Cellular energy needs are largely met by the mitochondrial oxidative phosphorylation system. The components of this system are encoded by both the nuclear and mitochondrial genomes. Given the greater energy needs of proliferating cells, it is not surprising that mitogenic factors trigger increased expression of mitochondrial genes while induction of cell quiescence has the opposite effect. An increase in both mitochondrial genome copy number and RNA level observed during terminal differentiation of myogenic cells to myotubes may be part of a myogenic differentiation program and may reflect mitochondrial response to metabolic factors that accompany their differentiation.

Insulin is the most potent anabolic hormone; its primary effect is to maintain blood glucose levels, but it also activates lipogenesis, protein synthesis and the mitogenic response. The cells most sensitive to insulin are muscle cells, liver cells and adipose cells. The stimulating effect of insulin on the mitochondrial capacity for oxidative phosphorylation may in part reflect increased expression of mitochondrial genes in skeletal muscle in situ.

Aim. The goal of this study was to quantify mitochondrial gene expression over the course of cellular quiescence and differentiation.

Materials and methods. Rat L6 myoblasts and HTC-IR hepatocytes were grown in DMEM supplemented with 10% FBS. Then, L6 cell differentiation was induced by culturing the cells in the presence of 2% FBS, and HTC-IR cells were made quiescent by lowering serum concentration in the medium to 1% FBS. RNA concentrations were quantified by RT-real time PCR. RNA was reverse transcribed using SuperScript II RT and random hexamers. The real-time PCR reactions were carried out with DNA-specific dye SYBR Green I. Myoblasts differentiation was analyzed by morphological markers (cells were considered fused if they contained at least three nuclei within one cytoplasmic continuity) and biochemical markers of myogenesis (immunostaining with antibodies to myogenin and myosin heavy chain). Cell proliferation was assayed by the incorporation of \(^{3}H\)-thymidine.

Results. Low growth factor concentration in medium decreased proliferation of both cell types and induced differentiation of myoblasts. The expression of all mitochondrial genes decreased in quiescent hepatocytes whereas it increased in quiescent differentiated myotubes, as compared with proliferating cells, similarly to reflecting the expression of the insulin receptor gene, both in myoblasts and hepatocytes. The kinetics of mitochondrial RNA levels were similar to the expression patterns of two nuclear genes, subunit e of mitochondrial ATP-synthase and uncoupling protein-2, however they did not reflect changes in mitochondrial DNA
content. Insulin accelerated myogenesis and expression of both mitochondrial and nuclear genes in differentiated myotubes but not in quiescent hepatocytes.

**Conclusion.** Our studies prove that myogenesis may require the orchestrated transcriptional activation of both mitochondrial and nuclear genes and provide additional evidence confirming the regulatory impact of insulin on the function of muscle mitochondria. Although the exact mechanisms controlling mitochondrial gene expression remain to be established, these studies support the interesting hypothesis that circulating insulin may play an important role in maintaining the physiological function of mitochondria in different cell types, including skeletal muscles. Conversely, altered insulin secretion may affect cellular energy balance and result in development of several pathophysiological conditions as a consequence of mitochondrial dysfunction.

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