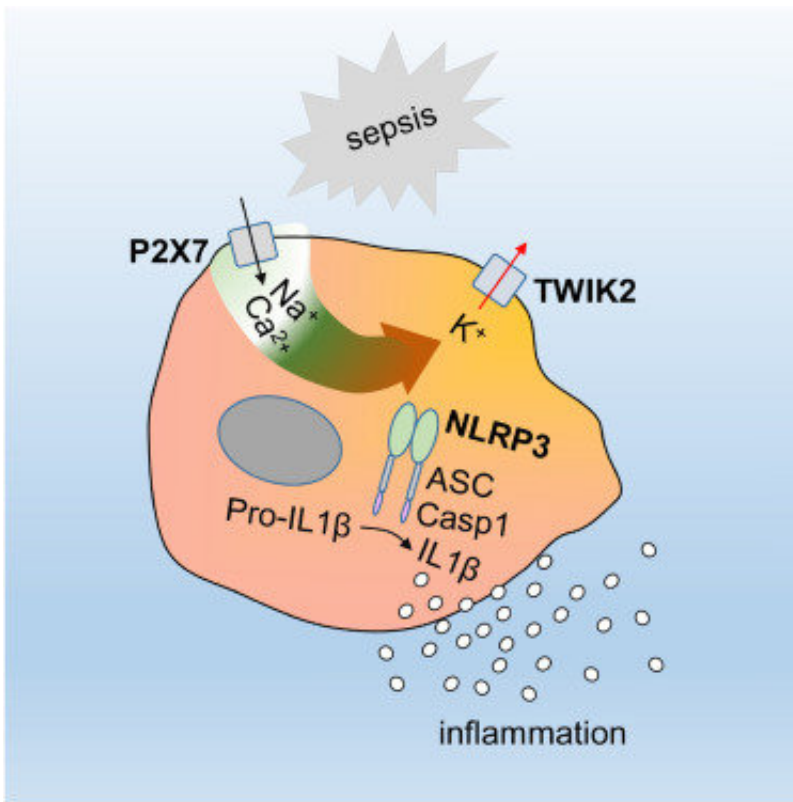


Researchers identify key protein involved in triggering inflammation

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Credit: *Immunity* (2018). DOI: 10.1016/j.immuni.2018.04.032

Researchers from the University of Illinois at Chicago have identified a protein that is crucial for activating inflammation—both the good kind of inflammation that leads to healing wounds and fighting infection, as well as excessive inflammation where the immune system can damage tissues and organs. The protein—an ion channel that spans the

membrane of immune cells—presents a new target for the development of drugs that can restrain overblown inflammatory responses. The researchers report their findings in the journal *Immunity*.

Scientists have long known that [inflammation](#) involves the activation of a structure within immune cells called the inflammasome, and that it is activated by an influx of potassium ions across the cell membrane through a protein [channel](#). However, the identity of this channel was not known until now.

Researchers led by Asrar Malik, Schweppe Family Distinguished Professor and head of pharmacology in the UIC College of Medicine, have now identified the channel, called TWIK2, and have studied its function in macrophages, a type of immune cell involved in fending off infections as well as clearing debris during inflammation.

"Now that we have identified this crucial channel, it opens up the possibility of developing targeted new anti-inflammatory drugs to modify its function and help and reduce inflammation," said Malik. While some drugs currently exist that target potassium channels, drugs specific to the TWIK2 channel still need to be developed.

Sepsis is a very serious condition and a potentially life-threatening complication due to infection in humans. In a mouse model of sepsis, where the immune system has an overblown response to a bloodstream infection, mice lacking the TWIK2 molecule had significantly reduced levels of inflammation, and activation of the inflammasomes in their macrophages was suppressed. Additionally, when the researchers transferred macrophages lacking TWIK2 into a mouse model of sepsis where native macrophages were depleted, inflammatory lung injury was prevented.

"Knowing that TWIK2 is the channel which leads to activate the

inflammasome allows us to dial down the [inflammation response](#) with a [drug](#) that inhibits TWIK2 when inflammation gets excessive," said Malik.

Interestingly, the researchers noted that quinine, a bitter crystalline compound present in cinchona bark that has been used since the 18th century as an antimalarial and anti-fever drug, actually inhibits the function of the TWIK2 channel in macrophages.

"Some of the fever-suppressing effects of quinine may be due to its effects on the TWIK2 channel," said Dr. Jalees Rehman, an associate professor of medicine and pharmacology in the UIC College of Medicine and a co-author on the paper. "We found that quinine reduced the levels of the inflammatory molecule interleukin 1-beta which is known to cause fever," said Rehman.

One of the challenges for treating excessive inflammatory responses is that many anti-inflammatory medications have major side effects. "By discovering new components of the inflammation pathways, we hope to pave the way for new personalized anti-inflammatory drugs which minimize the side effects for patients," Rehman said.

More information: Anke Di et al. The TWIK2 Potassium Efflux Channel in Macrophages Mediates NLRP3 Inflammasome-Induced Inflammation, *Immunity* (2018). [DOI: 10.1016/j.immuni.2018.04.032](https://doi.org/10.1016/j.immuni.2018.04.032)

Provided by University of Illinois at Chicago

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