

Dr Francesca Liccardo

Date of birth: January 25th, 1994.

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Nationality: Italian

Gender: Female

Professional Experience and Education**11/02/2023 to present: Post-Doctorate Position**

Team led by Dr Francesco Fazi

Department of Anatomical, Histological, Forensic Medicine and Orthopedic Sciences,
Sapienza University of Rome, Rome, Italy

Project: "Morphological and functional characterization of mechanotransduction in the
leukemic bone marrow microenvironment underlying AML therapeutic resistance"

01/11/2019 - 10/02/2023: PhD School in Morphogenesis and Tissue Engineering

Department of Anatomical, Histological, Forensic Medicine and Orthopedic Sciences,
Sapienza University of Rome, Rome, Italy

Supervisors: Dr Francesco Fazi and Dr Silvia Masciarelli

*Thesis: Retinoic Acid and proteotoxic stress induce myeloid leukemia progenitors cell
death overcoming the protective effects of the bone marrow niche mesenchymal cells*

01/10/2017 - 23/10/2019: Master in Genetics and Molecular Biology, vote 110/110 with honours

Department of Anatomical, Histological, Forensic Medicine and Orthopedic Sciences,
Sapienza University of Rome, Rome, Italy

Supervisors: Dr Francesco Fazi and Dr Silvia Masciarelli

*Thesis: Sviluppo di una strategia terapeutica combinata per indurre la morte cellulare
di progenitori mieloidi leucemici*

01/10/2013 - 22/06/2017: Bachelor in Biology, vote 110/110

Dept of Biology and Biotechnology "Charles Darwin", Sapienza University of Rome,
Rome, Italy

Supervisor: Dr Maria Bernardini

*Thesis: La sifilide e Treponema pallidum: l'uso di approcci moderni nella comprensione
di un'antica malattia*

15/09/2008 – 11/07/2013: High school diploma, vote 100/100

Liceo Scientifico "Luigi Siciliani", via Turco, 7, Catanzaro, Italy

Personal skills and competences

Mother tongue: Italian

Other languages: English; French.

Communication skills

Good written and verbal communication skills gained through the relationship with different persons. Capacity to adapt and provide problem-solving strategies. Good capacity to work with a team and interact with group components.

Organizational/managerial skills

Good capacity to independently organize the work, respecting deadlines and predetermined aims.

Professional skills and competences**Molecular Biology and protein analysis:**

DNA extraction from cell culture, RNA extraction from cells, cDNA reverse transcriptase and RT-qPCR, PCR, Western blot, FACS analysis, and confocal microscopy.

Cellular Biology:

Culture and co-culture of cell lines and primary cells, analysis with optical, electronic, and confocal microscopy, immunofluorescence, FACS analysis, trypan blue assay, efluor analysis, cell cycle analysis, oxidative stress evaluation through ROS levels measurement, MTT assay, Wright-Giemsa staining, isolation and analysis of cells from murine blood and bone marrow.

In vivo studies:

Generation of cell line-derived xenograft (CDX) murine models of human AML. Pharmacological administration of anti-tumoral drugs with therapeutic relevance for toxicity and efficacy studies to formulate new combined therapeutic strategies.

Computer skills and competences:

OS and Windows operating systems; European Computer Driving Licence (ECDL) released by AICA (Associazione Italiana per l'Informatica ed il Calcolo Automatico). Good use of Word, PowerPoint, Excel, Adobe Acrobat Professional, Adobe Illustrator, Adobe Photoshop, GraphPad-Prism, ImageJ and bibliographic software. Use of biological databases and software (Pubmed, GenBank, Human Protein Atlas, BLAST, Amplify4, circBase). Good use of 7500 Software (Applied Biosystem) 7500 SOFTWARE (Applied Biosystem) and QUANTSTUDIO™ 7 FLEX REAL-TIME PCR SYSTEM, programs for the analysis of Real-Time PCR data. Good use of FCS Express and CytExpert software for FACS analysis, ZEN dark, and ZEN blue edition for the analysis of confocal microscope acquisitions. Good ability to browse the internet.

Mentoring and training through research:

- Mentoring and research activities for students' degree course in Genetics and Molecular Biology, Sapienza University of Rome: teaching cellular biology and molecular biology techniques (8 hours every year).
- Mentoring Master's Students: Viviana Romano (09/04/2022-19/06/2023); Lavinia Pace (02/05/2024-present)

Other experiences

- Certificate of training for: Preclinical Testing and Animal Welfare, Sapienza University of Rome, 31/05/2023
- Course of "Statistics for Biologists" BeMM PhD School of Biology and Molecular Medicine, Sapienza University of Rome, 01/10/2021
- Course of "Enzyme Kinetics" BeMM PhD School of Biology and Molecular Medicine, Sapienza University of Rome, 10/09/2020
- "Corso di comunicazione scientifica" BeMM PhD School of Biology and molecular medicine, Sapienza University of Rome, 13/07/2020
- Course of "Public Speaking" BeMM PhD School of Biology and molecular medicine, Sapienza University of Rome, 26/06/2020

Publications

Total publications: 8 (3 first or co-first author)

1) Incocciati A, Cappelletti C, Masciarelli S, **Liccardo F**, Piacentini R, Giorgi A, Bertuccini L, De Berardis B, Fazi F, Boffi A, Bonamore A, Macone A. **Ferritin-based disruptor nanoparticles: A novel strategy to enhance LDL cholesterol clearance via multivalent inhibition of PCSK9-LDL receptor interaction.** Protein Sci. 2024 Sep;33(9):e5111. doi: 10.1002/pro.5111. PMID: 39150051; PMCID: PMC11328107.

Co-author (investigation, writing, review and editing, validation). The study proposes a new ferritin-based therapeutic strategy for the treatment of hypercholesterolemia. Engineered human ferritin nanoparticles can incorporate 24 copies of peptide Pep2-8, hence favoring LDL cholesterol clearance in HepG2 liver cell line.

Citations: 2 (Google Scholar)

2) Iaiza A, Mazzanti G, Goeman F, Cesaro B, Cortile C, Corleone G, Tito C, **Liccardo F**, De Angelis L, Petrozza V, Masciarelli S, Blandino G, Fanciulli M, Fatica A, Fontemaggi G, Fazi F. **WTAP and m6A-modified circRNAs modulation during stress response in acute myeloid leukemia progenitor cells.** Cell Mol Life Sci. 2024 Jun 23;81(1):276. doi: 10.1007/s00018-024-05299-9. PMID: 38909325.

Co-author (investigation, review). The research reveals that AML cells modulate specific circular RNAs bearing m⁶A-modification in response to bortezomib-mediated oxidative stress induction. The results reveal new insights to better define AML resistance mechanisms upon treatments inducing ER and oxidative stress.

Citations: 3 (Google Scholar)

3) Cardarelli S, Biglietto M, Orsini T, Fustaino V, Monaco L, de Oliveira do Rego AG, **Liccardo F**, Masciarelli S, Fazi F, Naro F, De Angelis L, Pellegrini M. **Modulation of cAMP/cGMP signaling as prevention of congenital heart defects in Pde2A deficient embryos: a matter of oxidative stress.** Cell Death & Disease. 2024 Feb 23; 15(2):169. doi: 10.1038/s41419-024-06549-1.

Co-author (design method, investigation, review). The study demonstrates the role of phosphodiesterase 2A in cardiomyocyte development and protection from oxidative stress to prevent mouse congenital heart defects (CHDs). This could pave the way for the design of new clinical studies for CHDs.

Citations: 4 (Google Scholar)

4) **Liccardo F**, Śniegocka M, Tito C, Iaiza A, Ottone T, Divona M, Travaglini S, Mattei M, Cicconi R, Miglietta S, Familiari G, Nottola SA, Petrozza V, Tamagnone L, Voso MT, Masciarelli S, Fazi F. **Retinoic acid and proteotoxic stress induce AML cell death overcoming stromal cell protection.** J Exp Clin Cancer Res. 2023 Aug 31; 42(1):223. doi:10.1186/s13046-023-02793-z.

First author. The article establishes the effectiveness of combining retinoic acid and proteotoxic stress induction against FLT3-ITD+ AML cell lines *in vitro*, on primary leukemic stem cells *ex vivo*, and in a murine model of orthotopic human AML *in vivo*. This has critical translational implications for AML treatment.

Citations: 4 (Google Scholar)

5) **Liccardo F**, Iaiza A, Śniegocka M, Masciarelli S, Fazi F. **Circular RNAs Activity in the Leukemic Bone Marrow Microenvironment.** Noncoding RNA. 2022 Jul 1;8(4):50. doi: 10.3390/ncrna8040050. PMID: 35893233; PMCID: PMC9326527.

First author. This review provides an overview of the most relevant annotated circular RNAs in AML and their possible role in bone marrow niche remodeling during leukemia onset and progression.

Citations: 7 (Google Scholar)

6) Śniegocka M, **Liccardo F**, Fazi F, Masciarelli S. **Understanding ER homeostasis and the UPR to enhance treatment efficacy of acute myeloid leukemia.** Drug Resist Updat. 2022 Sep;64:100853. doi: 10.1016/j.drug.2022.100853. Epub 2022 Jul 8. PMID: 35870226.

Co-first author. This review reports the most relevant literature on the unfolded protein response (UPR), a key multifaceted mechanism for AML progression and drug resistance.

Citations: 27 (Google Scholar)

7) Palombarini F, Masciarelli S, Incocciati A, **Liccardo F**, Di Fabio E, Iazzetti A, Fabrizi G, Fazi F, Macone A, Bonamore A, Boffi A. **Self-assembling ferritin-dendrimer nanoparticles for targeted delivery of nucleic acids to myeloid leukemia cells.** J Nanobiotechnology. 2021 Jun 9;19(1):172. doi: 10.1186/s12951-021-00921-5. PMID: 34107976; PMCID: PMC8190868.

Co-author (design method, investigation, review). This article shows that a self-assembling hybrid nanoparticle, engineered from Archaeoglobus fulgidus chimeric ferritin, can deliver pre-miRNAs to AML cells. Once entered, the nucleic acid is released into the cytosol and processed to mature functional miRNA. The results are promising for the development of new protein-based transfecting agents.

Citations: 57 (Google Scholar)

8) Masciarelli S, Capuano E, Ottone T, Divona M, Lavorgna S, **Liccardo F**, Śniegocka M, Travaglini S, Noguera NI, Picardi A, Petrozza V, Fatica A, Tamagnone L, Voso MT, Lo Coco F, Fazi F. **Retinoic acid synergizes with the unfolded protein response and oxidative stress to induce cell death in FLT3-ITD+ AML**. Blood Adv. 2019 Dec 23;3(24):4155-4160. doi: 10.1182/bloodadvances.2019000540. PMID: 31834935; PMCID: PMC6929380.

Co-author (design method, investigation, review). The study demonstrates that AML cell lines and primary blasts expressing FLT3-ITD mutation or fusion proteins involving the MLL gene are sensitive to a combination of ER stress and oxidative stress.

Citations: 31 (Google Scholar)

Abstracts in Congresses

- **Liccardo F**, Mazzanti G, Marcotulli M, Cidonio G, Ottone T, Travaglini S, Divona M, Voso M.T., Masciarelli S. and Fazi F. From in vitro to in vivo and back: unraveling treatment responsiveness of AML cells upon the interaction with bone marrow niche mesenchymal cells. XVII Congresso Nazionale SIES 2024, Florence, Italy, 07/03/2024.

- **Liccardo F**, Śniegocka M, Ottone T, Divona M, Miglietta S, Familiari G, Petrozza V, Tamagnone L, Voso M.T., Masciarelli S. and Fazi F. Retinoic acid and proteotoxic stress induce AML cell death overcoming bone marrow stromal cell protection. European School of Haematology, Estoril, Portugal, 29/10/2023.

- **Liccardo F**, Śniegocka M, Ottone T, Divona M, Miglietta S, Familiari G, Petrozza V, Tamagnone L, Voso M.T., Masciarelli S. and Fazi F. Retinoic acid and proteotoxic stress induce AML cell death overcoming bone marrow stromal cell protection. ABCD, Paestum, Italy, 21/09/2023.

- **Liccardo F**, Śniegocka M, Ottone T, Divona M, Miglietta S, Familiari G, Petrozza V, Tamagnone L, Voso M.T., Masciarelli S. and Fazi F. Retinoic acid and proteotoxic stress induce myeloid leukemia progenitors cell death overcoming the protective effects of the bone marrow niche mesenchymal cells. European School of Haematology, London, UK, 05/02/2023.

- Masciarelli S., **Liccardo F**, Śniegocka M, Divona M, Travaglini S, Ottone T, Miglietta S, Familiari G., Petrozza V, Tamagnone L, Voso M.T., Fazi F. Use of the combination of retinoic acid and proteotoxic stress as a therapeutic strategy to target FLT3-ITD⁺ myeloid leukemic cells. XVII Congresso Nazionale SIES 2022, Rome, Italy, 31/03/2022.

- Masciarelli S., Capuano E., **Liccardo F**, Śniegocka M, Ottone T, Lo-Coco F., Fazi F. Retinoic acid synergizes with the unfolded protein response and oxidative stress to induce AML cell death. 5th International Conference Acute Myeloid Leukemia “Molecular and Translational”: Advances in Biology and Treatment, ESH, Estoril, Portugal, 24/10/2019.

- Masciarelli S., Capuano E., **Liccardo F**, Śniegocka M, Ottone T, Lo-Coco F., Fazi F. Retinoic acid synergizes with the unfolded protein response and oxidative stress to induce AML cell death. ABCD Congress 2019, Bologna, Italy, 19/09/2019.

- Masciarelli S., Capuano E., **Liccardo F**, Ottone T, Lo-Coco F., Fazi F. Development of a combination strategy based on ER and oxidative stress in Acute Myeloid Leukemia. Gordon Research Conference on Stress Proteins in Growth, Development and Disease, Lucca, Italy, 07/04/2019.

Invited talks in Congresses

- **Liccardo F**, Śniegocka M, Ottone T, Divona M, Miglietta S, Familiari G, Petrozza V, Tamagnone L, Voso M.T., Masciarelli S., Fazi F. Retinoic acid synergizes with proteotoxic stress to induce cell death of FLT3-ITD⁺ acute myeloid leukemia progenitor cells. National PhD Meeting, Salerno, Italy, 24/03/2022.

- **Liccardo F**, Śniegocka M, Ottone T, Divona M, Miglietta S, Familiari G, Petrozza V, Tamagnone L, Voso M.T., Masciarelli S., Fazi F. Retinoic acid synergizes with proteotoxic stress to induce cell death of FLT3-ITD⁺

acute myeloid leukemia progenitor cells. Sessione Scientifica del Collegio Docenti di Istologia ed Embriologia, online session, 25/02/2022.

Prizes and Awards

Best Poster Award: Masciarelli S., **Liccardo F.**, Śniegocka M., Romano V., Ottone T., Travaglini S., Miglietta S., Nottola S. A., Familiari G., Petrozza V., Tamagnone L., Voso M.T., Fazi F. Bone marrow stromal cells support acute myeloid leukemia stem cells enhancing antioxidant defenses. 75° Congresso Nazionale SIAI, Padua, Italy, 14/09/2022.

Best PhD Thesis Award: Prize in memory of Sergio Adamo for the best presentation and scientific research of the Cycle XXXV of Morphogenesis and Tissue Engineering PhD School, Sapienza University of Rome, Rome, Italy, 10/02/2023.

Best Oral Presentation Award: **Liccardo F.**, Śniegocka M., Tito C., Iaiza A., Ottone T., Divona M., Mattei M., Cicconi R., Miglietta S., Familiari G., Nottola S.A., Petrozza V., Tamagnone L., Voso M.T., Masciarelli S. and Fazi F. Retinoic acid and proteotoxic stress induce acute myeloid leukemia cell death, overcoming the protective effects of the bone marrow niche stromal cells. Scientific session of Collegio Docenti di Istologia, Rome, Italy, 24/02/2023.

Academic memberships

European Association for Cancer Research (EACR37371); nominated for Full Membership in Sigma Xi, The Scientific Research Honor Society; Associazione di Biologia Cellulare e del Differenziamento (ABCD); Società Italiana Ematologia Sperimentale (SIES).

Other attended Congresses

- 2nd School of Acute Leukemia (SOHO Italy), Rome, Italy, 28/06/2022.
- SIBBM “Frontiers in Molecular Biology” Seminar: the RNA World 3.0, Rome, Italy, 20/06/2022.
- MINISIMPOSIO SU SPERIMENTAZIONE ANIMALE IN BIOMEDICINA - Sperimentazione animale: aspetti storici, etici, giuridici – Virtual event, 23/09/2021.
- SOHO 3rd ITALIAN CONFERENCE – Rome, Italy, 27/09/2021.
- 74° Congresso Nazionale SIAI 2021 – Virtual event, 24/09/2021.
- MINISIMPOSIO SU SPERIMENTAZIONE ANIMALE IN BIOMEDICINA - Ricerca sui primati non umani: quando, come e perché – Virtual event, 18/03/2021.
- Third International Workshop on Tumor Evolution (IRE) - Discovering and targeting therapeutic vulnerabilities in the tumor microenvironment – Rome, Italy, 07/04/2020.
- X BeMM Symposium - PhD School of Biology and Molecular Medicine, Rome, Italy, 22/11/2019.