Understanding nanoparticle accumulation in a complex *in vitro* tumour-on-a-chip model

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Microfluidic devices for cell biology research have revolutionized the way we can analyse nanoparticles (NPs) and novel drugs over the past 20 years.[1] These devices have shown great promise in being highly tunable, high throughput systems that can be used for a wide variety of biological experiments to better understand NP interactions on the cellular level.[2] In my work, I have designed a polydimethylsiloxane (PDMS) microfluidic device with the capability to culture multicellular tumour spheroids (MCTS) that can be imaged and analysed in real time to gain detailed understanding of NP interactions at the tumour site.[2] These MCTS are designed to incorporate cancer (SKOV-3), fibroblast (NIH/3T3) and macrophage (RAW264.7) cell lines to create a complex 3D model that better replicates the tumour microenvironment. Flow rate and sheer stresses can be appropriately scaled in this tumour-on-a-chip model, allowing for extravasation and accumulation of NPs to be understood through real-time imaging in a physiologically relevant environment. These devices are designed to be applicable to any library of NPs, this work is specifically looking at how soft nanoparticle size affects their ability to extravasate and accumulate within the tumour microenvironment as a "proof of concept". Through this research, we hope to show how a complex *in vitro* dynamic model such as the tumour-on-a-chip can better recapitulate the tumour microenvironment and therefore enhance our understanding of biological interactions with NPs and increase the success rate of NP formulations into the clinic.

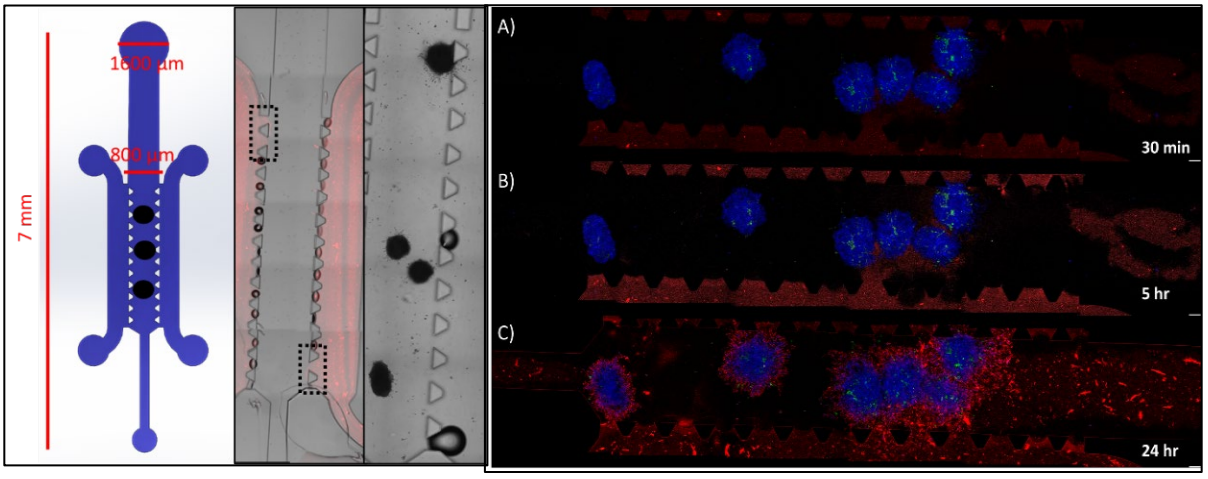

Figure 1: Graphical diagram (left) of the "tumour-on-a-chip" showing the key dimensions and where the spheroids will be entrapped (black circles). Middle panel shows a tile scan microscopy image of the middle channel (filled with 50% v/v Matrigel in DMEM media) separated from the side channels. Red colour is fluorescence from NPs showing sections where polymers can extravasate into the middle channel (black dashed boxes). NP association with embedded spheroids within the tumour-on-a-chip at various timepoints (A-C). Red is cy5 signal associated with NPs, blue showing SKOV-3 cells and green showing NIH/3T3 fluorescence. Scale bar denotes 100 µm.

References:

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