# **Extracellular vesicles derived from Citrus limon, Punica granatum, and** Actinidia deliciosa **modulate inflammation in Caco-2 cells**

Simona Di Giulio, Stefania Mariano, Marco Muci, Elisabetta Carata, Elisa Panzarini

Department of Biological and Environmental Sciences and Technologies (Di.S.Te.B.A.), University of Salento, 73100 Lecce, Italy

In recent years there has been an explosion of interest in plant extracellular vesicles (P-EVs) both to understand the role that they naturally play in plants and also for their therapeutic potential against several diseases. Like mammal EVs, P-EVs contain plant-specific small molecules with functional roles and therapeutic potential. While therapeutic interest in P-EVs began with the identification of antioxidant properties, many studies are suggesting a wide therapeutic potential, including the possibility of exploiting them as drug delivery vectors due to their relatively low production cost, good tolerability, and the absence of zoonotic or human viruses which may be present in mammalian EVs. Among the beneficial effects, the impact of P-EVs on gut inflammation is not yet well understood.

In this study, we evaluated the capability of *Citrus limon*, *Punica granatum*, and *Actinidia deliciosa***-**derived EVs in modulating inflammation and oxidation in Caco-2 cells, a human colon epithelial cancer cell line used as a model of human intestinal absorption of drugs and other compounds. Cells were treated with LPS and TNF-α, or $H_2O_2$ to induce inflammation or oxidation respectively. The anti-inflammatory effect was evaluated by analyzing cytokines gene expression with RT-qPCR. P-EVs exert both an antioxidant and anti-inflammatory activity upon internalization in Caco-2 cells visualized by confocal microscopy, suggesting the capability of P-EVs to modulate inflammation and their potential beneficial effect on intestinal mucosa.