Clues to thyroid cancer unlocked

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Researchers at the University of Toronto and Mount Sinai Hospital have utilized proteomic technologies to discover proteins secreted by thyroid cancer cell lines to identify and characterize potential biomarkers for the future management of thyroid carcinomas.

The study, recently published in the [Journal of Proteome Research](#), is of particular importance because these [biomarkers](#) have the potential to aid oncologists in determining the aggressiveness of the cancer so appropriate treatment plans can be developed for patients. [Thyroid cancer](#) represents 90 per cent of all endocrine malignancies, with an estimated annual incidence of 122,800 cases worldwide and approximately 33,000 newly diagnosed cases in North America.

"We know that about 10 to 15 per cent of thyroid cancers are aggressive. Our hope is that out of this research a diagnostic test can be developed that will allow us to detect aggressive forms of the cancer early so we create rigorous treatment plans that will help improve outcomes for patients," said Professor Emeritus Paul Walfish of medicine and an endocrinologist at Mount Sinai Hospital, senior author of the study. "On the other side of the equation, if we determine a patient's cancer is a non-aggressive form the treatment plan can be less intensive, making it easier for patients to tolerate, and have a lesser impact on their quality of life."

Walfish and his team employed liquid chromatography mass spectrometry for identification of proteins secreted by aggressive and non-aggressive thyroid cancer cell lines. Among the majority of the 46 high confidence secretory proteins identified, 31 have not yet been

reported in thyroid cancer demonstrating the ability of secretome analysis to identify potential biomarker candidates for correlation with clinical management of thyroid cancer.

"Six proteins secreted by thyroid cancer cells could be independently verified in cell lines, tumour xenografts in immunocompromised mice, as well as tumour tissues and blood samples of thyroid cancer patients," said Dr. Ranju Ralhan, co-director of the Alex and Simona Shnaider Research Laboratory in Molecular Oncology at Mount Sinai Hospital. "This underscores their potential as candidate thyroid cancer biomarkers. Clinical trials will still need to be undertaken to validate our research, but we are very hopeful that this will lead to a diagnostic test."

The studies also revealed that it's the nuclear and/or cytoplasmic localization of these proteins in human thyroid cancer tissues that might have clinical relevance. Notably, similar subcellular localization of these proteins could be observed in xenografts of thyroid cancer cells in NOD/SCID/gamma mice as well. Also, prothymosin alpha (PTMA) was particularly elevated in aggressive anaplastic thyroid carcinomas compared with the more differentiated papillary thyroid cancer, indicating it may serve as a marker for aggressive carcinomas upon validation in a larger study.

"To our knowledge this study is the first report on the identification of biotinidase and nucleolin in thyroid cancer," added Walfish. "Further, in-depth studies showed a protein called PTMA, a heterochromatin remodelling protein, is significantly elevated in well-differentiated thyroid carcinomas compared to adenomas and non-toxic goitres."

Large-scale analysis of these proteins in sera of thyroid cancer patients and characterization of their expression in cancer tissues may serve as the next step towards evaluating their suitability as candidate cancer markers. Thus, these researchers have successfully demonstrated the

application of proteomic technologies for discovery and verification of proteins secreted by cultured thyroid cancer cells and large-scale validation will pave the way for development of minimally invasive biomarkers for future clinical applications in thyroid cancer as well as other epithelial cancers.

Walfish and his team, including Ralhan, Dr. Christina MacMillan and laboratory co-workers Lawrence Kashat, Anthony So and X. Meng of the Department of Pathology and Laboratory Medicine, in collaboration with Dr. K.W. Michael Siu's team at York University and Dr. Laurie E. Ailles in the Ontario Cancer Institute, developed a strategy to identify thyroid cancer biomarkers.

  More information: An abstract of the study entitled Secretome-Based Identification and Characterization of Potential Biomarkers in Thyroid Cancer can be found online at www.ncbi.nlm.nih.gov/pubmed/20873772

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