

Mast cells get all touchy-feely

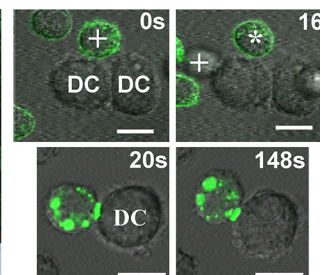
"Allergy" cells embrace dendritic cells to transfer antigens.

Dendritic cells are always on alert for pathogens. Carroll-Portillo et al. reveal that mast cells make contact with dendritic cells and pass on antigens that can stimulate an immune reaction (1).

Although mast cells are notorious for triggering allergic reactions and asthma, they have a positive role in our immune defenses. Along with receptors that recognize IgE antibodies linked to allergens, the cells carry Toll-like receptors and other pathogen detectors. One way that mast cells provide protection is to attack microbial invaders, but they also steer the responses of other immune cells, such as dendritic cells. The two types of cells hang out in the same locations in the body, and researchers have found evidence of indirect interactions between them (2, 3). Molecules released by mast cells spur dendritic cells to mature, migrate to lymph nodes, and instigate a Th2 response. Although some scientists have postulated that the two types of cells contact each other, nobody had been able to demonstrate a physical connection (4).

To look for signs of contact, Carroll-Portillo et al. put human tissue samples from the colon, small intestine, skin, and lungs under the microscope. Regardless of the tissue type, mast cells and dendritic cells were often in close proximity. In some of the skin samples, for example, almost 80% of mast cells were so close to dendritic cells that they appeared to make contact. However, the researchers couldn't prove that the cells were actually touching, so they turned to in vitro studies.

When the researchers allowed mast cells and dendritic cells to interact on a coverslip, the cells adhered to each other. If the mast cells hadn't been activated by exposure to an antigen, they stuck to dendritic cells for an average of 11 seconds. But activated mast cells clung to their dendritic partners for an average



AUTHOR PHOTOS COURTESY OF DIANE LIDKE (LEFT) AND SAM PORTILLO (CENTER)

FOCAL POINT

(Left to right) Diane Lidke, Alessandra Cambi, Amanda Carroll-Portillo, and colleagues showed that mast cells connect to dendritic cells before delivering antigens that can induce a response from T cells. When inactivated mast cells (the smaller cells in the top row) make contact with a dendritic cell, their interaction lasts only a few seconds. In contrast, an activated mast cell (the green cell in the bottom row) can remain attached to a dendritic cell for several minutes.

of 243 seconds. Using an atomic force microscope, Carroll-Portillo et al. found that it took almost twice as much force to pull the cells apart if the mast cells were activated.

Liaisons between activated mast cells and dendritic cells change both partners. For example, the researchers found that the cells released different amounts of certain cytokines after contact. The two cell types formed a specialized contact called an immunological synapse. Mast cell endosomes gathered at this contact site. These endosomes housed antigens, IgE antibodies, and IgE receptors internalized from the mast cell's plasma membrane.

Carroll-Portillo et al. determined that mast cells use exosomes to pass these proteins to dendritic cells. They also found that blocking integrins, which link cells together at immunological synapses, slashed the amount of material traveling between the cells, confirming the importance of contact for the transfer.

But do these intimate moments between mast cells and dendritic cells contribute to the body's defenses? To stimulate an immune response, dendritic cells process antigens that they've collected

and then present them to T cells. The team determined that dendritic cells do the same with the antigens they receive from mast cells. After activating mast cells by exposing them to OVA peptide, the researchers added the cells to a mixture of dendritic cells and T cells that respond to OVA. Levels of CD25 shot up on the T cells, an indication that they were stimulated. In contrast, when the researchers mixed activated mast cells with T cells but left out the dendritic cells, the T cells weren't switched on.

Dendritic cells are important antigen-presenting cells, but the study indicates that mast cells present antigens to dendritic cells. "The result implies an extra level of immune surveillance," says senior author Diane Lidke. What researchers now need to show, she says, is whether these interactions between mast cells and dendritic cells are important for detecting pathogens in vivo.

1. Carroll-Portillo, A., et al. 2015. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201412074>
2. Caron, G. 2001. *J. Immunol.* 167:3682–3686.
3. Dawicki, W., et al. 2010. *J. Immunol.* 184:2116–2123.
4. Dudeck, A., et al. 2011. *Eur. J. Immunol.* 41:1883–1893.

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