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CIC biomaGUNE
CENTER FOR COOPERATIVE RESEARCH IN BIOMATERIALS

seminar

Tuesday, 16th July, 12.00 pm, Seminar Room

Host: Dr. Maurizio Prato

Between Energy Conservation and Energy Dissipation: The Dual Life of F-ATP synthase

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Mitochondria can undergo a Ca^{2+}-dependent increase of inner membrane permeability (the permeability transition, PT) causing inner membrane depolarization and cessation of ATP synthesis. The PT is mediated by opening of a high-conductance channel, the PT pore (PTP) or mitochondrial megachannel (MMC). Prolonged opening of the PTP is a causal event in cell death which is favored by oxidative stress, while it is inhibited by matrix H^+ and Mg^{2+}/ATP(ADP). Cyclophilin D (CyPD) is the best characterized protein modulator of the PTP and the receptor for its inhibitor cyclosporin A (CsA). The pursuit of the PTP has taken a new course after the discovery that CyPD interacts with, and modulates, the F_1FO (F)-ATP synthase. The subsequent demonstration that bovine, human, yeast and drosophila F-ATP synthases form Ca^2+-activated channels set the foundation for the hypothesis that the PTP originates from specific conformations of F-ATP synthase, an issue that is the subject of controversy [1,2]. We will discuss recent advances in this rapidly moving field based on (i) reconstitution of channel activity with highly purified F-ATP synthase preparations, (ii) site-directed mutagenesis of selected residues of F-ATP synthase and (iii) development of novel inhibitors identified by high-throughput screening.

1. Bernardi P & Lippe G (2018) Channel Formation by F-ATP Synthase and the Permeability Transition Pore: An Update. *Curr Opin Physiol* **3**, 1-5.
2. Bernardi P (2018) Why F-ATP Synthase Remains a Strong Candidate as the Mitochondrial Permeability Transition Pore. *Front Physiol* **9**, 1543.