# O2k brief Ischemia-reperfusion

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**High-resolution respirometry: ischemia-reperfusion**

## Respiratory chain signalling is essential for adaptive remodelling following cardiac ischaemia

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## AOX (alternative oxidase) is catalytically engaged in post-anoxic heart mitochondria and lowers mitochondrial ROS production; but does not decrease acute I/R injuries

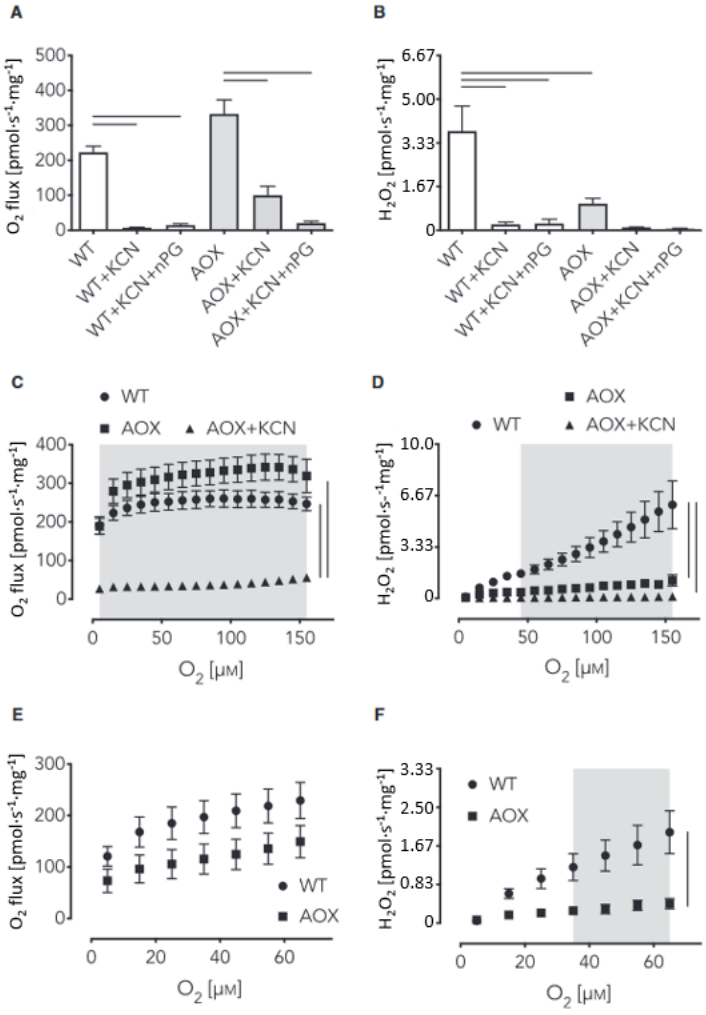


**Figure 1. (A-F)** Isolated WT and AOX heart mitochondria energized with CII substrate succinate and addition of inhibitors as indicated. KCN, CIV inhibitor potassium cyanide; nPG, AOX inhibitor n-propyl gallate. **(A)** Oxygen consumption. **(B)** Hydrogen peroxide flux. **(C)** Oxygen consumption in dependence of oxygen concentration. **(D)** Hydrogen peroxide flux in dependence of oxygen concentration. **(E)** Oxygen consumption during reoxygenation after 20 min of anoxia. **(F)** Hydrogen peroxide flux during reoxygenation after 20 min of anoxia.

Data shown as mean ± SEM of $N \geq 3$ experiments. Horizontal bars in (A, B) indicate significant differences with $P < 0.05$. Grey areas and vertical bars in (C-F) indicate significant differences with $p < 0.05$.

**AOX increases mitochondrial oxygen flux and decreases mitochondrial $H_2O_2$ flux in post-anoxic heart mitochondria energized with succinate**

**O2k-brief communicated by T Komlodi and L Tindle-Solomon**
**Oroboros Instruments**

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# Ischemia-reperfusion

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## AOX restores mitochondrial oxygen flux with NADH-linked substrates and Complex IV (CIV) activity 3 weeks after transient ischemia (45 min) followed by reperfusion

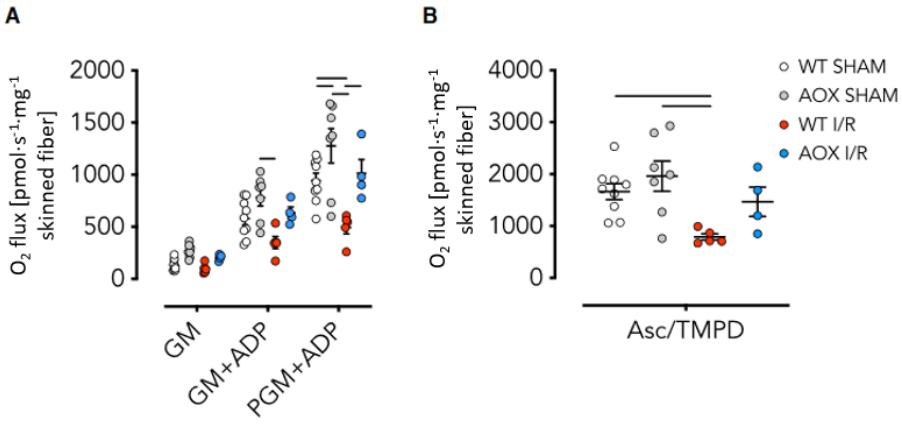
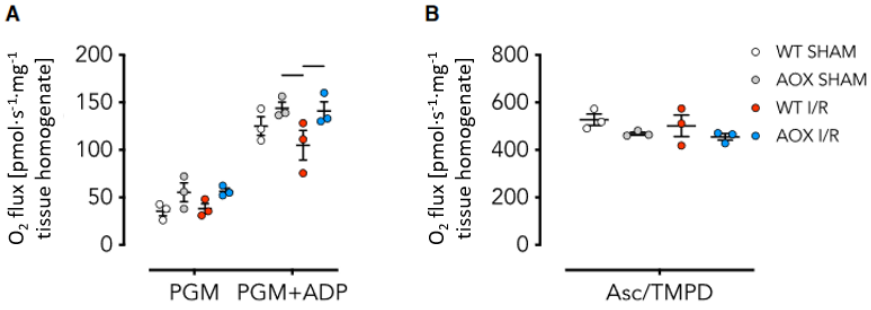



**Figure 2.** Oxygen consumption of isolated skinned heart fibers. **(A)** NADH-linked oxygen consumption driven by combinations of pyruvate (P), glutamate (G) and malate (M) as indicated, plus ADP. **(B)** C IV activity driven by ascorbate (Asc) and N,N,N′,N′-tetramethyl-p-phenylenediamine (TMPD). Data shown as mean ± SEM of $N \geq 4$ experiments. Horizontal bars indicate significant differences with $p < 0.05$.

## AOX restores mitochondrial oxygen flux with NADH-linked substrates 9 weeks after transient ischemia (45 min) followed by reperfusion

**Figure 3.** Oxygen consumption of heart tissue homogenate. **(A)** NADH-linked oxygen consumption driven by pyruvate (P), glutamate (G) and malate (M) plus ADP. **(B)** CIV activity driven by ascorbate (Asc) and N,N,N′,N′-tetramethyl-p-phenylenediamine (TMPD). Data shown as mean ± SEM of $N = 3$ experiments. Horizontal bars indicate significant differences with $p < 0.05$




**Restoration of mitochondrial oxygen consumption and decrease of mitochondrial ROS by AOX in the post-ischaemic heart are not sufficient to confer acute or chronic cardioprotection. Instead, AOX expression interferes with adaptive organ remodelling leading to contractile failure at 9 weeks but not 3 weeks after ischemia. Together, this indicates an essential role for ETS-derived signals during cardiac adaptive remodelling and identified ROS as a possible effector.**


Reference: Szibor Marten, Schreckenberg Rolf, Gizatullina Zemfira, Dufour Eric, Wiesnet Marion, Dhandapani Praveen Kumar, Debska-Vielhaber Grazyna, Heidler Juliana, Wittig Ilka, Nyman Tuula A, Gaertner Ulrich, Hall Andrew R, Pell Victoria, Viscomi Carlo, Krieg Thomas, Murphy Michael P, Braun Thomas, Gellerich Frank Norbert, Schlueter Klaus-Dieter, Jacobs Howard T(2020) Respiratory chain signalling is essential for adaptive remodelling following cardiac ischaemia. J Cell Mol Med [Epub ahead of print].



**Text slightly modified based on the recommendations of the COST Action MitoEAGLE CA15203.** Doi:10.26124/mitofit:190001.v6



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