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A novel Bio-printed 3D liver tissue platform: Tool for medical research

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Background: Bio¬engineered *in vitro* 3D human liver tissues, that are structurally and functionally accurate, provide an opportunity to reconstruct biological processes, both physiological and pathological. Normal cell physiology and function strongly depend on cell-cell and cell-extracellular matrix (ECM) interactions in the 3D tissue environment. Cells grown in 2D do not exhibit in vivo cell polarization and cellular interactions, and are generally non-viable after confluency within 3-5 days. The utility of co-culture of different cell types is limited by overgrowth of some cell types, especially fibroblasts using current two¬dimensional (2D) monolayer culture.

Methods: Hepatocytes and fibroblasts were encapsulated in an ECM-mimetic hydrogel, and 3D bio-printed as micro patterns with low aspect ratios. Typically 50,000 cells in 25 µl of hydrogel were extruded to about 5 mm in x and y directions, and 1 mm in the z direction. The hydrogel was then thermally cross linked to achieve the desired shape. These cell based tissue constructs were then cultured under standard conditions. Viability, histology, bio chemistry, gene and protein expression were observed at timely intervals.

Results: 3D bio-printed tissues express various critical liver functions such as production of albumin, cholesterol, fibrinogen, transferrin, urea, and inducible cytochrome P450 enzymatic activities (CYP1A2 and CYP3A4). Histology shows *in vivo* like cellular morphology. Viability and functionality of the 3D tissues could be maintained for 8 weeks, as compared to 5-7 days for conventional 2D cell culture. Hepatocytes and fibroblasts could be co-cultured in distinct hydrogel micro compartments, without fibroblast overgrowth and hepatocyte suppression. We present a novel 3D liver tissue platform that can be manufactured reproducibly, harbor multiple cell types in micro architectures, express functionality over an extended period of time, and thus can be used as a tool for translational medical research.

Biography

Sonal Asthana is a trained Hepatobiliary and Transplant Surgeon with work experience in leading centers in North America, UK and India. He has completed an American Society of Transplant Surgeons-Accredited Fellowship at the University of Alberta Hospital, Edmonton, Canada. The management of a transplant team requires a strong multidisciplinary approach to patient care, which is fairly different from the traditional hierarchical method still common in most surgical practice. Managing teams of highly skilled individuals working towards common goals will be a key skill for managers in modern medicine. He has authored more than 35 peer-reviewed papers, and has won international awards for basic and clinical research. His research has been supported by competitive grant funding from government and industry.

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