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Perspective

Stem Cell Therapy for Chronic Renal Failure

Lowell L Lewis*

Director, Montserrat Institute of Surgical Research and Education, Brades, Montserrat, West Indies

***Corresponding Author:** Lowell L Lewis, Director, Montserrat Institute of Surgical Research and Education, Brades, Montserrat, West Indies.

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Question

PCI– Percutaneous Renal Stem cell infiltration therapy.

Easier than renal transplantation.

Review Papers: Elsevier Biomaterials 2014.

Promotion of Cardiac differentiation of brown adipose derived stem cells by chitosan hydrogel for repair after myocardial infarction

Wang., *et al.* Tissue engineering Research Centre Academy of Military Medial Sciences Beijing China.

Other papers

Leiden University Medical Centre The Nederland's 2007.

Mesenchymal stem cells from ischaemic heart disease patients improve ventricular function after acute myocardial infarction in mice:

- (Bone marrow derived) Mesenchymal stem cells from ischaemic heart disease patients improve left ventricular function after acute myocardial infarction (Immuno-eficient mice).
- Preservation of Left Ventricular Function and Attenuation of Remodelling after Transplantation of Human Epicardium – Derived cells into the Infarcted mouse Heart

University of Western Ontario Canada 2014:

- Mesenchymal stem cell delivery strategies to promote cardiac regeneration following ischaemic injury.
- Xiamen University China in collaboration with University of Miami and Diabetes Research Institute Federation USA.
- Umbilical Cord Mesenchymal Stromal Cell with Autologous (iliac crest) Bone Marrow Cell Transplantation in established Type 1 Diabetes: A pilot randomized Controlled, Open Label Clinical Study, to assess Safety and Impact on Insulin Secretions.
- Different disease, but a good-example of multiple source stem cell therapy and proof that pluripotent Stem Cells delivered by intra-vascular end arteries do differentiate into the tissues of the target organ.
- Question? Why use Stem cells with the Diabetes defect gene.

Significance of this paper

- Different disease, but a good-example of multiple source stem cell therapy and proof that pluripotent Stem Cells delivered by intra-vascular end arteries do differentiate into the tissues of the target organ. Question? Why use Stem cells with the Diabetes defect gene.
- Includes use of percutaneous infusion of dorsal pancreatic artery.
- Confirms potential treatment of Pancreatic Carcinoma by percutaneous intravascular, or endoscopic pancreatic duct, ablation procedures, including laser activated Nano therapeutic agents.

Wang., *et al.* paper

Cardiac stem cell therapy

- Enhancing transplanted cell survival and engraftment.
- Genetic manipulation of stem cells.
- Beneficial environment.
- Non invasive delivery.

What are stem cells

Ovum and Spermatozoa

Figure 1

Human chromosomes

Figure 2

Stages of human fetus

Figure 3

Stem cell

Figure 4

Stem cells

- Pluripotent mesenchymal stem cell.
- "Orchestral Cascade of events, determined by a genetic code, that directs differentiation of stem cells, and the subsequent multiplication, changes in shape, content and functions of

their progeny, with specific instructions of when to be active or inactive, when to change from one tissue to another, what products to produce, when to multiply and when to die, depending on physical, chemical and electronic interactions in their environment".

Myocardial infarction

- Cause of death, No 1 global, 8.14 million.
- Years of life lost, 129 million DALYs.
- Real solution = Prevention (Diet and Smoking).

Canada mortality trends 2000 to 2010

Figure 5

Deaths from cardiac failure

?	per year	?% Deaths
Age	No	
25+	114	
35+	578	
45+	2,254	
55+	4,548	
65+	7,181	
75+	14,345	
85+	20,108	

Table 1

Interventions

- PCI– Percutaneous Renal Stem cell infiltration therapy.
- Easier than renal transplantation.

Heart vessels

Figure 6

Blocked vessels and infarct

Figure 7

Cardiac aneurysm

Figure 8

Percutaneous coronary angioplasty

Figure 9

Stenting

Figure 10

Thrombolysis

- TNKase Tenecteplase 50 mg $6,000.00.
- Plus Aspirin, Clopidogrel and Heparin.
- Question? TNKase + UCM Stem Cell Therapy.

Known

- Intra coronary autologous bone marrow cell transfer after myocardial infarction "The Boost Randomized Controlled Trial. By K Wollert., *et al*. Lancet July 2004.
- "Transfer of bone marrow cells enhanced Left Ventricular systolic function, primarily in myocardial segments adjacent to the infarcted area.

Study objective

- To prove that infarcted cardiac muscle can be repaired by localized delivery of a Mesenchymal Stem cells and Chitosan hydrogel therapeutic preparation.
- Chitosan will be described in the Method section of this presentation and the contents of following 3 slides are to be covered in remaining presentations.
- Question – Is Chitosan required to provide the structural framework for the mesenchymal cells to survive and to function.

Chitosan hydrogel

- A component of the crustacean skeleton, now utilized in the bioengineered 3D repair of cartilaginous, ligaments and skeletal injuries.
- Not produced by mammalian genomes, but has been shown to actively enhance collagen synthesis and increase the differentiation rate into cardiomyocytes.

Molecular structure of chitosan

De-acetylated Chitin, the structural element in the exoskeleton.

Figure 11

Rats

- Chitosan Hydrogel improves cell retention and survival.
- Replacing contractile cardio-myocytes an unmetchallenge.
- BADSC at Interscapular tissue of Sprague – Dawley Rats.
- Role of collagen synthesis in Extracellular Matrix on cardiac differentiation.
- Graft engraftment and survival assessed by optical bioluminescence.
- Structure and function determined by detailed histological analysisand echocardiography.
- Chitosan hydrogel delivery of BADSCs and effect on cardiac differentiation to be determined.

Questions

- Where are Nephrocyte precursors and progenitors?
- What is human equivalent of brown adipose tissue on the dorsal region of adult rats, which have enhanced cardiac differentiation in response to Chitosan components (D-Glu and N-AC-Glu)?
- Would umbilical cord or iliac crest bone marrow mesenchymal stem cell PCA delivered preparations achieve the same result?

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