MedicalXpress

A sip of resveratrol and a full p53: Ingredients for a successful cell death

November 13 2012

Researchers at the Universidade Federal in Rio de Janeiro in Brazil have found that introduction of a normal copy of the p53 gene in p53-defective cancer cell lines makes these cells sensitive to the anti-tumor proprieties of resveratrol, the naturally occurring dietary compound found in red wine.

Resveratrol is a naturally occurring dietary compound found in grapes, berries, and peanuts. This polyphenol protects plants against pathogens such as bacteria and fungi by inducing cell death in invading organisms. The compound was discovered in red wine in 1939 but by large did not attract the attention of the scientific community. More recently, pre-clinical studies have revealed the many beneficial properties of resveratrol. These include antidiabetic, cardioprotective, and chemopreventive effects. The latter has been associated to resveratrol antioxidant and anti-inflammatory proprieties.

A number of studies show that resveratrol induces cell death in different types of cancers, both in humans and animal models. However, the potential anti-tumor effect of resveratrol is still little understood as the compound seems to induce cell death in a number of cancer cells whereas in others no effect is observed, even when massive doses of resveratrol are used. A phase I study on the pharmacokinetic properties of resveratrol as a potential cancer chemopreventive agent has concluded that consumption of high levels of resveratrol would be insufficient to provide the amounts of resveratrol needed to elicit its chemopreventive proprieties. Nevertheless, a few ongoing clinical trials investigate the

effects of resveratrol on a number of diseases, including colon cancer.

More recently, the anti-tumor functions of resveratrol have been associated to p53, a protein responsible for suppressing tumor development in the body. p53 is one of the main blockers of the cell cycle, leading cells to the death row. A faulty p53 is unable to suppress cell growth, which ultimately results in tumor development. Indeed, studies have shown that p53 is either defective or simply absent in most cancers.

To investigate whether resveratrol anti-tumor effects, as observed in some cancer cell lines, depend on the status of the cell's p53 gene, a group led by Dr Jerson L. Silva at the Universidade Federal do Rio de Janeiro, Brazil, tested the effects of resveratrol in H1299, a human non-small lung carcinoma cell line carrying only a partial fragment of the p53 gene and compared the results with MCF-7, A549, and H460, which are cancer cell lines carrying normal copies of p53. The study shows that although resveratrol affects the viability of all cancer cell lines, MCF-7, A549, and H460 are more sensitive to the effects of resveratrol than H1299. While MCF-7 cell lines die after exposure to resveratrol, H1299 remains resistant. Additional findings indicate that the toxic effect of resveratrol on MCF-7, A549, and H460 cell lines is mediated by p53.

The research group then went one step further and asked what would happen if a normal copy of p53 is added to the previously p53-defective H1299 cancer cell line. The results, published this week in *PLOS ONE*, show that introduction of a normal copy of p53 in H1299 turns the cell line sensitive to the anti-tumor effects of resveratrol, similarly to that observed in other cancer cell lines (MCF-7, A549, and H460). "Our findings may have potential applications in cancer cell lines that are under p53 control," says Dr Danielly Ferraz da Costa, the first author of the study. "Also, the introduction of the p53 gene in p53-defective tumors, followed by resveratrol treatment, may represent a novel and

promising therapeutic approach in our fight against cancer," says the young author.

More information: "Transient transfection of wild-type p53 gene triggers resveratrol-induced apoptosis in cancer cells" www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0048746

Provided by Publicase Comunicação Científica