FIRST LATIN AMERICAN WORM MEETING

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Institut Pasteur de Montevideo
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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)

This Symposium was declared of Cultural and National interest by the Government of Uruguay.

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Characterization of the antiparasitic bephenium as an agonist of *Caenorhabidits elegans* levamisole-sensitive nicotinic receptors.

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Nicotinic acetylcholine receptors (nAChRs) are pentameric ligand-gated ion channels that mediate fast synaptic transmission and are involved in neuromuscular transmission. Nematode muscle nAChRs are of clinical importance because they are targets of anthelmintic drugs. The muscle nAChRs of nematode parasites fall into three pharmacological classes that are preferentially activated by levamisole (L-type), nicotine (N-type) and bephenium (B-type). *Caenorhabditis elegans* muscle contains the N-AChR and L-AChR types. We therefore sought to explore the action of bephenium at *C. elegans*. Behavioral studies reveal that wild type worms are sensitive to bephenium. The drug causes spastic paralysis but with less potency than levamisole. The*lev-8*and *unc-38* null mutant strains, which lack accessory (LEV-8) and essential (UNC-38) subunits of L- AChRs, show partial and full resistance to bephenium,respectively. To determine the mechanism of action of bephenium we used a primary culture system that allows differentiation of embryonic cells into L1 larva muscle cells *in vitro*. Our results reveal that bephenium (1-100 μM) activates a single population of ~3.6 pA amplitude channels (-100 mV) that correspond to the L-AChR channels. The open-channel lifetime is similar to that of ACh-activated channels (~0.2 ms). Because in parasites the receptor target of bephenium contains the ACR-8 subunit, and in *C. elegans* ACR-8 is a candidate subunit to replace LEV-8,we also evaluated the action of this drug in the *lev-8* null mutant strain. We found that bephenium also activates L-AChRs lacking LEV-8, although the activity pattern differs from that of wild-type L-AChRs. Overall, we characterized the agonistic action of bephenium, which is used for parasitic infections caused by intestinal helminths, at the *C. elegans* L-AChR.

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Characterization of DLK-1 function in neuronal regeneration induced entry into diapause

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Neuronal regeneration is the recovery of the axon's structure, to restore its morphology and function. *C. elegans* neurons regenerate after axotomy and spontaneous breakage in a process dependent on the function of DLK-1. DLK-1 is a kinase, with an essential role in the control of microtubule dynamics, associated with the formation of growth cone by the activation of p38 and Jnk pathways. We previously showed that sensory neurons that express a pro-degenerative trigger (*mec-4d*), are protected from death by diapause entry, degenerating again when development is resumed (Calixto *et al*., 2012). Importantly, we observed that in