids). Molecular markers of tumor behavior are not clear but needed to assist clinical decision making.

Methods: Gene expression profile of 7 NF-PNETs and 6 carcinoids was obtained through Affymetrix Human Gene 1.0 ST Array. The tumors were clinically classified by aggressiveness (indolent v. aggressive). The microarray data were analyzed using Genespring 11. Microarray data files were preprocessed with RMA algorithm. Genes were ranked according to expression levels and only those presented in top 80% in at least one sample were included for unpaired t-test. Benjamini Hochberg false discovery rate control was used for multiple test correction.

Results: For NF-PETs, 322 genes were differentially expressed >3-fold in indolent v. aggressive tumors, and 112 genes were differentially expressed with $p<0.005$. *ACMSD* (Aminocarboxymuconate semialdehyde decarboxylase), *FGB* (fibrinogen beta chain), *AGT* (angiotensinogen), *APOH* (apolipoprotein H), *HAO1* (hydroxyacid oxidase 1) were >8 fold upregulated in aggressive tumors. For carcinoids, 159 genes were differentially expressed >3-fold in indolent v. aggressive tumors, and 47 genes were differentially expressed with $p<0.005$. *SLC38A3* (solute carrier family 38, member 3) was 15-fold upregulated in aggressive tumors and *MX2* (myxovirus resistance 2) was 5-fold upregulated in indolent tumors. When taken as a group, 68 genes were differentially expressed >3-fold in indolent v. aggressive tumors, and 38 genes were differentially expressed with $p<0.005$. *MEP1B* (meprin A, beta) was ~10-fold upregulated in aggressive

tumors. Pathway analysis suggested interleukin 4 and 9 pathways were differentially regulated between indolent and aggressive NF-PETs.

Conclusion: Indolent and aggressive NETs, especially pancreatic ones, exhibit distinct gene expression profile. Specific genes are differentially expressed in indolent v. aggressive NETs and may serve as markers for tumor behavior.