Controlled Chemotactic Cell Migration in 3D Bio-printed Hydrogels

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The success of anti-angiogenesis drugs has encouraged many researchers to further develop angiogenesis models to increase the clinical success rates as the models can aid in personalised medicine and the understanding of angiogenesis on a molecular level.[1] Modelling the process of angiogenesis will enable the study of the role of different cells and extracellular matrix components which will allow for the development of better targeting drug complexes and help understand why current therapeutics are less effective than predicted.[2]

The tumour microenvironment surrounding angiogenesis has proven to be challenging to model due its complexity. The extensiveness of clinical *in vitro* drug assays demands for a reproducible high throughput angiogenesis model which has yet to be developed and translated to clinical applications.[3] It is well known and accepted that 3D cell models have several advantages over traditional 2D cell models as they can exhibit more *in vivo* tumour-like features. Drop-on-demand 3D bioprinters are capable of high-throughput printing of cellular aggregates, known as spheroids into 96-well plates.[4] Applying 3D bioprinting for high-throughput drug screening enables multiple parallel drug tests for drug screening, toxicity, disease formation and progression, and personalized medicine applications.[5] Advancement in the field of 3D bioprinting now enables the growth of spheroids inside tissue-like hydrogels made from synthetic peptides and polymers.[6]

The physical translocations (i.e. chemotaxis) of tumour cells are regulated by various chemical signals which creates a major challenge for reconstructing microenvironments in 3D cell cultures.[7] In chemotaxis, cells migrate towards or away from a stimulus molecule by sensing its molecular concentration gradient in the extracellular matrix.[8] Traditional 2D chemotactic models restrict observation of cell migration to two dimensions, reveals little about the stepwise dynamics of the migration process and are less physiologically relevant in comparison to 3D models.[9] In an approach to overcome this challenge this research focusses on the influence of chemotactic agents on the migration of cancer cells in 3D hydrogel tumour models. 3D bio-printed stimuli-responsive microcapsules containing chemotactic agents will be incorporated into the hydrogels to controllably release the chemotactic agent to produce an extracellular concentration gradient for the study of chemotaxis. Studying how cancer cells behave during chemotaxis in 3D tumour models will provide insight into the molecular mechanisms of angiogenesis and enable anticancer drug screening.

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