A Universal Microfluidic Platform for *In Vitro* Biomaterial Evaluation

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INTRODUCTION: Conventionally, the biological properties of biomaterials are evaluated using well plates. Although being a standardized method, it is static in terms of fluid flow and is far from the physiological conditions found *in vivo*. This work presents a versatile microfluidic system that allows for integration of different biomaterials (ceramic, metals and polymers) under dynamic conditions.

METHODS: The Universal Biomaterial-on-Chip (UBOC) consisted of two separate 3D printed (Polylactic acid, Ultimaker 2+) structures: the upper layer which contains the channel through which medium can flow (Fig 1A) and the bottom layer that holds and secures the biomaterial in place (Fig 1B). A glass coverslip was taped to the upper layer to tightly seal the channel. Subsequently, an oval Polydimethylsiloxane (PDMS) gasket (l=10mm, w=7mm, h=0.8mm) was inserted into the periphery of the channel in the upper layer. Furthermore, magnets (Ø=12mm, h=3mm) were glued on both sides of the bottom layer. To close the channel, two magnets were placed on the upper layer, causing attraction to the magnets in the bottom layer. The gasket would then directly interface with the biomaterial inside the bottom layer, creating a leak-free channel on its surface. MC3T3-E1 pre-osteoblasts were seeded in the UBOC platform (50,000 cells/cm^2) on calcium-deficient hydroxyapatite (HA) (Ø=15mm) and clinical grade titanium (Ti) (Ø=12mm). The cells were cultured for a period of 5 days at a flow rate of 2 µl/min using supplemented MEM-α medium (Hyclone, 10% FBS, 1% Pen-Strep). On day 5, the cells were stained on-chip with Live/Dead stain (Calcein, Propidium Iodide and Hoechst) and subsequently imaged.

RESULTS: HA and Ti samples were successfully integrated into the UBOC. Cells cultured on-chip displayed a high degree of viability and confluence on day 5 of culture on both HA and Ti substrates (Fig 2).

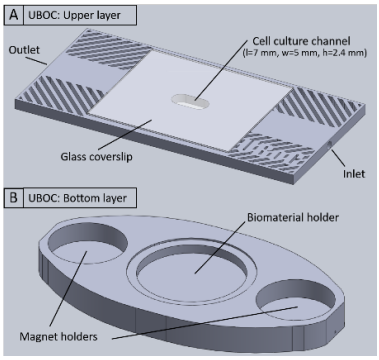

Fig. 1: 3D model for A) Upper and B) Lower layer of UBOC.

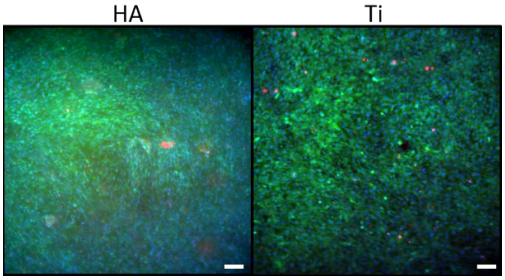

Fig. 2: MC3T3 culture on HA and Ti substrates in UBOC after 5 days (Scale bar is 100 µm).

DISCUSSION & CONCLUSIONS: UBOC presents the possibility for flexible *in vitro* biomaterial analysis as it allows for easy incorporation of flow to conventional cell culture regimes in a low-cost manner. Via this method, cells can be cultured on the biomaterial with exposure to fluid flow and controlled shear-stress. The platform is compatible with standard characterization methods, such as imaging and biochemical cell analysis. In addition, since the system is designed to be opened and closed, the biomaterial could be easily accessed, harvested and transferred to a regular tissue culture vessel, enabling standard off-chip biochemical assays and protocols to be performed for further analysis.

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