Medical Xpress

Scientists discover novel genetic defects which cause oesophageal cancer

March 31 2014

Latest findings by a team of international scientists led by Singapore-based researchers reveal the genomic landscape of oesophageal squamous carcinoma.

A team of scientists from the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore and National University Cancer Institute Singapore (NCIS), and their collaborators from the Cedars-Sinai Medical Centre, UCLA School of Medicine, demonstrated that a number of novel genetic defects are able to induce oesophageal cancer.

The research group, led by Professor H. Phillip Koeffler, Senior Principal Investigator at CSI Singapore and Deputy Director of NCIS, has conducted a successful comprehensive genomic study of oesophageal squamous carcinoma, a type of very aggressive cancer prevalent in Singapore and Southeast Asia.

This novel study was first published online in the prestigious journal *Nature Genetics* on 30 March 2014.

In this study, the researchers comprehensively investigated a large variety of genetic lesions which arose from oesophageal squamous carcinoma. The results showed enrichment of genetic abnormalities that affect several important cellular process and pathways in human cells, which promote the development of this malignancy. The scientists also uncovered a number of novel candidate genes that may make the cancer

sensitive to chemotherapy. The researchers' findings provide a molecular basis for the comprehensive understanding of the pathophysiology of oesophageal carcinoma as well as for developing novel therapies for this deadly disease. These groundbreaking results have immediate relevance for cancer researchers, as well as for clinical oncologists who currently do not have effective therapeutic agents to treat this type of cancer.

Dr Lin Dechen, Research Fellow at CSI Singapore and first author of the research paper, noted, "Our findings are very relevant to Singapore and the region because this disease is endemic to Southeast Asia. More importantly, many potential therapeutic drugs have surfaced from our analysis, with some of them already in use for treating other types of tumours. We are more than excited to test their efficacy in oesophageal cancer."

Prof Koeffler said, "Oesophageal squamous cancer is one of most common causes of cancer-related death, and is particularly prevalent in Southeast Asia. We wanted to understand this major burden on the local public health system and to help find solutions. By completely investigating all human genes at the single nucleotide level, our current findings provide an enhanced road map for the study of the molecular basis underlying this somewhat neglected malignancy."

With the discovery of these previously unrecognised genetic defects, Prof Koeffler and his team will explore the detailed molecular mechanisms in the next phase of research. In addition, the scientists will evaluate whether some of these defects can be used in the clinic to cure this disease.

More information: "Genomic and molecular characterization of esophageal squamous cell carcinoma." De-Chen Lin, Jia-Jie Hao, Yasunobu Nagata, et al. *Nature Genetics* (2014) DOI: 10.1038/ng.2935. Published online 30 March 2014

Medical Xpress

Provided by National University of Singapore

Citation: Scientists discover novel genetic defects which cause oesophageal cancer (2014, March 31) retrieved 4 May 2024 from https://medicalxpress.com/news/2014-03-scientists-genetic-defects-oesophageal-cancer.html

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