**THE ROLE OF THE THYMUS IN MYASTHENIA GRAVIS**

**Student:** Marta Prats Vallverdú; **Tutor:** Iñaki Álvarez

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**Introduction**

- Myasthenia Gravis (MG) is an autoimmune disease (AID) that causes muscle weakness and fatigue. It especially affects the ocular, facial and bulbar muscles.
- MG is caused by the production of antibodies against proteins of the neuromuscular junction:
  - Acetylcholine Receptor
  - Muscle Specific Kinase
  - Low-density lipoprotein receptor-related proteins

**Acetylcholine Receptor (AChR) structure**

**Muscles affected in MG**

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**Thymoma**

- Tumor of cortical epithelial cells of the thymus: types AB, B1 and B2.
- Changes in the thymus caused by thymoma:
  - Medullary area reduced compared to cortical area (imbalance in the cell density)
  - Low expression of AIRE (defect in negative selection)
  - High number of immature T cells (CD4+ and CD8+, DP)
  - High proliferation of cortical thymocytes increases genetic mutations
  - Reduced number of dendritic cells (defect in negative selection)
  - MHCI, deficiency (defect in positive selection)
  - FoxP3 deficiency (deregulation of Treg)
  - Treg deficiency (increases survival of autoreactive T cells in the periphery)
  - High levels of expression of type I interferons

**Thymic follicular hyperplasia**

- Many germinal centers (GCs) are formed in the thymus.
- Changes in the thymus caused by thymic follicular hyperplasia:
  - Thymus overexpression of proinflammatory cytokines and genes induced by IFN-γ
  - Abnormal cytokine network that alters the balance between Th1, Th2 and Th17
  - Defect in Treg (increases survival of autoreactive T cells in the periphery)
  - Reduced number of dendritic cells (defect in negative selection)
  - Low expression of AIRE (defect in negative selection)
  - High expression of TNF-α (chronic inflammation in thymus)
  - Expansion of perivascular spaces, displacement of mioid cells
  - The complement proteins and autoreactive T cells against AChR attacks mioid marrow cells
  - High expression of Bcl-2 prevent apoptosis of autoreactive cells

**Thymectomy**

- The removal of the thymus.
- Thymoma:
  - Eliminates the production site of autoreactive T cells
  - Thymic follicular hyperplasia: Eliminates the production site of antibodies anti-AChR

**Conclusions**

- Thymoma plays a very important role in the AChR-MG
- Thymoma affects the proper functioning of the thymus and favors the generation and the exportation of autoreactive T cells to periphery.
- The presence of GCs in the thymus increases antibody production, favours the exportation of antibody-producing cells to periphery and alters the thymus function.
- There is evidence that thymectomy is useful in some cases but not fully effective in others.

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**Bibliographic references**