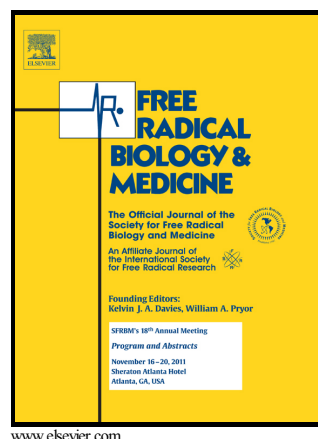


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In cellulo monitoring of quinone reductase activity and reactive oxygen species production during the redox cycling of 1,2 and 1,4 quinones

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ACCEPTED MANUSCRIPT

IN CELLULO MONITORING OF QUINONE REDUCTASES ACTIVITY AND
REACTIVE OXYGEN SPECIES PRODUCTION DURING THE REDOX CYCLING
OF 1,2 AND 1,4 QUINONES

Laure-Estelle Cassagnes^{a,b}, Pierre Perio^{a,b}, Gilles Ferry^c, Natacha Moulharat^c,

Mathias Antoine^c, Régis Gayon^d, Jean A. Boutin^c, Françoise Nepveu^{a,b §},

Karine Reybier^{a,b § *}

^a Université de Toulouse 3, UPS; UMR 152 PHARMA-DEV, 118 route de Narbonne, F-31062 Toulouse cedex 9, France

^b IRD, UMR 152, F-31062 Toulouse cedex 9, France

^c Biotechnologie, Pharmacologie moléculaire et cellulaire, Institut de Recherches Servier, 125, Chemin de Ronde, 78290 Croissy sur Seine, France

^d Vectalys SAS, Canal Biotech 2, 3 rue des satellites, 31400 Toulouse, France

§ These authors contributed equally to the work.

* Corresponding author: Tel: +33 562259804; Fax: +33 562259802, karine.reybier-vuattoux@univ-tlse3.fr

ABSTRACT

Quinones are highly reactive molecules that readily undergo either one- or two-electron reductions. One-electron reduction of quinones or their derivatives by enzymes such as cytochrome P450 reductase or other flavoproteins generates unstable semiquinones which undergo redox cycling in the presence of molecular oxygen leading to the formation of highly reactive oxygen species. Quinone reductases 1 and 2 catalyze the two-electron reduction of quinones to form hydroquinones which can be removed from the cell by conjugation of the hydroxyl with glucuronide or sulfate thus avoiding its auto-oxidation and the formation of free radicals and highly reactive oxygen species. This latter characteristic confers a detoxifying enzyme role to QR1 and QR2, even if this character is strongly linked to the excretion capacity of the cell. Using EPR spectroscopy and confocal microscopy we demonstrated that the amount of ROS produced by Chinese hamster ovary (CHO) cells overexpressing QR1 or

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