UGR study opens door to treatment for Papillon-Lefèvre syndrome

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Research news

Papillon-Lefèvre syndrome (PLS) is a rare disease with a very low prevalence rate that affects one in every million people. It is characterised by severe periodontitis and scaling of the skin, particularly on the palms of the hands and the soles of the feet, as well as increased susceptibility to infections. This inherited disease results from a mutation in an enzyme called cathepsin C (CatC), but the molecular mechanism behind this mutation was unknown until now.

A research study led by the University of Granada (UGR), in which scientists from the University of Seville, Pablo de Olavide University and Marche Polytechnic University (Ancona, Italy) have also participated, has revealed that the molecular mechanism by means of which a cleaning process occurs inside the cell, called autophagy, is blocked in the cells of patients suffering from Papillon-Lefèvre syndrome. At the same time, other cathepsin family proteins are over-expressed in order to compensate for this deficiency. These proteins are released from lysosomes, the organelles containing them, resulting in the activation of inflammatory pathways and oxidative stress. This process is called “autophagic dysfunction” and “ lysosomal permeabilization”.

Currently, there is no effective treatment for this disease, so researchers have created a recombinant cathepsin C in insect cells (specifically in a fall armyworm or Spodoptera frugiperda), the extracts of which have showed high enzyme activity.

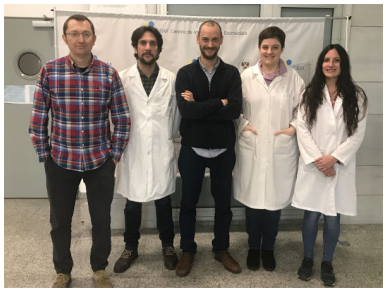
“Following the treatment of the cells in [PLS] patients, we have identified the alterations observed, activating autophagy, cell growth, and reducing inflammation and lysosomal permeabilization. In other words, the altered enzymatic processes are regulated”, explains Mario D. Cordero Morales, the main author of the paper and a researcher at the Department of Physiology of the UGR.

The research study led by the UGR has uncovered the molecular mechanism underlying the Papillon-Lefèvre syndrome, opening the door to a new treatment option called “enzyme replacement therapy”.

The research findings were recently published in the prestigious Journal of Allergy and Clinical Immunology.

Bibliographic reference:

Bullón P, Castejón-Vega B, Román-Malo L, Jimenez-Guerrero MP, Cotán D, Forbes-Hernandez TY, Varela-López A, Pérez-Pulido A, Giampieri F, Quiles JL, Battino M, Sánchez-Alcázar JA, Cordero MD. Autophagic dysfunction in Papillon Lefèvre síndrome is restored by recombinant Cathepsin C treatment. Journal of Allergy and Clinical Immunology. 2018 Feb 1. pii: S0091-6749(18)30144-1



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