Cardiac Mesenchymal Cells Cultured at Physiologic Oxygen Tension Have Superior Therapeutic Efficacy in Mice with Heart Failure Caused by Myocardial Infarction

RESULTS

Effect of 5% Oxygen Tension on Morphology of Mouse Cardiac Mesenchymal Cells at Passage 2

A. Mouse CMCs at passage 2 were cultured at 21% O₂ for 5 days. B. Mouse CMCs at passage 2 were cultured at 5% O₂ for 5 days. Sears: 100 μm

Effect of 5% Oxygen Tension on Morphology of Mouse Cardiac Mesenchymal Cells at Passage 5

A. Mouse CMCs at passage 5 were cultured at 21% O₂ for 4 days. B. Mouse CMCs at passage 5 were cultured at 5% O₂ for 4 days. Sears: 100 μm

Echocardiographic Measurements

Effect of CMCs Cultured at 5% Oxygen Tension on Left Ventricular Ejection Fraction in Mice with Heart Failure

Normal Control: 57% Pre-Infarction: 49% Post-Infarction: 21% 5% O₂ CMCs: 51% 21% O₂ CMCs: 61%

Figures 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11

CONCLUSIONS

These results demonstrate for the first time that, compared with CMCs cultured at 21% O₂, CMGs cultured at 5% O₂ not only have greater proliferation and resistance to stress in vitro but also are more potent in increasing viable heart tissue and improving the function of the failing heart after myocardial infarction in vivo.

IMPLICATIONS

Until now, stem cells have usually been cultured at 21% O₂. This study suggests that we should use lower (physiologic) O₂ tensions instead. Importantly, the concept may also apply to other stem cells besides CMGs.

Major Implications:

- Since physiologic 5% O₂ tension increases CMG proliferation, using 5% O₂ will save time and money to produce the desired numbers of cells. Also, foster cell culture will help patients who urgently need stem cells.
- Since CMGs grown at 5% O₂ are better able to withstand hypoxic stresses, they may be better able to survive after transplantation into the ischemic regions of the heart where oxygen is very low (1-2%).
- Since CMGs grown at 5% O₂ proliferate more rapidly in vitro, they may proliferate more rapidly in vivo after transplantation.
- Since CMGs grown at 5% O₂ are markedly more effective in improving LV function after myocardial infarction, they may provide a new therapy for millions of patients with heart failure caused by myocardial infarction (heart attack), who currently have few or no options.

MEDICAL SIGNIFICANCE

Heart failure is a major healthcare problem, affecting 6 million Americans, with a 50% mortality at 5 years. Mounting evidence shows that stem cell therapy is beneficial to these patients and may prolong their life and alleviate their symptoms. Thus, improving the efficacy and cost-effectiveness of CMGs and other stem cells could benefit millions of patients and have important social and medical implications.

5% Physiologic Oxygen Tension

Culturing stem cells at 5% O₂ may improve efficacy of cell therapy for heart disease.

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