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Dendritic cells as a new player in arteries and heart valves

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(PhysOrg.com) -- In 1973, Ralph M. Steinman launched a new scientific discipline when he published his discovery of the dendritic cell, an odd-shaped player in the immune system. Since then, dendritic cells have proved to be critical sentinels on the lookout for foreign invaders, involved in early immune responses such as graft rejection, resistance to tumors and autoimmune diseases. Now it appears they need to be considered in research on arterial and heart function, too, according to new experiments to be published February 16 in *The Journal of Experimental Medicine*.

Previous research had turned up indirect evidence of dendritic cells in the large arteries of both mice and people. But Jaehoon Choi, a postdoctoral associate in Steinman's Laboratory of Cellular Physiology and Immunology at The Rockefeller University, now has proof positive, at least in mice. More importantly, he and colleagues showed that the key immune cells sit just beneath the lining of the aorta and can project their dendrites into the bloodstream to capture foreign materials. "This has been seen in other linings like the airway and the intestine, but never in the major arteries," Steinman says.

Choi used genetically modified mice developed by Rockefeller Professor Michel C. Nussenzweig's lab that allowed him to tag a known marker for dendritic cells, a molecule called CD11c, with a fluorescent protein. High levels of CD11c are found in dendritic cells, and the fluorescing protein proved effective for identifying them in the heart. Choi's experiments showed not only that the tagged dendritic cells had

the requisite CD11c, but also turned up evidence of another immune system molecule involved in delivering foreign substances to the T cells that can kill them. Moreover, they isolated dendritic cells from the aorta and found that they were just as effective at handing over foreign substances and stimulating the immune system's killer cells as those in immune organs such as the spleen.

Still, the question of whether the dendritic cells could do their normal job in the intact heart remained. To test this, Choi injected mice with a model foreign protein, waited 20 hours, and then isolated the dendritic cells. He found that the isolated cells spurred the growth of the appropriate T cells, indicating that they had captured the invaders like they were supposed to and delivered them over for destruction. "We were the first to show the function of the dendritic cell in the aorta and cardiac valves," Choi says.

Now he is trying to figure out the role of dendritic cells in a mouse model of arteriosclerosis, a hardening of the arteries by plaques filled with lipids such as cholesterol. The recent research found ample evidence of dendritic cells in the aortic root, arch and descending aorta, the same areas that are prone to the disease.

"What does this really mean? Do they handle lipids or stimulate inflammatory response?" Steinman asks. "We don't know, but that's what we'd like to find out next."

More information: *The Journal of Experimental Medicine* online: February 16, 2009

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