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A major step toward a more targeted treatment for auto-immune diseases?

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More and more people in Western society are suffering from auto-immune diseases. Discovering the cause of these chronic inflammations is a first important step in the search for targeted medicines. VIB researchers connected to Ghent University and the Katholieke Universiteit Leuven joined forces and have elucidated the function of MALT1, a key player in controlling inflammatory reactions.

They are the first to show that MALT1 is able to cleave the A20 protein, which inhibits inflammation. Scientists hope that by counteracting MALT1 they will be able to restore the body's natural inhibition of inflammation and thus provide an alternative for treatments that tax the immune system. This would represent a profound improvement over current medicines. Their research will be published in the authoritative journal *Nature Immunology*.

Inflammations are our normal protective reactions against infections – they arise to help remove pathogenic organisms from our bodies. This immune response is very precise and is only possible after a complex cascade of signals. Sometimes something goes wrong in this chain of reactions, and the inflammation process becomes uncontrolled or even triggers undesired immune responses against the body's own substances. This can lead to auto-immune diseases such as rheumatism, Crohn's disease, psoriasis, and multiple sclerosis, and, in some cases, to cancer. Reining in the runaway immune system is the most obvious remedy for these kinds of diseases. But the major challenge is to do this in such a way that the immune system continues to perform its protective role.

And this requires a thorough understanding of the entire process.

It has long been known that the MALT1 protein plays an important role in initiating inflammation reactions. That's why VIB researchers Beatrice Coornaert (UGent), Rudi Beyaert (UGent), Thijs Baens (K.U.Leuven) and Peter Marynen (K.U.Leuven) set out to discover exactly what its particular role is. They have now succeeded in showing that MALT1 cuts the A20 protein into pieces. They are in fact the first to find that MALT1 is a protease (a protein that cleaves other proteins) and that A20 is the protein that is cut. In normal circumstances, A20 inhibits inflammatory reactions; and, by cleaving A20, MALT1 counteracts this inhibition, allowing the inflammation to progress freely. So, both proteins play very important parts in fine-tuning the intensity of inflammatory reactions.

Through their research, the VIB scientists are shedding light on an important part of the process that controls our immune response. Their findings offer possibilities for the development of new medicines that counteract MALT1 and thereby restore the natural 'brake' on the inflammation process. In this way, scientists hope to be able to provide an alternative for treatments that undermine the immune system. In addition, they hope to be able to apply this knowledge to the typical immunoreactions toward organ transplants or the treatment of cancer that is caused by genetic defects in MALT1, such as MALT lymphoma.

This research clearly shows the added value of combining expertise from different research groups. These important discoveries are the result of a close collaboration between researchers from the VIB Department for Molecular Biomedical Research (UGent) and the VIB Department of Molecular and Developmental Genetics.

Source: VIB (the Flanders Institute for Biotechnology)