

Researchers discover immune pathway

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Researchers from Aarhus University, Denmark, have now discovered an important mechanism behind one of our most fundamental lines of immune function. The discovery has been published in the esteemed scientific journal, The *Journal of Immunology*, where it has been highlighted as a top story.

In collaboration with colleagues from USA and Turkey, they have discovered exactly which enzymes collaborate in the first line of the [immune defence](#). Thus, they answer a central question about the so-called complement system, which has been a focal point of the scientific field for the past decade: which enzyme does what?

Using [blood samples](#) from a unique patient harbouring a rare genetic syndrome, the researchers from Aarhus University have now established that it is the enzyme MASP-1 that is key to the activation of the complement system.

"Understanding the immune system is a central goal in itself in scientific terms, especially for our research group conducting basic research. But in the longer run, it is also an important goal that this knowledge may help people and cure diseases", says postdoc Soeren Egedal Degen from Aarhus University, who is first author on the paper.

Big perspectives for patients

He believes that once one has defined how the complement system works, it will be possible to manipulate it:

"For example this system is important for the survival of patients undergoing chemotherapy, because this treatment suppresses other functions of the immune system - so in their case it is beneficial to "rev up" the system. But following a [heart attack](#) there may be reasons to instead dampen the system. The complement system has an unfortunate tendency to attack tissues that have suffered damage due to deprivation of oxygen, and thereby it exacerbates the damage already done to the heart", says Soeren Egedal Degn.

He notes however, that the new discovery is unlikely to result in concrete new treatment modalities in this decade.

MASP-1 and the lectin pathway

Behind the discovery of the central role of MASP-1 in the complement system is, apart from Soeren Egedal Degn, also the Aarhus professors Jens Chr. Jensenius and Steffen Thiel, who are considered international experts in the field. They have previously discovered the four other known proteins related to MASP-1, namely MASP-2, MASP-3, MAp19 and MAp44. Together, these proteins make up a central part of the activation pathway of complement known as the lectin pathway. The research group in Aarhus, which also includes the laboratory technicians Lisbeth Jensen and Annette G. Hansen, has been central in the elucidation of the lectin pathway through the past 15 years.

The enzyme MASP-1 is able to efficiently auto-activate, for example when it "senses" a bacterium. It then activates MASP-2, which in turn activates the rest of the complement system in a cascade-like manner, where a long list of enzymes sequentially activate each other - much like dominoes. The result is a signal to immune cells to home to the area in the body, where the system is activated, and to kill the intruding bacteria. The bacteria are also covered in "molecular tags", making it easier for the immune cells to recognize and efficiently engulf them. Finally, the

complement system directly "punches holes" in the bacteria, by forming pore-like structures in their membranes.

Provided by Aarhus University

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