



**COSTANZA EMANUELI**

**PROFESSOR OF VASCULAR PATHOLOGY AND REGENERATION  
BRITISH HEART FOUNDATION SENIOR FELLOW**



**Giornata della Scienza  
14 marzo 2014**

**Imperial College  
London**

 **University of  
BRISTOL**



Nata a Firenze (ospedale di Careggi) nel 1968

Scuola elementare Cesare Battisti

Scuola media Ottone Rosai

Liceo Scientifico GB Morgagni

Universita' di Firenze -Scienze Biologiche

Dottorato di Ricerca (una parte)

## I miei primi 25 anni



Firenze



Viareggio



Chianti

# ... e poi si cambia



San Francisco  
1995





**Bristol 2005**

**BHF Senior Lecturer /Ricercatore (2005)**

**Reader/ Professore Associato 2008**

**Professor/Professore ordinario 2010**



# Bristol University (my research lab team)



**Dr. Marie Besnier**  
Rouen University –  
Normandie - France



**Dr. Lynsey Howard**  
University of Glasgow –  
Glasgow, Scotland, UK



**Mr. Saran Shantikumar**  
University of Leeds/Oxford –  
England, UK

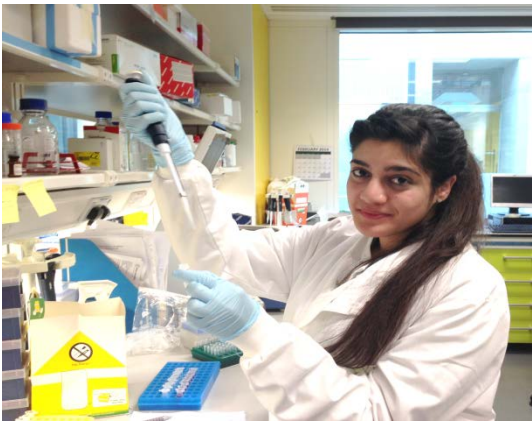


**Dr. Betty Descamps**  
Bordeaux Segalen  
University – Bordeaux -  
France



**Miss. Raheleh Amini**  
Shahid Beheshti  
University of Medical  
Sciences - Tehran -Iran

**6 new persons are joining soon**



**Huma Hossamudin,**  
**Medical student**  
**London, UK**



**Gianni Angelini**  
**BHF Professor of cardiac surgery**  
**Siena, Italy**

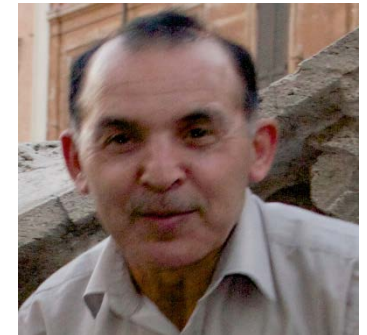


**Cristina Beltrami**  
**postdoc**  
**Lucca, Italy**



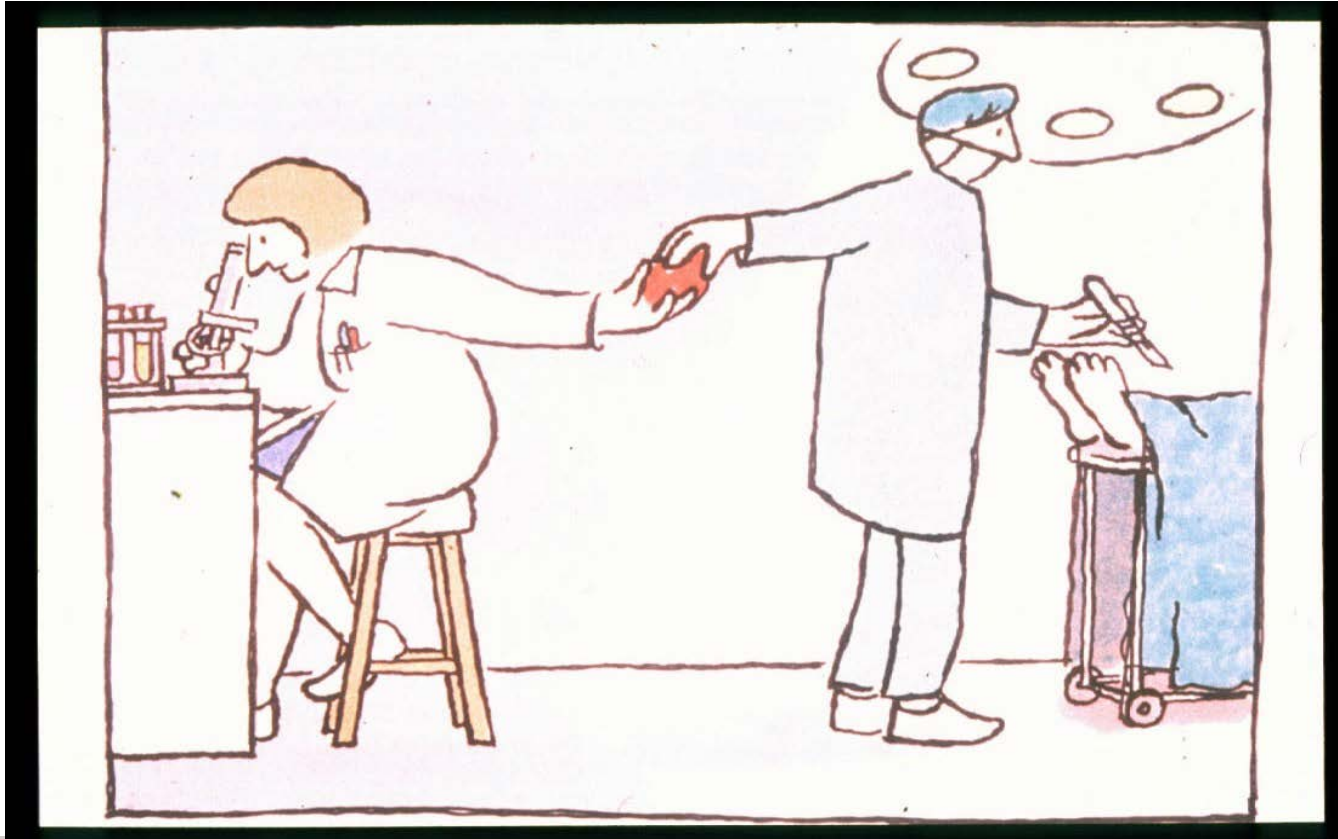
**Priyantha Kulatilake**  
**Medical student**  
**Cardiff, Wales, UK**

**Imperial college of London**  
**(my research team)**



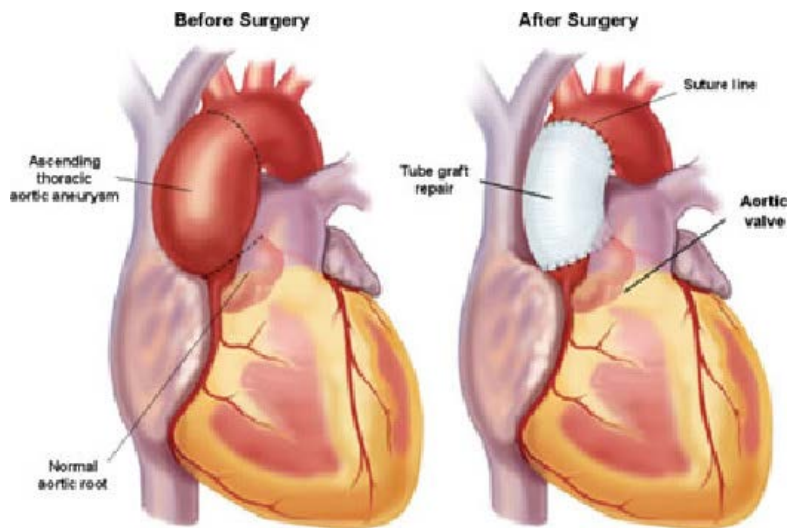
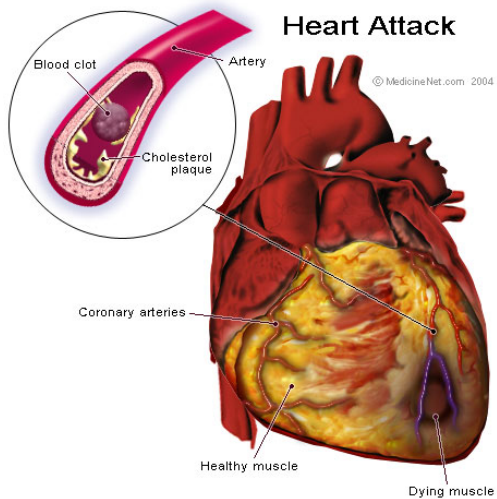
**Abas Laftha,**  
**Senior technician**  
**Basran, Iraq**

# Ricerca di base rivolta a migliorare le opzioni terapeutiche dei pazienti che necessitano chirurgia cardiovascolare

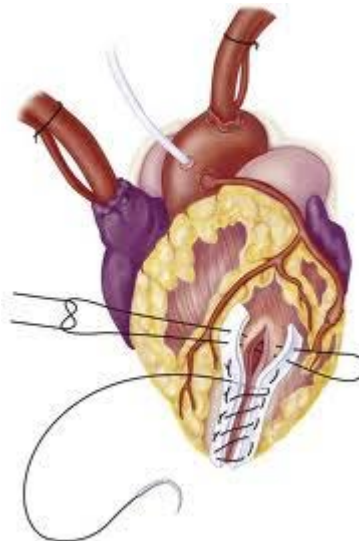


# Translational Focus of Bristol Regenerative Medicine

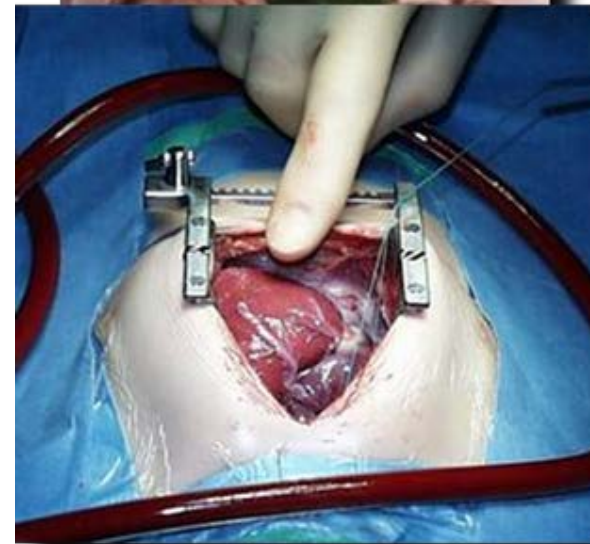
## ISCHAEMIC DISEASE



## THORACIC AORTA ANEURYSM



## SURGICAL THERAPIES FOR HF

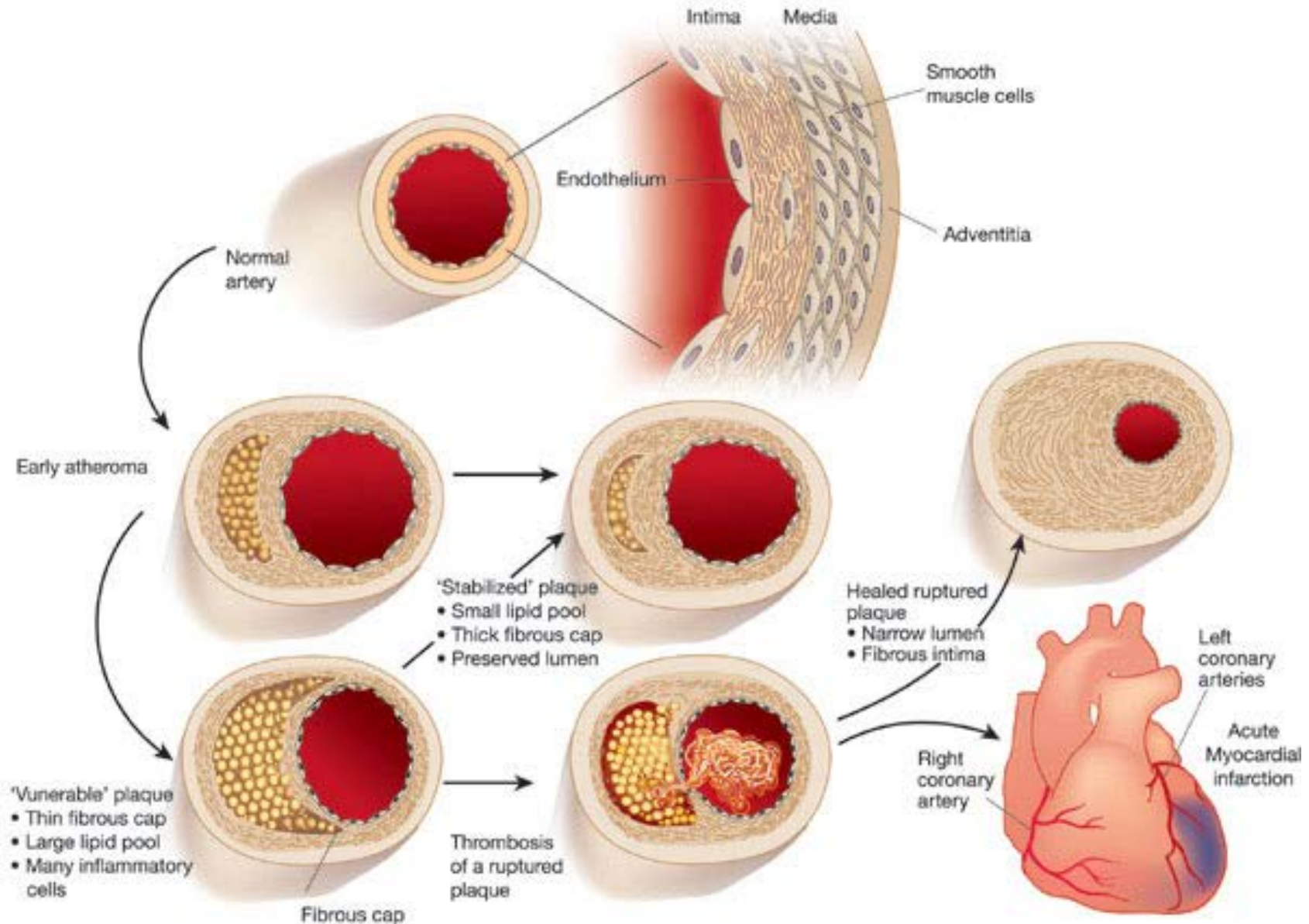


## CHD



# Myocardial infarct/heart attack:

What is the reason for coronary artery to be blocked?

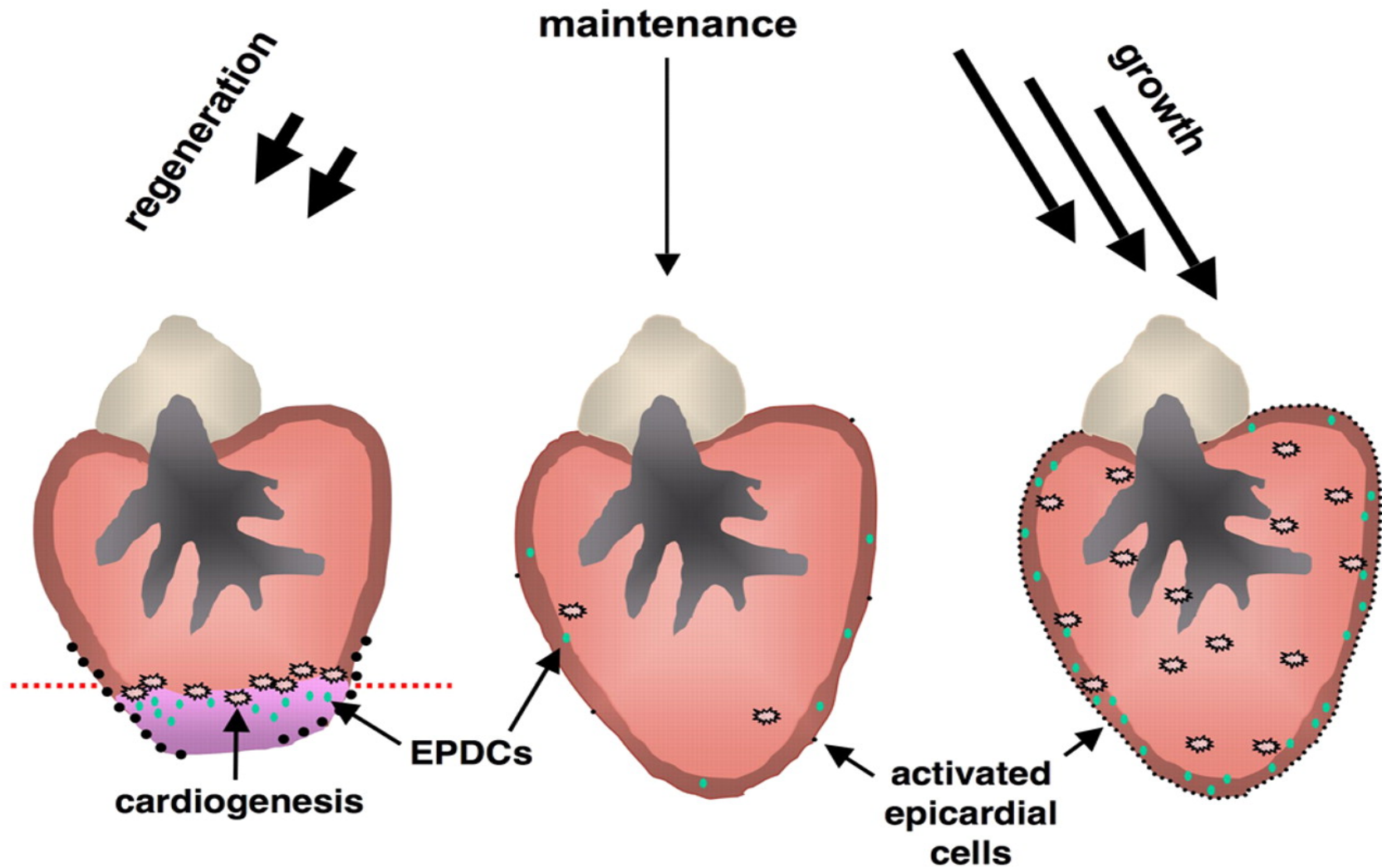


# Heart disease impact UK



- **Heart Attacks 250,000 p.a.**
- **Sudden death 120,000 p.a.**

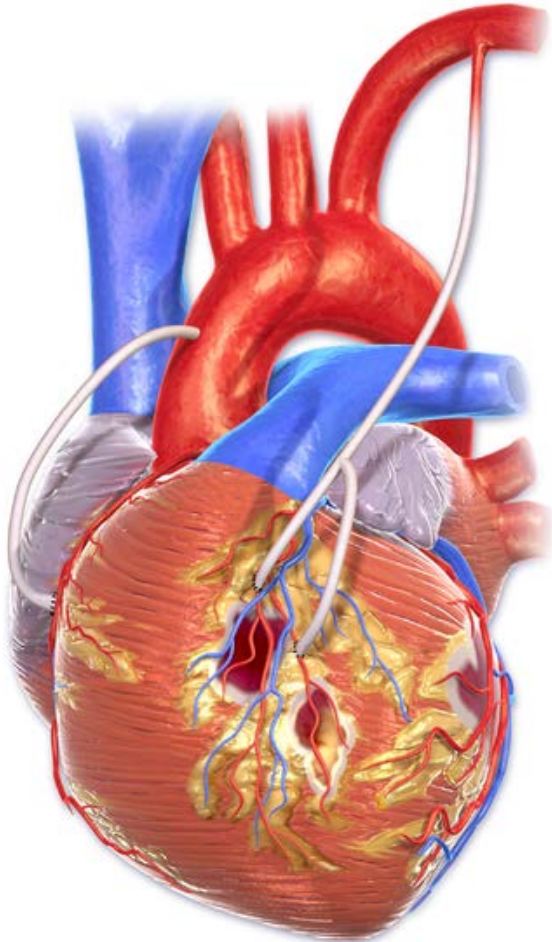
# The hearts of fish and primitive animal can regenerate But the human heart does not



# The new field of regenerative medicine



© Corbis Images



**Coronary Artery Bypass Graft (CABG)**  
*Triple Bypass*

**REGENERATION**

WITH PEOPLE THIS IS IMPOSSIBLE, BUT WITH GOD ALL THINGS ARE POSSIBLE. MATTHEW 19:26

**We'd like to play God!**

The graphic features a central red heart resting on a dark, cracked stone. The word "REGENERATION" is written in large, white, distressed letters across the top. Below the heart, the word "FLESH" is written in a curved path. Various biblical references are connected to the heart and stone by dotted lines, including:

- Knowledge of Sin (Romans 3:20)
- Sorrow for Sin (2 Cor. 7:10)
- Darkened, Ignorant (2 Pt. 1:17-18)
- Deal in
- Unbelief (John 6:63-64)
- Depraved Mind (Romans 1:28)
- Continually Wicked (Genesis 6-9)
- Alive with Christ (Ephesians 2:5)
- Renewed (Titus 3:5)
- State of Righteousness (Romans 6:6)
- Divine Workmanship (Ephesians 2:10)
- Born of God (1 John 5:1)
- Clean (Isaiah 35:8)

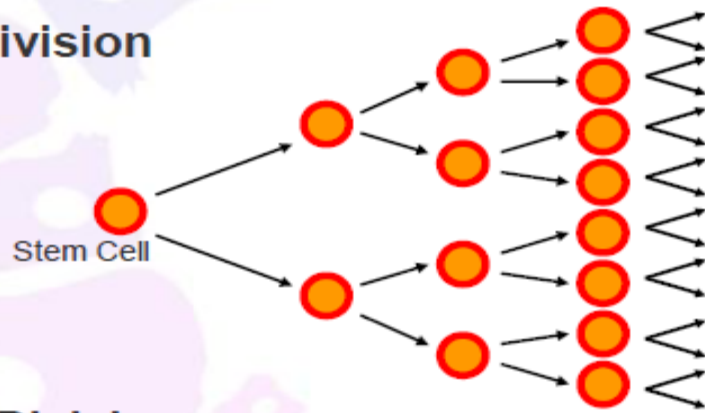
# What is a Stem Cell?



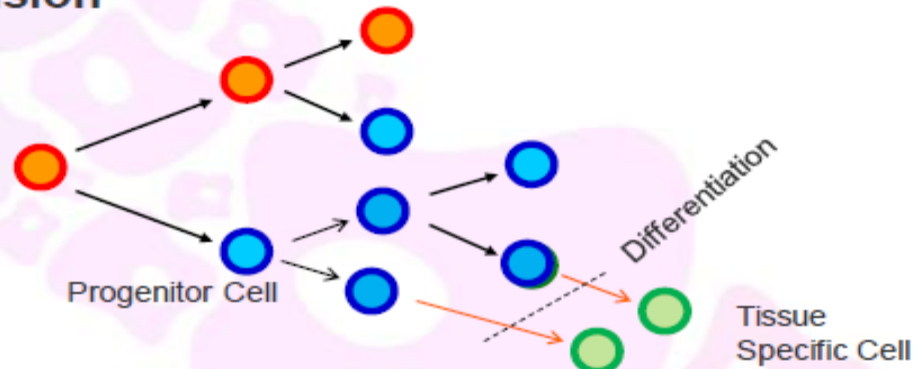
- A **Stem Cell** is a cell with the ability to divide for indefinite periods in culture that can give rise to specialized cells - including daughter stem cells.

# Stem Cell Division

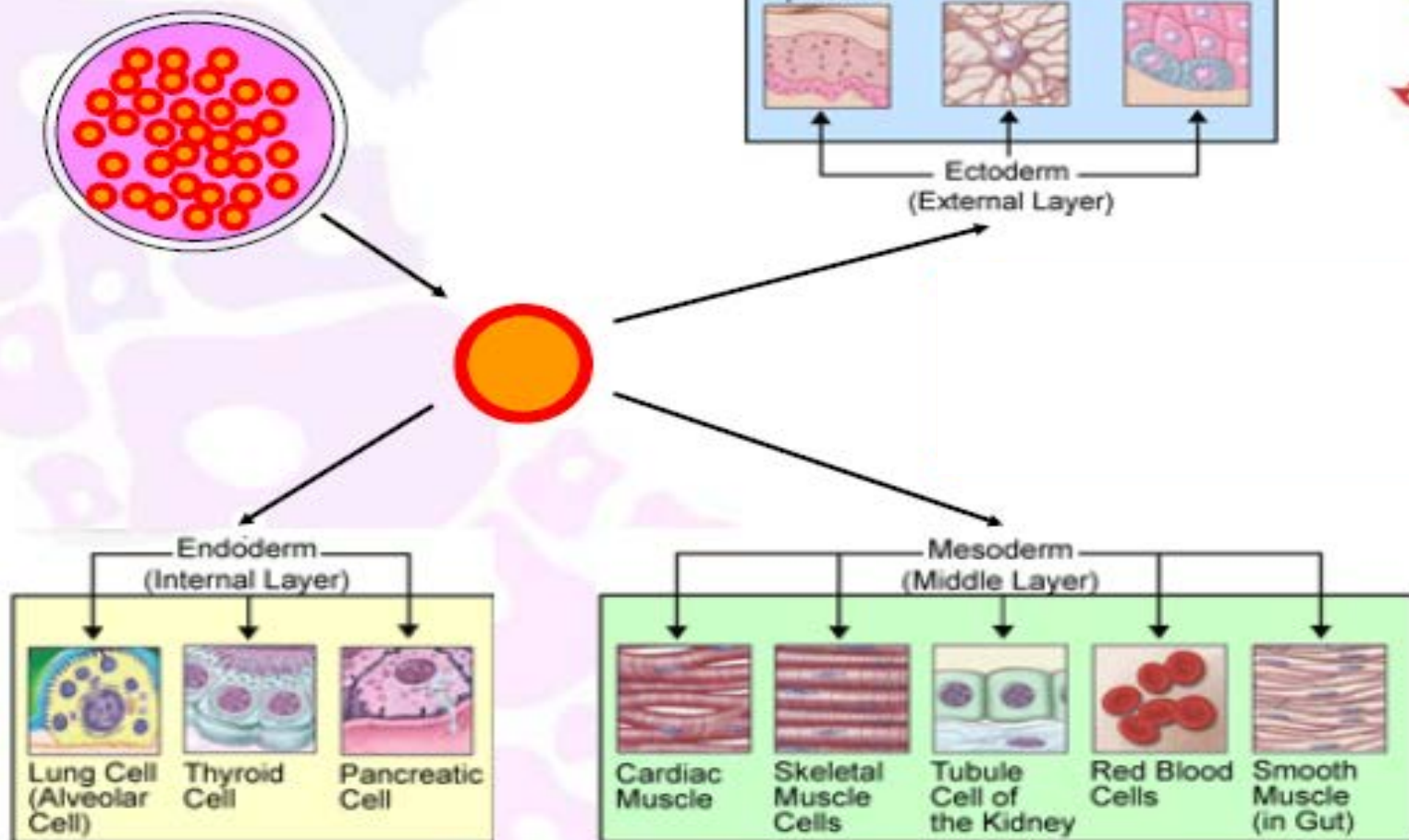
## Symmetric Division



## Asymmetric Division

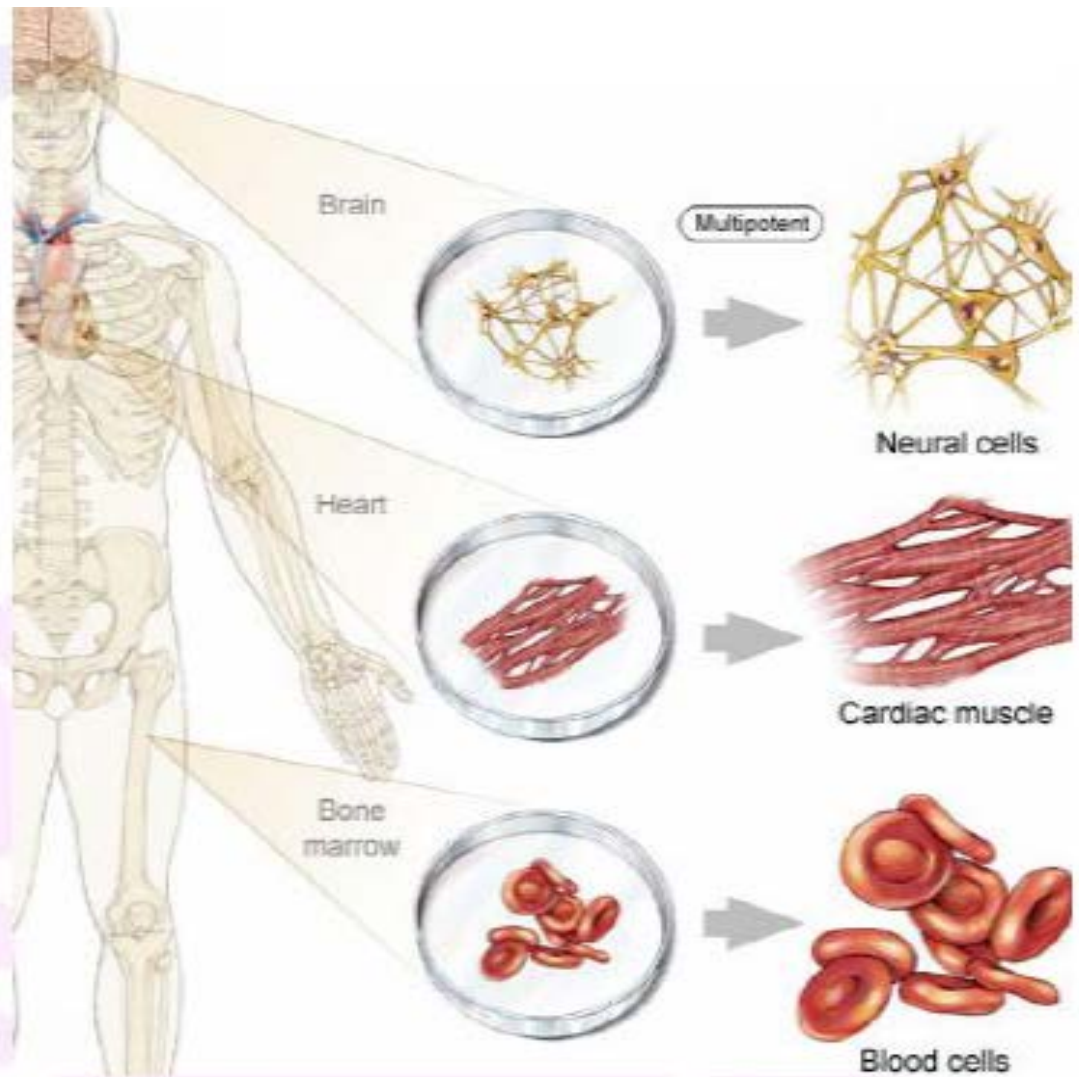


# ES Cell Differentiation



# 'Adult' Stem Cells

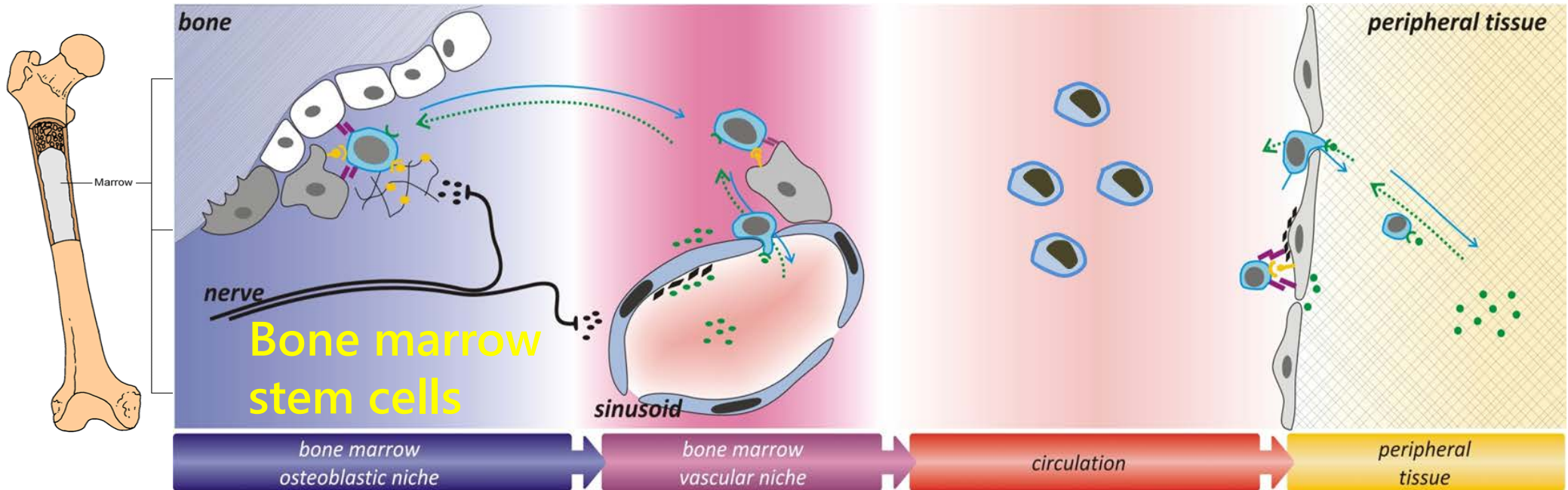
- Often referred to as **progenitor cells** or **somatic stem cells**
- Foetal, Newborn, Adult
- Multipotent – *can become any cell of parent organ*
- *Multiple sources of progenitors*





# Injury

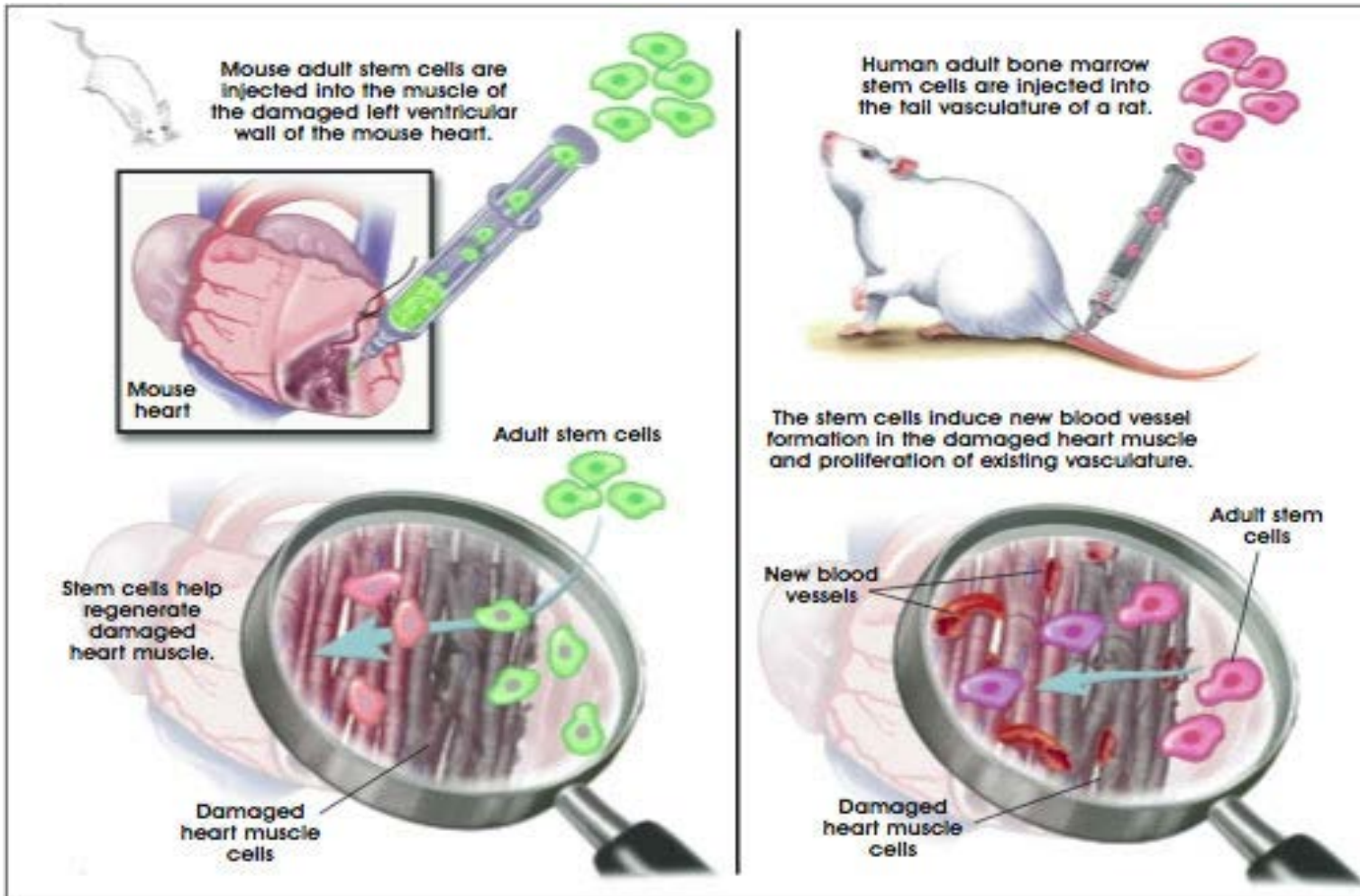
# Copying mother nature



**Bone marrow transplantation is a standardized procedure**

**Genial idea: Extract those precious cells and inject them into the heart**

# Preclinical research



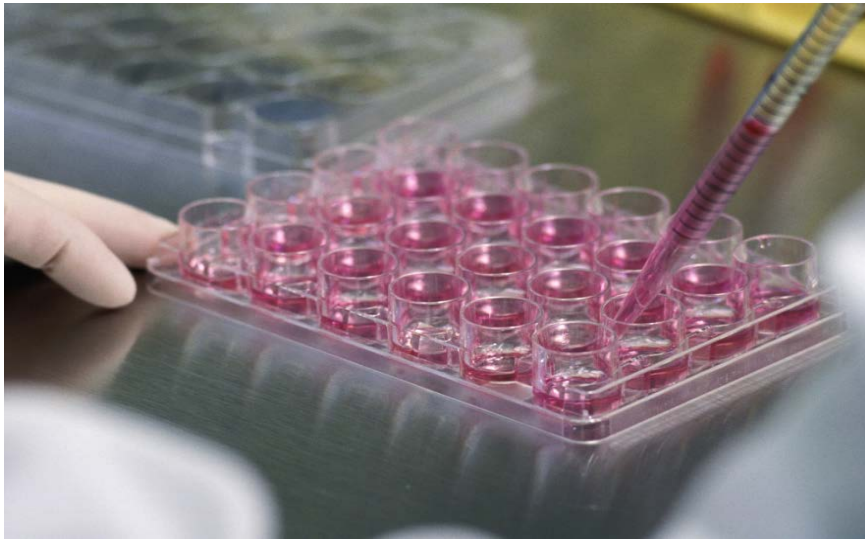
# Preclinical studies in large animals with in vivo MRI in Bristol GLP facility

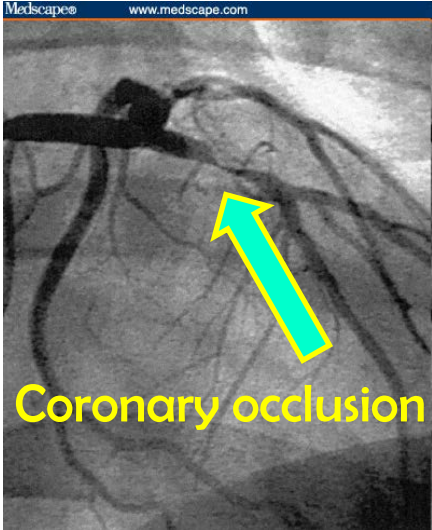


PIG ARRIVAL

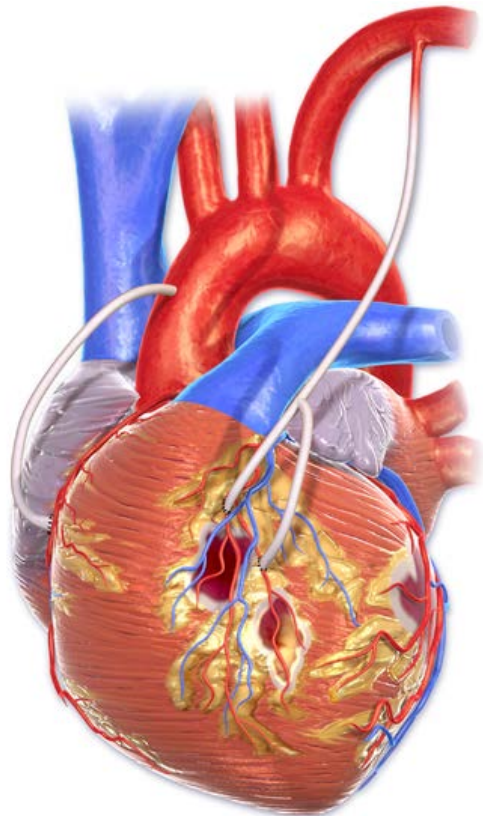
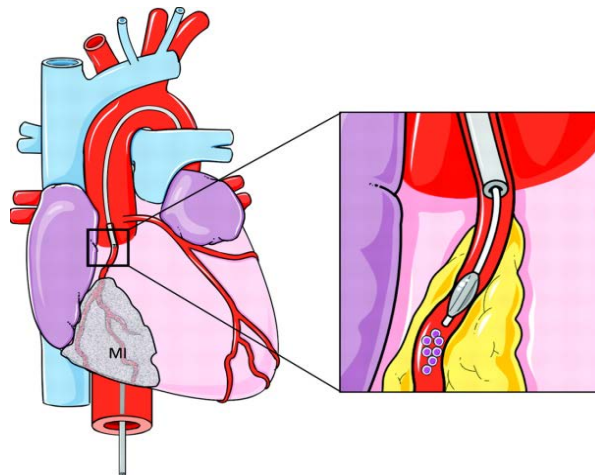
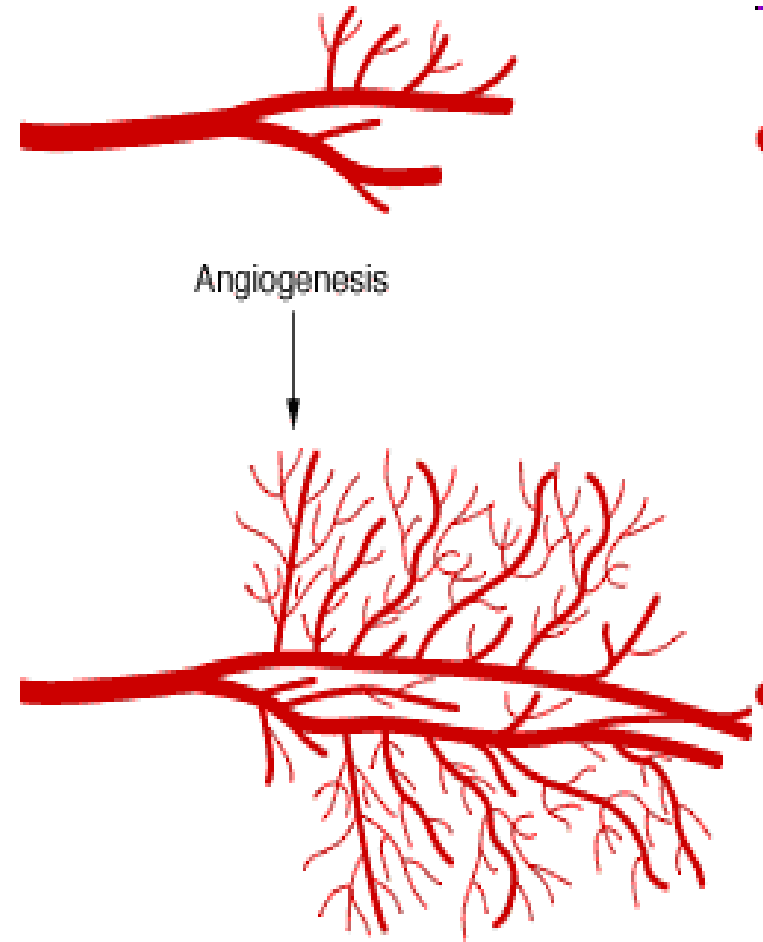
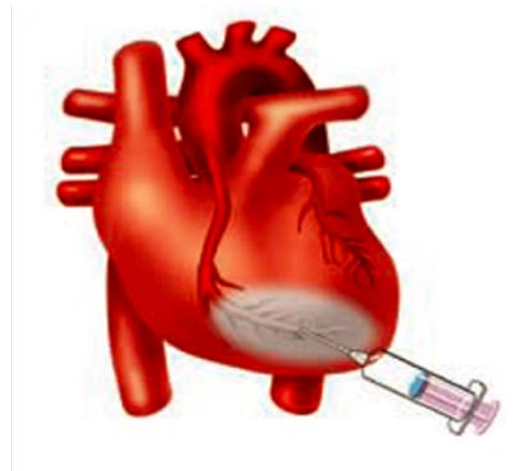


Sample Harvesting  
SACRIFICE





# Therapeutic angiogenesis using stem cells



**Coronary Artery Bypass Graft (CABG)**  
*Triple Bypass*

# TransACT 1 and 2 clinical trials

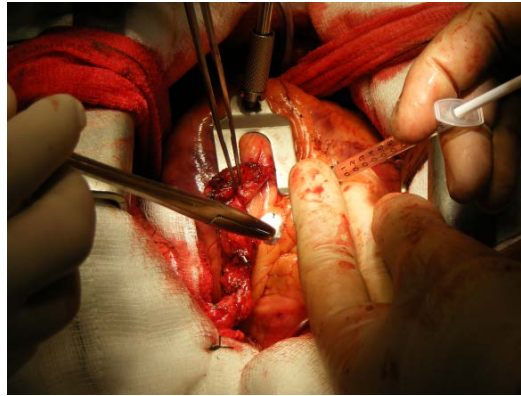
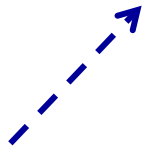


Prof Ascione

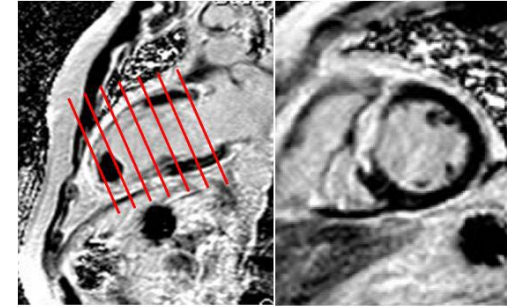


Dr Bucciarelli-Ducci

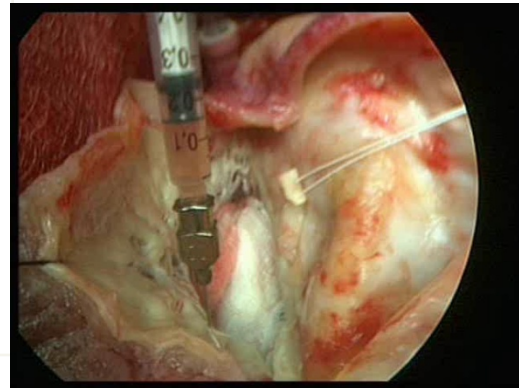
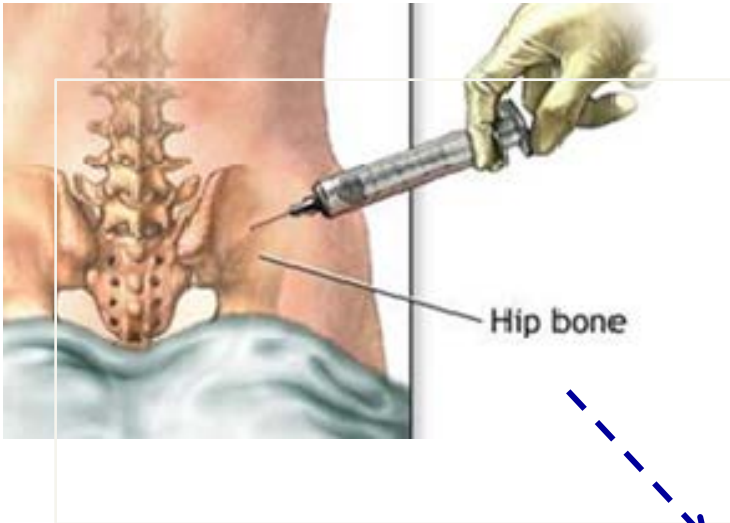
BM 133-pos cells



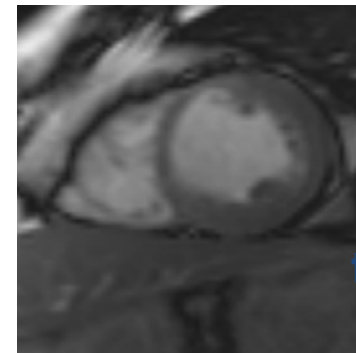
TransACT 1 CABG for MI



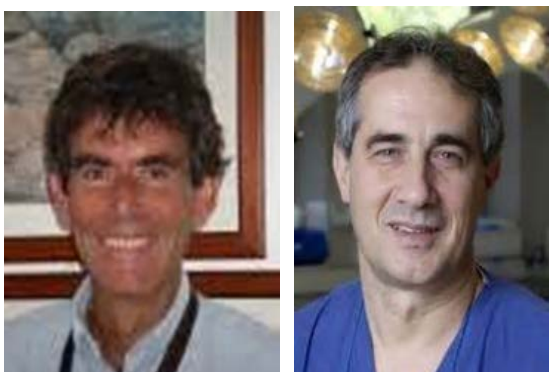
LV Scar size



TransACT 2 LV reshaping

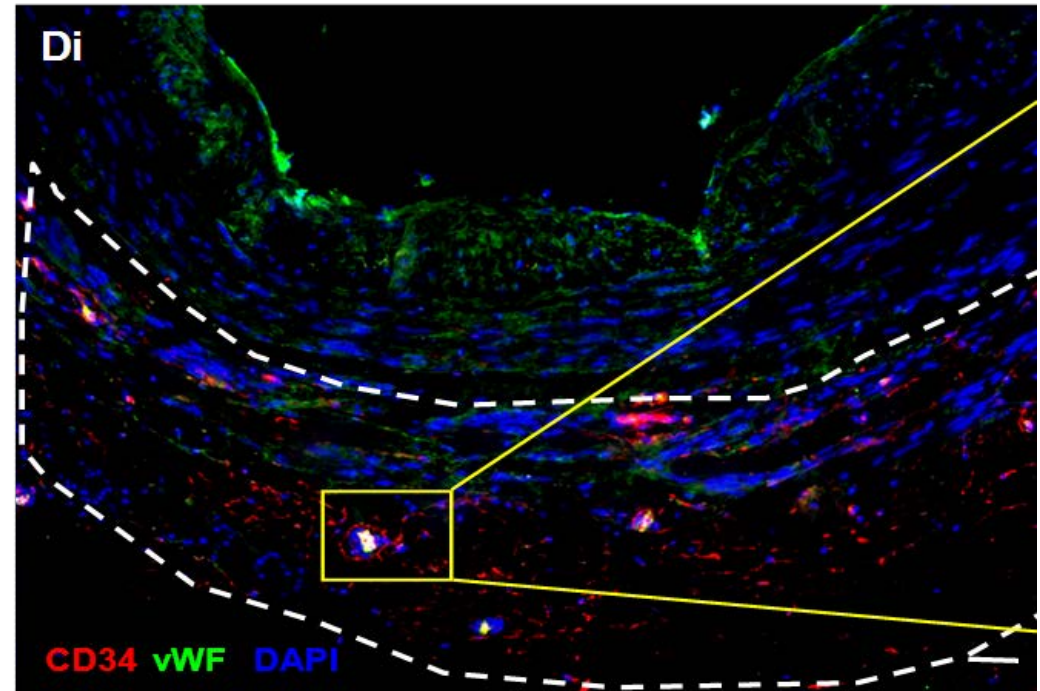
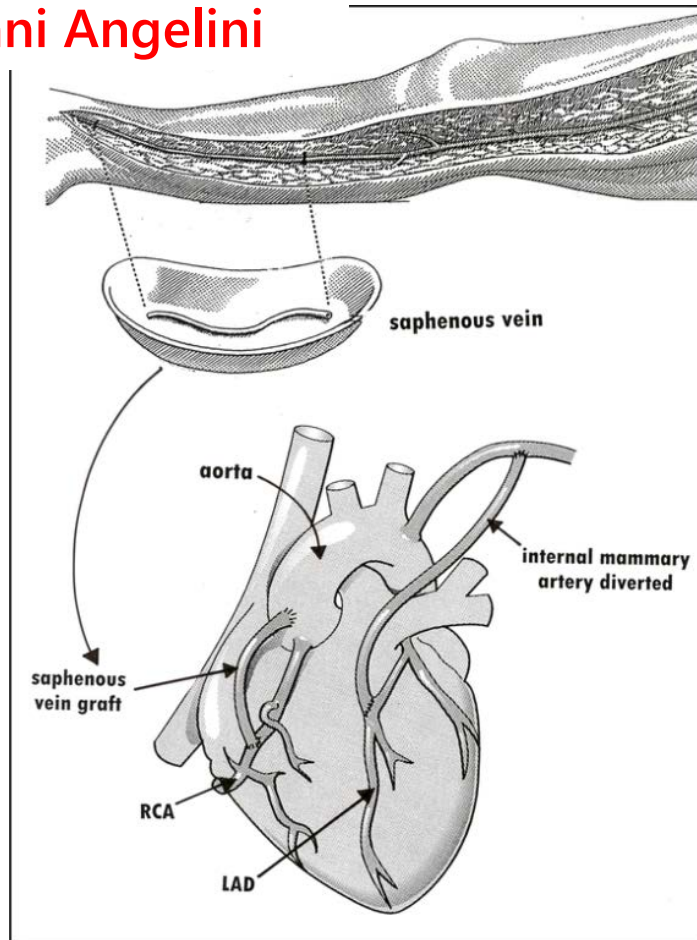
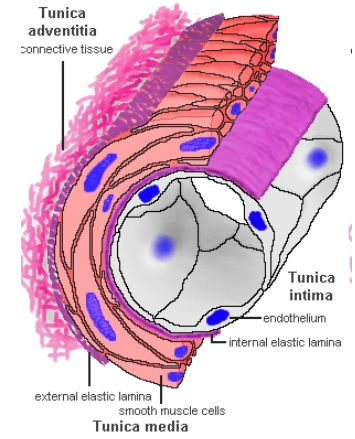


LV wall Thickening at the infarct site



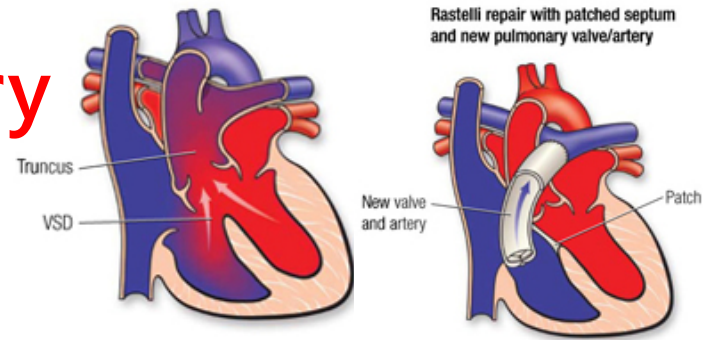
# The Bristol pericyte progenitor cells: almost ready for a clinical trial

Profs Paolo Madeddu and Gianni Angelini



Vena saphena leftover of what used for by-pass

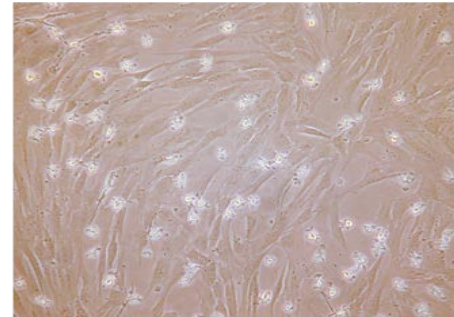
# Stem cells in congenital heart surgery



**Cell isolation and expansion**

→

**Stem Cells**



**Seeding graft**

→

**Bioreactor**



↓



**Seeded graft**

←



**Surgery**

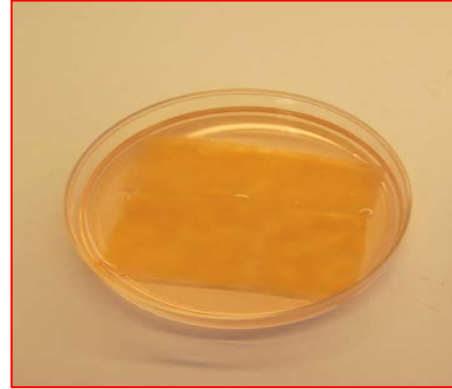
←



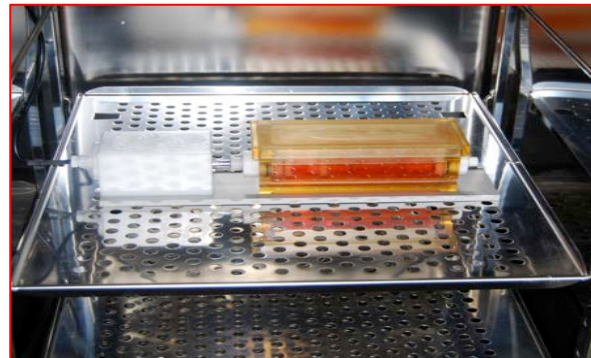
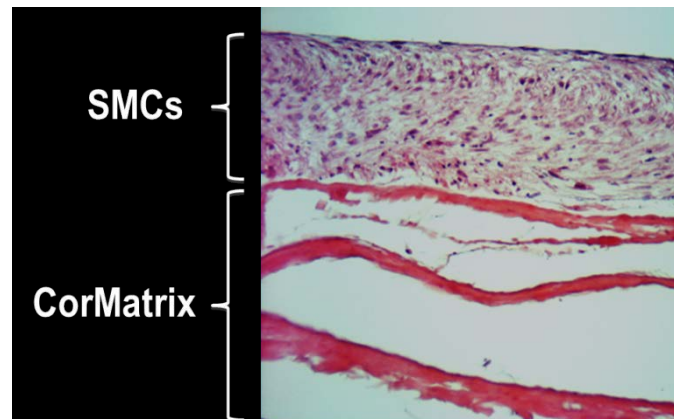
**Professor Massimo Caputo**



# CorMatrix<sup>®</sup> ECM<sup>®</sup> Technology for Tissue Engineering



SCs-derived SMCs are seeded and left on the scaffold for 2d before assembly the conduit ↓



Tissue engineered conduit is incubating in the bioreactor

## First "in Children" Trials

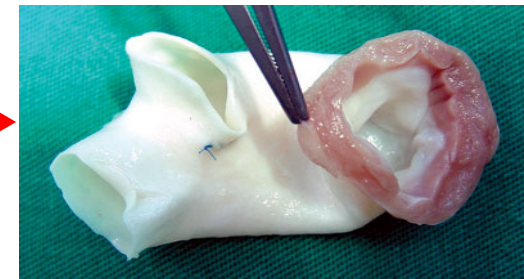
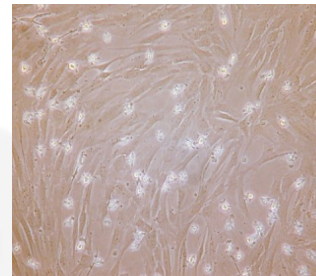
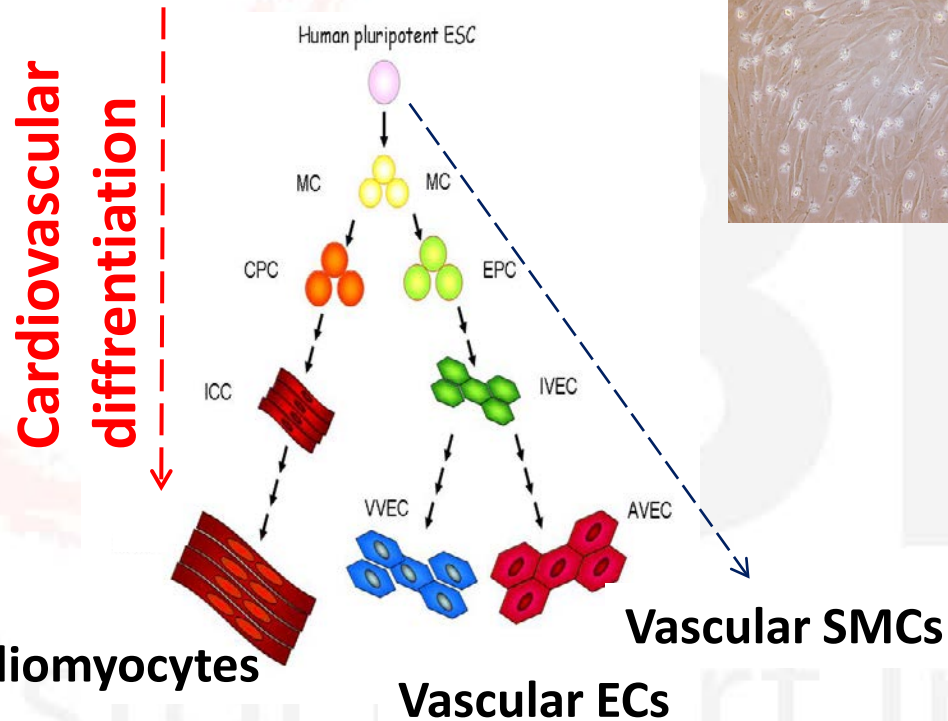
### Large Animal Model



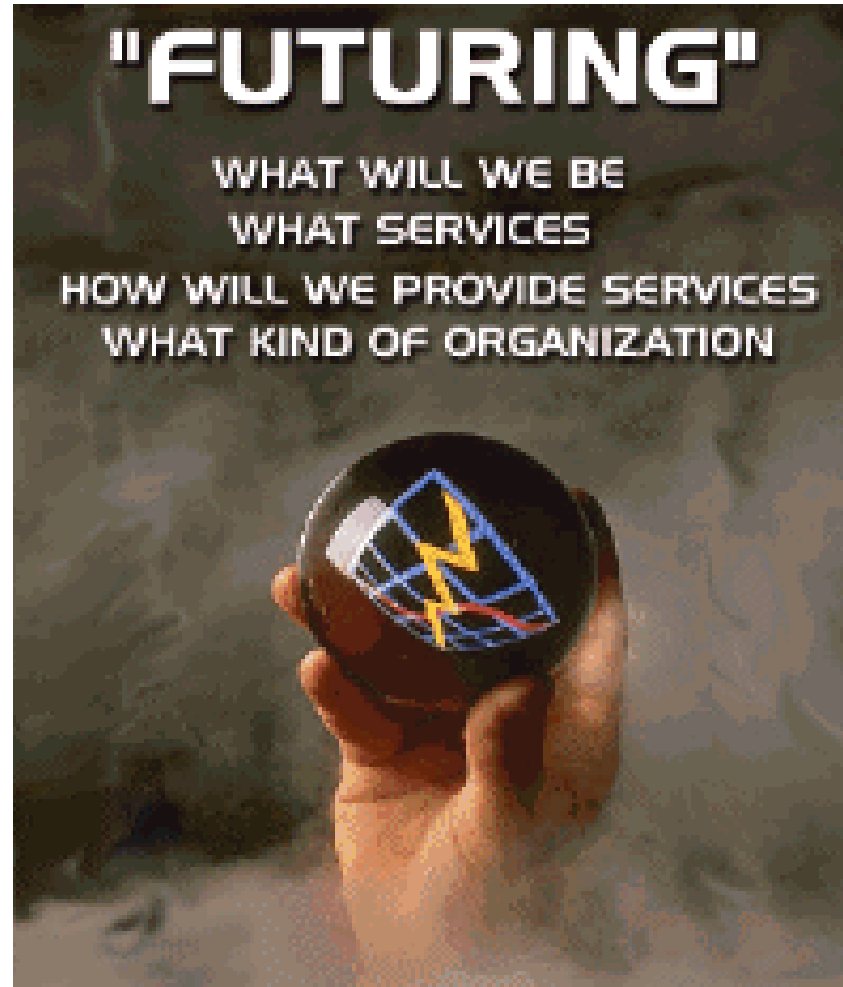
# Pluripotent stem cells-derived CV progenitor cells for CHD repair



## Clinical grade ESCs and autologous iPSCs



# The Future of Cardiovascular Medicine: INNOVATION



Keeping our patients SAFE (regulatory authorities)



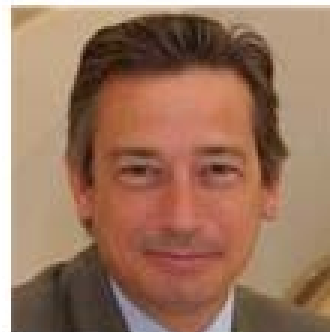
**Prof. Paolo Madeddu**  
HoS Reg Med



**BHF Prof. Gianni Angelini**  
Director of the Bristol  
NIHR-BRU in CV Disease



**Prof. Massimo Caputo**  
Congenital Heart Surgery



**Prof. Raimondo Ascione**  
Adult Cardiac Surgery





**British Heart Foundation**



**NHS**

*National Institute for  
Health Research*

