IMPACT OF HIGH EXTRACELLULAR LACTATE ON INDUCED PLURIPOTENT STEM CELL METABOLISM AND PLURIPOTENCY

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Induced pluripotent stem (iPS) cells hold the potential to drastically improve cell-based therapies in the near future. However, in order for stem cell therapies to become clinically feasible, these cells must be generated in sufficient quantity and quality. This aim will require a comprehensive understanding of how environmental conditions affect iPS cell metabolism and pluripotency. Rapidly proliferating cells, including cancer and iPS cells, consume glucose and secrete lactate at high rates, even in the presence of sufficient oxygen, a process referred to as the Warburg effect. In cancer cell metabolism, lactate accumulation is associated with cancer stem cell-like gene expression, drug-resistance, metastasis, and poor prognosis in breast cancer patients. Elevated lactate conditions have also been shown to preferentially cause iPS cells to differentiate into cardiomyocytes in glucose-deficient media. Yet, there remains an incomplete understanding of the role of lactate in stem cell metabolism and pluripotency in glucose containing media. This study examined the impact of extracellular lactate on the metabolic activity and pluripotency of iPS K3 cells grown with sufficient glucose. Extracellular glucose, lactate, and amino acid concentrations were monitored throughout the experiment to determine the extracellular consumption or production fluxes. High extracellular lactate resulted in altered cell metabolism, including decreased lactate production while glucose consumption remaining unchanged. These results support hypotheses that there is a possible redistribution of carbons within metabolism under high extracellular lactate, with a larger portion of carbon entering the tricarboxylic acid cycle. The implications of these findings towards understanding iPS cell metabolism and designing cell culture conditions to limit lactate accumulation will be discussed.