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Next generation *in vitro* liver model design: combining a permeable polystyrene membrane with a transdifferentiated cell line

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Abstract

Herein we describe the manufacture and characterisation of biocompatible, porous polystyrene membranes, suitable for cell culture. Though widely used in traditional cell culture, polystyrene has not been used as a hollow fibre membrane due to its hydrophobicity and non-porous structure.

Here, we use microcrystalline sodium chloride (4.7±1.3 μm) to control the porosity of polystyrene membranes and oxygen plasma surface treatment to reduce hydrophobicity. Increased porogen concentration correlates to increased surface pore density, macrovoid formation, gas permeability and mean pore size, but a decrease in mechanical strength. For tissue engineering applications, membranes spun from casting solutions containing 40% (w/w) sodium chloride represent a compromise between strength and permeability, having surface pore density of 208.2±29.7 pores/mm^2, mean surface pore size of 2.3±0.7 μm, and Young's modulus of 115.0±8.2 MPa.

We demonstrate the biocompatibility of the material with an exciting cell line-media combination: transdifferentiation of the AR42J-B13 pancreatic cell line to hepatocyte-like cells. Treatment of AR42J-B13 with dexamethasone/oncostatin-M over 14 days induces transdifferentiation towards a hepatic phenotype. There was a distinct loss of the pancreatic phenotype, shown through loss of expression of the pancreatic marker amylase, and gain of the hepatic phenotype, shown through induction of expression of the hepatic markers transferrin, carbamoylphosphate synthetase and glutamine synthetase.

The combination of this membrane fabrication method and demonstration of biocompatibility of the transdifferentiated hepatocytes provides a novel, superior, alternative design for *in vitro* liver models and bioartificial liver devices.

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