Abstract

The discovery of the molecular basis of Rotor syndrome consisting in biallelic inactivating mutations in both *SLCO1B1* and *SLCO1B3* genes encoding hepatic transporters OATP1B1 and OATP1B3, together with the previously described association of the rs4149056 variant in OATP1B1 with statin-induced myopathy (SM), led us to hypothesis that private variants in OATP1B1 and OATP1B3 confer predisposition to SM. This hypothesis was not supported by our study of 88 patients in whom exome sequencing was performed. Interestingly, we detected candidate variants in several genes mutated in recessively inherited muscle disorders, namely *CLCN1*, whose carriage may predispose to SM.

Pathogenic variants in several dozens of causative genes underlie hereditary cholestasis. We performed exome sequencing in 51 unexplained cases and revealed several unexpected diagnoses such as autosomal recessive polycystic polyposis, cutaneous porphyria or nephronophthisis. The most remarkable finding was that of yet unreported *F11R* deficiency due to a homozygous splice mutation found simultaneously in an index patient suffering from liver cirrhosis and her healthy sister. The F11R protein is involved in formation of tight intercellular junctions and mutations in *F11r* predispose to liver failure in mice. The finding of bialellic variants in *IFT172* associated with phenotypically variable ciliopathy, which we detected in two patients with isolated cholestatic liver disease, was fundamental.

Key words: whole exom sequencing, statin myopathy, cholestasis, CLCN1, IFT172