Clot-busting enzymes are working two jobs

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The body's blood clot-busting enzymes are much busier than previously imagined, with new research showing that they also dispose of every cell that dies prematurely from disease or trauma.

In research published today in *Cell Reports*, scientists from Monash University have demonstrated for the first time the enzyme t-PA, which plays a vital role in the removal of blood clots, is also a major player in the removal of necrotic, or dead, cells.

Necrosis occurs when cells in living tissue die prematurely due to external stress or injury. The body's system for removing waste associated with necrotic cell removal was not, until now, well understood.

Professor Robert Medcalf and Dr Andre Samson, of the University's Australian Centre for Blood Diseases (ACBD), led the research with Professor Stephen Bottomley of the Monash Department of Biochemisty and Molecular Biology.

The research team found that in the late stages of death, the injured cell undergoes a restructure and takes on a form not unlike a blood clot, to prepare for efficient removal from the body. This process had never been described before.

Professor Medcalf said the blood clot-like structure allowed the damaged cells to be recognised and removed by t-PA and its enzymatic waste disposal team.

"It's exactly the same principle as the formation and removal of a blood clot," Professor Medcalf said.

"In the process of a cell dying it goes through this unique form of aggregation to keep all the intracellular debris localised. Then, it can be taken out in an orderly fashion by the blood clot-busting enzyme system without causing damage to the body."

The researchers were studying brain tissue when they made the discovery, but have shown that the same process applies to every cell in the body.

"It's very efficient. Instead of doubling up, the body is using the same disposal system to eliminate a variety of unwanted waste products, be they dead cells or blood clots that have served their purpose," Professor Medcalf said.

"What this means is that t-PA and its team of enzymes recognises waste through structure or shape, not by the specific proteins involved."

The findings shed further light on the function and therapeutic uses of t-PA, which is used in the treatment of stroke and heart attack.

Researchers from Alfred Health and the Ludwig Institute for Cancer Researchers also collaborated on the study, which was funded by the National Health and Medical Research Council of Australia.

Provided by Monash University