

**P020** The role of oxidants and anti-oxidants in beta cell function and integrity

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**Background and aims:** The contribution of ROS and NO production to glucolipotoxic b-cell dysfunction and death are unknown. The aim of this work was to investigate the contribution of various antioxidants to protection from pro-inflammatory or glucolipotoxic conditions and in addition a possible novel role of Prx III the functionality of the insulin-secreting cells.

**Materials and methods:** Stably transfected rat insulinoma cells (RINm5F, exhibiting over or reduced expression of Prx III) or clonal BRIN BD 11 b cells or mouse islets were treated with various stressors (cytokines 0,3125U/ml IL-1 $\beta$ , 31,25U/ml TNF- $\alpha$ , 15,625U/ml IFN- $\gamma$ , hydrogen peroxide 0,3%, high glucose 25mM, or palmitic acid 0,1mM) in the presence or absence of antioxidants such as superoxide dismutase (20U/ml), catalase (100U/ml), NAC (0,2mM), Apocynin (0,2mM), or iNOS inhibitor (0,2mM). Disruption of the mitochondrial transmembrane potential was determined by DiOC<sub>6</sub>(3) absorption and fluorescence emission spectroscopy. Insulin secretion was determined from viable cells by ELISA. Cell viability was determined by MTS.

**Results:** Treatment with cytokines, hydrogen peroxide, but not palmitic acid, or high glucose reduced insulin secretion in the BRIN BD11 cell line. Moreover, in RINm5F cells exhibiting reduced expression of Prx III, addition of cytokines, hydrogen peroxide, or streptozotocin or alloxan caused cell death, which was associated with elevated levels of iNOS and cleavage of PARP. Furthermore, antioxidants such as catalase, superoxide dismutase and N-acetylcysteine protected against cytokines, hydrogen peroxide, and high glucose. Cells over-expressing Prx III were protected due to elevated mitochondrial antioxidant activity.

**Conclusion:** Cellular antioxidants play a crucial role in protecting from cytokine or chemical stimulated ROS production, thus maintaining insulin secretion and preventing  $\beta$ -cell death.