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Global redox potential: A extracellular biomarker of cellular metabolism

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Redox processes are at the core of cellular function. They play a signaling and regulatory role when the production of reactive oxygen species (ROS) is balanced by the organism's antioxidant defenses. However, when the production of oxidizing species is too intense and prolonged, the defenses can no longer manage the burden, leading to potential damage to proteins, lipids, and DNA. Today, it is possible to assess cellular redox metabolism by targeting specific mechanisms, such as the ubiquinol/ubiquinone couple, which reflects changes in cellular metabolism. It is therefore crucial to monitor the formation of these species within cells.

Mitochondria are essential organelles for the function of all eukaryotic cells, as they facilitate oxidative phosphorylation, a redox-dependent process, the consequence of which is ATP synthesis. Thus, stress on the mitochondrial respiratory chain triggers a cascade of redox changes, which can be detected through specific measurements. Our hypothesis is that measuring the global redox potential (ERedox) could provide an evaluation of redox modifications in the cellular environment, reflecting the metabolic stress imposed on the cells.

E_{Redox} is measured in the extracellular medium using a two-electrode electrochemical system. The indicator electrode is a 'lab-made' microelectrode with a 50 μm diameter wire, while the reference electrode is a Ag/AgCl microelectrode. Cells derived from a murine model are cultured under pharmacological stress on the mitochondrial respiratory chain for 48 hours. ERedox monitoring, along with measurements of the respiratory chain redox couples, is performed throughout the stressed culture. The observed changes in E_{Redox} demonstrate that global measurement serves as a marker of cellular metabolic adaptation to stress. These results are correlated with complementary biochemical analyses (enzymatic activities, mitochondrial respiratory activity, and redox couple assays) to create a 'redox map' of the cells. Continuous measurement of ERedox using a sensor that mitigates biofouling will enable more precise monitoring of extracellular redox modifications.

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