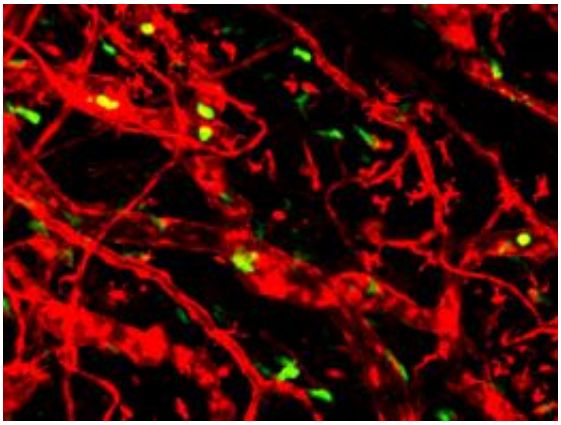
MedicalXpress

Preschool within lymphatic vessels

August 9 2012, By Fabio Bergamin



Microscopic photograph of dendritic cells (green) migrating actively in lymphatic vessels (red). Photo: Maximilian Nitschké / ETH Zürich

Not only infants crawl. ETH researchers have shown that so-called dendritic cells, important cells of the immune system, use a similar mode of movement more often than previously assumed. The scientists used intravital microscopy to image dendritic cells crawling within lymphatic vessels of living animals.

Just imagine a toddler crawling on the floor: it reaches forward with its hands and pulls the body and legs along before reaching out again in front. Dendritic cells, important cells of the immune system, move in a very similar pattern within lymphatic vessels. This was shown by researchers of the group of Cornelia Halin, Assistant Professor at the Institute of Pharmaceutical Sciences.

Dendritic cells, a specialized type of white blood cells, reside in most tissues of the body where they scan for foreign particles like germs or toxins. If they encounter such particles, known as antigens, dendritic cells take them up and then migrate from the tissue into small lymphatic capillaries. These capillaries merge into bigger lymphatic collecting vessels, which eventually lead to a draining lymph node. Here, dendritic cells can interact with other cells of the immune system – in particular with T-cells – and an immune response against the germ or toxin is initiated. Thus, dendritic cells play a central role in defending the body against foreign pathogens.

Active and passive movement

The mode of dendritic cell movement from a peripheral tissue to a draining lymph node has not been conclusively studied so far. It was already known that dendritic cells have to migrate actively through the tissue to reach the small lymphatic capillaries. In addition, it was observed that immune cells move passively within large lymphatic collecting vessels from where they are then flushed with the lymph flow into the draining lymph node. By contrast, it was unclear so far, how dendritic cells behave upon entry from the tissue into the small lymphatic capillaries. In analogy to their movement within collecting vessels, it was commonly assumed that dendritic cells are also passively transported by the lymph flow within lymphatic capillaries.

New scientific discoveries have now shown that this assumption was false. Researchers from the team of Cornelia Halin have confirmed an observation recently reported by another group: Similarly to their mode of migration within the tissue, dendritic cells continue to actively migrate upon entry into lymphatic capillaries: the cells slowly crawl along the vessel walls, like small children on the floor. In addition, the ETH scientists were able to gain initial insights into the molecular mechanism of this newly discovered mode of migration.

Cell protrusions to pull forward

Using transgenic mice with fluorescent blood and lymphatic vessels, the researchers were able to observe the movement of dendritic cells within the skin of anesthetized mice with intravital microscopy. “The cells form protrusions within lymphatic capillaries and pull themselves in the desired direction”, says Maximilian Nitschké, postdoctoral fellow in the group of Cornelia Halin and first author of the study. The ETH scientists have begun to identify which molecules play a role in the active migration of dendritic cells within lymphatic capillaries. In particular, an enzyme called ROCK, appears to play a central role in this process, as shown by in vivo experiments in which ROCK activity was pharmacologically blocked. The researchers assumed that dendritic cell use their protrusions to hold onto molecules expressed in the vessel wall. The enzyme ROCK is subsequently needed to break these bindings at the cell’s rear to allow the cell to move forward.

Better understanding of the immune system

Interestingly, the researchers observed, that dendritic cells appeared to “patrol” through the lymphatic capillaries: the cells did not only migrate in the direction of the presumed lymph flow but occasionally also crawled for some time in the opposite direction. In addition, the cellular crawling velocity within lymphatic capillaries appeared to be considerably slower than the speed of the lymph flow.

The reason why dendritic cells move in this seemingly inefficient pattern is still unclear. “It could be that, during this mode of slow migration, dendritic cells interact with other, yet to be identified cells and exchange important signals,“ says Maximilian Nitschké. However, he believes that the most likely reason for the active mode of dendritic cell migration might be the following one: “Although the lymph flow within small

lymphatic capillaries appears to be faster than the speed of the migrating cells, it might still not be sufficiently strong to allow for passive transport of the dendritic cells by flow." Thus, active crawling might be the only option for the cells in order to move forward within the lymphatic capillaries.

More research will be needed to complete our understanding of how dendritic cells migrate to lymph nodes and how this process affects the induction of the immune response. Basic insights gained from such studies might help to develop more potent vaccines in the future.

More information: M Nitschké et al.: Differential requirement for ROCK in dendritic cell migration within lymphatic capillaries in steady-state and inflammation. *Blood*, 2012, Online-Vorabveröffentlichung, doi: 10.1182/blood-2012-03-417923

Provided by ETH Zurich