

**BIOGRAPHICAL SKETCH**

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NAME: CHIARA PALMI

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

POSITION TITLE: Joung PI

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<br>(if applicable) | Completion Date<br>MM/YYYY | FIELD OF STUDY                                                     |
|--------------------------------------------|---------------------------|----------------------------|--------------------------------------------------------------------|
| University of Milan                        | M.S.                      | 10/2002                    | Medical Biotechnology                                              |
| Vita-Salute San Raffaele University, Milan | PhD                       | 01/2009                    | Molecular Medicine -<br>Section of Basic and<br>Applied Immunology |

**A. Personal Statement**

My academic training and research career have provided me with a multidisciplinary background in molecular and cell biology, cancer genetics and translational research, with a specific focus on pediatric acute lymphoblastic leukemia (ALL).

Since 2022 I'm a permanent staff member and Joung PI at Fondazione Matilde Tettamanti Menotti De Marchi ONLUS (Fondazione M. Tettamanti) in Monza, Italy, an internationally recognized research center in pediatric hematology.

My research focuses on:

- i) new prognostic and/or druggable gene lesions in childhood ALL: *CRLF2* alterations in B and T-ALL, *IKZF1* deletions in B-ALL, the profile *IKZF1*-plus in B-ALL and in DS-ALL (B-ALL in children with Down syndrome);
- ii) high-throughput drug screening and drug repurposing strategies to identify effective treatments for poor outcome subgroups of pediatric B and T-ALL;
- iii) characterization of ETV6::RUNX1 pre-leukemic cells (resistance to inhibitory stimuli, interaction with the bone marrow microenvironment with or without inflammation, cell cycle/senescence, DNA damage, self-renewal capacity, metabolic profile....) with the aim of identifying therapeutic targets to prevent pediatric leukemia development.

A defining component of my scientific training was the international research period undertaken during my doctoral studies, from 2004 to 2006, in the laboratory of Professor Mel Greaves, a world-leading expert in prenatal pre-leukemia, which led to the identification of dysregulated TGF- $\beta$  signaling in ETV6::RUNX1 pre-leukemic precursor B cells (Ford/Palmi et al., JCI, 2009) providing insight into early events of childhood leukemia initiation and a potential link between immune responses to infection and malignant evolution.

Over the course of my career, I have authored or co-authored 33 peer-reviewed publications in the field of pediatric hemato-oncology (one currently in press), including nine first-author and five senior-author papers. These works span mechanistic studies of pre-leukemic cells, prognostic markers, and therapeutic strategies. In parallel, I have been actively involved in training and mentoring young

scientists, supervising seven undergraduate students and five PhD students from different biomedical and medical programs at the University of Milan and the University of Milan–Bicocca.

I have been awarded competitive, peer-reviewed funding as Principal Investigator for the projects “New therapeutic strategies for children with high-risk acute lymphoblastic leukemia” (Ricerca Finalizzata 2016, Italian Ministry of Health) and “TEL/AML1 fusion gene in childhood acute lymphoblastic leukemia: unraveling the mechanisms sustaining the pre-leukemic cell in its bone marrow niche” (Cariplo Foundation, 2018). These awards laid the foundation for my scientific independence and the establishment of multidisciplinary collaborations.

Currently, my research team consists of 2 postdoctoral researchers and 1 undergraduate student in Medical Biotechnology.

## **B. Positions, Scientific Appointments, and Honors**

2022-present: **Joung PI with a permanent position** at Fondazione M. Tettamanti. Research activity: New therapeutic strategies for children with high risk acute lymphoblastic leukemia; ETV6::RUNX1 fusion gene in childhood acute lymphoblastic leukemia: unraveling the mechanisms sustaining the pre-leukemic cell in its bone marrow niche.

2020-present: qualification (National Scientific Habilitation, ASN) for Associate Professorship in Applied Biology (05/F1).

2019-2022: **project leader** at Fondazione M. Tettamanti (funded by Fondazione Monza e Brianza per il Bambino e la sua Mamma (MBBM), Monza). Research activity: New therapeutic strategies for children with high risk acute lymphoblastic leukemia; ETV6::RUNX1 fusion gene in childhood acute lymphoblastic leukemia: unraveling the mechanisms sustaining the pre-leukemic cell in its bone marrow niche.

2018-present: qualification (National Scientific Habilitation, ASN) for Associate Professorship in General Pathology and Clinical Pathology (06/A2)

2015-present: **member of the Commission** “Final contest of Under 40 in Hematology” (<https://under40.it/webcommunity/category/under40/>)

2009-2019: **Post Doc position** at Fondazione M. Tettamanti (2017-2018: winner of the Postdoctoral research fellowship “Assegno di Ricerca type A2-senior” - University of Milan-Bicocca; 2011-2014: winner of “Assegno di Ricerca type A”; 2009-2010: winner of “Assegno di Ricerca type B”). Research activity: Study of the ETV6::RUNX1 positive pre-leukemia; identification and functional characterization of new risk factors and potential therapeutic targets in childhood ALL.

2006-2008: **PhD student** at Fondazione M. Tettamanti (2008: winner of a “occasional work” contract with the University of Milan-Bicocca - Genopolis FIRB project 2003; Research activity: Functional characterization of the ETV6::RUNX1 pre-leukemic clone.

2004-2006: **scientific officer** and from 2005 **PhD student** at Prof. Mel Greaves laboratory - Institute of Cancer Research, London, UK. Research activity: Study of the role of ETV6::RUNX1 in apoptosis.

2002-2004: **graduate fellow** at Fondazione M. Tettamanti (2004: FIRC fellowship in Pediatric Oncology); Research activity: Molecular and functional analysis of the chimeric genes *PAX5::ETV6* and *TEL::ARG* (*ETV6::ABL2*);

2000-2002: **undergraduate student** at Fondazione M. Tettamanti (2001: Winner of a scholarship by Laura Coviello association); Research activity: Molecular and functional analysis of the chimeric gene *TEL::ARG* (*ETV6::ABL2*).

## Honors:

- 8-11 March 2019: Oral presentation awardee during the EMBO Workshop on “B cell development and leukemia”, Salamanca, Spain.
- 19-21 October 2016: “Best Abstracts” -“XIV Congresso Nazionale SIES”, Italy.
- 13-14 November 2014: **Winner first place** in the contest “Under 40 in Hematology”.
- 17-18 October 2012: Travel award -“XII Congresso Nazionale SIES”, Italy;
- 24-26 September 2008: Travel award -“X Congresso Nazionale SIES”, Italy.
- 15-18 June 2006: Travel award - “11th EHA Congress”, The Netherlands.
- 30 April-2 May 2006: Poster awardee as “the best poster” - 5th Bi-annual Symposium on Childhood Leukemia”- The Netherlands.
- 8-12 February 2006: Poster “Scholar in Training awardee” - “AACR Special Conference in cancer Research”, California (USA).

## Peer reviewed grants

As ‘PI’:

- “New therapeutic strategies for children with high risk acute lymphoblastic leukemia” (Call “Ricerca Finalizzata 2016” code: GR-2016-02364753) granted by the Italian Ministry of Health for 3 years (450.000 euro).
- “TEL/AML1 fusion gene in childhood acute lymphoblastic leukemia: unraveling the mechanisms sustaining the pre-leukemic cell in its bone marrow niche” (Call “Ricerca biomedica condotta da giovani ricercatori 2018” code: 2018-0339) granted by Cariplo Foundation for 3 years (250.000 euro).

As ‘Collaborator’:

- “Innovative strategies for advanced molecular and metabolic targeting of pediatric and adult acute lymphoblastic leukemia to personalize treatments (IMPACT-ALL)”, FRBB2024 From bed to bench: the way to innovation (3 years, 1.999.800 euro): PI=Dr. Giovanni Cazzaniga;
- “Before leukemia in children: PRE-disposition, PRE-leukemia for PRE-vention (PRE3vent). AIRC IG2023 (5 years, 1.026.000 euro): PI=Dr. Giovanni Cazzaniga;
- “Childhood Acute Lymphoblastic Leukemia: a path back, from genetic predisposition through pre-leukemia”. AIRC IG2018 (5 years, 673.450 euro): PI=Dr. Giovanni Cazzaniga;
- “Genomic profile and early response for improving cure rate and quality of life in childhood acute lymphoblastic leukemia”. AIRC IG2017 (5 years, 910.000 euro): PI= Prof. A Biondi;
- “Identification of stromal-derived signals driving leukemia by an innovative murine model of a human Bone-Marrow niche”. AIRC IG2014 (3 years, 232.155 euro): PI= Dr G. D’Amico;
- “Unraveling molecular pathogenesis on selected childhood ALL high-risk subsets to tailor novel targeted treatment”. AIRC IG2014 (3 years, 460.000 euro): PI= Prof. A Biondi;
- “Progenitor and non-progenitor functions of “mesenchymal” stem cells: fundamental mechanisms, role in disease, and harnessing for therapies”. PRIN 2012 (3 years, 153.971 euro): PI= Prof. Paolo Bianchi;
- “Identification and functional characterization of new risk factors in childhood acute lymphoblastic leukemia”. Fondazione Cariplo 2011 (3 years, 412.000 euro): PI= Dr. Giovanni Cazzaniga;
- “Molecular pathogenesis of childhood leukemia, from leukemia stem cells to functional modelling.” AIRC IG2010 (3 years, 450.000 euro): PI= Prof. Andrea Biondi;
- “Childhood ALL: from clinical studies to research questions to understand molecular history and pathogenesis”. AIRC IG 2007 (3 years, 270.000 euro): PI= Prof. Andrea Biondi.

## C. Contributions to Science

H index=20; Citations=1744(Scopus 21/01/2026)

1. Acunzo D, Bertagna M, Risca G, Beneforti L, Bresolin S, Galimberti S, Sánchez-García I, Biondi A, Cazzaniga G, **Palmi C**. Targeting oncogene-induced senescence in ETV6::RUNX1 pre-leukemic cells. Cell Death Discovery. In press.

2. Oikonomou A, Watrin T, Valsecchi L, Scharov K, Savino AM, Schliehe-Diecks J, Bardini M, Fazio G, Bresolin S, Biondi A, Borkhardt A, Bhatia S, Cazzaniga G, **Palmi C**. Synergistic drug interactions of the histone deacetylase inhibitor givinostat (ITF2357) in CRLF2-rearranged pediatric B-cell precursor acute lymphoblastic leukemia identified by high-throughput drug screening. *Heliyon*. 2024;10(13):e34033.
3. Oikonomou A, Valsecchi L, Quadri M, Watrin T, Scharov K, Procopio S, Tu JW, Vogt M, Savino AM, Silvestri D, Valsecchi MG, Biondi A, Borkhardt A, Bhatia S, Cazzaniga G, Fazio G, Bardini M, **Palmi C**. High-throughput screening as a drug repurposing strategy for poor outcome subgroups of pediatric B-cell precursor Acute Lymphoblastic Leukemia. *Biochem Pharmacol*. 2023;217:115809.
4. Lopes BA, Meyer C, Bouzada H, K lp M, Maciel ALT, Larghero P, Barbosa TC, Poubel CP, Barbieri C, Venn NC, Pozza LD, Barbaric D, **Palmi C**, et al. The recombinome of IKZF1 deletions in B-cell precursor ALL. *Leukemia*. 2023;37(8):1727-1731.
5. **Palmi C**, et al. Definition and Prognostic Value of Ph-like and IKZF1plus Status in Children With Down Syndrome and B-cell Precursor Acute Lymphoblastic Leukemia. *Hemasphere*. 2023;7(6):e892.
6. Fazio G, Bresolin S, Silvestri D, Quadri M, Saitta C, Vendramini E, Buldini B, **Palmi C**, et al. PAX5 fusion genes are frequent in poor risk childhood acute lymphoblastic leukaemia and can be targeted with BIBF1120. *EBioMedicine*. 2022;83:104224.
7. Dander E\*, **Palmi C**\*, et al. The Bone Marrow Niche in B-Cell Acute Lymphoblastic Leukemia: The Role of Microenvironment from Pre-Leukemia to Overt Leukemia. *Int J Mol Sci*. 2021;22(9):4426. \*=contributed equally to this work
8. Fazio G, Bardini M, De Lorenzo P, Grioni A, Quadri M, Pedace L, Corral Abascal L, Palamini S, **Palmi C** et al. Recurrent genetic fusions redefine MLL germ line acute lymphoblastic leukemia in infants. *Blood*. 2021;137(14):1980-1984.
9. Isidro-Hern ndez M, Mayado A, Casado-Garc a A, Mart nez-Cano J, **Palmi C**, et al. Inhibition of inflammatory signaling in Pax5 mutant cells mitigates B-cell leukemogenesis. *Sci Rep*. 2020 Nov 5;10(1):19189.
10. Beneforti L, Dander E, Bresolin S, Bueno C, Acunzo D, Bertagna M, Ford A, Gentner B, Te Kronnie G, Vergani P, Men ndez P, Biondi A, D'Amico G, **Palmi C**\*, Cazzaniga G\*. Pro-inflammatory Cytokines Favor the Emergence of ETV6-RUNX1-positive Pre-Leukemic Cells in a Model of Mesenchymal Niche. *Br J Haematol* 2020; Online ahead of print. \*=These authors share the senior authorship.
11. Lopes BA, Meyer C, Barbosa TC, Poubel CP, Mansur MB, Duployez N, Bashton M, Harrison CJ, Zur Stadt U, Horstmann M, Pombo-de-Oliveira MS, **Palmi C**, et al. IKZF1 Deletions with COBL Breakpoints Are Not Driven by RAG-Mediated Recombination Events in Acute Lymphoblastic Leukemia. *Transl Oncol*. 2019;12(5):726-732.
12. Portale F, Beneforti L, Fallati A, Biondi A, **Palmi C**, et al. Activin-A contributes to the definition of a pro-oncogenic bone marrow microenvironment in t(12;21) preleukemia. *Exp Hematol*. 2019;73:7-12.e4
13. Sarno J, Savino AM, Buracchi C, **Palmi C**, et al. SRC/ABL inhibition disrupts CRLF2-driven signaling to induce cell death in B-cell acute lymphoblastic leukaemia. *Oncotarget*. 2018;9(33):22872-22885.
14. Stanulla M, Dagdan E, Zali va M, M ricke A, **Palmi C**, et al. IKZF1plus Defines a New Minimal Residual Disease-Dependent Very-Poor Prognostic Profile in Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia. *J Clin Oncol*. 2018;36(12):1240-1249.
15. Schwartzman O, Savino AM, Gombert M, **Palmi C**, et al. Suppressors and activators of JAK-STAT signaling at diagnosis and relapse of acute lymphoblastic leukemia in Down syndrome. *Proc Natl Acad Sci U S A*. 2017;114(20):E4030-E4039.
16. Savino AM, Sarno J, Trentin L, Vieri M, Fazio G, Bardini M, Bugarin C, Fossati G, Davis KL, Gaipa G, Izraeli S, Meyer LH, Nolan GP, Biondi A, Te Kronnie G, **Palmi C**\*, Cazzaniga G\*. The histone deacetylase inhibitor givinostat (ITF2357) exhibits potent anti-tumor activity against CRLF2-rearranged BCP-ALL. *Leukemia*. 2017;31(11):2365-2375. \*=These authors share the senior authorship.

17. Serafin V, Lissandron V, Buldini B, Bresolin S, Paganin M, Grillo F, Andriano N, **Palmi C**, et al. Phosphoproteomic analysis reveals hyperactivation of mTOR/STAT3 and LCK/Calcineurin axes in pediatric early T-cell precursor ALL. *Leukemia*. 2017;31(4):1007-1011.
18. **Palmi C**, et al. CRLF2 over-expression is a poor prognostic marker in children with high risk T-cell acute lymphoblastic leukemia. *Oncotarget*. 2016;7(37):59260-59272.
19. Boer JM, Van der Veer A, Rizopoulos D, Fiocco M, Sonneveld E, de Groot-Kruseman HA, Kuiper RP, Hoogerbrugge P, Horstmann M, Zaliava M, **Palmi C**, et al. Prognostic Value of Rare IKZF1 Deletions in Childhood B-cell Precursor Acute Lymphoblastic Leukaemia: An International Collaborative Study. *Leukemia*. 2016;30(1):32-8.
20. Bugarin C, Sarno J, **Palmi C**, et al. On behalf of I-BFM study group. Fine tuning of surface CRLF2 expression and its associated signaling profile in childhood B cell precursor acute lymphoblastic leukemia. *Haematologica* 2015;100(6):e229-32.
21. Hasan MN, Queudeville M, Trentin L, Eckhoff SM, Bronzini I, **Palmi C**, et al. Targeting of hyperactivated mTOR signaling in high-risk acute lymphoblastic leukemia in a pre-clinical model. *Oncotarget*. 2015;6(3):1382-95.
22. **Palmi C**, et al. Cytoskeletal Regulatory Gene Expression and Migratory Properties of B Cell Progenitors are Affected by the ETV6-RUNX1 Rearrangement. *Mol Cancer Res* 2014;12(12):1796-806.
23. **Palmi C**, et al. Impact of IKZF1 deletions on IKZF1 expression and outcome in Philadelphia chromosome negative childhood BCP-ALL. Reply to "Incidence and biological significance of IKZF1/Ikaros gene deletions in pediatric Philadelphia chromosome negative and Philadelphia chromosome positive B-cell precursor acute lymphoblastic leukemia. *Haematologica* 2013;98(12):e164-5.
24. **Palmi C**, et al. What is the relevance of Ikaros gene deletions as a prognostic marker in pediatric Philadelphia-negative B-cell precursor acute lymphoblastic leukemia? *Haematologica* 2013;98:1226-31.
25. Fazio G, Cazzaniga V, **Palmi C**, et al. PAX5/ETV6 alters the gene expression profile of precursor B cells with opposite dominant effect on endogenous PAX5. *Leukemia* 2013;27(4):992-5.
26. Attarbaschi A, Morak M, Cario G, Cazzaniga G, Ensor HM, Te Kronnie T, Bradtke J, Mann G, Vendramini E, **Palmi C**, et al. Treatment outcome of CRLF2-rearranged childhood acute lymphoblastic leukaemia: a comparative analysis of the AIEOP-BFM and UK NCRI-CCLG study groups. *Br J Haematol* 2012;158(6):772-7.
27. **Palmi C**, et al. Poor prognosis for P2RY8-CRLF2 fusion but not for CRLF2 over-expression in children with intermediate risk B-cell precursor acute lymphoblastic leukemia. *Leukemia* 2012;26(10):2245-53.
28. Shochat C, Tal N, Bandapalli OR, **Palmi C**, et al. Gain-of-function mutations in interleukin-7 receptor- $\alpha$  (IL7R) in childhood acute lymphoblastic leukemias. *J Exp Med* 2011;208(5):901-8.
29. Ford A\*, **Palmi C**\*, et al. The TEL-AML1 leukemia fusion gene dysregulates the TGF $\beta$  pathway in early B lineage progenitor cells. *JCI* 2009;119(4):826-36. \*=contributed equally to this work.
30. Corradi B, Fazio G, **Palmi C**, et al. Efficient detection of leukemia-related fusion transcripts by multiplex PCR applied on a microelectronic platform. *Leukemia* 2008; 22 (2):294-302.
31. Fazio G, **Palmi C**, et al. PAX5/TEL acts as a transcriptional repressor causing down-modulation of CD19, enhances migration to CXCL12, and confers survival advantage in pre-B1 cells. *Cancer Res* 2008;68(1):181-9.
32. **Palmi C**, et al. TEL/ARG induces cytoskeletal abnormalities in 293T cells. *Cancer Lett* 2006; 241(1):79-86.
33. Tartaglia M, Martinelli S, Cazzaniga G, Cordeddu V, Iavarone I, Spinelli M, **Palmi C**, et al. Genetic evidence for lineage-related and differentiation stage-related contribution of somatic PTPN11 mutations to leukemogenesis in childhood acute leukemia. *Blood* 2004; 104(2):307-13.

#### Referee:

Reviewer of *Oncotarget*, *Haematologica*, *Genes*, *Chromosomes and Cancer*, *Leukemia & Lymphoma*, *Plos One*, *Frontiers in Immunology*, *Cytokine*.