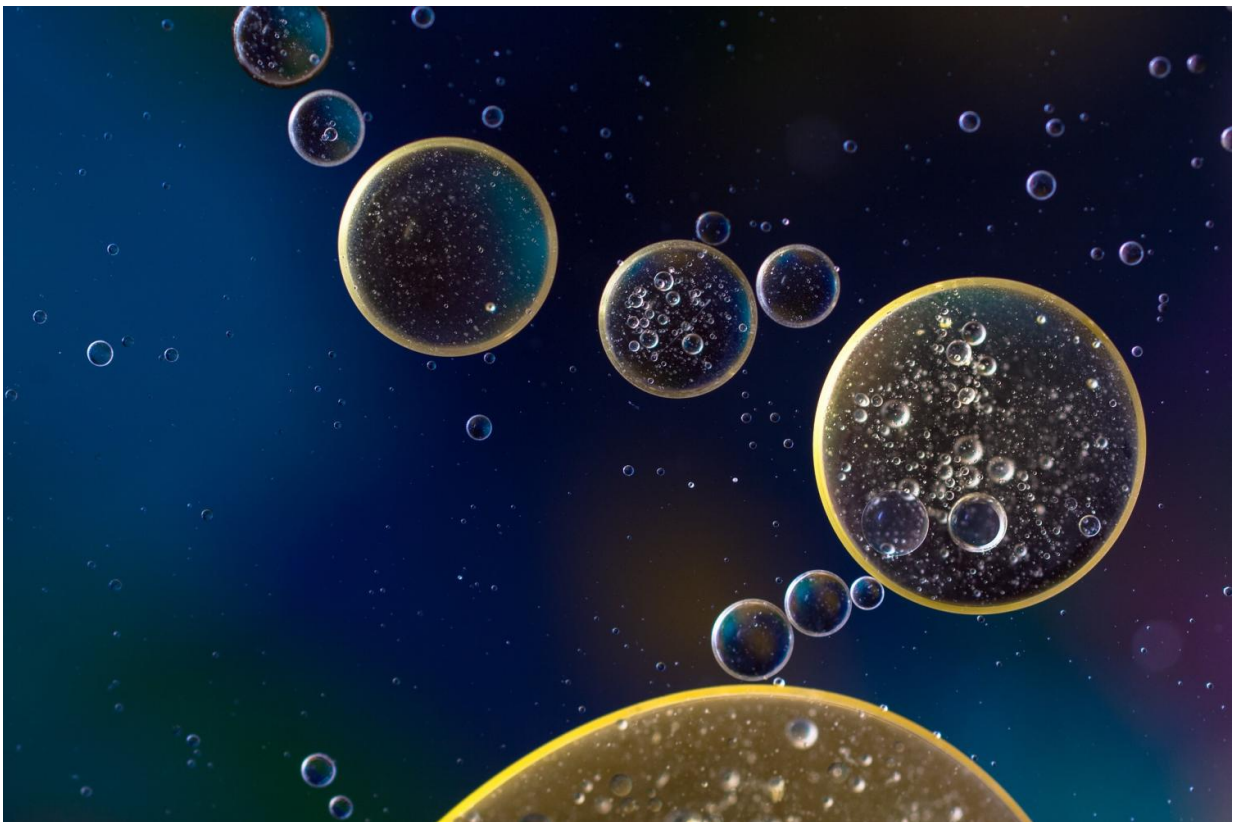


Immune cell steroids help tumours suppress the immune system, offering new immunotherapy targets

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A study has revealed that tumors can evade the immune system by telling immune cells to produce immunosuppressive steroids. Researchers from

the Wellcome Sanger Institute, Department of Pathology, University of Cambridge, and MRC Cancer Unit, discovered that immune T cells from mouse skin and breast tumors secrete steroids, and that preventing this steroid production reduced growth of tumors in mice. The study found that either removing a key steroid-producing gene, or switching it off with a drug, dramatically slowed the formation or progression of cancers.

Reported in *Nature Communications*, the mouse study revealed this steroid signaling pathway contained potential drug targets for developing new types of cancer immunotherapy, although further human studies are needed.

The immune system is extremely complex. While [immune cells](#) protect the body from tumors and infections, some chemicals produced in the body can dampen down the immune system. This makes it much harder for the body to fight against cancer, and cancer immunotherapies that restore the activity of the immune system are urgently needed.

A previous study had revealed that some immune [cells](#), known as T cells, produced steroids after an infection had passed, to reduce their activity back to low levels again. The researchers wanted to find out if [tumor](#) T cells could behave in the same way.

The team tested T cells from melanoma and [breast tumors](#) in mice, using single cell RNA sequencing to see exactly which genes were switched on in each individual cell. The researchers discovered that T cells from tumors did produce steroids, which could potentially reduce their effectiveness at battling the tumor.

Dr. Bidesh Mahata, the lead author from the University of Cambridge and the Wellcome Sanger Institute, said: "For the first time, we could see that mouse tumor T cells were producing immunosuppressive steroids,

even though T cells from healthy mice didn't. It appears that tumors could be instructing their T cells to produce steroids, which would then allow the tumors to evade the immune system and continue growing. This is a really exciting discovery as it means there might be a way of switching the steroid production off again to treat cancer. This is a new hope in cancer, particularly for those tumors that use this trick to suppress anti-tumor immunity."

To test switching off the steroid production, the researchers worked with mice that were missing a key steroid-synthesis gene—Cyp11a1—from their T cells. They discovered that whereas tumors developed rapidly in normal, wild-type mice, tumor growth was inhibited in these knockout mice with any tumors being much smaller and slower to grow. They also showed that a drug that inactivates the Cyp11a1 protein, aminoglutethimide, also reduced the tumors in normal mice.

Dr. Jacqui Shields from the MRC Cancer Unit Cambridge, said: "Using mouse models, we showed that preventing T cells from producing [steroids](#) made a huge difference to tumor growth, reducing it dramatically. We found that either removing the key gene, or preventing it from functioning with drugs, stimulated anti-tumor immunity. This suggests the steroid-production pathway could be a real contender in the search for drug targets for designing cancer immunotherapies, to help treat cancer patients."

Dr. Sarah Teichmann, a senior author from the Wellcome Sanger Institute, said: "This study may pave the way for new hope in cancer immunotherapy. While these results are from [mice](#), preliminary data from human tissues suggests that the same tumor defense may happen in people and we now need further research to show direct evidence in human [cancer](#). If this is confirmed, in the future, it might be possible to target this immunosuppressive pathway, to create new treatments to switch the [immune system](#) back on, and help save lives."

More information: Bidesh Mahata et al. Tumors induce de novo steroid biosynthesis in T cells to evade immunity, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-17339-6](https://doi.org/10.1038/s41467-020-17339-6)

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