we carried EST analysis which allowed us to identify different UCP genes and external and internal ND sequences. Expression was studied by semi-quantitative RT-PCR, in etiolated hypocotyls and heterotrophic cultured cells of *Glycine max* L. Merr treated with 1 mM SA for different times. Mitochondria from SA-treated hypocotyls had higher AOX capacity and protein content. Succinate oxidation was not affected while NADH respiration was reduced. A general up-regulation of energy dissipation systems is observed in both hypocotyls and cells. Interestingly, although the different AOX genes are expressed at different levels in both plant materials, as determined by the number of PCR cycles needed for amplification, the kinetics of induction, at the time-points analysed, was conserved between hypocotyls and cells.

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S12.27 Early mitochondrial damage in hippocampus of pilocarpine-treated epileptic rats

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An animal model which has been proven to be appropriate to study human temporal lobe epilepsy (TLE) with Ammon's horn sclerosis (AHS) is the pilocarpine-treated epileptic rat. In this model, the animals are treated systemically with a dose of the muscarinic agonist pilocarpine that induces an acute limbic status. The status epilepticus is terminated after 40 min with diazepam. This acute intoxication is followed by a 'latent' (i.e. seizure free) period lasting usually 1–2 weeks, followed by a chronic epileptic condition with spontaneous seizures, resembling human TLE. From the point of view of hippocampal pathology, pilocarpine-treated rats display changes closely resembling the AHS condition that is seen in the majority of TLE patients. It consists of segmental loss of pyramidal neurons in the CA1, CA3, and CA4 sectors of the Ammon's horn. In the present work we investigated the time course of hippocampal damage after systemic pilocarpine treatment applying metabolite determinations, determinations of hippocampal cell counts and determinations of mitochondrial function and of mtDNA copy numbers. We observed that the pilocarpine-induced status epilepticus is accompanied by early accumulation of lactate and succinate, decline of N-acetyl aspartate and decreased mtDNA copy numbers. These results can be explained as consequence of status epilepticus associated ROS formation.

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S12.28 Rescue of myopathic collagen VI null mice by genetic inactivation of mitochondrial cyclophilin d

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Progress in understanding the pathogenesis of collagen VI-diseases has been made in mice with disrupted *Col6a1* gene, which display an early-onset myopathy due to lack of collagen VI. Mitochondria in skeletal muscle fibers and in myoblasts from *Col6a1*$^{-/-}$ mice depolarize in presence of oligomycin, an anomalous response that is corrected by cyclosporin (CsA). This finding suggests that in collagen VI-myopathies flickering of the permeability transition pore (PTP) is increased and causes depletion of pyridine nucleotides, progressive impairment of respiration, and switch of the F1FO ATP synthase into an ATP hydrolase maintaining the membrane potential at the expense of glycolytic ATP. This interpretation is consistent with the therapeutic effect of treatment of *Col6a1*$^{-/-}$ mice with CsA, which desensitizes the PTP *in vivo*. To further test the role of the PTP in the pathogenesis of collagen VI-myopathies, we have generated *Col6a1*$^{-/-}$*Ppif*$^{-/-}$ mice (*Ppif* is the unique mouse gene encoding for mitochondrial cyclophilin, whose inactivation desensitizes the PTP). We will report the striking rescue of *Col6a1*$^{-/-}$*Ppif*$^{-/-}$ mice from the myopathy despite their total lack of collagen VI.

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S12.29 Mitochondrial respiration in skeletal muscle from Zucker Diabetic Fatty rats

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Mitochondrial dysfunction in skeletal muscle has been suggested to underlie the metabolic aberrations seen in type 2 diabetes mellitus, such as intramyocellular lipid (IMCL) accumulation and a decreased (fat) oxidative capacity. Here we tested this hypothesis by analyzing respiration in isolated mitochondria from 14 week-old Zucker Diabetic Fatty (ZDF) rats vs. healthy controls. At this age, ZDF rats are characterized by elevated IMCL levels and hyperglycemia. Our data show that state 3 respiration fuelled by pyruvate was slightly, but non-significantly, reduced (369.9±15.7 vs. 395.6±9.1 nmol O_2/mg/min; p=0.19; n=6) in mitochondria from ZDF rats as compared to healthy controls. Oligomycin-induced state 4 was significantly reduced in diabetic rats (9.7±0.4 vs. 11.9±0.5 nmol O_2/mg/min; p=0.008; n=8). Surprisingly, diabetic rats displayed an enhanced state 3 respiration fuelled by palmitoyl-CoA plus carnitine (157.0±9.5 vs. 123.4±12.8 nmol O_2/mg/min; p=0.06; n=6), while state 4o respiration remained unchanged (15.4±0.4 nmol and 15.2±1.1 O_2/mg/min (p=0.9; n=6) in ZDF vs. control. Furthermore, mitochondria from ZDF rats displayed a decreased sensitivity to fatty acid (FA)-induced uncoupling as evidenced by an increase in EC_{50} (372±19 vs. 283±16 nM free palmitate, p=0.01; n=4). This difference disappeared in the presence of the adenine nucleotide translocator (ANT) inhibitor carboxyactractyloside (Catr). Whether differences in muscular UCP3- or ANT levels contribute to these observations is currently under investigation. In conclusion, sensitivity for FA-induced uncoupling is reduced in 14-week old ZDF rats, but remarkably, mitochondrial fat oxidative capacity is improved.

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