

Key pathway to stop dangerous, out-of-control inflammation discovered

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A potential new strategy to developing new drugs to control inflammation without serious side effects has been found by Georgia State University researchers and international colleagues.

Jian-Dong Li, director of Georgia State's Center for Inflammation, Immunity and Infection, and his team discovered that blocking a certain pathway involved in the [biological process](#) of inflammation will suppress it.

Inhibiting a molecule called phosphodiesterase 4B, or PDE4B, suppresses inflammation by affecting a key gene called CLYD, a gene that serves as a brake on inflammation.

The research was published in the journal *Nature Communications*.

Li explained the process of overactive inflammation using a "police" analogy.

When a pathogen – such as bacteria or viruses—infects a patient, he said, it triggers an "alarm" to which the "police" of immune system respond. In turn, it triggers neutrophil attractant called cytokines to respond, leading to inflammation that serves to help rid the body of the pathogen. But if inflammation isn't stopped, [tissue damage](#) can result.

The pathways during the response are termed "positive," like a gas pedal on a car, and "negative," like a brake, with the process in the positive

pathway going down the line from the pathogen to inflammation, and negative going the other direction. PDE4B is involved in controlling the negative pathway.

Many researchers have been focusing on developing anti-[inflammatory agents](#) by stopping the positive pathway, but the discovery by Li and his colleagues gives scientists a new route to stop inflammation using safer or even existing drugs proven to be non-toxic as they have found that accelerating the negative [pathway](#) will reduce inflammation.

"This is the key negative regulator that we have been searching after for years, " Li said.

There is a need for better drugs to control inflammation, because current treatments come with serious side effects, Li said. Steroids are commonly used, but cannot be used over the long-term. Steroids suppress the immune system.

More information: The article is "Inhibition of PDE4B suppresses inflammation by increasing expression of the deubiquitinase CLYD," in *Nature Communications*, available at [hx.doi.org/10.1038/ncomms6274](https://doi.org/10.1038/ncomms6274)

Provided by Georgia State University

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