Calcium regulation of apoptosis in pancreatic acinar cells

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We have studied calcium regulation of induction of apoptosis in pancreas. In pancreatic acinar cells, the earliest events were found to be cytosolic calcium elevations due to release of calcium from intracellular stores. As a result of that calcium levels also increased in mitochondria aiding mitochondrial depolarization and mPTP. High mitochondrial calcium at the time of oxidant stress was found to be the crucial factor in the cell fate. When mitochondrial calcium was low, then apoptosis did not occur regardless of other stores' content. We also studied Bcl-2 family members, well known regulators of apoptosis involved in regulation of intracellular calcium homeostasis. Most interesting was a potential link between Bcl-2 family proteins and a passive calcium release from the intracellular stores. We found that BH3 mimetics induce calcium release from the ER that leads to the formation of calcium plateau. Inhibition of either IP3Rs or RyRs reduced but did not abolish BH3-elicited calcium release. Further, we have shown that loss of Bcl-2 protein decreases calcium release from the ER and increases cytosolic calcium clearance in pancreatic acinar cells.

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