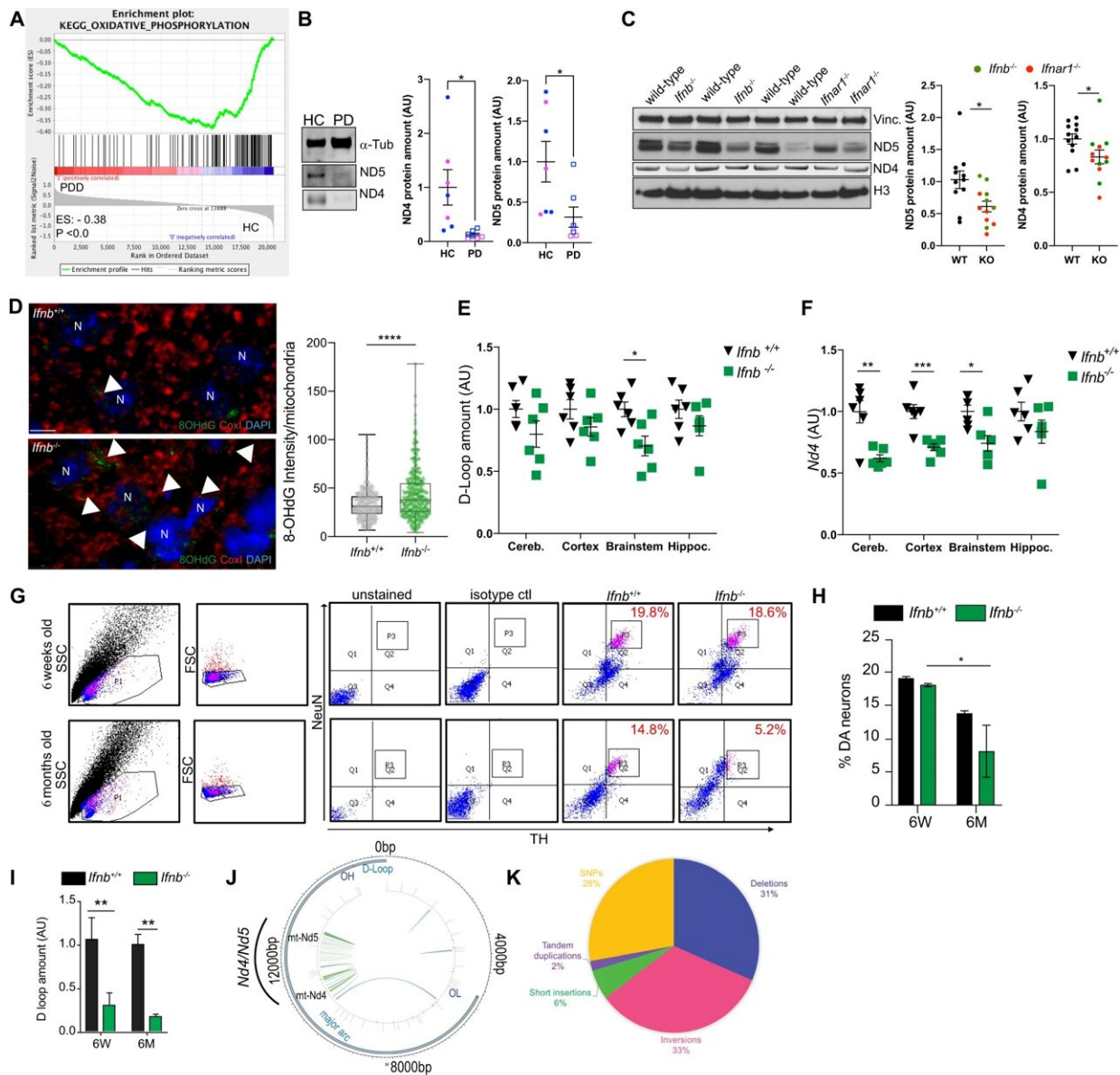


Researchers find mitochondrial DNA damage triggers spread of Parkinson's disease-like pathology

October 2 2023



Complex I respiratory chain subunits are altered in PD patients and PD models (*Ifnb^{-/-}/Ifnar1^{-/-}*) due to mtDNA damages. **A** Enrichment plot of KEGG-OXPHOS from microarray data comparing sporadic Parkinson's disease with dementia (sPDD/N = 13) and healthy controls (HC/N = 14). **B** Immunoblot showing loss of ND4 and ND5 proteins in the prefrontal cortex of healthy controls (HC) or Parkinson Disease patients (PD), with quantification. Pink indicates females and blue males. **C** Immunoblot showing loss of ND4 and ND5 proteins in the brainstems of 12-month-old mice, with quantifications. **D** Immunolabelling for 8-OHdG (pseudocoloured green), CoxI (mitochondria, pseudocoloured red) in mice midbrains. DAPI stains nuclei. Scale bars equal 5 microns. Quantification of 8-OHdG as integrated density of 8-OHdG in mitochondria of 3-month-old mice. Each dot represents a mitochondrion assessed ($N = 415$) from 3 biological replicates. **E** qPCR for D-loop in different brain regions in 6-week-old mice. **F** qPCR for major arc based on *Nd4* amplification in different brain regions in 6-week-old mice. For **E** and **F** each dot represents one individual animal, $N = 6$. **G** FACS cell sorting to isolate single dopaminergic (DN) neurons from midbrain of 6-week and 6-month-old mice. NeuN⁺ indicate neurons and NeuN⁺TH⁺, dopaminergic neurons. **H** Quantification of (**G**) in 6-week-old or 6-month-old mice. $N = 3$. **I** qPCR for D-loop in single isolated DN. Data are mean \pm SEM, $N = 3$ mice/group. **J** Position of SVs and SNVs detected with MitoSV-seq in 6-week-old *Ifnb^{-/-}* mice. Circos plots of mouse mtDNA genome displaying Heavy and Light Origin of replication (OH and OL, respectively), major arc and D-loop (outer blue circle). mtDNA genes are displayed in the middle circle (gray lines). SVs as arches with deletions (blue), tandem duplications, inversions and insertions (orange). Thickness of the arches correspond to SVs heteroplasmy. SNVs are marked with short red lines (—) according to their positions in mouse mtDNA. Intensity of red lines correspond to SNVs' heteroplasmy. **K** Pie chart showing the distribution of variation types detected in *Ifnb^{-/-}* mice; SNP: Single Nucleotide Polymorphism. For all graphs, * p

Citation: Researchers find mitochondrial DNA damage triggers spread of Parkinson's disease-like pathology (2023, October 2) retrieved 28 April 2024 from <https://medicalxpress.com/news/2023-10-mitochondrial-dna-triggers-parkinson-disease-like.html>

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