METHYLOMIC SIGNATURE AND MOLECULAR MODELLING TO BETTER UNDERSTAND AUTOPHAGY INDUCED BY PHYTOCHEMICAL IN CACO-2 CELLS

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The binomial "autophagy-cancer" is intricate and methylomic studies can help to understand it by changing point of view from a gene level to an -omic one. Recently, autophagy-modulating properties of several phytochemicals have attracted attention in anticancer research.

We evaluated whether Indicaxanthin (IND), the peculiar known beneficial phytochemical of prickly pear, seasonally available in the southern Italy, could induce autophagy in Caco2 cells, and whether it results from an epigenomic modification and/or a direct molecular interaction.

IND increased autophagy in Caco-2 cells; the methylomic signature, obtained by Reduced Representation Bisulfite Sequencing (15 million of clusters) reported that 14 main genes of autophagy, showed a different methylation consistent with the induction of this phenomenon. Among these: *MTOR*, *ATG13*, *BECN1*, *TFEB*, *ATG3*, *WIPI2*, *TECPR1*, *SNAP29*, *VPS11*, *VPS16*. By traditional approaches we confirmed the demethylation of *BECN1* gene and the increase of Beclin1 levels. By *in-silico* molecular modelling, we displayed a possible interference of IND, by competitive mechanisms, in the Beclin1-Bcl2 interaction.

Methylomic signature and molecular modelling has been helpful to understand autophagy IND-induced in intestinal epithelial tumour cells. Our results suggest that the pro-autophagic action promoted by this phytochemical involves both epigenomic modulation and post-translation mechanisms by direct interaction with key targets of autophagy pathway.

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