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Molecular profiling of melanoma tumours explains differences in survival after T cell therapy

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The more times metastasised melanoma has mutated and the patient's immune system has been activated against the tumour – the better the chances of survival after immunotherapy. This is what emerges from a research collaboration between Lund University in Sweden and Herlev university hospital in Denmark. The findings are now published in the scientific journal *Nature Communications*.

Using the body's own immune system to combat tumours, an approach known as immunotherapy, has brought a major breakthrough in cancer care. Whereas we previously had no treatments able to increase survival for certain cancer diagnoses, it is now possible to treat advanced melanoma, for example.

One such immunotherapy method currently under clinical trial on patients with advanced melanoma is adoptive T cell therapy. The treatment is demanding both in terms of resources and for the patient, who needs to be in a condition to withstand it.

Sharpens the T cells

In simple terms, the treatment entails first removing the patient's own T cells from the tumour. T cells are the part of the immune system that recognises tumour cells. The patient's cells are then cultured in the lab and subsequently injected back into the patient.

"The aim is for them to seek out and fight the tumour and the circulating tumour cells," explains Göran Jönsson, researcher at Lund University. He is collaborating with Herlev university hospital in Copenhagen, which is one of few hospitals in Europe currently conducting clinical trials of this form of immunotherapy.

Although the treatment outcomes are promising, only just below half of patients respond to this immunotherapy.

"Between 10 and 20 per cent of those affected by advanced melanoma can be cured with a single treatment of adoptive T cell therapy. On the other hand, the treatment is very intensive, and has many side effects. It is therefore important to be able to predict which patients stand to benefit from the treatment, so that we give it to the right ones," say Inge Marie Svane and Marco Donia, physicians at Herlev university hospital and researchers at the University of Copenhagen.

The more mutations, the better

In order to find such markers, the researchers studied a group of 25 patients who had all undergone adoptive T cell therapy for advanced melanoma, because they either did not respond to previous treatment or had a recurrence of disease during previous treatment. The researchers analysed tumour cells from the patients at the molecular level.

This revealed that the more mutations the tumour had, the better the result of the T cell therapy.

"We could show that the more mutations there were, the better. This is linked to the fact that every time the tumour mutates, new antigens are produced, known as neoantigens, that the T cells recognise as alien and want to fight. More mutations means more neoantigens for the immune system to discover," says Göran Jönsson.

It's like a game of hide and seek: the more people join, the easier it is for the person searching to find those who are hiding.

The researchers also saw that the survival rate was better if the part of the patient's immune system that infiltrates the tumour was active, even if the immune cells had not defeated the tumour.

"Because this treatment is not practised in many places in the world, the group of patients we can study is not very large, but our results clearly show a group of patients that can be identified on the molecular level who will have long-term benefits from the treatment," says Göran Jönsson.

More information: Martin Lauss et al. Mutational and putative neoantigen load predict clinical benefit of adoptive T cell therapy in melanoma, *Nature Communications* (2017). DOI: 10.1038/s41467-017-01460-0

Provided by Lund University