Cellular and Structural Modulation of p53 Tumor Suppressor Protein by Resveratrol

Costa, D. C. F.[1], Casanova, F.[1], Fialho, E.[2], Silva, J. L.[1]

[1]IBqM, UFRJ.
[2]INJC, UFRJ.

Resveratrol, a dietary constituent found in grapes, berries and peanuts, is one of the most promising agents for cancer prevention. The anti-tumoral activity of this compound is based on its capacity to inhibit diverse cellular events during all three stages of carcinogenesis (initiation, promotion and progression). The p53 tumor suppressor protein plays an essential role in preventing cancer development, by inducing cell cycle arrest or apoptosis in response to cellular stress. Resveratrol has been shown to induce p53 accumulation in different tumor cell lines. However, the mechanisms by which this compound modulates p53 activity are not completely understood. Firstly, we tested the effects of resveratrol on MCF-7 human breast cancer cells, which expresses constitutively wild type p53. MTT reduction cell viability assay showed that resveratrol promoted a cytotoxic effect on MCF-7 cells in a dose and time dependent manner. Resveratrol in a concentration of 150µM was able to impair 60% and 75% of cell growth after 24 and 48 hours of treatment, respectively. In addition, resveratrol (50-200µM) increased p53 protein levels in MCF-7 cells after 24 hours of treatment, without altering p53 transcript levels. In order to investigate a possible interaction between resveratrol and p53, we performed structural analysis using fluorescence spectroscopy. Resveratrol promoted a decrease in fluorescence intensity of both purified p53 core domain and full length p53. Taken together, our results provide evidence that resveratrol possibly induces the stimulation of p53 protein levels in MCF-7 cells by regulating post-transcriptional cellular processes. Moreover, structural data suggest that resveratrol might directly modulate p53 function by interacting with this protein.

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