CASE STUDY

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The Challenge

Laboratory tests for the assessment of lipid nano particles (LNPs) safety mainly consists of 2D experiments, however 3D experiments help better recapitulate the physiological environment seen in humans due to; better cell-to-cell interactions; allow for concentration gradients and more physiological adherence of cells to the environment seen in vivo. There is a disconnect between what is seen in testing between laboratory tests and ones done in animal models. This project aimed to begin to create a 3D model of the subcutaneous skin layer that could start to be used for assessing the interactions of LNPs with immune cells and help to determine the safety of LNPs for various indications.

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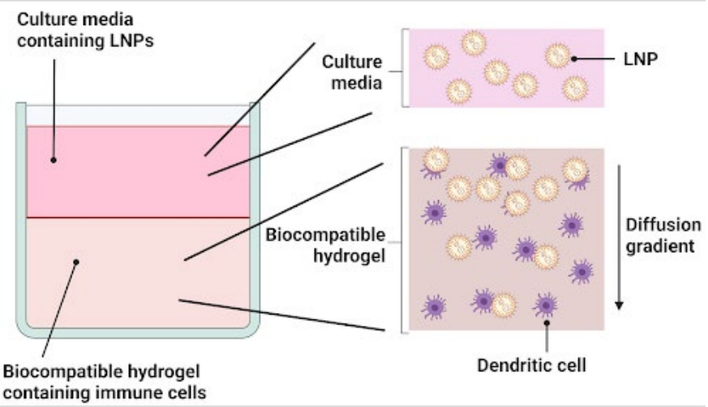
Innovation

To create this model I encapsulated immune cells in a hydrogel to allow for 3D encapsulation, I then added LNPs to the top and measured fluorescent cellular health dyes to determine the affects of the LNPs on the cells. The project required a lot of validation of gels and particles as well as using different types of equipment to validate the model.



Result

- Both the agarose and VitroGel hydrogels used in the project can both be used to image cells and particles in 3D.
- Cells can be imaged in multiple planes within the hydrogel.
- Fluorescent particles could also be imaged in the hydrogel and their uptake in cells visualised.
o There was better particle distribution and cell uptake of particles in the VitroGel.
- 3D printed gels were trialled to allow for more cpntrolled distribution of cells within the hydrogels. In the 3D printed hydrogels fluorescent particle uptake over 24 hrs was seen, but no LNP cellular transfection could be visualised.
- Successfully transferred the VitroGel experiment into a higher throughput format with the capacity to run up to 60 samples at a time. Using this experiment to determine stress levels in the cells using a fluorescent cell health reporter dye. LNP transfection was not detected and requires further validation.

Impact

3D hydrogel models can be useful to help determine better in vitro results that recapitulate in vivo responses, we are particular interested in how cells with different orientation of exposure to particles may alter their stress levels through cell-to-cell communications. These results have helped to create a basic SC model that requires further validation but has answered all the proposed project questions.

Having greater high throughput is important for models used in the earlier stages of therapeutic development as they can be more cost effective and not take up as much of time. Inevitably allowing greater numbers of samples to be tested in shorter periods, this was really key part of the project.

The project laid strong foundations for continued innovation, including plans to develop a user-friendly software interface and explore commercialisation opportunities. These developments will support future industry uptake and help establish reliability-based optimisation as a viable design pathway for next-generation FWT systems.

Danielle Brain

“This project has been a huge learning point in my career and has allowed me to further my expertise in microscopy, project management and allowed me to explore my own ideas away from my groups expertise. It has been crucial in in giving me a dedicated time to develop the 3D subcutaneous skin layer model for immune cell exposure of therapeutics.”

Medicines Discovery Catapult

“Through her committed and diligent work, Danielle has opened a new research avenue for Medicines Discovery Catapult. This study has provided foundation insight for subsequent commercial offerings that employ 3D cell cultures to study nanotherapeutics with fluorescence imaging.” - **Philip Auckland, Medicines Discovery Catapult.**

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