FIRST LATIN AMERICAN WORM MEETING

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Institut Pasteur de Montevideo
URUGUAY

Expanding *Caenorhabditis elegans* research: First Latin American Worm Meeting

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Place: Institut Pasteur Montevideo, Uruguay

Organizers:

Inés Carrera (Institut Pasteur de Montevideo)
Andrea Calixto (Universidad Mayor, Santiago, Chile)
Gustavo Salinas (Universidad de la República, Montevideo, Uruguay/Institut Pasteur de Montevideo)

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http://lasdb-development.org

Introduction: Organic solvent is a name for a group of organic chemicals that are widely used in industrial processes.The industrialized gasoline products have a variable composition of compounds and solvents, but basically consists of aromatic hydrocarbons. Toluene is one of the organic solvents present in gasoline that has a high degree of volatility, being absorbed mainly by the pulmonary route and reaches the central nervous system promoting toxic action. The present work aims to evaluate the effect of volatile exposure to toluene on the development, behavior, mortality and induction of cell death in the experimental model *Caenorhabditis elegans*. **Materials and methods:** N2 wild-type nematodes and a MD701 (CED-1::GFP) were used. Worms in the first larval stage were exposed to volatile toluene for 48 hours in a closed chamber at concentrations of 8.700, 14.500, 21.750 and 29.000 ppm. After 48 hours of exposure analyzes were carried out, such as mortality rate, development, behavior and observation of apoptotic events in germline cells. **Results and discussion:** We observed a significant increase in mortality (LD50= 22.594 ppm) and a significant developmental delay as we increased the concentration of exposure to toluene. We also observed a significant decrease in the swimming and increase in the number of cells in apoptosis, corroborating with some works present in the scientific literature. **Conclusion:** Based on the results obtained, toluene showed a significant toxicity where we can prove that it promotes cell death through the caspase pathway, also showed a significant toxic effect on development and on swimming behavior that is controlled by neuronal stimulation, this suggests possible neurotoxic effect.

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Screening of insulin like-peptides (ILPs) involved in the neural coordination of stress response in *C. elegans*

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The ability of organisms to appropriately respond to physiological and environmental challenges requires conserved mechanisms, known as the “stress response”. The nervous system plays a key role in the coordination of systemic stress response. Recently, we demonstrated that in basal conditions tyramine released from the RIM neuron inhibits stress response in worms. Moreover, we demonstrated that expression of the GPCR TYRA-3 in the intestine is essential

for this inhibition. When exposed to a stressor, such as heat, oxidative stress or lack of nutrients, tyramine signalling from the RIM should be stop to allow the animal to respond to these stressful conditions. We also observed that the insulin receptor DAF-2 is involved in this neural regulation of stress response, suggesting the compromise of insulin/insulin-like growth factor signaling (IIS) pathway. However, which are the signals that connect the intestine, where *tyra-3* is expressed, with DAF-2 in several other cells are completely unknown. With this aim, we analyzed expression pattern of some of the 40 insulin like-peptides (ILPs) of C. elegans. We found that INS-3 and INS-7 co-localize with TYRA-3 in intestine. Moreover, expression of *ins-7* in RIM neuron has been previously described. We also observed that null mutants of these ILPs are as resistant to thermal and oxidative stress as *tdc-1* (incapable of sinthetizing tyramine) and tyra-3 null mutants. We generated double null mutants of tdc-1 and tyra-3 with *ins-3* and *-7* in order to study epistatic relationships. Moreover, we are analizing the effects of exogenous tyramine on *ins-3* and *-7* expression. This study will contribute to understand molecular mechanisms involved in neuronal regulation of stress response in a multicellular organism.

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The role of serotonergic G-protein coupled receptors (GPCRs) in *Echinococcus granulosus* and other cestodes suggests future applications as drug targets of neglected diseases

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Introduction: Cestode parasites are a diverse group of organisms, many of them are cause of neglected zoonoses with major impact in health and economy. The adecuate nerve- muscle function is a classical target for cestocide drugs. Genomic and transcriptomic data of *E. granulosus* (Tsai *et al*., 2013) and experimental results showing the motor response to serotonin (5-HT) of the larval stage (Camicia *et al*., 2013) suggest the existence of serotonergic GPCRs (5-HT GPCRs) in this parasite. Drugs that could discriminate between parasite and human GPCRs receptors were not discovered yet.
Hypothesis: We propose the existence of 5-HT GPCRs with a major role in parasite movement. **Results:**The bioinformatics search of this kind of receptors in cestode parasites such as *Mesocestoides corti*, *Echinococcus spp.* resulted in the interesting finding of conserved sequences with identity to 5-HT GPCRs, some of them were already cloned and sequenced. The addition of 5-HT to the larval stages of *M. corti* and *E. granulosus* resulted in the stimulation of the motility, where as the addition of 5- HT GPCRs antagonists resulted in the inhibition of movement, supporting the importance of 5-HT GPCRs in the parasite movement.
Conclusion: The neuromuscular activity in the presence of serotonergic agonists-antagonists suggest the existence of 5-HT GPCRs in cestode parasites. The