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Phenylethanolamine N-Methyltransferase (PNMT) as a Novel Marker for Cardiomyocyte Progenitor Cells

Background

Phenylethanolamine n-Methyltransferase (Pnmt) is an enzyme that converts norepinephrine (NE) to epinephrine (EPI). EPI and NE are the major circulating catecholamines in most mammals. In adults they are primarily produced in adrenergic neurons and adrenal chromaffin cells. During periods of acute stress, EPI and NE are important modulators of "fight or flight" responses. Their actions induce significant metabolic and physiologic responses, especially in the cardiovascular system where they strongly increase cardiac output by stimulating both the rate and the force of cardiac contractions.

During embryonic development, Pnmt is expressed in the heart early, prior to initiation of the beating activity. The current invention describes the use of the Pnmt gene to identify a population of progenitor or stem cells that can be used to repair and/or regenerate diseased or damaged tissue, including cardiac and neural tissue. Pnmt-positive progenitor cells can be isolated from various pluripotent stem cell cultures (e.g. adult bone marrow-derived stem cells, adipose derived stem cells, cardiac-derived stem cells, neural-derived stem cells, embryonic stem cells, etc.), or from developing (e.g. embryonic) or adult tissue/organs (e.g. heart). The isolated progenitor cells can then be expanded ex vivo and the resulting cells transplanted back into the donor as an isograft. In the donor, the transplanted Pnmt-positive progenitor cells may differentiate to provide, for example, cardiomyocytes to replace cells lost due to myocardial injury from ischemic cardiomyopathy, congenital heart disease, or myocardial infarction.

Invention

The current invention allows for identification of a population of progenitor/stem cells using Phenylethanolamine n-Methyltransferase (PNMT) as a novel marker.

Application

The current invention can be used to isolate a population of Pnmt-positive progenitor cells to be used for cellular replacement therapy for myocardial injuries and neurodegenerative disorders.

Advantages

- Use in gene therapies as isograft or allograft transplantations
- Use for the ex vivo production of catecholamines such as adrenaline (epinephrine) • Ability to alter transplanted cells to render them less likely to cause immune reaction
- Transplanted cells can differentiate in situ and better adapt to the host environment
- Transferred progenitor cells can be monitored by MRI or by bioluminescence imaging (BLI) to physically and functionally assess the potential of novel cardiac progenitor cells to regenerate damaged myocardium

Lead Inventor

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Selected References

Ebert SN, Rong Q, Boe S, Thompson RP, Grinberg A, Pfeifer K. Dev Dyn. 2004; 231(4): 849-58.

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