

CURRICULUM VITAE ET STUDIORUM

Date Prepared: July 2026
Name: Giovanni Roti
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EDUCATION

1996	Bachelor of Science Diploma di Maturità Scientifica	B.S. 58/60	Liceo Scientifico L. Spallanzani, Reggio Emilia
2002	Medicine. Laurea Medicina e Chirurgia	M.D. 110/110	University of Parma
2006	Clinical Fellowship Hematology and BMT	50/50 cum lode	University of Perugia, Hematology
2011	Ph.D. Dottorato di Ricerca	Ph.D.	University of Perugia, Hematology
2025	Master's in healthcare management and Health Systems and Organizations		Ministry of Health

CLINICAL AND SCIENTIFIC TRAINING

1999-2000	MD student	Université "Claude Bernard" Lyon, France. Centre Hospitalier Lyon Sud HCL-Pierre-Bénite, France
2000-2002	Residency	Hematology and BMT unit, University of Parma
2002-2006	Clinical Fellowship	Hematology and BMT unit, University of Perugia
<i>Research Fellowships</i>		
2007-2011	Postdoctoral Research Fellow	Dana-Farber Cancer Institute/Broad Institute of Harvard/MIT Harvard Medical School

ACADEMIC POSITION

YEAR	POSITION	DEPARTMENT	INSTITUTION
2026-	Full Professor Hematology Principal Investigator	Medicine and Surgery, Hematology THEC laboratory	University of Parma
2022-2026	Associate Professor Hematology Principal Investigator	Medicine and Surgery, Hematology THEC laboratory	University of Parma
2020-2022	Assistant Professor Principal Investigator	Medicine and Surgery, Hematology	University of Parma

2019-2020	Research Scientist A.D.R.	Medicine and Surgery, Hematology	University of Parma
2016-2019	Ricercatore T.D.b Principal Investigator	Medicine and Surgery, Hematology	University of Parma
2011-2016	Ricercatore T.D.a	Medicine, Hematology	University of Perugia
2011-2016	Instructor in Pediatrics	Pediatric Oncology	Dana-Farber Cancer Institute Harvard Medical School
2007-2017	Research Associate	Cancer Program	Broad Institute of Harvard and MIT

CLINICAL RESPONSIBILITIES

<u>YEAR</u>	<u>POSITION</u>	<u>DEPARTMENT</u>	<u>INSTITUTION</u>
2023-	Head of the Hematology and BMT Unit	HEM-ONC	University of Parma, Hospital
2023-	Scientific Director, NGS Platform	HEM-ONC	University of Parma, Hospital

ADDITIONAL NATIONAL SCIENTIFIC QUALIFICATION FOR ACADEMIC RECRUITMENT

2026	Clinical Pathology	06/A2	09/07/2026 - 09/07/2038	Full professor
2026	Pediatrics	06/G1	10/06/2026 - 08/06/2038	Full professor

INTERNATIONAL EXPERIENCES

Postdoctoral Research Fellow (Laboratory: Kimberly Stegmaier, MD)
Department of Pediatric Oncology.
Leukemia Program (Head: Stuart H. Orkin, MD, PhD; David A. Williams, MD).
Dana-Farber Cancer Institute, Boston, MA, USA.

&
Postdoctoral Research Fellow
Harvard Medical School. Boston, MA, USA
from 02-01-2007 to 08-09-2011

Research Scientist
Cancer Program (Head: Todd R. Golub, MD)
Broad Institute of Harvard and MIT, Cambridge, MA, USA
from 02-01-2007 to 30-10-2016

Faculty Instructor in Pediatrics (Assistant Professor equivalent)
Harvard Medical School, Boston, MA
Department of Pediatric Oncology

Leukemia Program (Head: Stuart H. Orkin, MD, PhD; David A. Williams, MD; Scott A. Armstrong, MD, PhD)

from 08-09-2011 to 30-10-2016

HIGHLY SPECIFIC TRAINING

2005	Training in DHPLC technology in the laboratory of Dr. Marco Tartaglia, Istituto Superiore di Sanità, Rome, Italy
2006	Transgenomic course for Wave System, Pavia, Italy
2007	Broad Institute Gene Pattern Workshop
2008	Broad Institute Gene Pattern Workshop
2011	Broad Institute Gene Pattern Workshop
2015	Introduction to RNAseq Analysis (DFCI-Boston Children's Hospital)
2015	Technical training for <i>in vivo</i> mice work
2017	GCP Compliance Training for HCPs V2.0

MEMBERSHIP

2006-	Member, European Hematology Association (EHA)
2009-	Member, American Society of Hematology (ASH)
2016-	Italian Society of Experimental Hematology (SIES)

HONORS, AWARDS, AND PRIZES

2005	Travel grant. 40th Italian society of Hematology, Bergamo, Italy
2006	"Mauro Felli", Young Researcher Award. CIRIAF University of Perugia, Italy
2007-2008	European Hematology Association-American Society of Hematology (EHA-ASH) International Award
2008	Travel grant. 13 th European Hematology Association Congress
	Travel grant. American Society of Hematology 51 st Meeting
2009-2010	Lady Tata Memorial Trust. International Awards for Research in Leukemia.
2010	"Silvia Fiocco" Young Researcher Award for Excellence in Leukemia Research, Accademia Nazionale dei Lincei, Roma
2010-2013	Leukemia and Lymphoma Society "Special Fellow" Award
2011	ASH Abstract Achievement Award, American Society of Hematology
2014	Claudia Adams Barr Award, Dana-Farber Cancer Institute
	Young Investigator Award, Fondazione Guido Berlucchi
	ASH Abstract Achievement Award, American Society of Hematology
2016	ASH Abstract Achievement Award, American Society of Hematology
	Seal of Excellence. EU Framework Programme for Research and Innovation 2014-2020. Project proposal 750679
2017	Gianni Bonadonna Prize for New Drug Development in Oncology, Finalist
	Best abstract presented at the Italian Society of Experimental Medicine meeting. Parma
2018	Gilead International Scholar award
	Seal of Excellence. EU Framework Programme for Research and Innovation 2014-2020. Project proposal 838166
2019	Giovanni di Guglielmo Award for Excellence in Leukemia Research. Accademia Nazionale dei Lincei.
2019	AIMS Award: Artificial Intelligence Molecular Screen (AIMS) Awards program by Atomwise for academic researchers seeking novel compounds to treat disease
2021	Hollis Browstein scholar

FUNDING INFORMATION (PI)

1999	Grant "Erasmus". European Grant for academic mobility, Université Claude Bernard Lyon II, France	n/a
2007	Grant "L. Fontana e M. Lionello" 2007 FIRC (Fondazione Italiana per la Ricerca sul Cancro)	\$25.000
2007-2008	European Hematology Association-American Society of Hematology (EHA-ASH) International Fellowship Award	\$75.000
2009-2010	American-Italian Cancer Foundation International Postdoctoral Research Fellowship	\$70.000
2009-2011	Lady Tata Memorial Trust. International Awards for Research in Leukaemia	£50.000
2011-2012	Grant 2011-Progetti di Ricerca. Fondazione Umberto Veronesi, Italy	€100.000
2010-2013	Leukemia and Lymphoma Society "Special Fellow" Award	\$195.000
2011-2016	Italian Ministry of Health. Bando Ricerca Finalizzata Giovani Ricercatori	€317.767
2013-2016	International Fellowship. Fondazione Umberto Veronesi, Italy	€71.000
2014-2016	Claudia Adams Barr Program in Cancer Research/ Innovative Basic Science Research	\$380.000
2017-2021	Start-up GRANT. Associazione Italiana Ricerca sul Cancro (AIRC)	€1.000.000
2017	Horizon 2020-Research Infrastructure. Corbel EU program	€100.000
	Cariparma foundation research grant 3576/2017	€40.000
	Grande Ale research grant	€10.000
2018	Gilead International Scholar award	\$130.000
	Cariparma foundation research grant 0180/2018	€100.000
	Grande Ale research grant	€10.000
2019	University of Parma-Feliciani Ferretti grant	€24.000
	POR FESR 2014-2020. SUPER: Supercomputing Unified Platform Multi-PI grant from the Emilia Romagna health board	€50.000
2019	AIMS Award: Artificial Intelligence Molecular Screen (AIMS) Awards program by Atomwise for academic researchers seeking novel compounds to treat disease	€100.000
2019	AIRC-Investigator Grant. Co-PI. A Radio-Immuno-Genomic Approach to Identify Prognostic and Predictive Models for the Response to Immunotherapy in NSCLC. Task: Genomic and computational core.	€1.119.000
2020	Grande Ale research grant	€15.000
2020-2021	Leukemia Research Foundation	\$100.000
2021-	GIMEMA per le Idee (<i>collaborator</i>)	€192.000
2021-	FIN-RER (Regional Cooperative Project)	€400.000
2021-	IFAB Foundation	€136.000
2022-		€3.693.646,57
	Ministry of Health. "Creazione di un programma di medicina di precisione per la mappatura del genoma umano su scala nazionale" - Piano Sviluppo e Coesione Salute.	
2022-2026		€54,146
	PNRR – M4C2 – I1.1 - PRIN 2022 - ERC LS4 -Next Generation EU	
2023-		€1.093.721
	AIRC-Investigator Grant. Targeting the Atypical Kinome in T-cell Acute Lymphoblastic Leukemia (IG-2022)	
2023		€20.000
	Grande Ale research grant	

2023-2025	Call for IDEAs 2023 Fondazione TIM. Profilo Predittivo di Risposta ai Farmaci (P-DRP) nelle Leucemie “Hopeless”.	€369.000
2024	Grande Ale research grant	€20.000
2023-2027	GIMEMA AML2326 “Novel approaches to target MECOM/EV1 in Acute Myeloid Leukemia”	€160.000
2024-2025	PNRR- M4C2 – I1.4 Leukemia Drug Response Profile Screening (LDRscreen): a Multiomic Model - ERC LS4 -Next Generation EU	€400.000
2024-2026	PNRR-MCNT2-2023-12378065, “Novel approaches for characterization and therapeutic targeting of T-cell acute lymphoblastic leukemia (T-ALL)	€250.000
2025	Grande Ale research grant	€25.000
2025-2026	Human Technopole’s National Facilities Research Grant	€100.000
2026-	FIS-2024-05611, Fondo Italiano per la Ricerca, Bando FIS3, LS-I37	€1.864.975,76
2025	Grande Ale research grant	€30.000

FUNDING INFORMATION (Mentor)

2018	Matteo Marchesini, Ph.D. EHA-ASH Translational Research Training in Hematology (TRTH-Award)
	Claudia Sorrentino, Ph.D. Fondazione Umberto Veronesi Fellowship
2019	Claudia Sorrentino, Ph.D. Fondazione Umberto Veronesi Fellowship
2020	Anna Montanaro, Ph.D. student Rotary International Foundation
2020	Claudia Sorrentino, Ph.D. AIRC Fellowship
2020-21	Anna Montanaro, Ph.D. student Italian Society of Experimental Hematology International Fellowship
2020-21	Matteo Marchesini Ph.D., Italian Society of Experimental Hematology-Beat Leukemia Foundation Fellowship
2025	Luciano Nicosia Ph.D., AIRC Fellowship
2025	Maria Teresa Giaimo M.D., Fondazione Veronesi Clinical Fellowship Program
2025	Sabrina Testa M.D., Fondazione AIRC Physician Scientist Project
2025	Luciano Nicosia, Ph.D. AIRC International Fellowship
2026	Luciano Nicosia, Ph.D. Marie Skłodowska Curie Actions Fellowship

REFEREE ACTIVITY

Agency

2011-	Italian Ministry of Health; Harvard Catalyst, Harvard Medical School; American Society of Hematology; Research Foundation–Flanders (FWO); Italian Ministry of University and Research; Italian Medicines Agency (AIFA); University of Calabria; University of Parma Under 40 in Hematology; Leuka – Leading Leukaemia Research; KiKa Foundation.
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Journal

2011- *Among others:* Leukemia, Cell Death and Disease, Blood, Clinical Cancer Research, Annals of Hematology, Nature Communication, Scientific reports, Cancer Cell.

Scientific Board

2017- Grande Ale Foundation
2019- SIES. Italian Society of Experimental Hematology. Emilia Romagna Chapter
2023- IFAB-Foundation
2024- EHA Grants & Fellowship committee
2025 AIRC Grants & Fellowship committee

PRESENTATIONS

Works limited to oral presentation

International

2008 American Society of Hematology 50th Meeting, San Francisco
Leukemia/Lymphoma Society SCOR Meeting, Boston
13th European Hematology Association Congress, Copenhagen
2009 American Society of Hematology 51st Meeting, New Orleans
Leukemia/Lymphoma Society SCOR Meeting, Boston
2010 Broad Institute Cancer Program Meeting, Cambridge
Leukemia/Lymphoma Society SCOR Meeting, Boston
2011 American Society of Hematology 53rd Meeting, San Diego
Leukemia/Lymphoma Society SCOR Meeting, Boston
2013 Broad Institute Cancer Program Meeting, Cambridge
Leukemia/Lymphoma Society SCOR Meeting, Boston
2014 American Society of Hematology 55th Meeting, San Francisco
2015 Leukemia/Lymphoma Society SCOR Meeting, Boston
2016 Leukemia/Lymphoma Society SCOR Meeting, Boston
2017 T-ALL International Workshop, Leuven, Belgium
2019 International NOTCH meeting. Cyprus
2019 American Society of Hematology 61st Meeting, Orlando
2020 24th Congress of the European Hematology Association
2021 25th Congress of the European Hematology Association
2022 American Society of Hematology 63rd Meeting, New Orleans
ALL, Assembly 2022 Madrid, Spain
2023 American Society of Hematology 65th Meeting, San Diego
2024 3rd Translational research Conference on CLL, Vienna
European Hematology Association Hybrid Congress, Madrid
4th European School of Hematology, Stockholm
2025 4th Translational Research Conference Acute Lymphoblastic Leukemia, Malahide-Dublin
2026 European Hematology Association Hybrid Congress, Milan
5th European School of Hematology, Mandelieu-La Napoule
31st Congress of the European Hematology Association, Stockholm

National

2004 Italian Society of Experimental Medicine meeting, Pavia
2005 40th SIE meeting Italian society of Hematology, Bergamo
2009 1st Translational Research in Hematology Meeting, Città della Pieve
2011 Seminars in Molecular Medicine, Genomics and Cancer: New Frontiers, Perugia
2017 AIRC National Cancer Meeting. Napoli
2017 Italian Society of Experimental Medicine meeting, Parma
Keynote speech. Nerviano Medical Sciences. Oncology Seminars.

- 2018 Seminar in clinical medicine, Bologna
University of Trento: "Where Science Meets Technologies"
University of Padova: Seminars in Hematology
- 2019 Keynote speech. Italian Society of Experimental Hematology, Milano
Italian Society of Hematology Meeting. Piacenza
- 2021 Keynote speech. Italian Society of Experimental Hematology, Milano
"New Biological Insights and Novel Drugs in Acute Leukemia", Venezia
Keynote speech. Italian Society for Leukemia Research
"Can We Predict the Chemosensitivity of Leukemia", AIL-Leukemia, Rome
- 2022 Keynote speech. "Intersecting Genomic Medicine and System Pharmacology for Profiling
Therapeutic Sensitivity in Leukemia", Mestre, Italy
17th SIES Meeting Italian Society of Experimental Hematology, Roma
- 2024 18th SIES Meeting Italian Society of Experimental Hematology, Firenze
- 2025 52nd SIE Meeting Italian Society of Hematology, Milano
TECAN Innovation Day, Milano
Leukemia Academy, Milano
- 2026 XIX SIES Meeting Italian Society of Experimental Hematology, Firenze
AIRC Annual Meeting, Parma
Comprehensive Cancer Care and Research Network della Romagna
Leukemia Academy, Milano

SCIENTIFIC CONTRIBUTION

1. During my medical training, major advances were made in our understanding of the molecular basis of disease. My mentors at the University of Perugia, Prof. B. Falini and Prof. C. Mecucci, contributed to these advances through the groundbreaking identification of *NPM1* mutations in acute myeloid leukemia (AML). Although aberrant *NPM1* expression could be readily detected by immunohistochemistry, this approach was not suitable for directly screening mutations in large sample cohorts. Therefore, I developed what was considered at the time a high-throughput assay for detecting *NPM1* mutations in leukemia, based on denaturing high-performance liquid chromatography (DHPLC). DHPLC is a reverse-phase chromatography method used to detect base substitutions and small DNA deletions or insertions. This work resulted in a first-author publication and several co-authored studies. I also applied this approach to the identification of mutations associated with genetic diseases.
 - a) **Roti G**, Rosati R, Bonasso R, Gorello P, Diverio D, Martelli MF, Falini B, Mecucci C. DHPLC: a valid approach for identifying *NPM1* mutations in acute myeloid leukaemia. *Journal of Molecular Diagnostics*, 2006, 8: 254-259
 - b) Falini B, Martelli MP, Bolli N, Bonasso R, Ghia E, Pallotta MT, Diverio D, Nicoletta I, Pacini R, Tabarrini A, Verducci Galletti B, Mannucci R, **Roti G**, Rosati R, Specchia G, Liso A, Tiacci E, Alcalay M, Luzi L, Volorio S, Bernard L, Guarini A, Amadori S, Mandelli F, Pane F, Lo Coco F, Saglio G, Pelicci PG, Martelli MF, Mecucci C. Immunohistochemistry predicts nucleophosmin (*NPM*) mutations in acute myeloid leukemia. *Blood* 2006, 108(6):1999-2005
 - c) **Roti G**, La Starza R, Ballanti S, Crescenzi B, Romoli S, Foà R, Tartaglia M, Aversa F, Martelli MF, Mecucci C. Acute lymphoblastic leukemia in Noonan syndrome. *British Journal of Hematology* 2006, 133:448-450
2. In 2007, I joined Dr. Kimberly Stegmaier's laboratory at the Dana-Farber Cancer Institute and the Broad Institute of MIT and Harvard. In Dr. Stegmaier's laboratory, I initially extended the application of Gene Expression-Based High-Throughput Screening (GE-HTS) to the challenge of targeting transcription-factor abnormalities in cancer. I applied this platform to identify modulators of the oncogenic transcription factor AML1-ETO in acute myeloid leukemia (AML). This work led to the identification of corticosteroids and dihydrofolate reductase (DHFR) inhibitors as novel modulators of AML1-ETO, one of the most common chromosomal alterations in AML. Furthermore, I contributed to a project that identified GSK-3 α as a novel therapeutic target in AML. I served as a lead investigator or co-investigator in all these studies.

- a) Corsello SM[#], **Roti G[#]**, Ross KN, Chow KT, Galinsky I, Stone RM, DeAngelo DJ, Kung AL, Golub TR, Stegmaier K. Identification of AML1-ETO modulators by chemical genomics. *Blood*. 2009 Jun 11;113(24):6193-205. PMID: PMC2699238. *# These authors contributed equally to this work.*
- b) Banerji V, Frumm SM, Ross KN, Li LS, Schinzel AC, Hahn CK, Kakoza RM, Chow KT, Ross L, Alexe G, Tolliday N, Inguilizian H, Galinsky I, Stone RM, DeAngelo DJ, **Roti G**, Aster JC, Hahn WC, Kung AL, Stegmaier K. The intersection of genetic and chemical genomic screens identifies GSK-3 α as a target in human acute myeloid leukemia. *J Clin Invest*. 2012 Mar 1;122(3):935-47. PMID: PMC3287215.

3. NOTCH signaling represents a long-standing and central research focus of my laboratory. Our work aims to define the biological role of oncogenic NOTCH1 in lymphoid malignancies and to translate its vulnerabilities into selective therapeutic strategies. This program originated from the challenge of identifying the biologically relevant targets of compounds emerging from cell-based assays. To address this limitation, I integrated complementary chemical and genomic screens, combining a small-molecule screen for modulators of mutant NOTCH1 in T-cell acute lymphoblastic leukemia (T-ALL) with a cDNA-based screen for enhancers of a leukemia-associated NOTCH1 allele. SERCA emerged independently from both approaches, identifying calcium homeostasis and receptor trafficking as previously unrecognized vulnerabilities of NOTCH1-driven cancers. I subsequently demonstrated that SERCA inhibition disrupts the maturation and cell-surface trafficking of mutant NOTCH1 receptors, suppresses oncogenic NOTCH signaling, and induces G0/G1 cell-cycle arrest in NOTCH1-mutant T-ALL cells. The SERCA inhibitor thapsigargin showed on-target antileukemic activity in mouse models of human T-ALL and inhibited Notch signaling in *Drosophila*. Importantly, it preferentially affected mutant rather than wild-type NOTCH1 receptors, revealing a therapeutic window that is not observed with γ -secretase inhibitors or antibody-based approaches, which generally inhibit both oncogenic and physiological NOTCH signaling. These findings established SERCA as a therapeutic target in NOTCH1-mutant malignancies and provided the conceptual foundation for a major research program in my laboratory.

Because systemic administration of thapsigargin can disrupt intracellular calcium homeostasis and cause substantial toxicity, I next focused on developing strategies for its selective delivery. I demonstrated that T-ALL cells express high levels of folate receptors, enabling folate receptor-mediated drug internalization. In collaboration with James Bradner and Jun Qi at the Dana-Farber Cancer Institute, we developed a folate-conjugated thapsigargin prodrug as a first-in-class anti-NOTCH1 therapeutic with two complementary levels of selectivity: leukemia cells over normal tissues and mutant over wild-type NOTCH1 receptors. This work provided proof of principle that potent SERCA inhibitors can be pharmacologically redirected toward leukemia cells while preserving their preferential activity against oncogenic NOTCH1. Our studies also implicated calcium signaling more broadly in the regulation of NOTCH1. An expression-based screen identified the calcium-channel blocker bepridil as a NOTCH1 modulator in T-ALL, and subsequent studies demonstrated that this FDA-approved drug exerts antileukemic activity associated with NOTCH1-pathway inhibition in chronic lymphocytic leukemia (CLL). These findings expanded the relevance of our approach beyond T-ALL and reinforced the connection between calcium regulation and oncogenic NOTCH signaling.

At the University of Parma, I established an independent research program that further develops this therapeutic concept. Through a screen of approximately 191,000 compounds against P-type ATPases, my laboratory identified CAD204520, a novel SERCA modulator that binds to a site distinct from the thapsigargin-binding pocket. CAD204520 blocks oncogenic NOTCH1 signaling while showing a more favorable calcium-related toxicity profile. We demonstrated its activity in T-ALL and subsequently found that it selectively targets NOTCH1 PEST-domain mutations, including the most frequent class of NOTCH1 alterations in CLL and other lymphoproliferative disorders. These results have broadened the scope of our NOTCH program from T-ALL to additional NOTCH1-driven hematologic malignancies.

Overall, my laboratory has contributed to establishing a continuous translational framework for targeting oncogenic NOTCH1—from the discovery of SERCA through integrated genomic and

chemical screens, to leukemia-selective delivery of thapsigargin and the development of next-generation SERCA modulators. NOTCH biology therefore serves not only as a core disease model in my laboratory but also as a platform for integrating target discovery, chemical biology, drug development, and preclinical translation. This work complements our broader efforts to define the molecular landscape of acute lymphoblastic leukemia and develop new therapeutic approaches for high-risk T-ALL.

- a) Pagliaro L, Chen SJ, Herranz D, Mecucci C, Harrison CJ, Mullighan CG, Zhang M, Chen Z, Boissel N, Winter SS, **Roti G**. Acute lymphoblastic leukaemia. *Nat Rev Dis Primers*. 2024 Jun 13
- b) Pagliaro L, Cerretani E, Vento F, Montanaro A, Moron Dalla Tor L, Simoncini E, Giaimo M, Gherli A, Zamponi R, Tartaglione I, Lorusso B, Scita M, Russo F, Sammarelli G, Todaro G, Silini EM, Rigolin GM, Quaini F, Cuneo A, **Roti G**. CAD204520 Targets *NOTCH1* PEST Domain Mutations in Lymphoproliferative Disorders. *Int J Mol Sci*. 2024
- c) Marchesini M., Gherli A., Montanaro A., Patrizi L., Sorrentino C., Pagliaro L., Rompietti C., Kitara S., Heit S., Olesen C. E, Møller J. V, Savi M., Bocchi L., Vilella L., Rizzi F., Baglione M., Rastelli G., Loiacono C., La Starza R., Mecucci C., Stegmaier K., Aversa F., Stilli D., Lund Winther A.M., Sportoletti P., Bublitz M., Dalby-Brown W., **Roti G**. Blockade of Oncogenic NOTCH1 With the SERCA Inhibitor CAD204520 in T Cell Acute Lymphoblastic Leukemia. *Cell Chem Biol*. 2020 Apr 15;S2451-9456(20)30116-1
- d) **Roti G**, Qi J, Kitara S, Varca CA, Sanchez-Martin M, Kung AL, Ferrando AF, Bradner JE, Stegmaier K. Leukemia-Specific Delivery of Mutant NOTCH1 Targeted Therapy. *J Exp Med*. 2018 Jan 2;215(1):197-216
- e) **Roti G**, Carlton A, Ross KN, Markstein M, Pajcini K, Perrimon N, Pear WS, Kung AL, Blacklow SC, Aster JC, Stegmaier K. Complementary genomic screens identify SERCA as a therapeutic target in *NOTCH1-MUTATED CANCER*. *Cancer Cell*. 2013 Mar 18;23(3):390-405. PMID: PMC3709972.

As featured in Cancer Cell. 2013 Mar 18;23(3):267-9. Ilagan MX, Kopan R. Selective blockade of transport via SERCA inhibition: the answer for oncogenic forms of Notch?

As featured in Nat Med. 2013 May;19(5):546. Boettner B. Cancer therapy: A Notch further with SERCA.

As featured in Cancer Res April 1, 2013 73; 2023

- f) **Roti G**, Ross KN, Blacklow SC, Aster JC, Stegmaier K. Expression-based Screen Identifies the Calcium Channel Antagonist Bepridil as a Notch1 Modulator in T-ALL. Presented at the American Society of Hematology 51th Meeting, New Orleans 4-8 December 2009.
- g) Baldoni s, Del Papa B, Aureli P, Dorillo E, De Falco F, Varasano E, Cecchini D, Zei T, Di Tommaso T, Rosati E, Gabriela A, **Roti G**, Stegmaier K, Di Ianni M, Falzetti F, Sportoletti P. Bepridil exhibits anti-leukemic activity associated with NOTCH1 pathway inhibition in chronic lymphocytic leukemia. *International Journal of Cancer*. 2018 vol. 143, p. 958-970
- h) **Roti G** and Stegmaier K. New Approaches to Target T-ALL. *Front Oncol*. 2014 Jul 8;4:170. PMID: PMC4085879.

4. My research focuses on identifying novel therapeutic targets in pediatric and hematologic malignancies through the integration of complementary omics, functional proteomics, and genetic screening approaches. Most recently, the combination of functional proteomics with CRISPR-Cas9 screening led to the identification of WNK1 as a therapeutically relevant kinase in the aggressive TAL1-positive subgroup of T-cell acute lymphoblastic leukemia (T-ALL). In parallel, I have led a major research effort on acute myeloid leukemia (AML) with 3q26 rearrangements and *MECOM* overexpression, a particularly aggressive subtype associated with a life expectancy of less than 24 months. High-throughput screening of more than 10,000 compounds, followed by orthogonal proteogenomic analyses, identified a pharmacologically actionable PA2G4–MYC axis. These findings were validated in vitro and in preclinical models and subsequently translated into a clinical experience that demonstrated anti-leukemic activity in treated patients. We are currently leveraging these results to develop a new targeted inhibitor.

As an independent researcher at the University of Parma, I have also investigated epigenetic vulnerabilities in T-ALL, identifying an epi-metabolic dependency on the pharmacologically targetable methyltransferase EHMT2/G9a. This work builds upon my earlier contributions to the development of platforms for uncovering epigenetic dependencies and mechanisms of therapeutic response and resistance across leukemia, brain tumors, and neuroblastoma. These studies included the characterization of neuronal differentiation and cell-cycle programs associated with the

response to BET-bromodomain inhibition in MYC-driven medulloblastoma, the demonstration that selective HDAC1/HDAC2 inhibition induces neuroblastoma differentiation, and the development of integrated genetic and proteomic strategies for cancer-target discovery. I also contributed to defining how resistance to epigenetically targeted therapies can generate new tumor vulnerabilities through enhancer remodeling. Collectively, this research has established a coherent framework for translating multi-omic target discovery into pharmacological and, ultimately, clinical applications.

- a) Montanaro A., Monica G., D'Antuono A., Zamponi R., Andrei P., H. Su. A., Sammarelli G., Todaro G., La Starza R., Mecucci C., Elia L., Giaimo M., Gherli A., Vento F., Lorusso B., Lagrasta C., Simoncini E., Marchesini M., Pagliaro L., Jimenez C., Quaini F., Stegmaier K., and **Roti G.** Inhibition of the Atypical Kinase WNK1 as a Therapeutic Strategy in TAL1-related T-cell Acute Lymphoblastic Leukemia. *Blood*, 2026 May 19: blood.2025029901. doi: 10.1182/blood.2025029901. Online ahead of print.
- b) Marchesini M, Gherli A, Simoncini E, Tor LMD, Montanaro A, Thongon N, Vento F, Liveni C, Cerretani E, D'Antuono A, Pagliaro L, Zamponi R, Spadazzi C, Follini E, Cambò B, Giaimo M, Falco A, Sammarelli G, Todaro G, Bonomini S, Adami V, Piazza S, Corbo C, Lorusso B, Mezzasoma F, Lagrasta CAM, Martelli MP, La Starza R, Cuneo A, Aversa F, Mecucci C, Quaini F, Colla S, **Roti G.** Orthogonal proteogenomic analysis identifies the druggable PA2G4-MYC axis in 3q26 AML. *Nat Commun*. 2024 Jun 4
- c) Montanaro A, Kitara S, Marchesini M, Gherli A, Su A, Fioretzaki R, Ross L, Alexe G, Sabrina Bonomini S, Masselli E, Xiong Y, Jin J, Falco A, Knoechel B, Aversa F, Quaini F, Stegmaier K, **Roti G.** Identification of an Epi-metabolic dependency on EHMT2/G9a in T-cell Acute Lymphoblastic Leukemia. *Cell Death and Disease* 2022 (13):551.
- d) Bandopadhyay P, Piccioni F, O'Rourke R, et al. Neuronal differentiation and cell-cycle programs mediate response to BET-bromodomain inhibition in MYC-driven medulloblastoma. *Nat Commun*. 2019;10(1):2400. Published 2019 Jun 3. doi:10.1038/s41467-019-10307-9
- e) Frumm SM, Fan ZP, Ross KN, Duvall JR, Gupta S, VerPlank L, Suh BC, Holson E, Wagner FF, Smith WB, Paranal RM, Bassil CF, Qi J, **Roti G**, Kung AL, Bradner JE, Tolliday N, Stegmaier K. Selective HDAC1/HDAC2 inhibitors induce neuroblastoma differentiation. *Chem Biol*. 2013;20(5):713-725.
- f) **Roti G**, Stegmaier K. Genetic and proteomic approaches to identify cancer drug targets. *Br J Cancer*. 2012;106(2):254-261.
- g) Iniguez AB, Alexe G, Wang EJ, **Roti G** et al. Resistance to Epigenetic-Targeted Therapy Engenders Tumor Cell Vulnerabilities Associated with Enhancer Remodeling. *Cancer Cell*. 2018;34(6):922-938.e7.

5. More recently, I have focused on developing and clinically implementing a functional precision medicine platform for patients with high-risk, relapsed, or refractory leukemia. This platform combines ex vivo drug-response profiling of primary leukemia samples against curated libraries of approximately 80-200 approved small molecules with genomic and molecular characterization. By directly assessing individual patterns of drug sensitivity and resistance, this strategy aims to identify actionable therapeutic vulnerabilities and inform patient-specific treatment decisions, particularly when conventional therapeutic options are limited.

This work provided the foundation for the GIMEMA ALL2720 national clinical trial, which evaluates the integration of chemical and genomic profiling to guide treatment in relapsed or refractory T-cell acute lymphoblastic leukemia (T-ALL) and early T-cell precursor acute lymphoblastic leukemia (ETP-ALL). The trial represents the clinical translation of a chemogenomic framework developed to move beyond genomics alone and incorporate functional evidence of drug response into therapeutic decision-making. The design, implementation, and potential clinical applications of this strategy are described in our recent study in *npj Precision Oncology*.

The clinical value of the platform was further illustrated in a day-to-day clinical scenario involving a pediatric patient with high-risk acute undifferentiated leukemia carrying a *PICALM::MLLT10* rearrangement, in whom ex vivo drug-response profiling was used to guide therapy. This experience demonstrated the feasibility of applying functional drug testing to rare and biologically complex leukemias for which no established targeted treatment is available. The platform builds on our earlier identification of the combination of venetoclax and bortezomib as a potential therapeutic strategy for relapsed or refractory ETP-ALL. Collectively, these studies have enabled my laboratory to secure more than €5 million in funding over the past five years.

- a) Pagliaro L, Rosati R, Giaimo M, Bardelli V, Zamponi R, Tragni K, Montanaro A, Gherli A, Messina M, Picciocchi A, Marsili G, Crea E, Fazi P, Vignetti M, Papayannidis C, Giglio F, Cambò B, Chiaretti S, Piccini M, Lussana F, Sica

- S, Zappasodi P, Brunetti L, Beggiato E, Audisio E, Borlenghi E, Bocchia M, Bassan R, Di Trani M, Pessina A, Rinaldi A, Prezioso L, La Starza R, Mecucci C, **Roti G***. Advancing chemogenomic strategies for functional precision medicine in relapsed-refractory T-ALL and ETP-ALL: the GIMEMA ALL2720 trial. *npj Precision Oncology* 2026 in press.
- b) Mastrodicasa E, Pagliaro L, Pierini V, Bardelli V, Giaimo M, Zamponi R, Montanaro A, Tragni K, Arcaleni R, Massei MS, Capolsini I, Perruccio K, Varotto E, Buldini B, Gherli A, Romoli S, Matteucci C, Crocioni M, Arcioni F, Gurdo G, Cerri C, Caniglia M, **Roti G***, la Starza R*. Ex vivo drug response profiling guides therapy in a case of high-risk acute undifferentiated leukemia with PICALM::MLLT10. *Haematologica*. 2025 Feb 27. doi: 10.3324/haematol.2024.286815. Online ahead of print. *These authors contributed equally to this work.
- c) La Starza R, Cambò C, Pierini A, Bornhauser B, Montanaro A, Bourquin JP, Mecucci C, **Roti G**. Venetoclax and Bortezomib in Relapsed/Refractory Early T-Cell Precursor Acute Lymphoblastic Leukemia. *JCO Precision Oncology*, 2019 Sep 20;3:PO.19.00172.
- d) Omics approaches for Leukemia Target Identification and Matched Therapeutic Intervention FIN-RER 2020
- e) NCT04582487 GIMEMA National Trial ALL-2720. Advancing chemical and genomic strategies for relapsed/refractory T-ALL and ETP-ALL

CLINICAL CONTRIBUTION

- 1999-2000 Internship in Internal Medicine, (Centre Hospitalier Lyon Sud HCL-Pierre-Bénite, Université Claude Bernard Lyon II, France).
Inpatient care of general medicine patients, including Diabetes & Endocrinology; Hematology; Rheumatology; Cardiology (Hospital Cardiologique Louis Pradel Lyon, Université Claude Bernard Lyon II, France).
Internship in Orthopedic Surgery (Centre Hospitalier Lyon Sud HCL-Pierre-Bénite, Université Claude Bernard Lyon II, France).
- 2000-2002 Internship in Internal Medicine and Hematology, (Ospedale Maggiore di Parma, University of Parma, Italy). Inpatient care of general medicine patients, including: Diabetes & Endocrinology; Hematology; Respiratory Medicine; Gastroenterology; Cardiology; Nephrology.
- 2002 Out-of-hours General Practitioner's Service for the Emilia Romagna Health Board.
- 2002-2006 Fellow in Hematology and Bone Marrow Transplantation (BMT) (Ospedale S.Maria della Misericordia, University of Perugia, Italy). Hemato-oncologic inpatient management, including acute management of complications, high-dose chemotherapy, PBSC mobilization, autologous stem cell transplantation, allogeneic stem cell transplantation from matched and unmatched sibling donors. Management of general Hematology patients, including: hemoglobinopathies, acquired and inherited bleeding disorders. Management of hematological malignancy outpatients, including myeloproliferative disorders, myelodysplastic syndromes, plasma cell disorders, Hodgkin and non-Hodgkin lymphoma, chronic lymphocytic leukemia in the day-hospital setting. Outpatient management of new patients and their diagnostic workup for general Hematology and hemato-oncology.
- 2004-2006 Out-of-hours General Practitioner's Service for the Umbria Health Board.
- 2017-2024 Attending physician in the Hematology and BMT Unit, University teaching hospital, Parma, Italy
- 2023-** ***Clinical Pathology. Scientific Head of the Next-Generation Sequencing Platform for the Emilia-Romagna Northern Region. AOU-PR***
- 2019-2021 Attending physician in Internal Medicine, AO Mantova, Italy for COVID pandemic support
- 2024-** Head of the Hematology and Bone Marrow Transplant Unit. AOU-PR: The Hematology and Bone Marrow Transplantation Unit of the University Hospital of Parma is a Complex Clinical Unit within the Provincial Intercompany Integrated Onco-Hematology Department. It serves as a tertiary referral center for the province of Parma—an area with approximately 460,000 inhabitants—while also receiving patients from other provinces and regions. Its clinical and organizational responsibilities extend beyond the University Hospital through close integration with the Local Health Authority and other healthcare

providers operating across the province, ensuring continuity of care between hospital-based services, community facilities, primary care, and home-care programs.

The Unit provides comprehensive diagnosis and treatment for malignant hematologic diseases, including acute and chronic leukemias, myelodysplastic and myeloproliferative neoplasms, Hodgkin and non-Hodgkin lymphomas, multiple myeloma, monoclonal gammopathies, and chronic lymphocytic leukemia. It also treats nonmalignant hematologic disorders, including bone marrow failure, autoimmune cytopenias, hemoglobinopathies, platelet disorders, and paroxysmal nocturnal hemoglobinuria. Care is delivered through inpatient hospitalization, day-hospital treatment, and specialized outpatient clinics. The Unit works closely with the Bone Marrow and Hematopoietic Stem Cell Transplant Center and provides advanced diagnostic and disease-monitoring services encompassing morphology, cytogenetics, molecular hematology, next-generation sequencing, and cell processing for transplantation.

Its activity is based on an integrated multidisciplinary model connecting clinical care, advanced diagnostics, transplantation, research, and specialist training. Continuity of care is further supported by the *Emocasa* home-care program, developed in collaboration with AIL Parma, as well as psychological support and accommodation for patients arriving from outside the city. As part of the provincial onco-hematology network, the Unit contributes to the coordination of diagnostic and therapeutic pathways across the University Hospital of Parma, the Parma Local Health Authority, and the healthcare facilities distributed throughout the territory.

ACADEMIC CLINICAL TRIAL DEVELOPMENT

2020-	"Advancing chemical and genomic strategies for relapsed/refractory T-ALL and ETP-ALL"	GIMEMA ALL2720	National PI Local PI	NCT04582487
2021-	Novel Approaches to Target EVI1 in Acute Myeloid Leukemia	GIMEMA	National PI	NCT07445984
2022-	Integrative "omics" approaches for leukemia target identification and matched therapeutic intervention.	Emilia-Romagna Health Board	National PI	NCT06626893
2025-	Feasibility of a Multi-Omics Platform for Hematologic Malignancies	University of Parma	National PI	NCT07445438

TEACHING AND MENTORING ACTIVITY

2011-	My experience as a research supervisor began at Harvard Medical School, where I served as an Instructor in Pediatrics in the Department of Pediatric Oncology at the Dana-Farber Cancer Institute. During this period, I mentored students from Harvard Medical School and other Boston medical schools and supervised Ph.D. trainees who subsequently pursued postdoctoral research at prestigious academic cancer centers. I also closely supervised Angela Su and Samuel Kitara, two talented research technicians who joined the laboratory after college and worked with me from 2012 to 2016. Angela is now a senior laboratory manager and a researcher in the Pediatric Oncology Branch at the National Cancer Institute (NCI), while Samuel completed the highly competitive M.D./M.B.A. program at Yale University and subsequently joined Gilead. I supported Samuel's professional development, including his application to the Aga Khan Foundation International Scholarship Programme, which enables outstanding students from developing countries to pursue postgraduate education.			
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At the University of Parma, mentoring and career development have become central components of my academic responsibilities. Each year, I supervise at least two medical students, and I currently mentor three Ph.D. students and two postdoctoral fellows. Several former trainees have progressed toward independent academic careers. Matteo Marchesini, one of my first postdoctoral researchers in Parma, moved to the IRCCS Istituto Romagnolo per lo Studio dei Tumori “Dino Amadori” in Meldola, where he is now a Senior Researcher and Research Area Manager in Translational Hematology. He has also assumed principal-investigator responsibilities for an IRST research unit, demonstrating his transition toward scientific independence.

Anna Montanaro and Luca Pagliaro have likewise progressed from trainees in my laboratory to fixed-term researcher positions in the Department of Medicine and Surgery at the University of Parma, where they are developing increasingly independent research and teaching profiles.

More recently, Luciano Nicosia was awarded a highly competitive Marie Skłodowska-Curie Actions Postdoctoral Fellowship for a project on targeting EP300/CBP in AML, under my supervision. The fellowship was awarded in a call with an overall success rate of 9.4%, providing further recognition at the European level of our laboratory’s ability to support researcher development and career advancement.

2017-	Medical School. Hematology, University of Parma
2017-	Nursing School. Internal Medicine, University of Parma
2017-	Ph.D. Program. Department of Medicine and Surgery, University of Parma, Italy
2017-	Molecular Therapy. Bachelor of Science program. University of Parma, Italy
2020-	Master’s in Clinical Trials. University of Parma, Italy

TEACHING COURSES

CFU Courses (CDL) at University of Parma

1	“Prevention techniques in the environment and in the workplace (qualifying for the health profession of prevention technician in the environment and in the workplace) - Blood Diseases Module”
3	“Medical, veterinary and pharmaceutical biotechnologies - Molecular Therapies Module”
1	“Nursing (qualifying for the health profession of nurse) - Clinical Medical teaching - Specialized Medicine”
3	Medicine and Surgery – Hematology Module
1	“Fellowship program of Hematology”
1	“Fellowship program in Infectious and Tropical Diseases”
1	“Fellowship program of Pathology”

2017-	<i>Seminar Organization - University of Parma</i> Hematology & Oncology seminar series
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PUBLICATIONS

Complete List of Published Works in My Bibliography

<https://pubmed.ncbi.nlm.nih.gov/?term=Giovanni%20Roti&page=3>

ORCID ID: 0000-0002-8664-950X

ResearcherID: A-4234-2015

Scopus Author ID: 12808329800

SCOPUS

H-index: 28

Total citations: 2549

Mean citations: 33,86

Total Impact Factor: 696,092 – 2021 Journal Impact Factor

Mean Impact Factor: 12,2121

No. and total IF of publications where the candidate is first author equivalent (for the disciplines where the position in the list of authors corresponds to the role in the work presented): 9 – 116,721

No. and total IF of publications where the candidate is the last or corresponding author (for the disciplines where the position in the list of authors corresponds to the role in the work presented): 9 – 59,333

Pagliaro L, Rosati R, Giaimo M, Bardelli V, Zamponi R, Tragni K, Montanaro A, Gherli A, Messina M, Picciocchi A, Marsili G, Crea E, Fazi P, Vignetti M, Papayannidis C, Giglio F, Cambò B, Chiaretti S, Piccini M, Lussana F, Sica S, Zappasodi P, Brunetti L, Beggiato E, Audisio E, Borlenghi E, Bocchia M, Bassan R, Di Trani M, Pessina A, Rinaldi A, Prezioso L, La Starza R, Mecucci C, **Roti G**. Advancing chemogenomic strategies for functional precision medicine in relapsed-refractory T-ALL and ETP-ALL: the GIMEMA ALL2720 trial. *npj Precision Oncology* 2026 in press. **IF 9.9**

Montanaro A, Monica G, Zamponi R, D'Antuono A, Andreani A, Andrei P, Su A, Ciringione A, Sammarelli G, Todaro G, Rosati R, La Starza R, Mecucci C, Elia L, Gherli A, Vento F, Simoncini E, Lorusso B, Lagastra C.A.M., Giaimo M, Pagliaro L, Marchesini M, Jimenez C.R., Quaini F, Stegmaier K, **Roti G**. Inhibition of the atypical kinase WNK1 as a therapeutic strategy in TAL1-related T-cell Acute Lymphoblastic Leukemia. *Blood* 2026 May 19: blood.2025029901. doi: 10.1182/blood.2025029901. Online ahead of print. **IF 23.9**

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treatment for symptomatic splenic marginal zone lymphoma: long-term outcome and impact of early unmeasurable minimal residual disease attainment from the BRISMA/IELSG36 phase II study. *Haematologica*. 2024 Jul 1; 109(7):2297-2302. **IF 8.2**

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Pagliaro L, Cerretani E, Vento F, Montanaro A, Moron Dalla Tor L, Simoncini E, Giaimo M, Gherli A, Zamponi R, Tartaglione I, Lorusso B, Scita M, Russo F, Sammarelli G, Todaro G, Silini EM, Rigolin GM, Quaini F, Cuneo A, **Roti G**. CAD204520 Targets *NOTCH1* PEST Domain Mutations in Lymphoproliferative Disorders. *Int J Mol Sci*. 2024 Jan 7;25(2):766. doi: 10.3390/ijms25020766 **IF 4.9**

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Iesato, A., Li, S., **Roti, G.**, Hacker, M.R., Fischer, A.H., Nucera, C. Lenvatinib Targets PDGFR- β Pericytes and Inhibits Synergy with Thyroid Carcinoma Cells: Novel Translational Insights. *Journal of Clinical Endocrinology and Metabolism* 2021, 106 (12), pp. 3569-3590 **IF 5,958**

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Parma 10/08/2026

