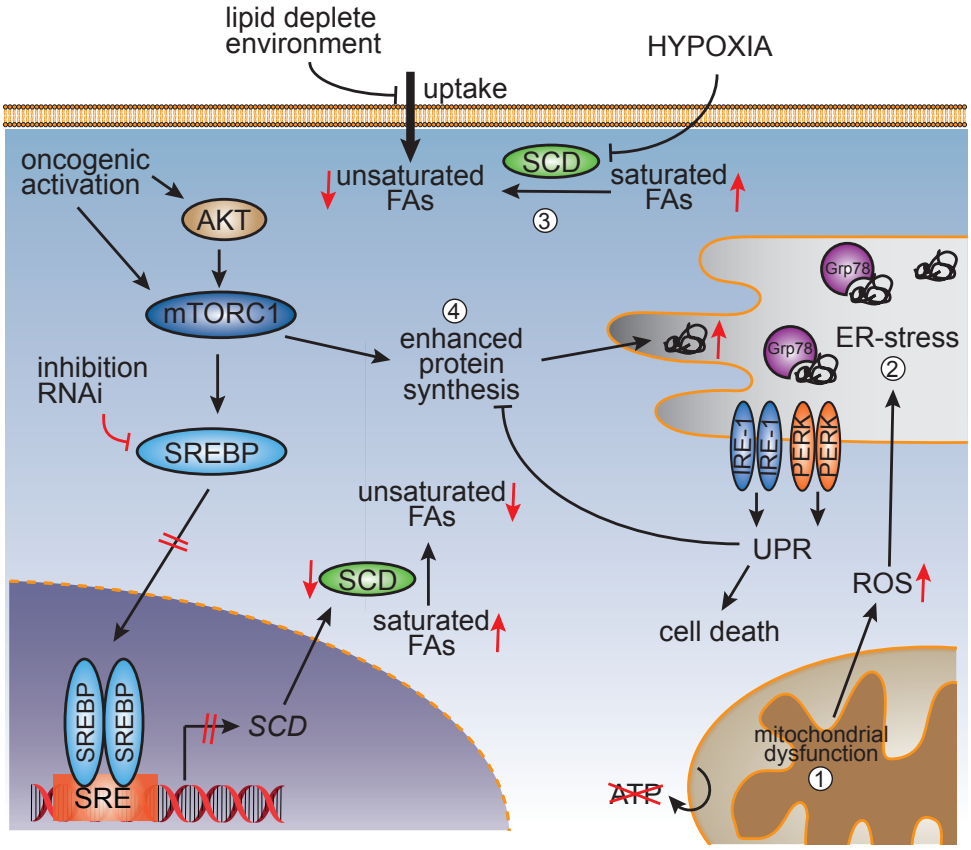
In format provided by Röhrig and Schulze (doi:10.1038/nrc.2016.89)



Supplementary Information S2 | **Induction of ER-stress by altered lipid saturation.** Activation of lipid synthesis through induction of sterol regulatory element binding protein (SREBP) and transcription of its target genes, in particular stearoyl-CoA desaturase (SCD), is an important function of the AKT-mTOR complex 1 (mTORC1) signalling pathway. Inhibition of SREBP blocks SCD expression leading to a reduction in mono-unsaturated fatty acids (mono-unsat. FAs). This changes cellular lipid composition and alters the function of cellular membranes, including the endoplasmic reticulum (ER) and mitochondrial membranes. Mitochondrial dysfunction (1) impairs ATP-generation and results in the accumulation of reactive oxygen species (ROS). Inhibition of SREBP also induces ER-stress and engages the unfolded protein response (UPR) either by directly altering the ER-membrane leading to activation of the endoplasmic reticulum to nucleus signaling 1 protein (ERN1, also known as IRE1) and the eukaryotic translation initiation factor 2 alpha kinase 3 (EIF2AK3, also known as PERK) or via ROS-mediated accumulation of unfolded proteins in the ER lumen leading to sequestration of the heat shock protein family A member 5 (HSPA5, also known as GRP78) (2). This blocks global protein synthesis and can lead to cell death. Reduced availability of lipids in the microenvironment or inhibition of fatty acid desaturation through SCD by hypoxia also restricts the availability of mono-unsaturated fatty acids in cancer cells (3). Oncogenic activation of AKT or mTORC1 increases the dependence of cells on lipid desaturation by enhancing protein synthesis (4) and increasing the accumulation of unfolded protein in the ER.