Maastricht University

Autoantibodies in the nervous system

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Propositions

Belonging to the PhD thesis

Autoantibodies in the nervous system:

pathophysiology and new therapeutic strategies

Marina Mané Damas,

Maastricht, 16th December 2020

1. The different mechanisms by which autoantibodies alter synaptic transmission likely impact the widespread function of neurons and neural networks, culminating in serious mental (and neurological) disturbances. (this thesis)
2. The burden of mental disorders continues to grow with significant impacts on health and major social, human rights and economic consequences in all countries of the world. (World Health Organization)
3. Autoantibodies to the NMDA receptor have been described in multiple different neurological disorders. The clinical and pathological significance of these antibodies depend on the IgG subclass, target subunit of the receptor, and presence of antibodies in the CSF. (Dalmau et al. Physiol Rev., 2017)
4. Cross-validated studies using different detection methods confirmed that pathogenic autoantibodies targeting neuronal surface antigens are very rare in psychotic disorders without any form of neurological manifestation. (this thesis)
5. Over the past decades, a sharp increase in autoimmune diseases has been noted worldwide. The cumulative prevalence of autoimmune diseases caused by autoantibodies is well over 2.5% of the population. (Ludwig R.J. et al., Front Immunol. 2017)
6. Manipulating the signalling path of these proteins by enhancing MuSK activation, one could improve the motor function and correct neuromuscular defects not only in myasthenia gravis but also in many other disorders of the neuromuscular junction. (this thesis)
7. The rapid ixazomib-induced depletion of plasma cells and thus of total IgG and AChR autoantibodies we observed in this study provides the basis for a clinical trial in AChR-MG patients. (this thesis)
8. A challenging strategy is to selectively deplete pathogenic long-lived plasma cells in an autoantigen-specific manner without removing long-lived plasma cells that provide protective humoral memory. (Hiepe, F. and Radbruch, A. Nat Rev Nephrol. 2016)
9. Pre-clinical studies are needed in order to formulate hypotheses that justify clinical trials. Without these preliminary studies in vitro and in vivo in selected animal species it would be unethical to test still unproven chemicals in humans. (Garattini S and Grignaschi G. European Journal of Internal Medicine, 2017)
10. Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less. (Marie Curie)