



Endogenous Myoglobin in Breast Cancer Is Hypoxia-inducible by Alternative Transcription and Functions to Impair Mitochondrial Activity

A ROLE IN TUMOR SUPPRESSION?*^[5]

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Representative trace of the protocol with intact breast cancer cells

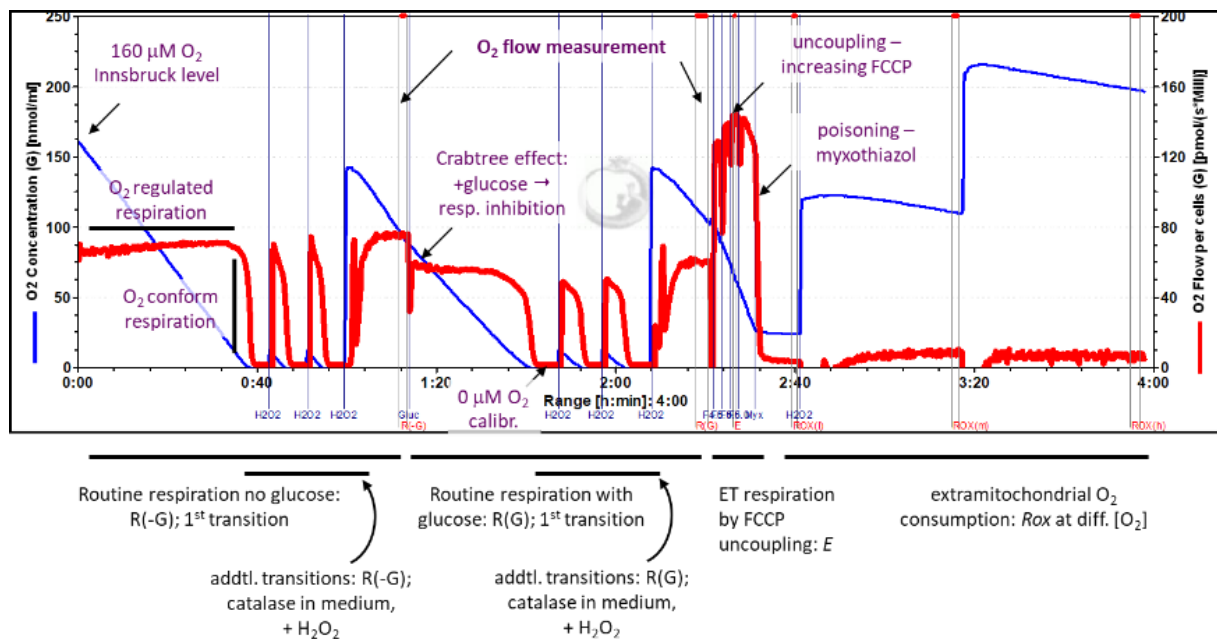


Figure 1. MDA-MB-468 cell respirometry showing the representative protocol to assess the Crabtree effect and the four cellular activity states studied (ROUTINE (-glucose), ROUTINE (+glucose), ET and ROX). The medium used was MiRO5 supplemented with catalase. H₂O₂ additions allows a controlled reoxygenation of the chamber to perform the oxygen kinetics.

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Respiration and oxygen kinetics as a function of respiratory state

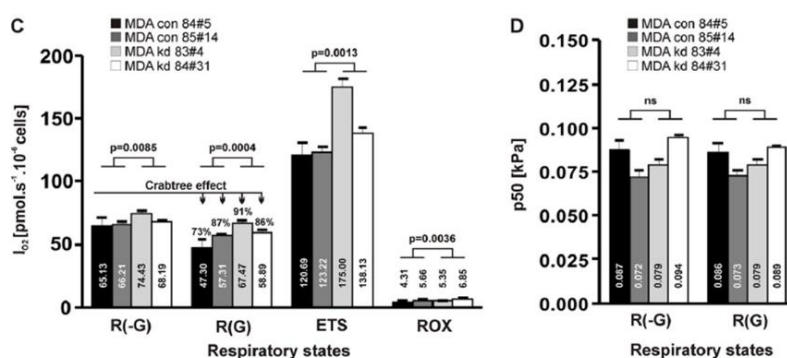


Figure 2. C. Oxygen consumption rates of myoglobin (Black) and myoglobin *knockdown* (Grey) clones for the ROUTINE (-glucose), ROUTINE (+glucose), ET and ROX states. **D.** Oxygen kinetic p_{50} for ROUTINE (-glucose), ROUTINE (+glucose). Mean p_{50} values are highlighted within the respective column. MDA-MB-468 shRNA clones derived from shRNA constructs 83, 84 and 85 were used for respirometry as controls (84#5 and 85#14) or *knockdown* (83#4 and 84#31).

Myoglobin abundance in breast cancer cells plays unconventional functions that are not directly related to the binding and transport of O_2 . We propose a role in the shuttle of fatty acids and in cell proliferation, broadening our view on the role of nonmuscle myoglobin in the biology of solid tumours

Reference: Kristiansen G, Hu J, Wichmann D, Stiehl DP, Rose M, Gerhardt J, Bohnert A, ten Haaf A, Moch H, Raleigh J, Varia MA, Subarsky P, Scandurra FM, Gnaiger E, Gleixner E, Bicker A, Gassmann M, Hankeln T, Dahl E, Gorr TA (2011) Endogenous myoglobin in breast cancer is hypoxia-inducible by alternate transcription and functions to impair mitochondrial activity: a role in tumor suppression? *J Biol Chem* 286:43417-28

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