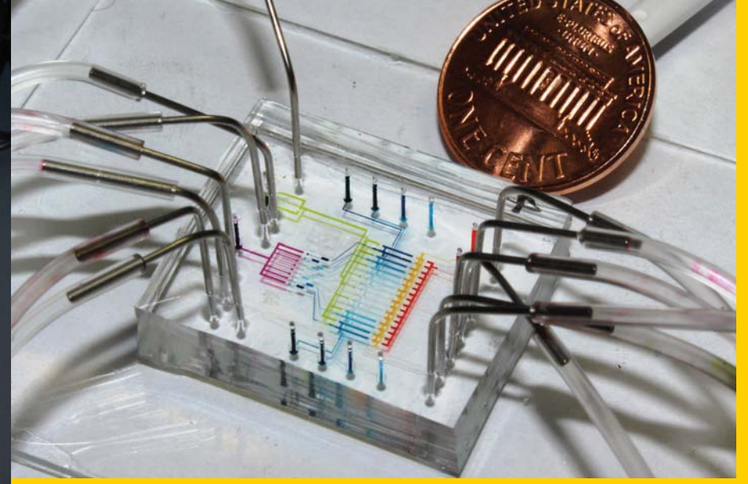

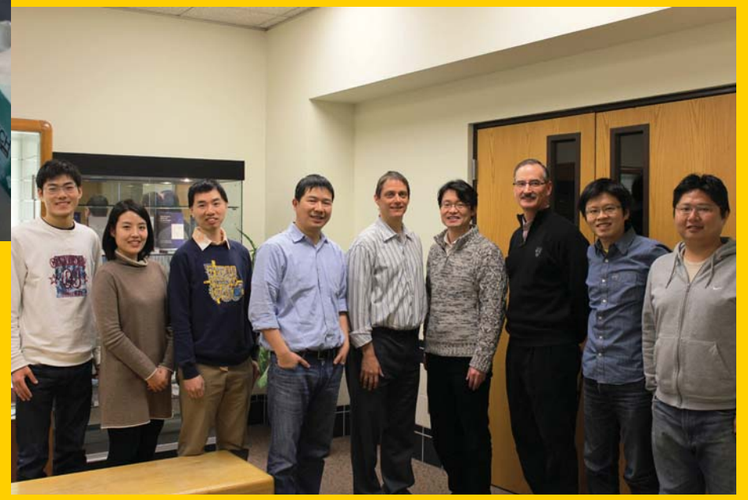

Lab-on-a-Chip

Novel Platform Speeds Immune System Monitoring

> It's motivating to know that what we're developing can benefit patients and have a real clinical impact.

FAR LEFT: Postdoc fellow Zeta Yu tests the integrated microfluidic chip he developed for functional immunophenotyping of patient blood samples.

TOP: A highly integrated microfluidics chip for rapid, automated, parallel quantitative immunoassays.

BOTTOM: Microfluidic immunophenotyping research team (from left to right) Xiang Li, Bo-Ram Oh, Zeta Yu, Jianping Fu, Timothy T. Cornell, Katsuo Kurabayashi, Thomas P. Shanley, Nien-Tsu Huang (now assistant professor at the National Taiwan University), and Weiqiang Chen (now assistant professor at New York University).

For critical care physicians, the ability to have an accurate picture of a patient's immune status can make the difference between life and death.

Doctors use information about immune status to monitor a patient's condition, determine whether treatments are working and to inform changes in treatment strategies if they are not.

But current immunological tests take 24 to 48 hours to deliver results, and they can require repeated sampling over time. Current tests also need large amounts of blood, which can be problematic for newborns and infants. And still, conventional tests don't provide as full a view of the immune system as clinicians might like.

"Doctors today have an arsenal of immune-modulating drugs available to them, but they can't always get the information they need as quickly as they need to prescribe the right drug," said assistant professor **Jianping Fu**, who leads the U-M Integrated Biosystems and Biomechanics Laboratory.

Timing is everything, Fu emphasized. "In patients with serious immune issues, such as sepsis, mortality increases by 7 percent per hour after onset."

Sepsis is a dangerous complication of infection. It occurs when immune cells release cytokines, molecules that can signal an inflammatory response throughout the body and can lead to organ failure. The mortality rate for severe sepsis can reach 60 percent.

Fu and ME Professor **Katsuo Kurabayashi,** co-principal investigator, are developing a "lab-on-a-chip" platform for rapid analysis of immune system function by quantifying different types of immune cells and the cytokines they release.

The two investigators are working with clinical collaborators from the U-M Medical School: Drs. **Timothy Cornell** and **Tom Shanley,** both pediatric intensivists at C.S. Mott Children's Hospital.

The new device uses microbeads coated with antibodies to recognize specific types of immune cells. A specially fabricated silicone membrane helps sort the target cells, which are routed through other components of the microscale system. Biosensors detect cytokine secretion from the cells attached to the beads.

The device can detect and analyze four types of immune cells and up to six cytokines for each type. This has the potential to supply clinicians with an expanded panel of biomarkers, giving a more detailed, actionable view of a patient's immune system status and function.

The device requires just a fraction of a drop of blood, and results take less than 30 minutes. In addition, the technology has the capability to achieve a detection sensitivity of just a single cell.

The project received seed funding from U-M's MCubed program and the Michigan Institute for Clinical & Health Research. Both paved the way for the team to win funding from the National Institutes of Health R01 Program, a significant milestone.

Through the U.S. Food and Drug Administration's Expanded Access program, a patient already has benefited from the team's invention.

In late 2014, a young girl with cancer was experiencing organ failure due to a severe immune system reaction to treatment. With results from the device, the patient's doctor was able to rapidly and accurately measure her cytokines and adjust therapy accordingly. She recovered.

"It's motivating to know that what we're developing can benefit patients and have a real clinical impact," said Fu.

In the future, patients undergoing organ transplants or cancer immunotherapy may also benefit from the technology. In the case of transplants, doctors suppress patients' immune systems to prevent rejection of the donated organ.

The new platform may instead enable doctors to suppress only the specific types of immune cells involved in organ rejection. With this approach, patients could still retain immunity to fight off everyday infections.

In cancer immunotherapy, one of most promising directions for cancer treatment today, there currently is no good way to tell whether the treatment has in fact stimulated the necessary immune cells to attack cancer cells.

"Today no available technology exists to effectively capture and examine those immune cells and see if they're working. I believe that's where our technology can go," Fu said.