

Research presents new ways of developing treatment of chronic inflammation

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Researchers from Aarhus University Hospital and Aarhus University in Denmark in collaboration with researchers from Colorado in the United States have found a new way to treat the inflammation involved in chronic diseases such as psoriasis, asthma and HIV. A group of transmitter substances (cytokines) in the immune system, the so-called IL-1 family, has been shown to play an important role in many of these diseases by regulating the body's immune responses.

Professor Charles A. Dinarello from University of Colorado Denver is also an honorary doctor at Aarhus University. He is an expert in regulation and transmission of these cytokines. He is primarily known for discovering the important cytokine IL-1(-?), which plays a significant role in countless diseases. In collaboration with Charles Dinarello, the Danish researchers have investigated a more efficient way of reducing the effect of the IL-1 family and in this way improve treatment of chronic inflammatory diseases.

Previous research has often focused on blocking a single cytokine or signaling pathway at a time. However, many diseases and sequela are driven

by more than one cytokine. This has caused researchers to wonder if it could be possible to block more important signaling pathways of the IL-1 family at the same time, and in this way make it possible to develop better treatments. The researchers try to find a broader anti-inflammatory treatment impacting several important cytokines at the same time, but also trying to avoid that this causes unintended side-effects.

In this study, the researchers have investigated if a receptor (IL-1R3), which is not just involved in the signaling of one but six different inflammatory cytokines in the IL-1 family, could be a possible target in the treatment of chronic inflammatory disease. Using an antibody to block the effect of IL-1R3, it was possible for the researchers to investigate the effects in both studies on cells and mice.

In this way, researchers could study some of the consequences of the blocking of this receptor on the immune system. At the same time, the researchers specifically studied the effect of blocking IL-1R3 in mice with either gout, acute allergic inflammation (asthma) or psoriasis.

"The experiments showed that it was possible to effectively block the receptor and reduce manifestation of diseases, which underlines the potentials in our new approach," says MD and Ph.D. Jesper Falkesgaard Højen.

"Even though new questions arise as a consequences of these results, we have managed to describe a new and effective approach to block IL-1 family driven inflammation, and in this way we have possibly contributed with a new direction to study and treat chronic inflammatory conditions driven by the IL-1 family."

More information: Jesper Falkesgaard Højen et al, IL-1R3 blockade broadly attenuates the functions of six members of the IL-1 family,



revealing their contribution to models of disease, *Nature Immunology* (2019). DOI: 10.1038/s41590-019-0467-1

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