ROLE OF TUMOR-ASSOCIATED MACROPHAGES IN PTC PROGRESSION

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Background/Purpose: Inflammation plays a key role in the progression of solid malignant tumors. Infiltrating macrophages secrete chemokines and cytokines which induces an epithelial to mesenchymal transition (EMT) in tumor cells which facilitates metastasis. Papillary thyroid cancer (PTC) infiltrated with macrophages portend a poor prognosis and higher metastatic propensity, but their role in thyroid cancer EMT is uncertain. The purpose of this study is to examine the cross-talk between macrophages and epithelial cells (and EMT) in the thyroid tumor microenvironment.

Methods: Nuclear and cytoplasmic extracts from cell lines of normal thyrocytes, PTC and follicular thyroid cancer cells were treated with macrophage-conditioned media (MCM) and analyzed for the expression of several EMT markers. Cell morphology, and migration/invasion assays were performed to examine *in vitro* phenotypic changes.

Results: The expression of EMT markers, including cadherin, catenin, vimentin, NFk-B and twist, are modulated by MCM. Further, snail and slug (transcription factors) translocated into the nucleus, indicative of the initiation of EMT. A statistically significant ($p<0.05$) upregulation of migration and invasion of cell lines (consistent with the mesenchyme phenotype) was induced by MCM.

Discussion & Conclusion: Our data provide evidence that macrophage-secreted proteins play a crucial role in EMT in thyroid tumor growth and metastasis. Validation of these findings in human PTC samples is underway to define the clinical relevance of EMT markers and their utility as therapeutic targets.