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Scientists study serious immune malfunction

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Defects in the gene that encodes the XIAP protein result in a serious immune malfunction. Scientists used biochemical analyses to map the protein's ability to activate vital components of the immune system. Their results have recently been published in *Molecular Cell*, a journal of international scientific repute.

Researchers at The Novo Nordisk Foundation Center for Protein Research at the University of Copenhagen have mapped how the XIAP protein activates a vital component of the immune defence system, specifically the component that fights bacterial infections in the gastro-intestinal system:

"Our results are an important step on the way to understanding the very serious – but fortunately rare – genetic immune disorder called X-linked lymphoproliferative syndrome type 2 (XLP2), which affects male children," says Associate Professor Mads Gyrd-Hansen from the The Novo Nordisk Foundation Center for Protein Research, and explains more about the disease:

"The gastro-intestinal system can be viewed as a long tube running through the body, absorbing nutrients and water. The contact surface between the intestinal system and the rest of the body is protected by an efficient immune barrier that confines the bacteria to the intestine. This barrier is not intact in XLP2 patients, who thus lack the necessary bulwark, so to say, between bacteria and body."

The new study published in Molecular Cell shows that genetic mutations

found in patients with XLP2 specifically destroy XIAP's ability to attach the signalling protein ubiquitin to other proteins. The attachment process is vital for activating the immune system and therefore for survival.

Important knowledge for leukaemia research

While the results from the study published in Molecular Cell are first and foremost relevant for XLP2 patients, cancer researchers can also benefit from the new discoveries:

"Several pharmaceutical companies have developed drugs to act on IAP proteins, including XIAP, as part of cancer treatment. Several of the drugs are currently being tested in clinical trials for their efficacy in treatment of leukaemia and other forms of cancer. It is therefore essential to know precisely which biological processes in the organism the treatment can potentially affect," continues Mads Gyrd-Hansen.

Mads Gyrd-Hansen and his colleagues at The Novo Nordisk Foundation Center for Protein Research have been collaborating for a good 18 months together with research groups in Germany, the UK and Australia, and the competencies of the individual groups have made it possible to rapidly achieve high-quality results quickly:

"International collaboration has made it possible – in a short time – to describe detailed molecular processes, to use the descriptions to create mouse models for further tests and thereafter to link the results of these tests to genetic mutations identified in patients."

Provided by University of Copenhagen