Supplementary Figure 1. Phylogenetic tree using human LIX1 as query. At the end of each branch, the species names of the LIX1 orthologs are indicated. The accession number of each protein is indicated on the right. The scale bar represents the evolutionary distance of the tree branches (A.U.). The figure was generated with the MAFFT and FastME programs (https://ngphylogeny.fr/).

Supplementary Figure 2. Confocal microscopy analysis (**A**) Endogenous LIX1 localization in GIST-T1 cells. Comparison with the mitochondrial marker COXIV. (**B**) LIX1/COXIV RGB profile analyzed at the level of the white line.

Supplementary Figure 3. Overexpression of mitochondrial catalase changes GIST cell identity. (**A**) Representative western blot showing TAZ and αSMA levels in parental GIST-T1 and GIST-T1 cells that overexpress mitochondrial targeted CATALASE (mt-CATA.) Equal loading was verified by GAPDH expression. (**B**) Quantification of CATALASE, TAZ and αSMA levels normalized to GAPDH and converted to fold change. Values are the mean ± SEM of n = 4 samples. **P* < .05 (two-tailed Mann–Whitney test). (**C**) RT-qPCR analysis of *MYOCD, ACTA2, ACTG2, CNN1, CYR61,* and *CTGF* transcript levels in GIST-T1- cells and GIST-T1 cells that overexpress mitochondrial targeted CATALASE. Data were normalized to the mean *HBMS* and *YWHAZ* expression, and converted to fold change. Values are the mean ± SEM of n = 4 samples. **P* < .05 (two-tailed Mann–Whitney test).

Supplementary Figure 4. LIX1 promotes mitochondrial fragmentation in HeLa cells. (A) MitoTracker staining of control HeLa cells (CTRL) and HA-LIX1-expressing HeLa cells. Nuclei were visualized with Hoechst. Scale bars, 10μm. **(B)** Quantification of the MitoTracker

data with the Mito-Morphology Macro in Image J. Values are the mean ± SEM of *n=36* HeLa control cells and *n=38* HA-LIX1-expressing HeLa cells. ***P <0.001; ****P <0.0001 (two-tailed Mann–Whitney test).

Supplementary Figure 5. Ultrastructure of mitochondria in GIST-T1-*Scrambled*, GIST-T1-*ShLIX1#1,* and -*ShLIX1#2* cells. These are tree other magnifications of the images shown in Figure 5C. Scale bars are indicated in each panel. Black arrows indicate the magnified areas.

Supplementary Figure 6. Supplementation with linoleic acid restores YAP/TAZ levels and GIST identity in GIST-T1-*ShLIX1 cells*. (**A**) RT-qPCR analysis of *CYR61, CTGF, MYOCD, ACTA2,* and *CNN1* transcript levels in GIST-T1-*ShLIX1#2* (+EtOH vehicle) and -*ShLIX1#2* (+50μM of linoleic acid) cells. Data were normalized to the mean *HBMS* and *YWHAZ* expression, and converted to fold change. Values are the mean ± SEM of n = 4 samples. **P* < .05 (two-tailed Mann–Whitney test). (**B**) Immunofluorescence analysis of αSMA expression in GIST-T1-*Scrambled* (+DMSO vehicle), GIST-T1-*ShLIX1#2* (+DMSO vehicle), and -*ShLIX1#2* (+50μm of linoleic acid) cells. Nuclei were visualized with Hoechst. Scale bars, 50 μm.