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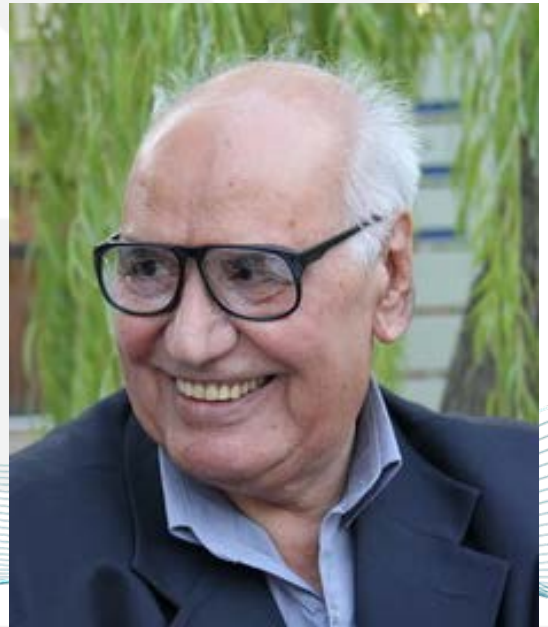
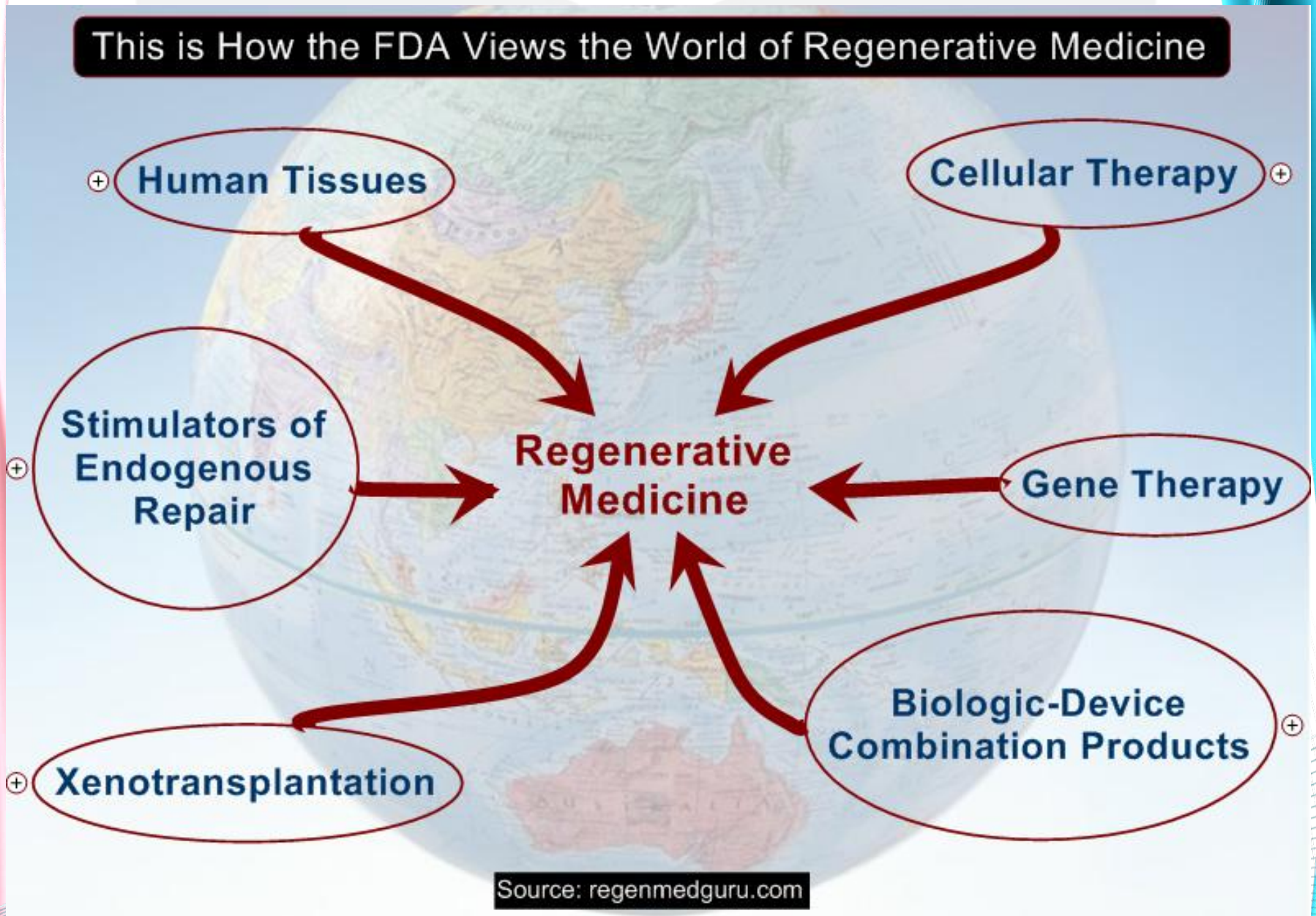
مردانی اند از جنس بلور و روشنایی



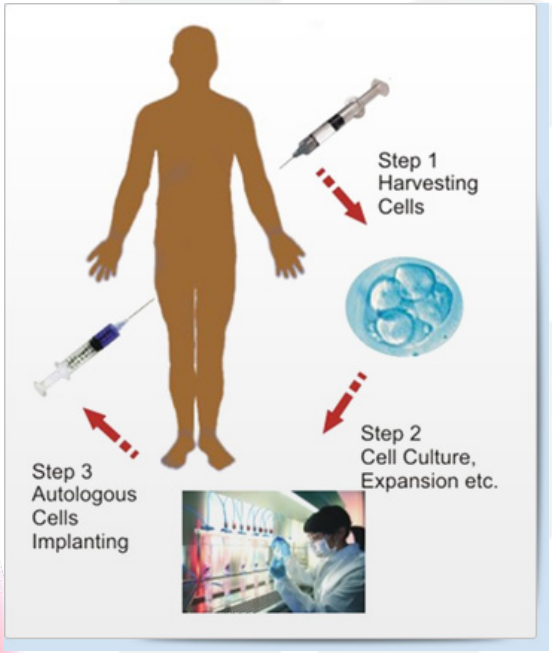
# Advances in Regenerative Medicine

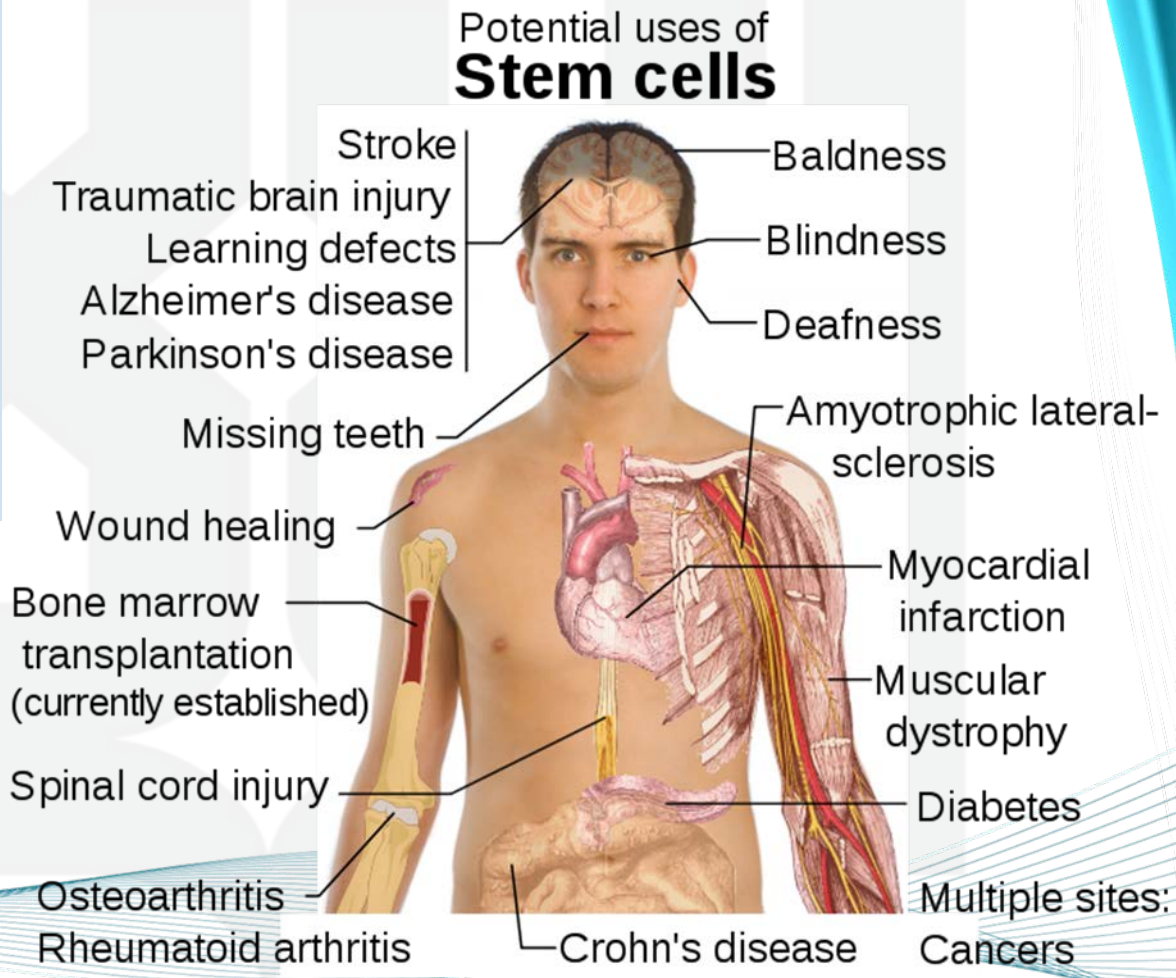
***Hossein Ghanbari, MD, PhD***

*School of Advanced Technologies in Medicine, TUMS, Tehran, Iran*

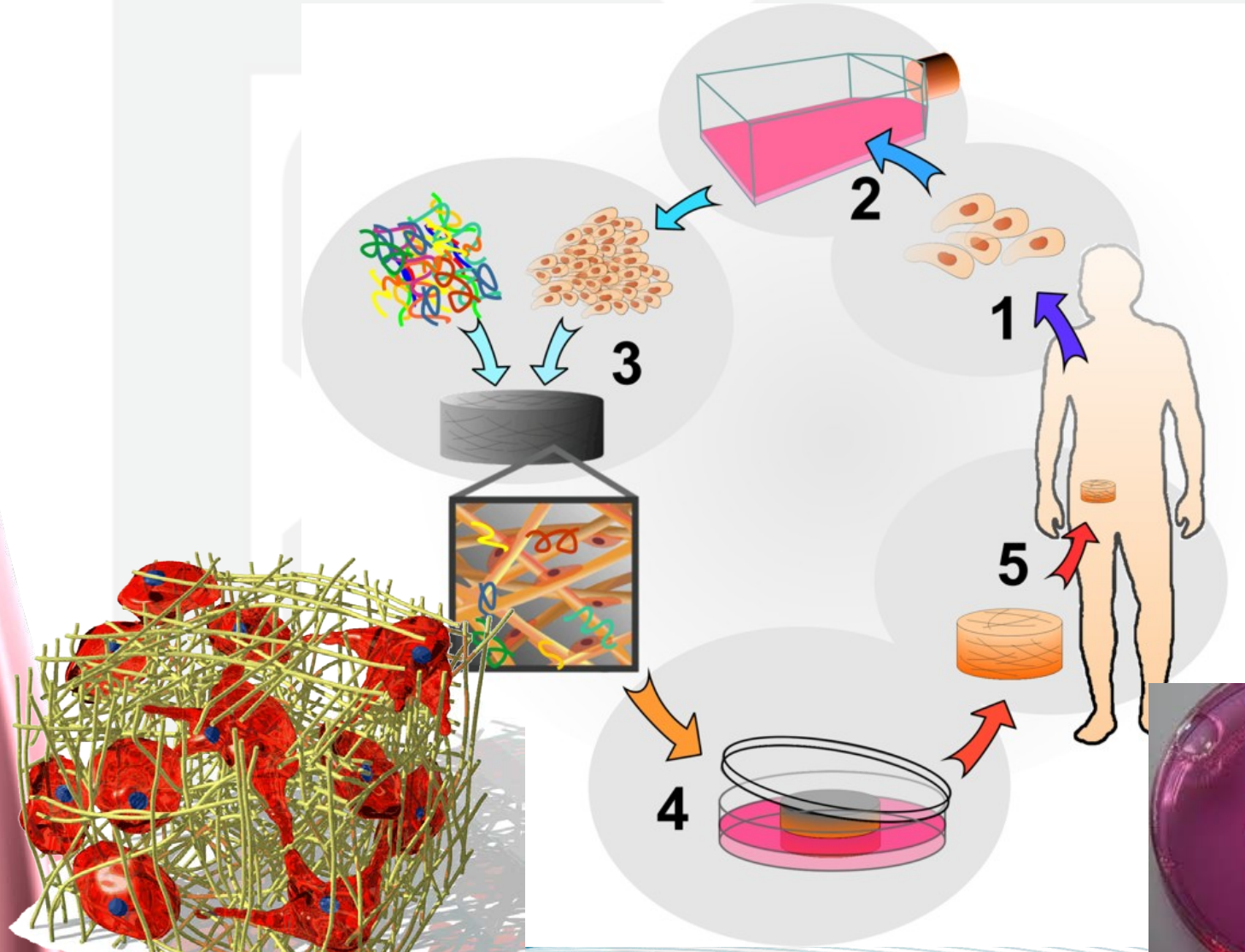

This is How the FDA Views the World of Regenerative Medicine
Human Tissues
Cellular Therapy
Stimulators of Endogenous Repair
Regenerative Medicine
Gene Therapy
Biologic-Device Combination Products
Xenotransplantation
Source: regenmedguru.com

# STEM CELL/CELL THERAPY



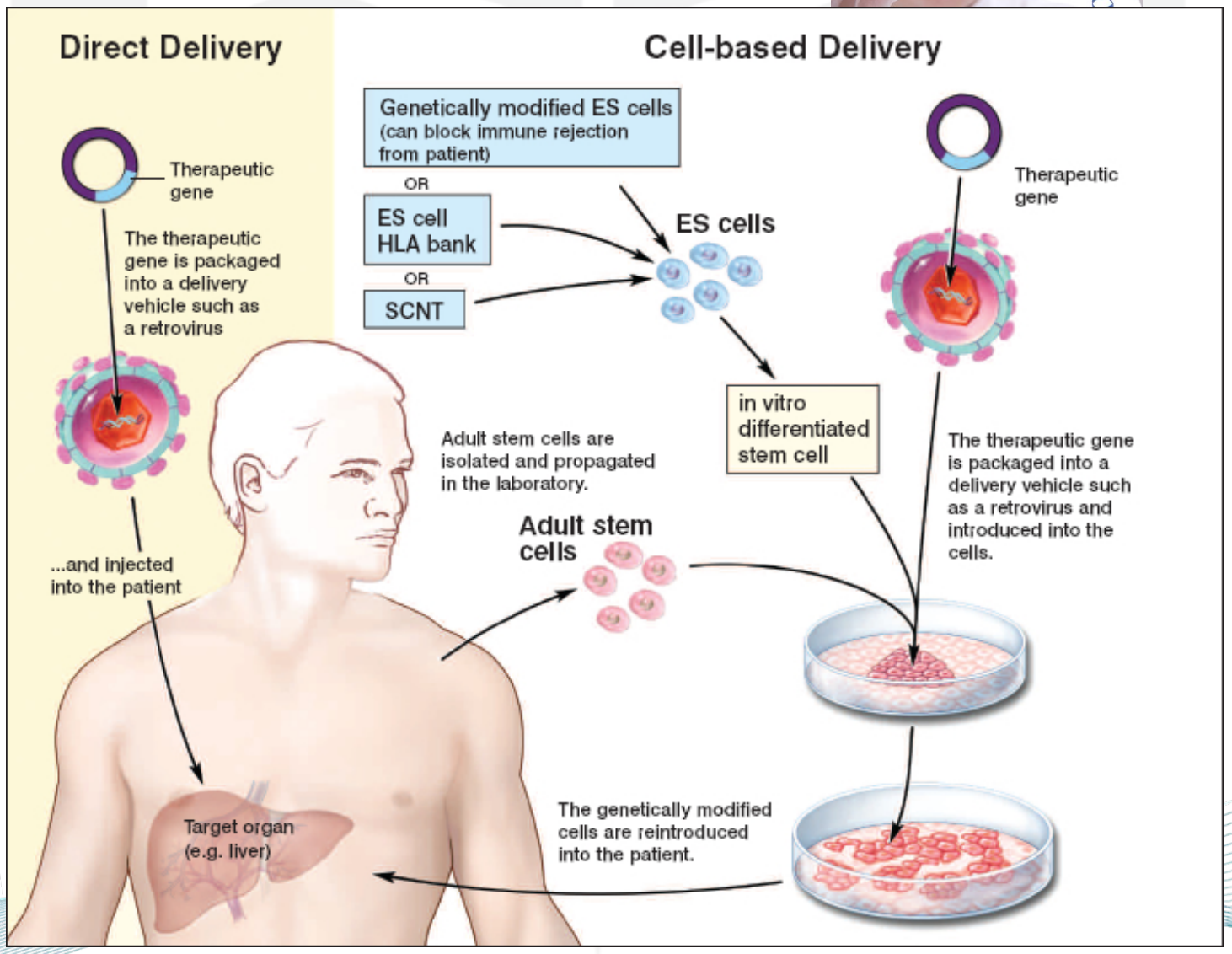



# TISSUE ENGINEERING

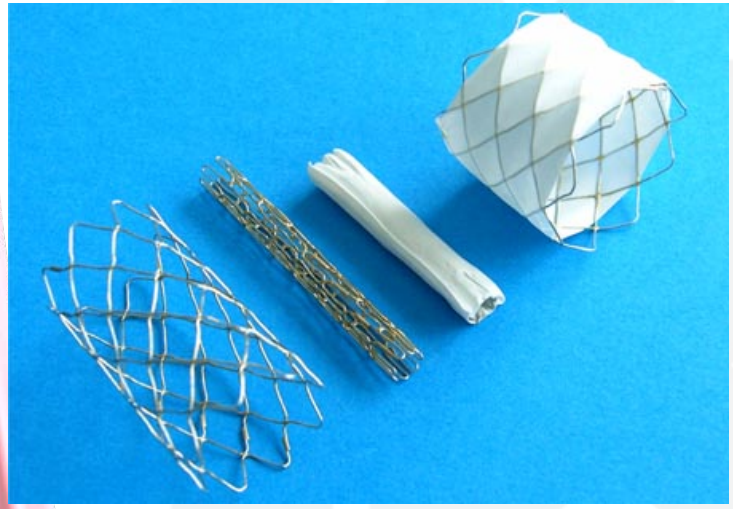


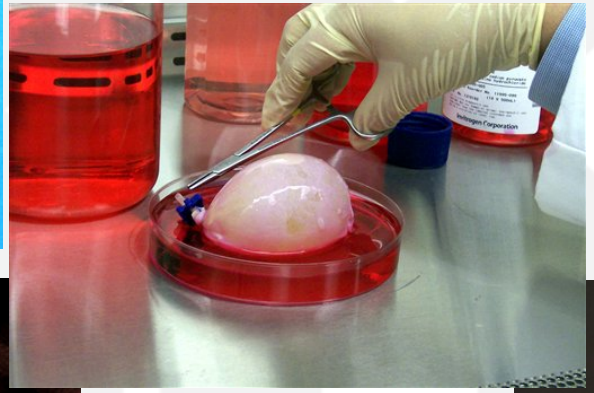



# GENE THERAPY

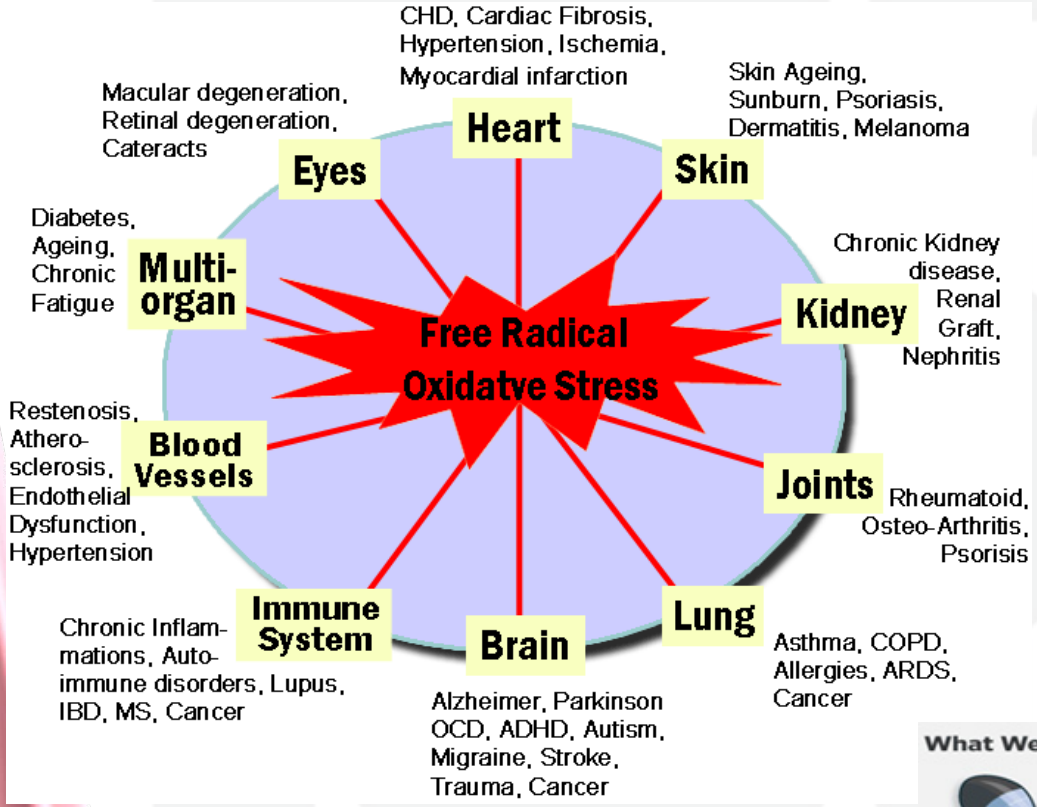


# BIOMATERIALS
# DEVICES/ IMPLANTS

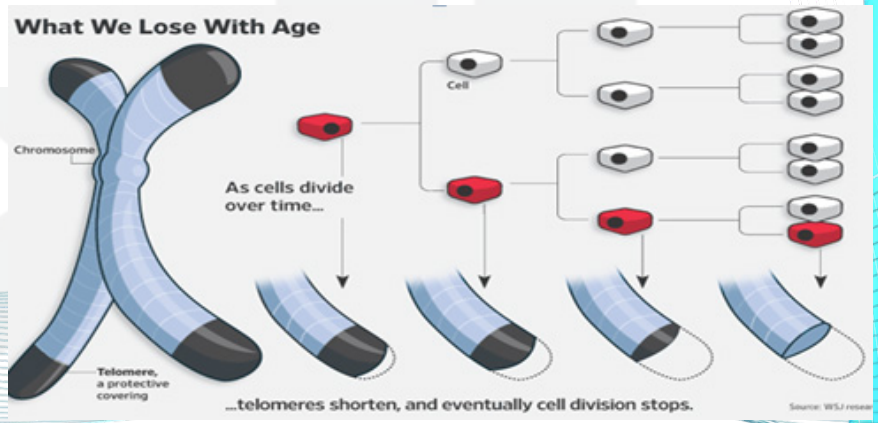




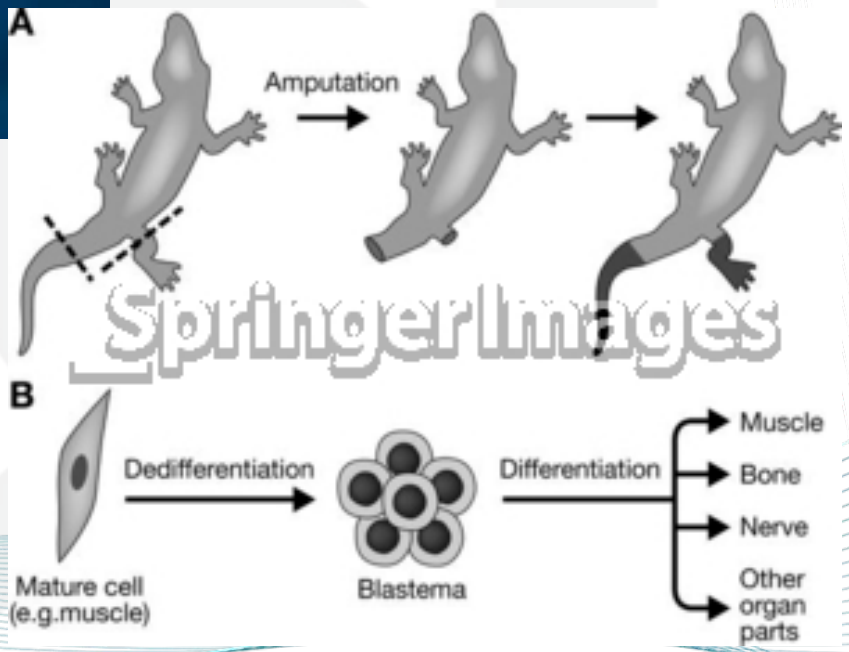
# ANTI AGING MEDICINE



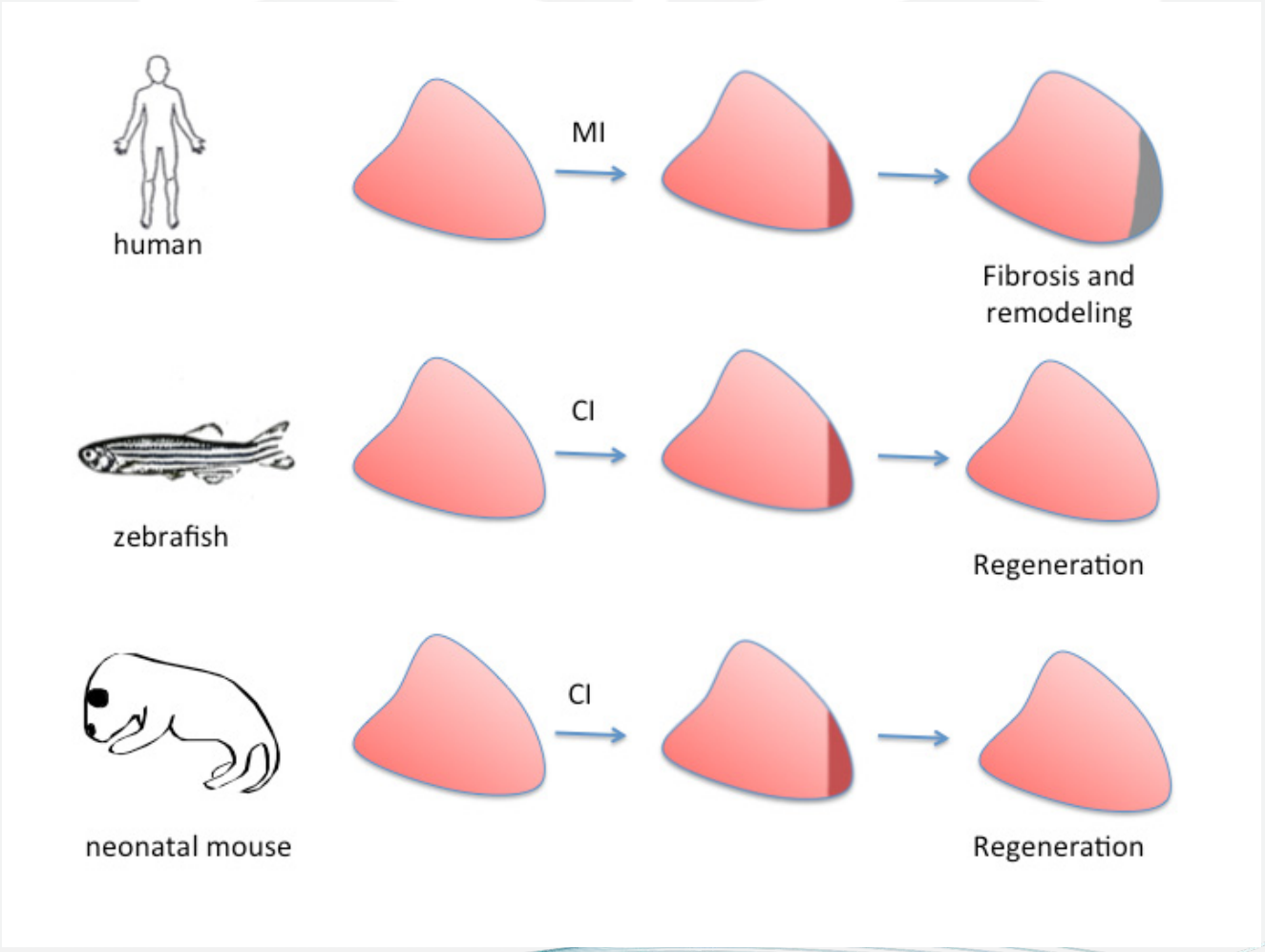

Early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases.

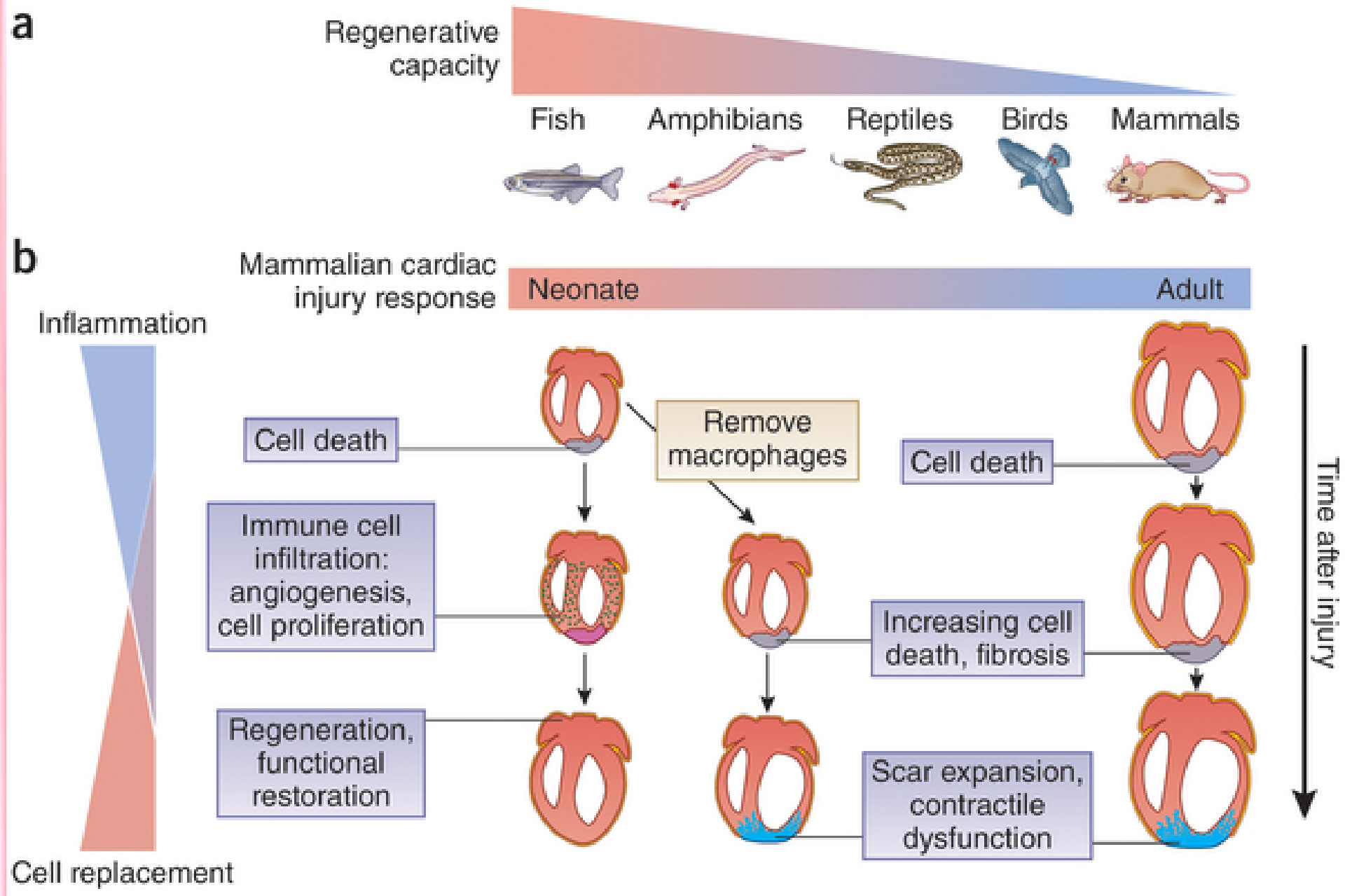



# ENHANCEMENT OF ENDOGENOUS REGENERATION

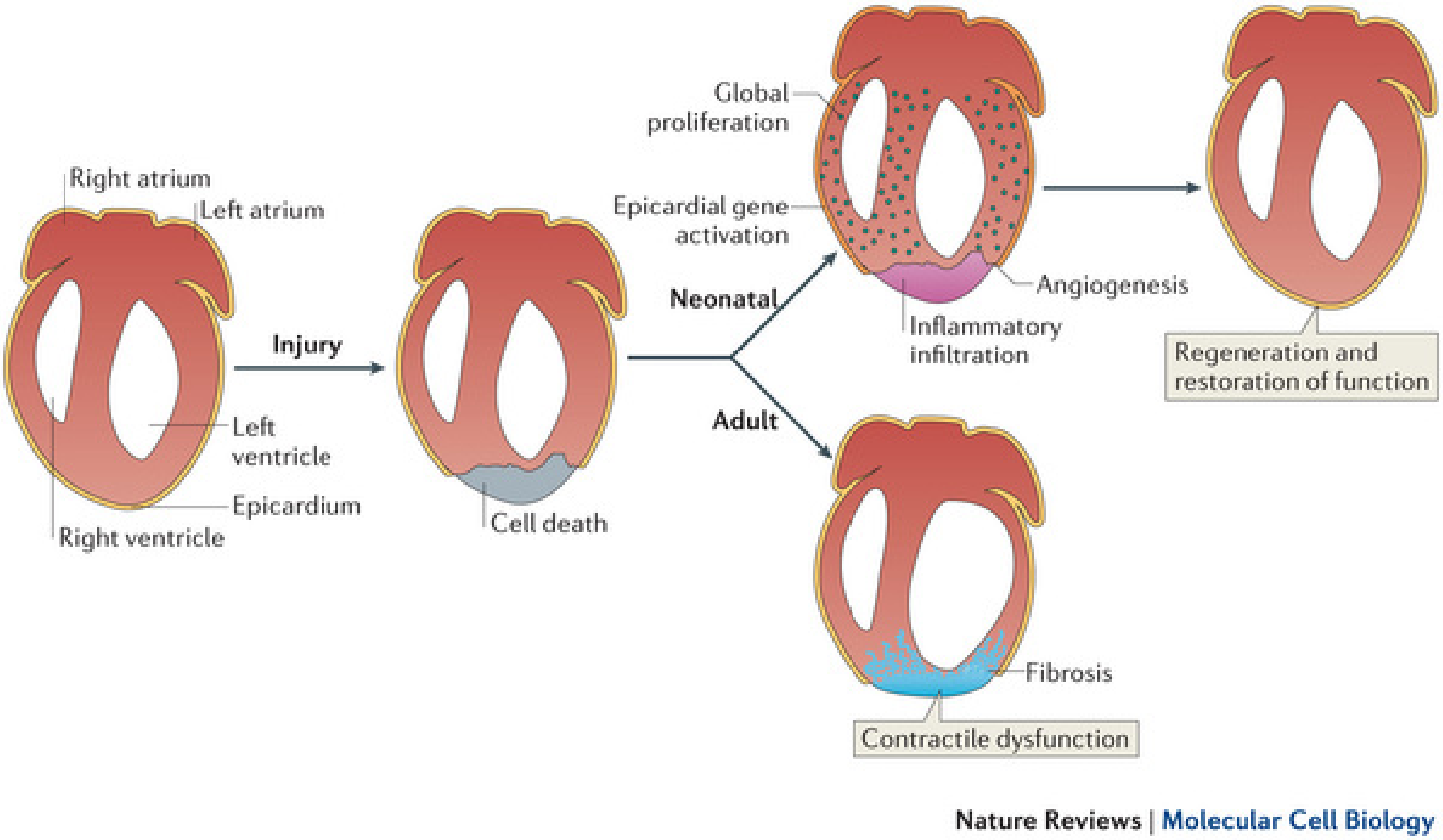



# DIFFERENT REGENERATIVE CAPACITIES OF THE HEARTS OF ADULT HUMANS, ADULT ZEBRAFISH AND NEONATAL MICE

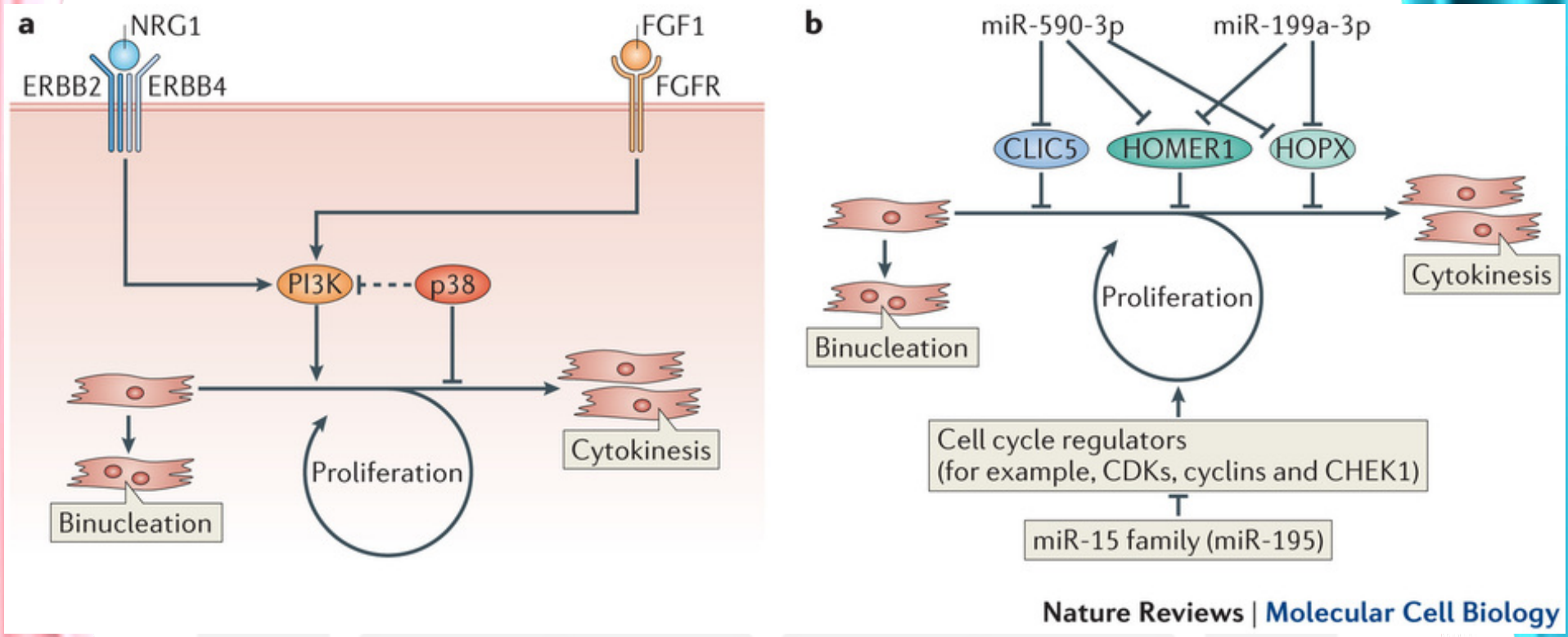



a
Regenerative capacity
Fish
Amphibians
Reptiles
Birds
Mammals
b
Mammalian cardiac injury response
Neonate
Adult
Inflammation
Cell replacement
Cell death
Remove macrophages
Immune cell infiltration: angiogenesis, cell proliferation
Regeneration, functional restoration
Cell death
Increasing cell death, fibrosis
Scar expansion, contractile dysfunction
Time after injury

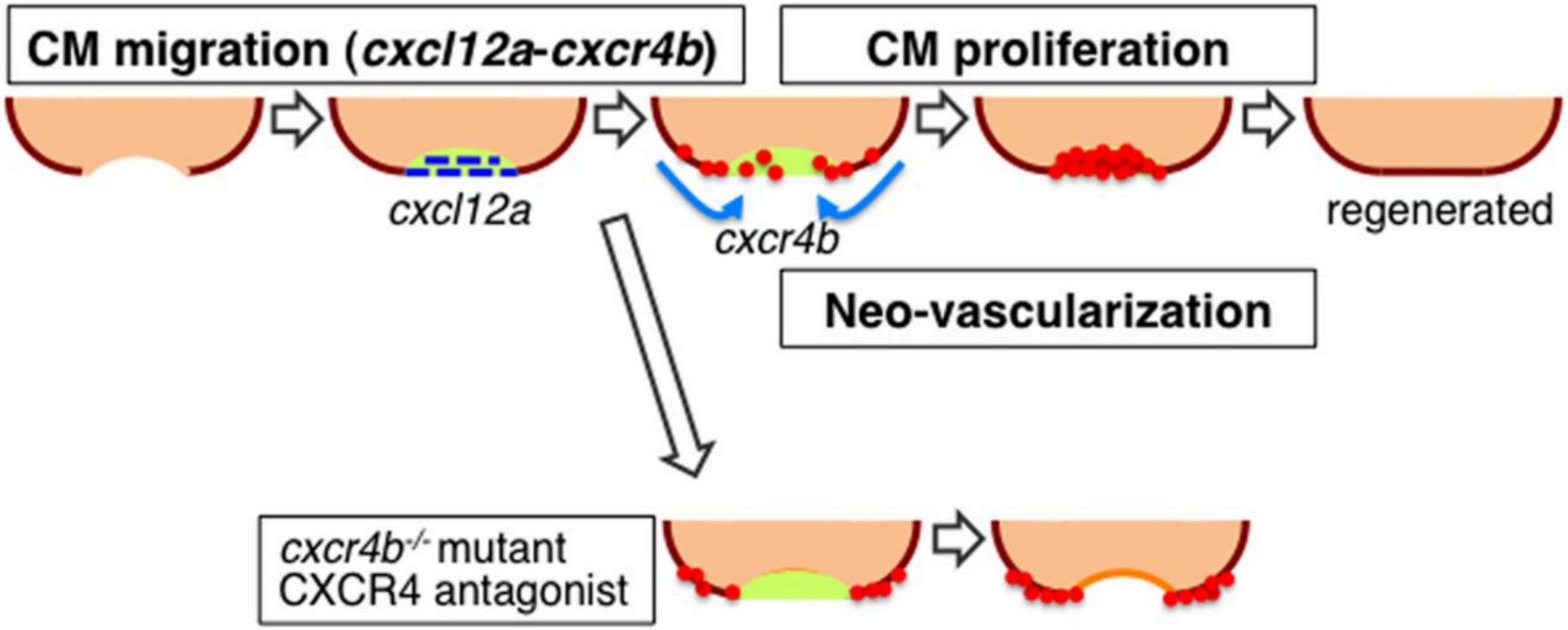
# REGENERATION OF THE MAMMALIAN NEONATAL HEART




In neonatal mice, the early response to cardiac injury-induced cardiomyocyte loss includes inflammatory infiltration, activation of epicardial-specific genes and angiogenesis. Global proliferation of cardiomyocytes in the injured heart replaces the scar tissue with cardiomyocytes and restores cardiac function within 3 weeks after the injury.



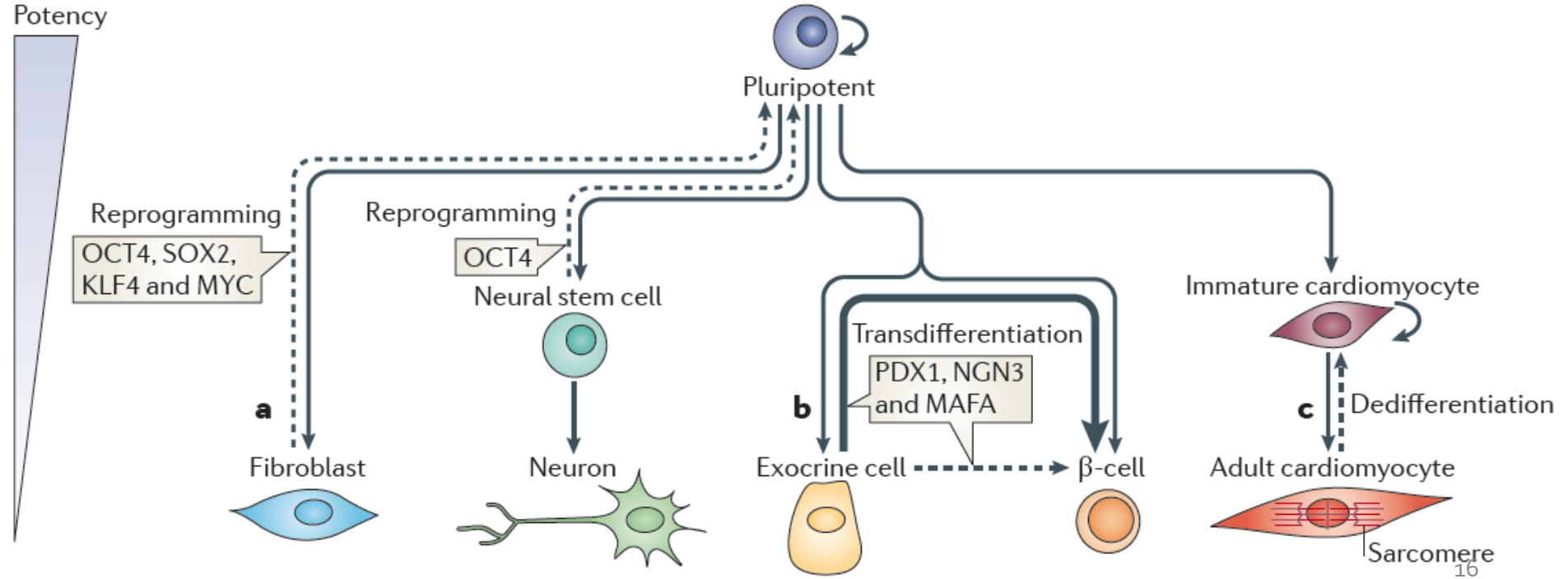

**a** | Regulation of cardiomyocyte proliferation by fibroblast growth factor 1 (FGF1) and neuregulin 1 (NRG1). Inhibition of the MAPK p38 in the presence of FGF1 or the activation of NGR1 signalling promotes cardiomyocyte re-entry into the cell cycle by activating PI3K, leading to DNA synthesis and cytokinesis. However, most cardiomyocytes in mice become binucleated shortly after birth as a consequence of DNA replication without cell division. **b** | Regulation of cardiomyocyte proliferation by microRNAs (miRNAs). miRNAs can positively (miR-590-3p and miR-199a-3p) or negatively (miR-15 family, including miR-195) regulate cardiomyocyte proliferation. miR-590-3p and miR-199a-3p promote cardiomyocyte proliferation by inhibiting the expression of genes encoding proteins that inhibit cell proliferation such as HOMER1, HOP homeobox (HOPX) and chloride intracellular channel 5 (CLIC5). The miR-15 family of miRNAs inhibits the cell cycle, and thus cardiomyocyte proliferation, by down-regulating genes encoding proteins that activate the cell cycle. CDKs, cyclin-dependent kinases; CHEK1, checkpoint kinase 1; FGFR, FGF receptor.



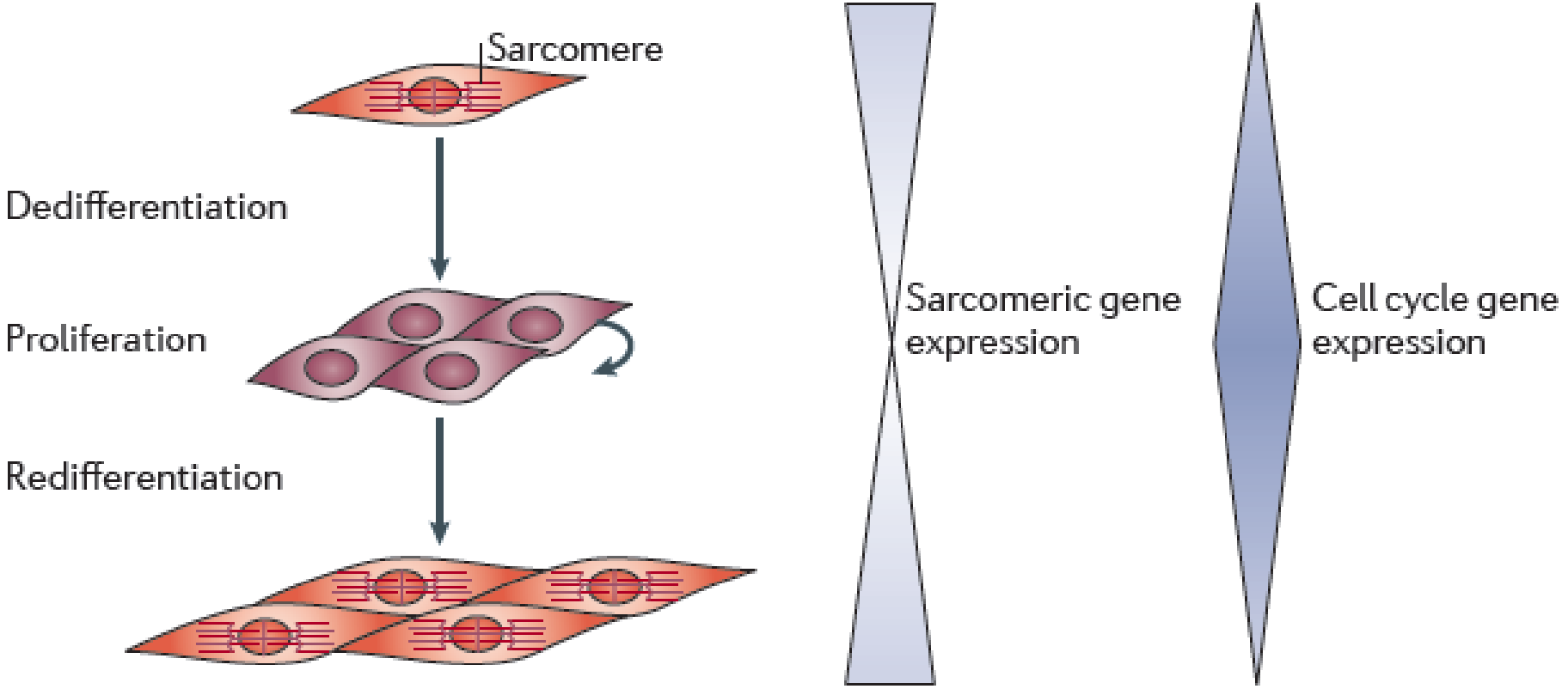

**A model of heart regeneration in zebrafish.** Amputation induces *cxcl12a-cxcr4b*-dependent directed migration of CMs into the injury site. CM proliferation and neo-vascularization are regulated independently from CM migration. Coordinated progression of these processes regenerates the injured heart. The orange circles represent proliferating CMs.

# ROUTES OF REGENERATION

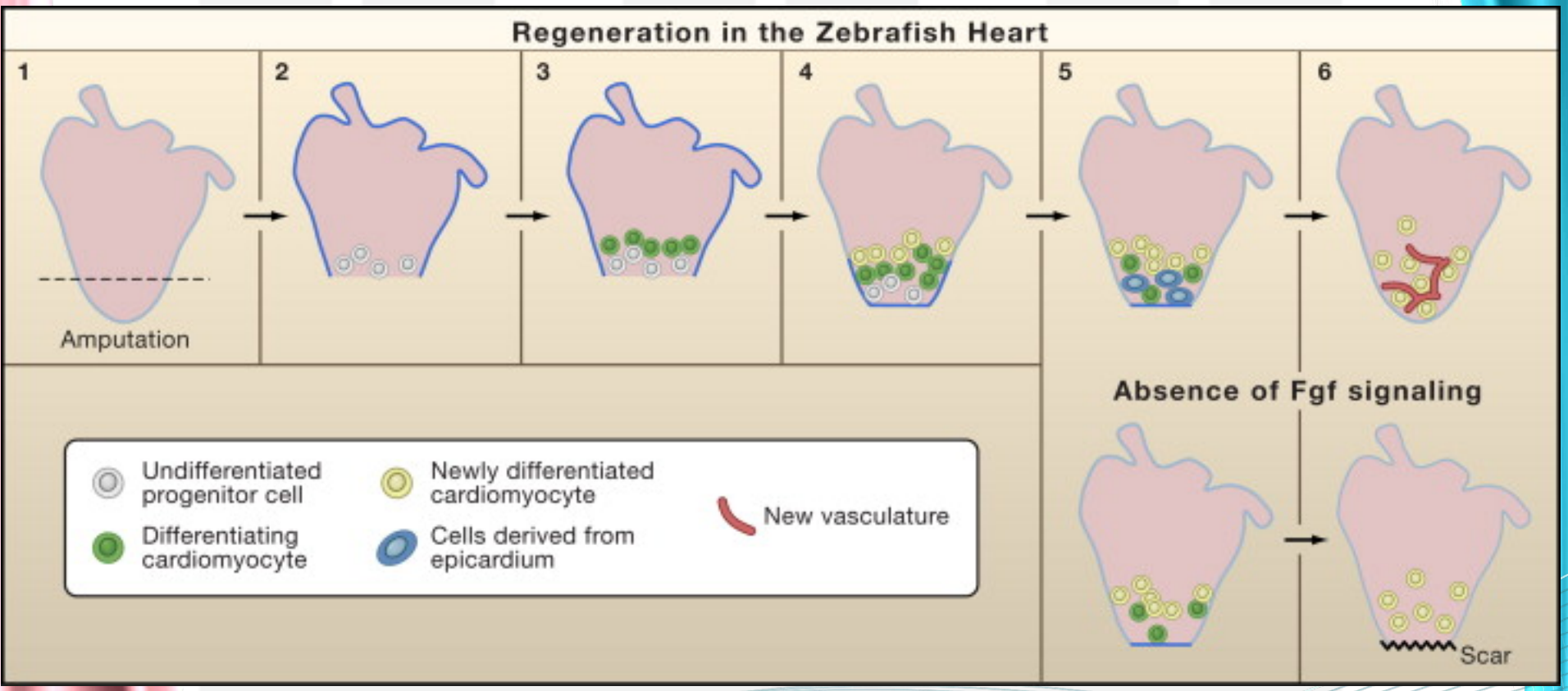
- Dedifferentiation
- Transdifferentiation
- Reprogramming



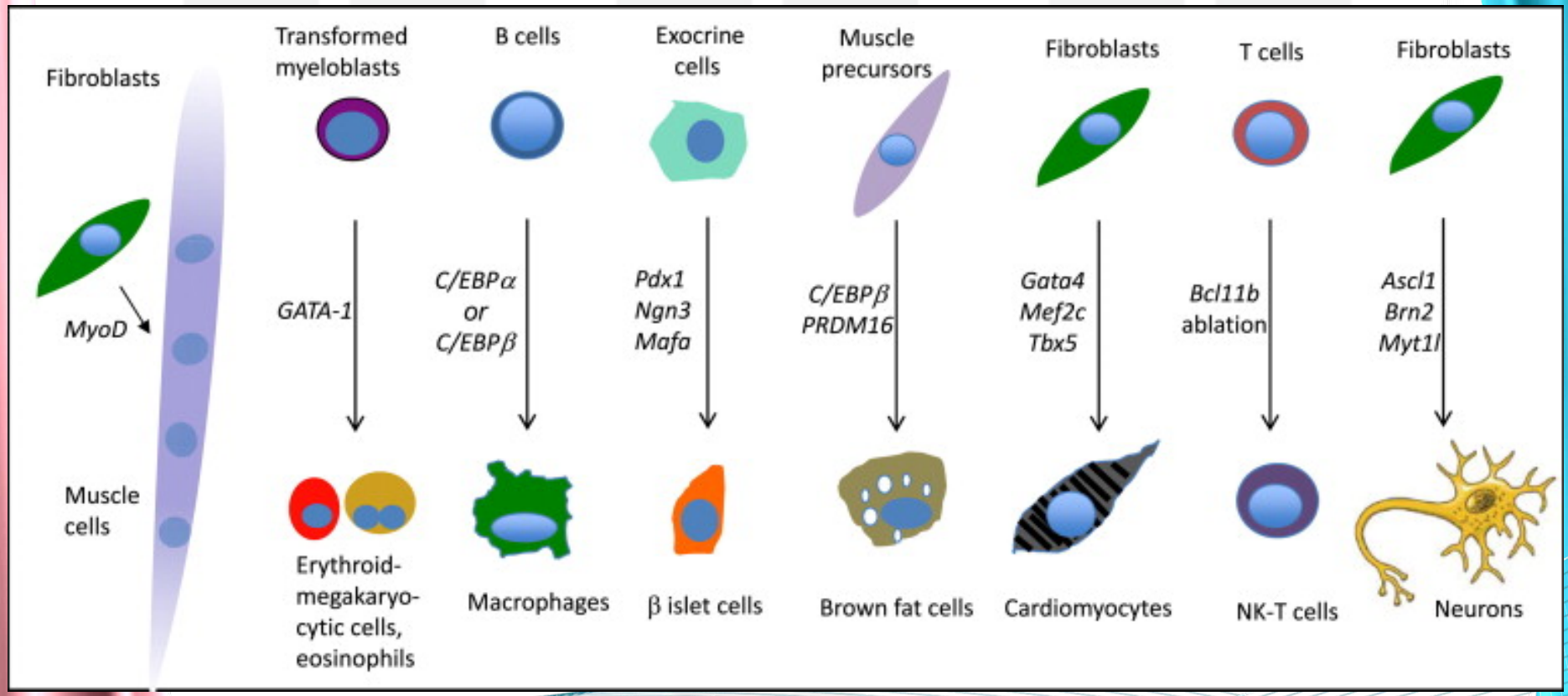
# DEDIFFERENTIATION AND HEART REGENERATION.

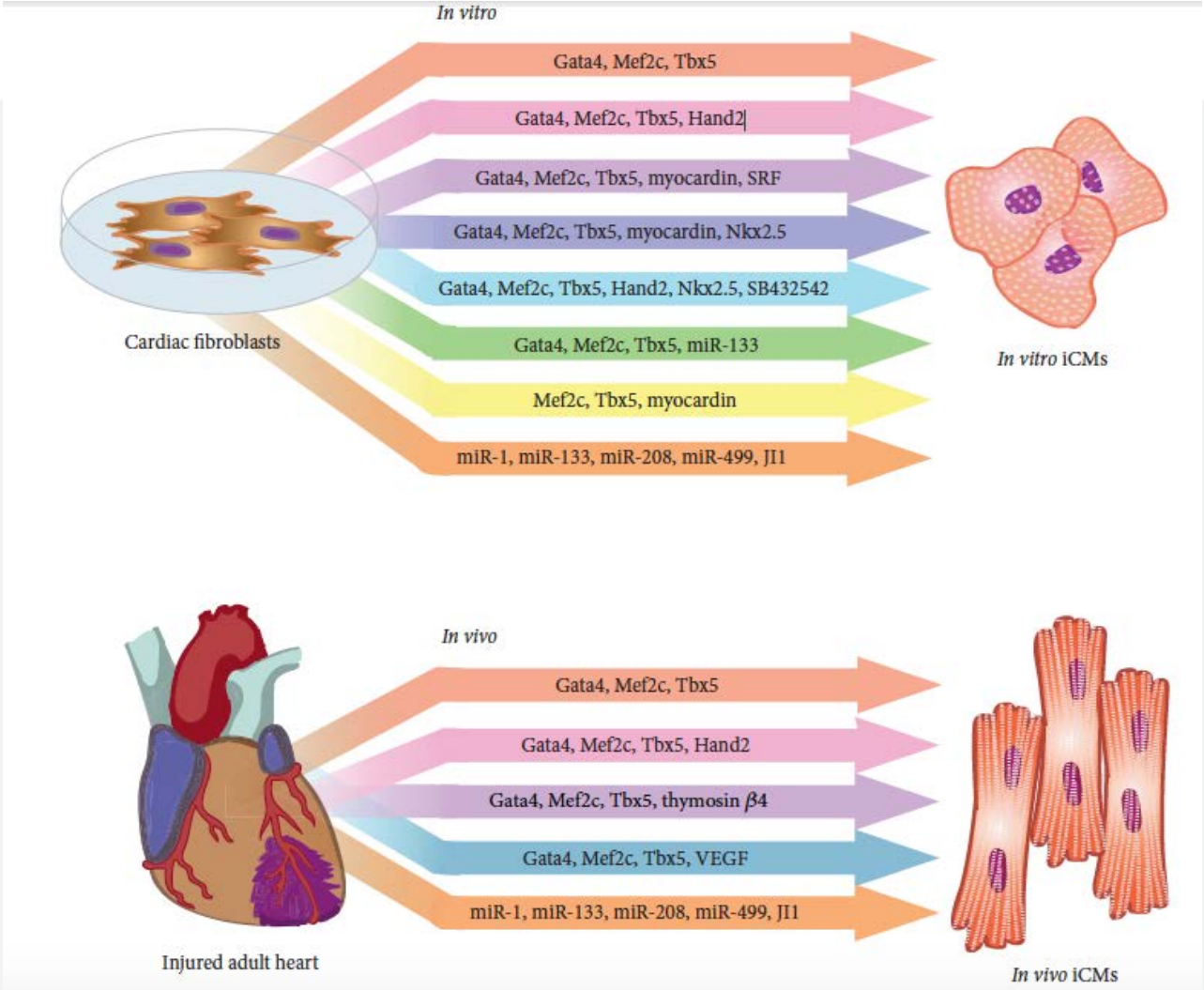


# DEDIFFERENTIATION AND HEART REGENERATION.



# EXPERIMENTAL TRANSDIFFERENTIATION

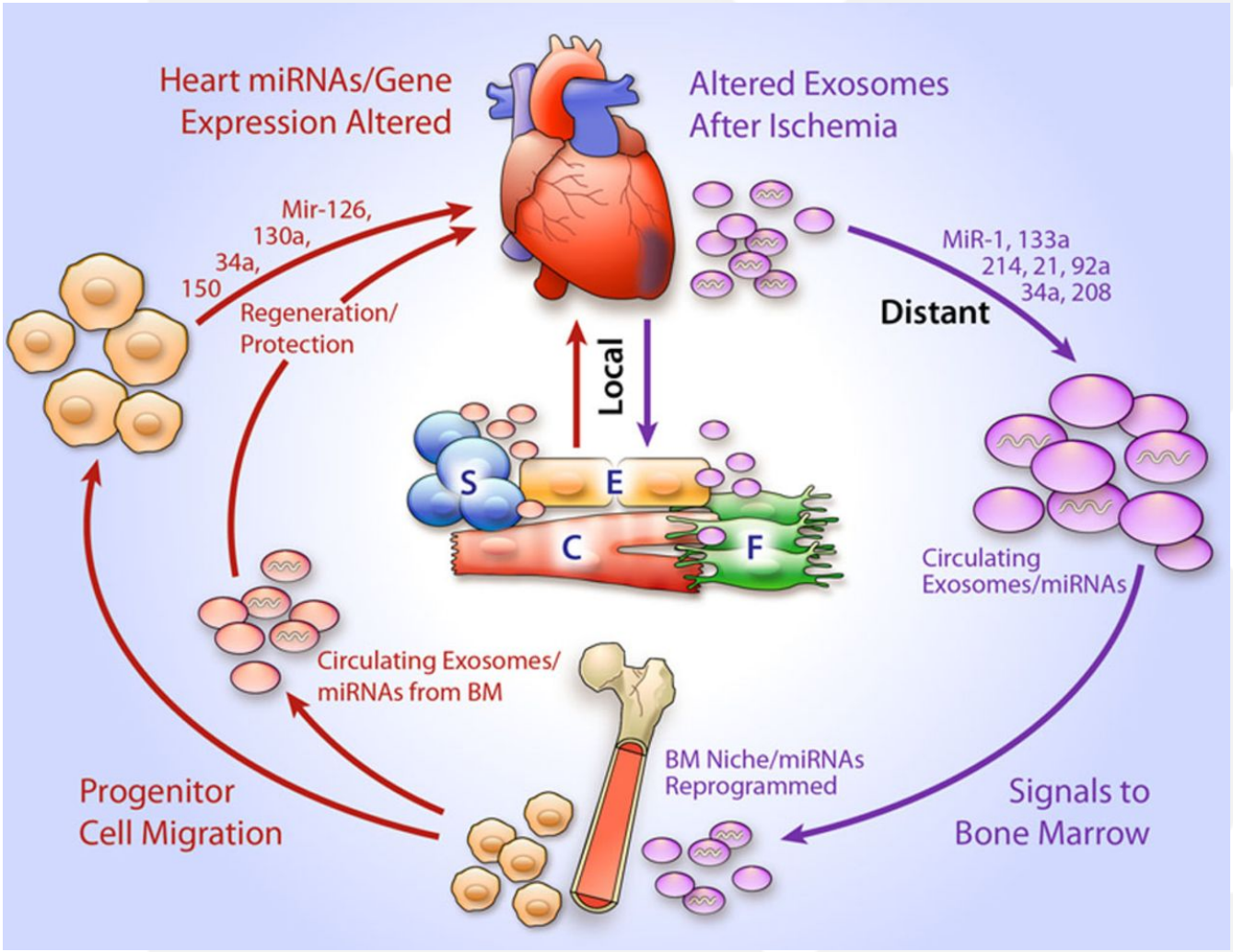





Methods of direct cardiac reprogramming. Several approaches for converting mouse or rat fibroblasts to cardiomyocyte-like cells in vitro and in vivo have been reported and are summarized here. In vitro reprogramming predominantly yields partially reprogrammed cells, while in vivo reprogramming yields more mature, fully reprogrammed cardiomyocyte-like cells. iCMs denotes induced cardiomyocytes

Chen H, et al. BioMed Research International Volume 2015, Article ID 580406, 8 pages

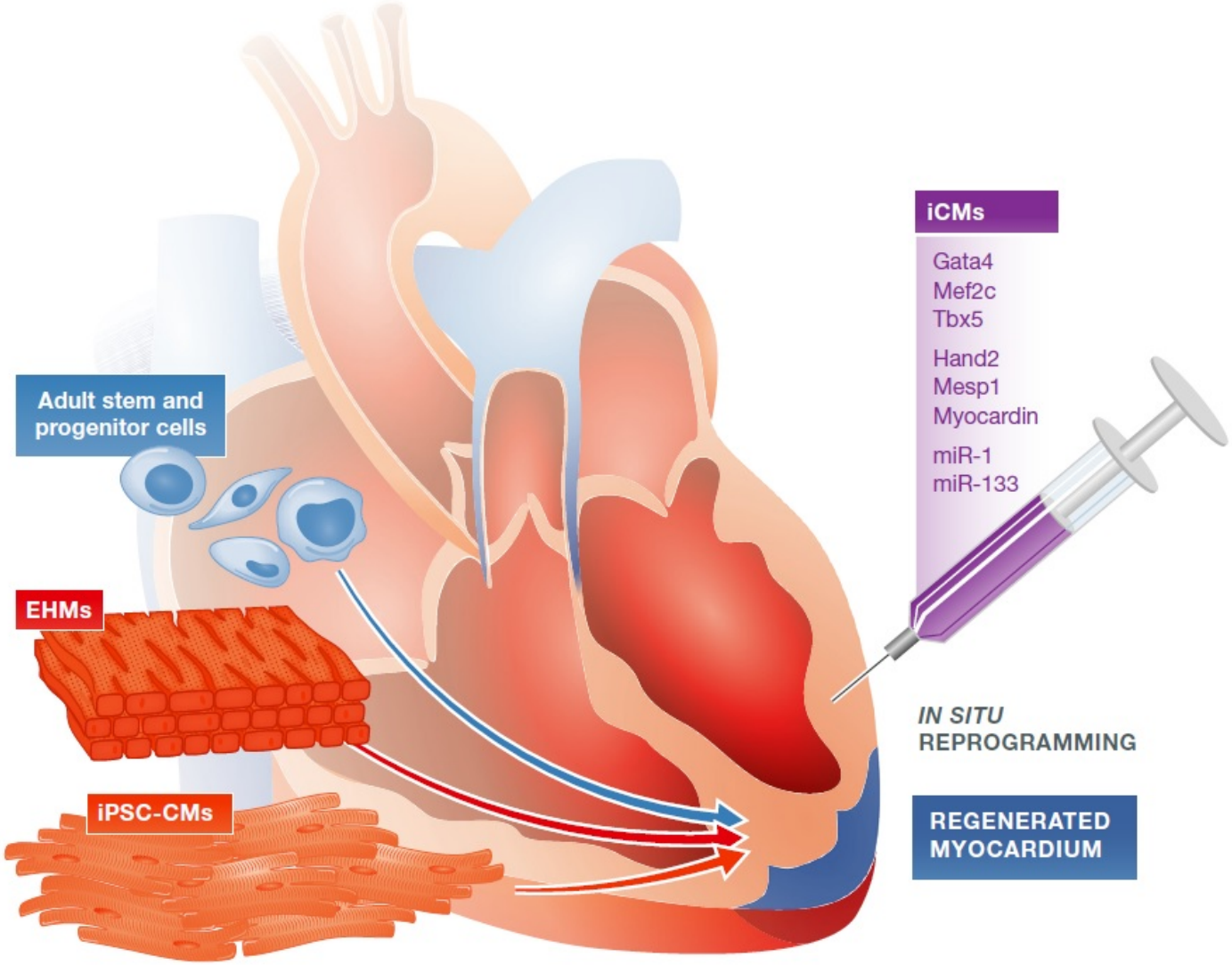
# A suggested hypothesis on the role of exosomes released from a damaged heart as a potential intercellular communicator.




Exosomes can carry signaling molecules to activate local tissues (C indicates cardiomyocytes; E, endothelial cells; F, fibroblasts; and S, stem cells) and distant organs such as bone marrow (BM). Furthermore, the exosomes released from progenitor cells and the reprogrammed BM can reprogram the ischemic tissues of the heart, inducing protection and regeneration (illustration credit: Ben Smith).

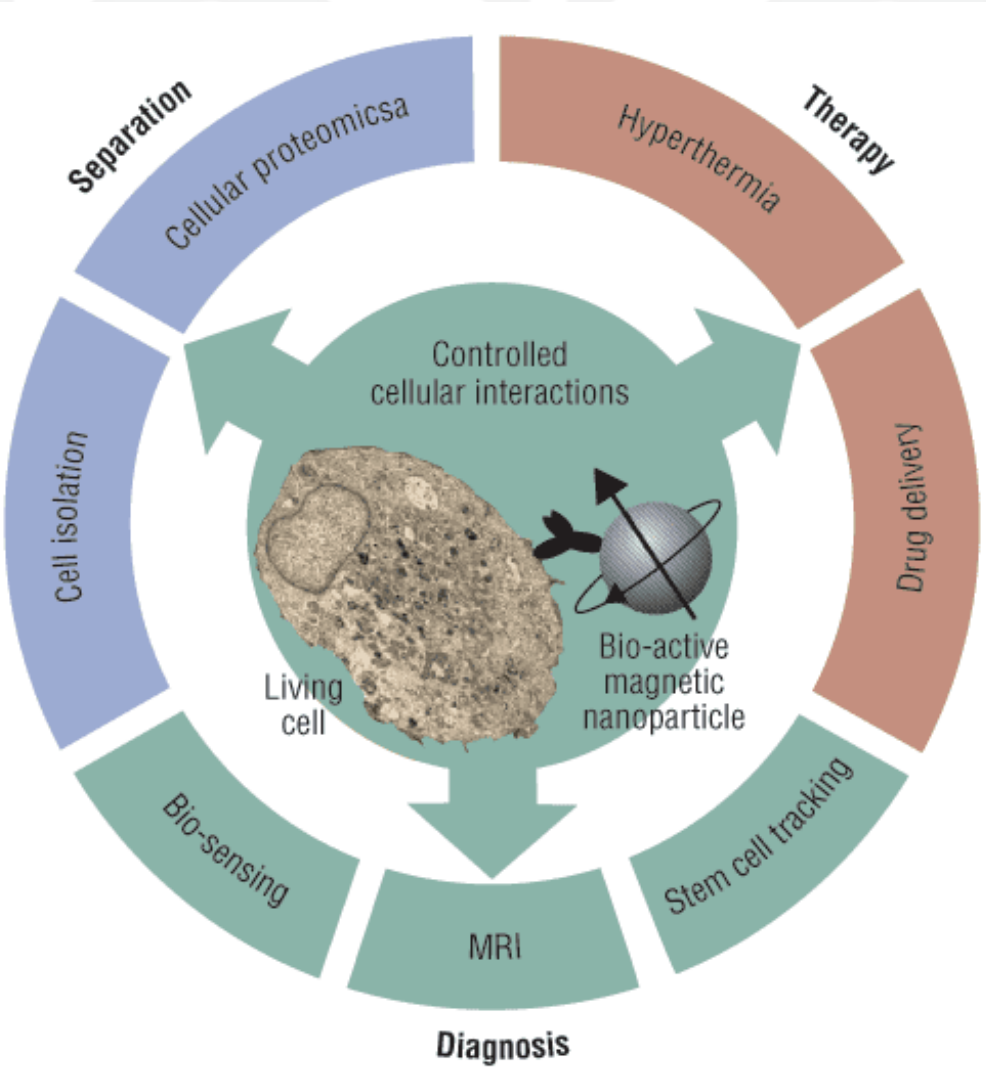
Susmita Sahoo, and Douglas W. Losordo Circulation Research. 2014;114:333-344

American Heart Association.

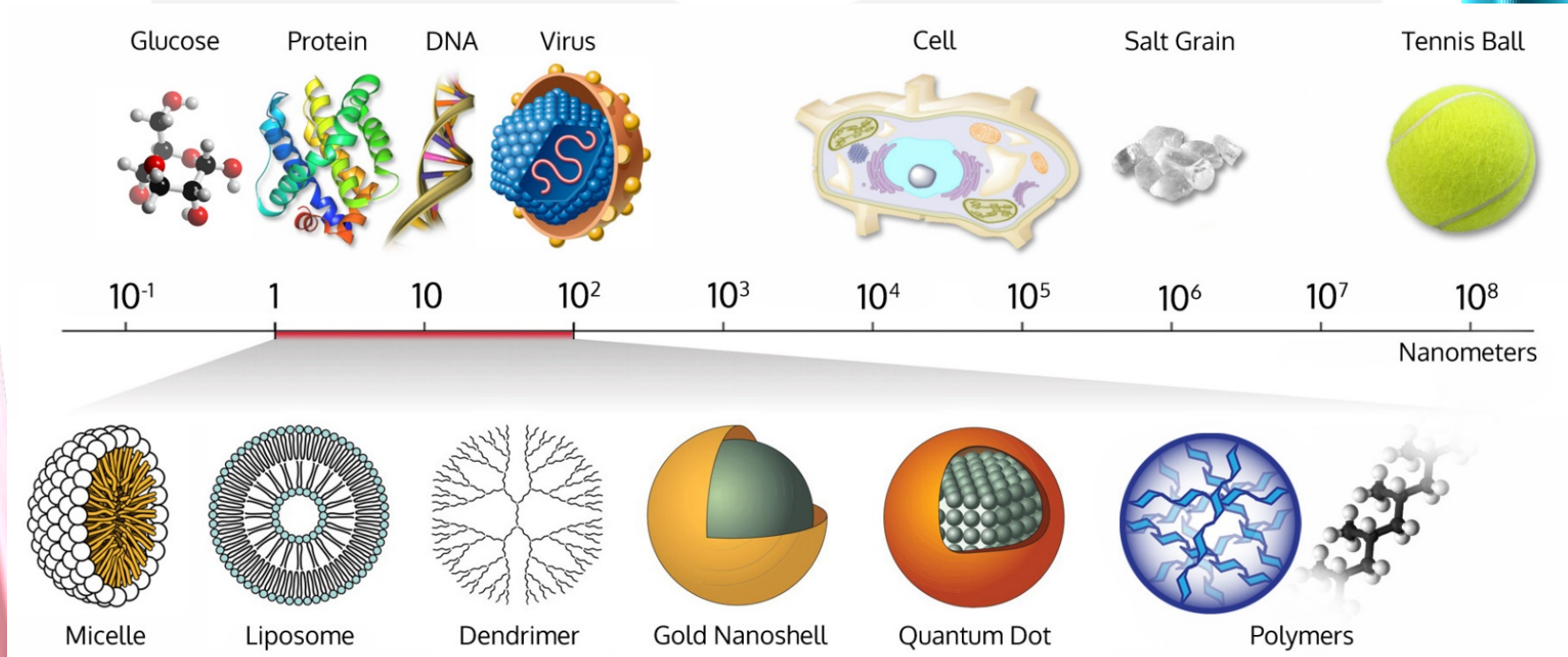


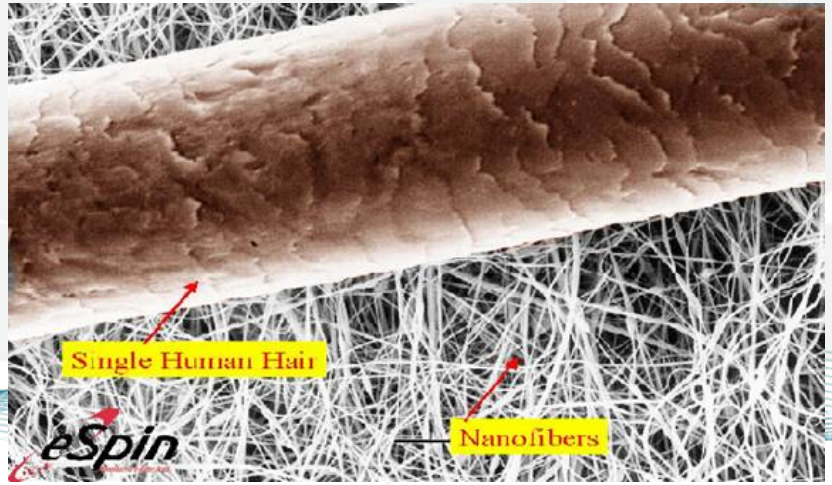

**Cell therapy and tissue engineering approaches for cardiovascular disease therapy.**
Heart failure due to ischemic heart disease or genetic disorders remains a major healthcare burden. Potential novel treatment options include transplantation of iPSC-CMs or ESC-CMs, as well as direct in vivo reprogramming of cardiac fibroblasts in the scar region to iCMs. The regenerative capacity of adult stem and progenitor cell populations is also being evaluated. Tissue engineering is a new method that aims to re-muscularize damaged myocardium via transplantation of in vitro engineered heart muscle made from iPSC-CMs or ESC-CMs. [EHM(Engineered Heart Muscles)]

# NANOTECHNOLOGY AND REGENERATIVE MEDCINE



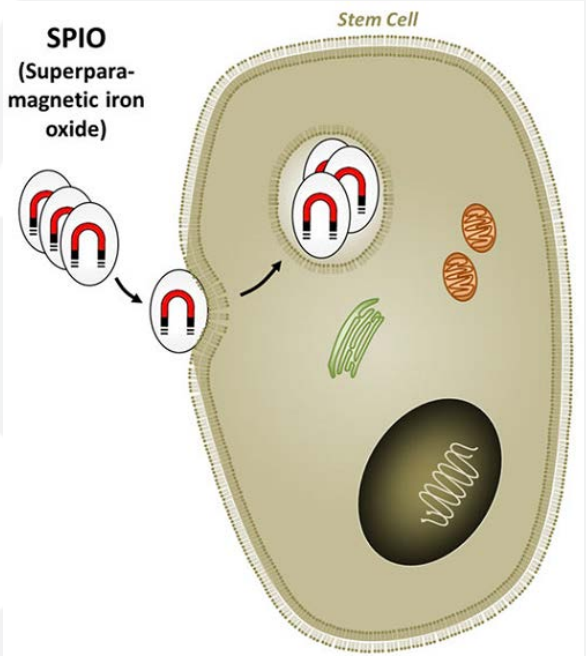
# NANOTECHNOLOGY



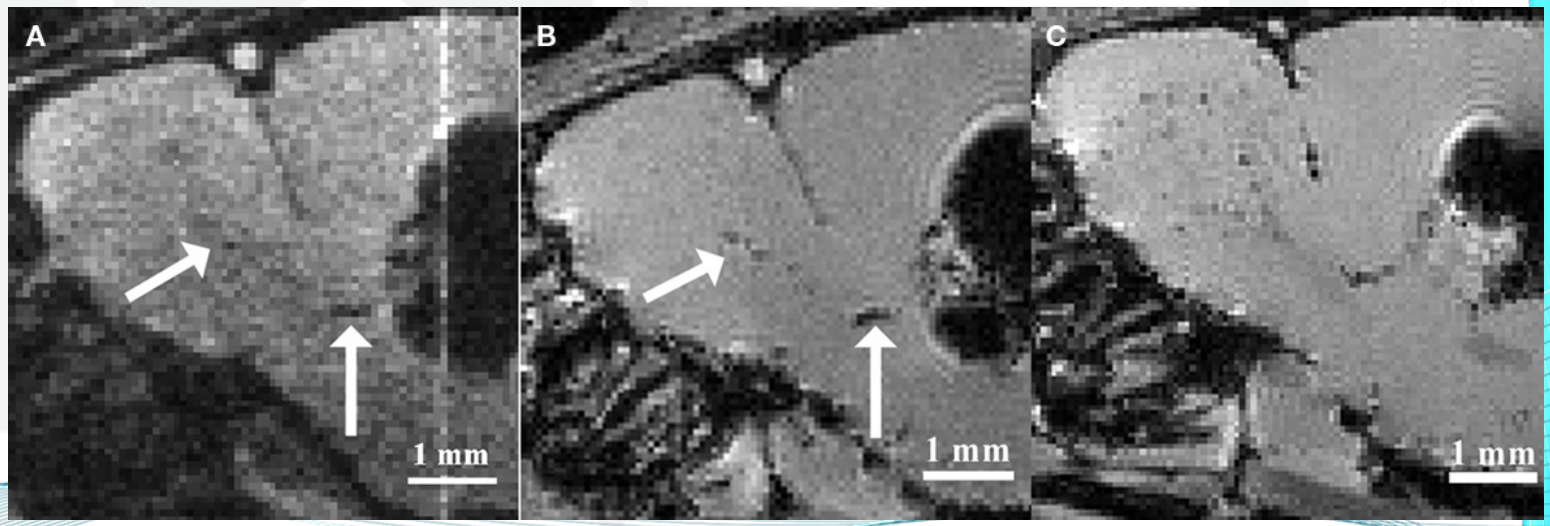



# NANOTECHNOLOGY IN CELL THERAPY

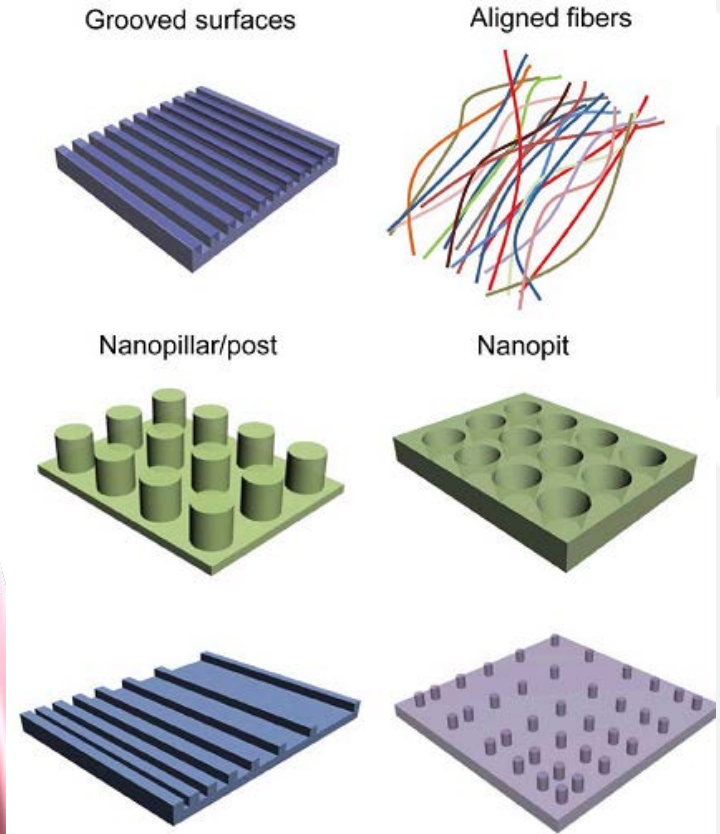
- Cell tracking & imaging
- Cell targeting
- Cell retention

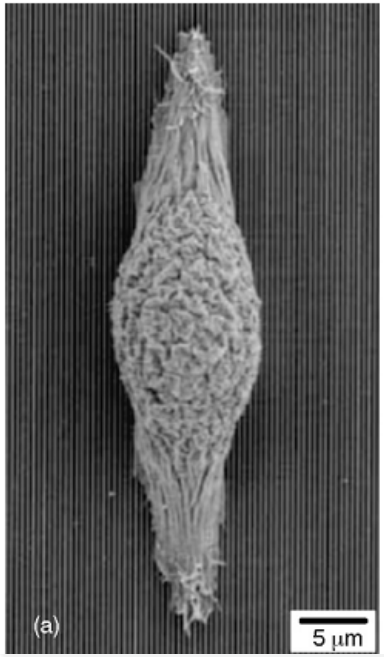


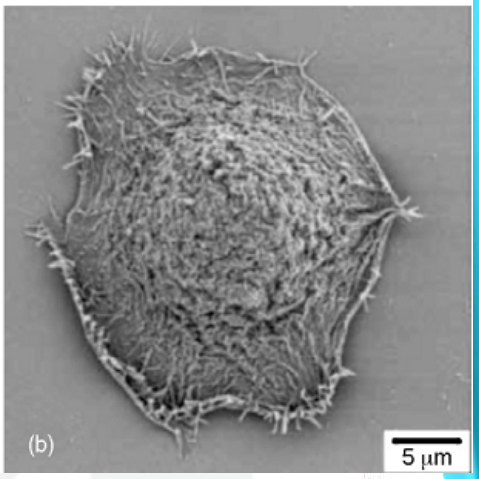

Magnetic resonance imaging of in situ labeled neural precursor cell migration.

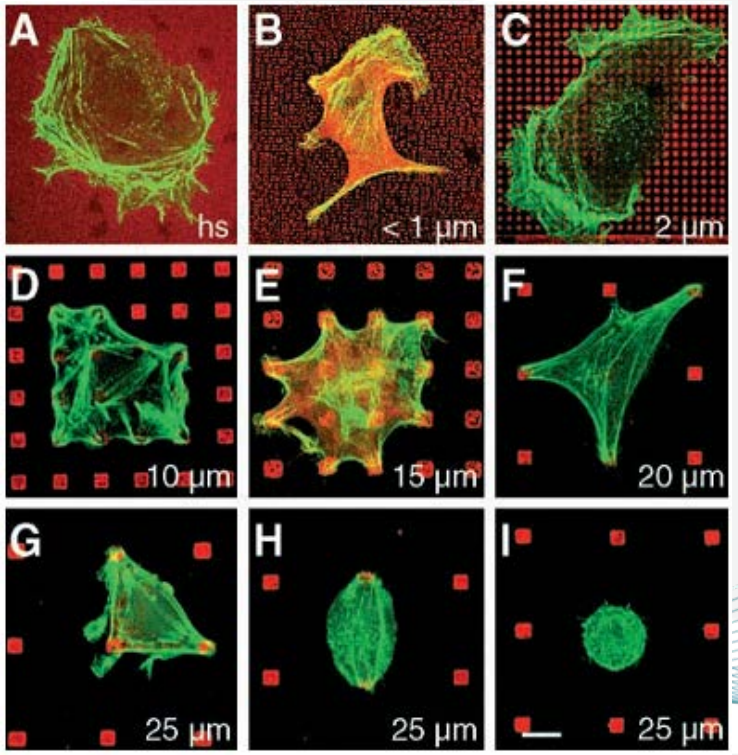


# NANOTECHNOLOGY IN CELL PROCESSING

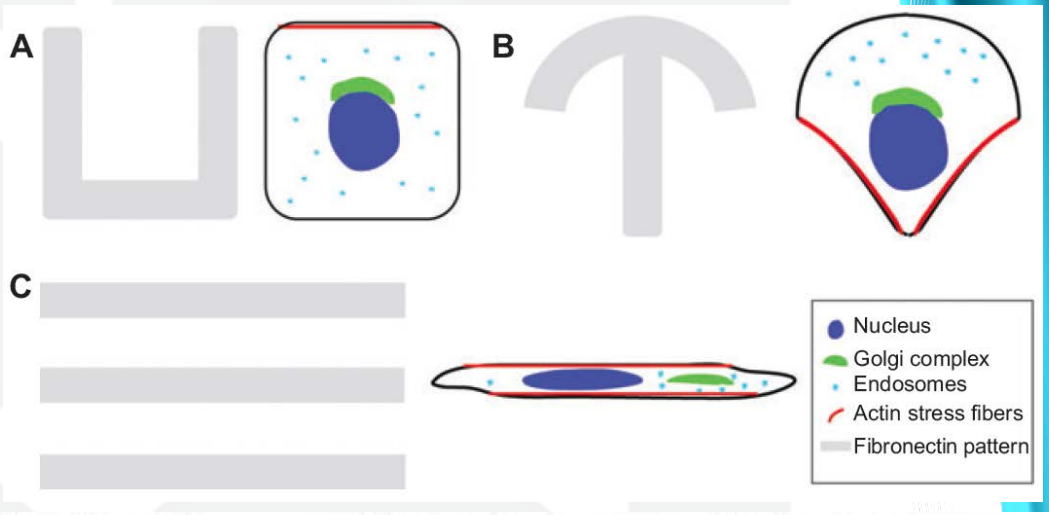


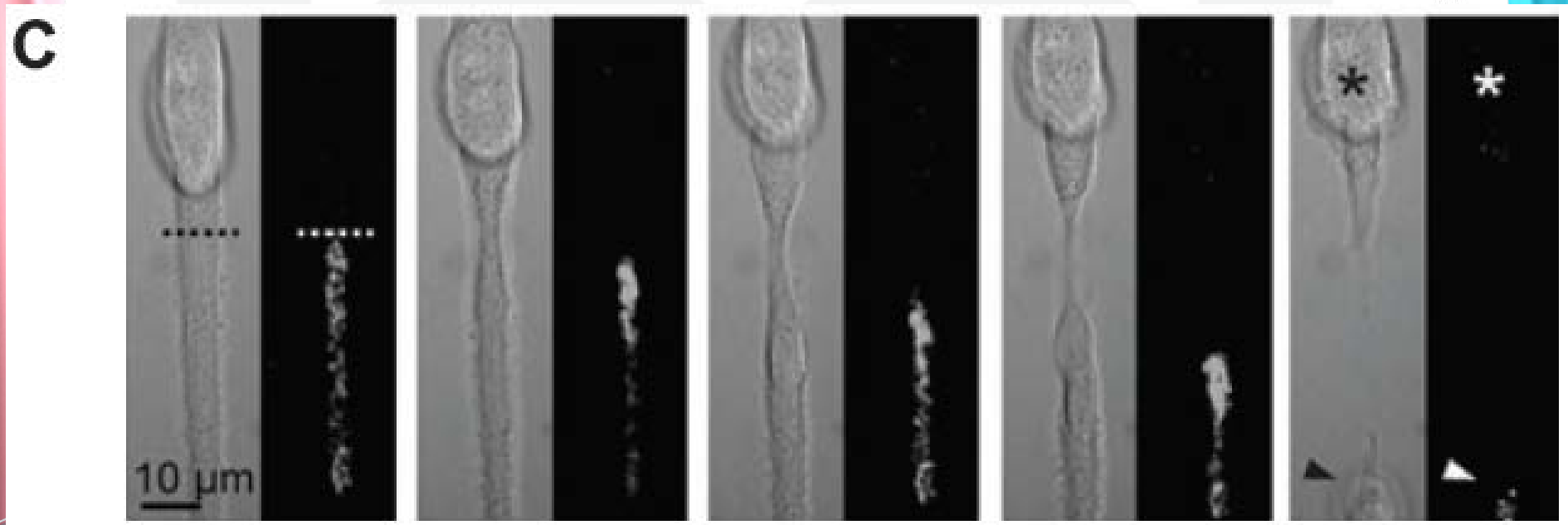



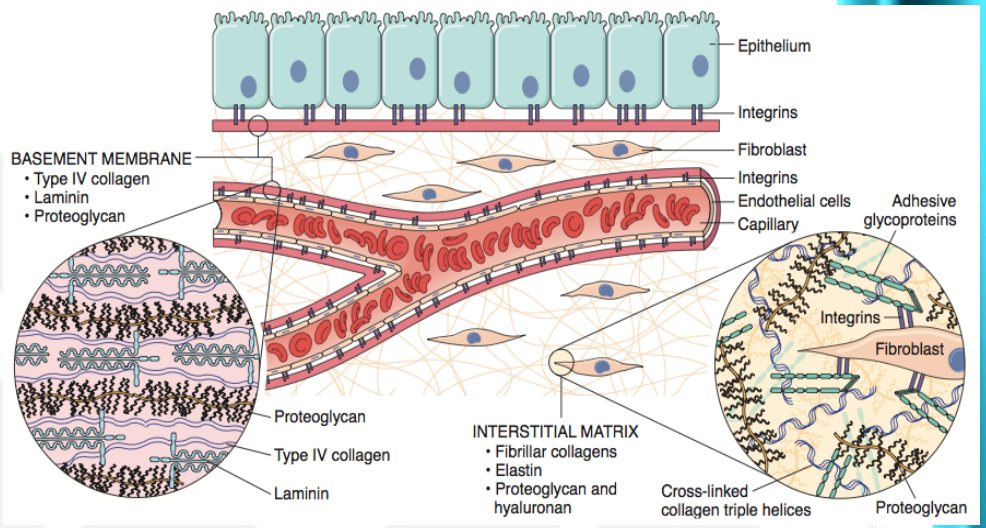
# INTRACELLULAR NANOSURGERY



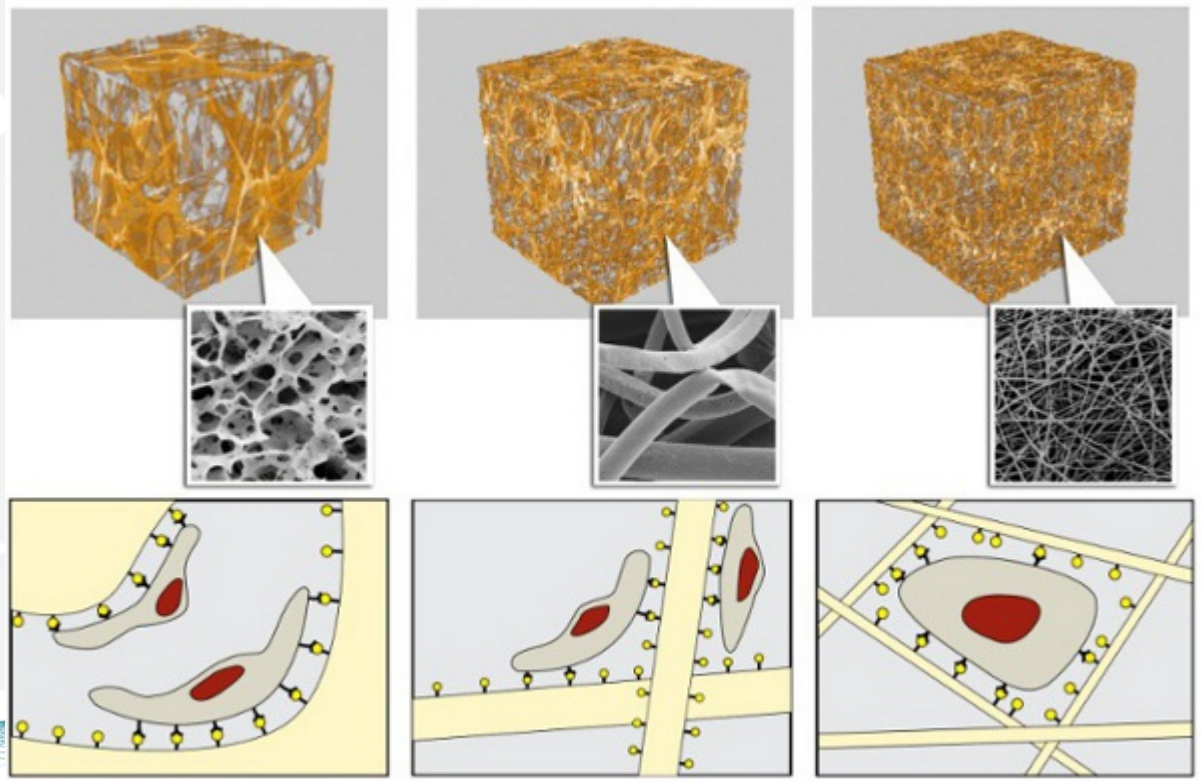

Removal of the Golgi complex from a living cell



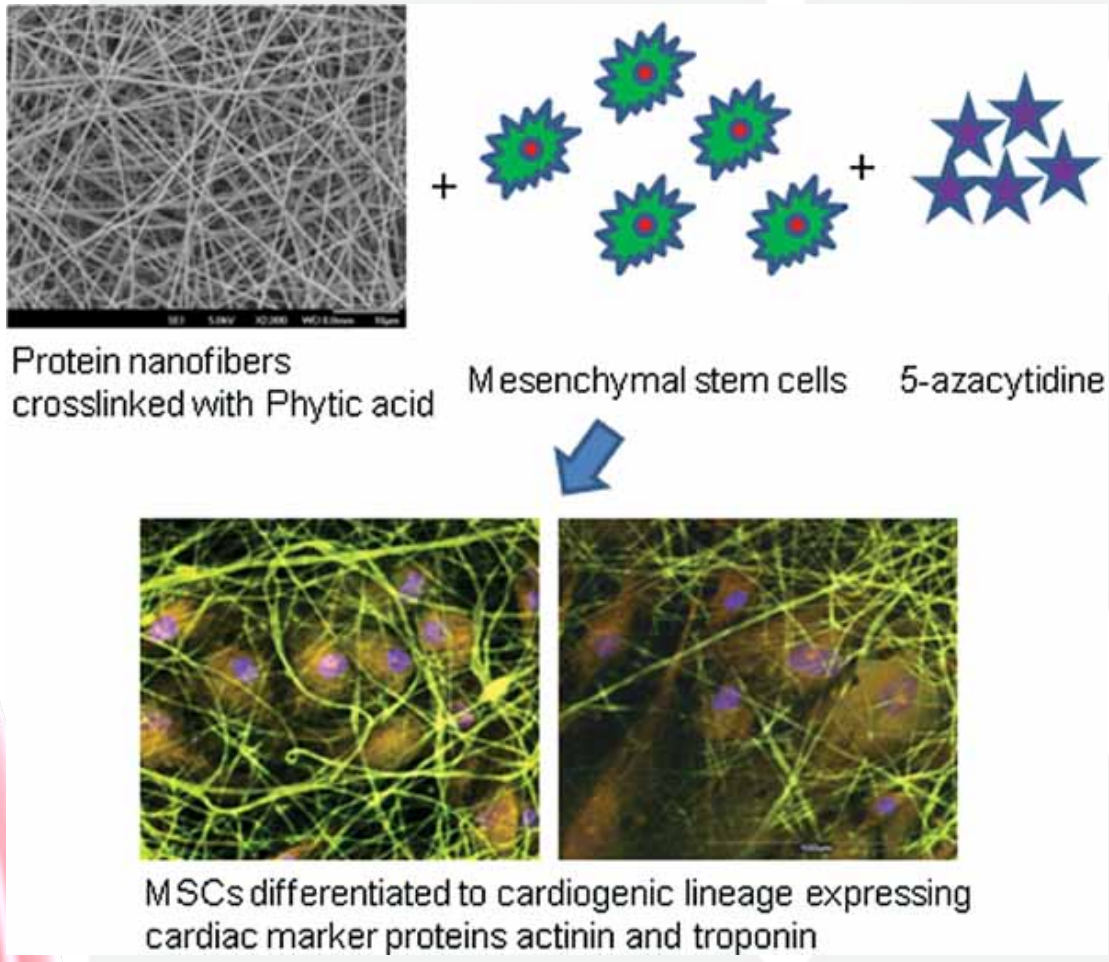
# NANOTECHNOLOGY IN TISSUE ENGINEERING




- Mimicking the nature!
- Smart scaffolds!



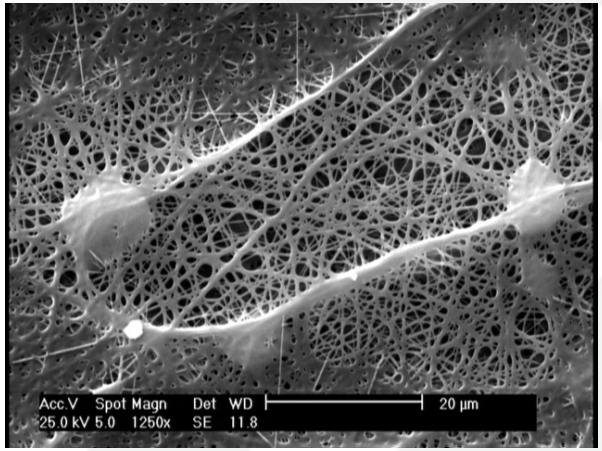
# Nanofibrous scaffolds

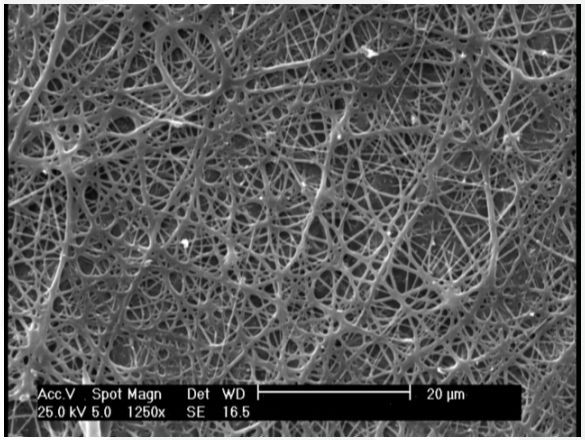


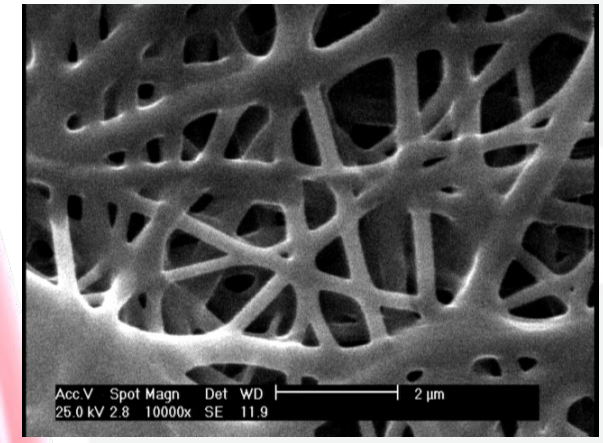

A functional scaffold developed from natural polymers (hemoglobin/gelatin/fibrinogen (Hb/gel/fib), crosslinked with a natural crosslinking agent, phytic acid. Pretreatment of mesenchymal stem cells (MSCs) using 5-azacytidine and such a functional nanofibrous construct having a high oxygen carrying potential could lead to enhanced cardiomyogenic differentiation of MSCs.

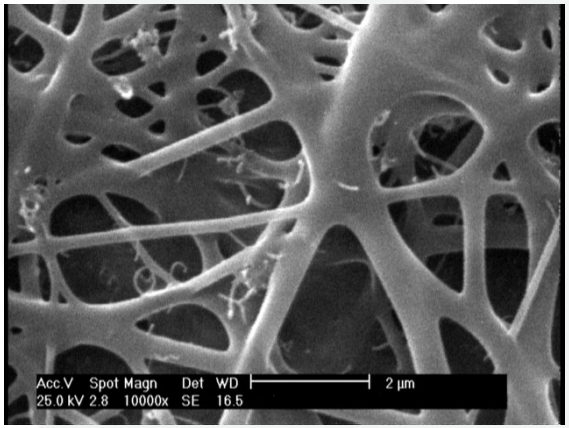
Ravichandran, R. et al. Macromol. Biosci. 2013, 13, 366–375

# CONDUCTIVE NANOFIBROUS CARDIAC PATCH



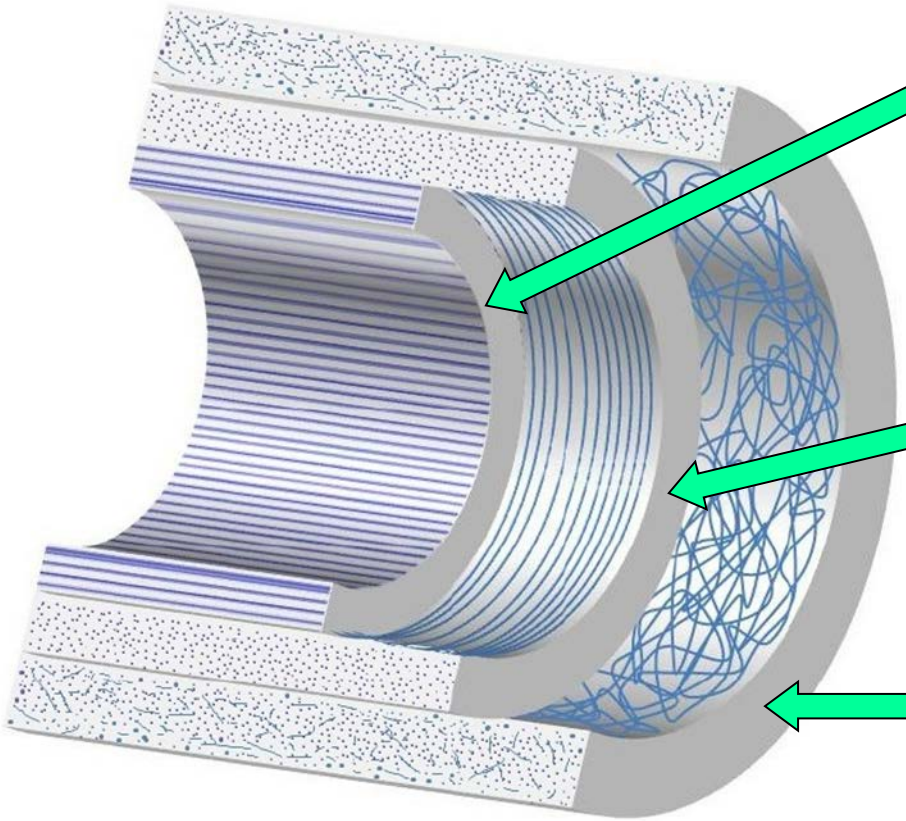




PU

PU+CNT

Ghanbari, H. et al.
unpublished data

# Nanofibrous Vascular Grafts



*Inner layer with linearly aligned nanofibers – providing longitudinal mechanical strength and laminar flow of the blood.*

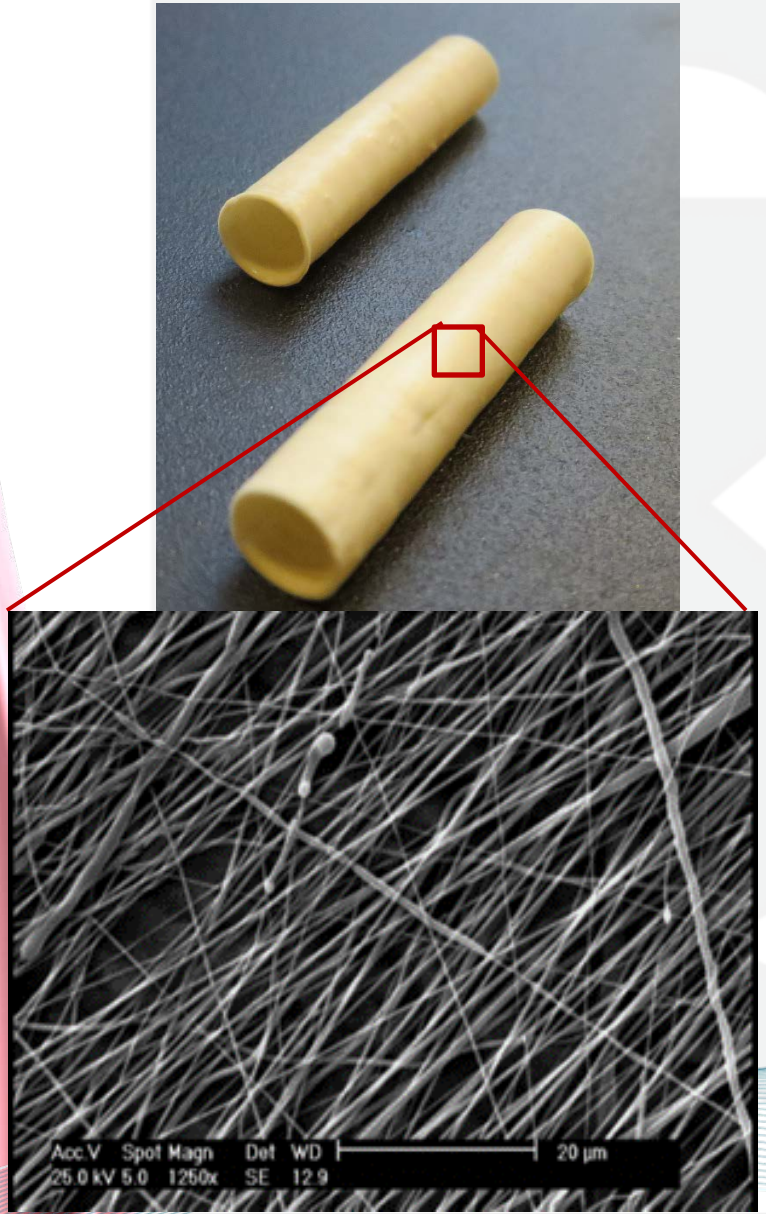
*Middle layer with perpendicularly wrapped nanofibers – main mechanical support preventing bursting of the graft.*

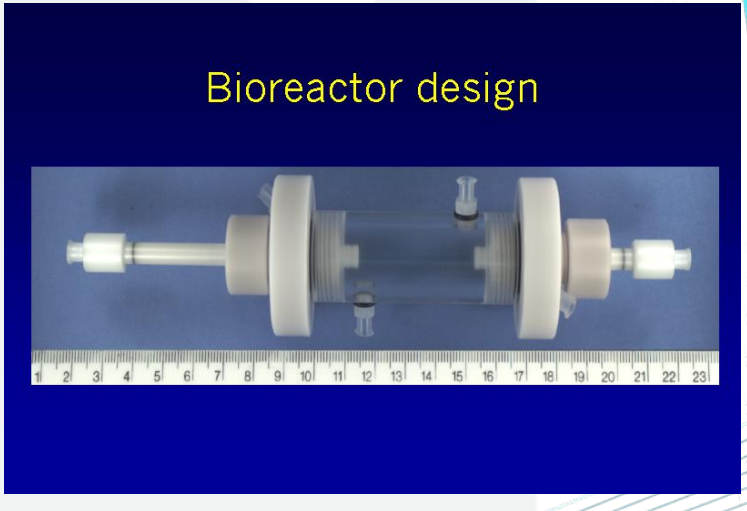
*Outer layer with randomly deposited nanofibers – providing integration with sorrounding tissues.*

*Schematic of a three-layered vascular graft scaffold with different fiber alignment for each layer.*

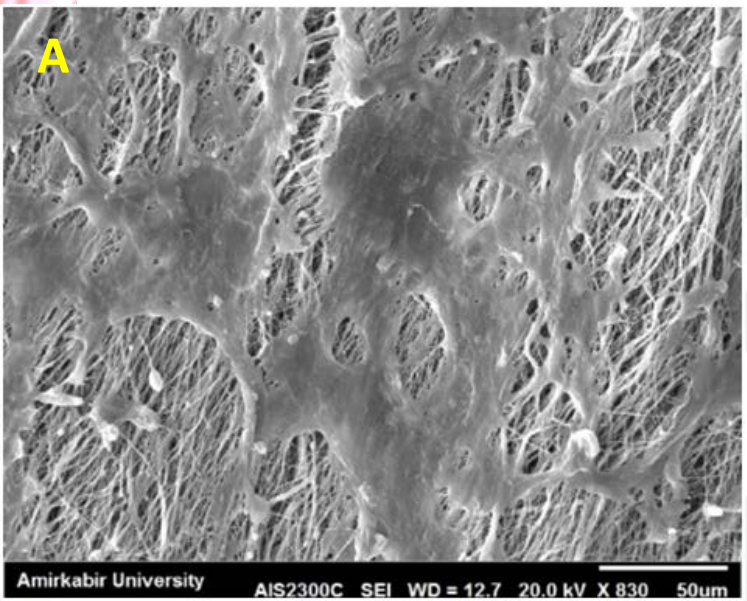
*Courtesy of Seeram Ramakrishna, NUS Center for Nanofibers & Nanotechnology*

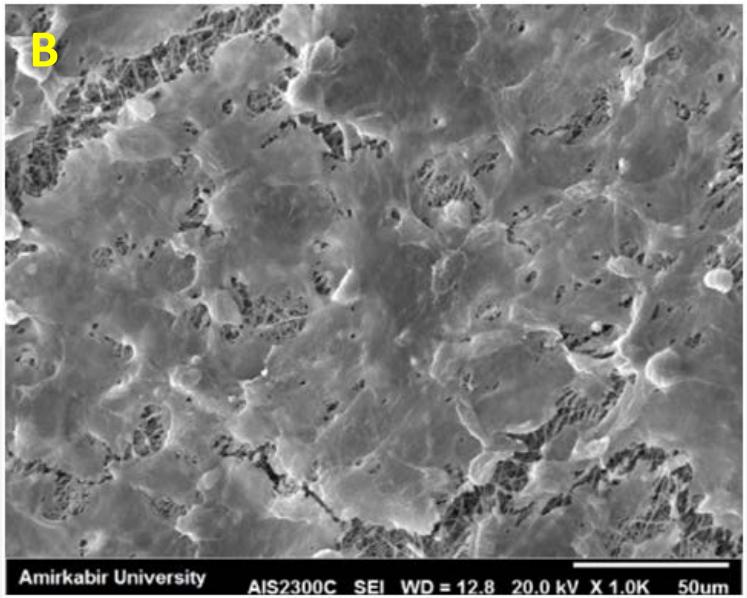
# Nanofibrous tissue engineering bypass graft (PU)



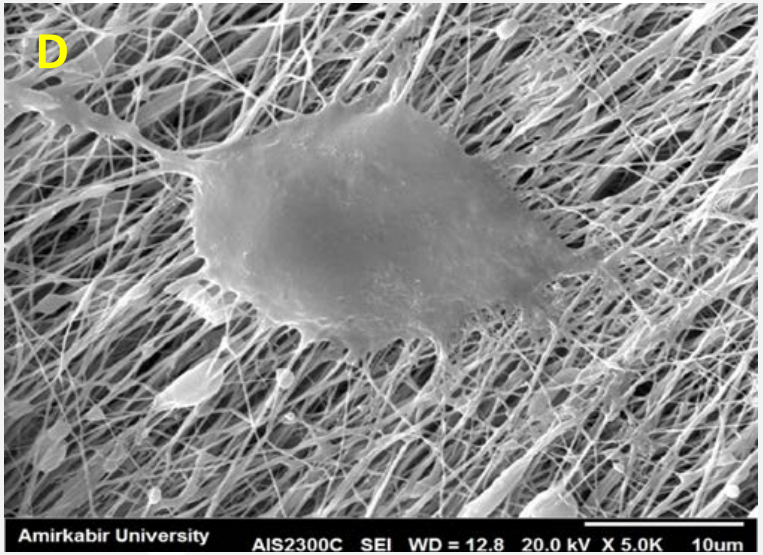




Ghanbari, H. et al. unpublished data



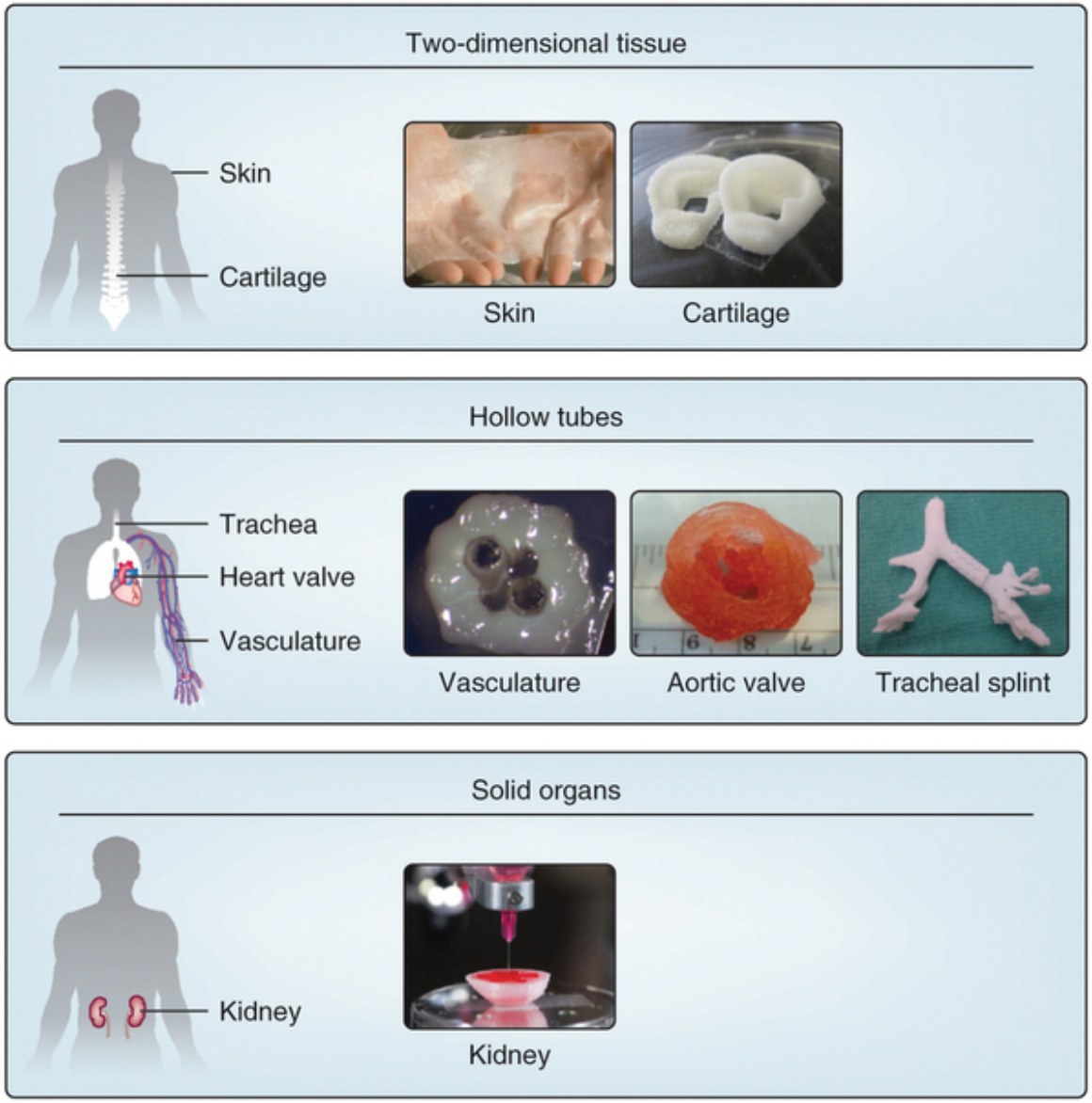





The effect of aminolysis on cell attachment and proliferation (HUVEC cells cultured on pristine PU (a,c) and aminolysed nanofibers (b,d)).

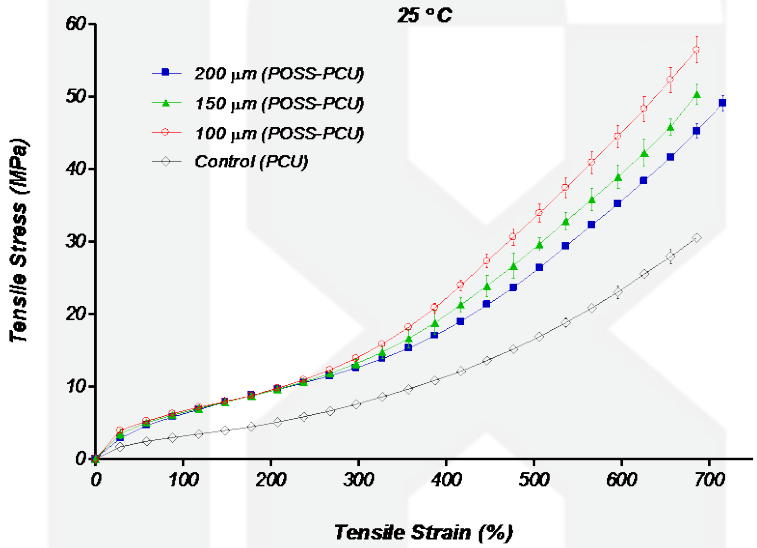
Ghanbari, H. et al. unpublished data

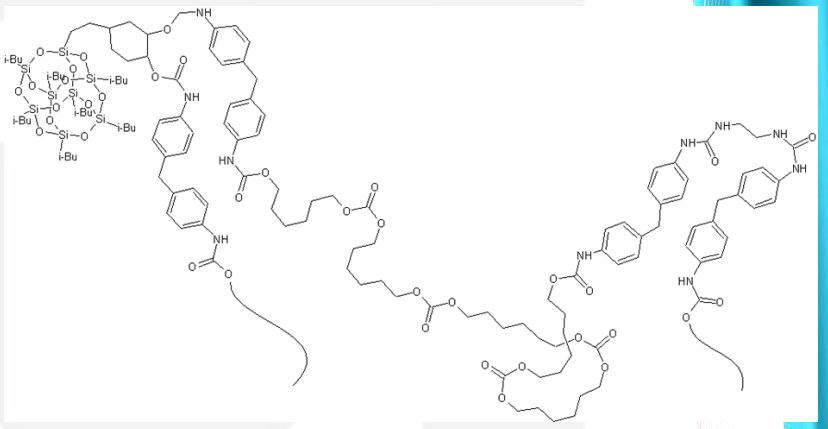
# 3D BIOPRINTING OF TISSUES AND ORGANS

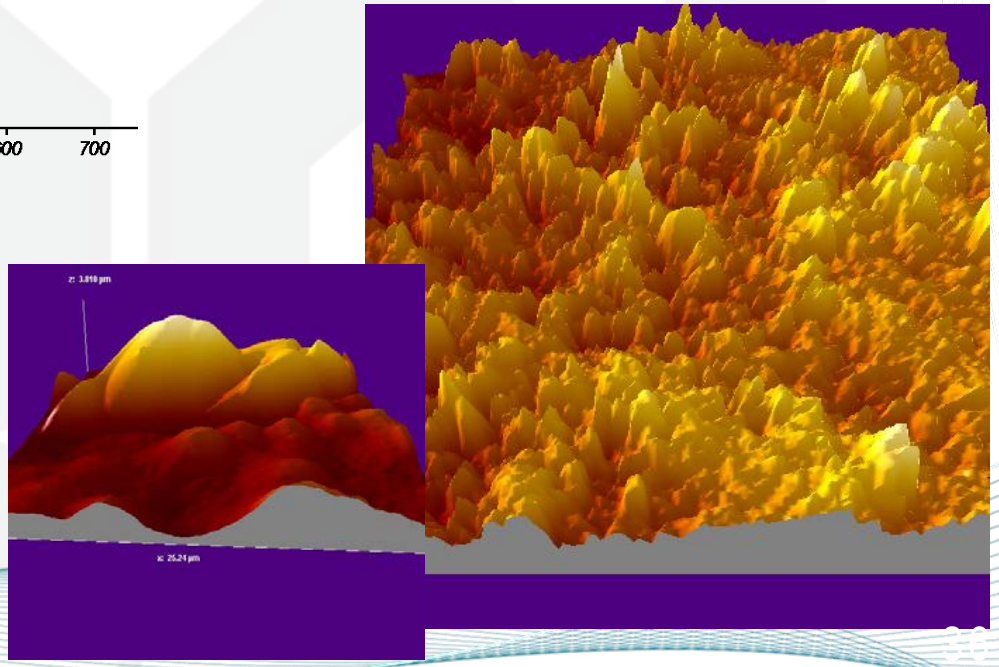




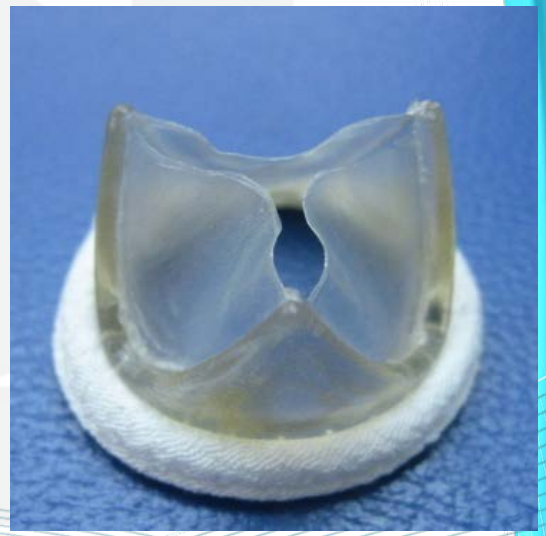
# NANOTECHNOLOGY AND MEDICAL IMPLANTS IMPLANTS



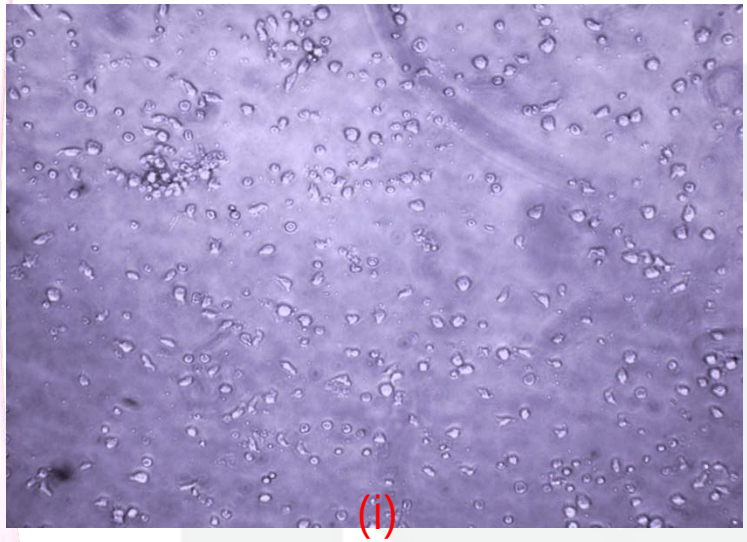





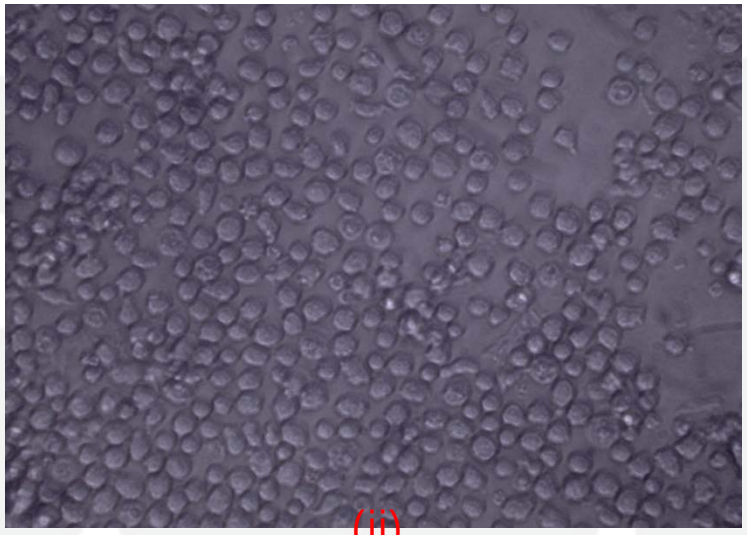
# Nanocomposite heart valve with self-endothelialisation potential



A

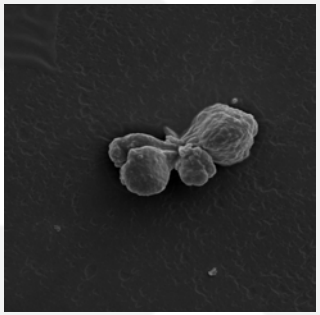


(i)



(ii)

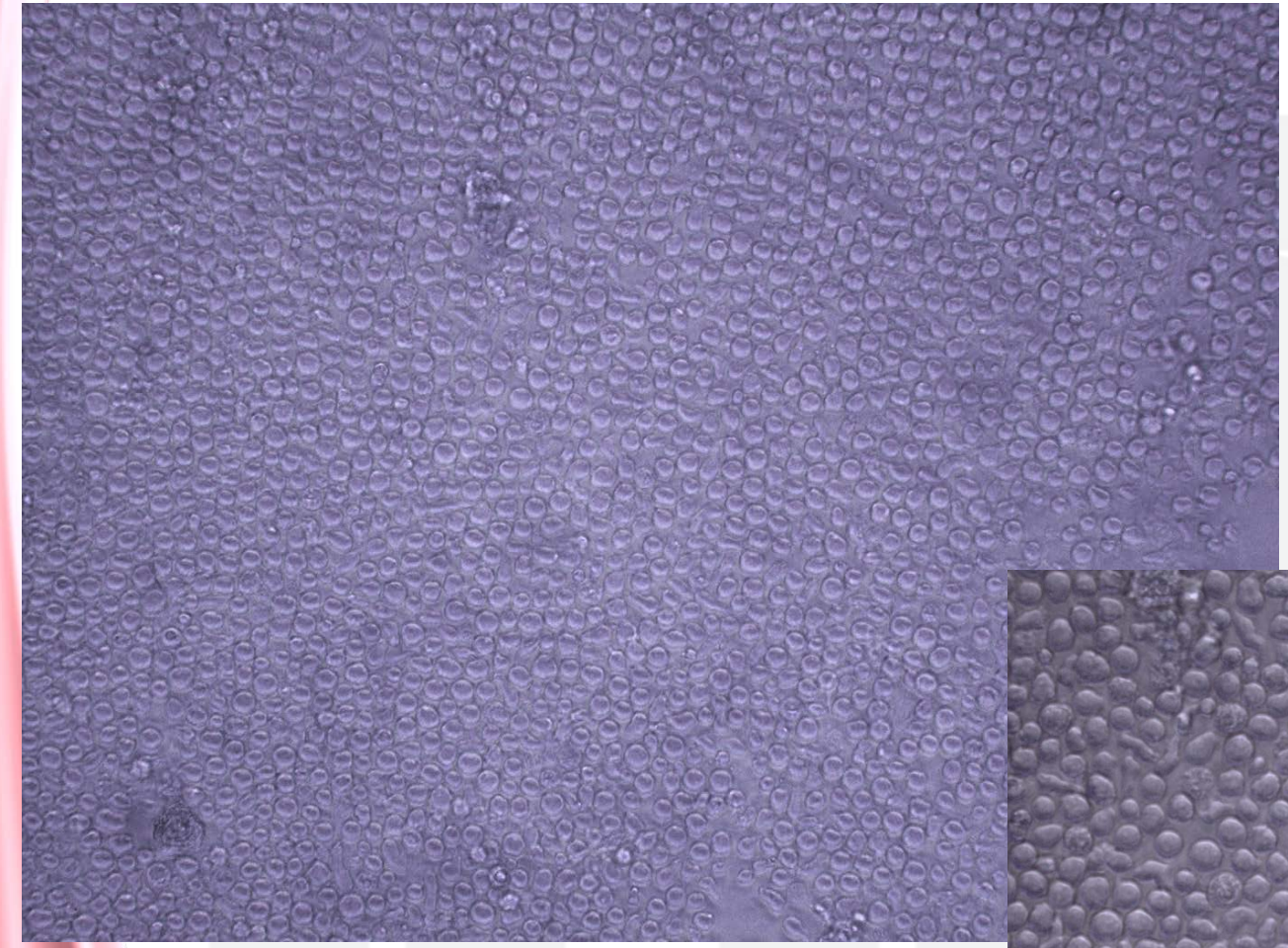
B



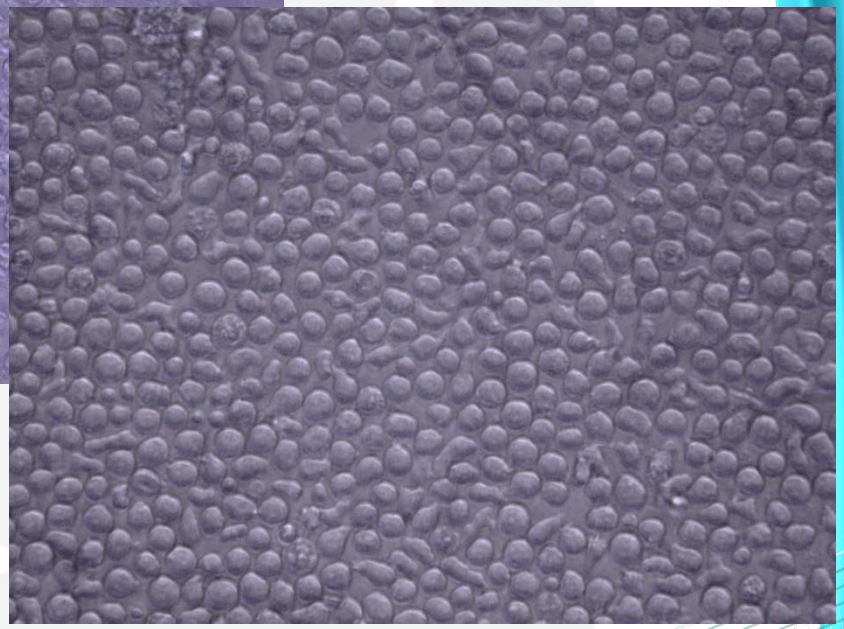
A) Live light microscopy images of EPC, cultured on nanocomposite (NC) samples in (i) day 7 and (ii) day 21, showing the early spindle-shaped morphology in day 7 has been dominated by the late cobblestone shaped phenotype in day 21. A colony of EPC is marked with arrow.

B) Scanning electron microscopy represents attachment and proliferation of EPC on nanocomposite samples. The inset shows cells undergoing division.

# CONFLUENT LAYER OF ECS

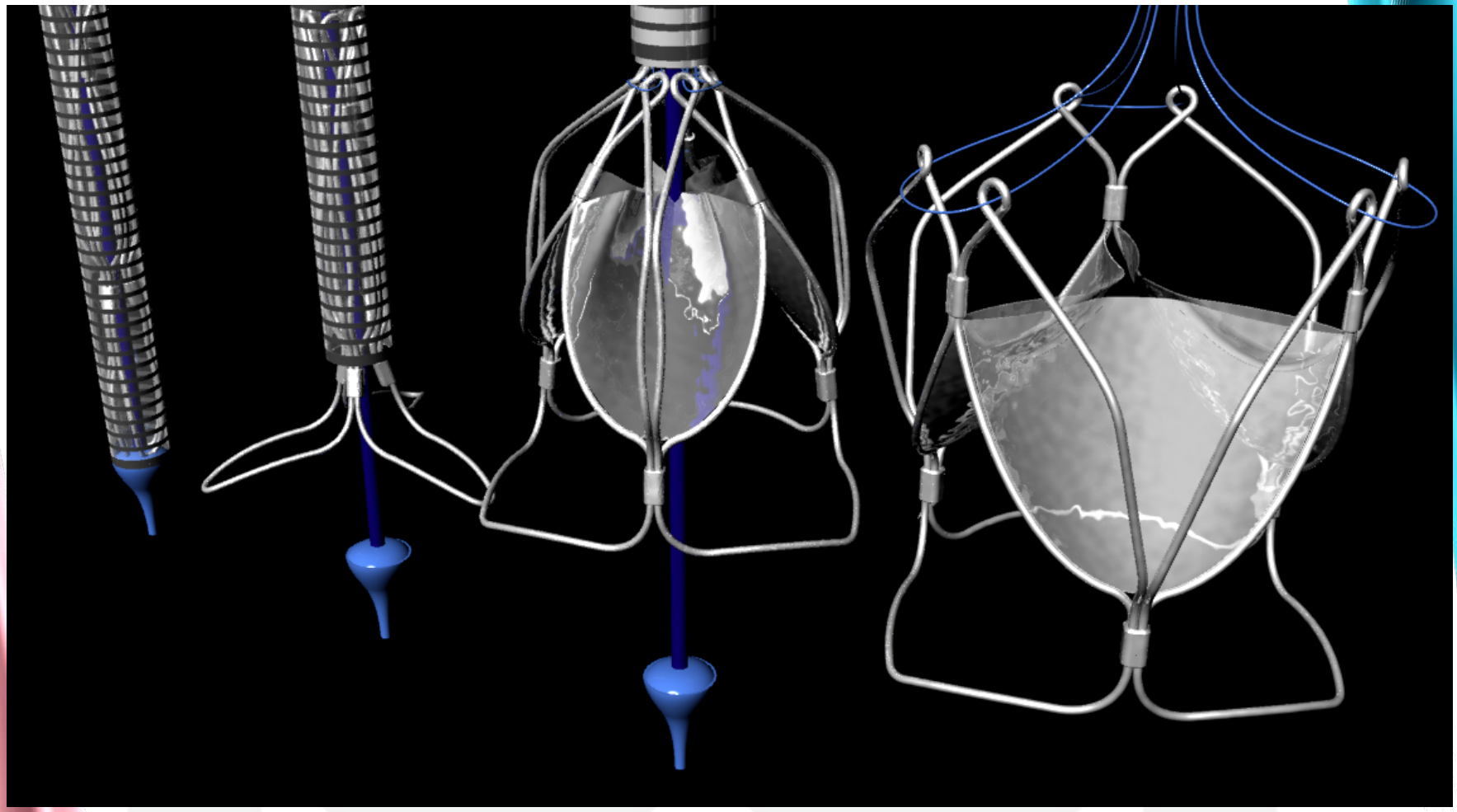


D21 (×20)



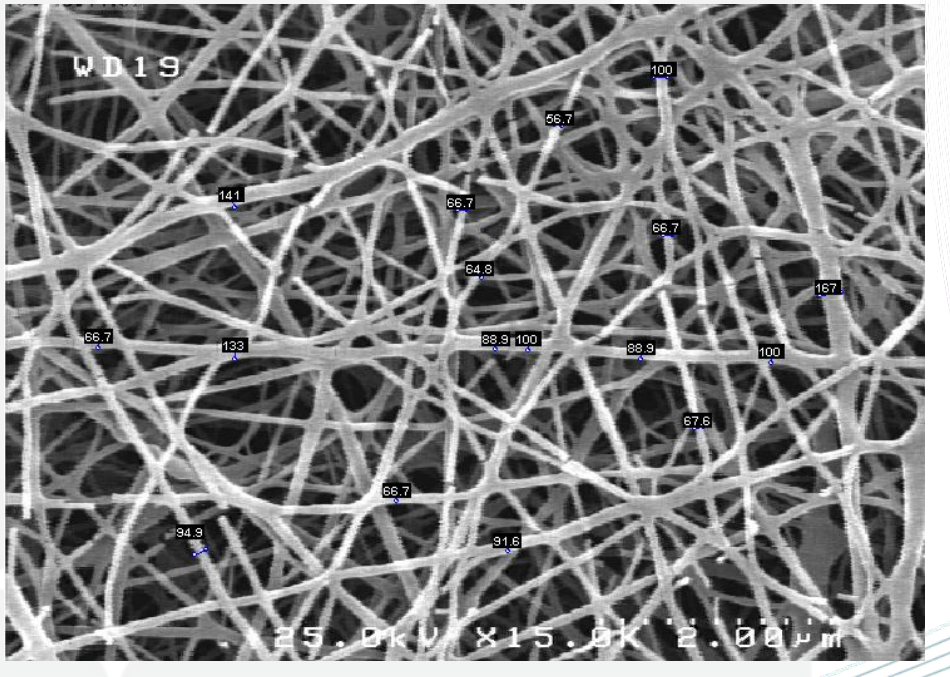
D21 (×40)

# PERCUTANEOUS HV

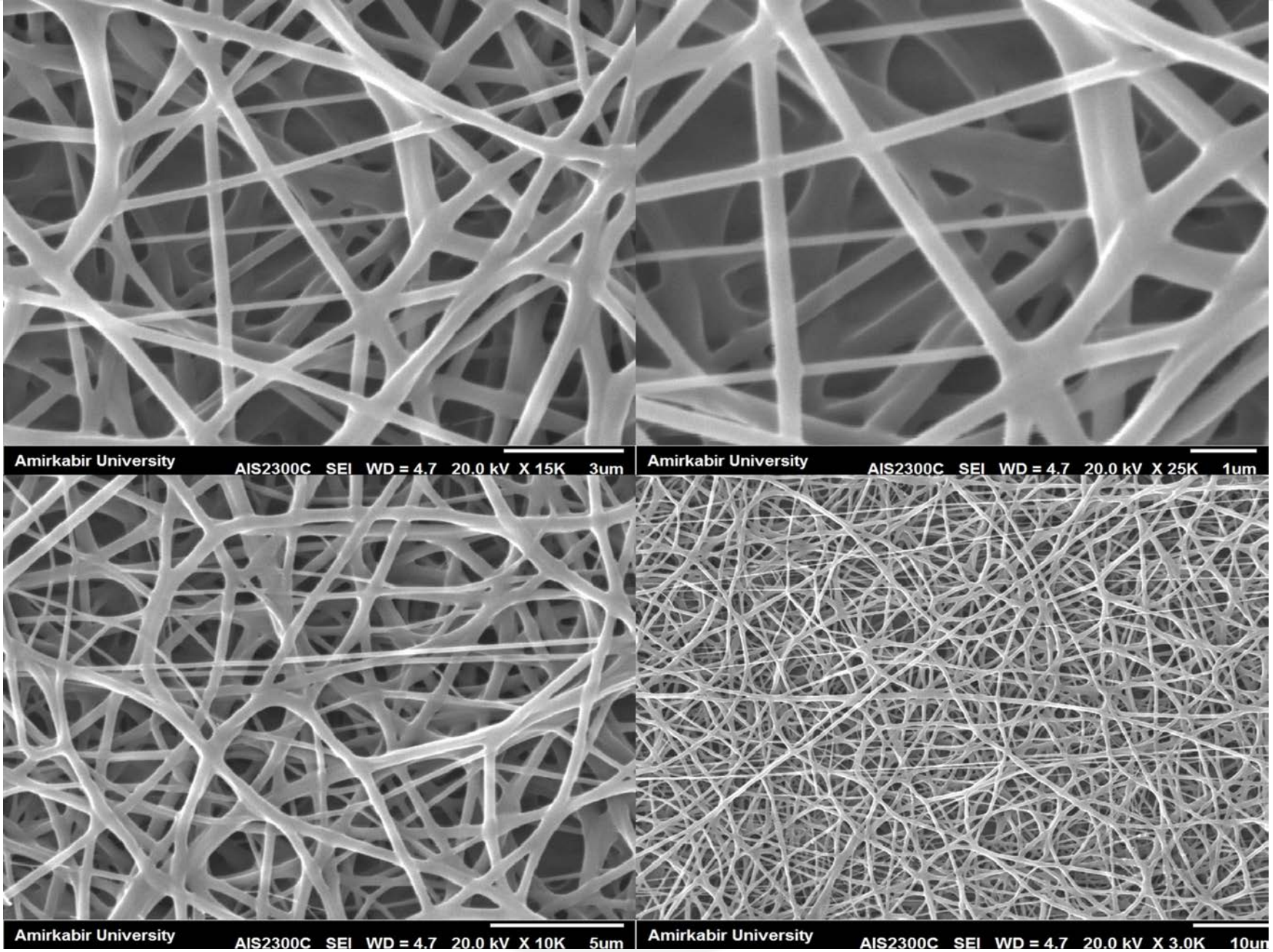


Fully retrievable and repositionable; ensures enhanced anchoring and sealing without applying excessive pressure on the annulus and allows to maximise the expanded/collapsed diameters ratio.

# NANOFIBROUS TISSUE ENGINEERING HEART VALVE

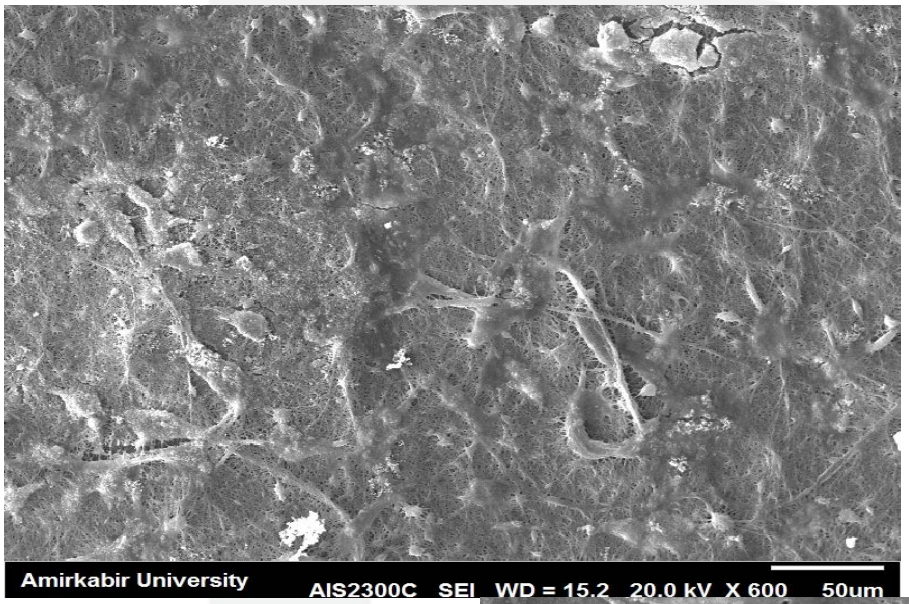


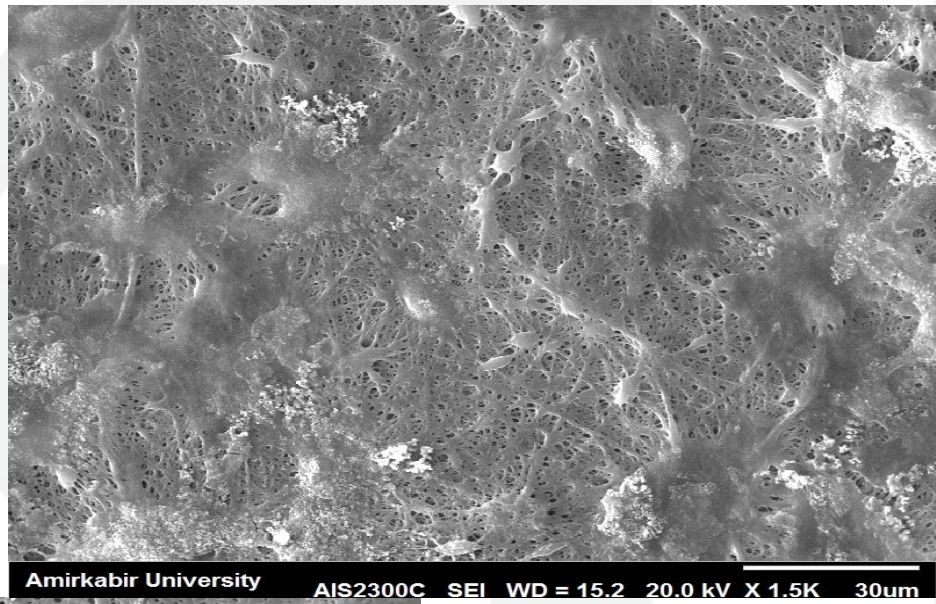

Ghanbari, H. et al. unpublished data

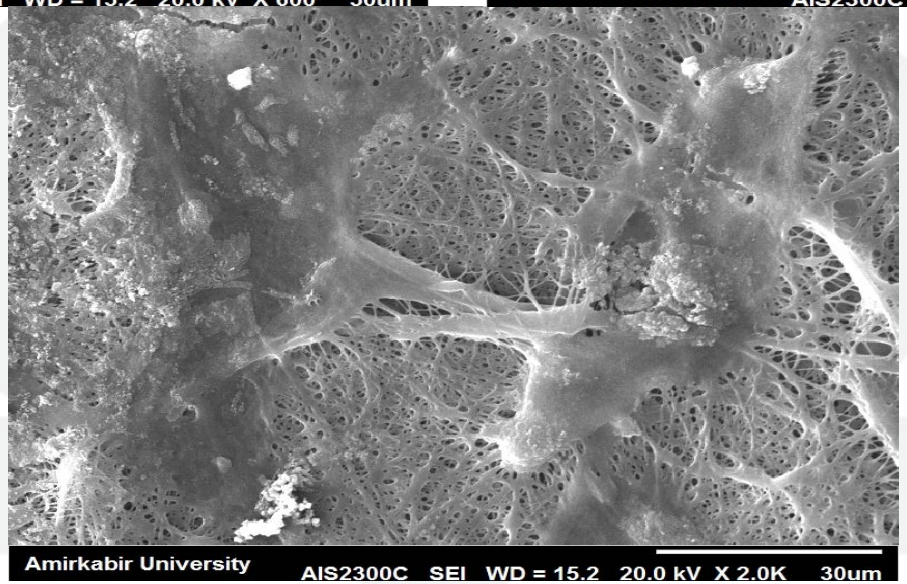



Ghanbari, H. et al. unpublished data

# HUVEC on nanofibrous scaffold

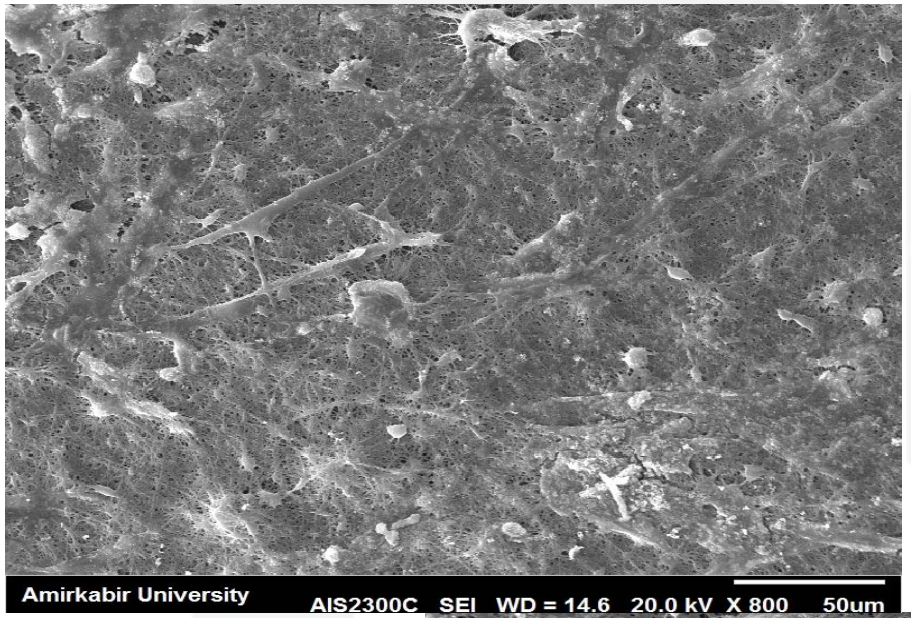


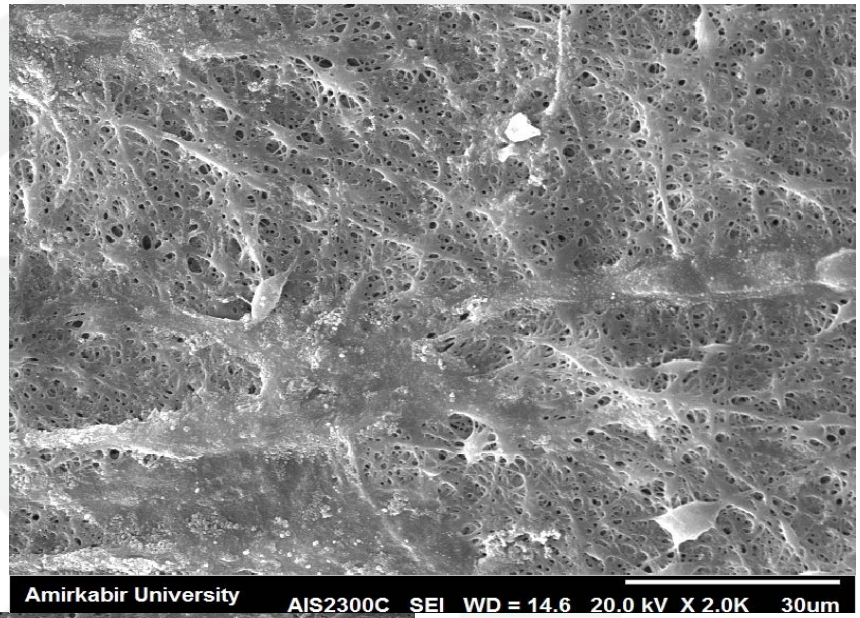




Ghanbari, H. et al. unpublished data

# T&G Myofibroblast on nanofibrous scaffold

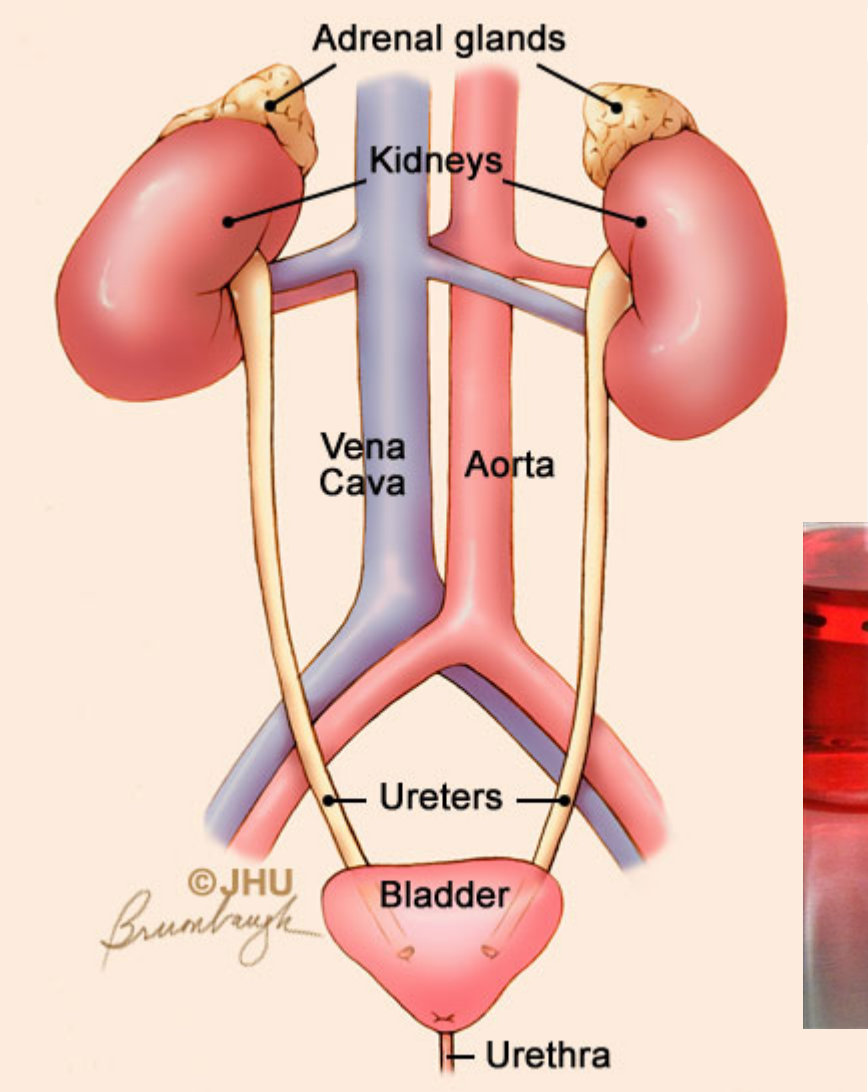


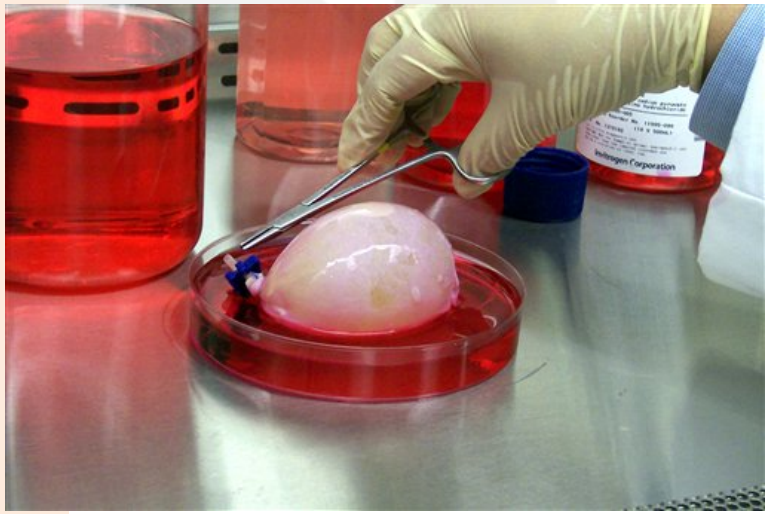



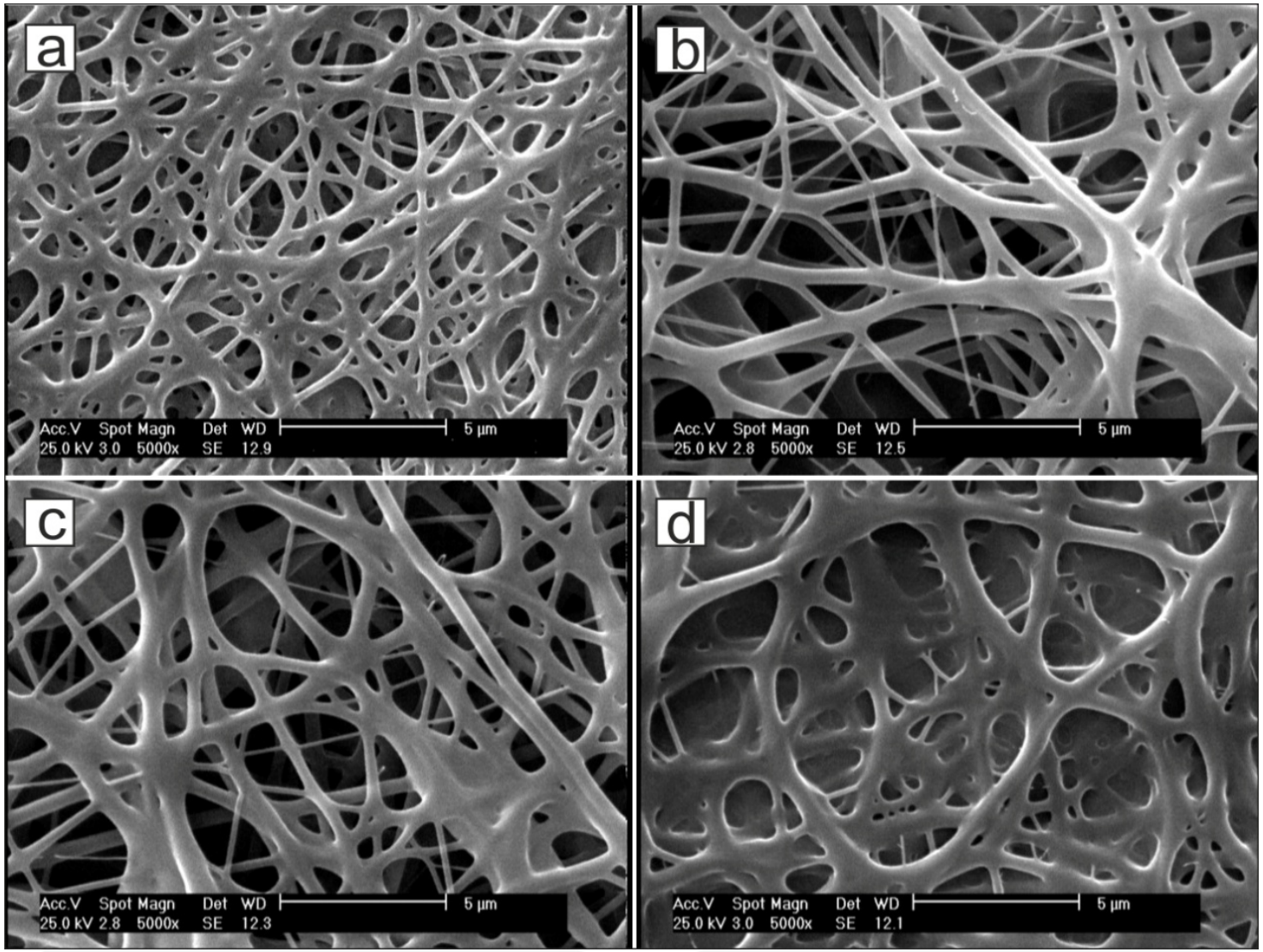


Ghanbari, H. et al. unpublished data

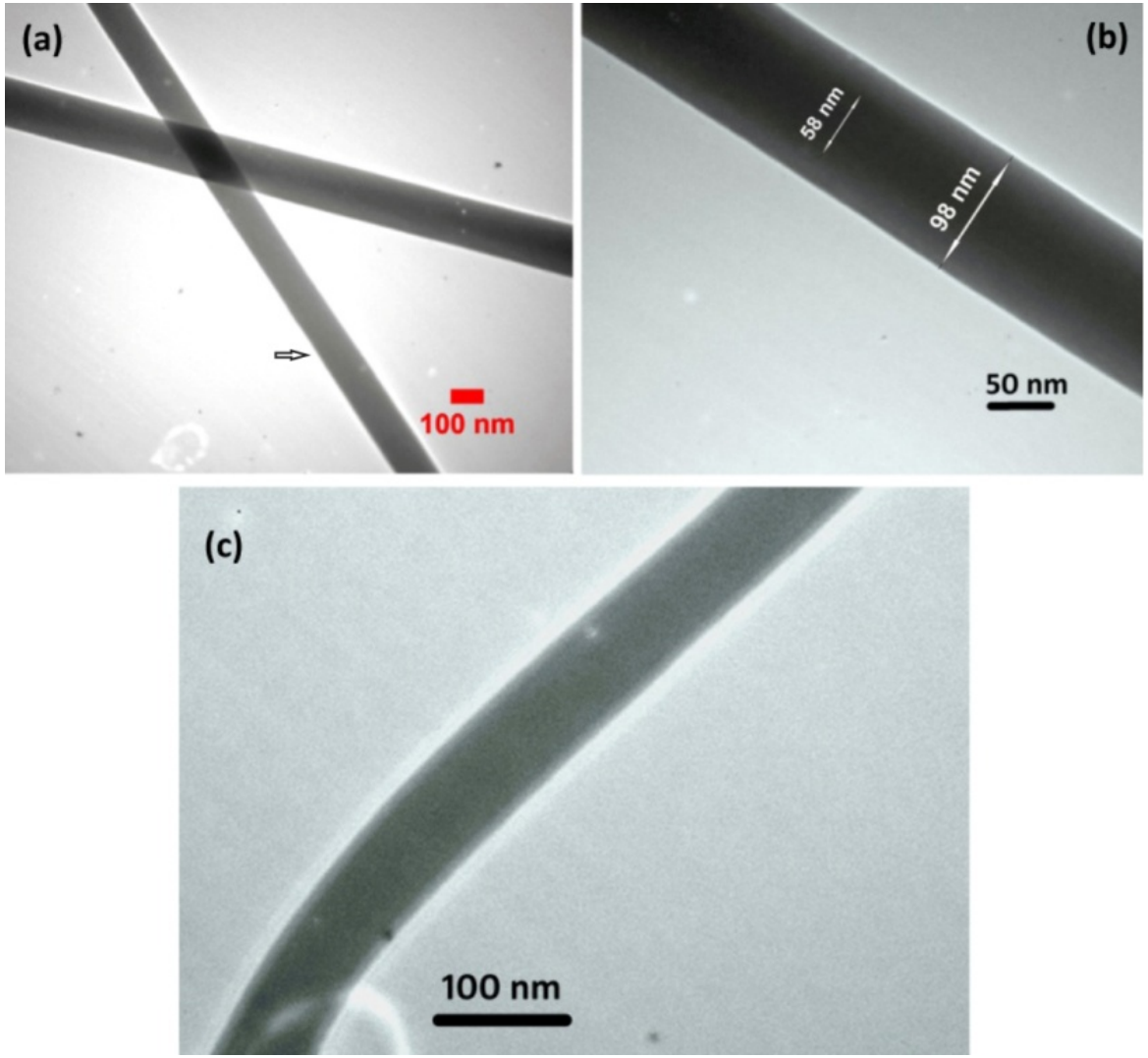
# Tissue engineering bladder



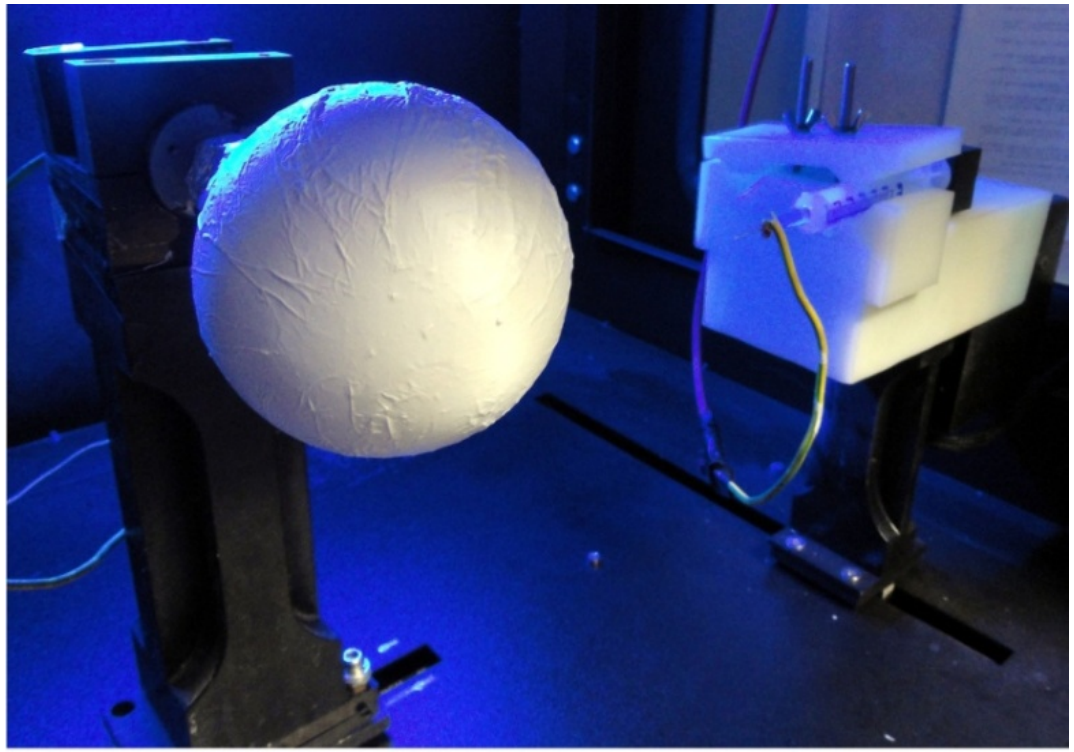



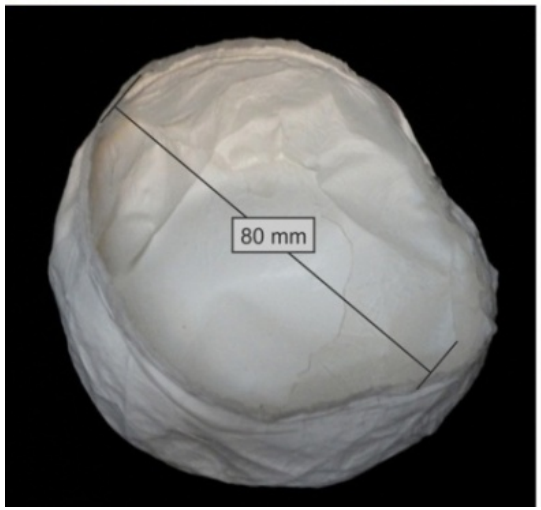



Core shell PEO/PU nanofibers for tissue engineering bladder, a)1%PEO, b)2% PEO, c)3% PEO and d) 4% PEO; submitted data

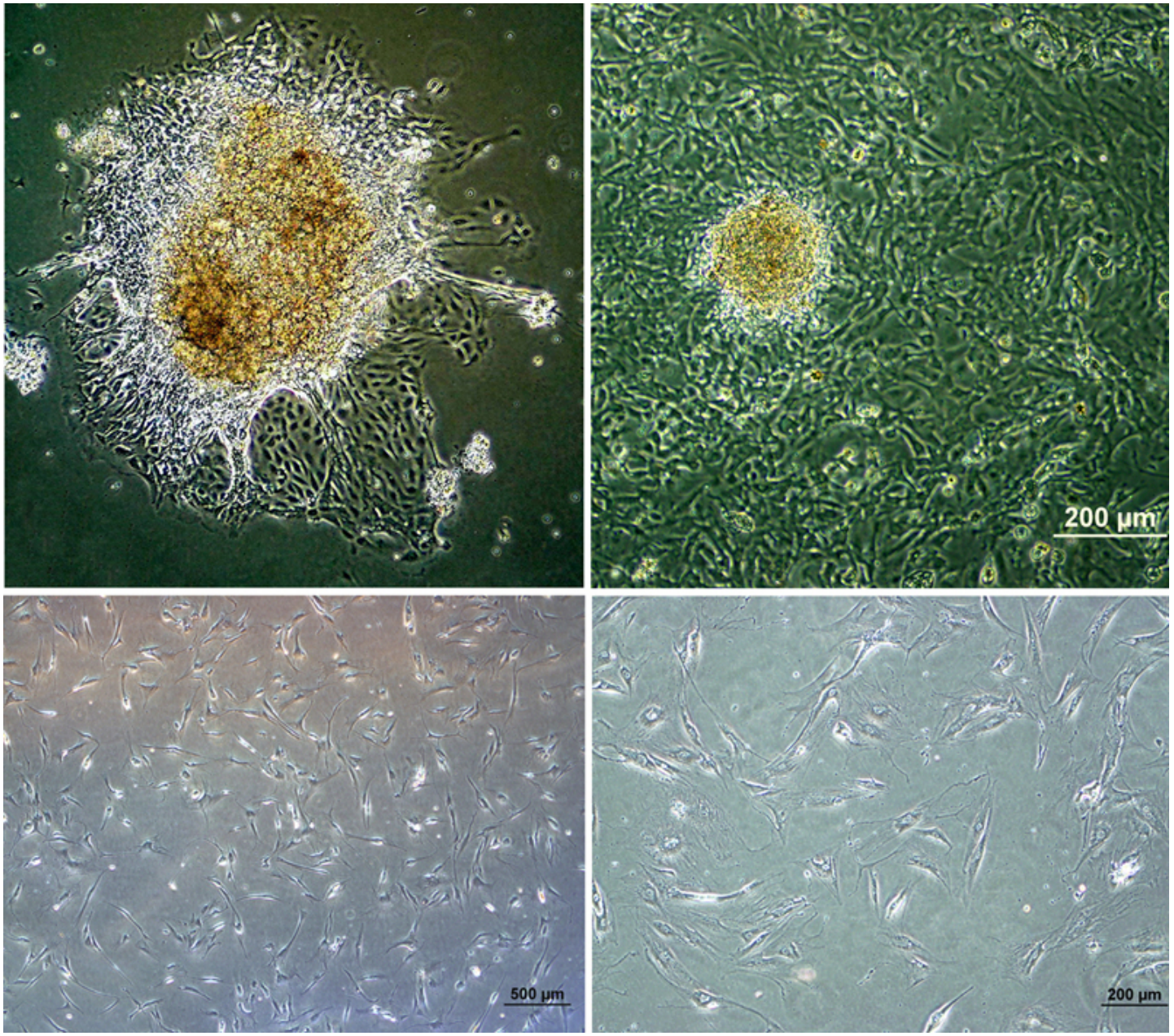



TEM images of PEO/PU core shell nanofibers






Core shell nanofibrous scaffold for Tissue engineering bladder, submitted data




Culture of SMC on nanofibrous scaffold

# Acknowledgments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- Ms. Shokrayi
- Mr. Salehi
- Ms. Amirian

# با سپاس از توجه شما