New study offers potential avenues for treatment of deadly nasopharyngeal cancer

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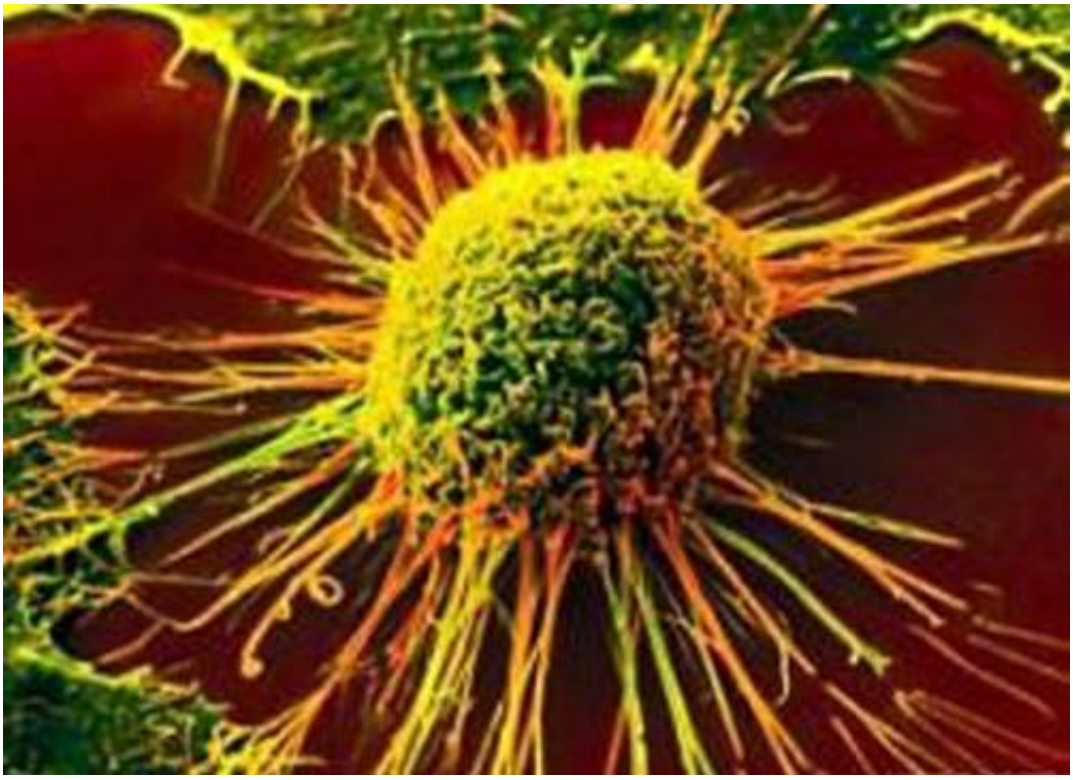

A team of scientists from the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore, National University Cancer Institute Singapore (NCIS) and National University Hospital Singapore (NUH), discovered a distinct mutational signature and nine significantly mutated genes associated with nasopharyngeal cancer,

paving the way to developing novel therapies for this deadly disease.

The research group, led by Professor H. Phillip Koeffler, Senior Principal Investigator at the CSI Singapore and Deputy Director of NCIS, has conducted the first successful comprehensive genomic study of nasopharyngeal carcinoma, which has a particularly high prevalence in Southern China and Southeast Asia, including Singapore. The findings provide an enhanced road map for the study of the molecular basis of this form of cancer.

The novel study was first published online in the prestigious journal *Nature Genetics* on 23 June 2014.

Nasopharyngeal carcinoma arises from the epithelial lining of the nasopharynx, the upper part of the throat behind the nose. Unlike cancers that have been extensively studied, such as breast and colon cancers, there is currently limited understanding of the molecular biology of nasopharyngeal cancer. To date, no targeted therapy has been established and there is an urgent need for a comprehensive genomic landscape of this disease to guide the development of novel therapies.

In this study, the researchers analysed the genomic DNA and proteins of over 100 nasopharyngeal cancer patients in Singapore through advanced biological technologies. The research revealed that many genes are mutated and dysfunctional in the nasopharyngeal tumour cells, and some of them cause and exacerbate the disease. The analysis also showed enrichment of genetic lesions which affect several important cellular processes and pathways. Furthermore, a number of novel druggable candidates, which are proteins that have the ability to bind with drugs with a high affinity, were uncovered through this comprehensive study.

Dr Dechen Lin, Research Fellow at CSI Singapore and first author of the scientific paper, said, "This malignancy has been somewhat neglected

because nasopharyngeal cancer is very rare in the US and Europe. However, the disease is particularly common in Southeast Asia, especially Singapore. Our current study offers immediate translational significance for nasopharyngeal cancer research, specifically, for identifying tailored targeted therapies for the patients, who continue to suffer because to date, no such regimens have been established."

Prof Koeffler said, "We wanted to boost the understanding of the etiology as well biology of nasopharyngeal cancer with the hope for improvements in diagnostics, prognostics and therapy, which will promote the well-being of Singaporeans. By completely deciphering all human genes at the single nucleotide level, our current findings provide an important foundation for the study of the molecular basis underlying this malignancy. More importantly, many potential therapeutic drugs have surfaced from our analysis, with some of them already in use for treating other types of tumours. Therefore, the results have the potential to rapidly facilitate the development of novel treatment strategies for nasopharyngeal cancer patients."

With the discovery of these previously unrecognised genetic defects in nasopharyngeal cancer, Prof Koeffler and his team will explore the detailed molecular mechanisms of these defects in the next phase of research. Associate Professor Loh Kwok Seng from NUH and NCIS, as well as Associate Professor Goh Boon Cher and Associate Professor Lee Soo Chin, from CSI Singapore and NCIS, who are authors of the paper and doctors to many of the patients involved in the study, will evaluate whether some of the genetic defects can be explored in the clinic to effectively treat this disease.

More information: The genomic landscape of nasopharyngeal carcinoma, DOI: 10.1038/ng.3006