Deadly disease can 'hide' from a Tasmanian devil's immune system

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The deadly facial tumour can hide itself from the Tasmanian devil's immune system. Credit: Andrew Flies, Author provided

The Tasmanian devil facial tumour (DFT) cells may use a molecular deception – common in human cancers – that could allow the deadly disease to avoid the animal's immune system, according to our new research published this month.

Recently it was discovered that DFT cells effectively hide from the

immune system by not expressing key immune recognition molecules.

Our new discovery that DFT cells contain this "molecular shield" in response to inflammation represents another important step towards understanding the disease and developing more potent ways of preventing or treating it.

So how does this shield work? First, we need to look at some of the recent developments in the treatment of cancers in general.

Cancer treatments

Cancer treatment has undergone a revolution in recent years. Gone are the days when surgery and harsh chemotherapy regimens are the only options.

Now cancer immunotherapy can stimulate the immune system to kill cancer cells. In 2013 this was named the breakthrough of the year in one of the top science journals in the world.

Since 2013 the immunotherapies that target what we call immune checkpoint molecules have continued to make great progress and have recently been approved as first line defences for some cancers.

Checkpoint molecules are critical for keeping the immune system in balance. Every time that the accelerator is pressed in the immune system, there is always at least one, and often several, means of stepping on the brakes.

These checks and balances are necessary because even though the primary job of the immune system is to protect us from disease, the immune system wields powerful weapons that can inflict collateral damage to critical tissues and organ systems when it is aimed at the

wrong target.

Programmed death

In recent years the aptly-named checkpoint molecules – "programmed death-1" (PD-1) and "programmed death ligand 1" (PD-L1) – have emerged to be critical regulators of the anti-cancer immune response.

The PD-L1 molecule is used by many types of cancer as a molecular shield to protect the malignant cells from anti-cancer immune responses.

The PD-1 molecule is found on several types of immune cells, but has particular relevance to the anti-cancer responses mediated by T cells.

When PD-1 on a cancer-killing T cell interacts with PD-L1 on cancer cells, the T cell is shut off. The T cell may undergo programmed death or it may linger and play no role in the anti-cancer response.

The worst possibility is that the former cancer-killing T cell hangs around and actually prevents other immune cells from killing cancer cells.

The Tassie devil's immune system

Our Tasmanian devil immunology team has recently demonstrated that these critical immune checkpoint molecules are also present in devils. This may play a role in the ability of the DFT's ability to evade the devil immune system.

There likely exists many additional mechanisms that the DFTs use to hide from or suppress the immune system of devils and ongoing research efforts aim to uncover and neutralise these mechanisms.

Recent evidence has shown that some devils have tumour regressions, showing that the tumours are not always able to hide from the immune system.

Spontaneous tumour regression is not common in humans, but it does occur in some people and is likely caused by the immune system recognising and killing tumour cells.

Another deadly disease

But the devils are not out of the woods yet for a few reasons. Only in 2014 a second transmissible cancer (devil facial tumour disease 2 or DFT2) was discovered in wild devils in southern Tasmania.

There are only a handful of naturally transmissible tumours known in the world, so a second transmissible tumour in devils is extremely surprising, like lightning striking the devils twice.

In order for the wild devil population to be truly safe from the transmissible tumours, they would need to have immunity to both the original transmissible tumour DFT and DFT2 and hope that no new transmissible cancers arise.

It remains unknown at this point how many different weapons the tumours use to evade or suppress the immune system.

The tumours themselves can also evolve rapidly in response to ecological and immunological pressure. In many cases, disease causing agents evolve to be less virulent (not kill the animal they infect), but only time will tell if that will happen in the curious case of the devil.

Our ongoing research aims to understand exactly which devil immune system switches can be turned on and off in order to stimulate immune

cells to kill cancer cells.

This will be particularly fruitful if we can pinpoint specific genetic and immunological mechanisms that are different in devils that kill tumour cells and those that don't.

It's not often that you cheer for the devil, but this is one situation where nearly everybody wants the devil to win!

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