cofactors such as transition metals, and their insertions into cognate subunits require specific maturation components distinct from the Ccm-system I. In recent years, we achieved significant progress on our understanding of how the single Cu_B atom is inserted into the catalytic site of the cbb_3-Cox heme-copper oxidase. The entire biogenesis process of the cbb_3-Cox from the maturation of its *c*-type cytochromes and the insertion of its catalytic heme-copper (Cu_B) center to the assembly of the subunits to yield complexes and supercomplexes will be discussed, focusing on studies carried out with the anoxygenic photosynthetic bacterium *Rhodobacter capsulatus*.

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Metabolic heterogeneity in molecular subtypes of diffuse large B cell lymphoma

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Cells adapt their metabolism to satisfy changing biosynthetic and bioenergetic needs. Investigation of metabolic reprogramming in cancer has provided insights into the metabolic control of proliferation and survival. While the initial focus of this field has been aerobic glycolysis (the Warburg effect), increasing evidence points to a complex landscape of tumor metabolic circuitries beyond aerobic glycolysis, including varied contribution of mitochondria to tumor metabolism as well as heterogeneity in fuel utilization pathways. Our integrative dissection of metabolomic and proteomic signatures in diffuse large B cell lymphomas (DLBCLs) has revealed metabolic subtypes and previously unappreciated quantitative differences in mitochondrial pathways in these groups of tumors. We show that unlike DLBCL subtypes that are dependent on the cell receptor (BCR) survival signals and have a Warburg-like phenotype, nutrient and energy metabolism in OxPhos-DLBCL have a significant mitochondrial component marked by elevated mitochondrial electron transport chain (ETC) activity, increased mitochondrial ATP production, greater incorporation of fatty acid- and glucose-derived carbons into the TCA cycle, and increased lipogenesis from these carbon substrates. These findings provide a clear example of heterogeneity in fuel utilization pathways and mitochondrial contribution to biosynthetic needs even within the same disease entity. Importantly, the distinct metabolic fingerprints we have identified are associated with survival mechanisms and predictable metabolic vulnerabilities. Metabolic signatures may provide important insights into the molecular heterogeneity of DLBCL and reveal rational targets in these lymphomas.

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NQO1 in aging and disease: Novel roles of a quinone reductase

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Can modification of VDAC(s) cysteine residues act as a sensor of oxidative state of the intermembrane space of mitochondria?

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Voltage-Dependent Anion selective Channels (VDAC) are pore-forming mitochondrial outer membrane proteins. The three VDAC isoforms show conserved sequences, similar structures and the same gene organization [1]. The meaning of three proteins encoded in different chromosomes must thus be searched for subtle differences at the amino acid level. Among others, cysteine content is noticeable. In humans, VDAC1 has 2, VDAC2 has 9 and VDAC3 has 6 cysteines. VDAC3, the least characterized isoform, presents a set of cysteines predicted to be exposed towards the intermembrane space [2], making them a preferred target for oxidation by ROS. By mass spectrometry we found in VDAC3 a single disulfide bridge and other cysteine oxidated states [3]. Chemico-physical techniques revealed an important function of cysteines in the structural stabilization of the pore. Selective deletion by mutagenesis of VDAC3 cysteines, followed by *in vitro* conductance experiments and complementation assays in *Δporin1* yeast, highlighted their influence on the protein function [3]. This work provides evidence for a complex oxidation pattern of VDAC3, even though it is not directly involved in electron transport. We propose a role of VDAC3 in buffering the mitochondria ROS load and in keeping track of the redox level in the intermembrane space, eventually signaling it through conformational changes.

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Mitochondrial ATP-sensitive potassium channels (mitoK$_{ATP}$): Molecular identity and physiological role

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