Survivin is a Negative Regulator of Apoptosis in Myasthenia Gravis: A Human and Animal Model Study

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Introduction: Myasthenia gravis (MG) is caused by autoantibodies directed against the neuromuscular junction, with the majority of patients expressing antibodies to acetylcholine receptor (AChR). Autoreactive cells that produce the disease evade the immune checkpoints by an unknown mechanism. Survivin is a member of the inhibitor of apoptosis family and known to be expressed in circulating lymphocytes from MG patients. Survivin expression may be part of a mechanism that inhibits the apoptosis of autoreactive B cells in MG.

Objective: To assess the role of survivin in myasthenia gravis

Methods: The peripheral blood mononuclear cells were obtained from MG patients and non-autoimmune controls and stained with anti-human CD45, T cell marker (CD4), B cell marker (CD20), and anti-Survivin. The extracellular or intracellular survivin expression on human CD20+ or CD4+ lymphocytes were viewed by using BD Celesta analyzer followed by FlowJo software. To target survivin, a monoclonal antibody was developed against survivin peptide (SVN53-67/M57). For the animal model, EAMG was induced and mice stratified into three treatment groups (PBS, anti-Survivin 20 mcg and 100 mcg). EAMG mice were assessed for disease severity, AChR-specific antibody production, and expression of survivin in splenocyte population.

Results: Significantly higher percentage of CD4- CD20+ human B cells showed intracellular survivin expression in MG patients compared to controls. In the animal model of MG, antibody to survivin treatment improved disease severity, reduced AChR-specific antibody titers, and decreased survivin expression in CD3- CD19+ splenic B cells compared to PBS controls.

Summary/Conclusion: Targeting survivin–expressing B cells for elimination may be an effective therapeutic approach