Effects of tyrosol and hydroxytyrosol in adenocarcinoma lung cancer cells exposed to hydrogen peroxide

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Non small cell lung cancer (NSCLC) represent the most common cause of cancer deaths worldwide (Zalcman et al., 2010). Several factors are involved in the development of this type of cancer. Significant role is played by the cigarette smoke (Halliwell et al., 1989), that recruiting within the air spaces inflammatory cells (MacNee et al., 1989) able to increases the levels of hydrogen peroxide (H2O2) (Thannickal et al., 2000). In vitro studies showed that H2O2 fosters the phosphorilation of MAPKs (ERKs1/2), this biochemical event is able to evocate the secretion by NSCLC of Interleukin (IL)-8 (Pelaia et al., 2004; Gallelli et al., 2014). Epidemiological studies suggested a positive correlation between olive oil consumption and a low incidence of inflammatory diseases, including cancer. In this concern, the scientific opinion is no longer out on the health benefits of olive oil with respect to cancer. Its beneficial effects are related to the high content of its antioxidants, among them tyrosol (Tyr) and hydroxytyrosol (H-Tyr) are the most abundant phenols components.
Here we evaluate the role of Tyr and H-Tyr on cell proliferation and viability as well as on inflammatory pathways and redox status in primary lung cancer cell (GLC) exposed to H2O2.
Adenocarcinoma lung cancer cells obtained from patients undergoing thoracic surgery were exposed to H2O2 (0.5 mM) for 30 minutes, in presence or absence of Tyr (100 mcM) and H-Tyr (140 mcM), initiated 24 h before cell exposure to H2O2. Culture supernatants were collected and assayed for IL-8 and redox status by ELISA using a commercially available kit (Peli-Kine kit; Eurogenetics (Hampton, UK); sensitivity limit, 1 pg/ml). Following this treatment, cells were lysed for western blotting in radioimmunoprecipitation assay (RIPA) buffer as previously reported (Gallelli et al., 2010). All data are expressed as mean ± standard error (SEM). Statistical evaluation was performed by analysis of variance (ANOVA). Differences identified by ANOVA were pinpointed by unpaired Student's t test. The threshold of statistical significance was set at $p < 0.05$. The exposure of cells for 30 minutes to Tyr and H-Tyr induced a significant decrease in cell number ($P<0.01$); in contrast H2O2 significantly increased ($P<0.01$) cell numbers, as detected by cell counts expressed as confluence percentages. The effects of H2O2 were significantly reduced ($P<0.01$) in cell pretreated with Tyr and H-Tyr. Moreover, Tyr and H-Tyr were able to reduce the effects of H2O2 of p-ERK1/2 on matrix metalloproteinases (MMP)-2 MMP-9 and NF-kB expression. Finally, the exposition of GLC to H2O2 (0.5 mM), induced a significant increase in the secretion of IL-8 and redox status, that were significantly ($P<0.01$) reduced by a 24-hour treatment with Tyr and H-Tyr administered 24-hour before the exposition to H2O2. These cancer-controlling properties of olive oil constituents are not a novelty and are generally referred as "antiproliferative" properties of olive oil. Our results settle the ability of Tyr and H-Tyr even in the growth control of lung cancer cells once they have already developed as happen for breast and colon cancer.

References

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