

New research solves old mystery of silent cell death

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Dr Michael White and colleagues have discovered how 'silent' cell death avoids activating the immune system. Credit: Walter and Eliza Hall Institute

Walter and Eliza Hall Institute researchers have for the first time revealed how dying cells are hidden from the immune 'police' that patrol the body.

The research answers a decades-old mystery about the death of cells, which in some situations can alert the [immune system](#) to potential danger, but in other circumstances occurs 'silently', unnoticed by [immune cells](#).

Silent cell death, or apoptosis, is a controlled way for the body to

eliminate cells that may be damaged, old, or surplus to the body's requirements, without causing collateral damage. This 'normal' cell death process is ignored by the immune system. In contrast, the death of cells at sites of infection or damage can alert the immune system to be on the lookout for danger.

Dr Michael White, Professor Benjamin Kile and colleagues from the institute have identified how apoptotic cell death is kept silent, in research published today in the journal *Cell*.

The team focused on the role of proteins called caspases, Dr White said. "Caspases hasten cell death by breaking down key components within the dying cell," he said. "Because apoptosis can still occur without the involvement of caspases, we investigated whether these proteins play any other role during cell death.

"We found that when cells undergo apoptosis without caspases, they release immune cell signaling molecules called interferons that set off the [immune response](#).

"By dissecting the step-by-step process that occurs within dying cells, we showed one of the key roles of caspases is to suppress interferon release. This confirmed that caspases are crucial for hiding apoptotic cell death from the immune system."

Professor Kile said the discovery provided new insights into the links between [cell death](#), the immune system and disease. "Our health relies on our immune system's ability to distinguish between the millions of cells that are supposed to die in our body every day to make space for new cells, and the unexpected death of cells that signals danger," he said. "The over-reaction of immune cells to apoptosis may be a factor contributing to inflammatory diseases such as rheumatoid arthritis.

The findings also provide important insights into how the body may tolerate potential new drugs, Professor Kile said. "Caspase-inhibiting medications are currently in clinical trials, for example being tested for their potential to keep [cells](#) alive during organ transplants. However, our work suggests that any use of these medications should be accompanied by careful monitoring of their effects on the immune system," Professor Kile said.

Provided by Walter and Eliza Hall Institute

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