Researchers develop platform to monitor hematopoietic stem cells

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A Canadian research team has developed an automated microfluidic cell culture platform to monitor the growth, survival and responses of hundreds of hematopoietic stem cells (HSCs) at the single cell level.

This new tool allows scientists to study multiple temporally varying culture conditions simultaneously and to gain new insights on the growth factor requirements for HSC survival.

"The ability to perform massively parallel cultures of single non-adherent mammalian cells will provide new avenues to explore complex biological questions," says Véronique Lecault, lead author of the study and a PhD candidate in the UBC Dept. of Chemical and Biological Engineering.

"Our results will find use in broader applications such as drug development, clone selection and culture optimization," says Lecault.

The findings appear in the May 22 issue of the online journal *Nature Methods.* The study is a collaborative project between the laboratories of Asst. Prof. Carl Hansen, UBC Physics and Astronomy, Centre for High-Throughput Biology, Prof. James Piret, UBC Chemical and Biological Engineering, Michael Smith Laboratories, Prof. Connie Eaves, Terry Fox Laboratory, BC Cancer Agency, and Dr. Keith Humphries, Terry Fox Laboratory, BC Cancer Agency.

Lecault explains that HSCs are found mainly in adult bone marrow and

have the astounding ability to sustain the continuous production of specialized blood cells.

These cells have major clinical implications, in particular for the treatment of cancer and blood-borne diseases, but the mechanisms regulating their division into stem cells (self-renewal) or more mature cells (differentiation) are not very well understood.

The heterogeneous nature of hematopoietic populations further complicates the study of these rare HSCs by hiding individual responses into average measurements. Single cell studies are therefore critical to elucidate these mechanisms but current techniques are labour intensive, require expensive reagents and provide limited flexibility to characterize cells or exchange culture conditions.

The team designed and fabricated microfluidic devices -- about the size of a matchbox -- containing 1,600 to 6,400 miniature culture chambers that can sustain robust cell growth, along with an automated time-lapse imaging system to track clones over multiple days as they expand from single cells.

"There are many challenges associated with the culture of suspension cells in nanolitre volumes including dehydration, nutrient limitations, and rapid variations if culture conditions are not well controlled," says Lecault.

The team was able to solve these problems by integrating an osmotic bath to block evaporation combined with a unique geometry that allows for automated medium exchange, immunostaining on live clones and cell recovery.

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