Physiologic Oxygen Tension Enhances Proliferation, Resistance to Hypoxic Stress, and Telomerase Activity of Mouse Cardiac Mesenchymal Stem Cells

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Stem cell therapy is a novel and promising strategy that shows strong potential to treat heart disease, particularly heart attacks (myocardial infarction) and heart failure. Stem cells are usually cultured at atmospheric oxygen tension (21%); however, the physiological oxygen tension in the heart is only 3-7%, raising the possibility that 21% oxygen may be toxic to the cells. This study used cardiac mesenchymal stem cells (CMCs), a type of adult stem cell recently discovered in the heart. The purpose of this project was to analyze the effect of culturing CMCs at physiological oxygen tension (5%) versus atmospheric oxygen tension (21%) in order to determine the optimal oxygen tension to culture CMCs and, possibly, other types of stem cells. CMCs were cultured for 7 passages at 21% or 5% oxygen tension and then subjected to severe hypoxic stress (1% oxygen tension) for 24 hours. Trypan Blue staining was used to measure cell number and viability, and spectrophotometric assays were used to measure lactic dehydrogenase (LDH) release and telomerase activity (ELISA). Compared with 21% oxygen tension, 5% oxygen tension consistently improved cell morphology throughout 7 passages in culture, and significantly ($P<0.001$) increased cell number, proliferation, telomerase activity, and the ability of CMCs to withstand severe hypoxic stress. These findings demonstrate that, compared with the commonly used 21% oxygen, culturing CMCs at 5% oxygen markedly enhances their proliferative activity and resistance to stress, possibly via enhanced telomerase activity. Therefore, CMCs cultured at 5% oxygen may be more effective in vivo.

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