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Mitochondrial MDM2 Regulates Respiratory Complex I Activity Independently of p53

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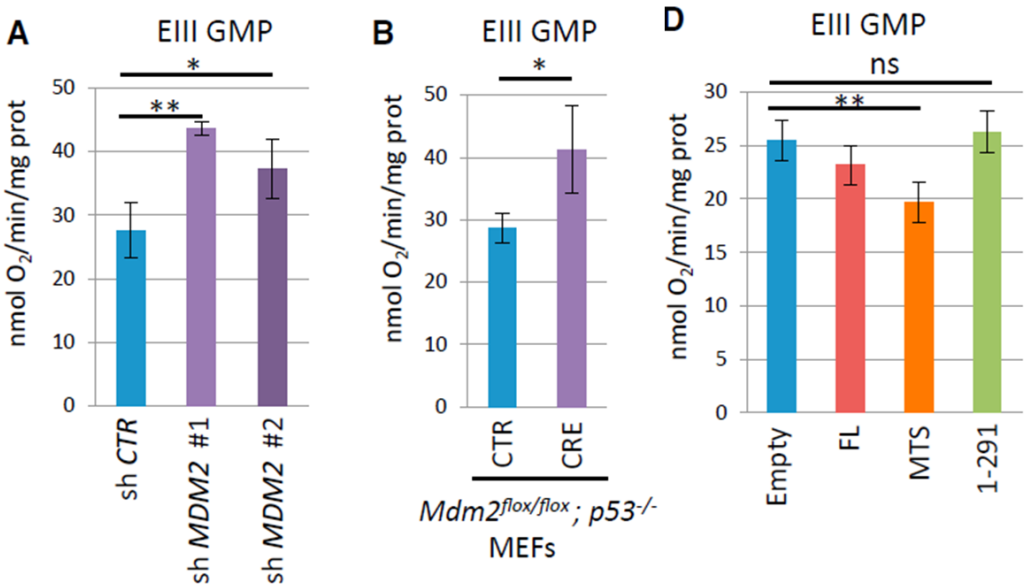
State III respiration linked to the electron transport chain (ETC) complex I (CI), measured in the presence of glutamine, malate, and pyruvate (EIII GMP) as substrates, increased significantly upon MDM2 depletion in H1299 cells, as well as after Cre-mediated inactivation of murine *Mdm2* in *Mdm2*$^{flox/flox}$; *p53*^{KO} primary mouse embryonic fibroblasts (MEFs).

mtMDM2 Controls ETC Complex I Activity and Respiration



(A) Oxygen consumption in H1299 cells transduced with lentiviruses encoding control or two independent MDM2 shRNAs. ETC CI-driven respiration, in the presence of glutamine, malate, and pyruvate (EIII GMP) as substrates, was measured by using a high-resolution Oxygraph respirometer (mean ± SEM; n = 3).
(B) ETC CI-driven respiration (EIII GMP) in Mdm2flox/flox; p53/ primary MEFs transduced with control (CTR) or CRE-expressing retroviruses (CRE) (mean ± SEM; n = four independent populations).
(D) ETC CI-driven respiration (EIII GMP) in H1299 cells expressing FL-MDM2 (FL), MTS-MDM2 (MTS), or MDM2 1-291 (1-291) and in control cells transfected with the corresponding empty vector (Empty) (mean ± SEM; n = 3).

Reference: Arena G, Cissé MY, Pyrdziak S, Chatre L, Riscal R, Fuentes M, Arnold JJ, Kastner M, Gayte L, Bertrand-Gaday C, Nay K, Angebault-Prouteau C, Murray K, Chabi B, Koechlin-Ramonatxo C, Orsetti B, Vincent C, Casas F, Marine JC, Etienne-Manneville S, Bernex F, Lombès A, Cameron CE, Dubouchaud H, Ricchetti M, Linares LK, Le Cam L (2018) Mitochondrial MDM2 regulates respiratory complex I activity independently of p53. Mol Cell 69:594-609.