Medical Xpress

Researchers discover new biomarker to identify agressive thyroid cancer

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Researchers at the University of Toronto and Mount Sinai Hospital have discovered a new way to identify aggressive thyroid cancer, as well as predict patient outcomes. The research was published late last week in the leading medical journal *BMC Cancer*.

“Our study shows, for the first time, a key biomarker that can be used in diagnostic, prognostic and therapeutic strategies for the future management of thyroid cancer,” said endocrinologist Paul Walfish, Alex and Simona Shnaider Research Chair in Thyroid Oncology at Mount Sinai Hospital, emeritus professor at the Faculty of Medicine and the senior author of the study.

Thyroid cancer occurs when some of the cells that make up the gland (a butterfly-shaped organ at the front of the neck) mutate and become cancerous. It is known that the epithelial cells lining the thyroid undergo cellular changes including the removal (or cleavage) of molecules attached to their surface. However until now, the role and significance of the intracellular product of this process were unknown.

To further understand the cellular changes occurring during the development and progression of thyroid cancer, Walfish and his team - including lead author Dr. Ranju Ralhan, Dr. Christina MacMillan, Dr. Jeremy Freeman (all of Mount Sinai Hospital) and Jun Cao (post-doctoral fellow) and Terence Lim (U of T medical student) - analysed 58 archived thyroid cancer tissue blocks from 34 patients and correlated them with survival analysis of these patients for up to 17 years.

The team discovered that increased intracellular levels of a specific biomarker named Ep-ICD can be used to diagnose an aggressive form of thyroid cancer. Ep-ICD forms intracellularly after cleavage from a precursor protein called epithelial cell adhesion molecule (Ep-CAM) which localizes on the membrane surface of normal and cancer cells.

“Our laboratory discovered that increased accumulation of Ep-ICD in the cytoplasm and nucleus of a thyroid cancer cell is associated with increased aggressiveness and poor prognosis,” said Walfish. “In patients with the most lethal form of thyroid cancer, the levels of Ep-ICD were remarkably higher than those with a more low-grade papillary thyroid cancer, where Ep-CAM remained predominantly on the membrane surface of their cancer cells.”

Statistical analyses showed that patients with increased cytoplasm and nuclear levels of Ep-ICD developed aggressive thyroid cancer and survived an average of five months after diagnosis, compared with those without such abnormal pathology who survived an average of 16 years.

“These findings add further support to a novel mechanism in the pathogenesis of aggressive thyroid cancer and demonstrate the importance of Ep-ICD in promoting such aggressiveness through its interaction with other proteins within the cell,” said Ralhan, co-director of the Alex and Simona Shnaider Research Laboratory in Molecular Oncology at Mount Sinai Hospital and lead author of the study.

Thyroid cancer is the most rapidly increasing cancer in Canada, with more than 3,000 Canadians - 80 per cent of them women - diagnosed annually. Thyroid cancer has one of the lowest death rates among cancers, however a sub-type, anaplastic thyroid cancer, has a high fatality rate and some patients may only live for four months after diagnosis in severe cases. Usually, the cause of thyroid cancer is unknown, although exposure to radiation has been linked to the

development of cancerous thyroid tumours.

Provided by University of Toronto