

BIOGRAPHICAL SKETCH

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NAME: Lazzari, Sara

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Post-doc in molecular and cellular biology

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Università Roma Tre, Rome, Italy	BS	06/2017	Biological sciences
Università La Sapienza, Rome, Italy	MS	01/2020	Genetics and molecular biology
Università La Sapienza, Rome, Italy	PHD	05/2024	Human biology and medical genetics

A. Personal Statement

As a dedicated researcher in human genomics, I have concentrated my efforts on elucidating the molecular foundations of rare diseases through a synergistic application of in silico and in vitro methodologies. My laboratory has extensively investigated the pathogenic mechanisms underlying these variations, with a particular emphasis on the GLUT1 protein and GLUT1 Deficiency Syndrome (GLUT1 DS) on which I conducted my Ph.D. project (thesis title "Molecular bases of GLUT1 Deficiency Syndrome: functional in vitro and in silico studies and a workflow implementation for variants' calling and annotation"). My research has focused on studying GLUT1 in cell models to elucidate its role in brain health, glucose metabolism, and disease. I analyzed GLUT1 variants showing reduced glucose transport and trafficking defects in some mutants. A novel NGS workflow was also developed to improve the interpretation of challenging variants, enhancing diagnosis and patient care. I also studied expression regulation of GLUT1 by a non-coding antisense RNA located head-to-head with GLUT1. Building upon these foundational studies, I am excited to introduce our collaborative project, "GLUT1 Dysregulation: From Mechanisms to Clinical Implications," in partnership with Prof. Viviana Caputo (Sapienza University of Rome), Dr. Chiara Parisi (CNR-IBBC), and Dr. Tommaso Mazza (Fondazione Casa Sollievo della Sofferenza). I am eager to contribute to this project investigating GLUT1's role in BBB function using GFP-tagged hCMEC/D3 cells. My expertise in protein dynamics, functional assays, and RNA regulation aligns with the project's goals, particularly in studying GLUT1 under glucose variation and developing advanced BBB models. I am committed to supporting impactful research on GLUT1's role in metabolic, neurological, and oncological diseases. I am confident that the research planned in this project will significantly advance our understanding of GLUT1 DS and related disorders, potentially leading to the development of novel diagnostic and therapeutic strategies.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 - Post-doc in molecular and cellular biology, Fondazione Casa Sollievo della Sofferenza, Rome

2020 - 2024 PhD fellowship, Università La Sapienza, Rome

Honors

2021 - 2022 Funding award "Progetti per avvio alla ricerca - tipo I", Università La Sapienza

C. Contribution to Science

1. As a dedicated researcher in human genomics, I focused on the study of the molecular bases of rare diseases through a combined approach of in silico and in vitro methods.

Our research has identified microRNAs that regulate pathways linked to tooth anomalies, such as the TGF β and Wnt signaling pathways, which are interconnected with odontogenesis. Additionally, we found associations with tumor-related pathways, suggesting a potential link between odontogenesis and oncogenesis processes. Giovannetti A, Guarnieri R, Petrizzelli F, Lazzari S, Padalino G, Traversa A, Napoli A, Di Giorgio R, Pizzuti A, Parisi C, Mazza T, Barbato E, Caputo V. Small RNAs and tooth development: The role of microRNAs in tooth agenesis and impaction. *Journal of Dental Sciences*. 2024 October; 19(4):2150- 2156. Available from:

<https://linkinghub.elsevier.com/retrieve/pii/S1991790224000783> DOI:10.1016/j.jds.2024.03.013

2. In another study, we assessed non-coding variants within the ACE2 gene, identifying significant single nucleotide variants in regulatory regions. Our analysis suggests that mutations in the ACE2 promoter could enhance promoter activity, potentially increasing the expression of specific ACE2 isoforms. Giovannetti A, Lazzari S, Mangoni M, Traversa A, Mazza T, Parisi C, Caputo V. Exploring noncoding genetic variability in ACE2: Functional annotation and in vitro validation of regulatory variants. *Gene*. 2024 Jul 15;915:148422. PubMed PMID: 38570058
3. We also developed tools like MiRLog and dbmiR to predict the functional impact of microRNA single nucleotide variants (SNVs). Our analysis uncovered several ultra-rare SNVs with potentially deleterious effects on miRNA biogenesis and function, representing putative contributors to human phenotypes. Giovannetti A, Bianco SD, Traversa A, Panzironi N, Bruxelles A, Lazzari S, Liorni N, Tartaglia M, Carella M, Pizzuti A, Mazza T, Caputo V. MiRLog and dbmiR: Prioritization and functional annotation tools to study human microRNA sequence variants. *Hum Mutat*. 2022 Sep;43(9):1201-1215. PubMed Central PMCID: PMC9546175.
4. Additionally, our research into the KCNH1 gene revealed its localization at the base of the primary cilium in human cells. We found that pathogenic missense variants disrupt cilia morphology, assembly/disassembly, and Sonic Hedgehog signaling, highlighting KCNH1's role in ciliogenesis and its potential implications in neurological phenotypes. Napoli G, Panzironi N, Traversa A, Catalanotto C, Pace V, Petrizzelli F, Giovannetti A, Lazzari S, Cogoni C, Tartaglia M, Carella M, Mazza T, Pizzuti A, Parisi C, Caputo V. Potassium Channel KCNH1 Activating Variants Cause Altered Functional and Morphological Ciliogenesis. *Mol Neurobiol*. 2022 Aug;59(8):4825-4838. PubMed Central PMCID: PMC9363390.