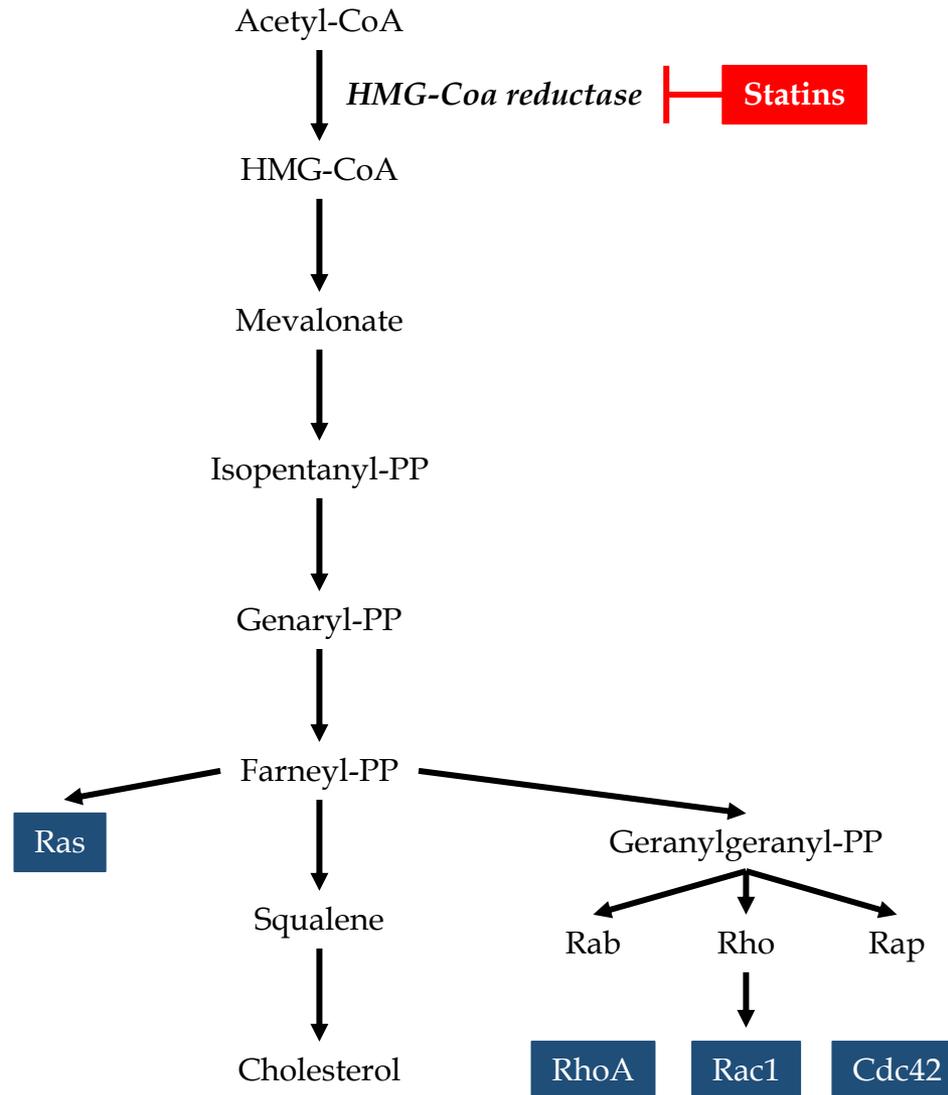
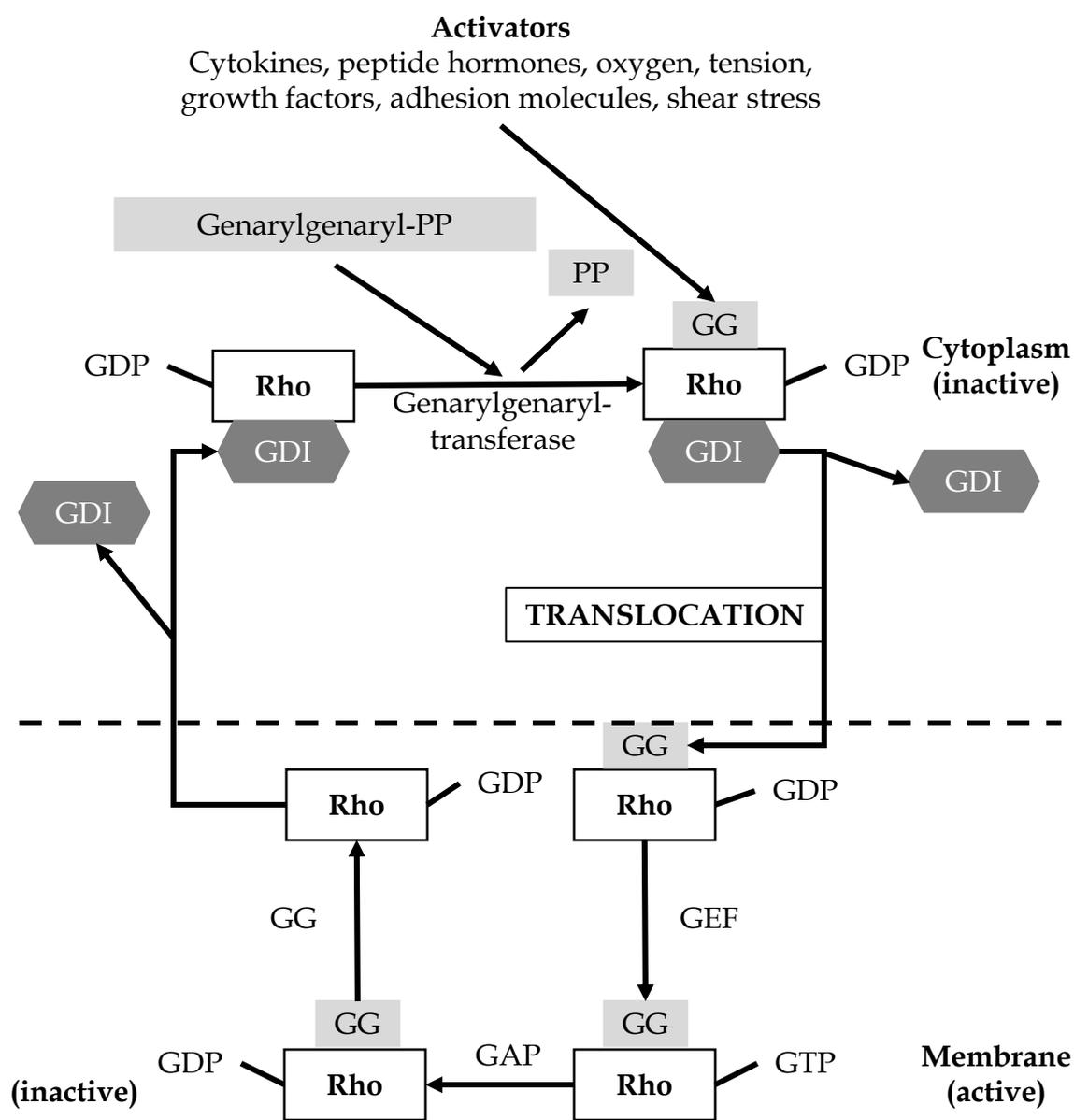


Supplementary material



Supplementary Figure 1 Cholesterol biosynthesis pathway and the effects of statins. Inhibition of HMG-CoA reductase by statins decreases isoprenoid intermediates such as farnesyl-PP and geranylgeranyl-PP, which leads to an inhibition of isoprenylation of small GTPases such as Ras, Rho, Rab, and Rap. Among the Rho GTPases are RhoA, Rac1, and Cdc42. CoA indicates coenzyme A, PP pyrophosphate.



Supplementary Figure 2 Regulation of Rho small GTPase by isoprenylation. Rho proteins change between a cytoplasm, inactive and GDP-bound state, and an active, membrane, GTP-bound state. Several cofactors, including generylgenaryl-PP, control this cycle. An important step in the activation of Rho small GTPase is the posttranslational isoprenylation, which allows the translocation of Rho to the cell membrane and the subsequent activation. GDP: guanosine diphosphate; GTP: guanosine triphosphate.

Supplementary Table 1 Simvastatin-drugs interactions: warning levels and usage recommendations

Level 1 (severe) Do not use	Level 2 (major) Use with caution	Level 3 (moderate) Less likely to cause severe drug interaction	Level 4 (mild) Unlikely to cause drug interaction
Protease inhibitors	Amiodarone	Afatinib	Barbiturates
Boceprevir	Amlodipine	Aprepitant	Carbamazepine
Clarithromycin	Conivaptan	Fosaprepitant	Clopidogrel
Cobicistat	Diltiazem	Bosentan	Nevirapine
Elvitegravir	Dronedarone	Colchicine	Oxcarbazepine
Emtricitabine	Efavirenz	Dalfopristin / quinupristin	Rifabutin
Tenofovir	Other fibrates	Daptomycin	Rifapentine
Cyclosporine	Fluconazole	Digoxin	Sofosbuvir
Danazol	Grapefruit juice	Esomeprazole	Lamivudine
Delavirdine	Imatinib	Fluvoxamine	Tenofovir
Erythromycin	Lomitapide	Fosphenytoin	
Gemfibrozil	Ranolazine	Lansoprazole	
Itraconazole	Simeprevir	Niacin, niacinamide	
Ketoconazole	Ticagrelor	Omeprazole	
Nefazodone	Troleandomycin	Pantoprazole	
Posaconazole	Verapamil	Phenytoin	
Red yeast rice	Daclatasvir	Quinine	
Telaprevir	Grazoprevir	Repaglinide	
Telithromycin	Elbasvir	Rifampin	
Voriconazole	Ledipasvir	St. John's wort	
Glecaprevir	Simeprevir	Warfarin	
Pibrentasvir	Velpatasvir		
Paritaprevir			
Ombitasvir			
Dasabuvir			

