In the past years it has been shown that bone marrow-derived mesenchymal stem or stromal cells (BM-MSCs) have a high potential for cell-based therapies and tissue engineering applications because of their multilineage differentiation potential and their immunomodulatory properties. However, bone marrow presents several disadvantages, namely low frequency of MSCs, high donor-dependent variations in quality and the isolation procedure is painful and implies the risk of infection. In search of alternative sources of MSCs, the umbilical cord (UC) tissue gained more and more attention. Since the UC is discarded after birth, the cells are easily accessible without ethical concerns. We isolated a population of plastic-adherent mesenchymal stem cell-like cells from human UC-tissue, which exhibit a high proliferative potential and express several MSC markers, including CD44, CD73, CD90 and CD105 (negative for CD31, CD34 and CD45). Moreover, the cells display multilineage differentiation potential. The aim of this study was to shape the microenvironment of the cells with regard to different oxygen concentrations and cell-cell interactions with immune cells. Therefore, the oxygen consumption, as well as the metabolic activity and HIF-1α target gene expression were determined. In addition, immunomodulatory properties of MSC-like cells were analyzed by direct and indirect co-culture experiments using peripheral blood mononuclear cells (PBMC) in CFSE-based proliferation assays. Our study revealed that UC-derived MSC-like cells consume 2-3 times less oxygen under hypoxic conditions (1.5% O\textsubscript{2}, 2.5% O\textsubscript{2} and 5% O\textsubscript{2}) as compared to 21% O\textsubscript{2} control. Hypoxic culture conditions caused stabilization of HIF-1α protein and subsequent regulation of its target genes, involved in glucose metabolism. Moreover, UC-derived MSC-like cells showed increased proliferation at 2.5% O\textsubscript{2}. Furthermore, our results demonstrated that MSC-like cells do not induce proliferation of allogeneic PBMCs in vitro. Additionally, coculturing of MSC-like cells and PHA-stimulated PBMCs in direct or in transwell co-culture experiments led to a decrease of PBMC proliferation compared to PHA-stimulated control PBMCs, indicating invivo immunomodulatory properties.