Abstract Preview - Step 3/4

- print version -

Topic: 4a Molecular and cellular biology: a. Cell cycle control / apoptosis

Title: INTERACTION OF APOPTOTIC AND CYTOPROTECTIVE BILE ACIDS WITH BIOMEMBRANES

Author(s): T. Sousa[1], S. Pinto[1], S.D. Lucas[2], R. Moreira[2], A. Coutinho[1], R.E. Castro[2], C.M. Rodrigues[2], M. Prieto[1], F. Fernandes[1]

Institute(s): *[1]Centro de Química-Física Molecular and Institute of Nanoscience and Nanotechnology, Instituto Superior Técnico, [2]Instituto de Investigação do Medicamento (iMed.ULisboa), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal*
E-mail: ruieduardocastro@ff.ul.pt

Text: **Background and aims:** The bile acid (BA) deoxycholic acid (DCA) is reported to induce cell death through the extrinsic and intrinsic pathways of apoptosis, while ursodeoxycholic acid (UDCA) has strong cytoprotective properties. We aimed to elucidate the mechanisms by which BAs trigger opposite cellular effects, using a membrane-focused approach.
Methods: Primary rat hepatocytes and HEK293 cells were incubated with unlabeled or NBD-fluorescent derivatives of DCA and UDCA. Permeabilization experiments used liposomes mimicking the plasma membrane and the mitochondrial outer membrane lipid composition.
Results: BAs were found at low concentrations in the plasma membrane of HEK293 cells and hepatocytes, but enriched in mitochondrial membranes, as seen by fluorescence microscopy. Unlabeled BAs had no effect on the fluidity of intracellular and plasma membranes of HEK293 cells, at apoptotic concentrations. On the other hand, the fluidity of intracellular membranes of hepatocytes was sensitive to all bile acid species, at both apoptotic and anti-apoptotic concentrations, while plasma membrane fluidity was mostly insensitive to the presence of BAs. Experiments with lipossomes indicated efficient permeabilization by DCA for different membranes. In particular, this phenomenon was more effective in membranes with high concentrations of cholesterol and sphingomyelin, like plasma membrane rafts. In contrast, cytoprotective BAs were significantly less effective in increasing membrane permeability.
Conclusions: Altogether, these results suggest that the pro- versus anti-apoptotic mechanisms of BAs do not primarily result from modulation of membrane fluidity. Instead, apoptotic bile acids, like DCA, strongly target and increase membrane permeability, likely constituting one of its first pro-apoptotic mechanisms of action.
(Supported by FCT, Portugal PTDC/QUI-BIQ/119494/2010; PTDC/QUI-BIQ/112067/2009)

Preferred Presentation Type: Oral Presentation

Conference: 2014 International Liver Congress TM · Abstract: A-627-0009-03283 · **Status: Submitted**

Print Back