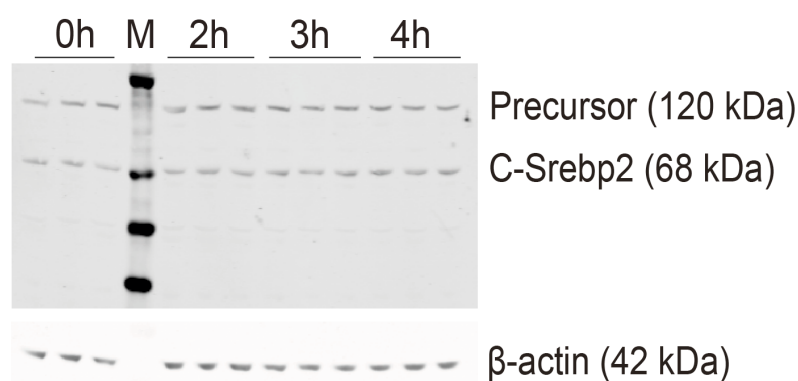
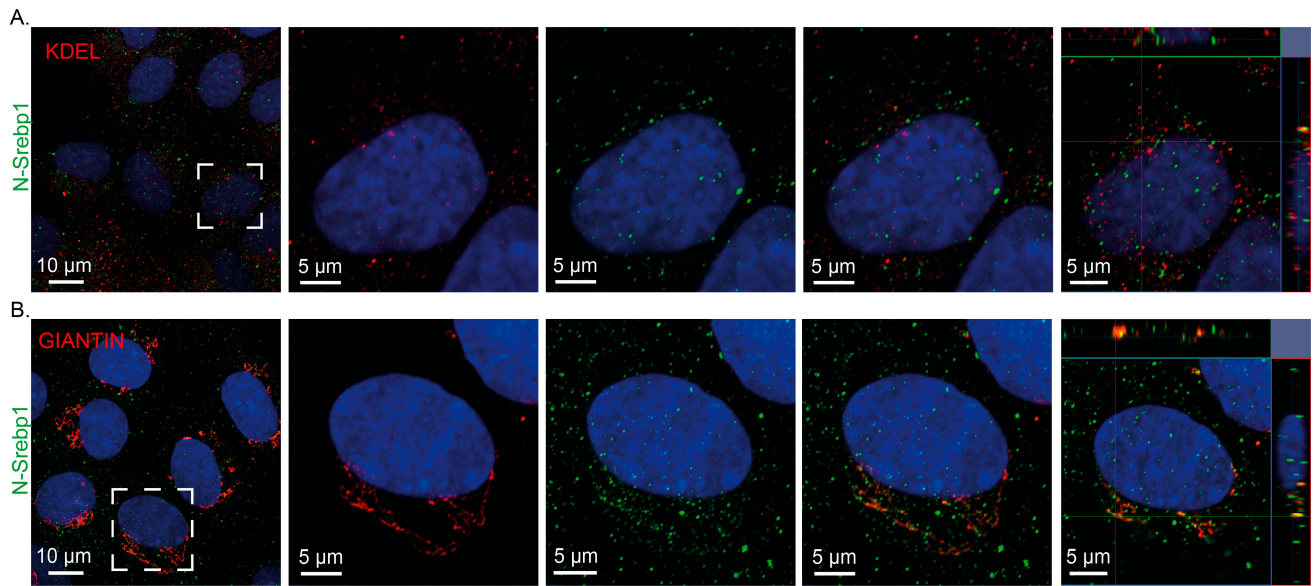


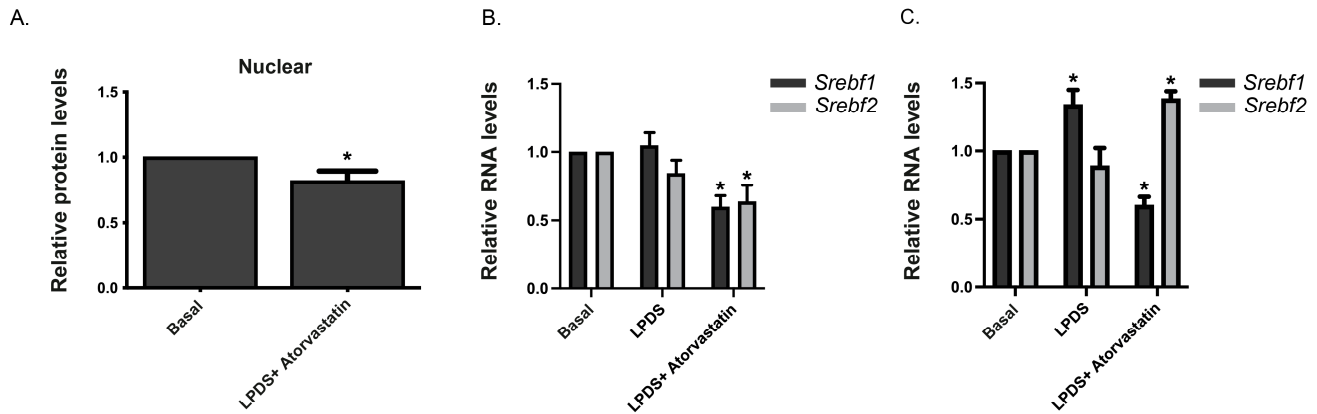
**Figure S1.** Atorvastatin does not produce a larger effect on HMGCR protein levels in McArdle-RH7777 cells switched to lipoprotein-depleted media for only 4-h. Western blot analysis of HMGCR (A) and C-SREBP2 (B) in whole-cell lysates of McArdle-RH7777 cells switched from basal media (0-h) to media containing lipoprotein-depleted serum (LPDS) and LPDS plus 1mM atorvastatin for the indicated time points. Three independent experiments, each containing three technical repeats were performed. Data (mean  $\pm$  SEM) normalised to b-actin are expressed relative to basal values. (C). Equivalent analyses for McArdle-RH7777 cells switched from basal media (0-h) to indicated media for 24-h. Values are from four independent experiments, each containing three technical repeats. Statistical differences from 0-h were determined by one-way ANOVA followed by Dunnet's multiple comparison test. Significance is indicated by asterisks: \*\*  $p < 0.01$ .



**Figure S2. Immunoblot of C-SREBP2-containing sequences in McArdle-RH7777 cells.** Representative Western Blot of precursor SREBP2 and of the C-SREBP2 fragment in three individual sets of whole cell lysates of McArdle-RH7777 cells switched from basal media (0-h, lanes 1-3) to media containing lipoprotein-depleted serum (LPDS) for the indicated time points (lanes 5- 13). M = size marker.



**Figure S3. Localization of Endogenous N-SREBP1 in McArdle-RH7777 cells.** Cells cultured under basal conditions were subject to indirect immunofluorescence using specified antibodies and counterstained with DAPI. Left-hand panels, maximum intensity projection images of representative field of cells. Right-hand panels, show expanded view of region highlighted by white squares. Enlargements show the separate channels (middle panels), and orthogonal views (XZ axis, right-hand side; YZ, top) of merged images through the centre of the nucleus. (A, B) N-SREBP1 (green), ER-marker KDEL (red); Golgi- marker Giantin (red).



**Figure S4. *Srebf1/2* RNA and Nuclear N-SREBP2 Protein Levels in Cells Incubated with Atorvastatin.** (A). Quantification of N-SREBP2 protein in nuclear extracts prepared from McArdle-RH7777 cells cultured under basal conditions and cells switched to lipoprotein-depleted media (LPDS) containing 1mM atorvastatin for 10-h. Values represent mean  $\pm$  standard error, from five independent experiments, each with three replicates. \* $p < 0.05$  by Student's t-Test. (B, C) RT-qPCR quantification of *Srebf1* and *Srebf2* in total RNA extracted from McArdle-RH7777 cells switched to LPDS and LPDS-atorvastatin-containing media for 11-h (B) and 12-h (C). Data (mean  $\pm$  SEM), normalised to *Ppia*, are from three independent experiments, each with three technical replicates. \* $p < 0.05$  versus cells at 0-h, determined by one-way ANOVA.

SFESGSGGWFDWMMPTLLLWLNVGVIVLSVFVKLLVHGEPVIRPHSRSSVTFWRHR	KQAD	582
LDLARGDFAAAAGNLQTCLAVLGRALPTSRLDLACSLSWNVIRYSLQKLRLVRWLLKKVF		642
QCRRTATPATEAGFEDEA	KTSARDAALAYHRLHQLHITGKLPAGSACSDVHMA	702
CAEEKIPPSTLVEIHLTAAMGLKTRCGGKLGFLASYFLSRAQSLCGPEHS	AVPDSLRLWC	762
HPLGQKFFMERSWSVKSAAKESLYCAQRNPADPIAQVHQAFCKNLLERAIESLV	KPQAKK	822
KAGDQEEESCEFSSALEYLKLLHSFVDSVGVMSPPLSRSSVLKSALGPDII	ICRWWTSAIT	882
VAISWLQGDAAVRSHFT	KVERIPKALEVTESPLVKAI	942
FHACRAMHASLPGKADGQQSSF		
CHCERASGHLWSSSLNVSGATSDPALNHVVQLLTCDLLLSLRTALW	KQASASQAVGETYH	1002
ASGAELAGFQORDLGSLRRLAHSFRPAYRKVFLHEATVRLMAGASPTRTHQLLEHSLRRRT		1062
TQST	KHGEVDAWPGQRRERATAILLACRHLPLSFLSSPGQRAVLLAEAARTLE	1022
KVGDRRSC		1141
NDCQQMIVKLGGGTAAAS		

**Figure S5. Sites of C-SREBP2 ubiquitination (red).** Data extracted from ubiquitinomes of HEK293T cells<sup>71–73</sup>.