Supporting Information

Mahdessian et al. 10.1073/pnas.1323785111

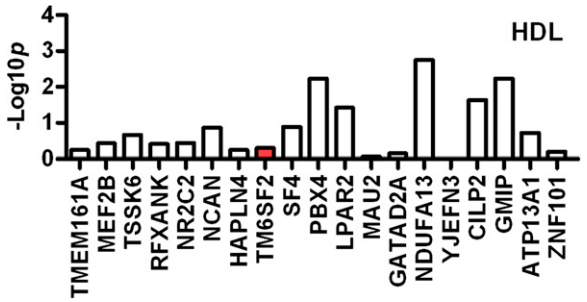

Fig. S1. Comparison of the -log[10] P values for the relationships between the mRNA levels of all 19 genes in the 19p12 locus and the plasma HDL cholesterol concentration analyzed in 206 individuals.

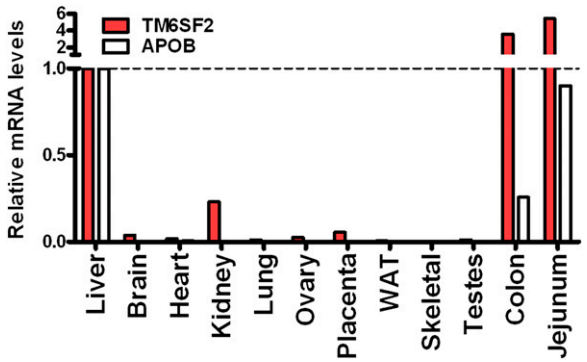

Fig. S2. Comparative analysis of transmembrane 6 superfamily member 2 (*TM6SF2*) mRNA levels in nine human tissues. *TM6SF2* and apolipoprotein B (*APOB*) mRNA levels were measured with quantitative real-time PCR (RT-PCR) and normalized with RPLP0. The data were expressed relative to the mRNA level in human liver and represent mean values of five independent experiments.

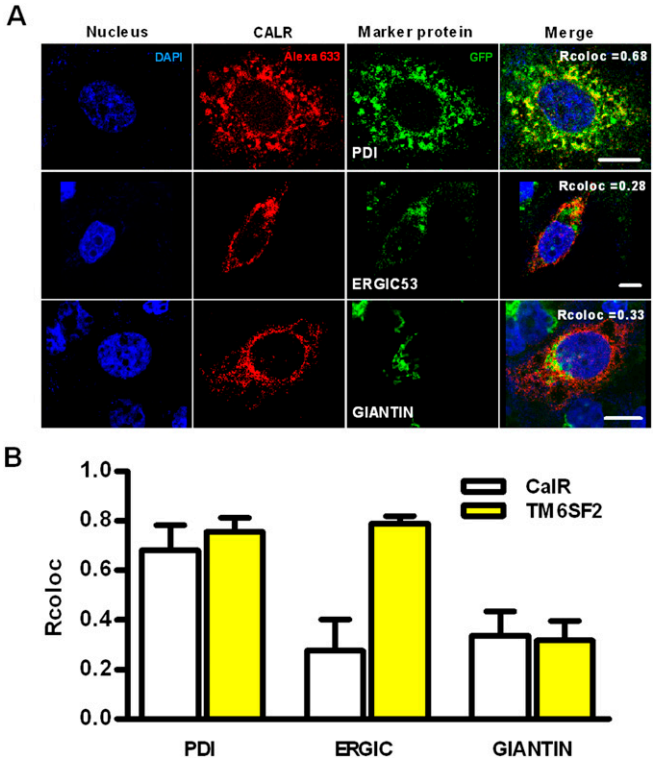

Fig. S3. Subcellular localization of calreticulin (CALR). (*A*) Human hepatoma Huh7 cells were transfected with GFP-tagged CALR, a marker for endoplasmic reticulum (ER). Following 48-h incubation, cells were fixed and stained for protein disulfide-isomerase (PDI), ERGIC53, or GIANTIN [markers for ER, ER-Golgi intermediate compartment (ERGIC), and Golgi, respectively]. (*B*) Colocalization was quantified using Pearson correlation (Rcoloc) and represents mean ± SD of four to six independent experiments. For comparison, the Rcoloc values reported in Fig. 2 are shown for colocalization of GFP-tagged TM6SF2 with PDI, ERGIC53, and GIANTIN. (Scale bar, 10 μm.)

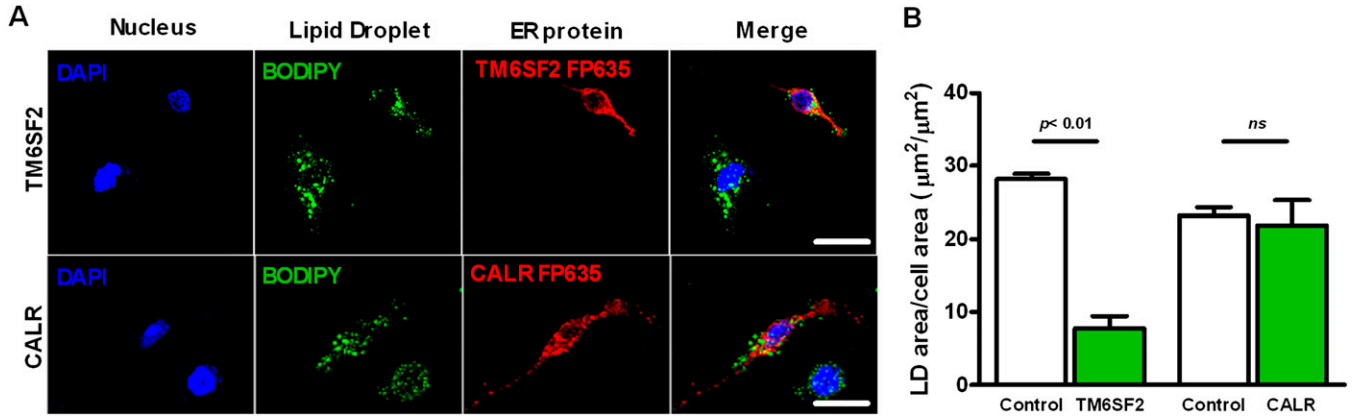

Fig. S4. TM6SF2 overexpression reduces lipid droplet content of human hepatoma Huh7 cells. Human hepatoma Huh7 cells were transfected with FP635-tagged TM6SF2 plasmids or FP635-tagged CALR (control) plasmids. Following 48-h incubation, cells were stained with BODIPY493/503 and analyzed by confocal microscopy. Huh7 cell pairs (composed of one cell expressing and the other cell not expressing the FP635-tagged protein) were identified and subjected to qualitative and quantitative analysis. (*A*) In *Upper*, a representative cell pair of TM6SF2 transfected cells is shown. Note that the lipid droplet content (green color) is considerably lower in TM6SF2 transfected cells (red color) compared with the nontransfected cell (absence of red color). In contrast, no difference in lipid droplet content is observed for a representative cell pair of CALR transfected cells, as shown in *Lower*. (*B*) Quantification of the lipid droplet content from four to six independent experiments shown in *A*. (Scale bar, 50 μm.)

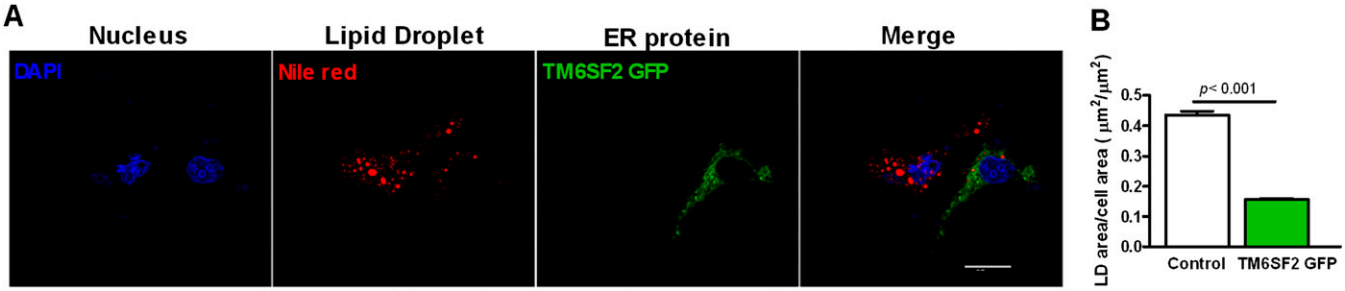

Fig. S5. Overexpression of GFP-tagged TM6SF2 reduces lipid droplet content of human hepatoma Huh7 cells. (*A*) Human hepatoma Huh7 cells were transfected with GFP-tagged TM6SF2 plasmids. Following 48-h incubation, cells were stained with Nile Red and analyzed by confocal microscopy. Huh7 cell pairs (composed of one cell expressing and the other cell not expressing the GFP-tagged protein) were identified and subjected to qualitative and quantitative analysis. Note that the lipid droplet content (red color) is considerably lower in cells expressing GFP-tagged TM6SF2 (green color) compared with cells that do not express GFP-tagged TM6SF2 (absence of green color). (*B*) Quantification of the lipid droplet content from four to six independent experiments shown in *A*. (Scale bar, 50 μm.)