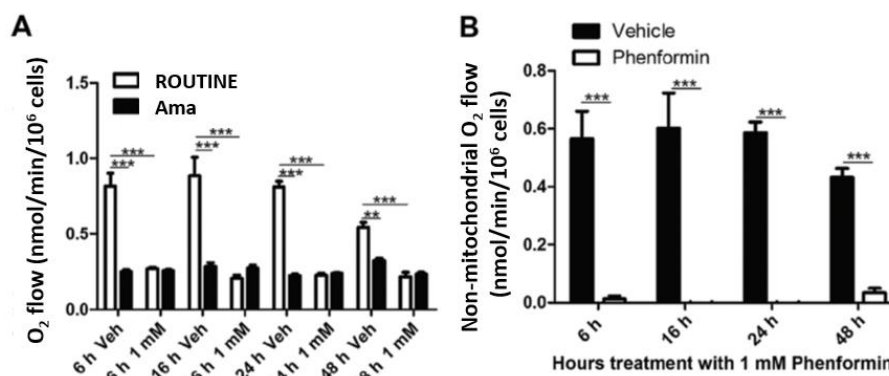


## Direct effects of phenformin on metabolism/bioenergetics and viability of SH-SY5Y neuroblastoma cells

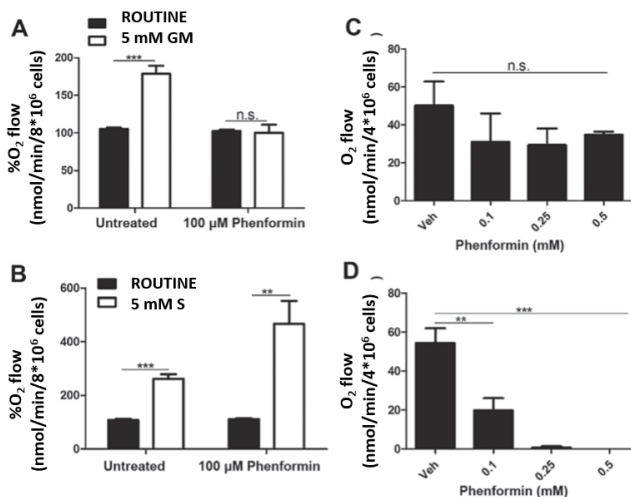
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**Figure 1.** Time-dependent inhibition of O<sub>2</sub> consumption in SH-SY5Y cells. Cells were treated with vehicle or phenformin and placed in the O<sub>2</sub>k containing F12 Dulbecco's modified Eagle's media. **(A)** ROUTINE respiration. **(B)** Non-mitochondrial respiration (ROX) within SH-SY5Y cells. Data is represented as the mean ± standard error. \**p*<0.05, \*\**p*<0.001, \*\*\**p*<0.0001.

### Inhibition of mitochondrial Complex I of SH-SY5Y cells by phenformin



**Figure 2.** Identification of Complex I as the target of phenformin inhibition in mitochondrial O<sub>2</sub> consumption. O<sub>2</sub> consumption in SH-SY5Y cells was measured using **(A)** NADH-linked substrates glutamate/malate (GM) or **(B)** succinate (substrate for complex II) in the presence and absence of phenformin. Independently, ROUTINE respiration was measured in SH-SY5Y cells treated with phenformin transfected with **(C)** an empty vector GFP tagged pAAV-MCS plasmid or **(D)** a pAAV-MCS plasmid encoding humanised Ndi1 (NADH:ubiquinone oxidoreductase). n.s., not significant. Data is represented as the mean ± standard error. \**p*<0.05, \*\**p*<0.001, \*\*\**p*<0.0001.

### Phenformin inhibits NADH- but not succinate-linked mitochondrial respiration

Reference: Geoghegan F, Chadderton N, Farrar GJ, Zisterer DM1, Porter RK (2017) Direct effects of phenformin on metabolism/bioenergetics and viability of SH-SY5Y neuroblastoma cells. *Oncol Lett* 14:6298-306.

Text slightly modified based on the recommendations of the COST Action MitoEAGLE CA15203. [Doi:10.26124/mitofit:190001.v4](https://doi.org/10.26124/mitofit:190001.v4)

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