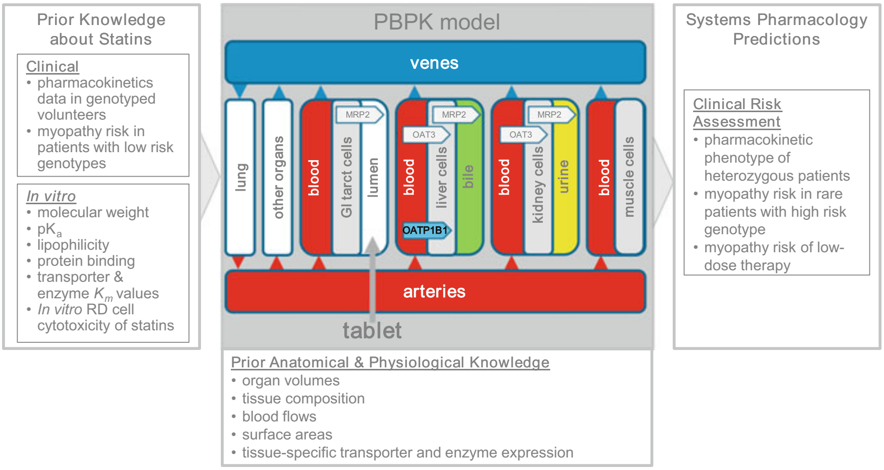

Fig. 7 The PBPK model for statins represents prior information in vitro and in vivo information about statins. In vitro properties of simvastatin and pravastatin are used to pre-parameterize the corresponding models. Clinical PK data for genotyped subjects are used to adjust the models. In combination with in vitro cytotoxicity data and clinical baseline myopathy risks, the PBPK models can be used to simulate clinical incidence rates in populations of high-risk patients underrepresented in small clinical trials due to their low prevalence (modified from Lippert et al. 2012)

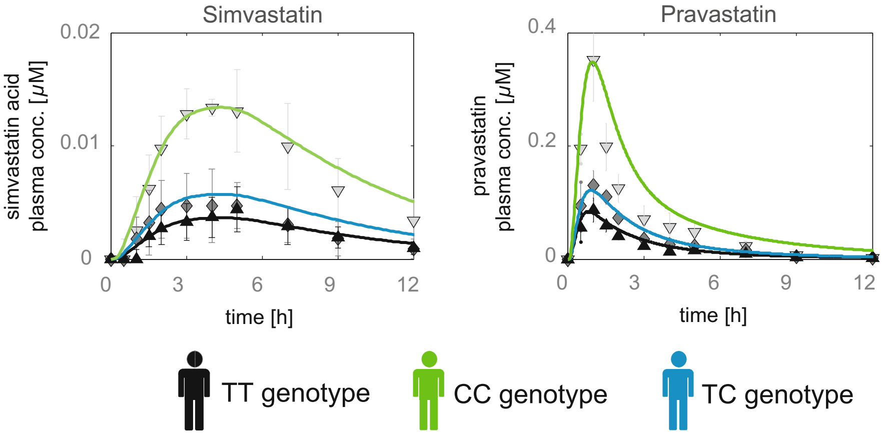

Fig. 8 Simulated simvastatin and pravastatin PK for subjects with different OATP1B1 genotypes. Data (symbols: *black triangles*, TT genotype; *diamonds*, TC genotype; *gray triangles*, CC genotype) for TT and CC genotype were used to adjust the PBPK models. Simulations (*black line*, TT; *blue line*, TC; *green line*, CC) for TC genotype are pure predictions based on the PBPK models for the homozygous genotypes and the assumption of an OATP1B1 activity in the TC subjects equaling the average level of TT and CC activity