Manchester BIOGEL

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CASE STUDY: The Growth and Differentiation of Kidney Organoids Within PeptiGel®

The Challenge

Induced pluripotent stem cell (iPSC) derived kidney organoids, or "mini kidneys", offer valuable insights into how the organ develops in the body. Kidney organoids have been shown to contain cell types of the developing organ and respond appropriately to forms of hereditary and environmental insult. While great strides have been made in recent years, a gap remains in our understanding surrounding the optimal conditions required for the generation of kidney organoids that faithfully mimic the in vivo organ.

The Solution

Self assembling peptide hydrogels offer the ability to fill this gap. The tunability of the peptide hydrogel allows for the environment in which the organoid is developing to be varied which will increase our understanding of kidney development. Additionally, low batch-to-batch variability of the hydrogels facilitates increased reproducibility of results amongst researchers.

The Science

iPSCs were differentiated over a 24-day period by applying growth factors at defined times. Cells were initially grown in monolayer and on Day 9, pelleted cells were encapsulated in Alpha 4 PeptiGel®. During the differentiation, the cells took on a renal fate, migrated and formed complex structures supported by the PeptiGel® matrix. Organoids grown on a Transwell insert acted as a control. The organoids were assessed by fluorescent confocal microscopy in order to visualise the cells types present and the resulting structures.

In association with CÚRAM
Supervised by Assoc. Professors
John Crean & Dermot Brougham

PeptiGel® due to its animal free, tuneable properties offers an ideal environment to grow organoids and gain a greater understanding of organ development

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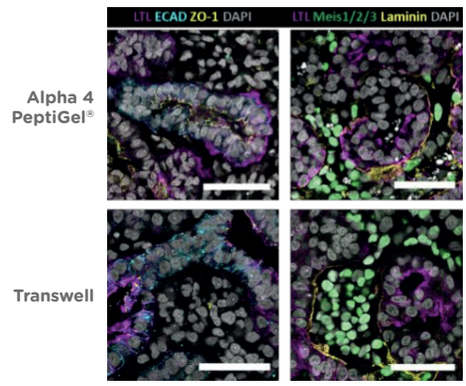
The Results



iPSCs directed towards a renal cell fate were pelleted and encapsulated within Alpha 4 PeptiGel® or placed on a Transwell insert. Following 24 days of growth, it was shown by fluorescent confocal microscopy that the peptide hydrogel successfully supported the differentiation of kidney organoids. PeptiGel® and Transwell organoids were shown to express key markers of renal differentiation including LTL+ve proximal tubules, ECAD+ve distal tubule/collecting duct and ZO-1+ve tight junctions. These cell types were supported by Meis1/2/3+ve interstitial cells and Laminin+ve basement membrane (scale bar = 50 µm).

The Future

The PeptiGel® range offers the ability to study organ development in a synthetic, tuneable, animal-free environment. This will lead to increased understanding of organ development and diseases processes, and is a step towards offering a new therapeutic for kidney disease.