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Adaptation of 3D printing bioinks to mimic the mechanical properties of embryonic tissue for the purpose of vascularization

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INTRODUCTION: In order for engineered tissue grafts and eventually organs to successfully integrate in a clinical setting, a functional vascular network is imperative. Current artificial vascular networks are insufficient in scale, poorly controlled regarding their sprouting length and direction and current biofabrication methods fail so far to mimic the dynamic process which occurs in nature[1]. Recently, it has been observed that embryonic tissue acts as a jammed suspension which can be locally unjammed by cellular forces. Embryonic vascularization occurs within this mechanical environment. In this work in order to mimic the embryonic environment, we created granular bioinks of different material compositions, which can be locally unjammed by HUVEC/SMC cells for the purpose of 3D printing microvascular structures.

METHODS: For the patterning phase of the granular inks we tested blended Agarose-Collagen conjugate particles with a diameter of 25μm. For the preparation the alginate granular ink, in-Air microfluidics technology were produced with the In-Air Microfluidics technology, and subsequently coated with 5% w/v collagen solution to allow DCAM cell adhesion onto the particles. 1:1 Human umbilical vascular endothelial cells (HUVEC) / Smooth Muscle Cells (SMC) Spheroids, functioning as the 3D tissues were used to dope randomly the granular ink in different ratios to find the maximum concentration of cells/ml that can be printed. SMC and HUVECs cell high concentration pellet was also mixed with the granular ink particles in order to find the maximum concentration of cells that can be loaded in the interstitial space of the granular ink. Optical and confocal microscopy was employed in order to characterize the samples.

CONCLUSIONS: The ability to 3D print and pattern microvascular constructs through granule size and composition modification and which offers an embryo-like mechanical environment, establishes that granular inks are a potent alternative to their shear thinning hydrogel counterparts.

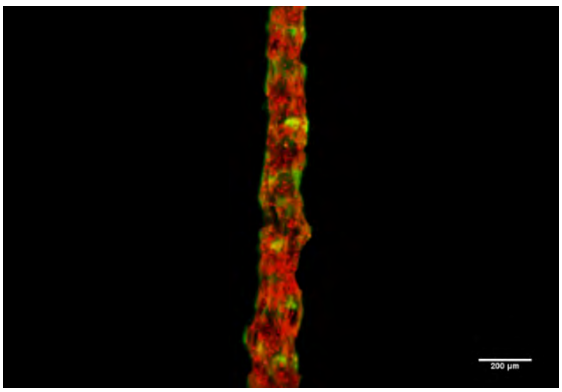

Figure 1: 3D printed granular agarose ink(red) doped with FITC dextran labelled 75μm 0.25% alginate microparticles(green) as proof of concept of a 3D printable doped granular ink.

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