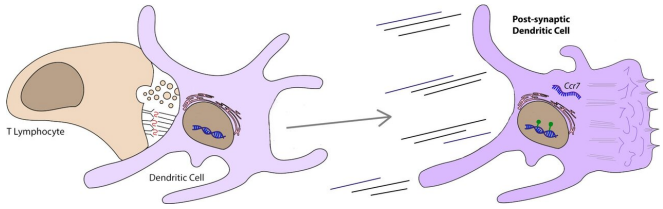
Scientists identify a mechanism through which dendritic cells improve their antiviral and immunotherapy strategies

3 February 2021



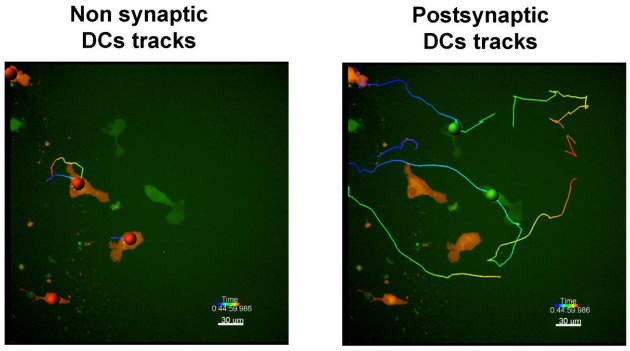
Left A dendritic cell presents foreign material to a T lymphocyte, preparing it to mount an effective immune response to it. Right Through genetic and epigenetic changes, this process also prepares the dendritic cell to meet future threats to the organism by increasing its tropism toward immune system control centers. Credit: CNIC

Researchers at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) led by Professor Francisco Sánchez-Madrid have found that dendritic cells, which initiate specific immune responses, can reprogram their genes to improve their immune response. The results of the study, funded by Fundación 'la Caixa' and published today in *Science Advances*, could have important applications in the development of new vaccination and immunotherapy strategies.

Dendritic cells are professional antigen-presenting cells that initiate adaptive or specific immune responses. As described by the research team, "dendritic cells capture possible pathogenic agents in different tissues and entry sites, process their components, and transport them to lymph nodes. Here, they establish communication with T lymphocytes through the formation of a specialized structure called the immune synapse. The immune synapse allows the dendritic cell to present processed components of the infectious agent to a T cell, so that they can be recognized and initiate a specific T cell immune response."

Until now, activation of T lymphocytes was thought to be dendritic cells' main function. However, Prof. Francisco Sánchez-Madrid's group, working together with the group led by Dr. Almudena R Ramiro, have discovered that the dendritic cell also receives information from the T cell via the immune synapse. "The T cell sends instructions that induce a change in the dendritic cell's gene-expression program, promoting the expression of genes related to motility, antiviral responses, and secretion and thereby increasing the dendritic cell's capacity to generate protective anti-pathogen immune responses," explained Sánchez-Madrid.

"This study describes how gene-expression changes are accompanied by changes in epigenetic marks on DNA. These epigenetic marks in turn produce transient changes in specific genes that promote or hinder their expression," explained first authors Irene Fernández Delgado and Diego Calzada Fraile.



A dendritic cells increases its motility after synaptic contact with a T lymphocyte. Post-synaptic trajectories are shown in green and trajectories absent synaptic interaction are shown in red. Credit: CNIC

One of the genes that increases its expression and accessibility is Ccr7, which encodes a cell migration receptor on the surface of dendritic cells that targets them to lymph nodes.

The research team found that, after participating in an immune synapse, dendritic cells migrate more efficiently to lymph nodes, where most processes involved in the activation of specific or adaptive immune responses take place.

The new study, carried out in close partnership with the CNIC Bioinformatics Unit (directed by Manuel Gómez and Fátima Sánchez-Cabo) and Genomic Unit (Ana Dopazo), describes a new mechanism that explains how dendritic cells improve their antiviral and immune-activation abilities.

The researchers conclude that their study shows that dendritic cells, responsible for initiating specific immune responses, reprogram their genes through altered epigenetic DNA marks after interacting with a cognate T cell. "These changes improve their motility, so that they arrive sooner at immune response activation sites, representing a new mechanism for potentiating the immune response."

The results also have potential applications in the development of new vaccination and immune therapy strategies. For example, the described mechanism could be used to generate super-migratory post-synaptic dendritic cells able to induce stronger and more effective immune responses.

More information: "Immune synapse instructs epigenomic and transcriptomic functional reprogramming in dendritic cells" *Science Advances* (2021). advances.sciencemag.org/lookup … .1126/sciadv.abb9965

Provided by Centro Nacional de Investigaciones Cardiovasculares Carlos III (F.S.P.)