

82P Dose differential modulation of the autophagic behaviour of estrogen expressing breast carcinoma cells

M.A. Fouad¹, M.W. Kamel¹, M. El Sawalhi², S.A. Shouman¹

¹Cancer Biology, National Cancer Institute, Cairo University, Cairo, Egypt, ²Biochemistry, Faculty of Pharmacy, Cairo, Egypt

Background: Breast cancer is a major public health problem among women. The use of phytoestrogens like Resveratrol (RSV) has been emerged as a promising chemopreventive and chemotherapeutic agent against breast cancer. However, its effect is reported to be variable according to the administered dose. So this study investigated the underlying mechanisms to the dual action of RSV on estrogen expressing type of breast carcinoma cells (MCF-7).

Methods: MCF-7 cells treated with different low and high doses of RSV and the consequent cytotoxicity, cell cycle, oxidative, angiogenic and inflammatory responses of the cells were evaluated. The autophagic behavior of MCF-7 cells was assessed by RSV combination with autophagic inhibitor (cloroquine). The effect of the combination on cell survival, autophagic markers expression along with acridine orange staining and cell apoptosis was determined.

Results: Compared to the higher concentration, low dose of RSV (10 µg/ml) exhibited significant anti-survival effect accompanied with cell accumulation at G0/G1 phase, higher MDA and VEGF secretion. Concerning the higher doses of RSV (30 and 50 µg/ml), more cells accumulated at S and G2/M phases, and significantly higher levels of GSH, COX-2, PGE2 and nitrate secretion were observed. Autophagic inhibition of RSV exhibited significant acidic lysosomal staining, anti-survival and pro-apoptotic effects on breast carcinoma cells. The combination of low RSV concentration (10 µg/ml) with autophagic inhibitor caused significant decrease in Beclin-1, LC3-B, BCL-2 and MCL-1 expressions, while higher doses of RSV (30 and 50 µg/ml) combination induced Beclin-1, BCL-2 and MCL-1 but reduced LC3-B expressions compared with the single treatment of RSV.

Conclusions: The cytotoxic effect of RSV depends on the autophagic response of breast carcinoma cells in relation to the applied dose.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.