

Mitochondrial bioenergetic background confers a survival advantage to HepG2 cells in response to chemotherapy

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Auteur	Loiseau, Dominique [1], Morvan, Daniel [2], Chevrollier, Arnaud [3], Demidem, Aicha [4], Douay, Olivier [5], Reynier, Pascal [6], Stepien, Georges [7]
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Mots-clés	Cancer [8], glycolysis [9], mitochondria [10], Oxidative [11], phospholipid [12] Cancer cells mainly rely on glycolysis for energetic needs, and mitochondrial ATP production is almost inactive. However, cancer cells require the integrity of mitochondrial functions for their survival, such as the maintenance of the internal membrane potential gradient ($\Delta\Psi_m$). It thus may be predicted that $\Delta\Psi_m$ regeneration should depend on cellular capability to produce sufficient ATP by upregulating glycolysis or recruiting oxidative phosphorylation (OXPHOS). To investigate this hypothesis, we compared the response to an anticancer agent chloroethylnitrosourea (CENU) of two transformed cell lines: HepG2 (hepatocarcinoma) with a partially differentiated phenotype and 143B (osteosarcoma) with an undifferentiated one. These cells types differ by their mitochondrial OXPHOS background; the most severely impaired being that of 143B cells. Treatment effects were tested on cell proliferation, O ₂ consumption/ATP production coupling, $\Delta\Psi_m$ maintenance, and global metabolite profiling by NMR spectroscopy. Our results showed an OXPHOS uncoupling and a lowered $\Delta\Psi_m$, leading to an increased energy request to regenerate $\Delta\Psi_m$ in both models. However, energy request could not be met by undifferentiated cells 143B, which ATP content decreased after 48 h leading to cell death, while partially differentiated cells (HepG2) could activate their oxidative metabolism and escape chemotherapy. We propose that mitochondrial OXPHOS background confers a survival advantage to more differentiated cells in response to chemotherapy. This suggests that the mitochondrial bioenergetic background of tumors should be considered for anticancer treatment personalization. © 2009 Wiley-Liss, Inc.
Résumé en anglais	<p>URL de la notice</p> <p>http://okina.univ-angers.fr/publications/ua306 [13]</p> <p>DOI</p> <p>10.1002/mc.20539 [14]</p>

Liens

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