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Therapies based on alpha defensins could help treat rheumatoid arthritis

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Arthritis and other inflammatory conditions could be helped by new insights into how the immune response is switched off.

Scientists have discovered how compounds produced by the body's immune system help to dampen inflammation and prevent damage to healthy tissues.

Their findings suggest that therapies based on these compounds could help to treat rheumatoid arthritis, which occurs when the immune system attacks the joints, causing pain and swelling.

The research could also lead to new treatments for sepsis, where a body-wide immune response causes lifethreatening tissue damage.

The compounds - called alpha defensins - are part of the body's first line of defence against infection. They help to stop bacteria and other infectious agents from reproducing.

Studies have suggested that the compounds may also act on cells of the immune system to prevent excessive inflammation but until now it was not clear how the process works.

In a study involving human cells, researchers at the University of Edinburgh have shown that alpha defensins are released by immune cells called neutrophils when they die.

The alpha defensins are then taken up by other immune cells called macrophages. The team found that the compounds prevent macrophages from producing messenger molecules called cytokines, which drive inflammation.

The overall effect is to limit excessive inflammation, restricting damage to healthy tissues without compromising the body's ability to clear the infection.

Researchers say their findings could lead to new treatments for chronic inflammatory disorders including rheumatoid arthritis. Such therapies could even prevent the condition from flaring-up in the first place, the team predicts.

The study, funded by the Medical Research Council and Arthritis UK, is published in the journal *Proceedings of the National Academy of Sciences*.

Dr Mohini Gray, of the University's MRC Centre for Inflammation Research, said: "This discovery opens the door to new approaches for the treatment and prevention of chronic inflammation. We are hopeful that with further research, these treatments could be exploited in the near future."

Stephen Simpson, Director of research and programmes for Arthritis Research UK, said: "There are over 400,000 people living with rheumatoid arthritis in the UK, a painful and debilitating inflammatory condition which can severely impact on the way people live their lives affecting their ability to walk, sit or move.

"This study, funded by Arthritis Research UK, reveals yet another layer of the immune system's complex control system. Understanding how the immune system works both in health and disease is crucial if we are to develop new and improved treatments for inflammatory conditions such as rheumatoid arthritis."

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University of Edinburgh