

ELISA LAZZARI PhD

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Profile:

As a highly trained and skilled post-doctoral researcher I have a strong interest in understanding disease processes at the biochemical and molecular level. I am enthusiastic, highly organized, hardworking and skilled in a wide range of laboratory techniques including molecular biology, protein purification and *in vitro* analysis and cell biology.

I have been lucky to be mentored throughout my career by excellent and inspiring scientists and I am now looking forward to follow their steps and to transmit my passion to the next generation of young scientists. I have a special interest into interdisciplinary projects going past the traditional boundaries of science and into outreach activities that allow me to share my knowledge with the public to help everybody understand the wonders and challenges of being a researcher.

Education and training:

- 2008 – 2012: PhD at the Royal College of Surgeons in Ireland, Molecular Immunology group
Thesis title: “Regulation of IRF5 activity in the TLR7 and type I IFN pathways”
(attached equipollence certificate)
- 2006 – 2008: MSc in Biomolecular Science and Technologies (V.O. 6/S) at Pisa University, Italy
Thesis title: “Structure and function of cytosolic 5'-nucleotidase (cN-II):
characterization of the site-specific mutants M436W and F127E”
Grade 110/110 *cum laude*
- 2002 – 2006: BSc degree course in Molecular Biology at Pisa University, Italy
Thesis title: “Evaluation of quality of fractionated blood plasma”
Grade 110/110 *cum laude*
- 2005: Professional training course “Biochemist Technician for Industry and Territory”
promoted by the Faculty of Mathematical, Physical and Natural Science of Pisa
University and Tuscany Region

Research and professional experiences:

- **March 2023 – present: Post-doctoral researcher, IRCCS “Burlo Garofolo” Trieste and Molecular Genetics Lab, University of Trieste (Italy)**
Study of the Opitz G/BBB syndrome gene product, MID1/TRIM18, and of its disease-associated variants in the regulation of protein homeostasis
 - Setting up of *in vitro* reactions to study the effect of pathogenic mutations on MID1 catalytic activity
- **April 2020 – December 2023: Post-doctoral researcher, Molecular Genetics Lab, University of Trieste (Italy) - Fondazione Umberto Veronesi post-doctoral fellow April 2020 - March 2021**
Role of TRIM32 in neuromuscular development and homeostasis
 - Set-up of NSC-34/C2C12 co-culture systems to investigate the neuromuscular junction (NMJ) synapse
 - Transcriptomic analysis of *Trim32* WT and KO NSC-34 clones
 - Generation of *Trim32* knock out clones of NSC-34 cells with CRISPR/Cas9 method and analysis of generated mutant clones
 - Quantitative analysis of neuronal morphology with ImageJ software
 - *In vitro* differentiation of murine motor neuron-like NSC-34 cells
 - Manuscripts writing and proofreading and writing of grant proposals

- **November 2015 – March 2020: Post-doctoral researcher, Molecular Genetics Lab, University of Trieste (Italy)**
Mechanistic study of TRIM32 E3 ligase activity in muscle differentiation and pathogenic role in muscular dystrophy
 - Generation of *Trim32* knock out clones of C2C12 cells with CRISPR/Cas9 method and analysis of generated mutant clones
 - Extraction of myofibers from murine muscular samples
 - *In vitro* differentiation of murine myoblast C2C12 cells and analysis of sub-cellular localization of endogenous and over-expressed TRIM32 (full length, deletion- and point-mutants) by epifluorescent microscopy
 - Culture and transfection of mammalian cell lines (C2C12, HEK293T, HeLa, COS-7)
 - Manuscripts writing and proofreading and writing of grant proposals
- **July 2014 – October 2015: Post-doctoral researcher, Cluster in Biomedicine and Elettra Synchrotron, Trieste (Italy)**
Biochemical and structural characterization of TRIM32
 - X-ray crystallography and SAXS analysis of TRIM32 alone and in complex with E2-ubiquitin
 - Analysis of TRIM32 oligomerization *in vitro* and *in vivo*
 - Assessment of TRIM32 E2 usage (*in vitro* and *in vivo* ubiquitination assay)
 - Assessment of TRIM32 activity on various substrates (*in vitro* and *in vivo* ubiquitination assay)
 - Expression and chromatographic purification of bacterially produced recombinant TRIM32 and E2-Ubiquitin
 - Manuscripts writing and proofreading and writing of grant proposals
- **14th January – 06th February 2015: Short Term Scientific Mission (PROTEOSTASIS COST Action STSM), Centre for Gene Regulation and Expression, Department of Life Sciences, University of Dundee (Scotland, UK)**
 - Expression and purification of E2 ubiquitin conjugating enzymes to be used for structural studies
 - *In vitro* conjugation of ubiquitin to purified E2 ubiquitin conjugating enzymes
- **December 2012 – December 2013: Post-doctoral researcher, Molecular Immunology Lab, Royal College of Surgeons in Ireland**
High throughput screening of TLR3 and TLR7 pathway inhibitors on behalf of Amgen pharmaceutical company
 - Set-up and troubleshooting of reporter gene assays to analyse the effects of small molecule inhibitors on TLR7-driven NF- κ B, IFNA4 and ISRE promoters and TLR3-driven IFNB promoter
 - Validation of assays to be used in the screen
 - Manuscripts writing and proofreading and reviewing of grant proposals
- **October 2008 – November 2012: PhD in Molecular Immunology, Royal College of Surgeons in Ireland**
Role of TRIM21 in TLR-mediated regulation of IRF5 isoforms stability
 - Culture and transfection of mammalian cell lines (HEK293T, HeLa, 2fTGH, THP-1)
 - Isolation of Peripheral Blood Mononuclear Cells (PBMCs) from whole blood
 - Analysis of the interaction between IRF5 isoforms and TRIM21 by co-immunoprecipitation
 - Purification of bacterially produced 6 \times His- and GST-tagged recombinant proteins for *in vitro* pull-down assays
 - Analysis of IRF5 isoforms stability by western blot, flow cytometry and High Content Analysis (HCA)

- Analysis of IRF5 isoforms and TRIM21 subcellular localization by epifluorescent and confocal microscopy
- Analysis of TRIM21-mediated IRF5 ubiquitination by *in vivo* ubiquitination assay
- Collaboration with other team members to generate data for publications and manuscripts writing and proofreading

Study of IRF5 activation downstream of the type I IFN receptor

- Analysis of IRF5 phosphorylation by co-immunoprecipitation using wild-type and mutant human and murine cell lines
- Analysis of IRF5 promoter binding by Chromatin Immunoprecipitation (ChIP) and gene expression by qPCR
- Generation of IRF5 point-mutants by mutagenic PCR and analysis of mutants activity by reporter gene assay
- Expression and purification of bacterially produced recombinant proteins for *in vitro* kinase assay

- **October 2007 – July 2008: Final Year Project in the Biology Department – Biochemistry Section, Pisa University, Italy**

Mechanistic study on cytosolic 5'-nucleotidase II

- Generation of cN-II point mutants by mutagenic PCR
- Purification of bacterially produced 6×His-tagged recombinant proteins and evaluation of enzymatic activity with radiochemical, chromatographical and spectrophotometric assays

- **October – December 2005: Training course, Kedrion Research Centre, Castelvechio Pascoli (Lucca), Italy**

Quality control of fractionated plasma

- Spectrophotometric and immunological assays (ELISA) on blood plasma samples to assess levels and activity of proteins involved in the coagulation cascade

Awards:

- Fondazione Umberto Veronesi (FUV) one year Fellowship (2020 program) awarded for the project “Role of TRIM32 in neuromuscular differentiation”
- COST-funded Short Term Scientific Mission (STSM) awarded to visit Prof Ron Hay’s lab, Centre for Gene Regulation and Expression, School of Life Sciences, University of Dundee, Scotland 14th January - 06th February 2015
- Keystone Symposia Scholarship (travel grant) awarded to attend the Keystone Symposia Meeting on Innate Immunity, Dublin June 2010

Additional information:

- **Teaching and mentoring**

- I have participated in the Molecular Biomedicine PhD program (University of Trieste) teaching week (Academic years 2019/2020 and 2020/2021) presenting the seminar: “The TRIM family of E3 ubiquitin ligases: Ubiquitination between health and disease”
- I presented the seminar “Generation of knock out cell lines with the CRISPR/Cas9 method: A practical example from the lab” as part of the Molecular genetics and genomic (SSD BIO/18) course (MSc in Functional Genomics, University of Trieste)
- I served as a Commissioner for TOLC tests at the University of Trieste
- I was involved as a demonstrator for practical lab lessons and in charge of marking of practical papers for students of the faculty of Pharmacy, RCSI
- I am experienced in mentoring undergraduate students and have fully supervised four BSc and four MSc students. I did cooperate with other colleagues in the lab for supervision of

several other undergraduate students and junior members assisting both during the lab activities and dissertations writing

- I have been the opponent for the thesis defense of five MSc students in the University of Trieste

- **Public outreach experiences**

- I participated in Trieste NEXT 2022 – UniTS booth “Ubiquitinazione: Anche la cellula fa la differenziata / Ubiquitination: The cell recycles too”
- I presented my research activities to high school students as part of the “Researchers in the classroom” program sponsored by Fondazione Umberto Veronesi – Polo “Fermi-Giorgi”, Lucca, October 2020
- I participated in the “Interview with the researcher” promoted by Fondazione Umberto Veronesi (<https://www.fondazioneveronesi.it/magazine/articoli/i-nostri-ricercatori/quale-ruolo-per-la-proteina-trim32-nelle-distrofie-muscolari>)
- I was involved in organizing and implementing RCSI Transition Year Students Program with the lecture "Introduction on weight, volume and concentration" and presented the lab research to high school students at RCSI “Innovation day”
- I served as a part-time co-operator for Pisa University (Italy) where I was involved in presentation of the Molecular Biology degree course as a consultant and assistant for prospective students

- **Lab managing skills**

- Creation and maintenance of lab ordering and inventory systems
- Creation and management of plasmids and transformed bacteria biobanks

- **IT skills and competency**

- I have an excellent knowledge of Microsoft products (Windows, Office) and related software
- Bioinformatic analysis of genomic sequences and protein structure (Blast, ClustalO, Protein Data Bank - PDB, homology modeling with Molecular Operating Environment – MOE, GeneSnap)

Poster presentations:

- May 2022, 1st ProteoCure Action Meeting, Ljubljana, Slovenia
Title: TRIM32 in neuromuscular differentiation and implications for LGMDR8 pathogenesis
- November 2016, 3rd PROTEOSTASIS Action Meeting, Lisbon, Portugal
Title: Structure and function of the E3 ubiquitin ligase TRIM32
- September 2015, EMBO conference “Ubiquitin and ubiquitin-like modifiers”, Cavtat, Croatia
Title: Structure and function of the E3 ubiquitin ligase TRIM32
- September 2013, Irish Society of Immunology and Ulster Immunology Group Joint Meeting, Dublin, Ireland
Title: TRIM21 differentially regulates the stability and activity of IRF5 isoforms
- September 2011, Irish Society of Immunology Meeting, Galway, Ireland
Title: Regulation of IRF5 stability by the E3 ubiquitin ligase TRIM21
- October 2010, Irish Society of Immunology 25th Anniversary Meeting, Dublin, Ireland
Title: Regulation of IRF5 activity by tyrosine phosphorylation in the type I IFN pathway
- September 2010, Irish Society of Immunology Meeting, Belfast, UK
Title: Regulation of IRF5 activity by tyrosine phosphorylation
- June 2010, “Innate immunity: mechanisms linking with adaptive immunity” Keystone Symposium, Dublin, Ireland
Title: Regulation of IRF5 isoforms stability by the E3 ubiquitin ligase TRIM21

- May 2010, “Viruses and Innate Immunity” EMBO workshop, Dublin, Ireland
Title: Regulation of IRF5 isoforms stability by the E3 ubiquitin ligase TRIM21
- September 2009, Irish Society of Immunology Meeting, Dublin, Ireland
Title: Role of TRIM21 in regulating IRF5 stability

Oral presentations:

- February 2017, University of Trieste, 1st Trilateral lab meeting on Embryological Syndromes and Treatments (TRI.E.S.T.)
Title: TRIM32, the E3 ubiquitin ligase mutated in Limb-Girdle Muscular Dystrophy 2H
- October 2013, Royal College of Surgeons in Ireland
Title: A novel role for IRF5 in the type I IFN pathway
- December 2010, Royal College of Surgeons in Ireland
Title: Role of IRF5 in Systemic Lupus Erythematosus (SLE)

Publications:

- Kumarasinghe L, Xiong L, Garcia-Gimeno MA, **Elisa Lazzari**, Sanz P and Meroni G “TRIM32 and Malin in Neurological and Neuromuscular Rare Diseases” *Cells*, 2021, *10*, 820
- **Elisa Lazzari**, El-Halawany M, De March M, Valentino F, Cantatore F, Migliore C, Onesti S and Meroni G "Analysis of the Zn-binding domains of TRIM32, the E3 ubiquitin ligase mutated in Limb Girdle Muscular Dystrophy 2H" *Cells*, 2019, *8*(3), 254
- **Elisa Lazzari** and G Meroni "TRIM32 ubiquitin E3 ligase, one enzyme for several pathologies: from muscular dystrophy to tumours" *International Journal of Biochemistry and Cell Biology* 2016, *79*; 469-477
- **Elisa Lazzari**, Korczeniewska J, Ní Gabhann J, Smith S, Barnes BJ and Jefferies CA "TRIPartite Motif 21 (TRIM21) differentially regulates the stability of Interferon Regulatory Factor 5 (IRF5) isoforms" *PLoS One*. 2014, *9*(8): e103609
- **Elisa Lazzari** and CA Jefferies "IRF5-mediated signalling and implications for SLE" *Clinical Immunology* 2014, *153* (2); 343-352
- Wynne C, **Elisa Lazzari**, Carty M, Mc Carthy EM, Smith S, Ní Gabhann J, Kallal LE, Higgs R, Cryan SA, Biron CA, Bowie AG and Jefferies CA "TRIM68 negatively regulates IFN- β production by degrading TRK fused gene, a novel component of TLR/RLR regulated pathways" *PLoS One*. 2014, *9*(7): e101503
- Byrne JC, Ní Gabhann J, **Elisa Lazzari**, Mahony R, Smith S, Stacey K, Wynne C, and Jefferies CA "Genetics of SLE: Functional Relevance for Monocytes/Macrophages in Disease" *Clinical and Developmental Immunology* 2012, Article ID 582352, 15 pages, doi:10.1155/2012/582352
- Meehan M, Parthasarathi L, Moran N, Jefferies CA, Foley N, **Elisa Lazzari**, Murphy D, Ryan J, Ortiz B, Fabius AWM, Chan TA and Stallings RL "Protein tyrosine phosphatase receptor delta acts as a neuroblastoma tumor suppressor by destabilizing the aurora kinase A oncogene" *Molecular Cancer* 2012, Feb 5; 11:6
- Higgs R, **Elisa Lazzari**, Wynne C, Ní Gabhann J, Espinosa A, Wahren-Herlenius M, Jefferies CA "Self protection from antiviral responses—Ro52 promotes degradation of the transcription factor IRF7 downstream of the viral Toll-like receptors." *PLoS One*. 2010, *5*(7): e11776

Reviewer activity:

- Bosnian Journal of Basic Medical Sciences
- Brain Sciences
- Molecules
- Marine drugs
- Disease Models & Mechanisms

- Genes
- International Journal of Molecular Sciences

Referees

- **Professor Germana Meroni (Post-doc supervisor)**
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Curriculum ai fini della diffusione online

