SUPPLEMENTAL DATA

Inhibition of Human Cytochrome P450 3A4 by Cholesterol

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 $FIGURE\ S1.\ \textbf{Lineweaver-Burk\ plots\ for\ cholesterol\ inhibition\ in\ human\ liver\ microsomes.}$

FIGURE S2. Lineweaver-Burk plots for cholesterol inhibition in a reconstituted recombinant P450 3A4 system.

FIGURE S3. Time course of cholesterol concentration in human hepatocytes.

FIGURE S1. Lineweaver-Burk plots for cholesterol inhibition in human liver microsomes. A, nifedipine oxidation; B, quinidine S3-hydroxylation; C, quinidine N-oxygenation. The lines represent the simultaneous fit to the corresponding models defined in Experimental Procedures at free cholesterol concentrations of 1.5 (\blacksquare), 6.6 (\blacksquare), 11.7 (\triangle), and 16.8 μ M (\bigcirc) (from Fig. 3 of main text). See Table 1 for K_i values.

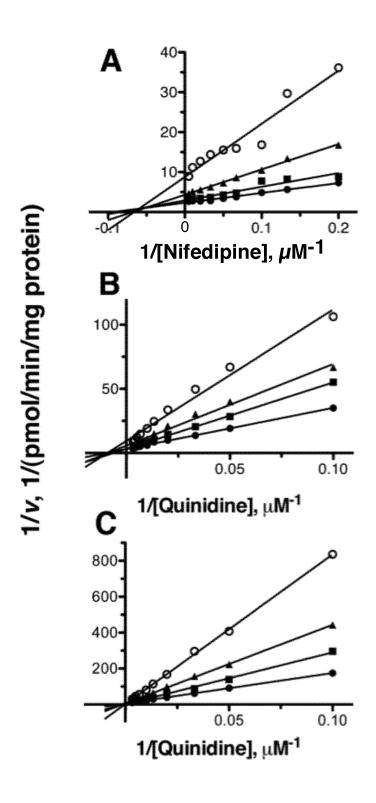


FIGURE S2. Lineweaver-Burk plots for cholesterol inhibition in a reconstituted recombinant P450 3A4 system. A, nifedipine oxidation; B, quinidine S3-hydroxylation; C, quinidine N-oxygenation. The lines represent the simultaneous fit to the corresponding models defined in Experimental Procedures at free cholesterol concentrations of $O(\bullet)$, 2.5 (\blacksquare), 5.1 (\blacktriangle), 10.2 (\bigcirc), and 15.3 μ M (\square). See Fig. 4 of main text and Table 1 for K_i values.

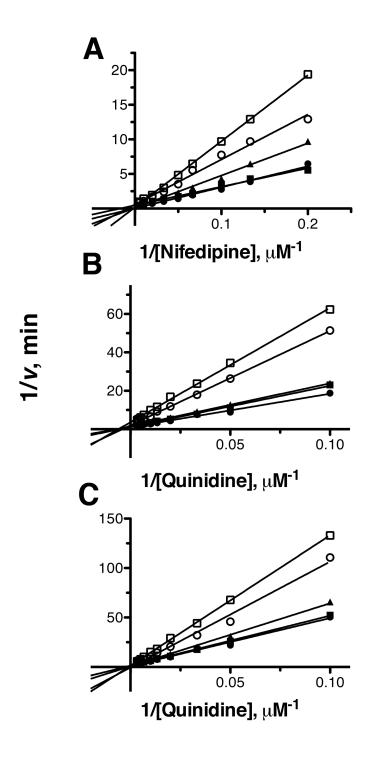


FIGURE S3. Time course of cholesterol concentration in human hepatocytes. \bullet , no treatment; \blacksquare , 200 μ M cholesterol; \blacktriangle , 30 μ M pravastatin.

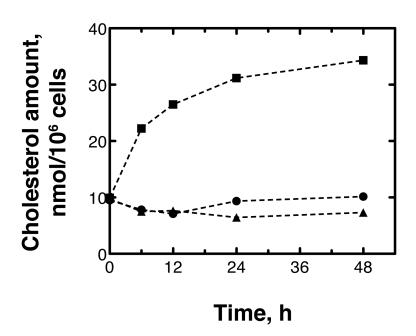


Fig. S3