Model tissue system reveals cellular communication via amino acids

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A team of researchers from the Massachusetts General Hospital Center for Engineering in Medicine (MGH-CEM) has found the first evidence of cell-to-cell communication by amino acids, the building blocks of proteins, rather than by known protein signaling agents such as growth factors or cytokines. Their report will appear in an upcoming issue of the *FASEB Journal* and has been released online.

"We were taken by complete surprise," says Rohit Jindal, PhD, a postdoctoral fellow at MGH-CEM and the paper's lead author. "Past reports have implicated various growth factors and the extracellular matrix proteins secreted by other cell types in regulating hepatocyte behavior, but to the best of our knowledge, this is the first evidence that cells can communicate by changing local amino acid concentrations."

The authors describe the development of a three-dimensional model of liver tissue in which hepatocytes (liver cells) are embedded in a layer of collagen and covered with a layer of endothelial cells - the cells that line blood vessels, which permeate the liver. In this model system liver cells recovered their metabolic activity much faster than in previous models - in two days instead of a week or longer. The fundamental discovery was that the amino acid proline was responsible for this enhanced recovery. A building block of collagen, proline was secreted by the endothelial layer of the liver model, taken up by hepatocytes and used to synthesize new collagen, leading to faster recovery of hepatocyte activity.

"Identifying this amino-acid-mediated communication points to the

importance of considering changes in metabolism while evaluating cell-to-cell communication," says Martin Yarmush, MD, PhD, director of the MGH-CEM and the paper's senior author. "Metabolic factors are gaining prominence in our understanding of a number of diseases, and establishing the contribution of different cell types to the metabolic milieu could provide new drug targets in the treatment of liver disease." Yarmush is the Helen Andrus Benedict Professor of Surgery and Bioengineering at Harvard Medical School (HMS).

Co-author Yaakov Nahmias, PhD, of MGH-CEM, adds, "It's not currently clear whether this mechanism occurs in living animals, but it could contribute to active liver remodeling during liver development or regeneration." Additional co-authors of the FASEB Journal paper are Arno Tilles, MD, and Francois Berthiaume, PhD, both of the MGH-CEM. The work was supported by grants from the National Institutes of Health and Shriners Hospitals for Children.

Source: Massachusetts General Hospital (news : web)