Aldamaria Puliti

Associate Professor

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Education and Training

2000

Residency in Medical Genetics

Thesis title: Syndromic forms of Hirschsprung disease associated with cardiac defects. Molecular cytogenetic analysis of the 22q11 region. (50/50).

University of Genoa – Genoa, Italy

1996

PhD in Human Genetics

Thesis title: Molecular genetics of Hirschsprung disease (HSCR): analysis of a human HSCR locus and the murine Dom model. (Awarded with highest distinction).

Université Paris XII–Créteil – Paris, France

1989

Master's Degree in Biological Sciences

Thesis title: Induction of chromosomal aberrations by metabolites of polycyclic romatic hydrocarbons in CHEL cells. *Graduated with honors* (110/110 cum laude).

University of Pisa – Pisa, Italy

Academic Experience

2020 – Present

Associate Professor

University of Genoa – Genoa, Italy

Lecturer in Medical and Human Genetics for degree programs in Medicine and Surgery, and Nursing Sciences.

Principal investigator of research projects.

2005 - 2020

University Researcher (Assistant Professor)

University of Genoa – Genoa, Italy

Lecturer in Medical and Human Genetics for degree programs in Medicine and Surgery, Nursing Sciences, Physiotherapy, and Molecular Health Biology.

Principal investigator of research projects.

1998 - 2005

University Researcher (Assistant Professor)

University of Pisa - Pisa - IT

Lecturer in Molecular Genetics for the Bachelor's program in Biological Sciences.

Principal investigator of research projects.

Language skills

English:	**French:**
Good	Advanced

Teaching Activities

Since my appointment as a university researcher, I have regularly taught courses in Human Genetics, Molecular Genetics, and Medical Genetics.
I also supervise undergraduate and master's theses in Biological Sciences, Molecular Health Biology, and Biotechnology.

Graduate and Postgraduate Teaching and Research Supervision

I am actively involved in supervising PhD students, residents, and postdoctoral fellows. My responsibilities include mentoring residents in Medical Genetics and overseeing both experimental work and thesis preparation of PhD students.

Academic Committee Memberships

- Member of the Academic Board of the PhD Program in Microbiology and Genetics, University of Pisa (2004–2005).
- Member of the Academic Board of the PhD Program in Pediatric Sciences – Genetics section, University of Genoa, from Cycle XXII (2006) to the current cycle (Cycle XL).
- Member of the Academic Board of the School of Specialization in Medical Genetics, University of Genoa (2005–present).
- Member of the Academic Board of the School of Specialization in Child and Adolescent Neuropsychiatry, University of Genoa (2005–present).

Research Interests

My primary research interest lies in elucidating the genetic and molecular mechanisms underlying inherited human diseases. I began my scientific career in Genoa, Italy, at the Molecular Genetics Laboratory of the Giannina Gaslini Institute, and later continued my work in Paris at INSERM Unit U468 and the Pasteur Institute.

My early research focused on identifying genes and mutations responsible for **Hirschsprung disease**, a congenital disorder characterized by aganglionosis of the colon. I contributed to the identification of two key genes involved in this condition, ***RET*** and ***SOX10***, and characterized a spontaneous murine mutation, $Sox10^{Dom}$, assessing its impact on neural crest–derived neuronal cells.

During my tenure at the University of Pisa, I expanded my research to include fundamental studies on **genome architecture** and **replication timing**, particularly in the context of chromosome 22 rearrangements associated with DiGeorge syndrome.

Since 2005, I have been leading research programs that investigate the pathogenesis of human diseases by integrating **human genetics**, **functional genomics**, and **both cellular and animal models**. My current research focuses on two main areas:

1. Pathogenic Mechanisms in Balance and Motor Coordination Disorders

I mapped and characterized the spontaneous murine mutation ***crv4***, which disrupts the gene encoding the **metabotropic glutamate receptor mGlu1**. The ***crv4* mouse** serves as a model for ***SCAR13* (spinocerebellar ataxia, autosomal recessive 13)**. Our findings demonstrated a compensatory mechanism involving **mGlu5**, which exacerbates the disease phenotype. Pharmacological inhibition of mGlu5 in a double mutant ($mGlu1^{-/-}/mGlu5^{-/-}$) model resulted in a marked improvement in motor coordination.

In collaboration with the Neuropharmacology group at the University of Genoa, I also investigate molecular mechanisms underlying **amyotrophic lateral sclerosis (ALS)**. In particular, we explore the therapeutic potential of targeting **presynaptic glutamate release** mediated by mGlu1 and mGlu5 to reduce excitotoxicity and improve disease phenotype in ALS animal models.

2. Autism Spectrum Disorders and Intellectual Disability

This line of research aims to deepen our understanding of the **genetic basis of neurodevelopmental disorders**, with a focus on **autism spectrum disorder (ASD)** and **intellectual disability**. The project is multidisciplinary, involving child neuropsychiatrists, psychologists, behavioral scientists, clinical geneticists, and molecular biologists.

At the Giannina Gaslini Institute, patients undergo standard genetic screening (e.g., **Fragile X syndrome** testing, **array-CGH** for genomic deletions/duplications). However, many cases yield negative or inconclusive results. Our group reassesses such cases using **next-generation sequencing**, particularly **whole-exome sequencing (ES) and genome sequencing (GS)**, to identify novel pathogenic variants.

In parallel, we investigate disease mechanisms by modeling neurodevelopmental gene function using **induced pluripotent stem cells (iPSCs)** derived from patients. The long-term goal is to advance our understanding of disease pathophysiology and identify novel **molecular targets** for therapeutic intervention.

Research projects funded on a Competitive Basis (from the most recent)

2020 – present

Multiomic strategies to implement the diagnostic workflow of rare diseases.
Italian Ministry of Health. PNRR Project 2020. Unit Principal Investigator

2020 – 2025

Unveiling the hidden side of NEUrodevelopmental DIsorder Genetics (NEUDIG): a multidisciplinary pathway to new molecular diagnoses by integrating genomic, transcriptomic, and functional analyses.
Ministry of Education University and Research. PRIN Project 2020. Collaborator

2018 - 2023

Implementing clinical exome sequencing into the diagnostic workflow of epileptic encephalopathies.
Italian Ministry of Health. RF 2016. Unit Principal Investigator

2013 - 2016

Hereditary ataxias: an integrated study from genomic approach to pathogenetic mechanisms using animal and cellular models.
Ministry of Education University and Research. PRIN Project 2010. Unit Principal Investigator.

2012 - 2016

Identification of genes for rare developmental disorders by next generation sequencing.
Italian Ministry of Health. RF 2010. Unit Principal Investigator.

2008 - 2010
Functional characterization of auto and hetero metabotropic glutamatergic receptors with presynaptic localization in the CNS.
Ministry of Education University and Research. PRIN Project 2007. Collaborator

2001 - 2005
RET as a dependence receptor involved in apoptosis neuronogenesis and tumorigenesis.
European Commission FP5-LIFE QUALITY EU
Grant QLG1-CT-2001-01646. Unit Principal Investigator

International Research Work Experience

From 1992 to 1995, I conducted my research in Paris at INSERM Unit U.468 of the Mondor Institute, directed by Prof. Michel Goossens, in collaboration with the Mammalian Genetics Research Unit at the Institut Pasteur, led by Prof. Jean-Louis Guenet.

I continued the studies initiated at the Molecular Genetics Laboratory of the Giannina Gaslini Institute in Genoa, with the goal of identifying the genetic basis of Hirschsprung disease. My early findings suggested that the condition was not solely due to mutations in the *RET* gene on chromosome 10, but that additional genes likely contributed—consistent with the heterogeneous genetic nature of the disease.

At INSERM Unit, I introduced the research on Hirschsprung disease genetics and led a project aimed at identifying the gene responsible for the Dom phenotype in the mouse, which corresponds to the human condition. I conducted this study alongside a team of junior students and fellows, collaborating with

colleagues expert in various fields. The work unfolded in several phases: **Genetic localization** of the murine mutation to a 1.6 cM interval; **Physical mapping** of the genomic region contained within this candidate 1.6 cM interval; **dentification of candidate genes** for the murine phenotype; **Mapping of the homologous human region**; **Expression analysis** in mouse embryos to characterize the developmental defect.
During this period, I also spent time at the Institute of Cellular and Molecular Embryology in Nogent-sur-Marne (France), directed by Prof. Le Douarin, to establish primary cultures of mouse neural crest cells—tissue that gives rise to the enteric ganglia implicated in Hirschsprung disease.
The insights gained from these experiences formed the foundation for subsequent studies I developed after returning to Italy.

Genoa, June 14, 2025