Identified: 15 genes that trigger rapid growth of head and neck squamous cell carcinoma

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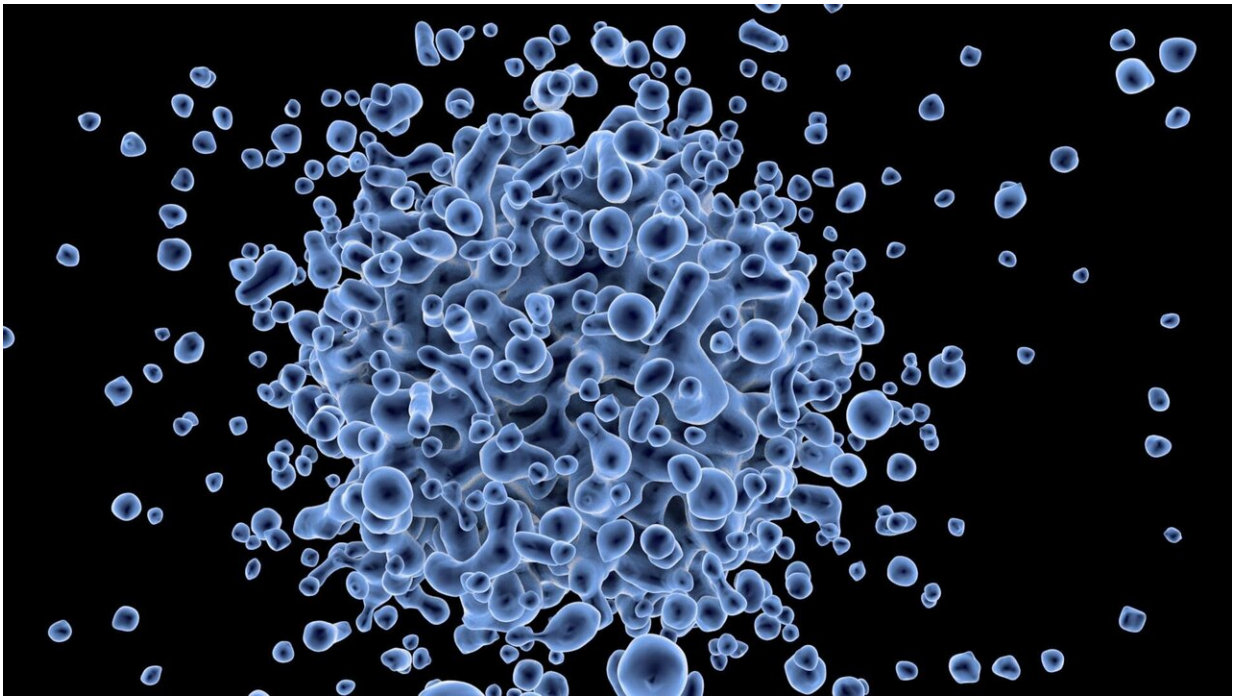

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A team of researchers affiliated with several institutions in Canada has identified 15 tumor suppressor genes that can trigger rapid growth of human head and neck squamous cell carcinoma (HNSCC) when they mutate. In their paper published in the journal *Science*, the group describes their reverse genetic CRISPR screen, which allowed them to analyze almost 500 long-tail genetic mutations that lead to HNSCC.

HNSCC is the sixth-most common type of human cancer, and sadly, has a low survival rate. As the researchers note, to date, most studies looking into a cure have focused on the few genes that mutate at a very high rate. This has given them a high profile. But there is another class of slower mutating gene that can lead to tumors in low numbers of patients. Prior research has shown that there are hundreds of these so called "long tail" genes, many of which have not been identified. In this new effort, the researchers used a reverse genetic CRISPR screen that allowed them to identify 15 of them.

The work focused on tumor suppressor genes that regulate cell division. When something goes wrong with them, such as a mutation, they lose their function and thus cannot prevent the cells they were regulating from mutating out of control. More specifically, the team focused their attention on the genes in cells that are part of the notch signaling pathway—in particular, those cells that develop into HNSCC tumors. All mammals have four kinds of notch receptors, which are used for communications between cells. The team carried out in vivo CRISPR screening on 484 long-tail gene mutations that had triggered the development of tumors in mice and identified 15 tumor suppressor genes . They then looked for the same types of mutations in human long-tail mutations and were able to calculate percentages for each.

The researchers conclude that 67 percent of human HNSCC cases occur along the notch signaling pathway, which suggests notch inactivation is a distinguishing characteristic of HNSCC.

More information: Sampath K. Loganathan et al. Rare driver mutations in head and neck squamous cell carcinomas converge on NOTCH signaling, *Science* (2020). DOI: 10.1126/science.aax0902