Supplementary material and methods:

Analysis of cellular DNA content by flow cytometry

Cells and supernatant were collected, cell pellet was resuspended in PBS and fixed in 85% ethanol at -20°C. After 24 hours ethanol was discarded and propidium iodide (Sigma) was added for 20 min. Cells were resuspended in FACS buffer and measured on FACS BD Calibur. Analysis was done with Flowjo V10.

Viability assay

$15*10^3$ cells were seeded equally in a 96 well plate. 48 hours after SR-BI knockdown Alamar blue (Invitrogen) was added and cells were incubated for 4 hours. The fluorescence was measured at wavelengths excitation 540 nm and emission 590 nm.

Cholesterol quantification

Gas chromatography (GC) was used to directly quantify the cellular content of free cholesterol, cholesteryl esters and triglycerides (44). Cells were detached using trypsin and lipids were isolated by standard Folch extraction. An aliquot of the pellet was used for cell protein determination by the Bradford assay. Analyses were performed on a GC-2010 gas chromatograph (Shimadzu, Kyoto, Japan). Tridecanoyl glycerol, cholesteryl myristate and trinonadecanoate (Sigma-Aldrich) were used as standards for free and esterified cholesterol and triglycerides. Chromatograms were quantified using GC Solutions 2.3 (Shimadzu) and results were normalized to cell protein.

Supplementary figure legends

S1. Comparing *SR-BI* mRNA distribution of (**A**) primary tumors (n=82) versus metastases (n=369), (**B**) non-metastatic primary tumors (n=56) versus metastatic primary tumors (n=26) and (**C**) regional cutaneous tissue (n=73), regional lymph node tissue (n=217) and distant metastasis (n=63) of the melanoma study TCGA. Ten year follow-up Kaplan-Meier survival curves of the mRNA dataset GSE19234 (n=44) for (**D**) *SR-BI* and (**E**) *LDLR*.

S2. Enrichment plots of the most modulated hallmark gene sets comparing SR-BI knockdown cells (upper panel) with BLT-1 treated cells (lower panel) of three metastatic human melanoma cell lines (MCM1DLN*, 1205Lu*, 451Lu*).

S3. (**A**) Sphere formation assays comparing diameter of control versus SR-BI knockdown cells with representative images. Quantitation illustrates sphere diameter (MCM1DLN*, n=4, *P*=0.1206; 1205Lu*, n=4, **P*=0.0285; 451Lu*, n=10, ****$P<0.0001$; mean±s.e.m). Scale bar, 300 μm. (**B**) Bar charts show measurement of viability of three metastatic human melanoma cell lines comparing control siRNA and SR-BI siRNA 48 hours post transfection. (**C**) PI-staining and FACS analysis of three metastatic human melanoma cell lines treated either with control or SR-BI siRNA over time. (**D**) Quantification of cholesterol (FC= free cholesterol, CE= cholesteryl ester, TC= total cholesterol, TG= triglyceride) was measured by gas chromatography of three metastatic human melanoma cell lines after SR-BI knockdown.

S4. (**A**) Immunofluorescence stained with WGA (green), a glycosylation marker, comparing control siRNA versus SR-BI siRNA. Nuclei are stained with DAPI. Scale bar, 10 μm. Quantitation shows intensity of WGA (1205Lu* cells, n=4, **P*=0.0252, 451Lu* cells, n=4, **P*=0.0286). (**B**) Densitometric analysis of detected glycosylated STAT5 on the Western blot. (**C**) Western blot analysis showing SR-BI and pSTAT5(Tyr694) expressions in MCM1DLN* cells. Cells were additionally treated with OSM and IL-6. α-tubulin was used as loading control. (**D**) Densitometric analysis of STAT5 binding EMSA. SP1 was used as reference.

S5. (**A**) RT-PCR of MCM1DLN* cells showing fold change of *STAT5b* versus *STAT5a*. (**B**) *STAT5* mRNA expression of MCM1DLN* cells showing the fold change of *STAT5a/b* knockdown efficiency.