New lab-on-a-chip system quickly identifies health aspects of a person's immune system

Reviewed by James Ives, M.Psych. (Editor) Sep 25 2019

Scientists from Nanyang Technological University, Singapore (NTU Singapore) have developed a lab-on-a-chip system that can identify the health aspects of a person's immune system from a drop of their blood, within minutes.

Using a combination of microfluidics - tiny microscopic channels that can isolate white blood cells from blood - and electrical sensors, the new chip was able to detect differences in the electrical properties of white blood cells taken from healthy and diabetic patients.

The proof of concept device may one day help doctors to quickly gain insight into a person's immune system, and spot early signs of inflammation and infection that could signal the need for further in-depth tests.

Designed and built by Assistant Professor Hou Han Wei and Assistant Professor Holden Li from the School of Mechanical and Aerospace Engineering, their invention, if successful in further laboratory and clinical assessments, could be turned into a portable device suitable for family clinics and polyclinics.

A prototype device and the engineering principles behind it were reported in two peer-reviewed journals:*Lab on a Chip* earlier this year and *Biosensors and Bioelectronics* in October last year.

As immune health is often implicated in cardiovascular diseases, the scientists say that their device can potentially be an additional screening tool for doctors to use for early detection of heart diseases. In Singapore, cardiovascular diseases accounted for 30.1 per cent of all deaths in 2017 while diabetes is a serious health problem which affects about 10 per cent of the world's population.

How the invention works

Asst Prof Hou, who is also a faculty member at the Lee Kong Chian School of Medicine at NTU, said that their chip detects electrical differences between a healthy white blood cell and an unhealthy one. Abnormal white blood cells have been reported as an early biomarker for increased risk of cardiovascular diseases and also suggests an ongoing inflammation.

Using very tiny channels, the chip first physically separates the various blood cells by size into the different outlets, like a coin-sorting machine. The isolated white blood cells are then run through a special channel where the electrical impedance is measured for each cell at a very high speed (hundreds of cells per second).

The electrical impedance of an abnormal cell is usually higher than the impedance of a healthy cell, given as abnormal cell is larger in size and has different membrane properties.

White blood cells form a significant part of the body's immune system and a key type known as neutrophils, are the first line of defence when infection or inflammation strikes.

> *Our chips can isolate thousands of white blood cells from a single drop of blood and, within minutes, tell if these cells are electrically different from normal, which would be an indicator of whether there is a health issue to be further investigated.More importantly, our process also does not use any chemical biomarkers or antibodies, which makes the assay cheap, easy to use, and that we can do further analysis on the same white blood cells we have already run through the chip."*
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> *Hou Han Wei, Assistant Professor, School of Mechanical and Aerospace Engineering, NTU Singapore*

Possible use in clinical testing

Asst Prof Holden Li says that the material used to make the new lab-on-a-chip is a common medical-grade polymer and is easily manufactured using existing machinery, and can be made into a desktop-sized machine for use in clinics.

"Our chip was designed for easy scale-up by companies, with an integrated system built from electronic components available on the market. Moving forward, we are looking to commercialise the technology with an industry partner, as we see that there are market demands -for a point-of-care device for doctors and as laboratory equipment for the study of neutrophils and drug screening," Prof Li said.

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The scientists added that they are also doing more research on the various electrical impedance levels and what each of them signifies, so as to build a sort of reference library for automated analysis, and will be working with doctors to test their prototype in the clinical setting.

Giving an independent opinion on the research,Professor Bernhard Boehm, Ong Tiong Tat Chair Professor of Diabetes Research at NTU's Lee Kong Chian School of Medicine, said many diabetic patients are also susceptible to chronic infections due to disease affecting the performance of the immune system.

"There are a number of limitations to using conventional diagnostic markers for patients with clinical suspicion of infection. In particular there is a need to improve early diagnosis of bacterial infections and to provide guidance for antibiotic therapy."

"Therefore, a test system that can rapidly guide decisions about initiation of specific therapies would be of great help in a clinical setting. However, this will need in the near future randomised controlled clinical trials to provide formal proof that the novel test system is superior to the currently used conventional diagnostic procedures," added Prof Boehm, who was not part of this study.

Tool in studying immune defence mechanisms

The new device could also be very useful for the study of NETosis, a newly discovered defence mechanism in the field of immunology.

During NETosis, neutrophils spit out DNA strands that trap bacteria and viruses, much like a spider's web, to impede their movements and to kill the trapped pathogens. However, too much NETosis also slows down wound healing in diabetes.

NETosis expert,Assistant Professor Christine Wong, from NTU's Lee Kong Chian School of Medicine who was not involved in this study, says the most widely adopted methodology for studying NETosis propensity currently is real-time imaging or microscopy of fixed neutrophils.

However, it is a laborious process for researchers to isolate the neutrophils for microscopy without affecting their native baseline state, and not influence experimental results.

"The new device by Asst Prof Hou and Asst Prof Li may enable rapid and non-biased NETosis experiments and quantification, which will be especially useful for drug screening ex vivo," Asst Prof Wong said in her independent comment.

"If the device can be modified to measure NETosis in mouse neutrophils, this would be delightful news for researchers using mouse models, as low neutrophil yield is a common obstacle in mouse neutrophil isolation due to the smaller blood volume available in mice and their lower myeloid cell

ratio when compared to humans."

Asst Prof Wong added that while the new device is unlikely to replace microscopy experiments, in particular when visualisation of cellular components during the NETosis process is the subject matter, the resources saved from NET quantification can could be diverted to those investigations.