M. leprae Modulates Glucose Uptake and Metabolism in The Host Cell

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INTRODUCTION: Leprosy is an infectious disease that affects mainly cells of the peripheral nervous system, causing axonal demyelization. Axonal homeostasis is dependent of Schwann cell lactate. Here we measured glucose metabolic parameters in M. leprae infected Schwann cells and in peripheral blood mononuclear cells (PBMC) of patients.

METHODS: Glucose uptake was analyzed in schwannoma cell line exposed to M. leprae by 2-NBDG incorporation. Lactate production was quantified by quinone imine generation. The activity of glucose 6-phosphate dehydrogenase (G6PD) and phosphofructokinase-1 (PFK) was monitored by the reduction of NADPH or oxidation of NADH, respectively. Mitochondria potential was determined in vitro-infected cells by TMRM. Cellular membrane potential was measured using a CCCP exposed control.

RESULTS AND DISCUSSIONS: Glucose uptake and G6PD activity where increased approximately 1.9x and 2.62x in infected cells, compared with the control. In contrast, PFK activity was 27.5 % reduced in infected cells, compared with the control. Lactate supernatant levels declined to 47% in infected cultures and halved in virchowian patients serum, when compared to control and healthy serum respectively. Curiously, a drastic reduction in mitochondrial activity, about 36% was observed by TMRM fluorescence in in vitro-infected cells.

CONCLUSIONS: A paradoxical reduction of both fermentative and oxidative pathways was observed in leprosy in vitro model. We believe that this phenomenon is a collateral effect of a strong anabolic demand for glucose, in order to provide carbon and NADPH for lipid synthesis. The observed reduction in Schwann cell lactate levels can be involved in the neuropathology of leprosy, low lactate levels can generate axonal energy deprivation. More studies on the bacterial modulation of these pathways could help identifying new therapeutic targets and understanding leprosy neuronal pathogenesis.

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