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Infected red blood cells: the microdevice separation technique

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At the Singapore–Massachusetts Institute of Technology (MIT) Alliance for Research and Technology centre in Singapore a collaboration of scientists from the National University of Singapore and MIT (MA, USA) have developed a microfluidic technique to separate malaria-infected red blood cells (iRBCs). In blood vessels with a diameter of less than 300 µm, RBCs migrate to the centre of the vessel due to the velocity gradient in the vessel. iRBCs are stiffer than noninfected cells and are displaced to the sidewalls, a process known as margination.

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The scientists were able to mimic cell margination to separate iRBCs from whole blood. An infected blood sample was applied to a long, straight-channel microfluidic device, which was fabricated in polydimethylsiloxane. Cell margination was directed along the channel with iRBCs aligning to each sidewall, which were then removed using a three-outlet system. Research lead Chwee Teck Lim (National University of Singapore) spoke to *Bioanalysis* about the difficulties that had to be overcome during the research: "the major issues associated with processing whole blood in microchannels are problems related to clogging due to the large cell numbers (~5 × 10^6 RBCs/µl) and the larger leukocytes. This was avoided by designing an effective filter region at the inlet. Another problem we encountered was related to cell sedimentation in the syringe during testing. This results in inhomogeneous hematocrit values, thus affecting margination efficiency. This problem was overcome by changing the density of the buffer using dextran as an additive. To be more cost effective, we also tried to avoid using chemicals or antibodies in this work."

The distribution of the iRBCs was analyzed across the microchannel width at the outlet. Flow cytometry analysis indicated a recovery of approximately 75% for early-stage and over 90% for late-stage iRBCs.

Lim spoke about the wider applications of the research, explaining that "the motivation behind this work was to develop a simple, cheap, effective and efficient microdevice that can be readily used in resource-poor settings for more accurate malaria diagnosis (reduce the number of false negatives). Besides malaria, this margination effect can also be applied for other diseases such as sickle cell anemia and cancer whereby the less deformable cells will also undergo margination to the sides. This will prove especially useful for disease detection by effectively reducing the sample blood volume to be tested, improving the throughput and shortening the processing time. There are a few other avenues where this simple device could find diverse applications."

Currently, the scientists are optimizing the channel design by changing the channel length and side-channel split to improve the efficiency of separation. In addition, they plan to integrate on-chip detection to directly identify iRBCs after enrichment at side outlets and they also intend to carry out testing of clinical samples at malaria-prone sites.

Source: Hou HW, Bhagat A, Chong A *et al.* Deformability based cell margination – a simple microfluidic design for malaria-infected erythrocyte separation. *Lab Chip* DOI: 10.1039/C003873C (2010) (Epub ahead of print).

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