### Cardiac Patch

Course: Drug Delivery Systems

Supervisor: Prof. Ghaee

Presenter: Morteza Khodaei

Spring 2025



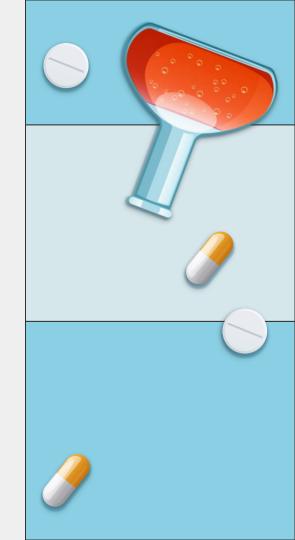
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Introduction

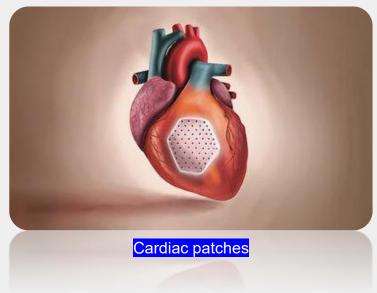




### Cardiac patches



- Cardiovascular diseases (CVDs) are the leading cause of death globally
- Current treatments for myocardial infarction(MI) have limited regeneration potential
- Cardiac patches offer a platform for localized
  drug delivery and tissue regeneration





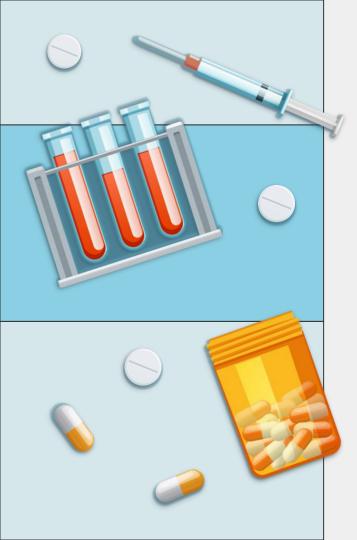
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Fundamentals

Drug Delivery Fundamentals

- Controlled release from patches enhances local efficacy
- Mechanisms: Diffusion, degradation, stimuliresponsive release
- Materials: Hydrogels, electrospun nanofibers,
  biodegradable polymers



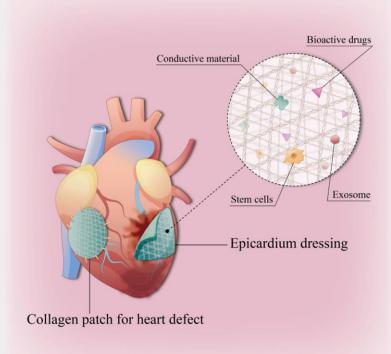


## 3 Materials

#### Materials Used in Cardiac Patches



- Natural polymers: Collagen, gelatin, fibrin
- Synthetic polymers: PLGA, PCL, PEG
- Smart materials:
  Thermo/pH/enzyme-sensitive
  materials



4

Case studies



# Case 1: Engineered heart muscle allografts for heart repair in primates and humans



#### Article

## Engineered heart muscle allografts for heart repair in primates and humans

https://doi.org/10.1038/s41586-024-08463-0

Received: 19 March 2023

Accepted: 27 November 2024

Published online: 29 January 2025

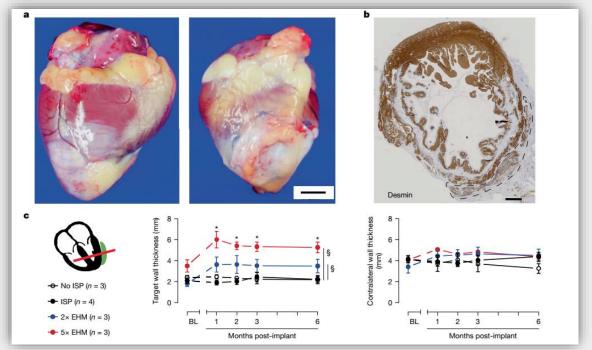
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Ahmad-Fawad Jebran<sup>12,29</sup>, Tim Seidler<sup>2,24,29</sup>, Malte Tiburcy<sup>2,5,29</sup>, Maria Daskalaki<sup>2,6</sup>, Ingo Kutschka<sup>12</sup>, Buntaro Fujita<sup>2,8</sup>, Stephan Ensminger<sup>2,8</sup>, Felix Bremmer<sup>2,9</sup>, Amir Moussavi<sup>2,10</sup>, Huaxiao Yang<sup>11,12</sup>, Xulei Qin<sup>11,12</sup>, Sophie Mißbach<sup>2,63</sup>, Charis Drummer<sup>2,6</sup>, Hassina Baraki<sup>1,2</sup>, Susann Boretius<sup>2,10</sup>, Christopher Hasenauer<sup>1,4</sup>, Tobias Nette<sup>1,4</sup>, Johannes Kowallick<sup>2,14</sup>, Christian O. Ritter<sup>2,14</sup>, Joachim Lotz<sup>2,14</sup>, Michael Didié<sup>2,3</sup>, Mathias Mietsch<sup>2,13</sup>, Tim Meyer<sup>2,5</sup>, George Kensah<sup>1,2</sup>, Dennis Krüger<sup>13</sup>, Md Sadman Sakib<sup>16</sup>, Lalit Kaurani<sup>15</sup>, Andre Fischer<sup>2,13,16,17</sup>, Ralf Dressel<sup>2,18</sup>, Ignacio Rodriguez-Polo<sup>2,6</sup>, Michael Stauske<sup>2,6</sup>, Sebastian Diecke<sup>19,20</sup>, Kerstin Maetz-Rensing<sup>21</sup>, Eva Gruber-Dujardin<sup>21</sup>, Martina Bleyer<sup>21</sup>, Beatrix Petersen<sup>2,22</sup>, Christian Roos<sup>22</sup>, Liye Zhang<sup>22</sup>, Lutz Walter<sup>2,22</sup>, Silke Kaulfuß<sup>23</sup>, Gökhan Yigit<sup>2,23</sup>, Bernd Wollnik<sup>2,17,23</sup>, Elif Levent<sup>2,5</sup>, Berit Roshani<sup>2,4</sup>, Christiane Stahl-Henning<sup>2,4</sup>, Philipp Ströbel<sup>9</sup>, Tobias Legler<sup>2,25</sup>, Joachim Riggert<sup>2,25</sup>, Kristian Hellenkamp<sup>3</sup>, Jens-Uwe Voigt<sup>26</sup>, Gerd Hasenfuß<sup>2,3</sup>, Rabea Hinkel<sup>2,31</sup>, Joseph C. Wu<sup>11,2</sup>, Rüdiger Behr<sup>2,6</sup> & Wolfram-Hubertus Zimmermann<sup>2,23,17,27,28,25</sup>



## Case 1: Engineered heart muscle allografts for heart repair in primates and humans





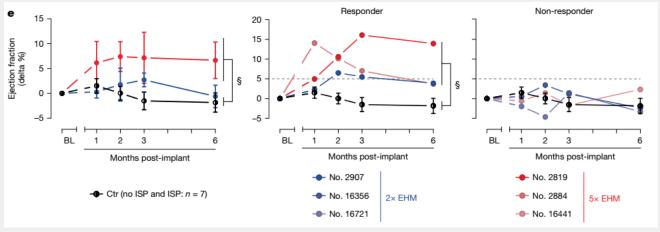








## Case 1: Engineered heart muscle allografts for heart repair in primates and humans













# Case 2: Living Nanofiber-Enabled Cardiac Patches for Myocardial Injury



### Living Nanofiber-Enabled Cardiac Patches for Myocardial Injury



Sukhwinder K. Bhullar, PhD,<sup>a</sup> Raneeta Thingnam, MSc,<sup>a</sup> Eryn Kirshenbaum, PhD,<sup>a</sup> Darya Nematisouldaragh, MSc,<sup>a</sup> Molly Crandall, MSc,<sup>a</sup> Stephanie M. Willerth, PhD,<sup>b</sup> Seeram Ramkrishna, PhD,<sup>c</sup> Inna Rabinovich-Nikitin, PhD,<sup>a</sup> Lorrie A. Kirshenbaum, PhD<sup>a,d</sup>

#### HIGHLIGHTS

- · Adverse cardiac remodeling following myocardial infarction is a leading cause of morbidity and mortality worldwide.
- Several impediments exist with current cell therapy approaches to repair damaged myocardium following injury, highlighting the need for alternative approaches.
- This review highlights a promising new approach of using biomaterial electrospun nanofiber patches for promoting tissue regeneration.



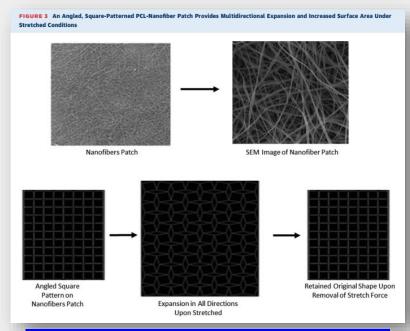


# Case 2: Living Nanofiber-Enabled Cardiac Patches for Myocardial Injury





- Tailored nanofiber geometry allows multidirectional expansion under cardiac stress
- Square-patterned PCL patch mimics myocardial mechanical dynamics



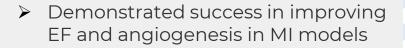
An Angled, Square-Patterned PCL-Nanofiber Patch



## Case 2: Living Nanofiber-Enabled Cardiac Patches for Myocardial Injury





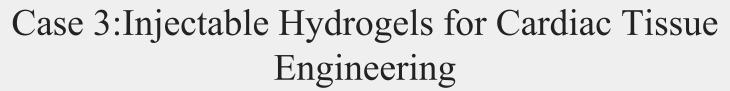


**TABLE 1** Nanofibers Cardiac Patches for Myocardial Regeneration

Biomaterials	Cellular Nanofiber Cardiac Patch	First Author
PCL-gelatin	hiPSC-CMs	Kumar et al <sup>26</sup>
PCL/GelMA-Ppy nanoparticles	Cardiomyocytes/fibroblasts	He et al <sup>31</sup>
PCL/gelatin	hiPSC-CMs	Sridharan et al <sup>36</sup>
Alginate/PCL	Cardiac progenitor cells	Karimi et al <sup>44</sup>
PCL-FN-immobilized nanofibers	UCB-MSC	Kang et al <sup>62</sup>
PLA, PEG, and PCL/collagen	HGF and IGF	Kerignard et al <sup>83</sup>
PCL	Sacrificial particles (PEO)	Wanjare et al <sup>84</sup>
Xylan (polysaccharides)/PVA	Acellular patch	Venugopal et al <sup>85</sup>
PLGA	Endothelial cells, VEGF	Fleischer et al <sup>86</sup>
β-PVDF	TiO <sub>2</sub>	Arumugam et al <sup>87</sup>
PEO	ECM	Shah et al <sup>76</sup>
PLA/PCL	Cardiomyocytes	Wei et al <sup>77</sup>
Alginate	Cardiomyocytes	Lee et al <sup>78</sup>
CNT/silk	Cardiomyocytes	Zhao et al <sup>79</sup>
PLA/PANI	Cardiomyoblast (H9c2)	Wang et al <sup>80</sup>
PCL/NO	NO <sub>2</sub>	Zhu et al <sup>81</sup>
PCL	hiPSC-CMs	Liu et al <sup>82</sup>

Nanofiber Cardiac Patches for Myocardial Regeneration







#### **REVIEW**

Hydrogels



#### Injectable Hydrogels for Cardiac Tissue Engineering

Brisa Peña, Melissa Laughter, Susan Jett, Teisha J. Rowland, Matthew R. G. Taylor, Luisa Mestroni, and Daewon Park\*





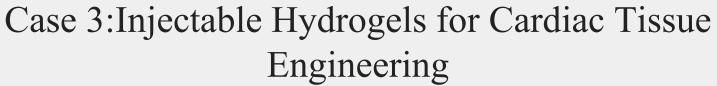


- Natural hydrogels often exhibit long gelation times (15 min – 3 hrs)
- Slow gelation risks cell loss and inefficient drug delivery

Table 2. Overview of the material properties of the natural injectable hydrogels used for cardiac tissue engineering.

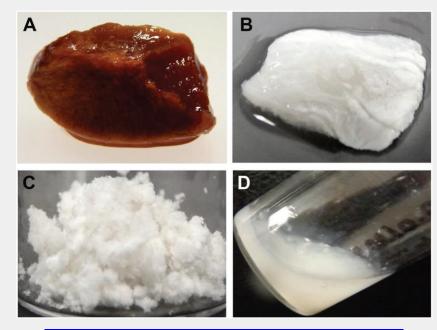
Refs.	Material	Mechanical properties >6 kPa	Conductive	Gel time	Gel stimuli	Degradable
[48]	CNT mixed in collagen type I hydrogel	Yes	Yes	≈15 min	Temp	Yes
[49]	Porcine ECM cross-linked with genipin	No	No	≈15 min	Temp	Yes
[50]	Fullerenol/alginate	No	No	5–10 min	Ca gluconate solution	Yes
[53]	Porcine ECM	N/A	No	N/D	Temp	Yes
[52]	Porcine ECM with mixed or conjugated doxycycline	No	No	N/D	Temp	Yes
[53]	Porcine ECM cross-linked with genipin or chitosan	Yes	No	3 h	Genipin/temp	Yes
[54]	Type I collagen	N/A	No	N/D	Temp	Yes
[55]	Decellularized cardiac and skeletal muscle ECM	No	No	1 h	Temp	Yes
[56]	Chitosan chloride-RoY	N/A	No	8–12 min	Temp	Yes
[57]	Fibrin gel with embedded GF and TIMP-3	N/A	No	N/D	Thrombin	Yes
[58]	Chitosan gel with mixed GN	Yes	Yes	Up to 50 min	BGP-Na salt solution	Yes
[59]	Chitosan hydrogel	Yes	No	s	pН	Yes

Gelation Time of Natural Injectable Hydrogels





Decellularization and digestion of porcine cardiac ECM tissue. The porcine cardiac tissue was sliced into A) sections and then B) decellularized. The decellularized tissue was further lyophilized and ground into C) powder, and then enzymatically digested into a liquid at D) room temperature.



ECM-Derived Hydrogel Injection and Effects on LV

#### Conclusion



Case	Material	Type	Mechanism	Result
1	Collagen + cells	Bio-patch	Cell therapy	↑ thickness, ↓ risk
2	Nanofibers + GF	Scaffold	Sustained release	† angiogenesis
3	Injectable hydrogel	In situ gel	pH/enzymatic	↓ inflammation

- > Cardiac patches integrate drug delivery and regenerative functions
- > Material design, responsiveness, biocompatibility, mechanics

