Mitochondrial respiratory chain sustains inflammation

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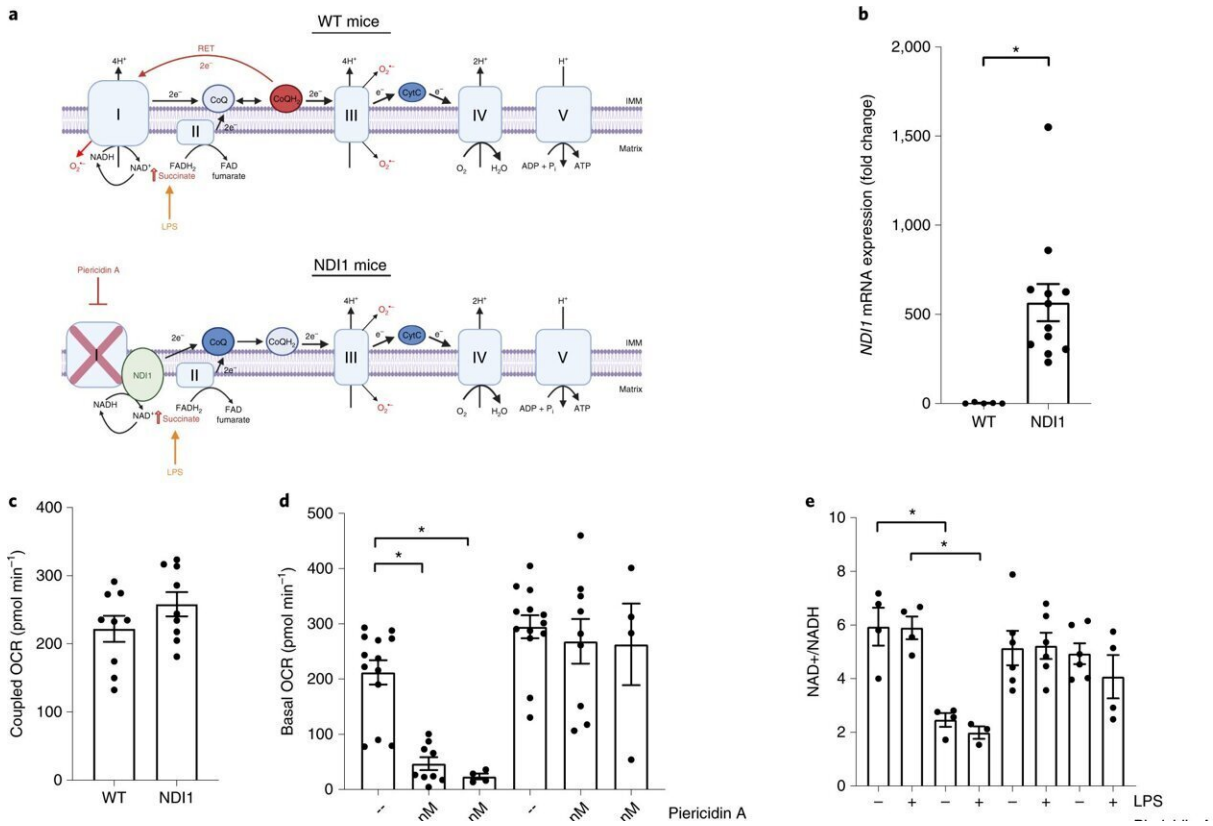

NDI1 expression confers resistance to mitochondrial complex I inhibitor piericidin A. a, Schematic of the mitochondrial electron transport chain in WT (top) and NDI1-expressing (bottom) BMDMs during LPS stimulation. Piericidin A inhibition of mitochondrial complex I on electron flow is rescued by NDI1 expression. IMM, inner mitochondrial membrane; RET, reverse electron transport. b, NDI1 mRNA levels ($\Delta\Delta C_t$) in WT and NDI1 BMDMs (n = 5 WT; n = 12 NDI1). c, Coupled OCR in WT and NDI1 BMDMs (n = 9 for each genotype). d, Basal OCR in WT and NDI1 BMDMs after 1 h treatment with 100

nM or 500 nM piericidin A (n = 13 vehicle for each genotype; n = 9 100 nM piericidin A for each genotype; n = 4 500 nM piericidin A for each genotype). e, NAD^+/NADH ratio in WT and NDI1 BMDMs after 4 h treatment with or without LPS (100 ng ml^{-1}) in the presence or absence of piericidin A (500 nM) (n = 3 WT LPS + piercidin A; n = 4 all other treatments). f, Rate of H_2O_2 production in WT and NDI1 BMDMs in the presence of succinate (500 μM) with or without piericidin A treatment (500 nM) (n = 9). g, Heatmap of significantly altered metabolites in WT and NDI1 BMDMs treated with LPS (100 ng ml^{-1}) alone, piericidin A alone (500 nM) or both LPS and piericidin A for 4 h. The relative abundance of each metabolite is depicted as z score across rows (red, high; blue, low) (n = 5 for all treatments). h, Arbitrary units of succinate in WT and NDI1 BMDMs with or without LPS (100 ng ml^{-1}) and piericidin A (500 nM) for 4 h (n = 5 for all treatments). Data are mean ± s.e.m. *P