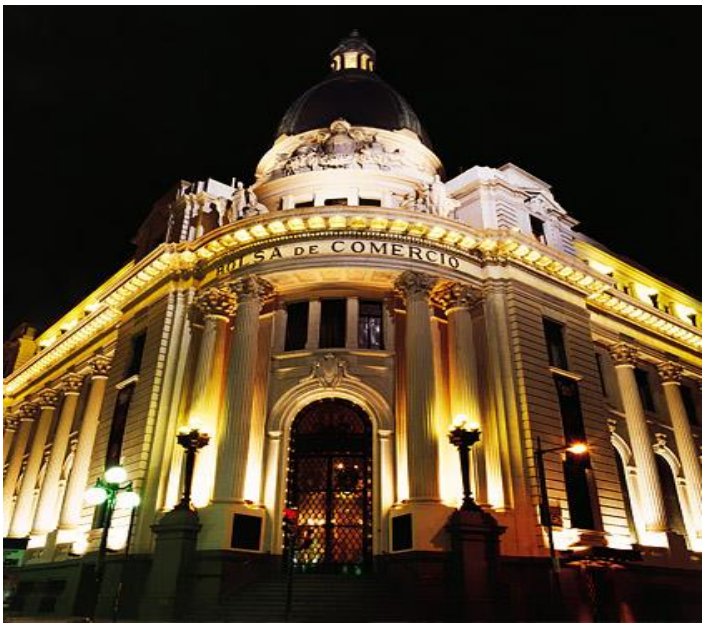
2nd Latin American Worm Meeting

February 19th-21st, 2020

Bolsa de Comercio de Rosario

Rosario, Argentina



Bolsa de Comercio de Rosario

Organizer: Diego de Mendoza

Co-organizers: Andrea Calixto, Inés Carrera, María José De Rosa, Daniel Hochbaum, Diego Rayes, Cecilia Mansilla, Oscar Fay, Eugenia Goya.

Scientific Committee

Andrea Calixto, Universidad Mayor, Chile

Inés Carrera, Universidad de la Republica, Uruguay

Diego de Mendoza, IBR, Argentina

Maria Jose De Rosa, INIBIBB, Argentina

Daniel Hochbaum, UBA, Argentina

Cecilia Mansilla, IBR, Argentina

Diego Rayes, INIBIBB, Argentina

4. Laboratory of Molecular Biology, Developmental Biology Section, NIDDK. NIH, Bethesda, Maryland

In harsh environments, *C. elegans* develops into the dauer larva, a stress-resistant and long-lived variant of the L2-stage larva. The nuclear receptor DAF-12 is one of the decisive checkpoints regulating worm aging and dauer formation, however the genes under its control remain largely uncharacterized. We used chromatin immunoprecipitation to identify DAF-12 regulated genes and ascertained relevant targets by RNAi screening for dauer suppressors. Inhibition of *chd-7* (chromodomain helicase DNA-binding protein) leads to developmentally arrested, abnormal dauers that are sensitive to SDS. Notably, deletion alleles *chd-7(gk290)* and *chd-7(tm6139)* form abnormal dauers with the same features as *chd-7*(RNAi), validating our screen. Moreover, *chd-7* mutants form reproductive adults in the *ts* allele *daf-7(e1372)*, suggesting that *chd-7* is downstream of both *daf-2* and *daf-7* signaling for dauer entry. Longevity of *daf-2(e1370)* and *glp-1(e2144)* mutants is also impaired in *chd-7(gk290)*. Scanning electron microscopy suggests cuticle defects upon *chd-7* inhibition and this was further supported by RNA-Seq analysis. *chd-7* shares more that 60% homology with human CHD7/8, which are associated with cognitive disorders, including CHARGE and Kallmann syndromes. Our ability to exploit *C. elegans* to analyze *chd-7* in the context of dauer formation creates an opportunity to identify relevant disease pathways regulated by this class of evolutionarily conserved chromatin modifiers involved.

The flight response induces the release of an insulin-like peptide from the intestine to inhibit cytoprotective mechanism in *C. elegans*

Tania Veuthey[1], Sebastián Giunti[1], María José De Rosa[1], Mark Alkema[2] and Diego Rayes[1].

1-Lab. Neurobiología de Invertebrados. Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB). Departamento de Biología, Bioquímica y Farmacia. Universidad Nacional del Sur. Bahía Blanca, Argentina. 2- Alkema Lab. Neurobiology. University of Massachusetts Medical School. tveuthey@uns.edu.ar

The perpetuation of the flight response inhibits defensive cytoprotective mechanisms, leading to reduced resistance to environmental stressors and shorter lifespan. We recently shown that, in *C. elegans*, the flight response induces neuronal release of Tyramine (TA), which stimulates the intestinal adrenergic-like receptor TYRA-3. This leads to DAF-2/Insulin/IGF-1 pathway activation and inhibition of cytoprotective mechanisms in intestine and other tissues. However, the signals that bridge intestinal TYRA-3 stimulation with DAF-2 insulin receptor activation in other tissues remain unknown. *C. elegans* genome encodes 40 Insulin-like peptides (ILPs) that bind to DAF-2, 28 of them expressed in the intestine. We test the resistance to environmental stressors (oxidative and thermal stress) silencing individual intestinal ILPs by RNAi. We found that silencing *ins-3* improves stress resistance. In contrast to control, exogenous

TA addition does not impair stress resistance in *ins-3*-silenced animals. Moreover, double-null mutants of *ins-3* and TA are as resistant to environmental stress as single mutants. This suggests that tyramine and INS-3 act in the same pathway. Since *ins-3* is also expressed in neurons, we performed tissue-specific rescues of *ins-3* in neuron and intestine to assess the tissue where *ins-3* is relevant for controlling stress resistance. Only intestinal *ins-3* restores the resistance to wild-type levels. Moreover, stress resistance of *ins-3 null-mutants* is mediated, at least partially, by DAF-16/FOXO. We propose that intestinal activation of TYRA-3 by the escape neurohormone TA leads to INS-3 release which acts as endocrine, autocrine and/or paracrine signal to activate DAF-2 in the intestine and distal tissues. Given the high degree of conservation of fundamental mechanisms among species, this study can contribute to understanding molecular pathways and cellular communication involved in neural regulation of stress response in multicellular organisms.

Liquid-Liquid Phase Separation in the Gonad of *C elegans* During Stress.

Navarro, R.E., Dámazo-Hernández, A., Fuentes-Jiménez, D.A., Morales-Oliva, E. Campos-Martínez, G. and Salinas, L.S.

Departamento de Biología Celular y Desarrollo, Instituto de Fisiología Celular, UNAM

In certain conditions, diffused RNAs and proteins can form liquid droplets, just like oil inside water to accomplish specific functions. This phenomenon is known as liquid-liquid phase separation or LLPS. Membrane-less organelles, like RNA granules, behave like LLPS. The adult hermaphrodite *C. elegans* gonad is an excellent model to study LLPS because is a syncytium and allows the study of this phenomenon in vivo.
We have observed that the *C. elegans* gonad possess many different types of RNA granules. In control conditions, germ cells present constitutively in their cytoplasm germ granules also known as P granules and processing or storage bodies. Under stress conditions, we and other groups have observed at least two different classes of stress granules: one that is mainly located in the distal core and another that is found in the most proximal part where oocytes are forming. Germ granules have been studied with more detail meanwhile processing bodies and stress granules formation, function and composition are not well understood yet.
The RNA binding proteins TIAR-1 and GLA-3 (TIA1/TIAR and TTP mammals homologs, respectively) are required for stress granule formation in the *C. elegans* gonad.
Using the transgene *gla-3a(tn1734[gfp::3xflag::gla-3a*]) (produced by the Greestein lab), we observed that the fusion protein GLA-3:GFP associates to stress granules during heat shock. Furthermore we observed that *gla-3* mutant animals are unable to form stress granules in their gonads during heat shock or starvation suggesting that this protein is important for the association of these RNP complexes. We tested the importance of gla-3 in germ cell quality by measuring the success of embryogenesis after young adults were exposed to heat shock and we found that gla-3 mutant animals embryo lethality increases considerably when animals are exposed to heat shock and