

Research opens up new treatment route for inflammatory rheumatism

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Enthesitis, inflammation of tendons where they attach to the bone, is a common medical problem which underlies various forms of inflammatory rheumatism. Although around 1% of the population is affected, the mechanisms driving this type of inflammatory condition is poorly understood. Research by Professor Dirk Elewaut (VIB-UGent/UZ Gent), in collaboration with Professor Geert van Loo (VIB-UGent) at VIB's inflammation research center (IRC), is now changing this. The researchers have demonstrated that macrophages, a particular type of white blood cell, play a key role. The findings reveal a mechanism which could lead to new treatments for certain types of inflammatory rheumatism.

Macrophages (which literally translates as 'big eaters') are types of white blood cells which attack foreign micro-organisms and remove harmful substances within the body. As a result, they form an essential part of our immune system. Professor Elewaut's research team has demonstrated that these macrophages can play a decisive role in enthesitis.

Prof. Dirk Elewaut (VIB-UGent/UZ Gent): "Achilles enthesitis is one of the most typical forms of chronic tendinitis. Our research demonstrates that macrophages which lack the anti-inflammatory protein A20 develop early on in their disease an enthesitis of the Achilles tendon. We were also able to demonstrate the underlying cause: A20 suppresses the activation of STAT1, a signalling molecule which seems to be key in initiating this [inflammation](#). The absence of A20 therefore leads to a significant increase in STAT1, which promotes the development of

enthesitis."

Successful treatment

JAK is one of the key molecules that controls STAT1. By blocking this molecule using a so-called JAK inhibitor, the researchers were able to prevent the increase of STAT1 and successfully treat the Achilles enthesitis.

Prof. Dirk Elewaut (VIB-UGent/UZ Gent): "Our findings underline the importance of macrophages in the development of enthesitis and the possibility of treating these conditions using JAK inhibitors. In several countries, this type of inhibitors is already available for the treatment of rheumatoid arthritis."

New therapeutic route

Many existing anti-inflammatory treatments used to date include TNF inhibitors. This is because the protein TNF plays an important role in inflammatory processes and numerous autoimmune disorders. Importantly, the occurrence of the inflammation in the A20 model is not dependent on TNF.

Prof. Dirk Elewaut (VIB-UGent/UZ Gent): "Our research opens up new prospects for patients in whom the existing TNF inhibitors offer no relief. In the first place, we wish to check whether this mechanism also plays a role in other places in the body, such as the spine. If so, the discovery may offer new options for patients with other forms of inflammatory rheumatic diseases such as spondyloarthritis, an umbrella term for several diseases characterised by inflammation of the spine and joints. It may also offer new treatment options for psoriatic arthritis, a very common form of joint inflammation in patients with psoriasis."

More information: Mira Merashli et al. Evidence of response to IL-6 inhibition in some cases of refractory spondyloarthritis-associated peripheral synovitis: Table 1, *Annals of the Rheumatic Diseases* (2016). DOI: [10.1136/annrheumdis-2016-209275](https://doi.org/10.1136/annrheumdis-2016-209275)

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