The morphology of mitochondrial network is highly variable and there is a substantial body of evidence for close relationship between cellular physiology and mitochondrial network organization. We set out to investigate whether pathology of diabetic β-cells is reflected by the altered morphology of mitochondrial network. Conventional confocal microscopy does not provide sufficient *z* axial resolution to realistically visualize 3D mitochondrial network, and therefore we applied high resolution 4Pi microscopy with *z* axial resolution of about 100 nm. Matrix-addressed GFP was lentivirally expressed in Langerhans islets isolated from diabetic Goto Kakizaki or control wistar rats. We demonstrate that β-cells within the Langerhans islets from diabetic Goto Kakizaki rats exhibited more disintegrated mitochondrial network compared to those from control Wistar rats. Observed average diameter of mitochondrial tubule was 236 ± 27 nm in Goto Kakizaki and 214 ± 16 nm in control rats. Our next aim was to characterize organization of mt nucleoids in primary β-cells of Langerhans Islets. To visualize mt nucleoids we used immunocytochemistry or lentiviral expression of GFP-labeled TFAM protein, which is known to have a crucial role in assembling of mammalian mt DNA.

doi:10.1016/j.bbabio.2010.04.423

18P.3 Mitochondrial fusion is an early and protective step of autophagy

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Autophagy is a catabolic process that allows the recycling of components of the cell under for instances conditions of nutrient depletion. Autophagy has been long regarded as an unselective process, but under some circumstances specific organelles like mitochondria are selectively engulfed by autophagosomes. We therefore explored whether mitochondrial morphological changes were associated with the onset of autophagy. Induction of autophagy led to mitochondrial elongation both *in vitro* and *in vivo*. Mitochondrial elongation correlated with increased fusion rate and required the core mitochondrial fusion proteins, as substantiated by a genetic analysis. A combination of real time imaging and the use of a pharmacological inhibitor indicated that cAMP-PKA axis mediates starvation-triggered mitochondrial elongation by blocking translocation of the pro-fission protein DRP1 to mitochondria. Elongation protected against mitophagy and was essential in the maintenance of ATP levels during periods of starvation. Ablation of the required pro-fusion genes converted mitochondria into sinks for ATP and caused starvation-induced death, showing a protective role for these morphological changes during periods of limited substrate supply. Thus, mitochondrial shape changes play an important role in the regulation of the fate of cells undergoing autophagy.

doi:10.1016/j.bbabio.2010.04.424

18P.4 Changes in sympathetic and parasympathetic regulation connected with succinate dehydrogenase and α-ketoglutarate dehydrogenase activity in different physiological states of the organism

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The study was carried out by a novel cytobiochemical method highly sensitive to changes *in vivo* due to preservation *ex vivo* the native structure of mitochondrial network [1]. Succinate dehydrogenase (SDH) and α-ketoglutarate dehydrogenase (KDH) activity was measured in glass-adhered lymphocytes in smear of blood by nitro-blue-tetrazolium reduction [1]. The set of selected maximally identical, premature (6 week) male rats (6–8) was investigated simultaneously. The following states were investigated: intact state, after adrenaline (ADR) administration, under emotional immobilization stress in a box, newborn, premature and soon after maturation, depending on mother suckling, and under the action of biologically active substances. Healthy volunteers and patients with hypertension were also examined. The quiescent state in all cases is characterized by low activities of SDH and KDH well balanced with a very small prevalence of KDH over SDH. Together with increase in influence of exogenous or endogenous ADR activation of SDH per 200–400% and more is observed. This is accompanied initially by activation of KDG too, but to a lesser extent, while under more strong ADR action KDH activity falls dramatically. The state of highly active SDH without controlling action of KGL oxidation is non-stable and transforms into inhibition of both dehydrogenases under progression of influence. The moderate SDH activation is accompanied by increase in succinate-dependent Ca^{2+} accumulation in mitochondria, while hyperactivation is connected with its fall. Phases of activation and hyperactivation are respectively connected with elevation and lowering of immune function of neutrophils. Under strengthening of cholinergic regulation, related to maturation of animal, in contrast, increase in KDG activity and diminishing of SDH activation by ADR were observed. The data obtained demonstrate on a larger scale the discovery in isolated mitochondria of unification of sympathetic and parasympathetic regulation in the single system with oxidation of only the two substrates — succinate and α-ketoglutarate and explain the finding receptors also to only these two intermediates of oxidation [1].

This work was supported by the Federal program “Scientific and scientific pedagogical staff of the innovation Russia” (project no. 02.740.11.0312).

Reference

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doi:10.1016/j.bbabio.2010.04.425

18P.5 Mitochondria from *Artemia franciscana* embryos exhibit a truncated form of ant, associated with atypical effects of its ligands on Ca^{2+} uptake capacity and unique morphology of matrix Ca^{2+} precipitates

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