

Severe viral infection overwhelms immune cells

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Suzanne Judd, Ph.D., an epidemiologist at UAB, explains what will lead to herd immunity and why it is important to remain vigilant in reducing the spread of COVID-19. Credit: CC0 Public Domain

Melbourne researchers have identified mechanisms leading to the functional deterioration of the immune system in response to severe viral infections, such as HIV or COVID-19.

It is widely known that severe viral infections and cancer cause impairments to the [immune system](#), including to T cells, a process called immune 'exhaustion'.

Overcoming immune exhaustion is a major goal for the development of new therapies for cancer or severe viral infections.

A team from the Peter Doherty Institute of Infection and Immunity (Doherty Institute) led by University of Melbourne's Dr. Daniel Utzschneider, Dr. Sarah Gabriel and Professor Axel Kallies has focused on the question of when and how T cells lose their function and become 'exhausted'.

It was previously thought that during severe infections, T cells lost their function slowly and over long periods of time.

This research published today in *Nature Immunology*, however, shows that T cells can be impaired within just a few days.

It also identifies several new mediators of immune exhaustion that maybe targeted in new therapies.

"This is an exciting finding, particularly in the context of COVID-19 as one of the big questions is why some people get severely sick, while others experience mild disease," Dr. Utzschneider said.

"We looked at both mild and overwhelming Lymphocytic Choriomeningitis Virus infections in mice, which serves as a model for severe viral infections in humans, early after onset of disease, and identified striking differences at the molecular and functional level."

Dr. Gabriel explained: "In response to overwhelming infections that are difficult to eliminate and may become chronic, we were able to show

that T cells down-regulate their function within days, while T cells responding to a weaker infection remained highly functional."

T cells are at the heart of immunotherapy for cancer. Therefore, understanding how T cell function is impaired is central to improving these therapeutic approaches and applying them to other diseases, such as [viral infections](#).

"These findings are extremely exciting. Our data show that T [cells](#) could be manipulated during early stages of severe viral [infection](#) to improve their activity," Professor Kallies said.

More information: Early precursor T cells establish and propagate T cell exhaustion in chronic infection, *Nature Immunology* (2020). [DOI: 10.1038/s41590-020-0760-z](#) , www.nature.com/articles/s41590-020-0760-z

Provided by University of Melbourne

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