STEM CELLS & TISSUE ENGINEERING
ASSOCIATED WITH POLYESTER MESH
SUPPORT DEVICE
FOR ISCHEMIC CARDIOMYOPATHY

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Cell transplantation has emerged as a novel strategy for myocardial regeneration.

Preliminary clinical results showed that cell bio-retention and engraftment within infarct is low and that extracellular matrix degradation and myocardial fibrosis contributes to LV dilatation and adverse remodeling.
Rationale of the Study

- The failing cardiac muscle needs to be supported to decrease ventricular wall stress.

- Isolated ventricular constraint therapy failed to demonstrate clear benefits.

- The goal of this experimental study is to evaluate intranfarct cell therapy associated with a polyester mesh cardiac wrap, using a collagen matrix as interface.
1. Ischemia - Reperfusion myocardial model (I/R)
2. Intrainfarct stem cell therapy
3. Ventricular constraint using a polyester mesh (Acorn-CorCap)
4. Implantation of cell-seeded collagen matrix between the heart and the polyester mesh
Surgical Steps

Cells Therapy

Mesh Wrap

Collagen Interface
GROUPS ( n = 15 sheep )

Ischemia (60 min) - Reperfusion (I/R)

Group 1: I/R without treatment (Control)
Group 2: I/R + Polyester mesh wrapping
Group 3: I/R + Stem Cells + Mesh wrapping
STUDY DESIGN

- Fat tissue biopsy
- Myocardial Ischemia + Cell therapy and/or Ventricular Constraint
  - Echocardiography
- Echocardiography Autopsy Histology

Timeline:
- J0: Cell Cultures
- J30
- J90
CELL THERAPY
In cooperation with Aalborg University, Denmark

Autologous adipose tissue derived stem cells (ASC)

- From sheep thoracic wall
- Cultivated in hypoxic conditions (5% oxygen)
- Labeled with BrdU (incorporated in cell ADN)

ADVANTAGES

- Easy sample removal (liposuction)
- Adipose tissue 100 times more abundant than bone marrow
- ASC can differentiate in endothelial cells and cardiomyocytes?
ADVANTAGES OF HYPOXIC CELL PRECONDITIONING

- STIMULATION OF PROTEINS EXPRESSION:
  HIF-1 (hypoxia-inducible factor), ANGIOPOIETIN-1, VEGF

- REDUCTION OF CELLULAR APOPTOSIS and CASPASE-3 ACTIVATION

- ALLOWS CELL TRAINING TO SURVIVE IN ISCHEMIC ENVIRONMENT
Methods

Myocardial Ischemia - Reperfusion

Cardiac Wrapping after Cell Tx
# RESULTS

## ECHOCARDIOGRAPHY

| Groups                  | LV end-diastolic Vol. (mL) |   | LV EF (%) |   | Deceleration Time (ms) |   |
|-------------------------|---------------------------|   |           |   |                         |   |
|                         | Pre Ischem.               | Post ischem | 3 mois   | Pre Ischem. | Post ischem | 3 mois | Pre ischem | Post ischem | 3 mois |
| Control                 | 39±2.5                    | 42.6±5.3    | 65±6.3   | 68.1±2.4    | 41±1.8      | 34.8±3.6 | 217±9.1     | 139±8.2      | 152±5.5 |
| Mesh Wrap               | 37.4±3.1                  | 39.8±4.5    | 35.6±5.1 | 67.5±1.6    | 39.7±2      | 44.1±2.3 | 212±6.1     | 142±7.3      | 136±4.7 |
| Stem Cells + Mesh Wrap  | 38±3                      | 42.4±4.3    | 32.6±4.1 | 68±2.1      | 38.8±1.9    | 55.8±3.8 | 215±8.0     | 140±6.3      | 195±9.5 |

**RESULTS**
RESULTS

ECHOCARDIOGRAPHY at 3 MONTHS

Control Group

Cell Tx + Cardiac Wrapping
Ventricular Constraint
Interface Heart - CorCap

Cell seeded collagen matrix
Treatment with Adipose Stem Cells

Myocardial Infarction

Angiogenesis
CONCLUSIONS

- Stem cell therapy reduces infarct size and fibrosis
- Ventricular wrapping limits adverse postischemic remodeling
- Collagen scaffold improves cell engraftment and reduces epicardial fibrosis
Cellular and tissue engineering associating a regenerative biological approach with a prosthetic support device should play a positive role in the treatment of ischemic heart failure.
The application of bioactive molecules and the recent development of nano-bio-technologies should open the door for the creation of « bioartificial myocardium »