



29

CONGRESO DE LA SOCIEDAD ESPAÑOLA DE FARMACOLOGÍA

TITULO: DRUG-INDUCED NEUROTOXICITY REGULATES APOPTOSIS, OXIDATIVE STRESS AND CELL CYCLE CONTROL GENE EXPRESSION

AUTOR PRINCIPAL: M. Pallàs

COLABORADORES: Jaume Folch³M. Yeste^{1,2}, D. Alvira^{1,2}, F.X. Sureda⁴, V. Rimbau^{1,2}, A. Camins^{1,2} M. Pallàs^{1,2}

CORREO ELECTRONICO: pallas@ub.edu

DNI: 36976145

TELEFONO FIJO: 93 4024531

TELEFONO MOVIL

FAX: 93 4035981

CENTRO DE TRABAJO: ¹Unitat de Farmacologia i Farmacognòsia ²Institut de Biomedicina (IBUB), Facultat de Farmàcia. Universitat de Barcelona. ³Grup de Farmacobiologia, Unitat de Bioquímica, ⁴Unitat de Farmacologia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili. Reus (Tarragona).

UNITAT DE FARMACOLOGIA. FACULTAT DE FARMACIA. UNIVERSIDAD DE BARCELONA

Indicar el formato de presentación deseado: *Oral* () *Póster* (x)

PALABRAS CLAVES : NEUROTOXICITY, APOPTOSIS, OXIDATIVE STRESS

Objectives: We analyzed the effects of the acute exposure to several xenobiotics (neurotoxic and non-neurotoxic: atropine, caffeine, colchicine, cycloheximide, digoxin, malathion, mercury (II) chloride, pentachlorophenol, phenobarbital, nicotine) in the transcriptional activity of genes related to cell death in cerebellar granule cells. **Methods:** We designed a low density array with a 32-assay format to detect possible gene targets. In the assay we included genes related to glutathione metabolism (Gsto1, Gpx1, Cat, Gsr, Gsta5, Sod1 and Sod2) genes related to cell cycle control (Ccn1, Cdk2, Cdk4, Cdk5) genes related to apoptosis (Bcl2, p53, Casp3, Casp8, Casp9, Diablo, Bid, Capn1, Bad) and neuronal-cell related genes (Gsk3beta, Pcna, Nptx1, Sirt2, Tgfbeta1, Mapk1, Mapk3 and Actb). Glyceraldehyde-3-phosphate dehydrogenase gene was used as housekeeping reference gene. Real-time RT-PCR data were quantified using the SDS 2.2 software package (Applied Biosystems). **Results:** We showed results obtained after treatment with colchicine slightly up-regulated the activity of genes related to oxidative stress: glutathione peroxidase 1 and catalase; altered significantly genes related to cell-cycle control: cyclin D1 and cyclin-dependent kinase 2; genes related to classical apoptosis pathway: p53, caspase 3 and caspase 8; and neuronal cell-related gene pentraxin 1. **Discussion and conclusions:** The exposition to selected drugs activates the classical apoptosis pathway, but also promotes the regulation of several genes related to oxidative stress and cell cycle-control. These results can constitute an alert to neurotoxicity based on short exposure times.

This study was supported by grants LSHB-CT-2004-512051 from EECC, SAF2005-01604 and SAF-2006-13092 from Ministerio de Educación y Ciencia, PI 041300, PI040376 (RT) and CIBER from Instituto de Salud Carlos III, 2005/SGR00893.

ENVIAR POR CORREO ELECTRONICO ANTES DEL 1 DE JUNIO DE 2007 A : farmacologia2007@accionmedica.com