

Discovery of the monocytes that secrete a pro-inflammatory protein

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Different populations of white blood cells secrete different levels of IL-1 β , a pro-inflammatory protein that normally helps the body fight off infection and injury, but may also trigger autoimmune disease and inflammatory diseases. An investigation by A*STAR researchers and collaborators shows that a regulatory protein called Hsp27 is responsible for some of these differences in subsets of monocytes.

The results help explain some of the diversity and sub-specialization of the immune system—and could yield new treatment strategies for patients with rheumatoid arthritis, colitis, diabetes and other ailments.

"These findings represent the first comprehensive and unifying data on IL-1 β production by monocytes, and identify the Hsp27 pathway as a main player and potential novel therapeutic target for inflammatory [disease](#)," says Wong Siew Cheng from the A*STAR Singapore Immunology Network, who led the research project.

Wong teamed up with Heather Wilson, an immunologist at the University of Sheffield in the United Kingdom, to study IL-1 β production in different subsets of monocytes. The two researchers jointly supervised a PhD student, Éva Hadadi, who used surface markers to sort monocytes isolated from human blood into three subpopulations: classical, intermediate and non-classical monocytes.

Hadadi then induced IL-1 β production and maturation through a two-step stimulation protocol. In this way, the researchers observed that classical and intermediate monocytes produced and released more than twice as much IL-1 β as non-classical monocytes.

They then searched exhaustively and systematically for reasons to explain this differential production of IL-1 β . Non-classical

monocytes were no less receptive to the stimulation protocol, they found, so that didn't account for their low IL-1 β output. Nor were these [white blood cells](#) generally deficient in their ability to produce pro-inflammatory signaling proteins or process their maturation.

"Instead," says Wong, "these cells expressed abundant Hsp27," an essential subunit of a [protein](#) complex involved in breaking down the RNA transcripts of IL-1 β before they can be turned into proteins. As a result of this differential Hsp27 activity, overall IL-1 β levels remained low in non-classical monocytes but high in classical monocytes.

The findings indicate that IL-1 β -spewing classical monocytes are the true culprits behind inflammatory disease and that therapies designed to boost Hsp27 levels in these cells might help tamp down unwanted inflammation. However, Wong notes that Hsp27 is also known to promote other pro-inflammatory molecules. "Hence," she says, "the type of treatment option to utilize will be based on the type of disease."

More information: Eva Hadadi et al. Differential IL-1 β secretion by monocyte subsets is regulated by Hsp27 through modulating mRNA stability, *Scientific Reports* (2016). [DOI: 10.1038/srep39035](https://doi.org/10.1038/srep39035)

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