Science Advances: Spanish scientists identify a mechanism through which dendritic cells improve their antiviral and immune-activation abilities

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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.

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 study, funded by Fundación 'la Caixa', reveals that the immune synapse initiates a genetic program that generates new protective mechanisms in dendritic cells

The new study, carried out in close partnership with the **CNIC Bioinformatics Unit** (directed by 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.

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