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Paradigm shift in immunology 'Adaptive Tolerance' balances autoimmune reaction

Immunologists at Ulm University and its Medical Centre have developed a new model that could revolutionise the treatment of autoimmune disease as well as vaccine development. As 'Adaptive Tolerance' demonstrates, autoreactive antibodies are by no means disease drivers which a healthy organism swiftly eliminates. Rather, they trigger the formation of a class of antibodies that protect the body's own structures. The researchers from Ulm led by Professor Hassan Jumaa first described this paradigm shift in the renowned EMBO Journal.

Autoimmune disease is prevalent in industrialised countries: Around 5 per cent of the population suffers from diseases such as type 1 diabetes or rheumatism, in which the immune defence is directed against the body's own structures. Thus far, so-called autoreactive antibodies, which are normally identified and removed during early B-cell development, were considered to be the disease drivers. As a reminder: B cells are a crucial component of the adaptive immune system and can trigger the formation of pathogen-specific antibodies.
Now, researchers led by Professor Hassan Jumaa, head of the Institute of Immunology in Ulm, have investigated and ultimately redefined the role of various autoreactive antibodies.

The research project focused on immunisation experiments in the mouse model, where human insulin was administered to healthy animals in the form of protein complexes to serve as autoantigen. The hormone insulin plays an important role in metabolism: In diabetics, insulin is deficient and must be supplemented.
'The mice were monitored closely for defence reactions using methods from diabetology. In the process, we came across autoreactive and thus harmful antibodies that, according to previous assumptions, should have been eliminated early on in the healthy mice,' explains Professor Jumaa. A hitherto-common hypothesis on autoreactive antibodies was hereby refuted. Furthermore, the immunologists found that re-administration of the insulin protein complexes caused the insulin-specific antibody titre in the mice to skyrocket. These so-called IgM antibodies were able to slow down the previously detected autoimmune reaction and prevent physical damage in those mice. The researchers from Ulm call this thus-far-unknown mechanism Adaptive Tolerance.

Research results transferable to humans

'Contrary to earlier assumptions, our research shows that a healthy defence reaction triggers the formation of protective IgM antibodies. This modulates the immune response and protects the body from autoreactive antibodies. It thus appears that a diverse B-cell repertoire is able to alleviate harmful autoimmune reactions through adaptive IgM antibodies,' first author Timm Amendt sums up the research results. Adaptive Tolerance is hence based on an interplay of different autoantigen complexes. When this balancing act is off-kilter, autoimmune disease can develop. The immunologists demonstrate that these research results can be transferred from the mouse model to humans in a further study that was recently published on a preprint server.

Overall, this paradigm shift from a static to a dynamic immunological model ('Adaptive Tolerance') provides undreamt-of insights into the development and treatment of autoimmune diseases. In the next step, the researchers led by Professor Hassan Jumaa want to use the new model to investigate whether adaptive IgM antibodies can be applied in the treatment or prevention of diabetes. Another area of application is, for example, vaccine development.

The studies were carried out at the Medical Faculty and the Institute of Immunology of Ulm University and were funded in parts by the German Research Foundation (DFG).

Reference:

Amendt T and Jumaa H (2021), Memory IgM protects endogenous insulin from autoimmune destruction, The EMBO Journal.

Preprint Study:
Amendt T, Allies G, Nicolo A, El Ayoubi O, Young M, Roeszer T, Setz CS, Warnatz W, Jumaa H (2021), Antibodies control metabolism by regulating insulin

homeostasis. https://www.biorxiv.org/content/10.1101/2021.08.10.455644v1

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Further information

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