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Benefits of a grape-rich diet on human health: a nutrigenomics study underlining the potential role of non-coding RNAs

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Grape (*Vitis vinifera L.*) is one of the most typical fruit of the Mediterranean diet, characterised by high polyphenols content with marked antioxidant and anti-inflammatory activities (Goszcz *et al.*, 2017). By using transcriptional profiling techniques, it has become increasingly clear that polyphenols can influence the expression of genes. Many of these genes are key elements of cell signalling cascades (Spencer 2009; Fraga and Oteiza 2011) and regulatory non-coding RNAs (ncRNAs) (Budisan *et al.*, 2017).

A previous study showed that table grape extracts exert a marked antithrombotic activity in vitro (Ammollo *et al.*, 2017). To shed light on the molecular basis of grape intake effects on human health and investigate the potential role of ncRNAs, we carried out a nutrigenomics study (Milella *et al.*, 2020a and 2020b). To this aim, 20 healthy subjects were enrolled to follow a grape-rich diet for 21 days. The gene expression profiles of peripheral blood mononuclear cells (PBMCs) extracted from six of these subjects, after 21 days of fresh table grape-rich diet and after an additional 28-day washout, were analysed. The results showed 930 genes differentially expressed. Among these genes, more than 200 are long ncRNAs (lncRNAs), almost all downregulated after the washout period when polyphenols' direct effect is supposed to be completely exhausted.

The functional analysis of differentially expressed genes revealed significant changes in processes critical for organismal and cell wellbeing such as inflammation and immunity, thrombosis, DNA and protein repair, autophagy and mitochondrial biogenesis. From our analysis of lncRNAs down-regulated in our study, we observed that many of them are over-expressed in many types of tumours, chronic diseases due to the persistency of inflammation and metabolic syndromes such as obesity. Altogether, these findings provide exciting clues for the crucial role of ncRNAs in grape intake's long-term effects on a series of biological processes. These lncRNAs would deserve to be further investigated for potential applications in the care of chronic diseases and cancer and their prevention.

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