Role of NCLX in the production of reactive oxygen species (ROS) in reoxygenation

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Ischemic pathologies, such as stroke and myocardial infarction, present a phase of cellular hypoxia followed by reoxygenation once blood flow has been restored. In both phases, but especially the latter, there is a burst of mitochondrial reactive oxygen species (ROS), which causes severe oxidative stress and is involved in the so-called ischemia-reperfusion injury.

Our group previously discovered that the mitochondrial sodium/calcium exchanger, NCLX, plays an important role in superoxide production during hypoxia due to the reduction of inner mitochondrial membrane fluidity caused by the interaction of sodium with phospholipids as it enters the matrix.

Since NCLX modulates ROS production in acute hypoxia, we wondered whether this exchanger would also play a role in ROS production during reoxygenation. To test this, we are trying to determine whether inhibiting NCLX in different cell types and animal models results in less ROS production upon reoxygenation after a period of hypoxia. To assess this, we are using dihydroethidium (DHE), a fluorescent probe that is oxidized in the presence of superoxide, as a marker of ROS production.

So far, our results have shown that acute inhibition of NCLX at the onset of reperfusion causes a significant reduction in superoxide production in mouse brain microvasculature endothelial cells, suggesting a role of NCLX in ROS production during reperfusion. Moreover, we are also using mice hippocampal slices to investigate the role of NCLX inhibition in animal brain tissue subjected to hypoxia and reoxygenation.