Review article

Fibers for hearts: A critical review on electrospinning for cardiac tissue engineering

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General Considerations

- Mimicking the fibrillar structure of the extracellular matrix is important for scaffolds.
- Clinical trails to date with cardiac stem cells, cardiospheres and adipose-driven stroma cells are minimal, unlike skeletal myoblasts and bone marrow derived cells.
- There is a low rate of engraftment and high mortality of the transplanted cells into diseased hearts. (From cell leakage due to inflammation, ischemia and apoptosis.)
- Tissue engineering provides a 3D environment similar to endogenous cardiac tissue, ability to deliver stems cells, support structures, and growth factors.

In electrospinning polymeric solution is fed through a thin needle opposite to a grounded collector and a high voltage is applied to form a jet of the solution that travels from the needle to the collector, where it is deposited in the form of dried nanofibers.

Electrospinning of synthetic and natural fibers is easy and cost effective.

Electrospun nanofiber matrices show morphological similarities to the natural ECM characterized by continuous fibers ranging from nano to micro scale, high surface-to-volume ratio, high porosity and variable pore size distribution.

Typical Electrospinning Setup

Scaffold Considerations

- Natural vs synthetic materials.
- Mimicking the aligned pattern of fibrous cells (microenvironment).
- Recognition of Young’s modulus for healthy and diseased tissue throughout the cardiac cycle.
- Conductivity (charge carriers).
- Biocompatibility and biodegradability.
  - Natural fibers may allow for better cell adhesion, differentiation, and proliferation, but have poorer mechanical properties. Their degradation products are less toxic and have a lower immune response.
- Replacing static seeding with dynamic, magnetic, vacuum, electrostatic, and centrifugal seeding.

Inducing Fiber Alignment

(a) Parallel electrodes.
(b) Rotating collector.
(c) Rotating jet method,
(d) Near field electrospinning

Natural Polymers for Electrospinning

- **Collagen (type I, III)**
  - Found in myocardial connective stroma.
  - Support H9c2 cardiomyoblasts culture.

- **Fibrinogen (glycoprotein)**
  - Ability to bind with high affinity to functional vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and a number of other cytokines.

- **Chitosan (polysaccharide)**
  - CM–fibroblast co–cultures resulted in polarized CM morphology and retained their morphology and function for long–term culture.
  - Fibroblast co–cultures demonstrated synchronized contractions involving large tissue–like cellular networks.

- **Elastin**
  - Used as a composite when electrospun.
- **Silk**
  - Glue-like sericin protein which role is to hold fibers together, and a fibroin filament component.
  - Good mechanical properties.
  - hAECs and hCASMCs demonstrate an affinity for the electrospun silk fibroin/PEO blend.

Poly(ε–caprolactone)-based scaffolds (PCL)
- Widely used.
- High stiffness and hydrophobicity do not provide significant cell attachment and proliferation in cardiac tissue engineering.
- PCL/gelatin scaffolds promote cell attachment and alignment.

Poly-(l–lactide) (PLLA), polyglycolide (PGA) and the copolymer poly(lactide–co–glycolide) (PLGA).
- PLLA scaffolds promoted better cell adhesion and mature cytoskeleton structure with well-defined periodic units in the contractile machinery (sarcomeres).
- Co-spinnning with gelatin and α-elastin lead to stable scaffolds in an aqueous environment without crosslinking.
Polyurethane (PU)
- Construction of heart valves.
Poly(ester urethane) ureas (PEUU)
Poly(glycerol sebacate) (PGS)
Poly(3-hydroxybutyrate) (PHB)
Surface Functionalization

Summary

- Mimicking the fibrillar structure of the extracellular matrix is important for scaffolds.
- Electrospun nanofiber matrices show morphological similarities to the natural ECM characterized by continuous fibers ranging from nano to micro scale, high surface-to-volume ratio, high porosity and variable pore size distribution.
- Electrospinning of synthetic vs natural fibers, co-spinning and surface functionalization.
- Clinical trails to date with cardiac stem cells, cardiospheres and adipose-driven stroma cells are minimal.