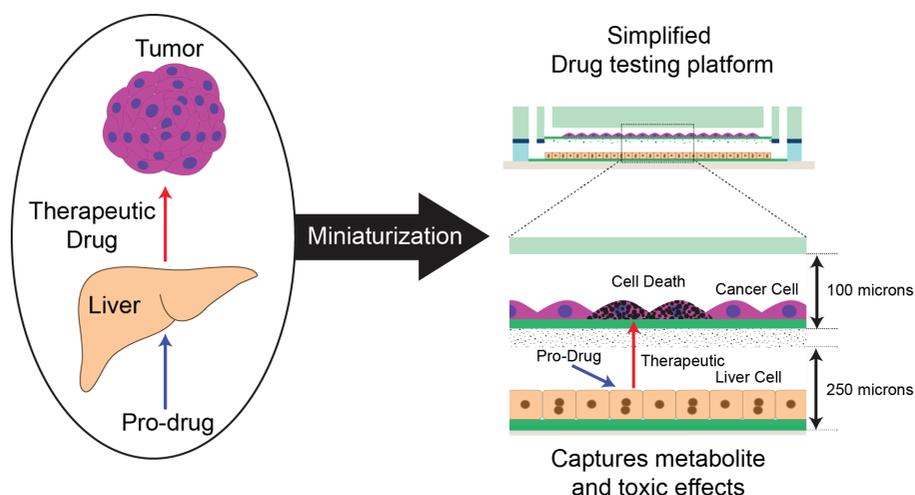


## PRESS RELEASE

# Microfabricated device allows evaluation of the efficacy, toxicity of drugs metabolized through the liver

**BOSTON — A team of researchers from the Massachusetts General Hospital Center for Engineering in Medicine (MGH-CEM) has developed a novel approach that dramatically simplifies the evaluation of the liver's drug-metabolizing activity and the potential toxic effects of the products of that activity on other organs. Their report appears in the forthcoming issue of the journal *TECHNOLOGY*.**



*A microfabricated device developed by the Massachusetts General Hospital Center for Engineering in Medicine is able to analyze the effects of pro-drugs — substances transformed within the liver into therapeutic agents — on cancer cells. The two-chamber microscale platform enables the culture of liver cells called hepatocytes and tumor cells in close proximity and in small amounts of supportive media. The microscale environment leads to the rapid accumulation of greater quantities of the desired metabolite and detection of its toxic effect on cancer cells. (Image Credit: Shyam Sundhar Bale, PhD, MGH Center for Engineering in Medicine.)*

“The liver plays a central role in drug metabolism, a process that has been exploited in the development of pro-drugs that are transformed by the liver into the ultimate therapeutic agent,” says Martin Yarmush, MD, PhD, director of the MGH-CEM and the paper’s senior author. “Currently, there is a large effort underway to create systems that enable evaluation of organ-to-organ interaction in the context of drug efficacy and toxicity. Most investigators in this field use approaches that rely on the flow of fluids between organs to achieve this interaction. But these systems can be cumbersome, with limitations in speed and undesirable excessive dilution. Our approach relies on capturing organ-to-organ interactions in a simple, static system that overcomes these limitations.”

The authors describe development of a microfabricated device that enables the separate culture of primary liver cells and cancer cells. The device contains two microchambers separated by a tissue-culture membrane allowing very small amounts

of the two different cell types to be cultured within the same device. The team demonstrated the efficacy of the system by analyzing the metabolic conversion in liver cells of Tegafur, a chemotherapeutic pro-drug, into the toxic metabolite 5-fluorouracil and its subsequent effect on cancer cells. The simplified platform eliminates the need for pumping and tubing connections and provides a novel, easy-to-use platform for studying drug metabolism, toxicity and interactions between multi-tissue systems, serving as a robust, valuable tool for screening drugs for toxic effects.

“This work is significant because many commercially available “organ-on-a-chip” devices are not truly microscale, and therefore can totally miss important biological and toxicological phenomena simply because sample volumes and dimensions are too large. This paper clearly demonstrates that critical, subtle interactions can be detected if the device is designed and fabricated properly,” says Shyam Sundhar Bale, PhD, a research fellow in the MGH-CEM and lead author of the paper. “Our method takes advantage of a microenvironment in which the cells can be cultured in much smaller quantities of supportive media than in traditional culture methods, enabling the accumulation of higher concentrations of the metabolized product. This methodology is particularly attractive in cases where in the toxic metabolite that is formed is either short lived or is processed further into other, non-toxic components.”

Co-senior author Rohit Jindal, PhD, of MGH-CEM, adds, “The microfabrication methods applied in this study are readily amenable to designing a device in which multiple two-chamber wells could be operated at the same time, dramatically increasing processing speed, that would be no larger than a standard, 96-well culture plate.” Jindal is an instructor in Surgery at Harvard Medical School.

Additional co-authors of the *TECHNOLOGY* paper are Gautham Vivek Sridharan, PhD, Inna Golberg, MS, Ljupcho Prodanov, PhD, William J McCarty, PhD, and Osman Berk Usta, PhD, all of the MGH Center for Engineering in Medicine. The work was supported by National Institutes of Health grants 5UH2TR000503, F32DK098905, and F32DK103500. The MGH has filed a patent application for the device described in this paper.

Massachusetts General Hospital, founded in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of more than \$760 million and major research centers in AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, human genetics, medical imaging, neurodegenerative disorders, regenerative medicine, reproductive biology, systems biology, transplantation biology and photomedicine.

**Corresponding authors for this study in *TECHNOLOGY* are Dr. Rohit Jindal, [RJINDAL@mgh.harvard.edu](mailto:RJINDAL@mgh.harvard.edu) or Dr. Martin L. Yarmush, [ireis@sbi.org](mailto:ireis@sbi.org).**

---

## About *TECHNOLOGY*

Fashioned as a high-impact, high-visibility, top-echelon publication, this new ground-breaking journal — *TECHNOLOGY* — will feature the development of cutting-edge new technologies in a broad array of emerging fields of science and engineering. The content will have an applied science and technological slant with a focus on both innovation and application to daily lives. It will cover diverse disciplines such as health and life science, energy and environment, advanced materials, technology-based manufacturing, information science and technology, and marine and transportations technologies.

## About World Scientific Publishing Co.

World Scientific Publishing is a leading independent publisher of books and journals for the scholarly, research and professional communities. The company publishes about 500 books annually and more than 120 journals in various fields. World Scientific collaborates with prestigious organisations like the Nobel Foundation, US National Academies Press, as well as its subsidiary, the Imperial College Press, amongst others, to bring high quality academic and professional content to researchers and academics worldwide. To find out more about World Scientific, please visit [www.worldscientific.com](http://www.worldscientific.com).