O2k brief Cancer
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High-resolution respirometry and cancer

Inhibition of mitochondrial respiration prevents *BRAF*-mutant melanoma brain metastasis

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ACTA NEUROPATHOLOGICA COMMUNICATIONS

In vivo drug screening

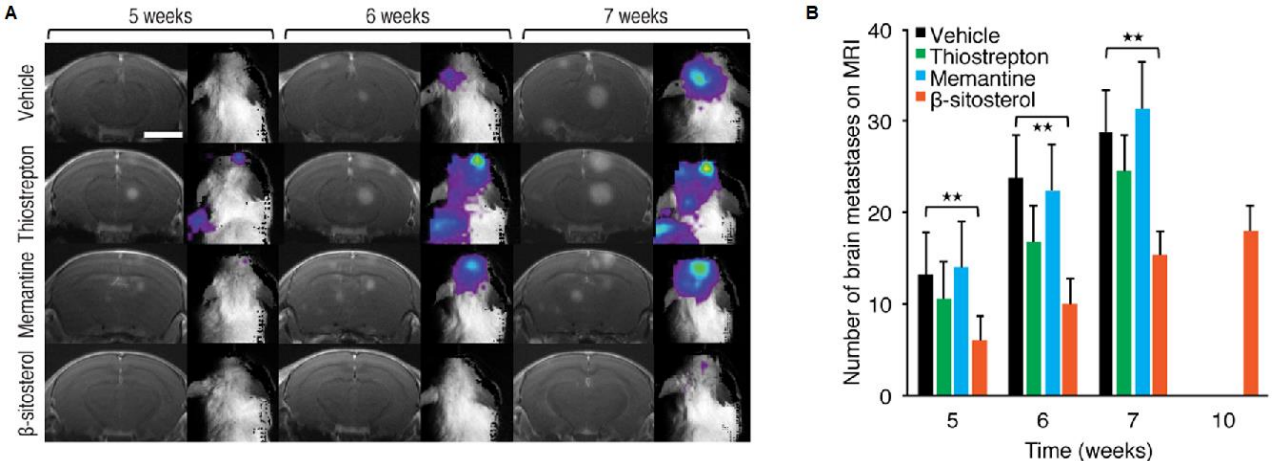
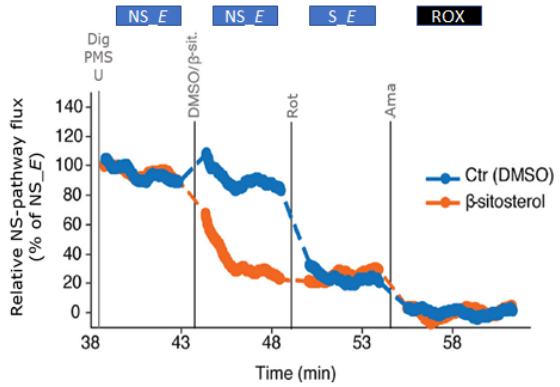


Figure 1. (A) Development of brain metastases visualized by MRI (T1-weighted images with contrast) and BLI at five, six and seven weeks. Scale bar MRIs, 0.25 cm. **(B)** Number of brain metastases at T1-weighted MRI with contrast (Student's *t*-test). There was no significant difference between vehicle- and memantine-treated mice. ** $p < 0.01$. All values are given as the mean ± SEM.



Effect of β-sitosterol on mitochondrial respiration

Figure 2. Analysis of β-sitosterol effect on respiration. The figure shows percent of O_2 flux relative to NS-pathway linked respiration in ET state. NS-linked respiration was estimated in permeabilized cells in the presence of pyruvate (P), malate (M) and succinate (S) and the uncoupler FCCP (U). The drug candidate β-sitosterol or its carrier, DMSO, were added to the chambers. Succinate-linked respiration, with electron flux through Complex II (CII) into the Q-junction (S-pathway) was obtained by inhibition of CI with rotenone (Rot). Inhibition of CIII by antimycin A (Ama) provided an estimation of residual oxygen consumption (ROX).

β-sitosterol inhibits mitochondrial respiration in tumor cells by acting as a Complex I inhibitor

Reference: Sundstrøm T, Prestegarden L, Azuaje F, Aasen SN, Røsland GV, Varughese JK, Bahador M, Bernatz S, Braun Y, Harter PN, Skaftnesmo KO, Ingham ES, Mahakian LM, Tam S, Tepper CG, Petersen K, Ferrara KW, Tronstad KJ, Lund-Johansen M, Beschorner R, Bjerkvig R, Thorsen F (2019) Inhibition of mitochondrial respiration prevents BRAF-mutant melanoma brain metastasis. Acta Neuropathol Commun 7:55.

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