

MEDIA RELEASE

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T cells team-up to protect the liver from infection

Researchers at the Centenary Institute have made an important breakthrough in understanding how the immune system fights off infections in the liver – paving the way for more specific and effective therapies to treat and prevent liver diseases such as viral hepatitis and fatty liver disease, and decrease the risk of liver transplant rejection.

The study discovered how two types of immune cells – CD4+ and CD8+ T cells interact and cooperate to generate an effective immune response in the liver to defend against harmful bacteria, viruses and parasites that cause liver diseases.

Associate Professor Patrick Bertolino, senior author in the study and Head of the Centre for Infection & Immunity at the Centenary Institute said that the study transforms our understanding of immune responses targeting the liver by revealing that the liver plays a more active role in immune responses than all current models suggest.

“T cells are key players in the body’s defence system. CD4+ T cells act as ‘helper’ cells coordinating and supporting the immune response by secreting various molecules required for the growth and survival of other immune cells or for regulating the immune system. In contrast, CD8+ T cells act as ‘killer’ cells targeting and destroying infected or abnormal cells” said Associate Professor Bertolino.

“While we knew that CD4+ T cells were important in CD8+ T cell responses against several diseases that specifically affect the liver, the nature of this cooperation and the site where CD4+ T cells help CD8+ T cells was previously unknown,” he said.

In the study, published in the prestigious journal *Nature Communications*, and involving mice, the scientists investigated the immune system's response to infection by introducing a fragment of virus into the liver. By tracking the response of T cells to this fragment, they saw that CD4+ and CD8+ T cells were activated and their numbers expanded in lymphoid organs such as lymph nodes and the spleen, where most immune responses are initiated. Subsequently, after activation, both types of T cells migrated to specific areas of the liver where they interacted and clustered with another type of immune cell called hepatic type-1 conventional dendritic cells (cDC1s).

“CD4+ T cells signalled liver resident cDC1s to turn on and further increase the number of ‘killer’ CD8+ T cells. This collaboration between three types of immune cells lead to the local amplification of the CD8+ T cell response in the liver, resulting in a more powerful immune response to fight infections,” said Associate Professor Bertolino.

“Our discovery helps us understand how different types of T cells work together to boost the immune response in the liver, offering valuable insights into the liver's defence mechanisms against infections,” he said.

First author of the study, Dr Kieran English, researcher at the Centenary Institute when the study took place and now a postdoctoral researcher at the VIB-UGent Center for Inflammation Research said that in addition to the remarkable teamwork shown between CD4+ and CD8+ T cells in safeguarding the liver from infections, the study reveals that the liver contains specialised areas where the immune response is amplified.

“As these areas are unique to the liver and play a key role in liver immune responses, they could be specifically targeted in future immune-based therapies to improve clinical outcome of liver diseases,” said Dr English.

“Current immune therapies used to treat liver diseases target the whole immune system. As we uncover intricate interactions among immune cells in specialised areas that are unique to the liver, we move closer to developing more precise and effective liver specific therapeutics that can treat potentially deadly liver diseases,” he said.

[ENDS]

Publication:

A hepatic network of dendritic cells mediates CD4 T cell help outside lymphoid organs.
<https://www.nature.com/articles/s41467-024-45612-5>

Image:

Associate Professor Patrick Bertolino:

https://drive.google.com/file/d/1mn_eWVPyJTbKvVeAdBCU4cdxvdvI5PYF/view?usp=sharing

Dr Kieran English: <https://drive.google.com/file/d/1TT0qjRiF59ntSDcFsB0QB9r24Nvl-mly/view?usp=sharing>

For all media and interview enquiries, please contact

Tony Crawshaw, Media and Communications Manager, Centenary Institute on 0402 770 403 or email: t.crawshaw@centenary.org.au

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