

**P057** Does Aminoacetone Accumulation Contribute to Pancreatic Beta-Cell Death in Diabetes?

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Aminoacetone (AA) is a threonine and glycine catabolite recently implicated as a source of methylglyoxal (MG) in *diabetes mellitus*. Oxidation of AA to MG, H<sub>2</sub>O<sub>2</sub> and NH<sub>4</sub><sup>+</sup> is catalyzed by a copper-dependent semicarbazide sensitive amine oxidase as well as by Cu(II) and Fe(II) ions. As MG and H<sub>2</sub>O<sub>2</sub> are reportedly toxic to pancreatic  $\beta$ -cells and AA is a potential source of oxyradicals by metal-catalyzed oxidation, we proposed a pro-oxidant role of AA in  $\beta$ -cells. AA toxicity to RINm5f cells was monitored with MTT at 24 h after AA (0.1–10 mM) treatment. AA-induced cell death was enhanced upon Cu(II) (5–100  $\mu$ M) administration and partially inhibited by the superoxide dismutase (50 U/mL), catalase (5  $\mu$ M)), bathocupreine (1 mM)), and *N*-acetylcysteine. Furthermore, AA was found to increase pro- (*Bax*) and anti-apoptotic (*Bcl-2*, *Bcl-xL*) expression proteins, raise Ca<sup>2+</sup> influx and increase mitochondrial inner transmembrane potential. Considering that AA is produced into the mitochondrial matrix and that  $\beta$ -cells display low expression of antioxidant enzymes, it is tempting to suggest that AA-generated H<sub>2</sub>O<sub>2</sub> reacts with Cu(I) to form reactive oxygen species and thereby contribute to pancreatic  $\beta$ -cell injury and death. Support: FAPESP, CNPq, Milênio Redoxoma.