Microfluidic array catches, holds single cervical cells for faster screening

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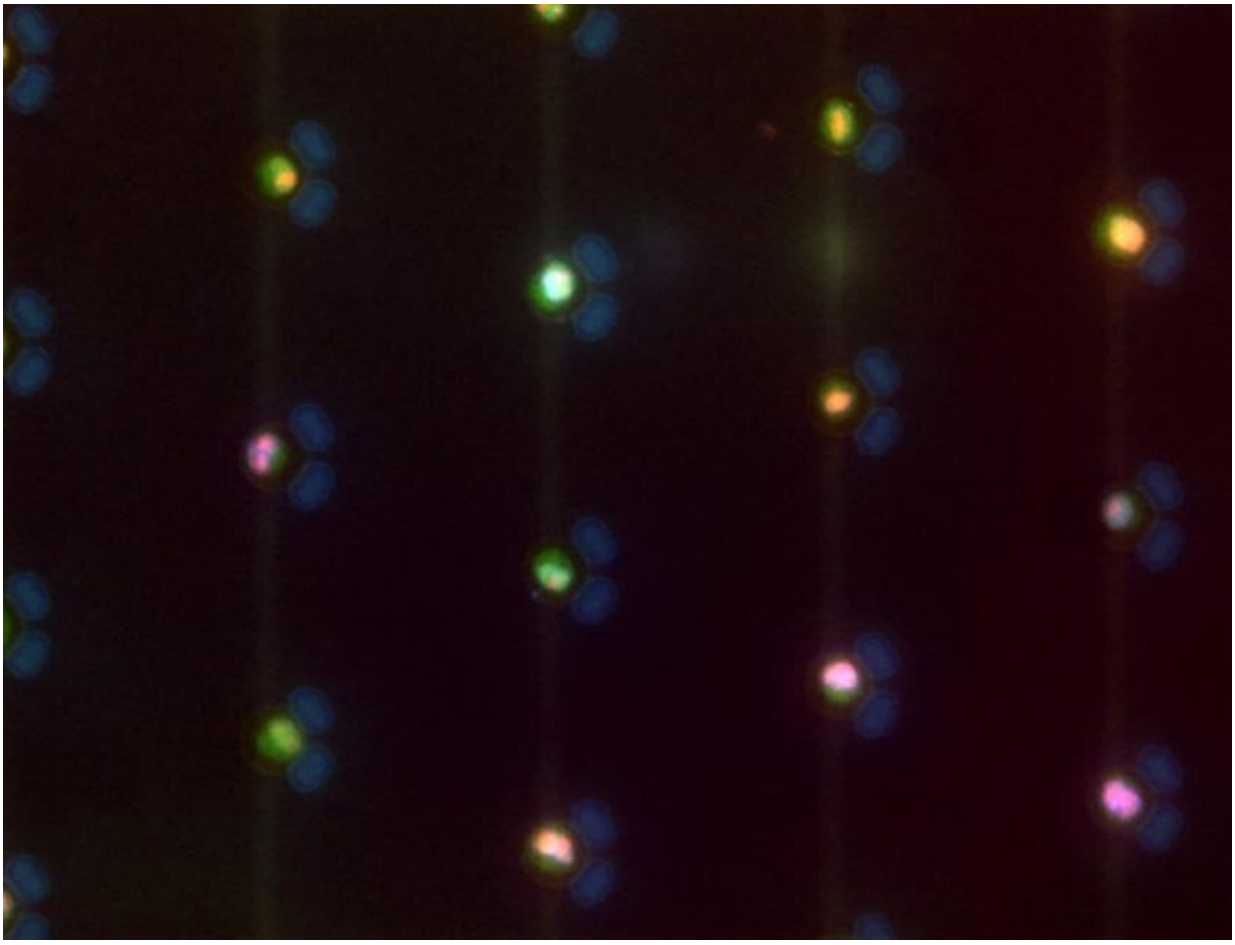

Experimental results of immunostained cells using the microwell array with barriers. Credit: Soo Hyeon Kim

Several screening tests for cervical cancer have been developed in recent years. One technique uses immunofluorescent staining to determine the levels of biomarkers to indicate a cell is undergoing HPV-related cancerous growth. Immunostaining for these proteins, however, can be time-intensive. One new approach, discussed in this week's *Biomicrofluidics*, looks to provide a way to screen cervical cells with immunostaining more efficiently, drawing inspiration from an unlikely source: Pachinko.

Researchers have demonstrated a new device that can trap and analyze single cells for HPV-related cervical cancer screening. The device uses an array of wells for single cells to sit in, each with microscopic electrodes lining the bottom, and an electrical phenomenon known as dielectrophoresis to trap those cells for analysis.

The design, said author Soo Hyeon Kim, was inspired by the game Pachinko, in which small steel balls navigate a board studded with brass pins toward baskets that denote various prizes.

"Major challenges were trapping suspended cells at the single-cell level and analyzing them using antibodies with minimum loss of trapped cells," he said. "By just putting a small structure behind the microwell, the cells were efficiently stayed in the microwells even with the unstable flow used for delivery of reagents."

Immunostaining involves creating antibodies that can enter a cell and bind to target proteins and fluoresce. Cells containing higher levels of two proteins related to cellular growth and proliferation, called p16 and Ki-67, reliably indicate the presence of cancerous cells.

Such techniques, though, often require researchers to carefully prepare one cell at a time. This can be particularly problematic, since sometimes not all cells from the same cancerous show the same abnormal behavior.

The group's approach, called electroactive microwell array with barriers (EMAB), is one of the first to combine electrostatic forces from each well's electrodes with a physical structure that acts as a Pachinko basket for each cell.

During experiments, the device effectively trapped 98% of the cells that passed through it and was able to hold on to 92% of them before analyzing them using immunofluorescent staining.

Kim said that combining EMAB with p16/Ki67 dual immunostaining could be a useful tool to provide molecular evidence that might help pathologists make a cervical cancer diagnosis. He hopes the technique evolves and can be adapted for use in diagnosing ovarian cancer and circulating tumor cells.

The group's next project is to use the device in the clinic.

More information: On-chip immunofluorescence analysis of single cervical cells using an electroactive microwell array with barrier for cervical screening, *Biomicrofluidics*, DOI: 10.1063/1.5089796

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