

Immune cell 'survival' gene key to better myeloma treatments

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A research team from Melbourne's Walter and Eliza Hall Institute of Medical Research have identified a gene that is essential for the survival of antibody-producing cells, which could lead to better treatments for diseases where these cells are out of control, such as myeloma and chronic immune disorders. Researchers (from left) are: Dr. Victor Peperzak, Dr. Ingela Vikstrom and Associate Professor David Tarlinton. Credit: Walter and Eliza Hall Institute

Scientists have identified the gene essential for survival of antibody-producing cells, a finding that could lead to better treatments for diseases

where these cells are out of control, such as myeloma and chronic immune disorders.

The discovery that a gene called Mcl-1 is critical for keeping this vital immune [cell population](#) alive was made by researchers at Melbourne's Walter and Eliza Hall Institute. Associate Professor David Tarlinton, Dr Victor Peperzak and Dr Ingela Vikstrom from the institute's Immunology division led the research, which was published today in [Nature Immunology](#).

Antibody-producing cells, also known as [plasma cells](#), live in the bone marrow and make [antibodies](#) that provide a person with long-term protection from [viruses and bacteria](#), Associate Professor Tarlinton said. "Plasma cells are produced after vaccination or infection and are responsible for the immune 'memory' that can persist in humans for 70 or 80 years. In this study, we found that plasma cells critically rely on Mcl-1 for their continued survival and, without it, they die within two days," he said.

Dr Peperzak said the team was surprised to find that plasma cells used this as a 'failsafe' mechanism in controlling their survival. "One of the interesting things we found is that because plasma cells rapidly destroy Mcl-1 proteins within the cell yet depend on it for their survival, they need continuous external signals to tell them to produce more Mcl-1 protein," Dr Peperzak said. "This keeps the plasma cells under tight control, with Mcl-1 acting like a timer that constantly counts down and, if not reset, instructs the cell to die."

Plasma cells are vital to the [immune response](#), but can be dangerous if not properly controlled, Associate Professor Tarlinton said. "As with any immune cell, plasma cells are really quite dangerous in many respects and need to be tightly controlled," he said. "When they are out of control they continue to make antibodies that can be very damaging if there are

too many. This happens in conditions such as myeloma – a cancer of plasma cells – and various forms of autoimmunity, such as systemic lupus erythamatosus or rheumatoid arthritis, where there are excessive levels of antibodies."

Myeloma is a blood cancer that affects more than 1200 Australians each year, and is more common in people over 60. It is caused by the uncontrolled production of abnormal plasma cells in the bone marrow and the build up of damaging antibodies in the blood. Rheumatoid arthritis and lupus are autoimmune diseases in which the antibodies produced by plasma cells attack and destroy the body's own tissues.

Associate Professor Tarlinton said that his hope was that the discovery could be used to develop new treatments for these conditions. "Myeloma in particular has a very poor prognosis, and is generally considered incurable," Associate Professor Tarlinton said. "Now that we know Mcl-1 is the one essential gene needed to keep plasma cells alive, we have begun 'working backwards' to identify all the critical molecules and signals needed to switch on Mcl-1 and keep the cells alive. Our hope is that we will identify some point in the internal cell signalling pathway, or a critical external molecule, that could be blocked to stop Mcl-1 being produced by the cell. This would be an important new platform for diseases that currently have no specific or effective treatment, such as myeloma, or offer new treatment options for people who don't respond well to existing treatments for diseases such as lupus or [rheumatoid arthritis](#)."

Provided by Walter and Eliza Hall Institute

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