O2k-brief Lymphocytes

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High-resolution respirometry lymphocyte and cancer

The metabolite BH4 controls T cell proliferation in autoimmunity and cancer

Cronin SJF, Seehus C, Weidinger A, Talbot S, Reissig S, Seifert M, Pierson Y, McNeill E, Longhi MS, Turnes BL, Kreslavsky T, Kogler M, Hoffmann D, Ticevic M, da Luz Scheffer D, Tortola L, Cikes D, Jais A, Rangachari M, Rao S, Paolino M, Novatchkova M, Aichinger M, Barrett L, Latremoliere A, Wirnsberger G, Lametschwandtner G, Busslinger M, Zicha S, Latini A, Robson SC, Waisman A, Andrews N, Costigan M, Channon KM, Weiss G, Kozlov AV, Tebbe M, Johnsson K, Woolf CJ, Penninger JM

Mitochondrial dysfunction in BH4-depleted T cells after activation

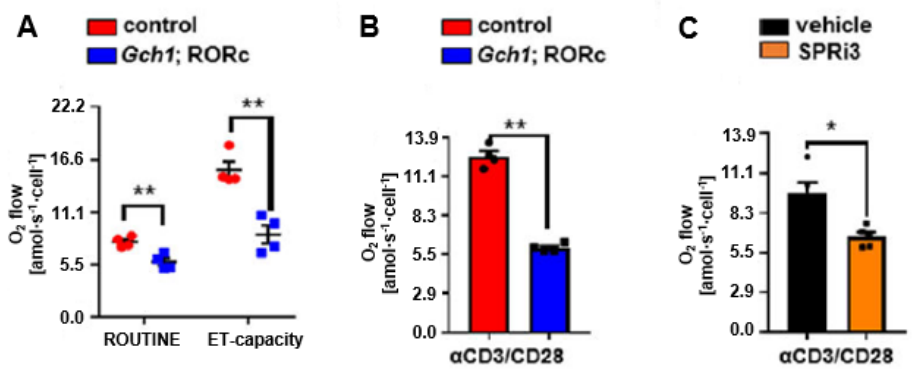

Figure 1. (A) ROUTINE and electron transfer-capacity respiration in intact, 16-h anti-CD3/CD28-stimulated CD4$^+$ T cells from control and Gch1; RORc mice. **(B)** Oxygen flow in permeabilized, 16h anti-CD3/CD28-stimulated CD4$^+$ T cells from control and Gch1; RORc mice and **(C)** wild-type CD4$^+$ T cells treated with DMSO or SPRi3 (50 µM)

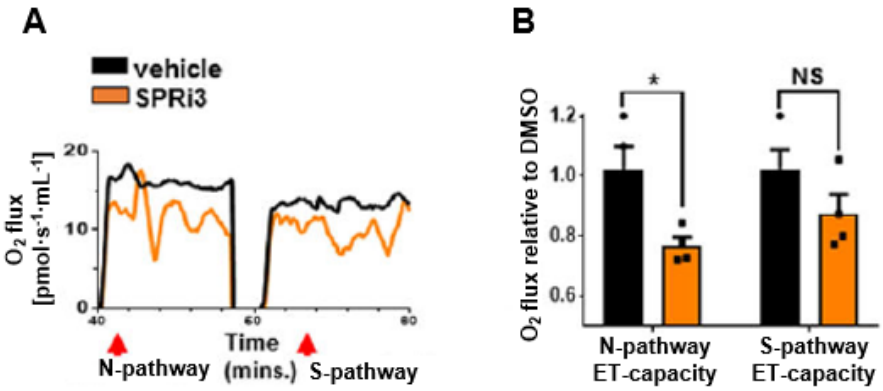

Figure 2. (A) Representative oxygen flux traces of NADH-linked (glutamate, malate and ADP) and succinate-linked ET activity (rotenone and succinate) from 16-h-activated wild-type CD4$^+$ T cells treated with vehicle or SPRi3 (50 µM). **(B)** Relative NADH- and Succinate-linked activities in activated control cells treated with vehicle (DMSO) or SPRi3 (50 µM).

Data from this paper indicate that antigen-receptor-stimulated, BH4- depleted T cells display a defective iron-redox cycling of cytochrome *c*, leading to mitochondrial dysfunction.

Reference: Cronin SJF, Seehus C, Weidinger A, Talbot S, Reissig S, Seifert M, Pierson Y, McNeill E, Longhi MS, Turnes BL, Kreslavsky T, Kogler M, Hoffmann D, Ticevic M, da Luz Scheffer D, Tortola L, Cikes D, Jais A, Rangachari M, Rao S, Paolino M, Novatchkova M, Aichinger M, Barrett L, Latremoliere A, Wirnsberger G, Lametschwandtner G, Busslinger M, Zicha S, Latini A, Robson SC, Waisman A, Andrews N, Costigan M, Channon KM, Weiss G, Kozlov AV, Tebbe M, Johnsson K, Woolf CJ, Penninger JM (2018) The metabolite BH4 controls T cell proliferation in autoimmunity and cancer. Nature 563:564-68.

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O2k-brief communicated by LF Garcia-Souza and L Tindle-Solomon
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