Methyl Jasmonate Effect on Proliferation and Energetic Metabolism of Breast Cancer Cells in vitro

Mendonça B.S., Figueiredo- Rodrigues M., Carvalho E., Amoedo N.D., Cesari I.M., Rumjanek F.D.

Laboratório de Bioquímica e Biologia Molecular do Câncer, Instituto de Bioquímica Médica, Universidade Federal do Rio de Janeiro, Ilha do Fundão - Rio de Janeiro - Brazil

Introduction. Methyl jasmonate (MJ) is a plant cyclopentanone lipid with potent anti-proliferative and pro-apoptotic activity against a variety of cancer cells with no toxic effects to normal cells. In these studies we evaluated MJ effects on growth, proliferation, bioenergetic metabolism, endogenous enzymes and redox activities in human ER<sup>+</sup> MCF-7 (non-invasive, less glycolytic/more oxidative) and ER<sup>-</sup> MDA-MB-231 (invasive, highly glycolytic/less oxidative) breast cancer cells, with the aim to further understand its mechanisms of action. Materials and Methods. In agreement with the literature for this lipid, MJ was tested at 0-10 mM on: (1) cell proliferation (SRB) and survival (MTT) at 24h/37°C under normoxia; (2) hexokinase (HK) and lactate dehydrogenase (LDH) activities; (3) glucose (Glc) uptake, by 2-deoxy-2-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]-D-glucose incorporation; (4) quantitation of lactate release in the medium; (5) real time cellular respiration by OROBOROS; and, (6) real time hydrogen peroxide [H<sub>2</sub>O<sub>2</sub>] production by AmpleRex. Results and Discussion. MJ inhibited proliferation (SRB) and survival (MTT) of both cell lines in a dose-dependent manner, MDA-MB-231 appearing to be more susceptible to MJ. Tested at 1.25 mM, MJ did not change the endogenous levels of LDH activity; at 2.5 mM, it increased the basal levels of lactate production in both cell lines, MDA-MB-231 cells producing higher amounts. However, no differences were found in Glc uptake between the cell lines. MJ [0.2 – 2 mM] caused a rapid and lethal dose-response inhibition of respiration in MDA-MB-231 cells. MJ induced also H<sub>2</sub>O<sub>2</sub> production in both cell lines, suggesting that some MJ effects are possibly mediated through ROS signaling. Conclusions. MJ exhibited differential anti-proliferative, anti-survival, and mitochondriotoxic activities against metabolically different invasive (MDA-MB-231) and non-invasive (MCF-7) breast cancer cells, leading however to their death; these results further support the outstanding anticancer activities of MJ, looking at its eventual use as an anticancer agent.

Key words: Bioenergetic Metabolism, Breast Cancer Cells, Methyl Jasmonate, ROS

This work was financed by: CNPq, FAF, and FAPERJ.