GLYCOLITIC AND MITOCHONDRIAL ALTERATIONS IN DENGUE-2 VIRUS INFECTED HUMAN HEPATIC CELLS

Pereira da Silva, AP¹; xxxxx, L²; Costa LS²; Galina A² and Da Poian AT².

¹Departamento de Química, Instituto de Ciências Exatas, Universidade Federal Rural do Rio de Janeiro, Rio de Janeiro;
²Instituto de Bioquímica, Universidade Federal do Rio de Janeiro, Rio de Janeiro.

Dengue virus (DENV), a mosquito-transmitted single-strand virus, is prevalent in over 100 tropical and subtropical countries. Approximately 390 million people are infected each year and 96 million manifest with clinically apparent disease. The molecular mechanisms involved in the cellular dysfunction of dengue severity remains poorly understood, however it is already known that viruses depend on host cellular metabolism and energetic homeostasis for their replication. For this reason we analyzed intracellular aerobic and anaerobic metabolic changes associated with DENV-2 infection of human hepatoma HepG2 cells. HepG2 cells seeded for 48 hours under standard growth condition were either mock-infected or infected at 1 p.f.u./cell with DENV-2 asiatic strain 16681. Assays were performed 16, 24 and 36 h post-infection. Glycolytic flux was evaluated through the spectrophotometric measurement of lactate in culture medium and activities of glycolytic enzymes hexokinase, phosphoglucose isomerase, phosphofructokinase, aldolase, gylceraldehyde-3-phosphate dehydrogenase, phosphoglycerate kinase, phosphoglycerate mutase, enolase, pyruvate kinase and the pentoses phosphate pathway enzyme, glucose-6-phosphatde dehydrogenase (G6PDH). At 24 hpi it was observed a decrease in the activities of hexokinase, piruvate kinase and G6PDH. For this reason this enzymes were also analyzed on an earlier time (16 hpi) and only the activity of G6PDH decreased. Despite these effects, NADPH levels and lactate release were not altered by infection. Aerobic metabolism was evaluated through measurement of oxygen consumption. DENV-2 promoted a decrease in several mitochondrial respiratory parameters studied. Although no difference was observed at 16 hpi, the basal and maximum oxygen consumption decreased on infected cells at 24 and 36 hpi while olygomycin-independent oxygen consumption was affected only at 36 hpi. Since these metabolic changes occur with no change of cell viability it is possible that these events are involved in cell damage that anticipates cell death.

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