DEVELOPMENT OF BIOINKS FROM HUMAN PLACENTA ECM FOR 3D BIOPRINTING OF ARTIFICIAL TISSUE CONSTRUCTS

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Introduction

Advancements in tissue engineering rely on bioactive scaffolds that strike a delicate balance between mechanical resilience and cellular support, while also facilitating vascularization and maturation. Although 3D bioprinting offers precise scaffold fabrication, the lack of suitable bioinks remains a challenge for creating functional tissue constructs. Extracellular matrix hydrogels, particularly those derived from human placenta (hpECM), offer a promising combination of natural composition, high bioactivity, and ethical acceptability, enhancing the properties of bioinks for tissue engineering. We envision that hpECM hydrogels and composites could revolutionize the development of innovative bioinks for 3D tissue printing, offering substantial potential for in vitro experimentation and the advancement of future implant technologies.

Materials and Methods:

We analysed the biological composition of hpECM hydrogels produced from different parts of the human placenta. Proteome analyses were used to break down the respective matrisome and enabled an evaluation of the manufacturing process as well as a direct comparison of hpECM hydrogels derived from different placental tissues such as the amnion, the chorion or the umbilical cord. We further were investigating the usability of hpECM hydrogels and various composites with silk or fibrinogen for 3D bioprinting processes. Therefore, printability studies and biomechanical tests were carried out for this purpose. To investigate bioactivity, primary cells were grown in 3D cultures using hpECM bioinks and various prevascularisation experiments were performed.

Results

Our manufacturing protocol results in reproducible hpECM hydrogels with preserved structural and functional proteins and minimal DNA content. Cell studies showed a high cytocompatibility of the hpECM bioinks, and vascularisation experiments demonstrate the importance of the matrix composition for tube formation. A previous study showed the successful enrichment of silk hydrogels with hpECM bioink to enhance bioactivity (1). Biomechanical analysis of these bioinks has now been performed and showed tunability of mechanical strength.
Furthermore, advanced 3D bioprinting with hpECM based bioinks enables the creation of high-resolution constructs, with promoting high cell viabilities as shown in Fig.1.

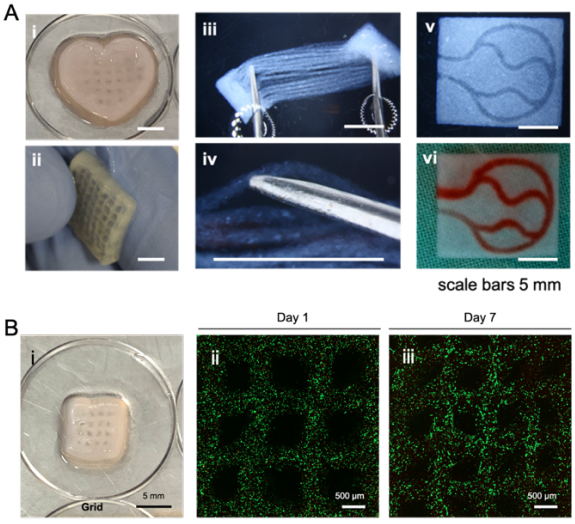

Figure 1: 3D bioprinted scaffolds using hpECM bioink. (A)(i-ii) grids in square and heart shape, (iii-iv, cardiac muscle fiber construct, (v-vi) perfusable loop empty and filled with red dye. (B)(i) grid in square shape, (ii) Calcein AM cell staining day 7, (iii) day 14 showing living cells in green.

Outlook

Ongoing efforts are focused on refining tissue models and improving mechanical properties in our bioinks. Studies on prevascularisation have shown that the composition of the bioink matrix has an effect on the formation of microvessels. We hope that these findings will enable us to control vascularization in 3D-printed tissues in the future.

References

1. Schneider KH, Goldberg BJ, Hasturk O, Mu X, Dötzlhofer M, Eder G, et al. Silk fibroin, gelatin, and human placenta extracellular matrix-based composite hydrogels for 3D bioprinting and soft tissue engineering. Biomater Res. 2023;27(1):117.