



XIX Italian Drosophila Research Conference

20-22 Giugno 2018

Aula Magna - Complesso Interdipartimentale "A. Vallisneri"

Abstracts book

CON IL CONTRIBUTO DI:

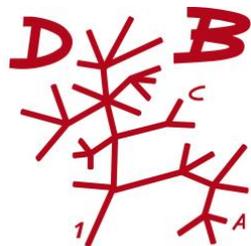
**PhD Program
in Biosciences**



**UNIVERSITÀ
DEGLI STUDI
DI PADOVA**



CON IL PATROCINIO DI:



**DIPARTIMENTO DI BIOLOGIA
UNIVERSITÀ DEGLI STUDI DI PADOVA**



**UNIVERSITÀ
DEGLI STUDI
DI PADOVA**

PROGRAMME

20 June 2018

13:30-14:15 **Registration**

14:15-14:30 **Welcome Address**

Gabriella Mazzotta

14:30-15:30 **LECTURE: New tricks for an old clock**

Ezio Rosato, University of Leicester, UK

(Chair: Gabriella Mazzotta)

15:30-16:10 **Mini SYMPOSIUM I: Circadian rhythms**

(Chair: Giorgio Gilestro)

Cryptochrome interacts with actin and enhances eye-mediated light sensitivity of the circadian clock in *D. melanogaster*

Gabriella Mazzotta, University of Padova

Modulation of miR-210 alters phasing of circadian locomotor activity and impairs projections of PDF clock neurons in *D. melanogaster*

Paola Cusumano, University of Padova

16:10-16:40 **Coffee break**

16:40-18:00 **Mini SYMPOSIUM II: Modeling human cancers in *Drosophila***

(Chair: Daniela Grifoni)

A neurogenic model of adult brain cancer in the fly

Simona Paglia, University of Bologna

***Drosophila* model to understand the role of autophagy in Glioblastoma**

Miriam Formica, University of Milan

***Drosophila* Multidrug Resistance Protein: new insights into unexplored functions of the ABC transporters**

Sara Monticelli, University of Bologna

Growth and tracheogenesis are separable traits in *Drosophila* cancers

Manuela Sollazzo, University of Bologna

21 June 2018

09:30-10:30 **LECTURE: New roles for old trafficking proteins**

Thomas Vaccari, University of Milan
(Chair: Cristiano De Pittà)

10:30-11:10 **Mini SYMPOSIUM III: Fusion and fission dynamics in *Drosophila***

(Chair: Patrizio Dimitri)

Studying how the SNARE protein Snap29 regulates membrane fusion at the Golgi apparatus during interphase and moves towards chromosomes at the onset of mitosis

Elisa Speranza, University of Milan

Shaping the endoplasmic reticulum: fusion and fission dynamics revealed in flies.

Diana Pendin, University of Padova

11:10-11:40 **Coffee break**

11:40-12:40 **Mini SYMPOSIUM IV: Lysosomal and ER disorders in *Drosophila***

(Chair: Thomas Vaccari)

Gaucher disease: a Hyper-Hippo syndrome?

Silvia Strocchi, University of Bologna

Characterization of Cathepsin F CRISPR/Cas9 mutants in *Drosophila* as a targeted *in vivo* model of type B Kufs disease

Marco Gualtieri, University of Milan

Translational control of the ODC/polyamine axis by CNBP is required for muscle function in *D. melanogaster*

Laura Ciapponi, University of Rome

12:40-12:50 **Sponsor Time: Biosigma**

12:50-14:00 **Lunch**

14:00-15:40 **Mini SYMPOSIUM V: Epigenetics and DNA damage response in *Drosophila***

(Chair: Maria Pia Bozzetti)

Unmasking the encrypted role of dTip60 chromatin remodeling complex in cell division

Giovanni Messina, University of Rome

HP1a interacts with NBS to maintain chromosome integrity in both *Drosophila* and human cells

Francesca Cipressa, University of Rome

Interactions between *pendolino* and histone modifiers reveal an epigenetic regulation of *Drosophila* telomere stability

Federica Mosti, University of Rome

Low doses of gamma irradiation render *D. melanogaster* resistant to the DNA damage

Antonella Porrazzo, University of Rome

The TGS1 hypermethylase plays a conserved role in the biogenesis of snRNAs

Grazia Daniela Raffa, University of Rome

15:40-16:10 **Coffee break**

16:10-17:10 **Mini SYMPOSIUM VI: Genome stability in *Drosophila***

(Chair: Gianni Cenci)

Roles of *dFmr1*, the *Drosophila* homolog of the human gene responsible for the Fragile X syndrome, in the genome stability

Antonietta Puricella, University of Salento

The magic inside: the universal promoter of two *Drosophila* transposons of the Bari family

Renè Massimiliano Marsano, University of Bari

Silencing of P-element mini-white reporters induced by functional domains of pericentric heterochromatin in *D. melanogaster*

Patrizio Dimitri, University of Rome

18:00-19:20 **Visit to the Scrovegni's Chapel**

20:00 Social dinner at **RISTOcaffè Nero di seppia** (Via S. Francesco, 161 - Padova)

22 June 2018

09:30-10:30 **LECTURE: A tale of sleepless flies and *ninna nanna*. How *Drosophila* changes what we know about sleep**

Giorgio Gilestro, Imperial College London, London, UK

(Chair: Paola Cusumano)

10:30-11:10 **Mini SYMPOSIUM VII: Analysis of behaviour in *Drosophila***

(Chair: Federica Sandrelli)

Opinion and behavior dynamics in fruitfly populations

Francesca Minchio, University of Padova

Mechanisms of selection for the control of action in *D. melanogaster*

Aram Meghian, University of Padova

11:10-11:40 **Coffee break**

11:40-13:00 **Mini SYMPOSIUM VIII: Modeling neurodegenerative and mitochondrial disorders in *Drosophila***

(Chair: Diana Pendif)

Effects of oxidative stress on locomotor behavior in *D. melanogaster*

Federica De Lazzari, University of Padova

Modelling the human mitochondrial disease related to APOPT1 in *D. melanogaster*

Michele Brischigliaro, University of Padova

Functional characterization of *dMpv17* in *D. melanogaster*

Samantha Corrà, University of Padova

Downregulation of glutamic acid decarboxylase in *Drosophila* TDP-43-null brains provokes paralysis by affecting the organization of the neuromuscular synapses

Fabian Feiguin., ICGEB, Trieste

13:00-13:15 **Closing remarks**

13:15-14:30 **Lunch**

New tricks for an old clock

Dr Ezio Rosato, University of Leicester, UK

Rhythmicity is a pervasive feature of life on our planet. A prominent example is the 24 h rotation of the earth around its axis, which has favoured the evolution of endogenous biological rhythms organised by a circadian clock. Since its inception, the study of circadian rhythmicity has made huge strides in the understanding of the molecular cycles that constitute the foundation of the clock. This has resulted in the award of the Nobel Prize for Physiology or Medicine to three *Drosophila* chronobiologists in 2017. However, we still do not fully understand how the neurons expressing the components of the clock, work together to generate rhythmic behaviour.

In my presentation, I will discuss the organisation of the circadian neurons in the brain of the fly and I will present some new techniques that we are using in my laboratory to characterise the 'logic' of the network that the circadian neurons form.

Mini SYMPOSIUM I

Circadian rhythms

Cryptochrome interacts with actin and enhances eye-mediated light sensitivity of the circadian clock in *Drosophila melanogaster*

Matthias Schlichting^{1,2}, Dirk Rieger¹, Paola Cusumano³, Rudi Grebler¹, Rodolfo Costa³, Gabriella M. Mazzotta^{3#}, Charlotte Helfrich-Förster^{1#}

(1) Neurobiology and Genetics, Biocenter, Theodor-Boveri-Institute, University of Würzburg, Germany; (2) Howard Hughes Medical Institute and National Center for Behavioral Genomics, Department of Biology, Brandeis University, Waltham, USA; (3) Department of Biology, University of Padova, Italy. (#) corresponding authors.

Cryptochromes (CRYs) are a class of flavoproteins that sense blue light. In animals, CRYs are expressed in the eyes and in the clock neurons that control sleep/wake cycles, and are implied in the generation and/or entrainment of circadian rhythmicity. Moreover, CRYs are sensing magnetic fields in insects as well as in humans. Here we show that in the fruit fly *Drosophila melanogaster* CRY plays a light-independent role as “assembling” protein in the rhabdomeres of the compound eyes. CRY interacts with actin and appears to increase light sensitivity of the eyes by keeping the “signalplex” of the phototransduction cascade close to the membrane. By this way, CRY also enhances light-responses of the circadian clock. The same might be true in humans, as human CRY does also interact with actin.

Modulation of *miR-210* alters phasing of circadian locomotor activity and impairs projections of PDF clock neurons in *Drosophila melanogaster*

Paola Cusumano¹, Alberto Biscontin¹, Federica Sandrelli¹, Gabriella M. Mazzotta¹, Claudia Tregnago², Cristiano De Pittà^{1,#} and Rodolfo Costa^{1,#}

(1) Department of Biology, University of Padova, 35121 Padova, Italy; (2) Department of Women and Children's Health, University of Padova, 35121, Italy. (#) corresponding authors.

Micro RNAs are endogenous single-stranded non-coding RNAs that modulate gene expression at the post-transcriptional level and can influence several phenotypic traits, ranging from development to behaviour. In recent years, the role of *Drosophila* micro RNAs in regulating and maintaining the 24h circadian rhythmicity has been recognized. We observed that depletion or over-expression of *miR-210* in the Pigment Dispersing Factor (PDF) positive clock neurons alters the locomotion phase of flies under both light-dark conditions or constant darkness. In addition, the up-regulation of *miR-210* dramatically altered the PDF positive clock neurons morphology, suggesting a role for *miR-210* in shaping neuronal projections. A transcriptomic analysis of *miR-210* over-expressing flies revealed differentially expressed genes implicated in circadian processes, neuronal development and photoreception. Our findings indicate that *miR-210* is involved in modulating circadian output and shaping the projections of PDF clock neurons, and suggest that *miR-210* may have pleiotropic effects on clock, light perception and neuronal development.

Mini SYMPOSIUM II

Modeling human cancers in Drosophila

A neurogenic model of adult brain cancer in the fly

Simona Paglia¹, Manuela Sollazzo¹, Simone Di Giacomo¹ and Daniela Grifoni¹

(1) Department of "Pharmacy and Biotechnology", University of Bologna, Italy.

Inactivation of the tumour suppressor gene *PTEN* is prevalent in primary Glioblastoma. In mammals, *PTEN* loss has been associated with the failure of a specific molecular axis, including aPKC and Lgl, responsible for the maintenance of the Glioblastoma Stem Cells (GSCs), a *reservoir* of self-sustaining cells with characteristics similar to neural progenitors.

Here we developed a neurogenic model of *Drosophila* brain cancer based on the dysfunction of the *PTEN*- aPKC-Lgl axis in type II neuroblasts (NBs), whose differentiation proceeds through transit-amplifying intermediate precursors, as it is for mammalian neural progenitors. We obtained neurogenic tumours that express high levels of MYC, keep growing in the adult and lead the animal to premature death, summarising several traits typical of human brain cancers.

Recently, our laboratory has demonstrated that the physiological phenomenon called MYC-Mediated Cell Competition (MMCC) is conserved in human cancers, where malignant cells are likely to use MYC activity to colonise the organ. Preliminary data will be presented about a possible correlation between MMCC and cell division in brain cancer development.

***Drosophila* model to understand the role of autophagy in Glioblastoma**

Miriam Formica¹, I. Busi², T. Vaccari^{1,2}

(1) Department of Biosciences, University of Milan, Milan, Italy; (2) IFOM- the FIRC Institute for Molecular Oncology, Milan, Italy.

Autophagy is a conserved catabolic mechanism that leads to degradation of cellular constituents in lysosomes. How autophagy acts in tumour growth is currently unclear. In my project, we used *Drosophila* as a model to understand *in vivo* the role of autophagy in the development of glioma. Glioblastoma (GBM), the most aggressive and incurable tumour of the central nervous system, often results from constitutive activation of the epidermal growth factor receptor (EGFR) and phosphoinositide 3-kinase (PI3K) pathways. Therefore, we overactivated these two pathways in *Drosophila* using the glial cell-specific driver Repo-GAL4. Such manipulation results in an overgrowth of the larval brain due to a glial expansion at the expenses of the neuronal compartment, that impairs neuronal function. Interestingly we found that, compared to control, the fly glioma displays high transcriptional and protein levels of the autophagy adapter Ref(2)P. However, other crucial regulators of autophagy, such as Atg8a, are not unregulated in the glial tumour. We also observed that down-regulation of components of the vacuolar-H+ATPase (V-ATPase), which is required for lysosomal acidification and completion of autophagy, strongly reduces tumour growth and prevents Ref(2)P accumulation. Collectively, our data suggest that autophagy might be required and limiting for glioma growth.

***Drosophila* Multidrug Resistance Protein: new insights into unexplored functions of the ATP Binding Cassette (ABC) transporters.**

Sara Monticelli¹, Giorgio Milazzo¹, Roberto Ciaccio¹, Stefania Purgato¹, Giorgia Giordani¹, Giuseppe Di Candia¹, Ettore de Giorgio¹, Laura De Grandis¹, Giovanni Perini¹ and Roberto Bernardoni¹

(1) Department of Pharmacy and Biotechnology, University of Bologna, Italy.

Neuroblastoma is the most common extracranial solid tumor of childhood. Among the prognostic markers of poor tumor outcome, we find *ABCC1* overexpression and *ABCC3* downregulation. These genes encode the ABC transporters MRP1 and MRP3, Multidrug Resistance associated Proteins known to confer chemoresistance to tumor cells promoting drugs efflux. Nonetheless, even in absence of chemotherapy, MRPs seem to play a substantial role in Neuroblastoma progression both in patients and murine models. To explore the still elusive MRPs physiological function, we silenced the *Drosophila melanogaster* homolog of MRP1 (dMRP) in the wing and observed an unforeseen phenotype consisting of blisters due to detachment of the dorsal and ventral wing epithelia. This phenotype is suppressed by null mutations in genes encoding different subunits of integrins, crucial proteins for wing epithelia adhesion. This suggests that dMRP could act as integrins negative regulator. Moreover, preliminary experiments show that the “blister” is partially rescued by expression of human *ABCC1* but enhanced by human *ABCC3*. This appears consistent with the antagonistic role of MRP1 and MRP3 and their different prognostic value. Altogether, our observations point to an unforeseen MRPs role in modulating integrins activity and cell adhesion, processes that can be crucial for Neuroblastoma progression.

Growth and Tracheogenesis are Separable Traits in *Drosophila* Cancers

Manuela Sollazzo¹, Francesca Froidi², Simone Di Giacomo¹, Silvia Strocchi¹, Simona Paglia¹, Daniela Grifoni¹

(1) Department of Pharmacy and Biotechnology, University of Bologna, Italy; (2) Peter MacCallum Cancer Centre, Melbourne, Australia.

Drosophila clonal cancer models provide an excellent contribution to the study of the molecular basis of tumorigenesis. A number of human cancer hallmarks are indeed functionally conserved; among them, overgrowth and vessel remodelling are particularly relevant to primary mass formation and cell dissemination throughout the organism.

We have previously identified MYC as a Hippo downstream target in *Drosophila* and demonstrated that cells with defects in polarity genes require MYC expression to overwhelm *wild-type* neighbours and develop into malignant masses. Recent data from our lab also showed that neo-tracheogenesis does occur in *Drosophila* cancers, and it is either functionally or molecularly analogous to mammalian tumour neo-angiogenesis.

Here I extended on previous work showing that, in *Drosophila* epithelial tumours, mass expansion and tracheogenesis are separable traits, dependent on MYC and FOS activity respectively. These two transcription factors are found at the intersection of the Hippo, JNK and Ras/MAPK signalling cascades, which are recognised as central actors in cancer progression.

New roles for old trafficking proteins

Thomas Vaccari, University of Milan

The Vaccari lab investigates fundamental questions concerning the role of membrane trafficking in tissue architecture in health and in disease. In particular, we focus on the function of trafficking regulators, such as Endosomal Sorting Required for Transport (ESCRT) proteins, vacuolar-H⁺ ATPase (V-ATPase) components and Soluble NSF Attachment Protein Receptors (SNAREs), such as Snap29, that control endocytosis and autophagy. Using *Drosophila melanogaster* as a model system, we have recently studied the role of lysosomal plasticity in regulation of Notch signaling (Tognon et al 2016 Autophagy) and the function of Snap29 in autophagy and in cell division (Morelli et al 2014 Autophagy; Morelli, Mastrodonato et al 2016 The EMBO Journal). During the seminar, I will discuss recent data about the novel function of Snap29 during mitosis and I will share unpublished data concerning the role of additional trafficking regulators that appear to play a role in neuronal health.

Morelli E, Ginefra P, Mastrodonato V, Beznoussenko GV, Rusten TE, Bilder D, Stenmark H, Mironov AA, Vaccari T (2014). Multiple functions of the SNARE protein Snap29 in autophagy, endocytic, and exocytic trafficking during epithelial formation in *Drosophila*. *Autophagy* 10(12):2251-68.

Morelli E, Mastrodonato V, Beznoussenko GV, Mironov AA, Tognon E, Vaccari T. (2016). An essential step of kinetochore formation controlled by the SNARE protein Snap29. *EMBO J* 35(20):2223-2237.

Tognon E, Kobia F, Busi I, Fumagalli A, De Masi F, Vaccari T. (2016). Control of lysosomal biogenesis and Notch-dependent tissue patterning by components of the TFEB-V-ATPase axis in *Drosophila melanogaster*. *Autophagy*. 12(3):499-514

Mini SYMPOSIUM III

Fusion and fission dynamics in Drosophila

Studying how the SNARE protein Snap29 regulates membrane fusion at the Golgi apparatus during interphase and moves towards chromosomes at the onset of mitosis

Elisa Speranza¹, Elena Morelli¹ and Thomas Vaccari¹

(1) *Department of Bioscience, University of Milano, Italy.*

Recently, it emerged that the soluble SNARE protein Snap29, known to control fusion between two membranes during interphase, has also a function in kinetochore formation during mitosis. It remains still obscure how Snap29 reaches kinetochores, whether it does it as part of membrane compartments or in complex with soluble proteins.

We previously found that Snap29 localizes at the Golgi apparatus during interphase both in *Drosophila* and mammals. Interestingly, preliminary analysis in human cells reveals that at the onset of mitosis the pool of human Snap29 (hSNAP29) at the Golgi apparatus moves toward chromosomes. Thus, we analyzed the behavior of a CFP-tagged version of *Drosophila* Snap29 (dSnap29) in S2 cells and embryos.

In addition, we observed that both proteins exert a role at Golgi, as their depletion leads to severe Golgi apparatus defects. In particular, as hSNAP29 collaborates with Sec22 and Stx18 to control COPI vesicles trafficking, we tested whether also dSnap29 interacts and localizes with Sec22 and Stx18 in S2 cells.

Our preliminary data indicate that the Snap29 function at Golgi is conserved in *Drosophila* and mammals and suggest that the pool of Snap29 at kinetochores derives from that at the Golgi apparatus.

Shaping the endoplasmic reticulum: fusion and fission dynamics revealed in flies.

Diana Pendin¹ Anna Shnyrova^{2,3,4}, Nicola Vajente¹, Vadim A. Frolov^{2,3,4}, Andrea Daga⁵.

(1) *Department of Biomedical Sciences, University of Padua, Padua, Italy;* (2) *Biofisika Institute (CSIC-UPV/EHU), Leioa, Spain;* (3) *Departamento de Bioquímica y Biología Molecular, Universidad del País Vasco, Leioa, Spain;* (4) *IKERBASQUE, Basque Foundation for Science, 48011 Bilbao, Spain;* (5) *E. Medea Scientific Institute, Conegliano, Italy.*

The endoplasmic reticulum (ER) is composed of a network of interconnected tubules that pervades the cytoplasm of eukaryotic cells. Network maintenance requires the controlled action of proteins producing membrane curvature and fusion (Pendin, 2011). We previously identify the GTPase Atlastin as the crucial mediator of homotypic fusion of ER membranes (Orso, 2009). Membrane fission antagonize the fusogenic activity of atlastin in the ER, however no dedicated fission machinery has been identified yet.

Using *Drosophila* as a model, we identified the molecular antagonist of atlastin, mediating fission of ER membranes. The concerted action of the two proteins ensures coordinated membrane remodelling, aimed at maintaining ER complex structure, which is essential for its proper function.

References:

Pendin D, McNew JA, Daga A. Balancing ER dynamics: shaping, bending, severing, and mending membranes. *Curr Opin Cell Biol.* 2011 Aug;23(4):435-42.

Orso G, Pendin D, Liu S, Tosetto J, Moss TJ, et al. Homotypic fusion of ER membranes requires the dynamin-like GTPase atlastin. *Nature.* 2009 Aug 20;460(7258):978-83.

Mini SYMPOSIUM IV

**Lysosomal and ER disorders in
*Drosophila***

Gaucher Disease: a Hyper-Hippo Syndrome?

Silvia Strocchi¹, Daria Messelodi², Andrea Pession^{2,3}, Daniela Grifoni¹

(1) Pharmacy and Biotechnology Department, University of Bologna; (2) Medical and Surgical Department, University of Bologna; (3) Inter-Departmental Centre of Cancer Research "Giorgio Prodi", University of Bologna.

The Gaucher Disease (GD) is a lysosomal disorder associated with mutations in the *GBA1* gene, encoding the acidic β -glucocerebrosidase. GD is characterized by a wide spectrum of phenotypic manifestations, the most severe of which involve the nervous system, with massive neuronal loss and microglial proliferation. Different symptoms are also observed in individuals bearing identical *GBA1* mutations, suggesting that additional players are involved in the disease.

Our hypothesis is that hyper-activation of the Hippo pathway, recently found involved in some neurodegenerative syndromes, may contribute to the dramatic outcome of the neuronopathic GD. We thus started an expression analysis of upstream and downstream Hippo pathway components in *Drosophila* *GBA1*-deficient larval and adult organs.

While some Hippo downstream targets resulted down-regulated in *GBA1*-deficient tissues, both in terms of transcript and protein content, Fat, an atypical cadherin upstream of the kinase complex involved in the regulation of glial and synapse development, was found up-regulated. In the light of this latter result, we are currently performing behavioural assays in flies where *GBA1* expression has been silenced in glial or neuronal cells, to find out possible cross-effects. Preliminary data will be presented about the implication of the Hippo pathway in the pathogenesis of the neuronopathic GD.

Characterization of Cathepsin F CRISPR/Cas9 mutants in *Drosophila* as a targeted *in vivo* model of type B Kufs disease.

M. Gualtieri¹, V. Alfred², T. Vaccari^{1,2}

(1) Department of Biosciences, University of Milan, Milan, Italy; (2) IFOM- the FIRC Institute for Molecular Oncology, Milan, Italy.

The human protease Cathepsin F (CTSF) is mutated in Type B Kufs disease, a lysosomal storage disorder (LSD) whose pathogenesis is unclear. Sequence similarity investigation led to the identification of CG12163 as the uncharacterized orthologue of CTSF. To study Cathepsin F in *Drosophila*, we generated knock-out mutants by CRISPR/Cas9 gene editing and we asked whether loss of CG12163, which we named *cathF*, could recapitulate the traits of type B Kufs disease *in vivo*. We have found that *cathF* mutants are viable and show no morphologic phenotypes. However, already at young age they present neurodegenerative traits such as impairment of motor function and brain vacuolization, which worsen with aging. We also observed accumulation of autofluorescence lipofuscin, a typical sign of the disease, both in larval organs and adult brains. Interestingly, by Western blot and immunofluorescence analyses, in *cathF* mutants we have also found alterations of autophagy that have not previously been associated to Type B Kufs disease. Altogether, our data indicate that *Drosophila cathF* mutants are a promising model to study Type B Kufs disease that might illuminate new aspects of the LSD pathogenesis and pave the way to future pharmacologic treatments.

Translational control of the ODC/polyamine axis by CNBP is required for muscle function in *Drosophila melanogaster*

Laura Ciapponi¹

(1) Department of Biology and Biotechnologies, C. Darwin, Sapienza, University of Rome, 00185 Italy.

CNBP (ZNF9) is a conserved CCHC-type zinc finger RNA binding protein that regulates translation and is required for normal mammalian development. Mutations in the first intron of the *CNBP* gene have been found in type 2 myotonic dystrophy, although it is still unclear whether the dystrophic phenotype is linked to a decrease of CNBP levels and/or to accumulation of toxic mRNAs. Here we show that dCNBP depletion in *Drosophila melanogaster* muscles causes locomotor defects due to impaired polyamine metabolism. Indeed, we demonstrate that the levels of ornithine decarboxylase (ODC) and polyamines are significantly reduced in dCNBP-depleted or mutant larvae compared to wild type controls, and that ODC depletion phenocopies the dCNBP-dependent locomotor defects. Mechanistically, we have found that dCNBP controls polyamine metabolism through dODC1 ribosomal entry site (IRES)-dependent translation. Of note, dCNBP locomotor defect is rescued by either polyamine feeding or dODC1 over expression. Together, our data illustrate an unprecedented mechanism whereby dCNBP controls muscle function by regulating the ODC/polyamine axis. This function of dCNBP may be evolutionarily conserved in vertebrates, with relevant implications in CNBP-related pathophysiological conditions.

Mini SYMPOSIUM V

**Epigenetics and DNA damage response
in *Drosophila***

Unmasking the encrypted role of dTip60 chromatin remodelling complex in cell division

Giovanni Messina^{1,2}, Maria Teresa Atterato^{1,2}, Francesca Delle Monache¹, Yuri Prozzillo^{1,2}, Manuela Leo¹, Stefano Cuticone^{1,2}, Patrizio Dimitri^{1,2}

(1) Department of Biology and Biotechnology "C. Darwin", Sapienza University of Rome, Italy; (2) Pasteur Institute - Fondazione Cenci Bolognetti, Sapienza University of Rome, Italy.

Cells utilize ATP-dependent nucleosome-remodelling complexes to regulate chromatin structure and gene expression ¹. In addition to its role in exchanging phospho-H2A.V with an unmodified H2A.V ², *Drosophila* Tip60 (dTip60) complex has been shown to be involved in cell cycle regulation. Indeed, 1) four subunits of the dTip60 complex, DOM-A, YETI, Tip60 and MRG15, are recruited to the mitotic apparatus in S2 cells ³; 2) subunits of two human chromatin remodelling complexes (SRCAP and P400/Tip60) related to dTip60 complex, relocate from chromatin to the mitotic structures ³; and 3) RNAi-depletion of these proteins affect chromosome segregation, leading to polyploidy and multinucleation ³. Thus, translocation of remodelling factors from interphase chromatin to the mitotic apparatus suggests highly regulated mechanism of localization possibly related to their function of poorly understood evolutionary conserved phenomenon which is worth elucidating.

For this purpose, we will exploit CRISPR/Cas9 technology to specifically destroy *dom*, *yeti*, *tip60* or *mrg15* genes, and repair them with the 'Auxin inducible'-tagged versions for rapid protein degradation. We plan to use *Drosophila* testis as the experimental system because of the peculiar ability of the meiotic cysts to undergo to synchronous divisions which can be easily imaged by using *in vivo* time-lapse microscopy to depict chromosome segregation and mitotic defects.

HP1a interacts with NBS to maintain chromosome integrity in both *Drosophila* and human cells

Bosso G.^{1,3}, Cipressa F.^{1,3}, Pennisi R.², Moroni M.¹, Ciapponi L.¹, Di Masi A.², Antoccia A.², Cenci G^{1,3}

(1) SAPIENZA Università di Roma, Rome, Italy; (2) Università di Roma Tre, Rome, Italy; (3) Fondazione Cenci Bolognetti/Istituto Pasteur, Rome.

The Heterochromatin Protein 1 a (HP1a) is a versatile protein known to be primarily involved in heterochromatin formation and gene silencing. Recent studies have also highlighted the importance of HP1-mediated chromatin remodeling and chromosome integrity, although its involvement in the latter function is still largely unexplored. Here we show that the *Drosophila* *Su(var)205*-encoded HP1a is able to physically interact with the Mre11-Rad50-NBS (MRN) complex in normal cells. GST-pulldown assays using different HP1a truncated forms revealed that MRN binds HP1 at the chromoshadow (CSD) domain and that this interaction depends on both CSD dimerization and the canonical HP1a interface. Interestingly, depletion of NBS, but not of Rad50 and Mre11, reduces HP1a levels while HP1 influences neither abundance nor localization of NBS. This indicates that NBS is required to regulate a proper HP1 turnover independently of Rad50 and Mre11. Moreover, the expression of a *HP1-RFP* encoding transgene reduces the number of spontaneous chromosome aberrations observed in *nbs* mutants, but has no effect on chromosome breaks generated as a consequence of *rad50* mutations, indicating that the NBS-dependent regulation of HP1 is important to prevent DSBs. We also show that, consistently with the results obtained in the *Drosophila*, siRNA-mediated depletion of hsNBS leads to a reduction of hsHP1a levels also in human fibroblasts. In addition, we have also observed by coIP that endogenous hsHP1 physically interacts with hsNBS. Altogether, our results suggest that the HP1-NBS relationship is evolutionarily conserved and might shed more lights on the pathogenic mechanisms associated with NBS dysfunction.

Interactions between *pendolino* and histone modifiers reveal an epigenetic regulation of *Drosophila* telomere stability

Federica Mosti¹, Marta Marzullo¹, Maurizio Gatti¹ and Laura Ciapponi¹

(1) Department of Biology and Biotechnologies, C. Darwin, Sapienza, University of Rome, 00185 Italy.

Drosophila telomeres are maintained by transposition to chromosome ends of specialized retroelements rather than telomerase activity. Fly telomeres are capped by the terminin complex that localizes and functions exclusively at telomeres, and by a number of non-terminin proteins that do not serve telomere-specific functions. *pendolino* (*peo*), encodes a non-terminin protein homologous to the E2 variant ubiquitin-conjugating enzymes. *peo* mutants exhibit frequent telomeric fusions (TFs) that preferentially involve the heterochromatin-associated telomeres. Mutations in *peo* strongly reduce di- and tri-methylation at lysine 9 (K9) of histone H3 in both heterochromatin and telomeres. Double mutants for *Su(var)3-9⁶*, a viable mutant allele in the histone H3 methyltransferase (HMTase) coding gene, and the *peo^h* allele, which is also viable, die during embryogenesis. In addition, mutations in *Su(var)3-9*, dominantly enhance the TF frequency in *peo* mutants. These results implicate for the first time H3K9 methylation in *Drosophila* telomere maintenance. We propose that when reduction of H3K9 methylation at telomeres falls below a critical threshold, telomeric DNA replication is severely disturbed resulting in the formation of fusigenic lesions at chromosome ends. Because methylated H3K9 is particularly enriched in heterochromatin, we envisage that heterochromatin-associated telomeres accumulate more fusigenic lesions than their euchromatin-associated counterparts.

Low doses of gamma irradiation render *Drosophila melanogaster* resistant to the DNA damage

Porrazzo A.¹, Cipressa F.^{1,4}, Morciano P.¹, Esposito G.², De Pittà C.³, Sales G.³, Tabocchini M.A.^{2,4}, Cenci G.^{1,4}

(1) SAPIENZA Università di Roma, Rome, Italy; (2) Istituto Superiore di Sanità (ISS) and INFN-Roma 1 Gr.coll.Sanità, Rome, Italy; (3) Università degli Studi di Padova, Padova, Italy; (4) Centro Studi e Ricerche "Enrico Fermi", Rome, Italy.

A major issue of radiation biology research is evaluating whether low doses of ionizing radiation (LDR) potentially affect human health. Despite the large number of studies addressing this issue, a mechanistic understanding of the effects of LDR in cells, tissues, organ and organisms is still elusive and the analysis of low dose radiation human risk continue to be a focus of intense debate and significant controversy. We have recently found that wild-type *Drosophila melanogaster* flies, chronically exposed to a priming γ -radiation dose of 40cGy, delivered at the LIBIS facility with a dose rate of 2.5 mGy/h during embryo-to-third instar larvae development, exhibited a strong reduction (~50%) of chromosome break frequency after a challenge dose of 10Gy with respect to untreated flies directly exposed to 10Gy. This indicates that a chronic exposure of 40cGy (dose rate of 2.5 mGy/h) renders flies more resistant to genotoxic threats suggesting that LDR can induce an adaptive response to DNA damage in *Drosophila* somatic tissues. This effect is associated with changes in the dynamics of γ -H2AV (the *Drosophila* H2AX ortholog) recruitment at DNA damage sites, as revealed by cytological and WB analyses. In addition our genetic and RNA-seq data indicate that this response largely depends on the genetic background and is associated with changes of few RNAs. As *Drosophila* is emerging as one of the most effective *in vivo* model for studying the consequences of radiation exposure, our data will shed more light on the *in vivo* effects of LDR also in humans.

The TGS1 hypermethylase plays a conserved role in the biogenesis of snRNAs

Francesca Bavasso¹, Paolo Maccallini¹, Veronica Lisi¹, Caitlin Roake², Steven Artandi², Maurizio Gatti¹, Grazia Daniela Raffa¹

(1) Sapienza Università di Roma; (2) Stanford University, California, USA.

Spinal muscular atrophy is a devastating neurodegenerative disease caused by mutations in SMN, an ubiquitous protein, conserved from flies to humans. SMN is a molecular chaperone, essential for snRNP assembly; however, why loss of SMN induces neuronal death and whether defects in snRNP lead to motor neuron disease are still unanswered questions. Recent work has shown that the *Drosophila* model allows identification of phenotypic modifiers of SMN function, thus uncovering genetic pathways important for SMA pathogenesis. We found that RNAi-mediated depletion of *Smn* in fly neurons results in locomotion and post-eclosion defects and that the *Smn* loss of function phenotypes are alleviated by overexpression of *Tgs1* (trimethylguanosine synthase 1). *Tgs1* is the enzyme responsible for the hypermethylation of the monomethylguanosine cap of several noncoding RNAs, including snRNAs and in human cells TGS1 cooperates with SMN in the biogenesis of snRNPs, although the precise role of cap hypermethylation is still unknown. We found that *Tgs1* loss results in a phenotype similar to that elicited by *Smn* depletion and that expression of a human *TGS1* transgene fully rescues the lethality of null mutations in *Tgs1*, thus indicating that TGS1 function is conserved across evolution. Here we investigated how *Tgs1* affects the biogenesis of snRNAs and explored the role of TGS1 as an *Smn* modifier and as a potential causative factor for SMA.

Mini SYMPOSIUM VI

Genome stability in *Drosophila*

Roles of *dFmr1*, the *Drosophila* homolog of the human gene responsible for the Fragile X syndrome, in the genome stability.

Antonietta Puricella¹, Simona D'Attis¹, Pierre Cattenoz¹, Celine Diebold¹, Angela Giangrande¹, Valeria Specchia¹ and Maria Pia Bozzetti¹

(1) DiSTeBA -Università del Salento, Lecce, Italy.

dFmr1 is the *Drosophila* homolog of the human gene responsible for the Fragile X syndrome which is the most common form of inherited mental retardation in humans. *dFmr1* is an RNA binding protein and contains evolutionary conserved domains: KH, RGG and two Tudor domains. The *dFmr1* protein is predominantly cytoplasmic, but it has also been localized in the nuclei. Some genetic and biochemical *dFmr1* interactors have been described, participating in clarifying its role in the nervous system and even in the gonads. *Drosophila melanogaster* is a good model for the study of the syndrome: *dFmr1* mutant flies exhibit phenotypes that correlate well with the neurological and gonadal defects shown by the Fragile X patients. Recently our group demonstrated a role of *dFmr1* in the piRNA-mediated silencing of the transposable elements in the gonads discovering an unexpected function of *dFmr1* in the genome stability. Here we present data on the role of *dFmr1* in the piRNA-mediated genome stability in the fly brain suggesting a possible role of the piRNA pathway in the nervous system. This new finding may open novel perspectives for the understanding of the molecular mechanisms underlined the severe neurological phenotypes of the Fragile X patients.

The magic inside: the universal promoter of two *Drosophila* transposons of the Bari family

Antonio Palazzo^{1,2}, Patrizio Lorusso¹, René Massimiliano Marsano¹

(1) Department of Biology, University of Bari, via Orabona 4, 70125 Bari, Italy; (2) Laboratory of Translational Nanotechnology, "Istituto Tumori Giovanni Paolo II" I.R.C.C.S., Viale Orazio Flacco 65, 70125 Bari, Italy.

The promoter has a crucial role in the initial expression and regulation of the enzymatic machinery mediating the movement of transposable elements. The promoters of transposable elements are poorly studied despite the great amount of data on their distribution and lot of studies on their biological activity. To start gaining information on this aspect of the transposon biology, we have started a preliminary study of the properties of the promoter of three Class I (*Copia*, *ZAM* and *Tirant*) and two Class II (*Bari1* and *Bari3*) *Drosophila* transposons. Using a simple approach, we have disclosed a unique feature of the *Bari* transposons' promoters, which are able to drive the expression of a reporter gene in distantly related organisms from eukaryotes to prokaryotes. Contrastingly, the transcriptional activity of the promoter of three Class I elements is mostly confined in the species of origin or, at least, in strictly related species. This "magic" feature could help explain why some transposable elements have an enhanced ability to be horizontally transferred. These findings are important for a complete understanding of the biology and ecology of transposable elements and could be relevant for the development of multi-host expression vectors.

Silencing of P-element mini-white reporters induced by functional domains of pericentric heterochromatin in *Drosophila melanogaster*.

E. Celauro¹, S. Cuticone¹, F. De Gori¹, P. Dimitri¹

(1) Dipartimento di Biologia e Biotecnologie, Sapienza Università di Roma, Roma, Italy.

P-element-derived reporter genes inserted throughout the *Drosophila melanogaster* genome are routinely used to monitor the functional state of chromatin regions. It is commonly thought that P element-reporter genes are subjected to PEV when transposed into pericentric heterochromatin, because they acquire heterochromatin-like epigenetic modifications that promote silencing. Pericentric heterochromatin of *Drosophila melanogaster*, in addition to highly repetitive satellite DNAs, contains islands of complex DNAs enriched in actively transcribed protein-coding genes. Thus, in principle, transcriptionally active heterochromatin domains should be able to drive proper expression of reporter genes inserted therein. Unexpectedly, our data indicate that domains of pericentric heterochromatin, albeit being capable of sustaining transcription of autochthonous protein-coding genes, can efficiently induce silencing of mini-white reporters. Surprisingly, while silencing of most mini-white reporters can be suppressed by different *Su(var)* mutations, two of them inserted into the coding regions of the *Yeti* gene are *Su(var)* insensitive. The molecular bases underlying this intriguing phenomenon (RNAi, chromatin modifications) will be discussed.

A tale of sleepless flies and *ninna nanna*.

How *Drosophila* changes what we know about sleep

Giorgio Gilestro, Imperial College London, London, UK

Our laboratory studies the neurobiology of behaviour in *Drosophila melanogaster*, with a strong emphasis on sleep. In particular, we are trying to uncover the still mysterious function(s) of sleep, using a systems neuroscience approach. The talk will present some of the recent and unpublished data of the lab as paradigmatic of what flies can teach us about sleep: I will introduce a new exciting gene regulating sleep in flies (*ninna nanna*) which uncovers new circuits and new, potentially conserved, molecular mechanisms. We will also revise the real consequences of sleep deprivation in flies, with unexpected and very surprising results.

Mini SYMPOSIUM VII

Analysis of behaviour in *Drosophila*

Opinion and Behaviour Dynamics in Fruitfly Populations

Francesca Minchio¹, Giovanni Frighetto², Angelo Cenedese^{1,5} Mauro A. Zordan^{3,5} and Aram Megighian^{4,5}

(1) Department of Information Engineering, University of Padova, 35131, via Gradenigo 6b, Padova, Italy; (2) Department of General Psychology, University of Padova, 35131, via Venezia 8, Padova, Italy; (3) Department of Biology, University of Padova, 35121, via G. Colombo 3, Padova, Italy; (4) Department of Biomedical Sciences, University of Padova, 35131, via U. Bassi 58/B, Padova, Italy; (5) Padova Neuroscience Center, University of Padova, Padova, Italy.

Drosophila melanogaster are insects that can detect and provisionally store notions of different types. Recently, studies on social learning in flies have been conducted. However, the extent to which they use and share such information with other flies remains unclear. To address this shortcoming, we wished to provide further elements to clarify this point. **Methods:** After building an agent-based network both intuitively and using a Hidden Markov Model (HMM) based approach, we implemented the popular DeGroot-Friedkin's reflected appraisal model, considering each fly as an agent of an influence network, i.e. a network where each individual's self-appraisal powers the dynamics of information spreading and knowledge distribution within the population. In particular, we allow the possibility that flies might never change their "opinions" despite social interactions, considering also the agents' "stubbornness". Finally, we evaluate the model by analyzing the equilibrium of opinions of several agent-networks, including a network obtained from a literature experimental dataset. **Results:** Same qualitatively results have been obtained both with the intuitive approach and the HMM, confirming the consistence of our model. Furthermore, investigating flies' social-learning performances, we found consistence between our results and the literature. **Conclusions:** In this study, we found that flies' opinions dynamics analysis is a good way to model the notion acquisition process, during flies' interactions, confirming *Drosophila*' low-level social skills.

Mechanisms of selection for the control of action in *Drosophila melanogaster*

Giovanni Frighetto¹, Umberto Castiello^{1,4}, Aram Megighian^{3,4} and Mauro A. Zordan^{2,4}

(1) Department of General Psychology, University of Padova, 35131, via Venezia 8, Padova, Italy; (2) Department of Biology, University of Padova, 35121, via G. Colombo 3, Padova, Italy; (3) Department of Biomedical Sciences, University of Padova, 35131, via U. Bassi 58/B, Padova, Italy; (4) Padova Neuroscience Center, University of Padova, Padova, Italy.

In the last few years several studies have investigated the neural mechanisms underlying spatial orientation in *Drosophila melanogaster*. Convergent results suggest that this mechanism is associated with specific neural circuits located within the Central Complex (CC). Furthermore such circuits appear to be associated with visual attention, specifically with selective attention processes implicated in the control of action. Our aim was to understand how wild-type flies react to the abrupt appearance of a visual distractor during an ongoing locomotor action. Thus, we adapted the well-known 'Buridan paradigm', used to study walking behaviour in flies, so we could specifically address the mechanisms involved in action selection. We found that flies tended to react in one of two ways when confronted with a visual distractor during ongoing locomotion. Flies either: (i) committed to a new path situated midway between the original target and the distractor, consistent with a novelty effect; or (ii) remained on the original trajectory with a slight deviation in the direction of the distractor. We believe that these results provide the first indication of how flies react, from the motor point of view, in a bi-stable context requiring the presence of selection-for-action mechanisms. Some considerations on the neural circuits underlying such behavioural responses are advanced.

Mini SYMPOSIUM VIII

**Modeling neurodegenerative and
mitochondrial disorders in *Drosophila***

Effects of oxidative stress on locomotor behaviour in *Drosophila melanogaster*

Federica De Lazzari¹, Giovanni Frighetto², Mauro Agostino Zordan¹, Aram Megighian³, Federica Sandrelli¹, Marco Bisaglia¹

(1) Department of Biology, University of Padova, Padova, Italy; (2) Department of General Psychology, University of Padova, Padova, Italy; (3) Department of Biomedical Sciences, University of Padova, Padova, Italy.

Imbalance in cellular redox state has been suggested as one of the major pathophysiological mechanisms underlying diverse motility disorders, such as Parkinson's disease and amyotrophic lateral sclerosis. In this scenario, the protective enzyme Superoxide Dismutase 1 (SOD1), which is involved in maintaining redox homeostasis, seems to play a central role. The activity of SOD1 relies on the presence of a copper ion in its active site, the insertion of which is mediated by the activity of a dedicated copper chaperone (CCS).

We exploited *Drosophila melanogaster* as an *in vivo* model to investigate the consequences of different oxidative conditions on locomotor behaviour, in wild-type as well as in Sod and Ccs mutant flies. Individuals were evaluated for resistance to oxidative insults and subsequently assessed for locomotor deficits by analysing climbing ability and a suite of locomotor activity parameters. As expected, *sod* mutants are short-lived and extremely sensitive to oxidative stimuli, while *ccs* null flies present a milder phenotype, which becomes evident under oxidative insult.

Furthermore, we were able to associate alterations in the oxidative state to locomotion defects and to discriminate between muscular and neuronal dysfunction.

Modelling the human mitochondrial disease related to APOPT1 in *D. melanogaster*

Michele Brischigliaro¹, Samantha Corrà¹, Eleonora Simonetto¹, Massimo Zeviani², Rodolfo Costa¹, Cristiano De Pittà¹

(1) Department of Biology, University of Padova, Padova, Italy; (2) MRC Mitochondrial Biology Unit, Cambridge CB2 0XY, UK.

Mitochondrial diseases (MD) are a clinically heterogeneous group of inherited disorders associated with defects in the oxidative phosphorylation system, with an estimated incidence range between 1:5,000 and 1:10,000 live births. Mitochondrial respiratory chain function depends on the coordinated expression of both mitochondrial and nuclear genomes. The large number of clinical traits of these disorders makes the diagnosis really challenging. Thanks to the advance in Next Generation Sequencing (NGS) techniques the identification of the genetic cause of MD has been considerably improved. However, only few diseases have been well-characterized and many genes related to MD are still being discovered. Mutations in the *APOPT1* gene have been identified in patients affected by COX deficiency with a peculiar brain MRI (magnetic resonance imaging) pattern showing early and rapid onset of cavitating leukodystrophy, neurometabolic decompensation, ataxia and spastic tetraparesis. To elucidate the role of APOPT1 in mitochondria homeostasis we exploited *dApopt1* (CG14806) knockdown (KD) flies. These flies show signs of neurodegeneration and locomotor defects, with a reduction in COX activity. Interestingly, *Apopt1* expression levels raise in wild-type flies in response to treatment with hydrogen peroxide. So, *D. melanogaster* can be considered a promising model for the study of this pathology because many of the defects found in patients with mutations in the *APOPT1* have been also found in *dApopt1* KD flies.

***Drosophila melanogaster* as a model to study dMpv17 role in mitochondrial DNA maintenance and metabolism**

Samantha Corrà¹, Michele Brischigliaro¹, Vanessa Checchetto¹, Emanuela Bottani², Chiara Rampazzo¹, Cristina Gagliani³, Katia Cortese³, Ildikò Szabò¹, Daniele Ghezzi^{4,5}, Massimo Zeviani², Rodolfo Costa¹, Cristiano De Pittà¹

(1) Dipartimento di Biologia, Università degli Studi di Padova, Padova, Italy; (2) MRC Mitochondrial Biology Unit, Cambridge, UK; (3) DIMES – Department of Experimental Medicine, University of Genova, Genova, Italy; (4) Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; (5) Fondazione IRCCS Institute of Neurology "Besta", Milano, Italy.

Mitochondrial disorders are defined as clinical entities associated with defects of oxidative phosphorylation, which are ultimately genetically determined. Mutations in *MPV17* are a prominent cause of hepatocerebral mitochondrial DNA depletion syndrome, accounting for about 50% of the cases. Patients are characterized by severe liver failure, steatosis, hypoglycemia, and neurological symptoms, leading to death in the first year of life. In *D. melanogaster*, *dMpv17* (*CG11077*) encodes a small hydrophobic mitochondrial inner membrane protein of 176 amino acids and its down-regulation causes a profound mitochondrial DNA depletion in fat bodies that can be considered similar to human liver and white adipose tissue. However, mitochondrial dNTPs pools are unaffected in *dMpv17* silenced cells. Similarly, to human condition, we observed an impairment of mitochondrial cristae morphology in fat bodies of *dMpv17* KD flies. Interestingly, we observed an altered expression profiles of genes involved in insulin signaling, lipid and glucose metabolism in *dMpv17* KO flies with respect to control. In starvation KO flies showed a significant decrease in survival. These results suggest an involvement of *dMpv17* in energy metabolism and in key endocrine pathways conserved from flies to humans.

Downregulation of glutamic acid decarboxylase in *Drosophila* TDP-43-null brains provokes paralysis by affecting the organization of the neuromuscular synapses

Giulia Romano¹, Nikola Holodkov¹, Raffaella Klima¹, Federica Grilli¹, Corrado Guarnaccia¹, Monica Nizzardo², Federica Rizzo², Rodolfo Garcia¹ and Fabian Feiguin¹

(1) International Centre for Genetic Engineering and Biotechnology, Padriciano 99, 34149 Trieste, Italy.

Amyotrophic lateral sclerosis is a progressive neurodegenerative disease that affects the motor system, comprised of motoneurons and associated glia. Accordingly, neuronal or glial defects in TDP-43 function provoke paralysis due to the degeneration of the neuromuscular synapses in *Drosophila*. To identify the responsible molecules and mechanisms, we performed a genome wide proteomic analysis to determine differences in protein expression between wild-type and TDP-43-minus fly heads. The data established that mutant insects presented reduced levels of the enzyme glutamic acid decarboxylase (*Gad1*) and increased concentrations of extracellular glutamate. Genetic rescue of *Gad1* activity in neurons or glia was sufficient to recuperate flies locomotion, synaptic organization and glutamate levels. Analogous recovery was obtained by treating TDP-43-null flies with glutamate receptor antagonists demonstrating that *Gad1* promotes synapses formation and prevents excitotoxicity. Similar suppression of TDP-43 provoked the downregulation of *GAD67*, the *Gad1* homolog protein in human neuroblastoma cell lines and analogous modifications were observed in iPSC-derived motoneurons from patients carrying mutations in TDP-43, uncovering conserved pathological mechanisms behind the disease.

Department of Biology
University of Padova
Via U. Bassi, 58/B
Padova

