

CLN8: an Atorvastatin-specific marker for common myalgia

¹Richard Seip, Ph.D., ²Paul D. Thompson, M.D., ³John P. Kane, ³Clive R. Pullinger, ⁴Alan H.B. Wu, Ph.D., ¹Gualberto Rúaño, M.D., Ph.D.

¹Genetics Research Center, Hartford Hospital, Hartford, CT 06106, USA

²Hartford Hospital, Hartford, CT

³Cardiovascular Research Institute, University of California, San Francisco, CA

⁴Department of Laboratory Medicine, University of California, San Francisco and the San Francisco General Hospital, San Francisco, CA

Background: Statin therapy is highly successful for the treatment of hypercholesterolemia and prevention of cardiovascular disease. Side effects including muscle pain (myalgia), weakness and/or increased serum CK activity (myositis) often disrupt treatment, with no unifying hypothesis to explain them. We used genome-wide association to investigate whether genetic links to myalgia may be statin-specific. **Methods:** We genotyped 812 statin-treated patients with an array of 865,483 SNPs. There were 328 patients on atorvastatin, 119 on simvastatin; 154 on rosuvastatin, 213 on other statins. Myalgia index was scored as 1 for myalgia presence in 377 patients and 0 for no myalgia in 416. **Results:** The SNP rs7014327 of the ceroid lipofuscinosis, neuronal 8 (*CLN8*) gene was associated with myalgia at a significance of $p < 2 \cdot 10^{-7}$ ($R^2 = 5.2\%$) in patients receiving atorvastatin only. In all patients the SNP was unassociated ($p < 10^{-5}$, $R^2 = 2.6\%$). *CLN8* encodes a protein implicated in Pompe's disease, whose hallmark is myopathy. **Conclusion:** We propose a new candidate for myalgia, *CLN8*, which has an effect only in atorvastatin patients. This drug dependent association supports the hypothesis of statin-specific pathways for statin myopathy.

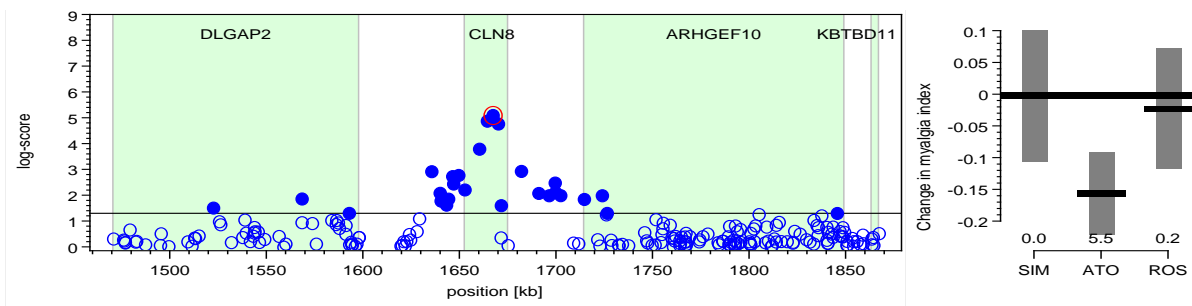


Figure legend. Left: *CLN8* genomic locus on chr 8p23 and effect on myalgia (all patients). Log-scores of p values for SNPs within 200 kb of the index SNP (red circle). Right: Effect of the SNP on myalgia index in patient subgroups taking simvastatin, atorvastatin, or rosuvastatin.