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RESEARCH AREA

For many cell types, the mitochondrial respiratory chain provides energy in the form of ATP, since the oxidation of nutrients takes place partially in mitochondria and requires oxygen from the air. In addition, the operation of other metabolic pathways - such as pyrimidine nucleotide synthesis or the conversion of certain amino acids - is also coupled to the activity of the respiratory chain. In tumor cells, mitochondrial respiration is often inhibited due to mutations in the protein complexes or as a result of a hypoxic environment. In such cases, the energy supply of the cell is disrupted, and the mitochondrion may shift from being an energy-producing organelle to an energy-consuming one. Despite the loss of its energy-producing function under these conditions, the residual activity of the respiratory chain may still play an important role in maintaining the aforementioned metabolic pathways. Our research group investigates enzymatic reactions that are capable of fuelling the respiratory chain via alternative routes when it is inhibited, thereby partially sustaining ATP production. In addition, our goal is to elucidate the significance of pathways that, independently of ATP synthesis, provide essential building blocks for tumor cell proliferation.

TECHNIQUES AVAILABLE IN THE LAB

Isolation of mitochondria from different mouse tissues, maintenance of cell cultures, measurement of mitochondrial bioenergetic parameters (oxygen consumption, membrane potential, NADH level, redox state of quinone pool) in isolated and in situ mitochondria, enzyme activity assays, western blot.

SELECTED PUBLICATIONS

Ravasz, D., Bui, D., Nazarian, S., Pallag, G., Karnok, N., Roberts, J., Marzullo, B. P., Tennant, D. A., Greenwood, B., Kitayev, A., Hill, C., Komlódi, T., Doerrier, C., Cunatova, K., Fernandez-Vizarra, E., Gnaiger, E., Kiebish, M. A., Raska, A., Kolev, K., Czumbel, B., … Chinopoulos, C. (2024). Residual Complex I activity and amphidirectional Complex II operation support glutamate catabolism through mtSLP in anoxia. **Sci Rep 14(1):** 1729.

Pallag, G., Nazarian, S., **Ravasz, D.**, Bui, D., Komlódi, T., Doerrier, C., Gnaiger, E., Seyfried, T. N., & Chinopoulos, C. (2022). Proline Oxidation Supports Mitochondrial ATP Production When Complex I Is Inhibited. **Int J Mol Sci 23(9):** 5111.

Ravasz, D., Kacso, G., Fodor, V., Horvath, K., Adam-Vizi, V., & Chinopoulos, C. (2018). Reduction of 2-methoxy-1,4-naphtoquinone by mitochondrially-localized Nqo1 yielding NAD+ supports substrate-level phosphorylation during respiratory inhibition. **Biochim Biophys Acta Bioenerg 1859(9):** 909–924.

Ravasz, D., Kacso, G., Fodor, V., Horvath, K., Adam-Vizi, V., & Chinopoulos, C. (2017). Catabolism of GABA, succinic semialdehyde or gamma-hydroxybutyrate through the GABA shunt impair mitochondrial substrate-level phosphorylation. **Neurochem Int 109:** 41–53.

Németh, B., Doczi, J., Csete, D., Kacso, G., **Ravasz, D.**, Adams, D., Kiss, G., Nagy, A. M., Horvath, G., Tretter, L., Mócsai, A., Csépányi-Kömi, R., Iordanov, I., Adam-Vizi, V., & Chinopoulos, C. (2016). Abolition of mitochondrial substrate-level phosphorylation by itaconic acid produced by LPS-induced Irg1 expression in cells of murine macrophage lineage. **FASEB J 30(1):** 286–300.