New molecules derived from cannabidiol are designed with more potent antioxidants

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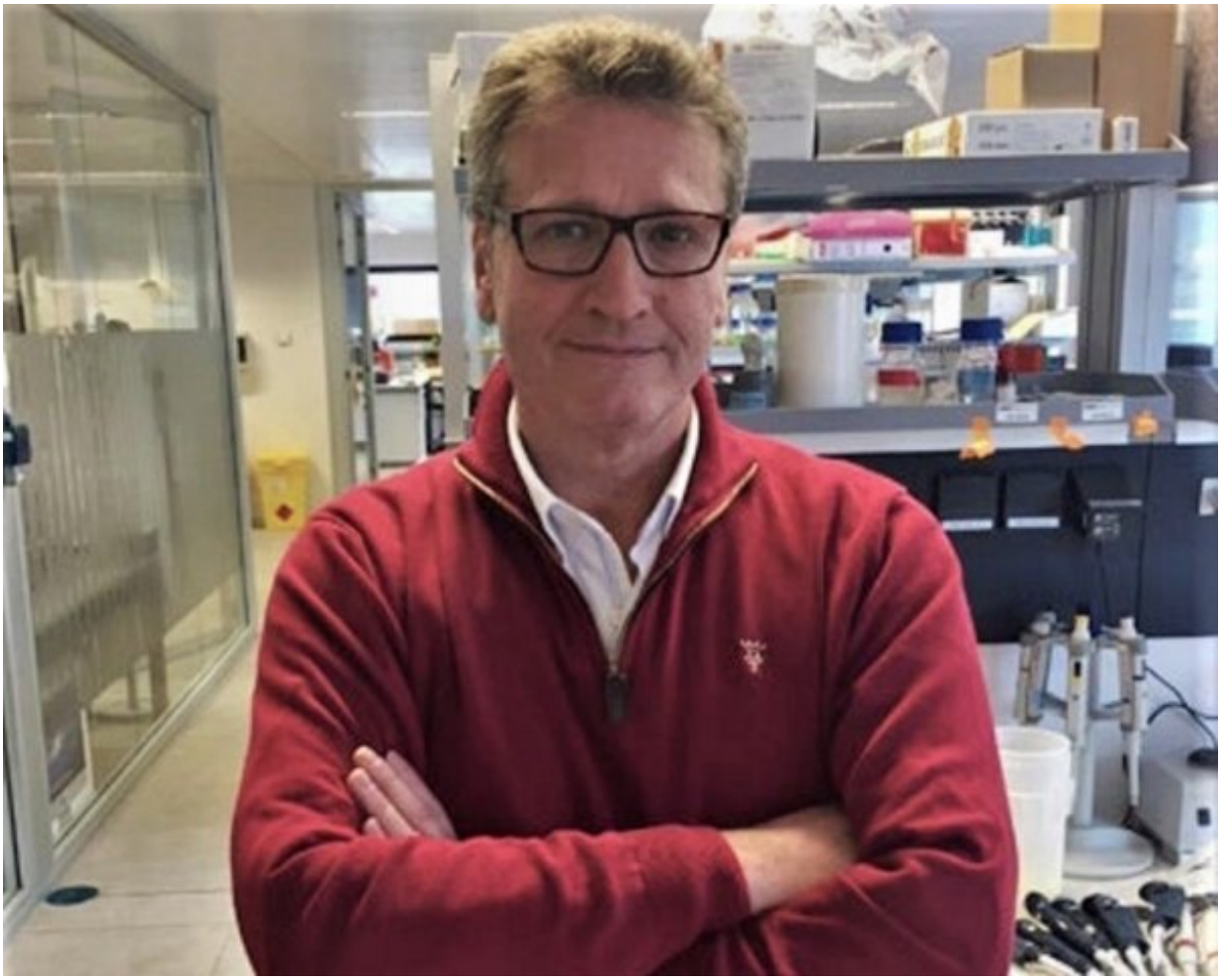

Immunology Professor Eduardo Muñoz. Credit: University of Córdoba

Nowadays, cannabidiol is a star component, not only in the world of cosmetics, but also in pharmaceutics and nutrition due to its antioxidant properties and its therapeutical potential. It is a natural molecule that comes from medicinal cannabis and that, despite being derived from it, is not a psychoactive compound, meaning that it has no effect upon the nervous system.

In spite of its successful sales, we still do not know how cannabidiol acts upon different skin cells in order to unleash its antioxidants. A collaborative partnership with the University of Cordoba and the University of Dundee demonstrated for the first time that cannabidiol induces the expression of heme oxygenase 1, an enzyme with antioxidant and anti-inflammatory properties, in the main cells on the top layer of the skin, called keratinocytes. This is done by reducing or silencing the protein that suppresses it, known as BACH1.

"Once we described the whole working mechanism, we have continued our partnership, making modifications to the cannabidiol molecule in order to try to improve its properties that fight against skin diseases," explains Immunology Professor Eduardo Muñoz, who is in charge of the BIO-304 "Immunopharmacology and Molecular Virology" research group at the University of Cordoba.

Hence, the international research team designed new molecules that, besides inhibiting the BACH1 protein, activate the NRF2 protein. This protein controls the way that certain genes are expressed. These specific genes help to protect cells against oxidative stress such as HMOX1, the one that encodes heme oxygenase 1, but also many others that work independently from BACH1.

So, the newly designed molecules that are derived from cannabidiol have double antioxidant activity: on the one hand, they supress BACH1 and with it, they induce the expression of heme oxygenase 1 and on the

other, they activate NRF2, which also induces the expression of heme oxygenase 1, in addition to other antioxidant genes. "When combining the inhibition of BACH1 with the activation of NRF2, the result is a very potent antioxidant and anti-inflammatory response and better therapeutic effects," says Eduardo Muñoz.

This action mechanism is very interesting for skin disease treatments such as atopic dermatitis and epidermolysis bullosa, a very rare disease on which there is little research. What is more, this molecule has great potential to be used in cosmetics due to its antioxidant properties.

In addition to the University of Dundee in Scotland and the University of Cordoba, the companies Emerald Health Biotechnology, in the field of developing new medicine, and Innohealth Madrid (acquired by Evonik Industries AG), which specializes in dermo-cosmetics made from natural ingredients, have also collaborated on this research. Both companies were set up stemming from the BIO-304 research group at the University of Cordoba.

Based on these studies, the research team will continue to modify the molecules in order to improve their properties and, further down the road, perform studies on animal models in order to understand its therapeutical potential for skin diseases and other inflammatory diseases.

More information: Laura Casares et al, Isomeric O-methyl cannabidiolquinones with dual BACH1/NRF2 activity, *Redox Biology* (2020). DOI: 10.1016/j.redox.2020.101689

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