

# T cell exhaustion - new insights



Researchers have just discovered a gene that exhausts T cells, which might provide new avenues for developing more potent immunotherapies.

White blood cells that fight cancer need to be robust, especially T lymphocytes or T cells, a subset of white blood cells that participates in the immune system's battle against cancer cells. However, during this conflict, T cells may become worn out. A gene that appears to contribute to this tiredness has just been discovered by researchers.

Since around 20 years ago, T lymphocyte fatigue has been recognised as a concern. T cells develop a state of weariness and lose some of their effectiveness after repeated exposure to tumour cells; even while they continue to detect the cancer cells as enemies, they generate less chemicals to destroy them. Additionally, they are unable to mature into memory T cells, which are crucial for sustaining the immunological response.

As a result, the study team worked to comprehend the processes that result in T cell depletion. They created a model based on human tumour cells and created worn-out lymphocytes that resembled those present in patient tumours. The CRISPR/Cas9 technique was then used by the scientists to individually inactivate a number of genes and assess the results.

They were able to find a gene that controls T cell fatigue as

a result. When this gene, known as SNX9, is inactivated, T cells continue to operate even after spending a prolonged time near a tumour. These results are quite encouraging because there aren't many targets to stop T cell fatigue, and the majority of studies to describe such targets have been carried out in mouse cells.

**Journal article:** Trefny, M.P., et al., 2023. [Deletion of SNX9 alleviates CD8 T cell exhaustion for effective cellular cancer immunotherapy.](#) *Nature Communications*.

*Summary by Stefan Botha*