

**S02-10.-Zebrafish models for human acute organophosphorus poisoning.** *Melissa Faria*<sup>1</sup>, *Natalia Garcia-Reyero*<sup>2,3</sup>, *Francesc Padros*<sup>4</sup>, *Patrick J. Babin*<sup>5</sup>, *David Sebastian*<sup>6,7,8</sup>, *Jérôme Cachot*<sup>9</sup>, *Eva Prats*<sup>10</sup>, *Eduardo Rial*<sup>11</sup>, *Anja Knoll-Gellida*<sup>5</sup>, *Guilaine Mathieu*<sup>5</sup>, *Tony Arick*<sup>2</sup>, *B. Lynn Escalon*<sup>3</sup>, *Antonio Zorzano*<sup>6,7,8</sup>, *Amadeu M.V.M Soares*<sup>1</sup>, *Demetrio Raldúa*<sup>12</sup>.- (Presenting Author: **Demetrio Raldúa**)

(1)Centre for Environmental and Marine Studies (CESAM), University of Aveiro, 3810-193 Aveiro, Portugal; (2)Institute for Genomics, Biocomputing & Biotechnology (IGBB), Mississippi State University, Starkville, Mississippi, USA; (3) Environmental Laboratory, US Army Engineer Research and Development Center, Vicksburg, MS, USA; (4)Pathological Diagnostic Service in Fish, Universitat Autònoma de Barcelona, 08190 Bellaterra, Spain; (5)Rare Diseases, Genetic and Metabolism (MRGM), Université de Bordeaux, EA 4576, F-3340 Talence, France; (6)Institute for Research in Biomedicine (IRB Barcelona), 08028 Barcelona, Spain; (7) Departament de Bioquímica i Biologia Molecular, Facultat de Biologia, Universitat de Barcelona, 08028 Barcelona, Spain; (8) Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), 08017 Barcelona, Spain; (9) EPOC, UMR CNRS 5805, Université de Bordeaux, 33405 Talence, France; (10) CID-CSIC, Jordi Girona 18, 08034, Barcelona, Spain; (11) Department of Cellular and Molecular Medicine, CIB-CSIC, Ramiro de Maetzu 9, 28040, Madrid, Spain; (12) IDÆA-CSIC, Jordi Girona 18, 08034, Barcelona, Spain

Terrorist use of organophosphorus-based nerve agents and toxic industrial chemicals based against civilian population constitute a real threat, as demonstrated by the terrorist attack against Japanese civilians in the 1990s or, more recently, by the attack against civilians in the suburbs of Damascus, Syria, in 2013. Thus, development of more effective countermeasures against acute organophosphorus poisoning is urgently needed. Here we have generated and characterized zebrafish models for mild, moderate and severe acute organophosphorus poisoning by exposure to different concentrations of the prototypic OP compound, chlorpyrifos-oxon. The main feature of the mildest grade was a moderate impairment in the visual and motor function correlated with the AChE inhibition. The clinical features of the larvae exhibiting the moderate grade were paralysis and tetany of the axial muscles. Finally, the severe grade was characterized by paralysis and cell death at the central nervous systems and axial muscles. Our results show that zebrafish models mimic most of the aspects of this toxidrome in humans, including acetylcholinesterase inhibition, NMDA-receptor activation and calcium dysregulation. The suitability of the zebrafish larvae to in vivo medium and high throughput screenings of small molecule libraries makes these models a valuable tool for identifying new drugs to be used in a multifunctional drug therapy against this toxidrome.

Supported in part by the US Army ERDC-IRO (W912HZ-13-BAA-01) and Environmental Quality Research Program, the National Science Foundation EPSCOR Grant EPS-0903787, the NATO SfP project 984777, the Advanced Grant ERC-2012-AdG-320737 and the Spanish Government (CTM2014-51985-R).