MONITORING MITOCHONDRIAL OXYGENATION

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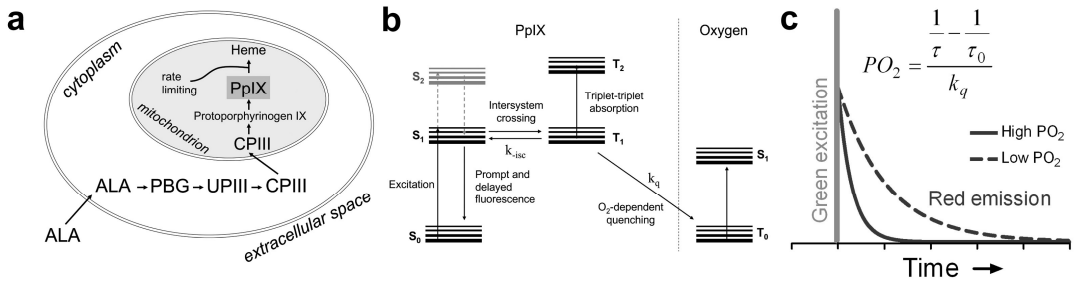
Introduction

The quantitative assessment of cellular oxygenation and metabolism in vivo has been a long time wish of both researchers and clinicians alike. The recent development of the first technique for measurement of mitochondrial PO_2 (mitoPO_2) in intact cells (1) has been demonstrated to be a big step forward to potential achievement of this goal. This optical technique is based on measurement of the oxygen-dependent lifetime of the delayed fluorescence of aminolevulinic acid (ALA) induced protoporphyrin IX (PpIX). The method has proven to be useful in vivo and has now been validated both in liver (2) and heart (3).

Methods



Principle of mitoPO_2 measurement by oxygen-dependent quenching of ALA enhanced PpIX. (a) Principle by which ALA administration enhances mitochondrial PpIX levels. ALA, 5-aminolevulinic acid; PBG, porphobilinogen; UPIII, uroporphyrinogen III; CPIII, coporporphyrinogen III; and PpIX, protoporphyrin IX. (b) Jablonski diagram of states and state transitions of PpIX and its interaction with oxygen. S_0, S_1, and S_2 represent the ground state and first and second excited singlet states, respectively. T_0, T_1, and T_2 represent the ground (triplet) state and first and second excited triplet states, respectively. k_q is the rate constant of T_1 quenching by oxygen. (c) PpIX emits delayed fluorescence after excitation by a pulse of green (510 nm) light. The delayed fluorescence lifetime is oxygen-dependent according to the Stern-Volmer equation (inset), in which k_q is the quenching constant and τ_0 is the lifetime at zero oxygen. (Adapted from reference 2)

Results/Discussion

This presentation will look back at the development of the technique, present some current work and will discuss potential clinical application of the technology.

Declaration of interest

E.G. Mik is founder and shareholder of Photonics Healthcare B.V., a company that holds exclusive licences to patents related to the discussed technology from both the Academic Medical Center Amsterdam and the Erasmus Medical Center Rotterdam.

References

1. Mik EG, Stap J et al. Mitochondrial PO_2 measured by delayed fluorescence of endogenous protoporphyrin IX. *Nat Methods*. 2006 Nov; 3(11): 939-45.
2. Mik EG, Johannes T et al. In vivo mitochondrial oxygen tension measured by a delayed fluorescence lifetime technique. *Biophys J*. 2008 Oct; 95(8): 3977-90.
3. Mik EG, Ince C et al. Mitochondrial oxygen tension within the heart. *J Mol Cell Cardiol*. 2009 Jun; 46(6):943-51.