NEW NANO DEVICE DETECTS IMMUNE SYSTEM CELL SIGNALING

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Scientists have detected previously unnoticed chemical signals that individual cells in the immune system use to communicate with each other over short distances.

The chemical signals cells exchange when they come into contact have been studied extensively. But it has not been possible to detect chemical messages that travel between cells that are nearby but not in contact – called paracrine signals – because they are highly localized and they are produced in concentrations that have been below detection levels.

A new technology, called a multi-trap nanophysiometer, was required to demonstrate the existence of non-contact signaling. This is one of the first microfluidic devices that has been applied successfully to the study of cell-to-cell signaling in the immune system.

The multi-trap nanophysiometer (MTN) was developed by a team of researchers at the Vanderbilt Institute for Integrative Biosystems Research and Education headed by John P. Wikswo, the Gordon A. Cain University Professor at Vanderbilt.

The dendritic cells, T-cells and B-cells in the immune system, which tend to concentrate in the lymph nodes spread throughout the body, function as individual, unattached cells.

If dendritic cells detect invaders in the body, they rapidly migrate to lymph nodes and have to find the appropriate T-cells to alert them. But how dendritic cells attract the right T-cells among millions of cells within the lymph nodes remains an immunological puzzle.

Scientists have been trying to develop systems for single-cell analysis for a number of years.

Because of the difficulty of keeping normal cells alive, they have been forced to use cells that have been genetically altered so they can be cultured indefinitely. Although the alteration “immortalizes” the cells, it also significantly limits their usefulness.

The MTN is the first system that can monitor biochemical changes in large numbers of normal or primary cells at the single-cell level for prolonged periods.

The new device consists of a series of hair-sized channels molded in a special kind of plastic that is glued onto the bottom of a glass microscope coverslip. A shoebox-sized pump pushes fluid (normally the media used to culture cells) through one channel that opens up into a chamber filled with hundreds of tiny, three-sided wells small enough to trap individual cells. When cells are injected upstream, they are passively trapped in the wells and are held there solely by the fluid flowing out even smaller holes in the well bottoms. By precisely controlling the flow rate, the researchers can keep normal cells alive for longer than 24 hours.

The researchers monitor the cells with a digital camera attached to a standard microscope, typically snapping images every 30 seconds.

Special attention should be focused on the fact that the researchers have written software that allows them to analyze the movements and reactions of individual cells. They can record various cell behaviors by injecting different fluorescent dyes into the cells.

The test reports say, for example, that when naive T-cells are primed for an immune response, the concentration of calcium ion in their cytoplasm jumps up. So when the cytoplasm contains a dye that fluoresces when it comes into contact with calcium, it glows brightly enough to be easily detected.

The surprise discovery of paracrine signaling was made by graduate student Shannon Faley, now a postdoctoral research associate at the University of Glasgow, Scotland. While experimenting with a nanophysiometer chamber she filled it with naive human T-cells and then added mature dendritic cells. She was looking for evidence of T-cell activation when the T-cells and dendritic cells were trapped in the same well and came into contact.

This kind of contact is part of the process that allows dendritic cells to convey information about potentially infectious invaders to the naive T-cells, which can then begin dividing to produce an army of effector T-cells custom-designed to attack the invaders.

By using new technology medical people will be able to contribute a lot to fighting immune system invaders.