

Curriculum Vitae

Marta Marzullo

CURRENT POSITION

01/01/2018-to date

Postdoctoral Researcher

Telomere and Genome stability group,
Insituto Gulbenkian de Ciência (IGC), Oeiras, Portugal

Advisor: Miguel Godinho Ferreira

Project: “Age as a Carcinogen – are Telomeres the culprit?”

I'm currently working on the characterization of the systemic effect of telomere shortening, using the model system *Danio Rerio* (Zebrafish). We use the telomerase mutant (*tert*^{-/-}) to dissect the consequences of telomere attrition at cell and tissue level. Ultimately, aiming to define the pathways involved in aging in human and to contribute to find therapy for aging-associated diseases.

PAST POSITION

15/11/2016- 30/11/2017

Postdoctoral Researcher

Department of Biology and Biotechnologies “C. Darwin”,
Sapienza, University of Rome. Italy

Advisor: Laura Ciapponi and Maurizio Gatti

Project: “Exploiting the *Drosophila* model system to investigate the function of human proteins involved in telomere maintenance”

01/11/2013- 31/10/2016

PhD student

Department of Biology and Biotechnologies “C. Darwin”,
Sapienza, University of Rome. Italy

Advisor: Laura Ciapponi and Maurizio Gatti

Project: “*pendolino (peo)*, a *Drosophila* gene preferentially required for heterochromatic telomeres protection”

EXPERTIS AND SKILLS

Lab Techniques

- Genetics and cytology:

Zebrafish- Maintaining Zebrafish stock (stocks maintenance, genotyping, crosses, mutant analysis).Genetic screening. Fish organs dissection and fixation. Histopathological analysis of specific tissues and cells (Beta-Gal assay, H&E, IF, etc). Induction of enterocolitis (through anal injection and or oral gavage).

Analysis of the main inflammatory pathways. Analysis of the consequences of telomere shortening.

Drosophila- Genetic screening. Culturing of *Drosophila* stocks, formal genetics analysis (stocks maintenance, mutant analysis, recombination, mutation induction). Chromosomes analysis, direct and indirect immunofluorescence. Mitosis and Meiosis analysis

- **Cell biology:** *Drosophila* cell cultures maintenance, transfection and manipulation.

- **Molecular Biology and Biochemistry:** Standard molecular biology techniques to analyze nucleic acids and proteins; DNA and RNA extraction, PCR, RT-PCR, Real-Time PCR, cloning, sequencing analysis, western blotting, protein purification, co-immunoprecipitation, GST-pulldown, ChIP, induction of Crispr-Cas9 mutation.

IT skills

Word, PowerPoint, Excel, Photoshop, Image J, FIJI, Image Lab, Sequencer

Languages

Italian: native

English: good level spoken and written

EDUCATION

25/02/2017

PhD degree in Genetics and Molecular Biology

Department of Biology and Biotechnologies “C. Darwin”,
Sapienza, University of Rome. Italy

Supervisor: Laura Ciapponi

Thesis title: *pendolino (peo)*, a *Drosophila* gene preferentially required for “heterochromatic telomeres” protection

Classification: Excellent

Project: I used molecular, biochemical and cytological approaches to characterize *Peo* molecular functions. I analyzed the effects of mutations in *peo* on the heterochromatin state and how changes of the epigenetic modifications could impair telomere stability leading to the formation of telomere fusions.

25/07/2013

Master’s degree in Genetics and Molecular Biology

Department of Biology and Biotechnologies “C. Darwin”,
Sapienza, University of Rome. Italy

Thesis title: Role of *pendolino* gene in the heterochromatic telomeres stability in *Drosophila melanogaster*

Supervisor: Laura Ciapponi

Vote: 110/110 summa cum laude

Project: I examined the particular telomere fusions phenotype of the *peo^h* allele analyzing the chromosomes morphology of the larval brain metaphases. I compared *peo* telomere fusion phenotype with those of other telomere mutants.

I analyzed the genetic interactions of *peo* with genes encoding for factors involved in heterochromatin and telomere maintenance. I also investigated through immunofluorescence experiments the localization of proteins required for telomere stability in *peo* mutants in different cell types.

28/10/2011

University degree in Biology

Department of Biology and Biotechnologies “C. Darwin”,

Sapienza, University of Rome. Italy

Thesis title: Identification of mutations in mitotic and telomeric genes associated to *Drosophila melanogaster* chromosome II

Supervisor: Laura Ciapponi

Vote: 110/110 summa cum laude

Project: I performed a screening on different mutant lines induced with EMS aimed to the identification of new gene involve in chromosomes stability. I analyzed the larval brain metaphases of the different mutants looking for chromosomal defects caused by the EMS-induced mutations. I identified a mutant line with a telomere fusion phenotype; a complementation test revealed that the mutation was a new mutation in the *pendolino* gene.

INTERNATIONAL PEER-REVIEWED PUBLICATIONS

1. **Marzullo M.**, El Maï M., Pimenta de Castro I. and Miguel G. Ferreira. Activation of the Akt/Foxo pathway switches apoptosis to senescence in *tert*^{-/-} zebrafish. *Manuscript in preparation*
2. **Marzullo M.**, Gatti M. and Ciapponi L. Interactions between *pendolino* and histone modifiers reveal an epigenetic regulation of *Drosophila* telomere stability. *Manuscript in preparation*
3. **Marzullo M.**, Andreyeva E.N., Gatti M. and Ciapponi L. SUUR is a telomere-associated protein that interacts with *Pendolino* and plays a role at *Drosophila* telomeres. *Manuscript in Summary 1+2: This two works represent the follow up of the Plos Genetics 2015 first paper on pendolino, and represent my own work done during the master degree and PhD. In this two paper we characterize the role of pendolino in heterochromatin maintenance and DNA replication, discovering for the first time a relationship between histone modification and telomeric fusions. We found that peo interacts with factor required for both heterochromatin formation and replication and that mutation in peo strongly affect both methylation and ubiquitination on the heterochromatin. Thus, the results of this two paper will give a great relevance to Peo and to its epigenetic at telomere, also on the light of the role of its human homologue AKTIP.*

My contribution to this work has been almost totally, I performed all the experiments present in 1 and 2, except for some interaction of telomeric factors with the replication protein SUUR. I performed experiment of cytology, molecular biology and biochemistry both on Drosophila flies and cell line.

- 3 Razzoli M., Dufe K., Gurney A., Erickson C., McCallum J., Spielman N., **Marzullo M.**, Patricelli J., Kurata M., Touma C., Palme R., Largaespada D., Allison D.B., Bartolomucci A. Social Stress Regulates Lifespan in Mice. *Aging Cell*. 2018 May 28:e12778. doi: 10.1111/accel.12778.

Summary: In this paper, using a mouse model of chronic psychosocial stress we identified a causal role for psychosocial stress on shortening lifespan and increasing the risk of cardiovascular disease in mice. Thus this model demonstrated a conserved role for the negative impact of social stress on survival implicating mechanisms of increased risk of cardiovascular disease.

My contribution to this work was to design an assay to analyze telomere length in different tissues of the stressed mice to find a correlation between telomere shortening and shortening of the lifespan.

- 4 Blum J.A., Bonaccorsi S., **Marzullo M.**, Palumbo V., Barbash D.A. and Gatti M. The Lhr-Hmr complex is required for sister chromatid separation during anaphase but not for centromere/kinetochore function. *Genetics*. 2017;207: 1457–1472. doi:10.1534/genetics.117.300390

Summary: In this manuscript we analyze the role of the proteins Hmr and Lhr in chromosome segregation and telomere maintenance. Both Hmr and Lhr localize at telomere and interacts with telomeric proteins. We therefore analyzed the chromosomal phenotype of larval brains from Hmr and Lhr null mutants and from Hmr; Lhr double mutants. We found that these mutants exhibit very low levels of telomeric fusions (TFs) and relatively high frequencies of incomplete chromosome breaks, but we did not observed aneuploidy suggesting that the complex Hmr-Lhr is not required for proper centromere/kinetochore function.

My contribution in this work was to perform cytological analysis to analyze the chromosomes aberration in the single and double mutants Lhr; Hmr.

- 5 **Marzullo M**, Gatti M. Telomere fusion in *Drosophila*: The role of subtelomeric chromatin. *Fly (Austin)*. 2015 Jul 3;9(3):121-5. doi:10.1080/19336934.2015.1131882.
C = 0, IF(5Y) = 2.8
- 6 Cenci G, Ciapponi L, **Marzullo M**, Raffa GD, Morciano P, Raimondo D, Burla R, Saggio I, Gatti M. The Analysis of *Pendolino* (*peo*) Mutants Reveals Differences in the Fusigenic Potential among *Drosophila* Telomeres. *PLoS Genet*. 2015 Jun 25;11(6):e1005260. doi: 10.1371/journal.pgen.1005260. eCollection 2015 Jun.
C = 8, IF(5Y) = 7.058 , Q1 (top 10%) in Genetic and Heredity

Summary: In this paper we describe a Drosophila gene, pendolino (peo), identified by mutations that preferentially induce TFs between telomeres associated with constitutive heterochromatin. The Peo protein binds terminin but does not have the typical terminin properties, as it is conserved in mammals and associates with several chromosomal sites. In addition, Peo is required for PCNA recruitment and for general DNA replication. We thus propose that loss of peo function results in specific fusigenic lesions concentrated in heterochromatin-associated telomeres, and that these lesions might be generated during telomere replication.

I strongly contribute to the publication of this paper, I identified the peo^h allele and conducted half of the experiments described in the paper, specifically: the comparative analysis on telomeric fusion, the WB and IF on Peo expression and localization, the assays on replication and PCNA localization and the analysis of the effect of aphidicolin treatment on telomeric fusion.

Bibliometric analysis according to Web of Science (C) and Journal Citation Reports (IF and Journal rankings, 2016)

HONOR AND AWARD

- 2017 **Best PhD thesis prize** “Ferruccio Ritossa” for the years 2015/16/17, awarded by AGI (Associazione Genetica Italiana)
Thesis title: *pendolino (peo)*, a *Drosophila* gene preferentially required for “heterochromatic telomeres” protection
- 2015 **Best poster prize** awarded by VI BEMM (Biology and Molecular Medicine PhD School) symposium, Rome 30th November 2015 (Annual meeting)
Title: Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication

ORAL COMMUNICATIONS

Presenting author underlined

Invited speaker

1. **Marta Marzullo**, Maurizio Gatti and Laura Ciapponi. Interactions between *pendolino* and histone modifiers reveal an epigenetic regulation of *Drosophila* telomere stability.
EMBO Workshop “Telomeres in Health and Human disease” Troia (PT) 1st-6th May 2018.
2. **Marta Marzullo**, Evgeniya N. Andreyeva, Maurizio Gatti and Laura Ciapponi. The role of *pendolino* in epigenetic regulation of *Drosophila* telomere capping
3. I EMBL-SAPIENZA PhD meeting “Chromatin and Epigenetics”, Rome 26th-27th **September 2016**.
4. **Marta Marzullo**, Evgeniya N. Andreyeva, Maurizio Gatti and Laura Ciapponi. Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication
5. XVIII Italian *Drosophila* Research Conference (IDRC), Bologna 14th-16th **September, 2016**.

6. **Marta Marzullo**, Giovanni Cenci, Grazia D. Raffa, Patrizia Morciano, Domenico Raimondo, Romina Burla, Isabella Saggio, Maurizio Gatti and Laura Ciapponi. *Pendolino* (*peo*), a *Drosophila* gene preferentially required for “heterochromatic telomeres” protection.
7. XVII Italian *Drosophila* Research Conference (IDRC), Anagni (FR) 6th-8th **October, 2014**.

POSTER COMMUNICATIONS

Presenting author underlined

1. **Marta Marzullo**, Evgeniya N. Andreyeva, Maurizio Gatti and Laura Ciapponi. Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication
EMBO/FEBS lecture course “Chromatin & Environment”, Spetses island (ATH) 8th-14th **August, 2016**. Poster P46.
2. **Marta Marzullo**, Giovanni Cenci, Patrizia Morciano, Maurizio Gatti and Laura Ciapponi. Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication
VI BEMM (Biology and Molecular Medicine PhD School) symposium, Rome 30th **November 2015**
Annual meeting. Poster P33.
3. **Marta Marzullo**, Giovanni Cenci, Patrizia Morciano, Maurizio Gatti and Laura Ciapponi. Functional characterization of *pendolino*, a *Drosophila* gene required for telomere protection and DNA replication (A-160)
XXIV European *Drosophila* Research Conference (EDRC), Heidelberg 9th-12th **September, 2015**. Poster P35.
4. **Marta Marzullo**, Giovanni Cenci, Maurizio Gatti and Laura Ciapponi. The analysis of *pendolino* reveals unexpected differences between euchromatic and heterochromatic *Drosophila* telomeres
Conference AGI (Associazione Genetica Italiana), Cortona (SI) 25th-27th **September, 2013**. Poster 5.7 and short talk.
5. **Marta Marzullo**, Giovanni Cenci, Maurizio Gatti and Laura Ciapponi. *Pendolino*, a *Drosophila* gene that controls the behavior of heterochromatic telomeres
XVI Italian *Drosophila* Research Conference (IDRC), Palermo 1st-3rd **October, 2012**. Poster.

SUPERVISION OF MASTER'S & UNDERGRADUATE STUDENTS

- 2017 **Co-supervision of three undergraduate students** at the Sapienza, University of Rome, Rome, Italy
Students' names: Luca Venditti, Claudio Paoletti and Federica Mosti
Principal supervisor: Laura Ciapponi
- 2015-2017 **Co-supervision of a lab Master's student** at the Sapienza, University of Rome, Rome, Italy
MSc Student: Elena Gentile
Principal supervisor: Laura Ciapponi

PARTICIPATION IN RESEARCH PROJECTS

Role as Principal Investigator

1. *pendolino* (*peo*), a *Drosophila* gene preferentially required for heterochromatic telomeres protection. (2016) **Avvio alla ricerca 2016. Funded by Sapienza, University of Rome**. Amount funded: 1.000€
2. Functional characterization of *pendolino* a *Drosophila* gene required for both telomere protection and DNA replication. (2015) **Avvio alla ricerca 2015. Funded by Sapienza, University of Rome**. Amount funded: 1.000€

Role as Team Member

1. Exploiting the *Drosophila* model system to investigate the function of human proteins involved in

telomere maintenance. (2017). **Funded by AIRC**. Principal Investigator: Maurizio Gatti. Amount funded: 702.975,00 €

2. Protein ubiquitylation is required for *Drosophila* telomere maintenance. (2015). **Funded by Sapienza, University of Rome**. Principal Investigator: Laura Ciapponi. Amount funded: 20.000 €

ORGANISATION OF SCIENTIFIC MEETINGS

2016 **Member of organizing committee:** VII BEMM (Biology and Molecular Medicine PhD School) symposium- 18th November 2016, Rome, Italy

TEACHING ACTIVITIES

2014-2016 **Supervisor of practice activity:** *Drosophila* manipulation for students of Genetics courses, Sapienza, University of Rome, Rome, Italy

INSTITUTIONAL RESPONSIBILITIES

2019 **PostDoc Committee member:** for the PostDoc Community of the Instituto Gulbenkian de Ciéncia (IGC), Oeiras, Portugal

2013-2016 **PhD students Rep:** for the students of the XXIX PhD course in “Genetics and Molecular Biology”
Sapienza, University of Rome, Rome, Italy

PARTICIPANT IN PROFESSIONAL TRAINING COURSES

2018 Theoretical and practical SPCAL course on Laboratory Animal Science

Topics

- Portuguese and european legislation for the protection of animals used for experimental and other scientific purposes
- Ethics and the 3rs
- Anatomy and physiology of rodents and lagomorphs
- Anatomy and physiology of teleost fish
- Feeding and nutrition of rodents and lagomorphs
- Housing and accommodation of rodents and lagomorph
- Animal transport
- Zebrafish (*danio rerio*) - methods for husbandry and maintenance of teleost fish
- Behaviour and environment in rodents
- Animal welfare and signs of disturbance
- Fish psychological stress and welfare
- Microbiological standardisation
- genetic standardisation and manipulation of laboratory animals
- Methods of handling, restraint and identification of laboratory rodents
- Administration of substances and collection of samples
- Pre and post surgical care and basic principles of surgery
- Euthanasia of laboratory animals: rodents and lagomorphs
- Anaesthesia and analgesia
- Experimental design and scientific integrity
- Health and safety

2015 Theoretical and practical course of statistic:

- Introduction to theory of test and hypothesis verification, significance tests and p-value

- Test on normal population, example on single sample, double paired samples and independent samples
- Non parametric test to hypothesis validation
- Application of R program

MAJOR COLLABORATIONS

- 2018-2019 **Dr. Jean-Philippe Pradère and Cedric Dray laboratory**
 Adipocyte secretions, Obesities and related Diseases lab
 UMR INSERM-UPS U1048 - Equipe 3, Toulouse, France
- We collaborate on a project on the characterization of the HFD(High Fat Diet) effect on senescence and telomere length in the zebrafish model system
- 2017 **Dr. Fabian Feiguin laboratory,**
 ICGEB (International Center for Genetic Engineering and Biotechnology),
 Area Science Park, loc. Padriciano, Trieste, Italy
- May 2017 I spent 1 month in the Dott. Feiguin lab to conduct ChIP experiments on old and young flies heads, to analyze the epigenetic status of TBPH gene locus during aging.
- 2014 **Prof. Alessandro Bartolomucci laboratory,**
 Department of Integrative Biology and Physiology (IBP),
 University of Minnesota, Minneapolis, USA
- 7 I collaborate with the prof. Bartolomucci lab to design an experiment to analyse telomere length in stressed mice. The results of this experiments are published on *Aging cell* doi: 10.1111/acel.12778.
- 2013-to date **Prof. Igor Zimulev laboratory,**
 Institute of Molecular and Cellular Biology, Siberian Branch of the Russian Academy of Sciences, Novosibirsk 630090, Russian Federation
- We collaborate on a project on the SUUR factor (suppressor of Underreplication), a protein required for heterochromatin replication and maintenance in *Drosophila*, and with a role in telomere protection.