Mitochondrial defects, such as mutations caused by reactive oxygen species (ROS), might be associated with pancreatic beta-cell failure in the course of diabetes. The weak expression of natural enzymatic defences, e.g. catalase and superoxide dismutase, renders beta-cells particularly susceptible to ROS. Mitochondria are the principal source of ROS. Such mitochondrial ROS generation is favoured by various conditions; e.g. aging, mutations of the mitochondrial genome, or lipotoxicity. For instance, ROS content in isolated islets of Zucker diabetic fatty rats is higher, suggesting that ROS may participate in the impairment of glucose-induced insulin secretion observed in association with type 2 diabetes. However, molecular mechanisms responsible for ROS induced impairment of metabolism secretion coupling are not fully understood. It has been well characterized that transient exposure of beta-cells to oxidative stress interrupts the transduction of signals normally coupling glucose metabolism to insulin secretion. Then, one can ask the question if such a transient oxidative stress in insulin secreting cells could cause long-term impairment of beta-cell function. Recent data from our laboratory show that INS-1E beta-cells can memorize one single transient oxidative stress as revealed by dysfunction of mitochondrial metabolism and glucose-stimulated insulin secretion. This memory was promoted by transient ROS exposure that induced molecular changes maintaining subsequent endogenous ROS generation.