Public summary of PhD-thesis of Sergio Spaans
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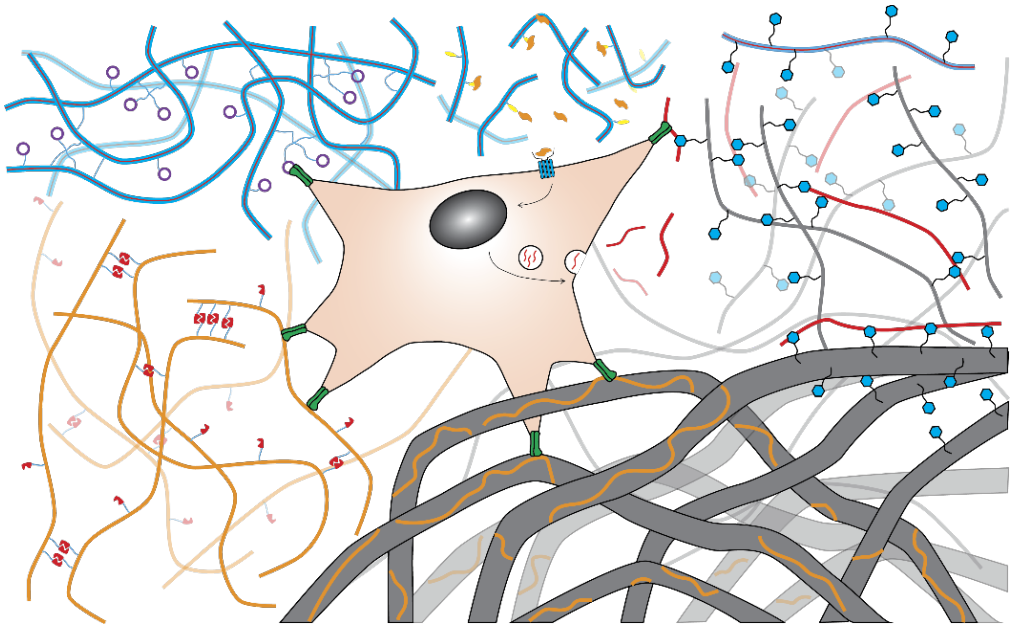
Jelly-like materials to heal an infarcted heart

Cells of the human body are surrounded and protected by a complex environment, the extracellular matrix. During a heart attack, the composition and structure of the extracellular matrix are altered. Biomedical Engineer Sergio Spaans from Eindhoven University of Technology has developed jelly-like materials ('hydrogels') that, once injected in the human heart, mimic the organization and functioning of a healthy extracellular matrix. These hydrogels can be used as carriers for the delivery of healthy cardiac cells directly in infarcted area of the heart and offer improved therapies for patients that suffered a heart attack.

PhD candidate Sergio Spaans (photo: TU/e)

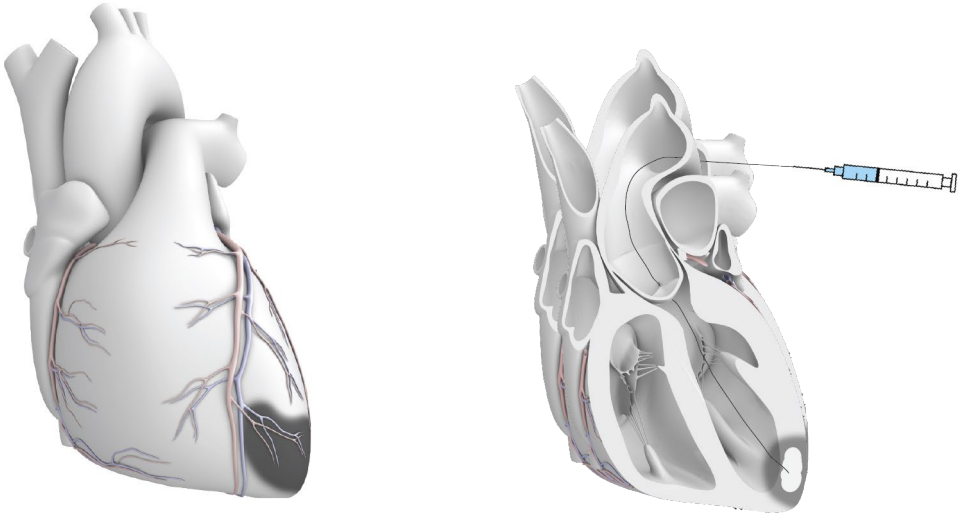
Cells of the human body are surrounded by a supporting structure, the so-called extracellular matrix. The natural extracellular matrix is an organized and dynamic environment which guarantees the biological activity and survival of cells. Throughout life, the extracellular matrix and the embedded cells are in a continuous and bidirectional communication, which is interrupted during life-threatening events. "Take the case of a heart attack", explains Spaans, "during which a massive amount of cardiac cells - the contractile units of the heart - dies as a result of oxygen deprivation. Following this event, a cascade of cellular processes takes place that results in the disorganization of the extracellular matrix."



Human cell and its surrounding environment (Illustration: Sergio Spaans)

Stem cells-based therapies

Unfortunately, the heart has a very limited capacity to 'heal itself', meaning that it is not able to replace its own damaged cells. Current therapies for patients that suffered a heart attack are largely based on the use of stem cells. The strategy is simple enough, in principle. Stem cells, which by definition can proliferate indefinitely and transform into other type of cells, are injected directly in the infarcted area of the heart and can then transform 'on site' into cardiac cells. In practice, however, the process is beset with tremendous challenges. Stem cell-derived cardiac cells should resemble exactly the original cardiac cells and be able to perfectly 'integrate' within the damaged heart. "Once injected", explains Spaans, "stem cells hardly adhere to the surrounding tissue. For this reason, cells based therapies offer only modest and temporary improvements."



Infarcted area (black) after a heart attack (left); stem cells injection (right)
(Illustration: Sergio Spaans and ICMS Animation Studio)

Biomaterials-based therapies

One possible way out would be the creation of an artificial matrix that can literally 'entrap' these stem cells. Spaans: "To develop these matrices, we took inspiration from the function and structure of the natural surroundings of cells: the extracellular matrix. We used hydrogels, network of polymers that soaks up lots of water to form jelly-like structures". The hydrogels developed by Spaans are modular structures, which can be assembled starting from an entire library of building blocks – or 'Lego bricks', as researchers in the field like to define them. These building blocks can be combined simply by mixing and matching them. The mixing is possible because these bricks 'self-assemble', meaning that they spontaneously get together to form complex structures.

Collagen inspired peptide

"Also", continues Spaans, "because bricks with different functionalities can also be combined, we decorated the structural blocks of the hydrogels with special peptides that would help cells adhere better." For example in one of the studies of his PhD project, Spaans took inspiration from collagen, which is the most abundant protein of heart tissue. The peptide was used to create soft and stiff collagen-mimicking hydrogels and to culture cardiac cells in the laboratory. "We discovered", explains Spaans, "that cellular adhesion and proliferation to these hydrogels really not only depends on the type of hydrogels, but also on its rigidity, with stiffer hydrogels performing much better than soft ones." As poor cellular adhesion and engraftment are still major limitations of stem cells based therapies, these results suggest new guidelines for the development of hydrogels to be applied, in the coming future, for cardiac repair.

Sergio Spaans will defend his PhD thesis on March 13th at TU/e. The Title of the PhD-thesis is "Engineered cardiac microenvironments based on supramolecular biomaterials". The supervisors of this project are Patricia Dankers (First promotor, TU/e), Carlijn Bouten (Second Promotor, TU/e) and Noortje Bax (Co-promotor, TU/e).