

"PANDER/FAM3B Overexpression Inhibits Cell Death and Affects Cell Migration in MDA-MB-231 Breast Tumor Cells

<u>Caldeira, I.D.S.^{1,3}</u>; Cruz, R.M.A.R.²; Nunes, V.A.³; Belizário, J.E.¹; Garay-Malpartida, H.M.^{1,3}.

¹Department of Pharmacology, Biomedical Sciences Institute, University of São Paulo, Brazil; ² College of Veterinary Medicine, University of São Paulo; ³ School of Arts, Sciences and Humanities, University of São Paulo, Brazil.

Background: FAM3B/PANDER(Pancreatic-derived factor) is a novel cytokine that induces apoptosis in pancreatic beta-cells and regulates the effects of insulin in peripheral tissues. Our previous results reveal that increased FAM3B expression in DU145 prostate tumor cells inhibits cell death and promotes tumor growth. Aims: We evaluate the role of this cytokine in cell death and migration of a breast adenocarcinoma cell line. Methods: We used the breast tumor cell line MDA-MB-231-overexpressing FAM3B and cells transfected with the empty vector as control. Cell viability and apoptosis of MDA-MB-231 cells stimulated by apoptosis inducers (TNF-a plus cycloheximide, staurosporine) were measured by using MTT assay and DNA fragmentation by flow cytometry. The gene expression of Bcl-2 family members was guantified by real-time PCR and western Blot. Caspase-3 activity was measured by using fluorometric assays. Cell migration was mesuared with wound healing assay. Results: Cell viability and DNA fragmentation analysis revealed that overexpression of FAM3B inhibits significantly cell death induced by TNF-a plus cycloheximide and staurosporine. The survival advantages provided by FAM3B are accompanied by increasing expression of anti-apoptotic genes Bcl-2 and Bcl-XL and decreasing of caspase-3 activity. In addition, wound healing assay, shown increased rates of cellular migration on cells overexpressing FAM3B. Conclusions: In agreement with previously demonstrated role in prostate tumor cells, FAM3B also was capable to activates pro-survival mechanisms and cell migration in MDA-MB-231 breast tumor cells. These roles involve, at least in part, the activation of Bcl-2mediated pathways.

key words: FAM3B, cell death, cell migration.