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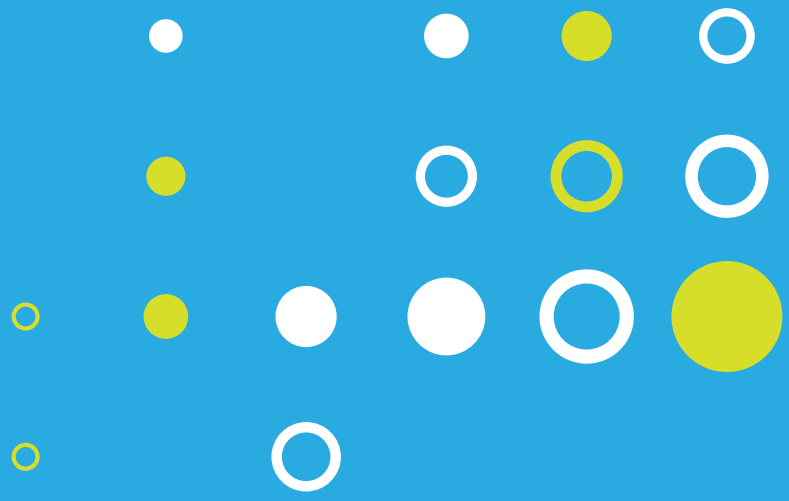

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CD melting assays indicate that the same SNPs induce G4 stability changes. In agreement, 1D ^{1}H NMR spectroscopy confirmed that SNPs induce quantitative and qualitative changes for the SNP-PG4s identified for *c-MYC* and *NRAS*. Finally, SNP-PG4s that produced significant structural variations *in vitro* were cloned into a pGL3 promoter vector (for PG4s controlling transcription) or into a psiCHECK-2 vector (for RNA PG4 controlling translation) and were transfected into HEK293 cells, revealing that SNPs altered luciferase reporter activity. Results gathered in this work suggest that SNP-PG4s that alter G4 folding may be the cause of differential expression of oncogenes leading to tumor predisposition, establishment, progression or metastasis and should be considered as a novel molecular etiology mechanism for the predisposition or establishment of diseases.

CB-C09
CONVERGENT APPROACH TO THE STUDY OF LONGEVITY OF *CERATITIS CAPITATA* AND *DROSOPHILA MELANOGASTER* MALES

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Our main objective is to correlate the physiological and gene expression profiles from fly males showing unusual longevity. We studied two classical models for senescence profiles: the Medfly *Ceratitis capitata* and the vinegar fly *Drosophila melanogaster*. We developed laboratory studies of behavioral parameters of male medflies in a novel arena containing lek-like arrangements of three flies. We were able to determine that young males showing none or very low rate of spontaneous supine falls (VLS males) and showing significant higher adult mean life expectancy (46.9 days of VLS males instead 27.1 days of supine males:), were significantly more longevous. Thus, we considered the supine behavior as a longevity predictor. We then studied the longevous and non-longevous male gene expression. In a completely different but convergent approach, we studied for the first time, the physiological characteristics and adult senescence profiles of the *D. melanogaster* mutant *tan-1*, unable to hydrolize N-β-alanyl-dopamine; that were compared to those of wild type Canton-S and mutant *ebony-1* (unable to synthesize N-β-alanyl-dopamine). We then demonstrated that *tan-1* was significantly longevous (up to 75.7 days-old instead of WT 60.8 days and 58.8 days of *ebony-1*). When performing qPCR studies in these peculiar longevous flies, the results showed that, as somehow expected, the expression of "antioxidant" genes in *tan-1* was higher than the one in wt (a 1.5-fold increase in SOD-2 mRNA and a 2-fold increase in Catalase expression). Strikingly, we found that in VLS male Medflies the expression of these enzymes was normal but was enhanced in "Supine" males. When the expression from VLS and normal Medfly male brains was compared, by RNASeq studies, the results revealed that other key genes significantly changed more than 2.5 times in longevous flies, thus pointing to a polygenic contribution to longevity, as also expected. Most significant were xenobiotic detoxification and ROS detoxification systems as well as genes involved in neural system connectivity and innate immune response.

CB-C10
EVIDENCE OF ALTERED ENDOMEMBRANES IN FISSION YEASTS LACKING GLUCOSIDASE I, A MODEL FOR HUMAN CONGENITAL DISORDER OF GLYCOSYLATION CDG IIb

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Glucosidase I (GI) is an endoplasmic reticulum (ER) membrane protein that removes the outermost glucose from the glycan $Glc_3Man_9GlcNAc_2$ (G3M9) immediately after protein *N*-glycosylation. Mutations in GI-encoding gene (*gls1*$^{+}$*)* result in human congenital disorders of glycosylation (CDG) IIb, also called MOGS-CDG. Using the fission yeast *Schizosaccharomyces pombe* lacking GI as a model organism we demonstrated that the main cause of the morphological and growth defects observed in mutant cells was the persistence of G3M9 structures in glycoproteins, as a second mutation in *alg10+* gene (which is responsible for the addition of the last Glc during the lipid-linked G3M9 synthesis) substantially suppressed the observed defects. The sick phenotype of *Δgls1* mutant cells could not be ascribed to a product inhibition of oligosaccharyltransferase transfer reaction, to the inability of glycoproteins to enter into calnexin-folding cycles, or to a potentially reduced ER-associated degradation. Glycan elongation of glycoproteins in the Golgi and the overall cell wall (CW) monosaccharide composition of *Δgls1* mutants were indistinguishable from those observed in cells lacking glucosidase II (*Δgls2α*), which display a wild type phenotype. However, transmission electron microscopy (TEM) showed that the CW of *Δgls1* mutants was thicker than *WT* and *Δgls2α* ones, presenting a feathered appearance, and a disorganized arrangement without its characteristic three-layered structure. Endomembrane system was also altered in cells lacking GI as: 1) subcortical ER structures localized below the plasma membrane were apparently absent or mislocalized in mutant cells observed by TEM, 2) CW glycoproteins region was wider in *Δgls1* cells than in WT ones as revealed by staining with fluorescent-labeled lectins *Griffonia (bandeiraea) simplicifolia* (recognizes Galactose terminal residues) and Concanavalin A (recognizes high-mannose glycans) , and 3) the lack of GI produces cells with highly fragmented vacuoles in hypotonic conditions (revealed by FM4-64 staining) which possibly cannot undergo homotypic fusion. Collectively, these results suggest the occurrence of alterations in the secretory/endocytic pathway in cells lacking GI and shed light on the underlying molecular and cellular mechanisms of CDG IIb disease.

CB-C11
THE FLIGHT RESPONSE INDUCES THE RELEASE OF AN ILP FROM THE INTESTINE TO INHIBIT CYTOPROTECTIVE MECHANISMS IN *CAENORHABDITIS ELEGANS*

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The perpetuation of the flight response inhibits defensive cytoprotective mechanisms, leading to reduced resistance to environmental stressors, early onset of age-related disorders and shorter lifespan from invertebrates to mammals. We have recently shown that, in *Caenorhabditis elegans*, the flight response induces the neuronal release of Tyramine (TA, the invertebrate analog of adrenaline), which stimulates the adrenergic-like receptor TYRA-3 in the intestine. This leads to the activation of the DAF-2/Insulin/IGF-1 pathway and the inhibition of cytoprotective mechanisms, such as translocation of DAF-16/FOXO or HSF-1, not only in the intestine but also in other tissues. However, the signals that bridge the stimulation of TYRA-3 in the intestine with the activation of the DAF-2 insulin receptor in other tissues remain unknown. *C. elegans* genome encodes 40 Insulin-like peptides (ILPs), which in principle could bind to DAF-2, and many of them are expressed in the intestine. We, therefore, used RNAi to individually silence intestinal ILPs and test the resistance to environmental stressors such as oxidative and thermal stress. We found that the silencing of one of those ILPS, *ins-3*, improves the resistance to environmental stressors. In contrast to control, the addition of exogenous TA does not impair the oxidative or thermal stress resistance in *ins-3*-silenced animals. Moreover, we generated double null mutants of *ins-3* and TA-deficient mutants and found that this double mutant is as resistant to environmental stress as single mutants. This suggests that tyramine and INS-3 act in the same pathway to control stress resistance. Since *ins-3* is also expressed in neurons, we injected *ins-3* cDNA driven by intestinal and neuronal promoters to *ins-3* null mutant animals, to assess the tissue where the expression of *ins-3* is relevant for controlling stress resistance. We found that only intestinal expression of *ins-3* restores the resistance to wild-type levels. Moreover, we found that the stress resistance of *ins-3 null mutants* is mediated, at least partially, by DAF-16/FOXO. We, therefore, propose that the activation of the intestinal GPCR TYRA-3 by the escape neurohormone TA leads to the release of INS-3 which acts as endocrine, autocrine and/or paracrine signal to activate the insulin receptor DAF-2 not only in the intestine but also in 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.

LIPIDS

LI-C01
α-SYNUCLEIN AND LIPID METABOLISM: INTERSECTING PATHWAYS

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α-synuclein (α-syn) aggregation and fibrillation is a hallmark of a class of neurodegenerative disorders known as synucleinopathies. An intriguing and not completely clarified feature of α-syn is the many ways in which it interacts with lipids. In the present study, we aimed to investigate the effect of α-syn overexpression on neuronal lipid metabolism. For this purpose, human IMR-32 neuroblastoma cells stably transfected with either pcDNA3 vector (control) or pcDNA3-WT-α-syn (WT α-syn) were used. We observed that α-syn overexpression induced the accumulation of cytosolic lipid droplets (LD) and cholesterol (Chol) in lysosomes. LD increase was coincident with a rise in triacylglycerol (TAG) and Chol esters content. To ascertain the mechanism involved in LD accumulation, pharmacological inhibitors of proteasomal degradation and autophagy were used. Whereas autophagy inhibition did not affect neutral lipids content, the blockage of proteasomal degradation was able to increase LD accumulation in WT α-syn cells. *In silico* analysis performed with MyProteinNet server (Yeger-Lotem lab) postulates a positive correlation between α-syn and sterol regulatory element-binding gen (SREBF-2). To corroborate these data in our experimental model, we evaluated the status of the transcription factors SREBP-1 and SREBP-2. SREBP-1 nuclear localization was slightly diminished by α-syn overexpression with decreased levels of fatty acid synthase protein expression. In contrast, α-syn overexpression promoted SREBP-2 nuclear translocation, with no increment in the expression levels of the downstream genes related to Chol synthesis. Intriguingly, fatty acid Coenzyme A esterification and acylation into Chol and diacylglycerides were increased in WT α-syn cells. To elucidate the source of fatty acids availability, we measured phospholipid content and TAG hydrolysis. WT α-syn cells displayed diminished levels of cardiolipin and phosphatidic acid with no changes in TAG hydrolysis. Our results allow us to conclude that: α-syn overexpression induces a metabolic switch that triggers the neuronal accumulation of neutral lipids by activating several mechanisms: (i) increased phospholipid hydrolysis, (ii) a rise in fatty acids esterification into Chol and diacylglycerols, and (iii) Chol accumulation in lysosomes probably due to an increment in its uptake. *Funding: ANPCyT, CONICET, and UNS.*

LI-C02
LIPID DROPLETS POPULATIONS IN THE INSECT VECTOR OF CHAGAS DISEASE (*TRIATOMA INFESTANS*)