

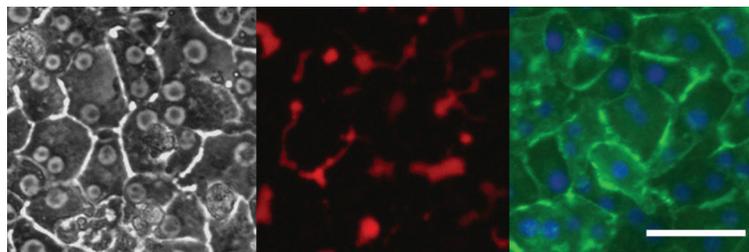
PRESS RELEASE

An ultrathin collagen matrix biomaterial tool for 3-D microtissue engineering

March 4, 2014 — A novel ultrathin collagen matrix assembly allows for the unprecedented maintenance of liver cell morphology and function in a microscale “organ-on-a-chip” device that is one example of 3-D microtissue engineering.

A team of researchers from the Center for Engineering in Medicine at the Massachusetts General Hospital have demonstrated a new nanoscale matrix biomaterial assembly that can maintain liver cell morphology and function in microfluidic devices for longer times than has been previously reported in microfluidic devices. This technology allows researchers to provide cells with the precise extracellular matrix cues that they require to maintain their differentiated form and liver-specific functions, including albumin and urea production. The novel technique reported offers a new tool for basic science and pre-clinical investigations, and allows for the creation of stable liver microtissues for use in organ-on-a-chip devices to mimic healthy liver physiology, investigate liver diseases, and test the toxicity of potential therapeutic drugs before using animals or clinical studies. This report appears in the current issue of the journal *TECHNOLOGY*.

“This is a clever combination of the well-known layer-by-layer deposition technique for creating thin matrix assemblies and collagen functionalization chemistries that will really enable complex liver microtissue engineering by replicating the physiological cues that maintain the state of liver cell differentiation,” says Martin Yarmush, M.D., Ph.D., of the Massachusetts General Hospital and senior author on this paper. “The ultrathin collagen matrix biomaterial and its ability to keep liver cells functional for longer periods of time in chip devices will undoubtedly be a useful tool for creating liver microtissues that mimic the true physiology of the liver, including cell and matrix spatial geometries”. By creating polyanionic and polycationic solutions of collagen, a ubiquitous extracellular matrix molecule, and alternately exposing liver cells seeded



An ultrathin collagen matrix assembly maintained the morphology and function of primary liver hepatocytes in a microfluidic organ-on-a-chip device for two weeks. Three images of the hepatocytes after two weeks in a microfluidic device: A phase contrast image of cell morphology at two weeks showing dense cytoplasm, distinct nuclei, and bright cell borders; bile canalicular network development (red); and cell nuclei (blue) and actin (green) organization demonstrating cell polarity. Scale bar: 50 microns. (Credit: William McCarty, the Center for Engineering in Medicine at the Massachusetts General Hospital, Harvard Medical School, and the Shriners Hospitals for Children-Boston)

in microfluidic devices to the solutions, the investigators were able to create a nanoscale assembly of collagen on top of the cells. This process can be used to form biologically relevant coatings on many types of charged surfaces to direct cell alignment, increase attachment efficiency, and maintain morphology and function.

“This technique is a nice example of how the translation of established methods for cell culture into microfluidic devices can produce new tools for understanding biological systems, such as cell-matrix interactions,” says William McCarty, Ph.D., the lead author on this paper. The team from the Massachusetts General Hospital plans to use this technology in a variety of engineering applications, including constructing liver microtissues by layering together the different types of cells that make up the liver. The liver plays a central role in human-drug interactions and is a common target for drug-induced toxicity, which can result in costly, late-stage and post-approval drug failures when animal models fail to predict human toxicity reactions. To address the current lack of predictive *in vitro* tools, the investigators are developing scalable liver microtissues that could be used to better understand the toxic effects of drugs, as well as provide a high throughput system for testing drug-drug interactions.

Additional co-authors of the TECHNOLOGY paper are O. Berk Usta, Ph.D., Martha Luitje, Shyam Sundhar Bale, Ph.D., Abhinav Bhushan, Ph.D., Manjunath Hegde, Ph.D., Inna Golberg, Rohit Jindal, Ph.D., and Martin L. Yarmush, M.D., Ph.D., all from the Center for Engineering in Medicine at the Massachusetts General Hospital, Harvard Medical School, and the Shriners Hospitals for Children-Boston.

This research was supported in part by grants from the National Institutes of Health (UH2TR000503 and F32DK098905 for W.J.M.).

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