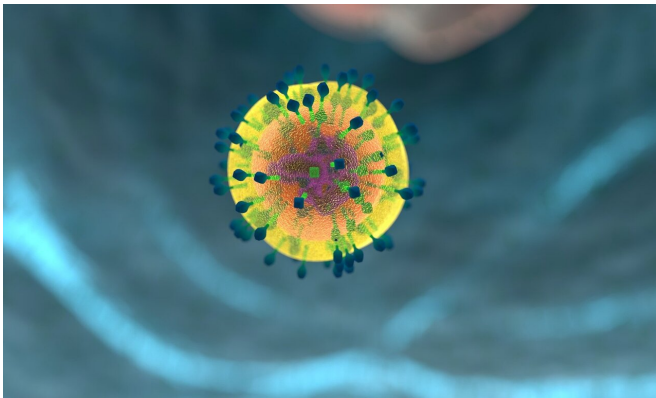


Study provides new insight into fundamental workings of the immune system in response to therapy to treat skin cancer

16 September 2021



Credit: CC0 Public Domain

New research led by the University of Birmingham suggests that skin cancer patients could have a better prognosis if their T cells send messages from five specific genes in their immune response to drugs given to treat the disease.

The research, carried out in mice, cells in the laboratory, and using publicly available data from patients with advanced melanoma before and after treatment with Nivolumab therapy, publishes today in the journal *Immunity*.

T cells are [white blood cells](#) that protect the body from harm from viruses, bacteria, and [cancer](#) cells, and explore their environments by using their T cell receptor (TCR) to recognize fragments—called antigens—of microbes or damaged [cancer cells](#).

The TCR controls the behavior of the T cell and can send messages to the T cells' command center to kick-start an [immune response](#). This

process is important for vaccine research and treatment of autoimmune conditions, but is particularly of interest for cancer treatments to improve the anti-tumor function of T cells.

The researchers carried out the study to better understand how the amount of antigen controls how the TCR sends messages to the T cells' command center, and how this affects the type of immune response. They wanted to explore how antigen amounts control the expression of so-called 'immune checkpoints' that act as brakes on immune responses. It is these immune brakes, such as one called PD1, that are the target of drugs that seek to increase the immune response in cancer immunotherapy.

Lead author Dr. David Bending, of the University of Birmingham's Institute of Immunology and Immunotherapy, explained: "Through our research we discovered that the amount of antigen determined how many immune checkpoints or immune brakes a T cell had on its [cell surface](#).

"When we exposed T cells to the highest amounts of antigen, they stopped sending signals to their command center, and this was because they had increased the number of immune brakes, which shut down the messengers. This made these T cells unable to respond to antigens for a period."

By blocking one of the immune brakes, called PD1, the researchers were able to re-awaken some of these 'unresponsive' T cells. They found that these re-awakened T cells not only started sending messages to their command centers, but the messages they sent were louder and clearer.

"The response from the command center was that

the T cells started to increase the number of messages from five [specific genes](#)," added Dr. Bending. "By looking for the messages from these five genes, we were able to show that these stronger and louder messages were increased in melanoma patients who survived for longer on drugs that block the immune brake PD1. We think that this means that those cancer patients whose immune cells can send messages from these five genes in response to drugs that target PD1, a good outcome is far more likely."

The researchers said their finding shows that the immune system likely requires an optimal level of stimulation to mount the most effective immune response in skin cancer patients.

Dr. Bending added: "Our research gives us interesting insight into fundamental workings of the immune system. It suggests that both the amount of antigen around a T cell and also the number of immune brakes the T cells have at their surface are very important in controlling immune responses. Furthermore, we have shown that we can alter the balance of the immune response through stopping some of these immune brakes, which results in a stronger T cell response."

The study has generated a new potential readout to monitor patients on drugs targeting PD1 in cancer. It also may be useful for exploring the potential of combinations of drugs that target multiple immune checkpoints to try to further re-awaken T [cells](#) in cancer patients.

More information: Antigen and checkpoint receptor engagement recalibrates T cell receptor signal strength, *Immunity* (2021).
doi.org/10.1016/j.immuni.2021.08.020

Provided by University of Birmingham

APA citation: Study provides new insight into fundamental workings of the immune system in response to therapy to treat skin cancer (2021, September 16) retrieved 7 October 2022 from <https://medicalxpress.com/news/2021-09-insight-fundamental-immune-response-therapy.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.