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Researchers prove antitumoral potential of a compound derived from olives

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Researchers from the universities of Granada, Barcelona and Jaen prove that maslinic acid, a natural triterpene found in high concentrations in the waxy skin of olives is effective in Caco-2 p53-deficient colon adenocarcinoma cells in just a few hours.

Researchers from the University of Granada (UGR), in collaboration with the universities of Barcelona and Jaen, have established the antitumoral nature of maslinic acid (a compound derived from olives) in Caco-2 p53-deficient colon adenocarcinoma cells in the short term.

Maslinic acid (MA) is a natural triterpene found in high concentrations in the waxy skin of olives, obtained through a method patented by professors Andrés García-Granadados López de Hierro and Andrés Parra Sánchez from the UGR department of Organic Chemistry, and currently used by the company Biomaslinic S.L.

The results of this research, recently published in the renowned *PloS ONE* magazine, show without a doubt how maslinic acid is capable of inducing the extrinsic cellular death pathway in Caco-2 cells that don't express protein p53 (known for its pro-apoptotic capacity).

In previous work, professor Lupiáñez Cara's research team reported that maslinic acid induces apoptotic cell death via the mitochondrial apoptotic pathway in cancer cell lines.

In the paper published in *PloS ONE*, the researchers have shown that MA

induces apoptosis in Caco-2 colon cancer cells via the extrinsic apoptotic pathway in a dose-dependent manner in the short term (4 hours).

A quick response

Maslinic acid triggers a series of effects associated with apoptosis and increased the levels of the pro-apoptotic protein t-Bid within a few hours of its addition to the culture medium. This triterpene has no effect on the expression of the Bax protein or the release of cytochrome-c (proteins involved in the mitochondrial apoptotic pathway), or on the mitochondrial membrane potential.

This suggests that MA triggered the extrinsic apoptotic pathway in this cell type, as opposed to the intrinsic pathway found in the HT29 colon-cancer cell line (cells which do have the tumor suppressor gene p53 and, as a result, express the protein p53.

The results published in *PloS ONE* suggest that the apoptotic mechanism induced in Caco-2 may be different from that found in HT29 colon-cancer cells, and that in Caco-2 cells maslinic acid seems to work independently of the presence of p53. Natural antitumoral agents capable of activating both the extrinsic and intrinsic apoptotic pathways could be of great use in treating colon-cancer of whatever origin.

The studies currently being carried out by the team are focused on finding compounds chemically derived from maslinic and oleanolic acids that are related with anti-proliferative, anti-tumoral and anti-angiogenic tasks as well as pharmacokinetic tasks at different levels (sub-molecular, molecular and cellular), in order to establish both their mechanism of action and the link between the various by-products and their effect on the cells.

More information: Fernando J. Reyes-Zurita et al. Maslinic Acid, a

Natural Triterpene, Induces a Death Receptor-Mediated Apoptotic Mechanism in Caco-2 p53-Deficient Colon Adenocarcinoma Cells, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0146178