

Researchers find protein target for anaplastic thyroid carcinoma

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Anaplastic thyroid carcinoma (ATC) is an aggressive type of cancer with a poor prognosis for which there is currently no effective treatment. Researchers from the National University of Singapore (NUS) have discovered for the first time that an epithelial basement membrane protein, called laminin-5 gamma-2 (LAMC2), has the potential to be an ideal target for the treatment of ATC.

Led by Professor H. Phillip Koeffler, Senior Principal Investigator, and Dr Manoj Garg, Research Fellow, at the Cancer Science Institute of Singapore (CSI Singapore) at NUS, the team is also the first to demonstrate that effect of LAMC2 on cell growth, [cell cycle](#), migration and invasion in ATC cells. This novel study was published in the *Journal of Clinical Endocrinology and Metabolism* last month.

Thyroid [cancer](#) is the most common cancer of the endocrine system. ATC are undifferentiated tumours of the thyroid follicular epithelium. This type of cancer has a [poor prognosis](#) due to their extremely aggressive nature and resistance to treatment. Overall survival from diagnosis is typically six months or less. As such, new therapeutic targets are needed to improve the clinical care of these patients.

In their study, the researchers found that LAMC2 is over-expressed in a large cohort of ATC patient samples. Analysis of RNA data of ATC cells showed that LAMC2 is likely to play a role in the formation of tumours. They discovered that silencing of LAMC2 in ATC cells reduced their cell growth, migration and invasion. In addition, silencing

of this protein impaired the cell cycle of ATC cells by arresting them at the growth phase to DNA replication phase, or the G1 to S phase transition, of their cell cycle.

At the same time, the study found that LAMC2 enhanced activation of growth signals through a cell surface protein called epidermal growth factor receptor (EGFR) in ATC cells. EGFR plays an important role in the behaviour of malignant cells in a variety of human tumours by increasing proliferation. Increased expression of epidermal growth factor and EGFR has been detected in 58 per cent to 87 per cent of ATC when compared with normal tissue. The researchers demonstrated that simultaneous silencing of LAMC2 combined with various ways of silencing EGFR effectively inhibited the growth of tumour [cells](#).

The novel study provides a foundation for further investigation of LAMC2 as a promising target for developing novel therapeutic approaches for the treatment of ATC.

Said Prof Koeffler, "Our findings provide a novel target for therapeutic research. We are now extending these investigations to additional types of frequent cancer subtypes."

More information: "Laminin-5 γ -2 (LAMC2) Is Highly Expressed in Anaplastic Thyroid Carcinoma and Is Associated With Tumor Progression, Migration, and Invasion by Modulating Signaling of EGFR." Manoj Garg, Deepika Kanojia, Ryoko Okamoto, Saket Jain, Vikas Madan, Wenwen Chien, Abhishek Sampath, Ling-Wen Ding, Meng Xuan, Jonathan W. Said, Ngan B. Doan, Li-Zhen Liu, Henry Yang, Sigal Gery, Glenn D. Braunstein and H. Phillip Koeffler. *The Journal of Clinical Endocrinology & Metabolism*. Volume 99 Issue 1 | January 2014. dx.doi.org/10.1210/jc.2013-2994

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