

## Molecular profiling of papillary thyroid cancer identifies functional biomarkers

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The ACS estimates that there will be ~56,000 new cases of thyroid cancer in 2012, approximately 80% of which will be papillary thyroid carcinomas (PTC), an increasing number since 1980. Molecular profiling of PTC offers a valuable tool for identifying genes that can be used as diagnostic and prognostic markers. Molecular profiling of PTC samples and paired controls identified 177 differentially expressed genes (98 upregulated and 79 downregulated). The upregulation of potential biomarkers was verified in expanded sample sets by qRT-PCR and immunohistochemistry, and included arachidonic acid 5-lipoxygenase (ALOX5), urokinase plasminogen activator and its receptor (uPA/uPAR) and kallikreins 7 and 10 (KLK7/KLK10). ALOX5 expression was elevated in PTC (22.57 fold) and demonstrated a direct correlation with tumor invasiveness. Transfection of ALOX5 into the PTC cell line, BCPAP, resulted in increased collagenase activity, MMP-9 secretion and invasiveness. Inhibitors of MMP-9 and ALOX5 reversed the ALOX5-enhanced invasion. uPA and uPAR transcription was increased in PTC (2.4 and 10.1 fold, respectively) and in BCPAP, relative to a normal thyroid cell line. siRNA-mediated downregulation of uPAR in BCPAP cells resulted in decreased activity in the FAK/PI3K/Akt signaling pathway, proliferation, clonogenicity and migration/invasion. KLK7 and KLK10 RNA expression in PTC was upregulated (21.0 and 22.0 fold) and immunohistochemical analysis on patient samples revealed increased and coordinated expression. These data provide new evidence of ALOX5 and uPA/uPAR system's functional roles in PTC invasion/metastasis, and demonstrate their attractiveness as molecular biomarkers and therapeutic targets. The role of KLKs in PTC pathogenesis is currently under investigation.

### Biography

Dr. Geliebter received his PhD from SUNY, Downstate Medical Center and completed postdoctoral research at The Albert Einstein College of Medicine, Bronx, NY. He has held faculty positions at The Rockefeller University and the Albert Einstein College of Medicine and he is currently a Professor in the Departments of Microbiology & Immunology and Otolaryngology at New York Medical College and the Resident Research Coordinator at New York Eye and Ear Infirmary. He has published more than 60 papers in peer-reviewed journals in the fields of thyroid and prostate cancer and molecular genetics of the immune system.

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