

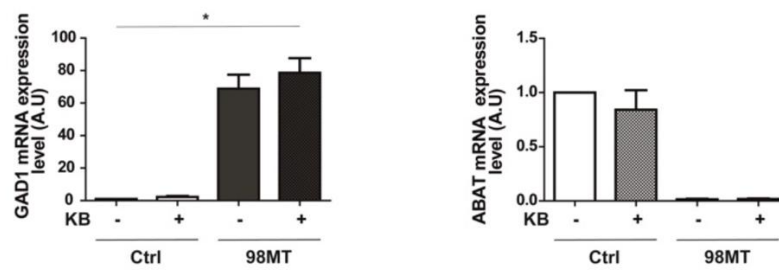
**Figure S1. The Glutamate pathway is also affected in 143B osteosarcoma MELAS cybrid cells.**

**(A)** Intracellular levels of glutamate in 143B osteosarcoma cybrid cells. Cybrid control (Ctrl) cells and MELAS 98% mutant (MT) cells. Results are presented as means  $\pm$  SEM relative to Ctrl cells of at least 4 independent experiments. Statistical differences are indicated with an asterisk between 98% MT and Ctrl cells (\* $p < 0.05$ ).

**(B)** Glutamate impacts mitochondrial morphology in 143B cybrid Ctrl cells. Ctrl cells in standard medium (1), with ketone bodies (KB) (2), with 30mM glutamate, with KB + 30mM glutamate (4).

**(C)** Intracellular level of glutamate in Ctrl cybrid cells exposed for 15h to 20 and 30 mM glutamate.

**(D)** Glutamate impacts on mitochondrial network structure in control cells in the presence or absence of ketone bodies (KB). Results are presented as means  $\pm$  SEM relative to Ctrl cells of at least 4 independent experiments. Statistical differences are indicated with an asterisk between 98% MT and Ctrl cells (\* $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ). Representative images of cells stained with MitoTracker (green) and Hoescht-DNA staining (blue) incubated for 15h in standard medium (1), with KB (2), with 30mM of glutamate (3), or with KB + 30mM of glutamate (4).



**Figure S2. Gene expression of *GAD1* and *ABAT* by quantitative PCR**

Gene Expression showing *GAD1*, *ABAT* expression levels in Ctrl and 98% MT cells, treated for 48h with (+) or without (-) KB.