

# Novel strategies for making myasthenia less gravis : targeting plasma cells and the neuromuscular junction

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## Statements

Belonging to the PhD thesis

### **Novel strategies for making myasthenia less gravis: targeting plasma cells and the neuromuscular junction**

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Maastricht, 22<sup>nd</sup> November 2013

1. Depletion of plasma cells is a therapeutic strategy for efficiently reducing autoantibody titers in experimental autoimmune myasthenia gravis. (*this thesis*)
2. The proteasome inhibitor bortezomib eliminates plasma cells and blocks autoantibody production in cultures of thymic cells from myasthenia gravis patients. Consequently, bortezomib is a promising therapy for rapidly reducing autoantibody titers in severely-affected myasthenia gravis patients. (*this thesis*)
3. Down-regulation of the muscle protein Dok-7, involved in AChR-clustering at the neuromuscular junction, increases the susceptibility to experimental passive-transfer myasthenia gravis, but is not essential for the recovery of the neuromuscular junction after antibody-mediated damage. (*this thesis*)
4. In the event of an autoimmune attack at the neuromuscular junction, the muscle responds with changes in its cytoplasmic proteins that are similar to the changes observed in other contraction-impairing conditions (myositis, aging and denervation). Some of these differentially-expressed proteins might represent novel targets for symptomatic treatment in myasthenia gravis. (*this thesis*)
5. All antibody responses are not created equal. T-cell-independent antibody responses are known to be short-lived, whereas T-cell-dependent antigens elicit immunity that lasts for decades or, in some cases, may be maintained for a lifetime. (*I. J. Amanna, M. K. Slifka; Immunol Rev, 2010*)
6. The severity of autoimmune disease depends not only on the magnitude of self-destructive immune response but also on the susceptibility of target tissues to the damage caused by a given level of response. (*R. Medzhitov; Science, 2012*)
7. Essentially, all scientific models are wrong, but some are useful. (*George E. P. Box*)
8. Tell a man that there are 300 billion stars in the universe, and he'll believe you. Tell him that a bench has wet paint upon it and he'll have to touch it to be sure. (*A. Einstein*)
9. Nothing in life is to be feared, it is only to be understood. (*Marie Curie*)
10. What a man thinks of himself, that is which determines, or rather indicates, his fate. (*H. D. Thoreau*)