MedicalXpress

Integrins losing their grip drive activate T cell immune responses

October 29 2014

When integrins let go of their ligands and the actin cytoskeleton inside the dendritic cell, the activity of another cell surface receptor, the GM-CSF receptor, rises. This increased signaling induces the dendritic cells to head to lymph nodes to activate T cells.

Integrins are adhesion molecules expressed on the surface of cells. They play a crucial role in "integrating" the cell exterior and the interior cytoskeleton in cells. The beta2-integrin family members are highly expressed in dendritic cells that are very important in immune responses. Dendritic cells pick up antigens in inflamed tissues and move to lymph nodes where they present the antigen to T cells and activate them to help fight infection.

Dr Susanna Fagerholm's groups at the Institute of Biotechnology in Helsinki, Finland, and at the University of Dundee, UK, found out that one of the first steps in this activation chain is taken when the integrins lose their grip of their ligands in tissues and the actin cytoskeleton inside the dendritic cells.

"This leads to increased signaling through another cell surface receptor, the GM-CSF receptor, in dendritic cells. The increased signaling results in reprogramming of the dendritic cells to a mature, migratory phenotype and induces them to migrate to lymph nodes to activate T cells," says Susanna Fagerholm.

Susanna Fagerholm's research teams in Helsinki and Dundee, and

collaborators in Dundee, Glasgow and Manchester, used a novel knock-in mouse model of the beta2-integrin and in vivo immunological assays, combined with next generation RNA sequencing technology to investigate the roles of beta2-integrins in dendritic cells.

"Better understanding of this chain of events may help in the design of targeted therapies to block unwanted immune responses, such as those associated with autoimmunity. This type of research may also help to design more effective immune-based cancer therapies."

More information: Vicky Louise Morrison, Martyn John James, Katarzyna Grzes, Peter Cook, David Gavin Glass, 5, Terhi Savinko, Hwee San Lek, Christian Gawden-Bone, Colin Watts, Owain Richard Millington, Andrew Scott MacDonald, Susanna Carola Fagerholm. "Loss of beta2-integrin-mediated cytoskeletal linkage reprograms dendritic cells to a mature migratory phenotype." *Nature Communications*. DOI: 10.1038/ncomm6359

Provided by University of Helsinki