The host-cell fermentative metabolism is modulated during *Mycobacterium leprae* infection: New targets to control leprosy.

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Introduction: Leprosy is a chronic mycobacterial infection that causes axonal degradation, fibrosis and demyelination of peripheral nerves. Multidrug regimens are used worldwide,However, in countries where leprosy is endemic the number of new cases remains stable during the last decades. Lactate is a product of aerobic glycolysis that plays important roles in the axonal metabolism, which is released by Schwann cell, representing the main fuel source for axons and neurons. **Objectives:** To evaluate the release of lactate and modulation of glucose metabolism in infected Schwann cells. **Material and Methods:** lactate concentration measurement made by lactate kit liquiform and the analysis of the genes was observed through RT-PCR**. Results and Discussion**: Our results indicate that Schwann cells infected with *Mycobacterium leprae* showed a two-fold reduction in lactate release to the supernatant. In contrast we observe over expression of the genes corresponding to extracellular monocarboxylate transporter MCT1, MCT2 and MCT4, which are responsible to transport lactate, pyruvate and ketone bodies. When using 6-ANAM, an inhibitor of the key enzyme of the oxidative phase of pentose phosphate pathway, the Glucose-6-phosphate dehydrogenase (G6PD) we successfully recovered lactate release of infected Schwann cells, concomitantly with the reduction of viability of *Mycobacterium leprae*. The pentoses pathway it's an important pathway that generates NADPH for reductive biosynthesis and glutathione regeneration. We observed that infected Schwann cells presents an increase in G6PD activity and expression, being more resistant to oxidative stress generated by H_2O_2. This oxidative stress protection was avoided by 6-ANAM or by the glutathione synthesis inhibitor BSO, an inhibitor of gamma-glutamylcysteine synthetase. **Conclusions**: Reducing the level of lactate released by Schwann cells can result in deprivation of energy to the axons, highly dependent on this source of carbon. Inhibition of pentose pathway could provide therapeutic effects on leprosy, combined with the restoration of lactate for neuronal nutrition.