

## Gene mutation that makes the body turn lifesaving immune cells into a rare and dangerous cancer

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The cause of a rare and highly aggressive form of non-Hodgkin lymphoma that attacks the face has been discovered by an international genome-scanning research project.

The team found that people with a mutation in a gene that helps the body recognize foreign invaders had almost twice the risk of developing the cancer known as extranodal <u>natural killer</u> T-cell lymphoma (NKTCL).

Study co-author, Chiea Chuen Khor, a medical doctor and group leader at the A\*STAR Genome Institute of Singapore, said natural killer T cells normally played a crucial role in rapidly responding to both tumor cells and viruses.

These cells destroy pathogens before they take hold in the body by recognizing tiny molecules on their surface and launching an attack.

"When people have this mutation, instead of destroying pathogens, some of the natural killer T cells can betray the body and turn malignant," he says. "These <u>cancerous cells</u> can eat away at tissues in the face".

If it is not discovered early, about half of all sufferers die within five years.

"Our study suggests that the way in which the person's <u>immune cells</u>



initiate their immune response is critical," Khor says. "Initiating too weak an <u>immune response</u> encourages the tumor cells to proliferate and causes the tumor to embed and grow."

Khor's team examined 514 people with the cancers and more than 5,800 unaffected people across parts of China, Hong Kong and Singapore. They found a mutation in a gene called HLA-DPB1 increased the likelihood of the cancer by 84 per cent.

"HLA-DPB codes for the critical role of presenting foreign antigens to the immune system to initiate its response," Khor says. "When HLA genes are involved, it is a delicate balance between killing invading germs and <u>tumor cells</u>, and avoiding the friendly fire of autoimmunity."

People with a mutation in HLA-DPB also appear more susceptible to Beryllium disease, in which the immune system attacks the lungs.

Previous research has linked NKTCL with infection with Epstein-Barr virus, which Khor says is usually relatively harmless in the body.

It is still not known why Epstein-Barr could trigger NKTCL, although it has also been linked to the development of another type of nasal cancer.

"Normally our immune system is good, strong, and is able to control the viral well. However, sometimes, when the immune system is weaker, the virus is not so well controlled. In that light, perhaps the virus could have malignant transformative potential," Khor says.

**More information:** Zheng Li et al. Genetic risk of extranodal natural killer T-cell lymphoma: a genome-wide association study, *The Lancet Oncology* (2016). DOI: 10.1016/S1470-2045(16)30148-6



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