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New discovery of biomarker to improve diagnosis, prognosis and treatment of esophageal squamous cell carcinoma

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Esophageal squamous cell carcinoma (ESCC), the major histological form of esophageal cancer, is the leading cause of cancer death worldwide. Scientists from the National University of Singapore (NUS) have discovered a biomarker, called adenosine deaminase acting on RNA-1 (ADAR1), which has the potential to improve the diagnosis, prognosis and treatment of this disease.

Led by Dr Polly Chen from the Cancer Science Institute of Singapore (CSI Singapore) at NUS, the team is also the first to demonstrate that the editing of protein-making sequences promotes the development of ESCC. This novel study was first published online in *Cancer Research* on 4 December 2013.

Currently, there is poor prognosis for ESCC patients and the five-year overall survival rate ranges from 20 to 30 per cent. As such, there is an urgent need for biomarkers which can diagnose this disease as early as possible, estimate reaction to chemotherapy or radiotherapy in patients and predict the overall survival rate of patients undergoing treatment.

In normal human cells, deoxyribonucleic acid (DNA), which comprises the genetic code, serves as a template for the precise production of ribonucleic acid (RNA) such that the DNA code and RNA code are identical. Editing is a process in which RNA is changed after it is made from DNA, resulting in an altered gene product. This RNA editing is

likely to play a role in the formation of tumours by either inactivating a tumour suppressor or activating genes that promote tumour progression.

In their study, the NUS researchers discovered that the RNA editing enzyme ADAR1, which catalyses the editing process, is significantly over-expressed in ESCC tumours. They observed that ADAR1 changes the product of the AZIN1 protein to a form which promotes the development of the disease. Clinically, the tumoural over-expression of ADAR1 was correlated with the shorter survival time of ESCC patients.

The findings suggest that ADAR1 can serve as a useful biomarker to detect disorders leading to ESCC and as a potential therapeutic target. The study may also provide the key to a biological process for drug development in the treatment of ESCC

Said Dr Chen, "Investigating the connection between ADAR1-mediated RNA editing and cancer progression is only the initial step in this research. The tumoural over-expression of ADAR1 can be used as an early warning sign of ESCC and halting or reversing the process may block the cells' conversion from normal to malignant.

Moving forward, the researchers will further investigate the key RNA editing events regulated by ADAR1 during ESCC development. They plan to develop a method to correct the RNA editing process through restoring ADAR balance by silencing ADAR1 and reinstating a specific hyper-edited or hypo-edited transcript.

More information: "Adenosine-to-Inosine RNA Editing Mediated by ADARs in Esophageal Squamous *Cell* Carcinoma." Yan-Ru Qin, Jun-Jing Qiao, Tim Hon Man Chan, Ying-Hui Zhu, Fang-Fang Li, Haibo Liu, Jing Fei, Yan Li, Xin-Yuan Guan, and Leilei Chen. *Cancer Research*. Published Online First December 3, 2013; DOI: 10.1158/0008-5472.CAN-13-2545