SUPPORTING INFORMATION

Table S1. Human cell lines used in these studies and their respective biomarker status and subtype. ER (estrogen receptor), PR (progesterone receptor), HER2 (ErbB2).

Cell Line	Source	Tumor Type	Subtype	ER	PR	HER2
BT-474	Primary breast	Ductal carcinoma	Luminal B	+	+	+
DU4475	Mammary gland	Epithelial cell	TNBC, IM subtype	-	-	-
HeLa	Cervix	Adenocarcinoma	N/A			
MCF-7	Pleural effusion	Invasive ductal carcinoma	Luminal A	+	+	-
MCF10A	Primary breast	Epithelial cell, nontumorigenic	Basal	-	-	-
MDA-MB-231	Pleural effusion	Adenocarcinoma	Claudin-low or basal-like	-	-	-
LiSa-2	Pleomorphic liposarcoma	Liposarcoma	N/A		+	
SKBR3	Pleural effusion	Adenocarcinoma	Luminal	-	-	+
T47-D	Pleural effusion	Invasive ductal carcinoma	Luminal A	+	+	-

Table S2. Gene primer sequences used for detection in qRT-PCR analysis.

Gene (GenBank)	Product Designation
ACACA	Hs01046047_m1 ACACA
ACLY	Hs00982738_m1 ACLY
ACSS2	Hs01122829_m1 ACSS2
Cyc	4310883E
CD36	Hs00354519_m1 CD36
DGAT1	Hs01020362 g1
FASN	Hs01005622_m1 FASN
GPIHBP1	Hs01564843_m1 GPIHBP1
HMGCR	Hs00168352_m1 HMGCR
LDLR	Hs 01092524_m1 LDLR
LMF1	Hs01071616_m1 LMF1
LPL	Hs00173425_m1 LPL
PLIN2	Hs00605340_m1 PLIN2
SCD	Hs01682761_m1 SCD

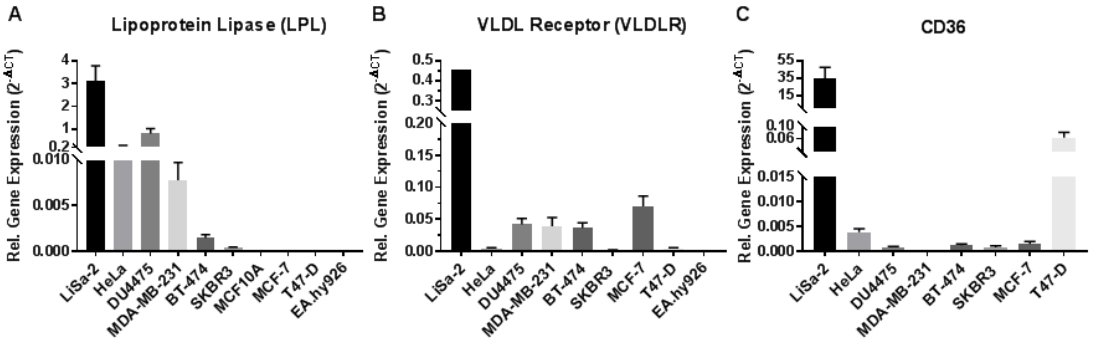

Figure S1. Cell line expression of select genes involved in FFA and VLDL uptake. Basal gene expression of (**A**) LPL, (**B**) VLDLR, and (**C**) CD36 was assessed using qRT-PCR (note different scales). Relative expression values are displayed as $2^{-\Delta CT}$, with Cq of the target normalized to that of cyclophilin. Data are mean +/- SEM of > 3 experiments.

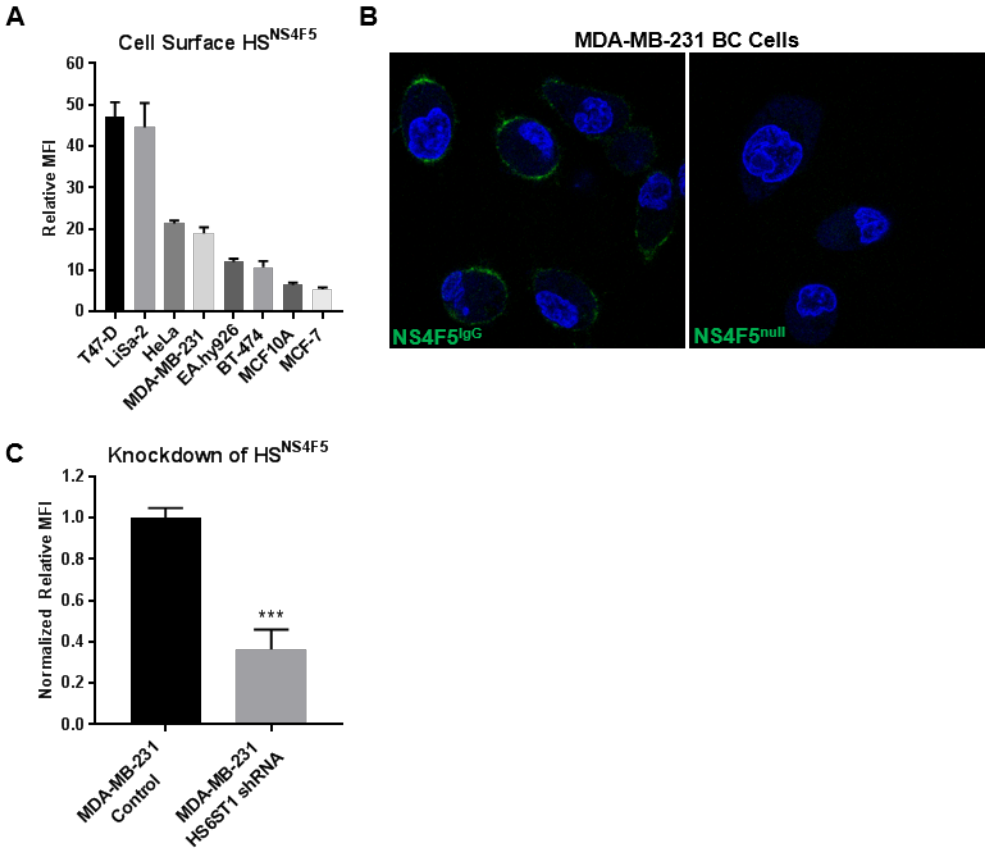

Figure S2. The HSPG Motif (GlcNS6S-IdoA2S)$_3$, a binding site for LPL, is expressed on the surface of cancer cells. (**A**) The abundance of HS^{NS4F5} on the surface of cell lines was assessed by flow cytometry. Relative MFI is the median fluorescence of cells stained with the NS4F5^{IgG}-Dylight 650 antibody normalized to the NS4F5^{null}-Dylight 650 control. (**B**) Confocal microscopy of MDA-MB-231 cells stained with Hoechst 33342 nuclear stain (blue) and DyLight 650 NS4F5^{IgG} or NS4F5^{null}antibody (green) for 30 min at 4°C localizes HS^{NS4F5} to the cell surface. (**C**) shRNA knockdown of heparan sulfate 6-O-sulfotransferase 1 (HS6ST1) reduces HS^{NS4F5} on the surface of MDA-MB-231 BC cells, assessed by flow cytometry. Relative MFI represents the median fluorescence of cells stained with the NS4F5^{IgG}-Dylight 650 antibody normalized to those stained with the isotype control, NS4F5^{null}-Dylight 650. ***$p < 0.001$, two-tailed unpaired t-test with Welch's correction.

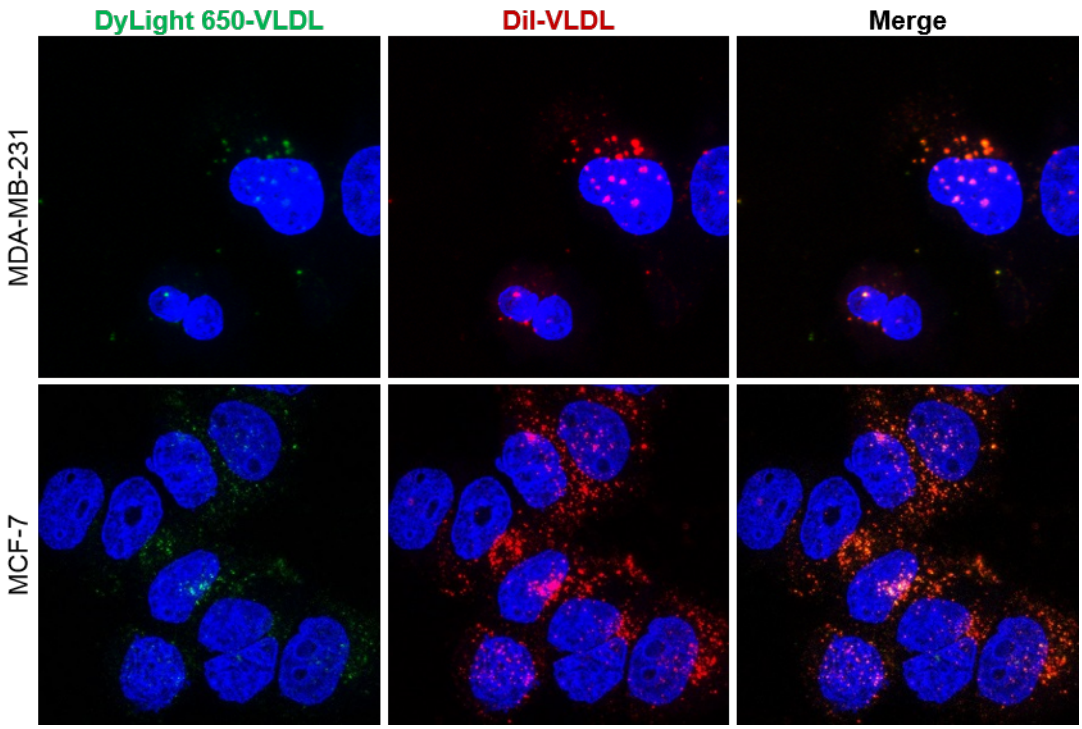

Figure S3. Both lipid and protein component of VLDL particles bind to- and are internalized by MDA-MB-231 and MCF-7 BC cells. Confocal microscopy of BC cells incubated with DiI (lipid-) and DyLight 650 (protein-) co-labeled VLDLs. Three channels are shown: Hoechst 33342 nuclear stain (blue), DiI-VLDL (red), DyLight650-VLDL (green). Orange spots (in merged channel) are where DiI and DyLight650 fluorescence coincide.

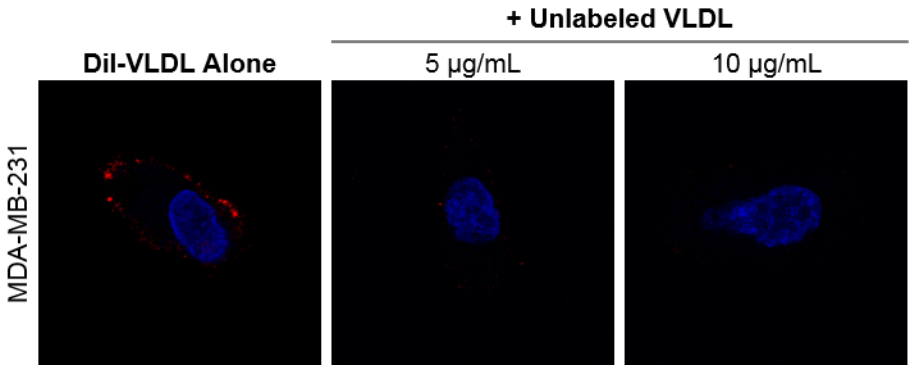

Figure S4. Cell surface DiI-VLDL binding is specific. Competition with excess unlabeled VLDL inhibits DiI-VLDL binding at 4°C. MDA-MB-231 cells were treated with DiI-VLDL (5 µg/mL) with or without unlabeled VLDL (5 or 10 µg/mL). DiI-VLDL (red); DAPI nuclear stain (blue).

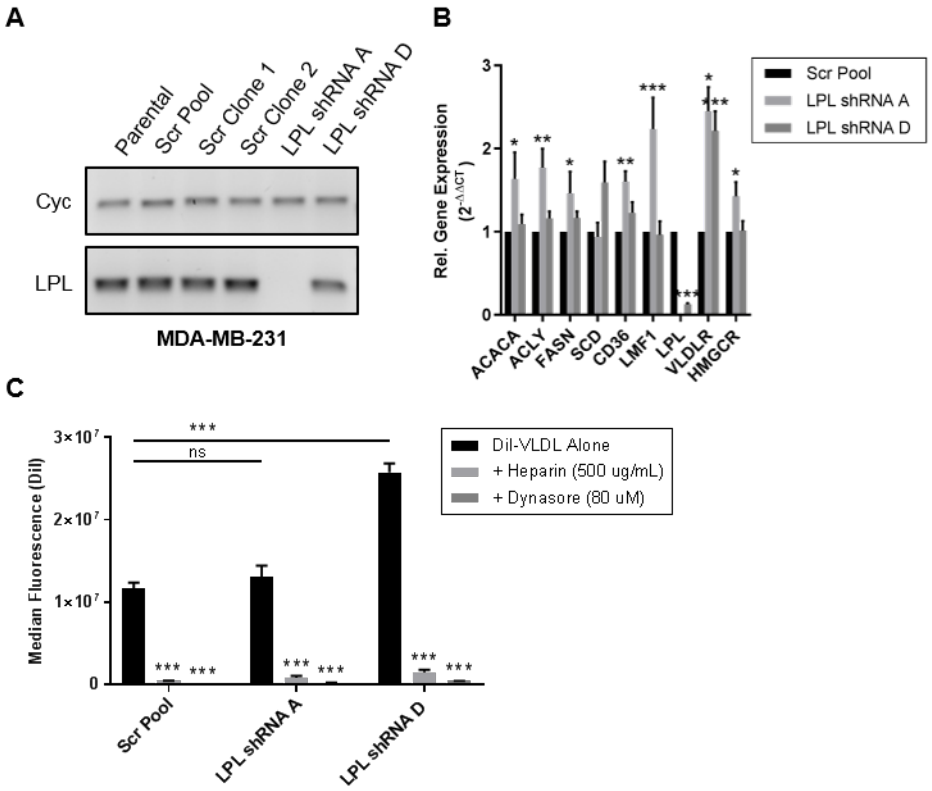

Figure S5. Characterization of MDA-MB-231 LPL shRNA cell lines. (**A**) qRT-PCR products run on agarose gels. Parental and scrambled shRNA cell lines are compared to LPL shRNA A (complete knockdown of LPL) and LPL shRNA D (partial knockdown). (**B**) qRT-PCR of MDA-MB-231 manipulated cell lines normalized to the pooled control. LPL shRNA A cells exhibit significant upregulation of mRNAs involved in *de novo* lipid synthesis (ACACA, ACLY, FASN), cholesterol synthesis (HMGCR), and FA uptake (CD36, LMF1, VLDLR). MDA-MB-231 LPL shRNA D (partial LPL knockdown) cells display a significant upregulation of VLDLR expression alone. *P < 0.05, **p < 0.01, ***p < 0.001. Error is SEM. (**C**) Comparison of DiI-VLDL uptake in Scr and LPL shRNA cells with and without treatment (heparin 500 μg/mL; dynasore 80 μM), measured by flow cytometry. MDA-MB-231 LPL shRNA D cells had significantly higher DiI-VLDL uptake than either the Scr control or LPL shRNA A cells, ***p < 0.001. All three cell lines showed significant reductions in DiI-VLDL uptake following treatment with heparin or dynasore, ***p < 0.001.

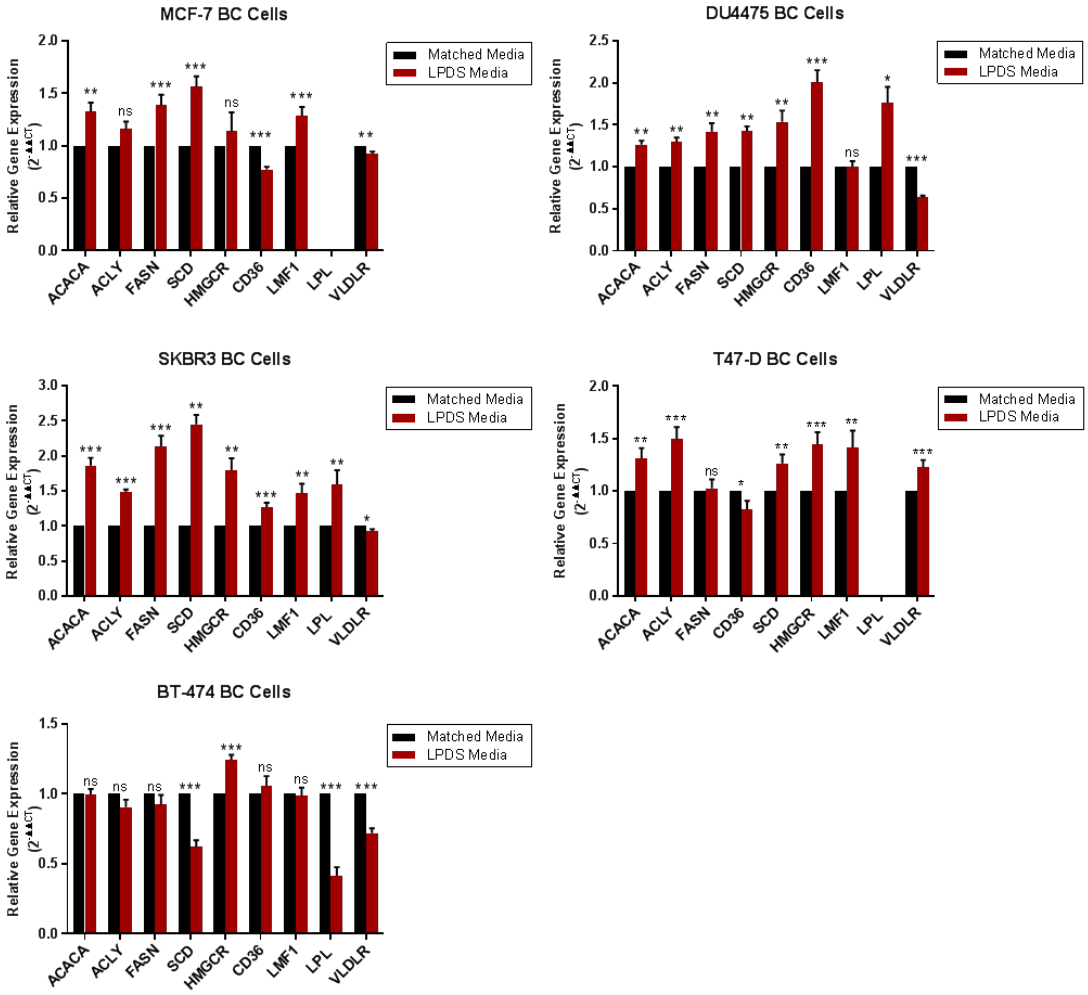

Figure S6. Trends in the expression of FA metabolic genes in BC cell lines cultured in lipoprotein-depleted serum media for 96 h. Gene expression was measured using qRT-PCR. Results were calculated using the $2^{-\Delta\Delta CT}$ method first normalized to cyclophilin, and then made relative to that of the matched FBS media control. Data are from > 3 experiments; error is SEM. Statistical significance determined using two-tailed unpaired t-tests: *P < 0.05, **p < 0.01, ***p < 0.001.