UNIVERSITÄT HEIDELBERG
ZUKUNFT SEIT 1386

Bioartificial insulin-secreting tissue to treat diabetes mellitus

Technology Offer

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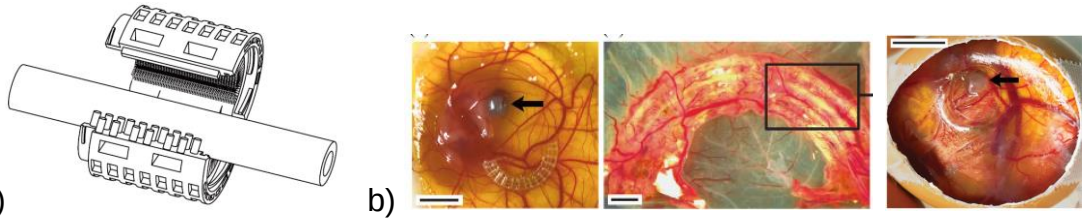

Fig. 1 a) CAD drawing of hybrid perivascular device **b)** Transplantation of the perivascular device into the CAM of fertilized chicken eggs shows survival and vascularization.

Category

Perivascular implant

Keywords

Diabetes mellitus, bioprinting, tissue engineering, artificial organs, scaffolds

Development stage

Preclinical

Seeking

Licensing

Collaboration

IP status

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Background

Transplantation of islets of Langerhans to selected patients with type 1 and type 3c diabetes mellitus (DM) is an established treatment option. Its limitations include a shortage of donor material but also a substantial loss of islets and impaired long-term function post-transplantation. Scaffold-based tissue engineering approaches extend the range of possible transplantation sites and might present a long-term curative treatment.

One major limitation in current development of tissue engineered products is practical applicability and a lack of vascularization, causing insufficient nutrition, hypoxia, and immunological host-graft reactions. While a multitude of studies focusing on aspects of the tissue engineering network exist, those have not yet consolidated into an entire process leading towards artificial organs.

This technology, developed by scientists of the University of Heidelberg, is an end-to-end concept to address the challenges of hybrid scaffold fabrication. Experimental proof of concept is provided by a 3D-bioprinted hybrid scaffold for insulin-secreting cells that is designed for clinical applications.

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Technology

Hybrid scaffold building blocks

were fabricated by 3D-(bio)printing using PCL mesh as a permeable outer shell to support the inner insulin-secreting gelatine methacrylate hydrogel core. The PCL component was further surface-heparinized that improved vascularization and in vivo, and increased cell adhesion. Importantly, PCL is FDA-approved as a drug delivery device and is used in medical devices because of its biocompatibility and low immunogenicity.

Cellular integration

was investigated *in vitro* and *in ovo* by means of morphology, viability, proliferation, cell migration, apoptosis staining, and transcriptome alterations of pseudo-islets. The bio-printed, multicellular hydrogel provides a microenvironment for insulin-secreting cells to form islet-like structures.

- Total mRNA sequencing revealed that morphological pseudo islet formation in 3D culture correlates to upregulation of β-cell-specific proliferative pathways and insulin secretion signalling cascades.
- Transplantation of the PCL scaffold to the CAM of fertilized chicken eggs revealed survival, viability, and insulin secretion of pseudo-islets.
- Immuohistochemical analysis proved not only extensive peri-islet vascularization but also intra-islet vascularization.

In summary, this end-to-end concept of 3D bioprinting of a perivascular implant is a promising future curative treatment for patients suffering from either type 1 or type 3c diabetes mellitus.

Benefits

- End-to end concept based on building-block concept
- Functional evaluation *in silico*, *in vitro*, and *in ovo*
- Novel treatment option for patients with insufficient insulin-secretory function

Applications

- Bioartificial organs
- Treatment option for patients with insulin secretion deficiency
- Treatment for patients with cell-based therapies / tissue engineered product development

Publications

- Gabriel A Salg, et al. Toward 3D-bioprinting of an endocrine pancreas: A building-block concept for bioartificial insulin-secreting tissue, *Journal of Tissue Engineering,* 2022; Volume 13
- Gabriel A Salg, et al. The emerging field of pancreatic tissue engineering: A systematic review and evidence map of scaffold materials and scaffolding techniques for insulin-secreting cells, *Journal of Tissue Engineering*, 2019; Volume 10

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