

# Identification of Novel NLRP3 Inflammasome Inhibitors

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## BACKGROUND

The NLRP3 inflammasome is a molecular machine that becomes activated during acute and chronic inflammation and leads to production of biologically active IL-1 $\beta$  and IL-18 that initiate inflammatory responses triggered by tissue damage. The NLRP3 inflammasome has also been implicated in many chronic inflammatory and degenerative diseases from gout, osteoarthritis, atherosclerosis to Alzheimer's disease. Currently, there are no effective ways to inhibit the NLRP3 inflammasome, thus there is a therapeutic need for this class of molecule.

## TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have identified a novel kinase whose inhibition prevents NLRP3 inflammasome activation by all its known stimuli, and the researchers have identified its essential catalytic pocket and mechanism of action.

## APPLICATIONS

Aberrant NLRP3 activation is the key promoter to many chronic diseases. Specific inhibitors to this new kinase identified should be useful to treat cryopyrin-associated periodic syndromes, gouty arthritis, osteoarthritis, Alzheimer's disease, type 2 diabetes, atherosclerosis, lupus, macular degeneration and cancer.

## ADVANTAGES

NLRP3 inflammasome activation is required for production of IL-1 $\beta$ . Antibodies to IL-1 $\beta$  have been proven useful in a number of inflammatory diseases and can even reduce the likelihood of secondary cardiovascular events for heart attack victims. IL-1 $\beta$ , however, is also important for protection from infection and IL-1 $\beta$ -blocking drugs can increase infection risk. The researcher's approach will avoid such a risk because it only blocks IL-1 $\beta$  production that depends on the NLRP3 inflammasome, which is not involved in the response to microbial or viral infections.

## STATE OF DEVELOPMENT

At this point collaboration with a pharma/biotech company to identify small molecule inhibitors of this kinase would be of interest as well as licensing the technology for further development by the pharma/biotech company.

## INTELLECTUAL PROPERTY INFO

A provisional patent has been submitted and the technology is available for licensing.

## RELATED MATERIALS

- ▶ Zhong Z, Liang S, Sanchez-Lopez E, He F, Shalapur S, Lin XJ, Wong J, Ding S, Seki E, Schnabl B, Hevener AL, Greenberg HB, Kisseleva, Karin M. New mitochondrial DNA synthesis enables NLRP3 inflammasome activation. *Nature*. 2018 Jul 25. doi: 10.1038/s41586-018-0372-z. - 07/25/2018

## PATENT STATUS

Patent Pending

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## OTHER INFORMATION

### KEYWORDS

Inflammation, NLRP3 inflammasome, IL-1 $\beta$ , cryopyrin-associated periodic syndromes, inhibitors, chronic inflammatory diseases

### CATEGORIZED AS

- ▶ **Medical**
  - ▶ Disease: Autoimmune and Inflammation
  - ▶ Therapeutics

### RELATED CASES

2017-302-0