New class of 'dancing' dendritic cells derived from blood monocytes

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Dendritic cells, known to be the prime movers of the body's immune response, are still notoriously difficult to study in humans. Samples, which come primarily from bone marrow or lymphoid tissue, are simply too difficult to obtain. But new research at Rockefeller University has shown scientists a way to study "authentic" dendritic cells from mouse monocytes, which are abundant in the blood, a much more accessible source in humans. The discovery, published last week in *Cell*, promises to accelerate research into therapeutic uses of dendritic cells in people, particularly in vaccine development and cancer treatment; it comes from the lab of Ralph M. Steinman, who first published his discovery of dendritic cells in 1973.

“So much of the work has been done in mice because of the logistics of getting the dendritic cells to work with,” says lead researcher Cheolho Cheong, a postdoc in the Laboratory of Cellular Physiology and Immunology at Rockefeller University. “We are filling in the gap between mice and humans with this new way to produce dendritic cells originated from the blood monocytes of living animals.”

Cheong’s breakthrough is in defining and isolating a new class of dendritic cells, called monocyte-derived dendritic cells, from the other types of specialized dendritic cells that reside in the lymph nodes, known as classical dendritic cells. After several years of searching, he found antibodies that would attach to a protein called DC-SIGN particular to the surface of monocyte-derived dendritic cells, a “handle” he could biochemically grab hold of to separate out the cells. Using this tool,

Cheong was able to show that monocytes, facing an infection of gram-negative bacteria such as *Escherichia coli* or their cell wall component called lipopolysaccharid in the blood, migrate to lymph nodes, where they quickly develop into fully fledged monocyte-derived dendritic cells, capable of stimulating T cells and fighting the infection.

When he segregated the cells and looked at them in the microscope, he saw that they had developed the unusual shape and manner of dendritic cells, with extended arms actively probing the environment for infectious particles, taking them up and presenting them to T cells. “It looks like these regular T cells are dancing with the stars,” he says. The monocyte-derived dendritic cells he had discovered outnumbered the classical dendritic cells in the infected mice and appeared to be as efficacious as their relatives in presenting invading particles to T cells, although more experiments will be required to determine their exact function in the immune response.

The work contributes to an increasingly detailed picture of how dendritic cells are derived, including work published last year in *Science* by Steinman’s colleague and former protégé Michel C. Nussenzweig. Nussenzweig and colleagues clarified the lineages of different types of dendritic cells and in particular the point at which classical dendritic cells separate from the closely related monocytes, even though they share a common ancestor in the bone marrow.

The research also shows that monocyte-derived dendritic cells are in fact “authentic” dendritic cells, with the same functional properties as their classical cousins. Although Cheong performed the work in mice, the discovery that real dendritic cells can be coaxed from blood monocytes promises to accelerate the study of dendritic cells in humans, because it is much simpler clinically to culture monocytes from a blood sample than classical dendritic cells from lymph tissues.

“If we better understand the human counterpart of monocyte-derived dendritc cells in mice, we can design better dendritic cell-based therapeutics for human use,” Cheong says.

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More information: Cell 143: 416–429 (October 29, 2010). Microbial Stimulation Fully Differentiates Monocytes to DC-SIGN/CD209+ Dendritic Cells for Immune T Cell Areas by Cheolho Cheong et al. http://www.cell.com/abstract/S0092-8674(10)01125-6

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