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# Programme & Abstracts

AAI ABCD AGI SIB SIBBM SIBE SIBV SICA SIF SIGA SIMAG SIMGBM SIP MeT SIPaV

## P13.1 - The inhibition kinetics of the $Ca^{2+}$-activated F-ATPase by F1 inhibitors strengthens its role in the mitochondrial permeability transition pore formation

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The mitochondrial F-ATPase is responsible for ATP production, but also, most likely, forms the mitochondrial permeability transition pore (MPTP), in turn involved in mitochondrial dysfunctions and cell death. $Ca^{2+}$ can replace the natural cofactor $Mg^{2+}$ in the F-ATPase catalytic site and $Ca^{2+}$ increase in mitochondria triggers MPTP. Kinetic analyses point out a different response of the $Ca^{2+}$-activated F-ATPase with respect to the $Mg^{2+}$ F-ATPase to $F_1$ inhibitors. Quercetine inhibition of the $Mg^{2+}$ F-ATPase depends on ATP concentration, while the $Ca^{2+}$-F-ATPase inhibition only depends on $Ca^{2+}$ concentration. The $Mg^{2+}$ F-ATPase inhibition by NBD-Cl decreases when ATP decreases, while the $Ca^{2+}$-activated F-ATPase inhibition by NBD-Cl is lowered by both $Ca^{2+}$ and ATP reduction. However, NBD-Cl exerts on the two differently activated F-ATPases the same uncompetitive inhibition with respect to ATP and mixed-type inhibition with respect to either divalent cations. The uncompetitive inhibition between $Ca^{2+}$ and $Mg^{2+}$ and the higher steric hindrance of $Ca^{2+}$ suggest that, with respect to $Mg^{2+}$, $Ca^{2+}$ interacts with different aminoacids to activate the enzyme which would dissipate ATP and open the MPTP.

## P13.2 - Role of paraoxonase-2 in chemoresistance in T24 human bladder cancer cells

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Paraoxonase-2 (PON2) is an intracellular antioxidant and anti-apoptotic enzyme. An increased PON2 expression was described in several tumors, including bladder cancer (BC). The aim of this study was to investigate the role of PON2 in chemoresistance of T24 cells, a cell line from human urinary bladder carcinoma.T24 cells were transfected with pcDNA3-PON2 plasmid vector. Control cells were transfected with empty vector (pcDNA3) or treated with transfection reagent (mock). Transfected cells were treated with gemcitabine and cisplatin, drugs used in the BC management, and cell proliferation was measured by MTT assay.

Real-Time PCR and Western blot analysisshowed that, compared with mock and pcDNA3-treated cells, T24 transfected with pcDNA3-PON2 displayed significantly increased PON2 expression. PON2 upregulation led to a significant increase in cell growth, despite the treatment with gemcitabine and cisplatin.

Our results are the first evidence suggesting that PON2 overexpression could be involved in the increased chemoresistance of T24 cells and seem to suggest PON2 as a potential target for silencing in BC to improve the susceptibility to chemotherapeutics.

## P13.3 - The approach of intrasite differential inhibition of aldose reductase in counteracting the onset of diabetic complications and inflammation

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Aldose reductase (AR), a NADPH-dependent reductase, is involved in the onset of diabetic complications. Nevertheless, the ability of AR to reduce both aldoses and cytotoxic aldehydes, generated from lipids peroxidation, poses the question of whether AR might be classified as a detoxifying enzyme. In addition, AR is able to reduce glutathionylhydroxynonanal, thus leading