MedicalXpress

Adaptive immune response: new cofactor of roquin identified

January 19 2018

Roquin has a key role in the adaptive immune response. It controls the activation and differentiation of T cells and thus helps to make the decisions whether or not and which type of immune response will be mounted. Now, a team of scientists of Helmholtz Zentrum München in cooperation with scientists of Ludwig-Maximilians-Universität and the Helmholtz Centre for Environmental Research in Leipzig have identified NUFIP2, a protein with a previously unknown function, as cofactor of Roquin and discovered that NUFIP2 enhances Roquin's regulatory function.

In previous studies, the research group led by Professor Vigo Heissmeyer, head of the Research Unit Molecular Immune Regulation (AMIR) at Helmholtz Zentrum München (HMGU) and professor at Ludwig-Maximilians-Universität (LMU) in cooperation with research groups from the Institute of Structural Biology (HMGU) showed that Roquin binds to the folded regions of the 3' UTR of certain mRNAs with its ROQ domain. This reduces spontaneous activation of T cells and controls differentiation decisions after activation, thereby limiting immune responses to specific reactions and preventing inflammatory reactions in the absence of pathogens. It became now clear that Roquin does not carry out these tasks alone. "We have discovered that Roquin recognizes mRNA and induces degradation together with NUFIP2," said Heissmeyer. "Such cooperative regulation of mRNA transcripts ensures that T cells produce fewer costimulatory receptors and immune responses are attenuated," added Professor Dierk Niessing, research group leader at the STB.

"The NUFIP2 protein, which I have identified in a high-throughput screen, binds directly to Roquin with high affinity, thus altering the Roquin-mediated recognition of target mRNAs. In return, this binding stabilizes NUFIP2 in the cell," said Nina Rehage, a former doctoral student at HMGU. "For ICOS and Ox40 in particular, we were able to demonstrate that the complex of NUFIP2 and Roquin reinforces the recognition of unconventional tandem structures in the 3' UTRs. ICOS and Ox40 are costimulatory receptors for T cells and are therefore crucial for the development of specific immune responses. Their regulation is therefore very important," explained Elena Davydova, Ph.D. student at the STB, and Christine Conrad, Ph.D. student at Ludwig-Maximilians-Universität.

Since T lymphocytes are involved in many diseases, especially autoimmune diseases, allergies and chronic inflammatory reactions, the key to new therapy options lies in the knowledge of the underlying molecular mechanisms. We think that this research contributes to a better understanding of the immune response and may at one point enable new therapies," said Heissmeyer.

More information: Nina Rehage et al. Binding of NUFIP2 to Roquin promotes recognition and regulation of ICOS mRNA, *Nature Communications* (2018). DOI: 10.1038/s41467-017-02582-1

Provided by Helmholtz Association of German Research Centres