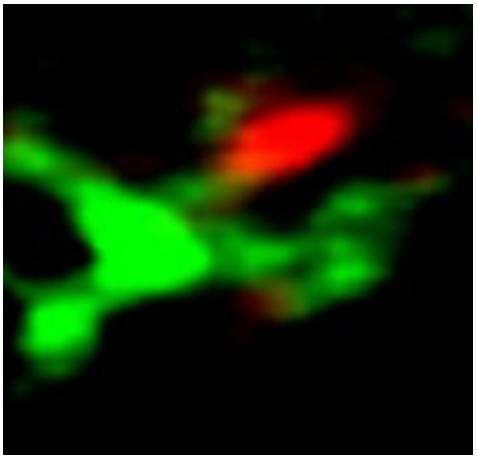
Immune cells can simultaneously stimulate and inhibit killer cell activity

October 22 2007



Receptive party. Both activating (red) and inhibiting (green) receptors are present when dendritic cells synapse with natural killer cells. This dual setup teaches the natural killer cell to become aggressive while preventing it from attacking its dendritic cell instructor. Credit: Rockefeller University

Dendritic cells, which are responsible for teaching other immune cells to attack infected or mutated cells, face a dangerous predicament. To demonstrate that an enemy has invaded, they must change to look a little bit like the invader. And once they look like an enemy, they risk being treated like one by their newly trained pupils. New research from Rockefeller University shows how the body's immune system gets around this paradox by using simultaneous signals to both activate and inhibit a killer cell's immune response.

Natural killer cells, which serve as a critical line of defense against invaders, can only attack efficiently after dendritic cells have programmed them to turn aggressive. The immunity-directing dendritic cells bind to the natural killer cells in order to activate the “seek and destroy” receptors on their surface. The two types of cells then form a synapse through which they communicate.

Typically, these synapses consist of either activating or inhibitory receptors, allowing for the natural killer cells to be turned on or off. But when assistant professor Christian Mьnz, head of the Laboratory of Viral Immunobiology, and postdoc Fabienne Brilot looked closely at the structure of the synapse between natural killer and dendritic cells, they found that both receptor types were present but that they were segregated, each located in different areas of the synapse.

Their research, published online this week in *The Journal of Clinical Investigation*, describes an interaction that had never been seen before. “It’s a novel regulatory synapse,” Mьnz says. “It seems like inhibitory and activating domains are localized to the center of synapse and signal in parallel, mediating both activating and inhibitory signals.” The dendritic cells give different signals to the natural killer cells, inhibiting their cell-killing or “cytolytic” function while at the same time activating them to divide, emit signaling molecules called cytokines and transform into better killers.

How dendritic cells are able to spur other immune cells into action without getting destroyed in the process is a problem that relates not just to natural killer cells but also to T cells, which must also be activated to kill. The researchers are still just figuring out the basic biology of these synapses and plan to look next at naпve T cell activation. But ultimately, Mьnz says, what they’re finding could have implications for immune reactions that occur after organ transplantation. If they could find a way to prevent natural killer cells from recognizing dendritic cells, it might

be possible to prevent the dendritic cells from activating the host's immune system to attack the transplanted organ.

Citation: *The Journal of Clinical Investigation* 117(11): November, 2007

Source: Rockefeller University