Scientists identify an essential role of the immune receptor CD69 in psoriasis

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Scientists at the Centro de Investigaciones Cardiovasculares Carlos III (CNIC) have defined the key role of an immune-system receptor in the development of psoriasis, suggesting that it could serve as a therapeutic target for the control of this disease. The study was carried out by Dr. Danay Cibrián and directed by Dr. Francisco Sánchez-Madrid, who heads the Intercellular Communication group at the CNIC. The study establishes the role of the leukocyte activation receptor CD69 in the control of aminoacid uptake, activation of the aryl hydrocarbon receptor (AhR), and the expression of inflammatory interleukins such as IL-22 in gamma delta and Th17 T cells, indicating that CD69 contributes to the development of psoriasis. The study, published in *Nature Immunology*, also indicates that CD69 might also participate in other inflammatory diseases such as aterosclerosis.

Psoriasis is a chronic inflammatory disease of the skin that affects approximately 2-3% of the world population and has a negative impact on patients' physical and mental health. The prevalence of psoriasis in Spain has increased by 1% in the last 15 years, and the disease now affects an estimated 1 million people across the country.

The skin is the first line of defense against many kinds of infection, trauma, and radiation. Dr. Francisco Sánchez-Madrid explains that "the skin contains many populations of specialized immune cells that act together to guarantee defense and protection." The leukocyte activation receptor CD69 is present in inflammatory cells in the skin. Dr. Francisco Sánchez-Madrid continues "These cells consume free essential

aminoacids like tryptophan by using specialized transport systems present in the cell membrane, such as LAT1 (SLc7a5). Consumption of aminoacids by inflammatory cells in the skin increases sharply during the inflammatory reaction because it is important for their proliferation and activation and for the secretion of inflammatory molecules that amplify tissue damage, like interleukins 22 and 17 (IL-22 and IL-17)."

Tryptophan

Using mice whose immune cells lack CD69, the research team showed that the expression of this molecule is important for the development of psoriasis. "We found that CD69 associates in the cell membrane with LAT1, regulating its level of expression and the uptake of aminoacids such as tryptophan," explains Dr. Danay Cibrián, adding that "tryptophan metabolism generates intermediate metabolites that activate the AhR, which in turn regulates the expression of inflammatory interleukins such as IL-22. Increases in the circulating levels of tryptophan favor the development of psoriasis by leading to increased levels of IL-22 in the skin." The importance of tryptophan metabolism in the secretion of the interleukins that mediate the development of psoriasis has been demonstrated in patient studies.

The researchers conclude that their study demonstrates the importance of CD69 in the development of psoriasis and opens the way to its possible use as a future therapeutic target for the treatment of this disease.

The research was led by Dr. Francisco Sánchez-Madrid, Profesor at the Universidad Autónoma de Madrid and Head of the Immunology Service at the la Princesa University Hospital, and was conducted through collaborations with CNIC researcher Dr. Pilar Martín, the CNIC Proteomics Unit, directed by Prof. Jesús Vázquez, the Dermatology Service at La Princesa university hospital, directed by Dr. Esteban

Daudén, and Professor Manuel Fresno of the Centro de Biología Molecular Severo Ochoa in Madrid.

More information: Danay Cibrian et al, CD69 controls the uptake of L-tryptophan through LAT1-CD98 and AhR-dependent secretion of IL-22 in psoriasis, *Nature Immunology* (2016). DOI: 10.1038/ni.3504

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