Boosting the anti-inflammatory action of the immune system

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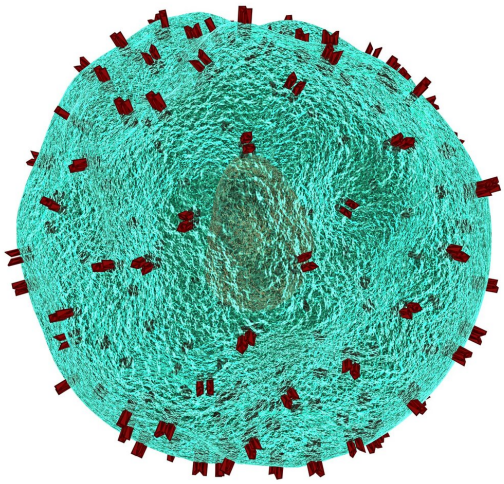

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Researchers at the University of Illinois at Chicago have identified a molecular switch that causes immune cells called macrophages to clean up cellular debris caused by infections instead of contributing to inflammation and tissue injury. Their findings are reported in the journal *Proceedings of the National Academy of Sciences*.

Macrophages are a type of immune cell found throughout the body. These cells can produce inflammation, which is good in moderation because inflammatory signals bring other immune cells to a specific location to clear an infection. However, when inflammation gets out of control, as it can in cases of inflammatory diseases, it can cause excess cellular and tissue damage, contributing to a vicious cycle that is very difficult to reverse. But macrophages also play a significant role in reducing inflammation when they engulf cellular debris or foreign microbes that contribute to inflammation. The mechanism behind macrophages' ability to switch back and forth between these two diametrically opposed roles has long-puzzled scientists.

Researchers led by Saroj Nepal, research assistant professor in the department of pharmacology at the UIC College of Medicine, have found that a molecule called Gas6 is required to induce macrophages to perform their anti-inflammatory role by engulfing and digesting cellular debris that can contribute to inflammation. The molecule could serve as a potential drug target for drug makers interested in coaxing the cells toward their anti-inflammatory state to help treat people.

In a mouse model of acute lung injury, Nepal and colleagues found that lung macrophages expressed both inflammatory and anti-inflammatory proteins. One of the anti-inflammatory proteins was Gas6. In a mouse model of acute lung injury where the animals' macrophages were artificially depleted of Gas6, clearance of inflammatory molecules and proteins in the lungs was severely impaired, and the inflammation could not be resolved. When they artificially boosted levels of Gas6 in the mouse macrophages, inflammation was resolved much faster than in mice with normal macrophages.

"Harnessing the anti-inflammatory function of macrophages using the Gas6 switch holds great potential for treating diseases ranging from heart disease to cancer to rheumatoid arthritis, where inflammation is a key underlying feature," Nepal said.

More information: Saroj Nepal et al. STAT6 induces expression of Gas6 in macrophages to clear apoptotic neutrophils and resolve inflammation, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1821601116

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