The Impact Of ALDH-2 Activity On Mitochondria Bioenergetic Functions In Endothelial Cells

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Even though endothelial cells (ECs) seem to generate most of their energy anaerobically, they have an extensive mitochondrial network and consume oxygen.

It is shown that mitochondria in endothelial cells are highly coupled and possess a considerable bioenergetic reserve. This reserve capacity is important in responding to oxidative stress but the mechanistic aspects of this crosstalk and the link between metabolism and angiogenesis have only started to become apparent, with numerous questions remaining to be addressed (Carmeliet et al., 2017). Mitochondrial aldehyde dehydrogenase (ALDH2) is responsible for the metabolism of acetaldehyde and other toxic lipid aldehydes. Our data documented that mitochondrial ALDH2 in the endothelium is a target for the vascular effect of Aβ peptides, including acquisition of premature senescent phenotype producing alterations in endothelial functions (Solito et al., 2010).

Aim: The aim of the study has been to investigate the role of ALDH2 on HUVECs bioenergetic functions focusing on mitochondrial function.

Materials and methods: To assess mitochondrial function in intact endothelial cells, extracellular flux analysis and TMRM probe were used to determine rates of O2 consumption and mitochondrial function in situ, respectively. In these experiments we defined mitochondrial function in HUVECs silenced for ALDH2 or treated with Aβ1-40 by sequentially adding pharmacological inhibitors to probe the function of individual components of the respiratory chain. The analysis of the different components of oxygen consumption rate allows calculation of a number of parameters that characterize mitochondrial bioenergetics in intact cells such as basal respiration, ATP-linked oxygen consumption, and reserve capacity of the cells (Dranka et al., 2010).

Results: Preliminary results suggest that the treatment with Aβ1-40 and ALDH2 silencing reduce mitochondrial reserve capacity. A loss of mitochondrial reserve capacity is expected to lead to decreased ability to respond to secondary energetic stressors. Exposure of endothelial cells to high concentrations of aldehydes or an impairment of ALDH2 activity then could lead to an impaired angiogenesis.

Conclusion: These results might provide useful information about the concept that enhancing ALDH2 activity, which preserve mitochondrial reserve capacity in stress condition, could represent novel therapeutic strategies for the treatment of angiogenic or metabolic disease.

Acknowledgment: work was supported by Prin - Bando 2015 Prot. 20152HKF3Z

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