Autism

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High-resolution respirometry: Autism

An mtDNA mutant mouse demonstrates that mitochondrial deficiency can result in autism endophenotypes

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Differential mitochondrial respiration of *ND6^{P25L}* versus WT mice

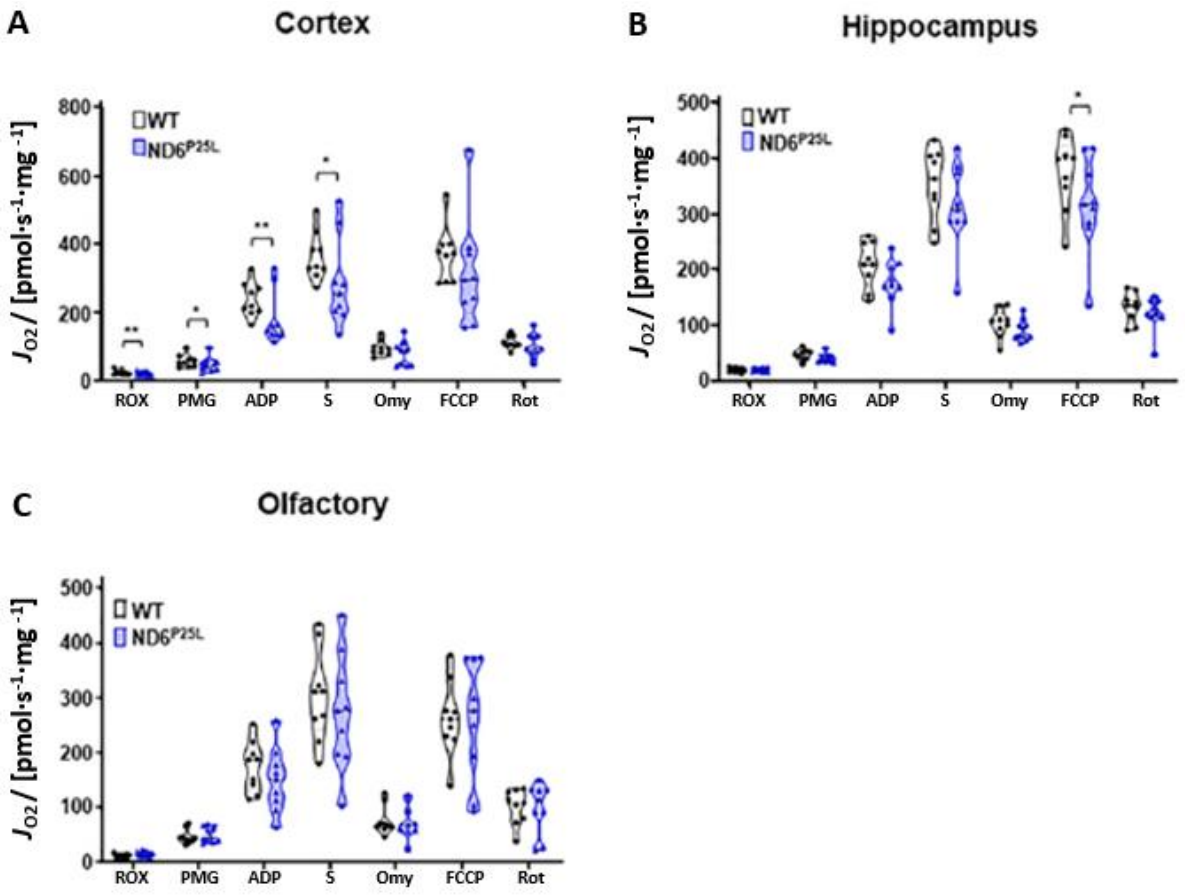

Figure 1. Oxygen flux (J_{O2}) of cortex **(A)**, hippocampus **(B)**, and olfactory bulb **(C)** of *ND6^{P25L}* versus WT mice. ROX: residual oxygen consumption; PMG, Complex I (NADH)-linked LEAK respiration (substrates: pyruvate, malate, and glutamate); ADP, ADP-stimulated OXPHOS capacity; S, OXPHOS capacity with succinate and PMG; Omy, LEAK respiration with oligomycin; FCCP, electron transfer capacity, uncoupled mitochondria; Rot, rotenone inhibitor of Complex I demonstrating Complex II (succinate)-linked respiration. Each dot represents an individual mouse. Black (WT mice), blue (ND6^{P25L} mice). *P < 0.05, **P < 0.01

O2k-brief communicated by T Komlodi and L Tindle-Solomon
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Differential mitochondrial reactive oxygen species generation in *ND6^{P25L}* versus WT mice

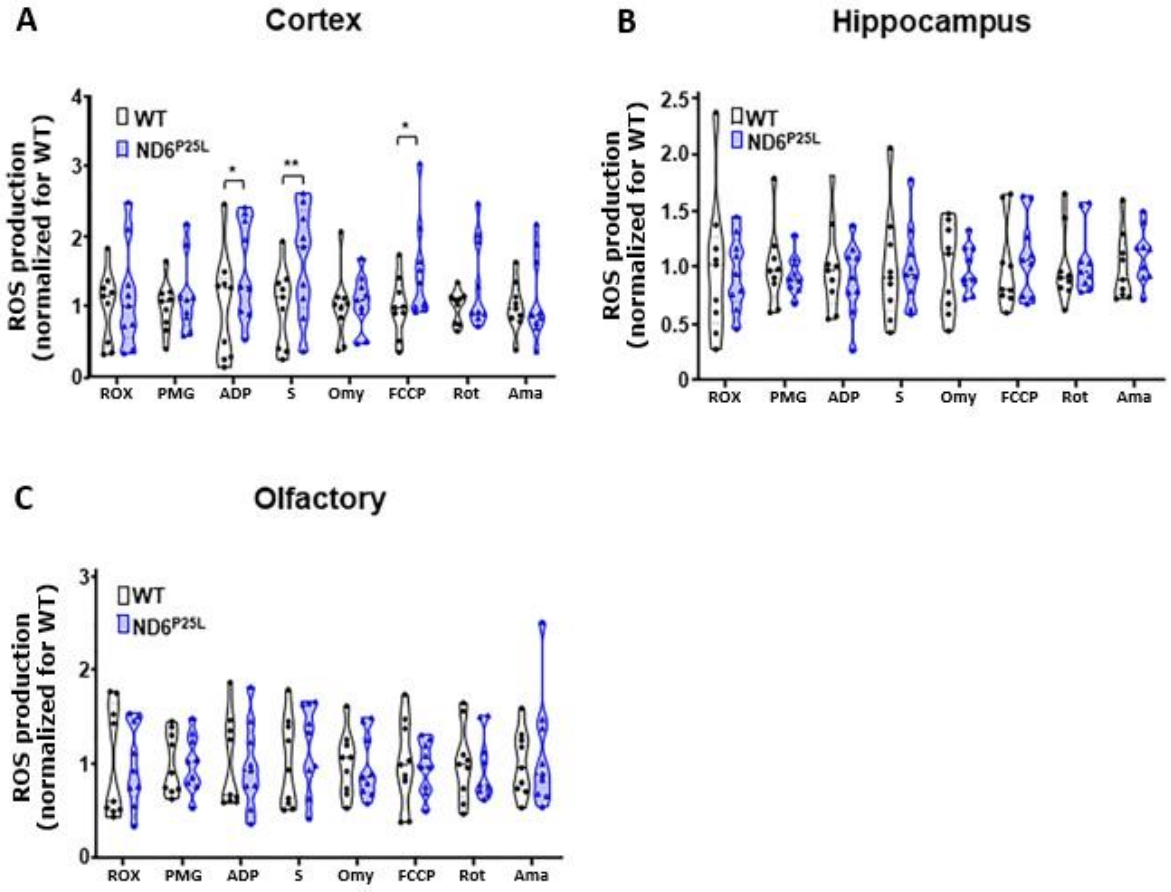

Figure 2. Differential mitochondrial reactive oxygen species (ROS) production in the cortex **(A)**, hippocampus **(B)**, and olfactory bulb **(C)** of *ND6^{P25L}* versus WT mice. ROX: residual oxygen consumption; PMG, Complex I (NADH)-linked LEAK respiration (substrates: pyruvate, malate, and glutamate); ADP, ADP-stimulated OXPHOS capacity; S, OXPHOS capacity with succinate and PMG; Omy, LEAK respiration with oligomycin; FCCP, electron transfer capacity, uncoupled mitochondria; Rot, rotenone inhibitor of Complex I demonstrating Complex II (succinate)-linked respiration; Ama, antimycin A inhibitor of Complex III demonstrating ROX. Each dot represents an individual mouse. Black (WT mice), blue (ND6^{P25L} mice). *P < 0.05, **P < 0.01

Introduction of an mtDNA *ND6* gene missense mutation (*ND6^{P25L}*) into the mouse germline caused autism spectrum disorder endophenotype, which correlates with impaired cortical and hippocampal mitochondrial respiration and increased reactive oxygen species production in the cortex.

Reference: Yardeni T, Cristancho AG, McCoy AJ, Schaefer PM, McManus MJ, Marsh ED, Wallace DC (2021) An mtDNA mutant mouse demonstrates that mitochondrial deficiency can result in autism endophenotypes. Proc Natl Acad Sci U S A 118:e2021429118.

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