Abstract:

We can meet pathological hypoxia in the cases of hearth attack, ischemic stroke, but also during tumor invasion, thanks to insufficient angiogenesis. The activation of HIF-1 factor during hypoxic conditions is crucial for the cell survival. This factor modulates energetic metabolism in favor of fast progressing glycolysis (with the contribution of glutaminolysis) which provides to cell enough ATP and "building blocks", while suppressing Krebs cycle and respiration because of shortage of oxygen. The thesis studies energetic metabolism of HepG2 cells (derived from liver carcinoma) which are cultivated in the media with various energetic substrates, i. e. glucose or galactose (always together with glutamine and pyruvate) under the hypoxic conditions (5% O_2). HepG2 cells use particularly oxidative metabolism for ATP and "building blocks" production under the normoxic conditions while hypoxic environment causes metabolic shift in glycemic condition. Interestingly, cells cultured in galactose (glutamine) didn´t switch the energy metabolism from oxidative to aerobic glycolysis such as cells cultivated in glucose, although HIF-1 factor was stabilized. We found that enhanced activity and integrity of mitochondria, enhanced maximal capacity and reserve capacity of respiration chain correlates with preserved respiration and oxidative phosphorylation of HepG2 cells cultured in galactose and hypoxia. The process of respiration and oxidative phosphorylation require enough substrate derived from Krebs cycle which correlates with low production of lactate. HIF-1 causing changes of energetic metabolism towards fast aerobic glycolysis in HepG2 cells cultured in glucose under hypoxic conditions is reflected in fast proliferation and resistance of these cells to oxygen shortage. However, the cells cultured in galactose proliferate two times slower than the cells cultured in glucose under hypoxic and normoxic conditions which reflects slow processing of galactose.

If we know that tumors which use oxidative metabolism are less resistant and proliferate slowly, such switch of energetic metabolism could be used in cancer therapy.

Key words: Hypoxia, HepG2, HIF-1, energetic metabolism, galactose, glucose, mitochondria, aerobic glycolysis.