

A protein that controls inflammation

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A study by the research team of Prof. Geert van Loo (VIB-UGent Center for Inflammation Research) has unraveled a critical molecular mechanism behind autoimmune and inflammatory diseases such as rheumatoid arthritis, Crohn's disease, and psoriasis. They discovered how the protein A20 prevents inflammation and autoimmunity, not through its enzymatic activities as has been proposed, but through a non-

enzymatic mechanism. These findings open up new possibilities for the treatment of inflammatory diseases. The results of the study are published in the leading journal *Nature Immunology*.

Inflammatory autoimmune diseases

Inflammatory autoimmune diseases such as rheumatoid arthritis, inflammatory bowel diseases, psoriasis, and multiple sclerosis are amongst the most common diseases. Their prevalence has been rapidly expanding over the last few decades, which means that currently millions of patients are under constant treatment with [anti-inflammatory drugs](#) to keep their condition under control.

As an example, about 1% of the western population is affected by [rheumatoid arthritis](#) (RA), a chronic and progressive inflammatory disease of the joints that severely affects the patients' quality of life. The [molecular mechanisms](#) that cause diseases such as RA need to be better understood in order to be able to develop new therapies to treat patients suffering from inflammatory pathologies.

An anti-inflammatory domain

Arne Martens in the research group of Prof. Geert van Loo investigated the molecular signaling mechanism by which the protein A20 controls inflammatory reactions. The current study builds further upon earlier work at the VIB-UGent Center for Inflammation Research which demonstrated that A20 acts as a strong anti-inflammatory mediator in many models of inflammatory disease.

In this study, the researchers show that the anti-inflammatory activity of A20 depends on the presence of a specific domain within the protein that is able to bind to ubiquitin, an important modification on other

proteins. This allows A20 to interfere with signaling pathways within the cell and as such prevent the activation of a cellular response that would normally result in [inflammation](#) and disease development.

New therapies for the treatment of inflammation.

Prof. van Loo explains the importance of their findings: "Our results are important from a scientific point of view since they help us understand how A20 prevents inflammatory reactions in the body's cells. However, this knowledge also has therapeutic implications, and suggests that drugs based on that specific A20 domain could have strong anti-inflammatory activities. Therefore, such drugs could be effective in the treatment of RA and various other inflammatory and autoimmune diseases."

More information: Arne Martens et al, Two distinct ubiquitin-binding motifs in A20 mediate its anti-inflammatory and cell-protective activities, *Nature Immunology* (2020). [DOI: 10.1038/s41590-020-0621-9](https://doi.org/10.1038/s41590-020-0621-9)

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