

Figure S8. G-MAD confirms the involvement of BOLA3 in mitochondrial respiration.

A-D, *BOLA3/Bola3/bola-3* associates with mitochondrial respiratory chain modules in human (**A**), mouse (**B**), rat (**C**), and *C. elegans* (**D**). The threshold of significant gene-module association is indicated by the red dashed line. Modules are organized by module similarities. Known modules connected to *BOLA3/Bola3/bola-3* from annotations are highlighted in red (no connected modules for *BOLA3/Bola3/bola-3*), and other modules with GMAS over the threshold are colored in black. Dot sizes reflect the GMAS of *BOLA3* against the respective modules.

E, Silencing *BOLA3* expression in HEK293 cells decreases expression levels of indicated genes involved in mitochondrial respiratory chain complexes. Error bars represent standard errors. *, p < 0.05; **, p < 0.01; ***, p < 0.001. n=9.

F, *BOLA3* knockdown leads to the reduction of oxygen consumption rate (OCR) as a reflection of mitochondrial respiration activity in human HEK293 cells. Addition of specific mitochondrial inhibitors, including the oligomycin (ATPase inhibitor), FCCP (uncoupling agent), and rotenone/antimycin A (electron transport chain inhibitors) are indicated.