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Study finds 600 new genes mutated in stomach cancer

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Singapore: A collaborative study conducted by three research groups affiliated with the Duke-NUS Graduate Medical School (Duke-NUS) and the National Cancer Center Singapore (NCCS) has identified over 600 novel mutated gene associated with stomach cancer. The research was headed by Dr Patrick Tan, Dr Steve Rozen and Dr Teh Bin Tean and has been first published in Nature Genetics.

The researchers have used a strategy that focusses only on the protein-coding portions of 18,000 genes, known as exons, instead of the entire genome in each tumor and tissue sample. Through sequencing the exomes from 15 patients, the researchers were able to identify over 600 gene mutations that were previously not known to be mutated in stomach cancer. The study paves way for treatments tailored to the genetic make-up of individual stomach tumors.

Two of the 600 stomach cancer-associated genes identified, FAT4 and ARID1A, stood out because of their roles in mediating cell adhesion and chromatin remodeling, respectively. Mutations in the cell adhesion gene, FAT4, may potentially increase the mobility of cancer cells into surrounding tissue and to other parts of the body as metastases. Chromatin remodeling genes like ARID1A are responsible for altering the chromatin structure of the DNA and maintaining the stability of the genome. Mutations in ARID1A may lead to abnormal chromatin structures, genomic instability, and the accumulation of further genetic abnormalities.

To find out if FAT4 and ARID1A are frequently mutated in stomach tumors, the researchers analyzed a larger sample of about 100 stomach tumors and found these genes to be mutated in five percent and eight percent of stomach cancers, respectively. In some patients, portions of the chromosome containing the two genes were found to be missing, evidence that genetic defects affecting these genes occur frequently in stomach cancer. Further experiments in the lab demonstrated the importance of these two genes in driving stomach cancer, as manipulation of FAT4 and ARID1A function altered the growth of stomach cancer cells.

Dr Tan, associate professor, Duke-NUS and leader of the Genomic Oncology Program at the Cancer Science Institute of Singapore and group leader at the Genome Institute of Singapore, said that, "Until now, the genetic abnormalities that cause stomach cancers are still largely unknown, which partially explain the overall poor treatment outcome. More research is required to realize the clinical implications of these findings. ARID1A and FAT4 are likely also involved in many other cancer types, not just stomach cancer."