Researchers find potential genetic marker linked to better survival outcomes in patients with head and neck cancer

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Researchers from the UCLA Health Jonsson Comprehensive Cancer Center have shown for the first time that a gene usually linked to giant

axonal neuropathy, a rare and severe neurological condition, also plays a role in inhibiting aggressive tumor cell growth in head and neck cancers.

Their study is published in *Cancer Research Communications*.

The team found that when the specific genetic variant (GAN gene exon 8 SNP T allele) of the GAN gene is not present, it leads to the production of certain proteins that make cancer cells more likely to spread and become resistant to treatment.

These findings suggest that the presence of the genetic variant and higher expression of the GAN gene product gigaxonin may contribute to better survival in head and neck cancers and could potentially be used as diagnostic markers for identifying less aggressive forms of the disease.

There are multiple neurodegenerative diseases that are associated with an increased risk of cancer. This increased risk is often associated with gene mutations that hinder the cell's ability to repair DNA damage properly. Giant axonal neuropathy, a rare genetic disorder that leads to progressive damage to the peripheral nerves and central nervous system, is caused by mutations in the GAN gene, resulting in loss of expression of the protein called gigaxonin. This protein is crucial for maintaining the structural integrity of cells.

In previous studies related to head and neck cancer, the UCLA team found that gigaxonin interacts with another protein called p16 to add a molecule called ubiquitin to a protein called NF-κB. This process, known as ubiquitination, is a way cells regulate the activity of proteins.

However, the exact role of gigaxonin in cancer has not yet been well understood. Here, authors show that ubiquitination of NF-κB results in downregulation of Snail, a protein associated with epithelial to mesenchymal transition (EMT), also known as metastasis. Thus,

expression of gigaxonin suppresses aggressive growth of human cancer cells.

To gain insight into the role of gigaxonin in tumor development, investigators analyzed normal and tumor DNA from cervical and head and neck cancers. They also examined cancer cell lines with different genetic variations to understand the relationship between the genetic variation, gigaxonin expression, and the growth of cancer cells, including their response to cisplatin, a type of chemotherapy. Additionally, they investigated how gigaxonin is involved in ubiquitinating a transcription factor NF-κB and possibly associated with the development of head and neck cancer.

The study provides insights into the molecular mechanisms underlying head and neck cancer progression. If validated in additional studies, the use of gigaxonin as a diagnostic marker could help lead to the development of targeted therapies based on the gigaxonin pathway.

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