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Agonistic antibody diseases = Autoimmune diseases? From bench to bedside

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In recent years, the number of diseases in which autoantibodies (AAB) against G Protein-coupled receptors (GPCR) have been detected has continued to increase. Because they act in a bioassay similar to the physiological ligands of GPCR, the term "agonistic autoantibodies" (agAAB) was established early on. The proportion of patients with a clinically diagnosed disease in whom agAAB has been detected in the blood can be very different. Currently agAAB can be determined against 8 different GPCRs. The probably most important ones are directed against the adrenoceptors (AR) α, ß1, ß2 and the angiotensin2 receptor type 1 (AT1-R). The AAB binding epitopes are located on the extracellular 1st or 2nd loop and are consistently constant.

For a few diseases such as dilated cardiomyopathy (DCM, ß1-AR, α-AR), pre-eclampsia (AT1-R) and vascular necrotic kidney transplant rejection (AT1-R), antibodies could be induced in animal experiments by immunisation with the extracellular loop peptides and subsequently produce a disease pattern similar to that of humans. In the development of vascular M. Alzheimer's disease (VAD), animal experimental findings according to agAAK against α-AR could also play a role in cerebral vascular obliteration. For most of the diseases associated with agAAB, the pathological significance of the proven agAAB has not yet been clarified. They may be an epiphenomenon, but can also be pathologically amplifying bystander or even cause the disease.

The above agAABs often occur in typical combinations, and we do not yet know anything about their possible interference or parallel involvement in the respective disease. The distribution patterns of agAAK in diseases such as DCM, VAD, diabetes type 2 (DM2), primary open-angle glaucoma (POAG), thromboangiitis obliterans (TAO) or chronic fatigue syndrome (CFS) observed so far suggest that there are pathophysiological similarities between the very different diseases in the clinical symptoms. This is particularly noticeable in diseases with vascular contribution.

Up to now, agAAB's participation in a disease beyond the classics such as DCM has not been taken into account therapeutically. The abundance of data on the prevalence of agAAB in a wide variety of diseases makes it almost necessary to search for new terms to take these conditions into account. One possible approach would be to label patients with different diagnoses and positive antibody status with the additional diagnosis"agonistic antibody disease". In specific individual cases, new therapeutic options may then become apparent.