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# Research defines dendritic cell lineage

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(PhysOrg.com) -- Dendritic cells were discovered more than 30 years ago, but their pedigree has never been fully charted. They were known to be key immune system cells born in bone marrow, but their adolescence remained a mystery, their path to infection-fighting adulthood confused. Now, in experiments published in *Science*, researchers at The Rockefeller University have identified these special cells' rites of passage: They have shown the developmental point when dendritic cells part ways with closely related immune cells known as monocytes, at least in mice. The findings could have important implications for research on dendritic cell-based vaccines all over the world.

"So far, people in clinics are trying to make vaccines — cancer vaccines and others — based on dendritic cells without fully taking into account the different types," says Michel C. Nussenzweig, head of the Laboratory of Molecular Immunology, where the research was conducted. "The different types have different biological properties. Defining how they arise is important in terms of being able to target individual types, which could be very significant for vaccine development."

Prior research had shown that two kinds of dendritic cells, classical spleen dendritic cells (cDCs) and plasmacytoid dendritic cells (pDCs), as well as monocytes have a common ancestor cell in bone marrow. Kang Liu, a postdoctoral associate in Nussenzweig's lab, led the genealogical research into where the lines diverged, a question that has sparked controversy ever since dendritic cells were discovered. She focused the investigation on cDCs, which are expected to be more useful for vaccine

development than the monocytes commonly used now.

*Awkward adolescents. Three hours after being introduced in a mouse, precursors for classical spleen dendritic cells (pre-cDCs, green) attach to blood vessels near where B cells (blue) and T cells (red), other important players in the immune system, are active. New research has solved the long-standing problem of how to differentiate pre-cDCs from other dendritic cells and their cousins, monocytes.*

Liu had a hunch about how an adolescent classical spleen dendritic cell might look. She deduced that it would express one cell receptor common to all known dendritic cells, Flt3, but would lack a certain protein that enables the grown-up cell to capture bacteria or viruses and present them to other immune cells for destruction. She developed markers for these theoretical dendritic adolescents and found them in bone marrow, blood and lymph organs such as the spleen and lymph node, which filter bodily fluids. She named these cells preclassical spleen dendritic cells (pre-cDCs), and found that wherever they were from, they grew into adult dendritic cells in mice within days.

Using a two-photon microscope and other biochemical tests, Liu and her collaborators Gabriel Victora and Tanja Schwickert were able to trace the life cycle of cDCs from their original ancestor to their transformation into fully committed pre-cDCs in the bone marrow, their migration in the blood and growth into full-fledged cDCs dancing around the lymph system. The pre-cDCs they injected grew up to behave just like the native cDCs in mice. Liu also unveiled the related but distinct lineages of plasmacytoid dendritic cells and monocytes.

“We identified the migrating dendritic cell precursor and really took it as a tool to understand the differentiation of dendritic cells from head to toe, from the early stage in bone marrow to the late stage development and regulation in the lymph organ,” Liu said.

The discovery of the dendritic cell precursor could have important applications in immunotherapy. Many immunotherapies today are based on monocytes, which can be chemically prodded to develop dendritic cell-like characteristics but are not the genuine article.

More information: *Science* online: March 12, 2009. In Vivo Analysis of Dendritic Cell Development and Homeostasis. Kang Liu, Gabriel D. Victora, Tanja A. Schwickert, Pierre Guermonprez, Matthew M. Meredith, Kaihui Yao, Fei-Fan Chu, Gwendalyn J. Randolph, Alexander Y. Rudensky and Michel Nussenzweig

Provided by Rockefeller University (news : web)