

BIOGRAPHICAL SKETCH

NAME: RONZONI, LUISA

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

POSITION TITLE: medical doctor-researcher

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Milan, Milano	Single-cycle master's degree	07/2002	Medical Biotechnology Degree
University of Milan, Milano	PhD	01/2006	Molecular Medicine
University of Milan, Milano	Single-cycle master's degree	03/2011	Medical Degree
University of Milan, Milano	Specialization	07/2016	Clinical Genetic Residency

A. Personal Statement

I'm a Clinical Geneticist, specialized in the genetic diagnosis and counseling of rare diseases.

I have a first degree in Medical Biotechnology, a second degree in Medicine, and a PhD in Molecular Medicine from the University of Milan, Italy.

I have a consolidated experience in genomic analysis and genetic counseling, both in prenatal settings and in children and adults. During the last five years, I have also developed a clinical background in rare liver diseases as well as in transfusion medicine and immunohematology, and I have applied my genetic expertise within these fields. My main research interest is in understanding the genetic basis of rare diseases and applying these discoveries to the clinical management of patients, through the identification of novel biomarkers, therapeutic strategies, and clinical algorithms in a personalized medicine approach.

I have been involved in research projects aimed at evaluating the clinical utility of genetic analysis for defining a diagnosis in a prenatal setting (Co-PI for the project "Clinical Exome in Prenatal Diagnosis," Fondazione IRCCS Cà Granda) or in adults with rare liver diseases (participant in the project "Impact of Whole Exome Sequencing on the Clinical Management of Patients with Advanced Nonalcoholic Fatty Liver and Cryptogenic Liver Disease," RF-2016, or in ongoing projects on microcirculation diseases "INNOVA", Italian Ministry of Health, PNRR PNC-E3-2022-23683266, PNC-HLS-DA).

Currently, I work at the Precision Medicine Lab, Biological Resource Center Unit, Department of Transfusion Medicine at Fondazione IRCCS Ca' Granda, Ospedale Policlinico of Milan, where I coordinate the Genetic Counseling Service for Rare Liver Diseases; I'm responsible for genetic counseling and next-generation sequencing (NGS) analysis, coordinating a team of biologists involved in sample processing and data analysis. Since 2023, I'm Co-PI for the Blood Transfusion Genomics Consortium (BGC), an international network of transfusion centers responsible for introducing NGS for blood typing.

In my research career I have been an inspiring and supportive mentor for biotechnology students (n=9) and genetic residents (n=7). In the last four years, I was giving lectures on genetic analysis and rare diseases at the Medical Biotechnology and Molecular Medicine master program and in the clinical pathology specialization program at the University of Milan. Finally, I perform peer-review activities for high-impact journals, including Liver International, Frontiers, and Prenatal Diagnosis.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021-now	Clinical Geneticist - Researcher Translational Medicine - Biological Resource Center Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico - Milan
2023-now	Co-PI for the Blood Transfusion Genomics Consortium (BGC)
2023-now	Member, Italian Society for Liver Study (AISF)
2016 - 2020	Clinical Geneticist UOSD Clinical Genetic Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico - Milan
2016-now	Member, Italian Society Human Genetic (SIGU)
2012 - 2016	Clinical Genetic Residency University of Milan – Milan Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico – Milan University of Pavia - Pavia
2006 - 2012	Post-doctoral fellowship – “Centro Anemie Congenite” – Department of Internal Medicine - Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico – Milan
2003-2006	PhD student - Department of Internal Medicine - Fondazione IRCCS Ca'Granda- Ospedale Maggiore Policlinico – Milan

Honors

2016	Specialization in Clinical Genetic; Dean's Award
2011	Master degree in Medicine and Surgery; Dean's Award
2002	Master degree in Medical Biotechnology; Dean's Award

C. Contributions to Science

1. My last publications clearly evaluate and underline the impact of genetic analysis on the diagnosis and management of patients with cryptogenic liver disease.

In recent years, the implementation of next-generation sequencing (NGS) in the diagnostic work-up of adult patients with unexplained liver disease has significantly helped patients who remained undiagnosed despite intensive clinical and instrumental evaluations. In this context, I actively contributed to evaluating the clinical utility of whole exome sequencing (WES) or targeted gene panel sequencing (TS) for the diagnosis of steatotic liver disease (SLD). First, we validated a customized targeted NGS panel including 82 liver and lipid metabolism-related genes and demonstrated that its detection rate and specificity were comparable to those of WES, confirming its utility as a first-tier genetic test. We then examined the diagnostic uptake of the customized validated TS panel in a cohort of unrelated adult patients with SLD and a suspected genetic component, finding a diagnostic uptake of 22% for Mendelian disorders; the complementary evaluation of common variants, as captured by the SLD-Polygenic Risk Score (PRS), increased the overall utility of the genetic examination.

We also evaluated the role of WES in providing a diagnosis in a small cohort of adult patients with liver disease not fully accounted for by known risk factors or associated with a strong family history. Reaching a definitive diagnosis is useful not only for patient management but also for genetic counseling and family studies.

Finally, we reported on the use of WES in a cohort of patients with cholestatic liver disease, yielding a definite genetic diagnosis in 24% of patients with a meaningful impact on their clinical management.

- Ronzoni L, et al. "Validation of a targeted gene panel sequencing for the diagnosis of hereditary chronic liver diseases." *Front Genet.* 2023; 14:1137016
- Ronzoni L, et al. "Diagnostic uptake of targeted sequencing in adults with steatotic liver disease and a suspected genetic contribution", *Liver Int.* 2025;45(3):e70010.
- Pelusi S*, Ronzoni L*, et al. "Clinical exome sequencing for diagnosing severe cryptogenic liver disease in adults: a case series." *Liver Int.* 2022 Apr;42(4):864-870. *co-first.
- Pelusi S*, Ronzoni L*, et al. "Prevalence and determinants of liver disease in relatives of Italian patients with advanced MASLD." *CGH* 2024; S1542-3565(24)00046-6; *co-first.
- Scaravaglio M*, Ronzoni L*, et al. "Diagnostic yield of whole exome sequencing in adult-onset cholestatic liver disease" *CGH*, under review; *co-first.

2. In addition to the contributions described above, I directly documented the effectiveness of genetic analysis in the diagnosis of rare diseases in prenatal setting or in childhood, with important clinical implications not only for the patients but also for their families and for reproductive risk assessment. For instance, WES was instrumental in diagnosing fetuses with multiple congenital anomalies or children with severe intellectual disability and liver involvement, with important implications for clinical management and presymptomatic screening of first-degree relatives. Similarly, CGH-array allowed to establish a diagnosis in patients with suspected rare syndromes, enabling to set-up an appropriate clinical follow-up. I also contributed to highlight the role of genetic counseling for the appropriate management of a genetic diagnosis or at-risk results after prenatal screening tests.

- Ronzoni L et al. "Prenatal ultrasound findings associated with PIGW variants: One more piece in the FRYNS syndrome puzzle? PIGW-related prenatal findings." *Prenat Diagn.* 2022;42(12):1493-1502
- Ronzoni L, et al. "Liver Involvement in Patients with Rare *MBOAT7* Variants and Intellectual Disability: A Case Report and Literature Review." *Genes (Basel).* 2023;14(8):1633
- Ronzoni L, et al. "7p22.1 microduplication syndrome: refinement of the critical region." *Eur J Med Genet.* 2017;60(2):114-117
- Ronzoni L, et al. "Increased risk for 47,XXY on cell-free DNA screen: not always Klinefelter syndrome." *Prenat Diagn.* 2021 Sep;41(10):1255-1257

3. In collaboration with the research group I currently work with, I contributed to research projects aimed at understanding the molecular mechanisms underpinning steatotic liver disease and its progression to hepatocellular carcinoma, with a particular focus on the role of germline and somatic variants.

- Marchetti A,Ronzoni L,...et al. "Impact of clonal hematopoiesis of indeterminate potential on hepatocellular carcinoma in individuals with steatotic liver disease." *Hepatology.* 2024 Oct 1;80(4):816-827.
- Cherubini A, ...EPIDEMIC Study Investigators et al. "Interaction between estrogen receptor- α and PNPLA3 p.I148M variant drives fatty liver disease susceptibility in women." *Nat Med.* 2023; (10):2643-2655
- Valenti L, ...Ronzoni L, ...et al. "Clinical and genetic determinants of the fatty liver-coagulation balance interplay in individuals with metabolic dysfunction." *JHEP Rep.* 2022;4(12):100598
- Moore MP, ...Ronzoni L, ...et al. "Low *MBOAT7* expression, a genetic risk for MASH, promotes a profibrotic pathway involving hepatocyte TAZ upregulation." *Hepatology.* 2025;81(2):576-590).

Moreover, during the COVID-19 pandemic, I evaluated the role of genetic susceptibility to SARS-CoV-2 in children and in multisystem inflammatory syndrome in children (MIS-C), highlighting the role of rare and common variants in disease susceptibility and progression. I contributed to confirm the role of ABO locus in SARS-CoV-2 susceptibility in a local cohort and helped to delineate the role of rare genetic variants identified through WES in COVID-19 severity.

- Di Pietro GM*, Ronzoni L*, et al. "SARS-CoV-2 Infection in Children: a 24 Months Experience with a focus on risk factors in a Pediatric Tertiary Care Hospital in Milan, Italy." *Front Pediatr.* 11:1082083. *co-first

- Ronzoni L, et al. Genetic predisposition to multisystem inflammatory syndrome in children in an Italian cohort, unsubmitted
- Valenti L, ...Ronzoni L, ...et al. "Trends and risk factors of SARS-CoV-2 infection in asymptomatic blood donors." *Transfusion*. 2021;61(12):3381-3389)
- Boos J,...Ronzoni L, ...et al. "Stratified analyses refine association between TLR7 rare variants and severe COVID-19." *HGG Adv*. 2024;5(4):100323;
- Malvestiti F,.....Ronzoni L, Valenti L. "IFNAR2 p.F8S variant predisposes to severe COVID-19 by enhancing immunoreactivity in dendritic cells." *Nature Communications*, under review
- Schaefer B, ...Ronzoni L, ...et al. "The common genetic variant rs1278960 determining expression of interferon-lambda predicts inflammatory response in critically ill COVID-19 patients." *Scientific Reports*, 2025, in press

4. In my first publications, I contributed to evaluate the role of iron overload and hemoglobin switching in beta-thalassemia pathogenesis. I set up an in vitro model to recapitulate erythroid differentiation, starting from peripheral undifferentiated CD34+ cells. This in vitro model was then used to study the mechanisms involved in thalassemic erythropoiesis, to evaluate potential biomarkers of ineffective erythropoiesis, and to test potential therapeutic drugs aimed at inducing fetal hemoglobin expression and increasing hemoglobin levels in thalassemia.

- Ronzoni L, et al. "Erythroid differentiation and maturation from peripheral CD34+ cells in liquid culture: cellular and molecular characterization." *Blood Cells Mol Dis*. 2008;40(2):148-155.
- De Franceschi L, Ronzoni L, et al. "K-Cl co-transport plays an important role in normal and thalassemic erythropoiesis." *Haematologica*. 2007;92(10):1319-1326
- Ronzoni L, et al. "Growth Differentiation Factor 15 expression and regulation during erythroid differentiation in non-transfusion dependent thalassemia." *Blood Cells Mol Dis*. 2015;54(1):26-28
- Ronzoni L, et al. "Modulation of gamma globin genes expression by histone deacetylase inhibitors: an in vitro study." *Br J Haematol*. 2014;165(5):714-721