Slow-channel congenital myasthenic syndrome models have different responses to atorvastatin

Congenital myasthenic syndromes (CMS) are a family of rare inherited disorders caused by mutations in the nicotinic acetylcholine receptor (nAChR) at the neuromuscular junction (NMJ) that result in muscle weakness and fatigue. Slow-channel CMS (SCCMS) is promoted by mutations that increase the receptor's response to ACh in muscle. Interestingly, the muscle nAChRs interact with cholesterol through the transmembrane domain, which ultimately promotes stabilization and proper ion channel functioning. Consequently, mutations in this receptor can also alter the cholesterol-nAChR interaction. Studies have shown that statins, drugs prescribed to lower serum cholesterol levels, unmask neuromuscular conditions in asymptomatic patients with latent neuromuscular disorders. This, coupled with findings supporting that elevated blood serum creatine kinase (CK) levels are indicative of intrinsic muscular problems, position the CK as an indicator of neuromuscular pathologies. Using a panel of SCCMS transgenic mice models, we evaluate the consequences of atorvastatin consumption to further assess the effects of statin prescription to SCCMS patients. To this end, we analyzed serum samples from mice carrying SCCMS-associated mutations (αC418W, δS262T, and αV249F) after atorvastatin administration for different time periods. CK blood serum levels were later quantified and used as a measure of muscular damage. Our results have shown differences between basal CK levels from each mutant as compared to wild-type mice. Additionally, similar to what we hypothesized, atorvastatin administration seems to affect CK blood serum levels in SCCMS mice. Altogether, our experiments have further assessed the different pathological effects atorvastatin exerts on each mutation, while also providing valuable insights into the impact of statin consumption in SCCMS mice models. Finally, quantification of CK blood serum levels has proven to be a useful method to measure muscular atrophy related to this disease.