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A molecular switch to stop inflammation

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Our immune system is vital to us and can sometimes overreact causing chronic illnesses, such as for instance rheumatism and allergy. Now, researchers from Umeå University and University of Gothenburg have identified a molecular switch – MYSM1 – that can suppress such an overreaction and avoid inflammation. The study is published in the prestigious journal *Immunity*.

"The discovery of MYSM1 is a major milestone in our understanding of how our immune system works, and how its response could be controlled in order to prevent inflammatory diseases such as sepsis," says Nelson O. Gekara, research leader at MIMS, Molecular Infection Medicine Sweden at Umeå University.

Our innate immune system is activated when our body needs to protect itself against pathogens, for instance bacteria and viruses, as well as for tissue healing. In some people, the immune system overreacts which can cause chronic inflammatory diseases and result in tumour development. The innate immune system is activated by receptors that recognise certain molecular patterns found on microbes or dead cells. These receptors are called pattern-recognition receptors (PRRs).

"Most infectious or inflammatory situations are associated with the simultaneous or sequential activation of multiple PRR pathways. Therefore, it is essential to avert a disproportionate self-destructive immune response in a synchronised fashion once activated. How this is accomplished has been unclear," says Nelson O. Gekara.

Nelson O. Gekara's at Umeå University and his doctoral student Swarup Panda are now closing in on a solution. For years, they have been searching for possible genes required for the regulation of the immune system. Together with Professor Jonas A Nilsson at Sahlgrenska Cancer Center at the University of Gothenburg, the Umeå researchers have now identified MYSM1 – a molecule in the cell core (nucleus) of resting cells. For the first time, the researchers are now able to show that during infection or inflammation MYSM1 accumulates outside of the nucleus, in the cytoplasm where it disrupts the function of signalling molecules involved in activation of PRR pathways, thereby terminating inflammation.

"MYSM1 can be said to act like a molecular switch that can turn off several inflammatory pathways. Therefore lack of MYSM1 in animal results in unrestrained activation of the innate immune system, leading to inflammatory diseases" says Nelson O. Gekara.

His research team is now screening for small molecule compounds that are able to modulate the MYSM1 molecule activity. The hope is to find new therapeutics against infections and other inflammatory diseases.

More information: "Deubiquitinase MYSM1 Regulates Innate Immunity through Inactivation of TRAF3 and TRAF6 Complexes." *Immunity* 43, 1–13, October 20, 2015; DOI: 10.1016/j.immuni.2015.09.010

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