

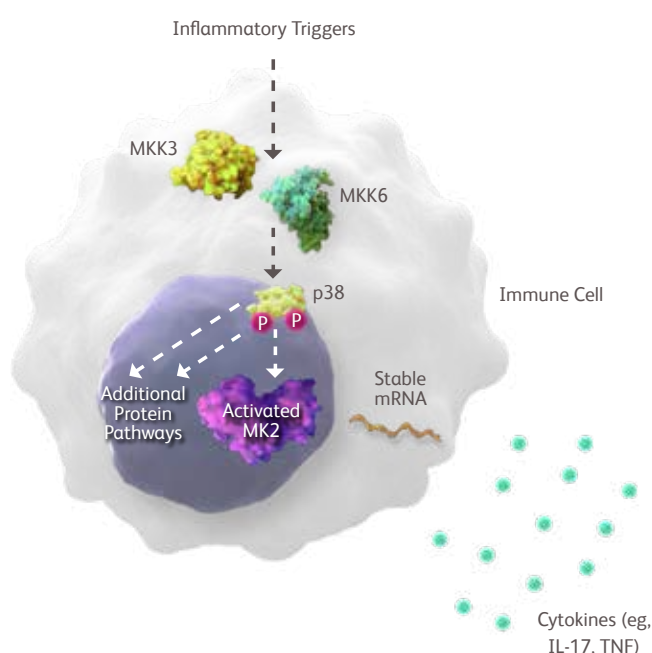
Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) Pathway

About MK2

MK2 is with an enzyme that plays a key role in a pathway responsible for producing signaling molecules (cytokines) that promote inflammation.

This pathway, present in immune cells, is activated by stress and inflammatory triggers.

When MK2 is activated, it enables the **stabilization of the mRNA** that codes for the proinflammatory cytokines, such as TNF and IL-17 among others, enabling their production.¹



MK2 and Inflammatory Diseases

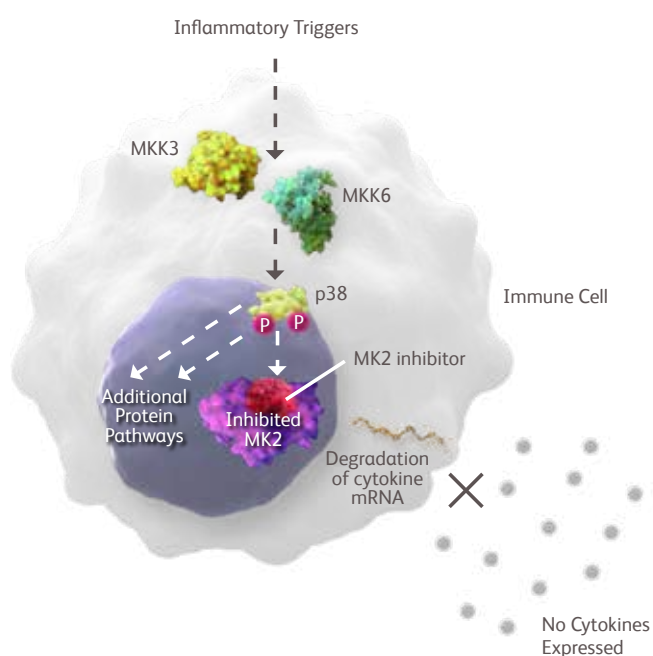
Inflammation is an important part of the immune system and plays a key role in protection from infection. However, **uncontrolled** or **misdirected** inflammation can contribute to the damage of otherwise healthy cells, resulting in immune-mediated diseases.²

MK2 can drive the uncontrolled or misdirected immune response through its role in production of proinflammatory cytokines that promote inflammation, contributing to inflammatory diseases.²

Research Implications

Researchers are investigating potential ways to prevent activation of this pathway to lower the production of pro-inflammatory cytokines in immune-mediated diseases.

One strategy involves **inhibiting the activation of MK2**, resulting in destabilization of cytokine mRNA that is degraded within the cell. Without this mRNA, the proinflammatory cytokines cannot be produced, which leads to a reduction of inflammation.³



At Bristol Myers Squibb, we continue to pioneer novel approaches by leveraging our depth of experience to advance research in immune-mediated diseases.

1. Gaestel M. MAPKAP kinases - MKs - two's company, three's a crowd. *Nat Rev Mol Cell Biol.* 2006;7(2):120-130. doi:10.1038/nrm1834

2. Duraisamy S, Bajpai M, Bughani U, Dastidar SG, Ray A, Chopra P. MK2: a novel molecular target for anti-inflammatory therapy. *Expert Opin Ther Targets.* 2008;12(8):921-936. doi:10.1517/14728222.12.8.921

3. CC-99677: A Novel, Oral, Selective MK2 Inhibitor with Sustainable Multi-Cytokine Inhibition for the Treatment of Ankylosing Spondylitis and Other Inflammatory Diseases. *ACR Meet Abstr.* Accessed April 26, 2022.

<https://acrabstracts.org/abstract/cc-99677-a-novel-oral-selective-mk2-inhibitor-with-sustainable-multi-cytokine-inhibition-for-the-treatment-of-ankylosing-spondylitis-and-other-inflammatory-diseases/tive-mk2-inhibitor-wit-h-sustainable-multi-cytokine-inhibition-for-the-treatment-of-ankylosing-spondylitis-and-other-inflammatory-diseases/>