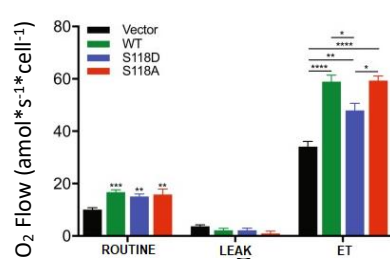




Non-canonical BAD activity regulates breast cancer cell and tumor growth via 14-3-3 binding and mitochondrial metabolism

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Novel mechanism of BAD-mediated growth in breast cancer: BAD promotes mitochondrial

Figure 1. Cell respiration by high-resolution respirometry in MDA-MB-231 expressing pcDNA3.2-V5-DEST vector control, WT-BAD, BAD-S118D (phosphomimetic) and BAD-S118A (non-phosphorylatable) cell lines. Bar graph showing the coupling control states in living cells (Data shown as mean ± SEM of 6 independent experiments).

BAD increases NADH-OXPPOS capacity and Complex I activity of the ETS

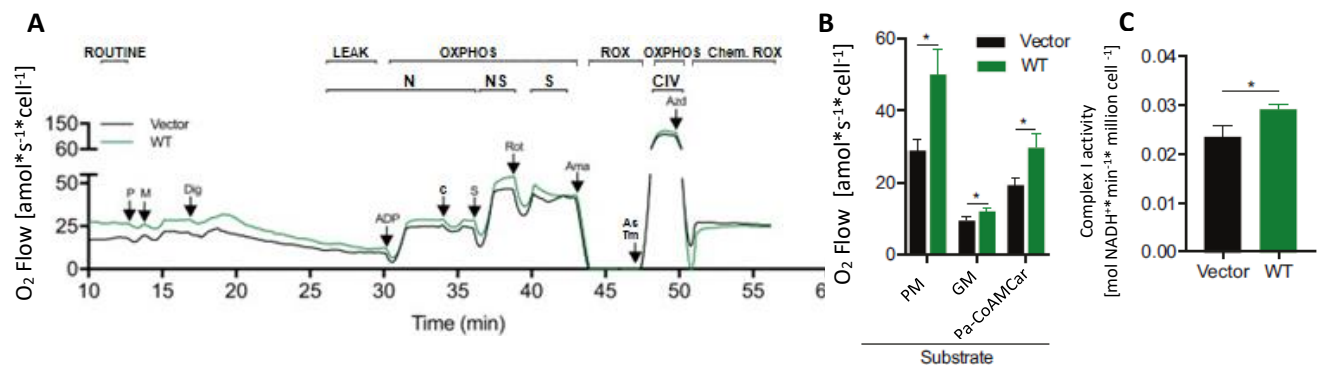
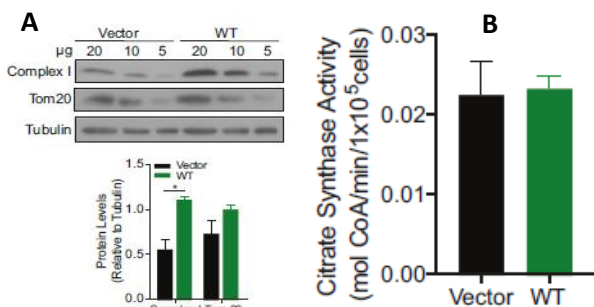


Figure 2. (A) O2k representative trace showing oxygen flow as a function of time by high-resolution respirometry: pyruvate (P), malate (M), digitonin (Dig), adenosine diphosphate (ADP), cytochrome c (c), succinate (S), rotenone (Rot), antimycin A (Ama), tetramethylphenylenediamine (Tm), ascorbate (As), and azide (Azd). **(B)** Mitochondrial respiration in permeabilized cells with substrates for NADH and FAO&NADH pathways: pyruvate&malate (PM), glutamate&malate (GM) and Palmitoyl-CoA&malate&carnitine (Pa-CoAMCar); (Data shown as mean ± SEM of minimum 5 independent experiments). **(C)** Complex I activity measured at 540 nm and normalized to cell number (Data shown as mean ± SEM of 4 independent experiments).



BAD-expressing cells show higher levels of Complex I but not mitochondrial content

Figure 3. (A) Complex I and Tom20 levels in MDA-MB-231 cell lines expressing pcDNA3.2-V5-DEST vector control and WT-BAD cells. (Data shown as mean ± SEM of 3 independent experiments). **(B)** Citrate synthase activity measured at 412 nm and normalized to cell number (Data shown as mean ± SEM of 3 independent experiments).

BAD, located at the mitochondria, can stimulate cell cycle progression through increased NADH-OXPPOS capacity and CI activity

Reference: Mann J, Githaka JM, Buckland TW, Yang N, Montpetit R, Patel N, Li L, Baksh S, Godbout R, Lemieux H, Going IS (2019) Non-canonical BAD activity regulates breast cancer cell and tumor growth via 14-3-3 binding and mitochondrial metabolism. *Oncogene* 38(18):3325-3339.

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