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PRESS RELEASE

Microfluidic platform enables measurement of neutrophil directional migration from a droplet of blood

Sept. 15, 2013 — Neutrophils are a vital part of the body's immune system. Recognized as the most abundant type of white blood cell present in human blood, neutrophils function primarily as the body's first line of defense against infection and inflammation. Within minutes of stimulation, neutrophils migrate, or chemotax, from the blood to tissue where they accumulate at sites of infection. Alterations in neutrophil ability to migrate could lead to infections that are hard to control, chronic inflammatory diseases, and tissue injury.

The alterations of neutrophil migration are most often transient, consequence of other diseases, and rarely permanent consequence of genetic defects. However, despite its importance, neutrophils' ability to migrate is rarely measured in the clinic This due largely to limitations in current technologies including a lengthy neutrophil isolation procedure that requires trained personnel, and often complex neutrophil migration assays.

To address the limitations of current technologies and enable practical applications in the clinic, a team of researchers from the The BioMEMS Resource Center at Massachusetts General Hospital (MGH) has designed a miniaturized silicon-based device that can be used to measure neutrophil's migration pattern from just a finger prick of blood. The device is made using advanced technologies borrowed from the electronics industry. Within the new device, neutrophil cells will migrate towards a chemoattractant, an agent that causes cells movement, allows migration pattern to be measured without requiring neutrophil cells to be pre-concentration from whole blood. This device has the potential to be use in the clinical setting to help physicians to better monitor the immune system in patients with likely infections, including burn, trauma, major surgery, HIV and cancer patients during chemotherapy. The report appears in this first issue of the journal *Technology*.

"Neutrophils are fascinating cells and their complex functional status is really under appreciated in the clinic. The neutrophils are assumed to be always fully functional and ready to protect us against bacteria and fungi. Thus, the only measure of neutrophil in the clinic is the absolute neutrophil count (ANC), part of the standard cell blood count. However, ANC gives no insight into neutrophil ability to move and reach the locations where they could perform their functions. Without neutrophils being able to get to the place in the body where the microbes are, all other functions become irrelevant. Current assays to measure neutrophils ability to move are laborious, imprecise, and are rarely performed in the clinic. To circumvent these limitations we designed a novel device. This device should enable frequent neutrophil measures and could eventually become a useful tool in the hands of physicians, for monitoring of the risk for infections or the course of chronic inflammation in their patients." says Daniel Irimia, MD,

PhD, an assistant professor of Surgery at Harvard Medical School and Massachusetts General Hospital, and who is also affiliated with Shriners Hospital for Children.

"The whole blood microfluidic device allows you to measure neutrophil chemotaxis from a droplet of blood in just minutes, and does not require hours of tedious processing common using traditional techniques," says Caroline N. Jones, Ph.D. one of the paper's lead authors. "This timely information will be invaluable in the clinic when treating or predicting infection, for example in patients after burn injuries."

It is known that many factors in whole blood, including serum and platelets, affect neutrophil function. It is therefore advantageous to minimize sample processing to maintain the *in vivo* microenvironment of the neutrophil when measuring variations in chemotaxis *in vitro* for clinical diagnostic purposes.

The device design includes strategic turns in the migration channels to block other cells in the blood from entering the neutrophil migration channels. These filtering channels selectively block the entrance of other blood cells based on size, deformability, or motility; but do not prevent neutrophil cells from entering the channel and migrating towards the collection chamber. The researchers demonstrated that this device gives robust and reproducible neutrophil accumulation numbers, velocity and directionality in healthy donor finger prick and venous blood sources. They also utilized the device in the clinic to measure neutrophil chemotactic impairment in a patient with large burn over a three week treatment period.

Additional co-authors of the *Technology* paper are Anh N. Hoang, PhD, Laurie Dimisko, Bashar Hamza, Joseph Martel, PhD, Nikola Kojic, PhD. The work was supported by grants from the National Institutes of Health (NIH).

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