
BIOGRAPHICAL SKETCH

NAME: Vincenzo Giambra

CREDENTIAL: Ph.D.

POSITION TITLES:

- Group Leader, Institute of Stem Cells Biology, Regenerative Medicine and Innovative Therapies (ISBReMIT), "Fondazione IRCCS Casa Sollievo della Sofferenza" (San Giovanni Rotondo, Italy);
 - Affiliate Assistant Professor, Department of Pathology and Laboratory Medicine, University of British Columbia, (Vancouver, Canada)
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EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	COMPLETION DATE	FIELD OF STUDY
University of Palermo (Italy)	B.Sc.	07/2000	Biology
"Tor Vergata" University of Rome (Italy)	M.Sc.	12/2003	Biotechnology
"Tor Vergata" University of Rome (Italy) and Albert Einstein College of Medicine - AECOM (USA)	Ph.D.	05/2007	Molecular and Cell Biology
BC Cancer Research Institute - BCCRI (Canada)	Postdoctoral Fellow	12/2016	Leukemia stem cells, T-cell leukemia

A. Personal Statement

Over the past ten years, I have conducted extensive research in both human and mouse models to decipher the properties of leukemic and hematopoietic progenitors responsible for the generation and propagation of hematological malignancies, such as the acute lymphoblastic leukemia of T-cell lineage (T-ALL). In my current positions, as a Group Leader in the ISBReMIT Institute at the "Fondazione IRCCS Casa Sollievo della Sofferenza" in Italy and an Affiliate Assistant Professor at the University of British Columbia in Canada, I am particularly focused on investigating the role of molecular pathways in the maintenance and development of leukemia stem cells in T-cell leukemias and the dynamics of recurrent and aggressive subclones in patients with T-ALL before and after conventional therapies. As a Principal Investigator (PI), my goal is to build and lead a strong research team dedicated to dissecting the key molecular events that drive aggressive disease behavior in T-cell leukemia.

Through my scientific career, I authored a total of 63 peer-reviewed publications, including manuscripts in *Nature Medicine* (2012) and *Blood* (2015) as first author and in *Cell Stem Cell* (2018), *Molecular Cancer* (2022) and *Blood* (2023, 2025) as a corresponding author and PI. I also received several scientific awards and funds, such as the Gilead Fellowship award in onco-hematology from Gilead Sciences srl, and the Michael Smith Foundation for Health Research Fellowship in Canada. To date, as Principal Investigator (PI) I have attracted ~10M Euros of peer-reviewed active funding from different international funding agencies, including the Worldwide Cancer Research, the Italian Association for Research on Cancer (AIRC), the Italian Ministry of Health and "With the South" Foundation. I have also received funds as a co-PI from the Canadian Institutes of Health Research (CIHR) and recently as a PI, I am leading a consortium of four international teams for the Joint Transnational Call for Proposals 2023 (TRANSCAN) by the European Union.

B. Positions and Employment

2001 - 2003 Master, Dr. D. Frezza' lab, Biology Department, "Tor Vergata" University, Rome, Italy
2003 - 2005 Ph.D., Dr. D. Frezza' lab, Biology Department, "Tor Vergata" University, Rome, Italy
2005 - 2007 Visiting Scientist, Dr. B. Birshstein lab, Albert Einstein College of Medicine, New York, USA
2007 - 2016 Postdoctoral Fellow, Dr. A. Weng lab, TFL, BC Cancer Agency, Vancouver, Canada
2017 - present Affiliate Assistant Professor, Dep. of Pathology, University of British Columbia, Vancouver, Canada
2017 - present Group Leader, ISBReMIT, "Fondazione IRCCS Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy

Other Experience and Professional Memberships

2010 – 2011 Member of International Society for Stem Cell Research (ISSCR)
2011 – 2013 Member of International Society for Experimental Hematology (ISEH)
2014 – 2015 Member of International Society for Experimental Hematology (ISEH)
2019 – present Reviewer, Blood, Haematologica, Oncotarget and Leukemia Research journals
2018 – present International Member of American Society of Hematology (ASH)
2021 – present Member of European Association for Cancer Research (EACR)
2021 – present Member of Società Italiana di Cancerologia (SIC)
2023 – present Scientific Panel member, South African Medical Research Council, South Africa
2023 – present Scientific Advisory Board, Worldwide Cancer Research, United Kingdom

Honors and Awards

2001 "Best method in Biotechnology" Award, Bionova 2001, Padova, Italy
2010 Travel Award, 52nd ASH Annual Meeting and Exposition, Orlando, USA
2011-2012 Research Trainee Award, Michael Smith Foundation for Health Research (MSFHR)-BC Cancer Foundation Post-Doctoral Fellowship–, Vancouver, Canada
2012 Travel Award, ISEH Annual Scientific Meeting, Amsterdam, Netherlands
2012 Travel Award, TFRI Annual Scientific Meeting, Victoria, Canada
2013 Keystone Symposia Scholarship, Keystone Meeting, Banff, Canada
2014 Travel Award, ISSCR Annual Scientific Meeting, Vancouver, Canada
2015 Abstract Achievement Award, 57th ASH Annual Meeting and Exposition, Orlando, USA
2022 Gilead Fellowship award in onco-hematology, 2022 Gilead Sciences s.r.l., Italy
2023 Europe-Africa Personalized Medicine (EU-Africa PerMed) Travel Award

C. Contribution to Science

1. As a Postdoctoral Fellow in the laboratory of Dr. Andrew P. Weng at the Terry Fox Laboratory of BC Cancer Research Institute in Vancouver (Canada), I investigated LIC activity in a NOTCH1-induced mouse model of T-ALL. Specifically, I demonstrated that active Wnt signaling is restricted to LIC-enriched subpopulations and that β -Catenin inactivation severely reduces LIC frequency. Additionally, I showed that β -Catenin transcription is upregulated by hypoxia via Hif1 α stabilization, and deleting either β -Catenin or Hif1 α reduces LIC frequency without affecting bulk tumor growth. I also identified a CD44⁺ subset with low reactive oxygen species (ROS) as highly enriched for LICs, where ROS accumulation is restrained by PKC- θ downregulation, regulated by NOTCH1, RUNX3, and RUNX1. These findings highlight Wnt, Hif1 α , and PKC- θ pathways as potential therapeutic targets.

- **Giambra V**, Jenkins CR, Wang H, Lam SH, Shevchuk OO, Nemirovsky O, Wai C, Gusscott S, Chiang MY, Aster JC, Humphries KR, Eaves C, and Weng AP, Notch1 promotes T cell leukemia-initiating activity by RUNX-mediated regulation of PKC- θ and reactive oxygen species, *Nature Medicine*, 18, 1693-1698 (2012). PMID:23086478.

- **Giambra V***, Jenkins C, Lam SH, Hoofd C, Belmonte M, Wang X, Gusscott S, Gracias D, and Weng AP*, Leukemia stem cells in T-ALL require active Hif1 α and Wnt signaling, *Blood*, 2015 May 1. PMID: 25934477 ***corresponding author**
2. As young principal investigator (PI) at the "Fondazione IRCCS Casa Sollievo della Sofferenza" (Italy) and in collaboration with Dr. Andrew P. Weng at the BC Cancer Research Institute (Canada), I demonstrated that although HSPCs derived from fetal liver and adult bone marrow produce highly similar primary leukemias, they differ in their ability to propagate disease in secondary recipients. I also showed that age-related epigenetic programming by the histone methyltransferase EZH2 alters the accessibility of the IGF1 locus to NOTCH1. The data suggest that reversing EZH2 mark or enforced IGF1 signaling in adult-programmed leukemia cells recapitulate fetal-like features including a reduced capacity for in vivo propagation.
 - **Giambra V***, Gusscott S, Gracias D, Raymond S, Lam SH, Panelli P, Tyshchenko K, Jenkins CE, Hoofd C, Lorzadeh A, Carles S, Hirst M, Eaves CJ, and Weng AP*, Epigenetic extinction of fetal programming promotes leukemia stem cell activity, *Cell Stem Cell*, 2018 Sept 19, PMID: 30269902 ***corresponding author**
 3. As principal investigator (PI) at the "Fondazione IRCCS Casa Sollievo della Sofferenza" (Italy), and in collaboration with Dr. F. Bianchi's group at the CSS in Italy, I reported that T-ALL-secreted extracellular vesicles (EVs) contain NOTCH1-dependent microRNAs (EV-miRs), which regulate oncogenic pathways by acting as autocrine stimuli, ultimately promoting the expansion/survival of highly proliferative cell subsets of human T-ALL. I also found that NOTCH1-dependent EV-miRs mostly comprised members of miR-17-92a cluster and paralogues, which rescued the in vitro proliferation of T-ALL cells, blocked by γ -secretase inhibitors (GSI) and regulated a network of genes associated with relapsed/refractory ETP-ALLs.
 - Colangelo T, Panelli P, Mazzarelli F, Tamiro F, Melocchi V, De Santis E, Cuttano R, Palumbo O, Rossi G, Bianchi F*, **Giambra V***, Extracellular vesicle microRNAs contribute to Notch signaling pathway in T-cell acute lymphoblastic leukemia. *Mol Cancer*. 2022 Dec 22;21(1) PMID: 36550553 ***corresponding author**
 4. As a principal investigator at the "Fondazione IRCCS Casa Sollievo della Sofferenza" (Italy), I identified functional mechanisms involved in the activity of leukemia-initiating cells (LICs) in T-cell acute lymphoblastic leukemia (T-ALL). Specifically, I highlighted relevant protein interactions of β -Catenin as well as mediators of CLOCK and BMAL1 transcription factors. Through single-cell gene expression analysis of leukemic cells from primary patients at the diagnosis and minimal residual disease (MRD), I also revealed that the expression of β -Catenin and FOXO3 dependent genes is high in the CD82+CD117+ cell fraction, which is substantially enriched with LICs in early T-cell precursor acute lymphoblastic leukemia (ETP-ALL).
 - Panelli P, De Santis E, Colucci M, Tamiro F, Sansico F, Miroballo M, Murgo E, Padovano C, Gusscott S, Ciavarella M, Chavez EA, Bianchi F, Rossi G, Carella AM, Steidl C, Weng AP, **Giambra V***, Noncanonical β -catenin interactions promote leukemia-initiating activity in early T-cell acute lymphoblastic leukemia. *Blood*. 2022 Oct 31: PMID: 36315912 ***corresponding author**
 - Murgo E, De Santis E, Sansico F, Melocchi V, Colangelo T, Padovano C, Colucci M, Carbone A, Totti B, Basti A, Gottschlich L, Relogio A, Capitanio N, Bianchi F, Mazzocchi G*, **Giambra V***, The circadian clock circuitry modulates leukemia initiating cell activity in T-cell acute lymphoblastic leukemia. *J Exp Clin Cancer Res*. 2023 Aug 24;42(1) PMID: 37620852 ***corresponding author**

5. As a principal investigator at the Fondazione IRCCS Casa Sollievo della Sofferenza (CSS) in Italy, I demonstrated that NOTCH1 dimeric signaling is crucial for T-cell leukemogenesis of human hematopoietic stem/progenitor cells (HSPCs). I identified a Notch-dimerization-dependent gene signature, including HES4, which promotes proliferation and survival by enforcing $\Delta 133p53$ expression and BCL2L1 activation. Using genetically modified models, RNA/ChIP-seq, and scRNA-seq profiling, I revealed T-ALL subsets with this signature, correlating with poor prognosis. These findings highlight NOTCH1 dimeric signaling as a key driver of human T-ALL.
- Tamiro F, Padovano C, De Santis E, Di lasio S, Sansico FD, Canistro V, Colucci M, Di Nunzio C, Bruno G, Doshi K, Totaro A, Gu E, Santodirocco M, Weng AP, **Giambra V***, NOTCH1 dimeric signaling is essential for T-cell leukemogenesis and leukemia maintenance, *Blood*. 2025 Feb 26. PMID: 40009499 * **corresponding author**

Selected First and/or Corresponding author publications

- Tamiro F, Padovano C, De Santis E, Di lasio S, Sansico FD, Canistro V, Colucci M, Di Nunzio C, Bruno G, Doshi K, Totaro A, Gu E, Santodirocco M, Weng AP, **Giambra V**, NOTCH1 dimeric signaling is essential for T-cell leukemogenesis and leukemia maintenance, *Blood*. 2025 Feb 26. PMID: 40009499
- Padovano C, Bianco SD, Sansico F, De Santis E, Tamiro F, Colucci M, Totti B, Di lasio S, Bruno G, Panelli P, Miscio G, Mazza T, **Giambra V**, The Notch1 signaling pathway directly modulates the human RANKL-induced osteoclastogenesis, *Sci Rep*. 2023 Dec 1;13(1):21199. PMID: 38040752
- Colucci M, Trivieri N, Mencarelli G, De Santis E, Sansico F, Tamiro F, Visioli A, Barile C, Pracella R, Rossi G, Binda E, **Giambra V**, A functional role of Ephrin type-B receptor 6 (EPHB6) in T-cell acute lymphoblastic leukemia, *Biomark Res*. 2023 Oct 20;11(1):92 PMID: 37858274
- Murgo E, De Santis E, Sansico F, Melocchi V, Colangelo T, Padovano C, Colucci M, Carbone A, Totti B, Basti A, Gottschlich L, Relogio A, Capitanio N, Bianchi F, Mazzocchi G, **Giambra V**, The circadian clock circuitry modulates leukemia initiating cell activity in T-cell acute lymphoblastic leukemia. *J Exp Clin Cancer Res*. 2023 Aug 24;42(1) PMID: 37620852
- Colangelo T, Panelli P, Mazzarelli F, Tamiro F, Melocchi V, De Santis E, Cuttano R, Palumbo O, Rossi G, Bianchi F, **Giambra V**, Extracellular vesicle microRNAs contribute to Notch signaling pathway in T-cell acute lymphoblastic leukemia. *Mol Cancer*. 2022 Dec 22;21(1) PMID: 36550553
- Panelli P, De Santis E, Colucci M, Tamiro F, Sansico F, Miroballo M, Murgo E, Padovano C, Gusscott S, Ciavarella M, Chavez EA, Bianchi F, Rossi G, Carella AM, Steidl C, Weng AP, **Giambra V**, Non-canonical β -catenin interactions promote leukemia-initiating activity in early T-cell acute lymphoblastic leukemia. *Blood*. 2023 Mar 30;141(13) PMID: 36315912
- Sansico F, Miroballo M, Bianco DS, Tamiro F, Colucci M, Santis E, Rossi G, Rosati J, Di Mauro L, Miscio G, Mazza T, Vescovi AL, Mazzocchi G, **Giambra V**, On Behalf Of Csx-Covid Group. COVID-19 Specific Immune Markers Revealed by Single Cell Phenotypic Profiling, *Biomedicine*. 2021 Nov 29;9(12):1794. PMID: 34944610
- Tamiro F, Weng AP, **Giambra V**, Targeting Leukemia-Initiating Cells in Acute Lymphoblastic Leukemia, *Cancer Res*. 2021 Jan 7. (2021) - PMID: 33414170 Review

- **Giambra V**, Gusscott S, Gracias D, Song R, Lam SH, Panelli P, Tyshchenko K, Jenkins CR, Hood C, Lorzadeh A, Carles A, Hirst M, Eaves CJ, Weng AP, Epigenetic restoration of fetal-like IGF1 signaling inhibits leukemia stem cell activity, *Cell Stem Cell*, 2018 Nov 1. PMID: 30269902
- **Giambra V**, Jenkins C, Lam SH, Hoofd C, Belmonte M, Wang X, Gusscott S, Gracias D, Weng AP, Leukemia stem cells in T-ALL require active Hif1 α and Wnt signaling, *Blood*, 2015 May 1. PMID: 25934477
- **Giambra V**, Jenkins CR, Wang H, Lam SH, Shevchuk OO, Nemirovsky O, Wai C, Gusscott S, Chiang MY, Aster JC, Humphries KR, Eaves C, Weng AP, Notch1 promotes T cell leukemia-initiating activity by RUNX-mediated regulation of PKC- Θ and reactive oxygen species, *Nature Medicine*, 18, 1693-1698 (2012) - PMID:23086478.

Complete List of Published Work:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Giambra+V>

D. Additional Information: Ongoing Research Support

1. *Proposal Title*: Unveiling the Epigenetic Landscape and Therapeutic Implications of Epigenetic Modifiers in Human T-cell Leukemia Initiation and Progression
Funding Source and Program: European Union, TRANSCAN-3 - JTC 2023
Period: 5/2024 - 6/2026
Amount: 1,170,223 (Euro)
Role: Principal Investigator
Research focus: The TRANSCAN-3 project aims to characterize the functional role of loss of distinct epigenetic modifiers in the context of T-ALL pathogenesis and maintenance.
2. *Proposal Title*: Genotypic, metabolic and immunophenotypic characterization of Early T-cell Precursor (ETP) Acute Lymphoblastic Leukemia (ALL) for the preclinical development of CAR-T cells
Funding Source and Program: Italian Ministry of Health, PNRR: M6/C2_CALL 2023
Period: 5/2024 - 6/2026
Amount: 1,000,000 (Euro)
Role: co-Principal Investigator
Research focus: This project aims to reveal the genotypic, metabolic and immunophenotypic profile of human ETP-ALL to generate novel CAR-based therapeutics.
3. *Proposal Title*: Characterization of IMmunoinflammatory mechanisms and immunonutrients action on cognitive ageing and Alzheimer's disease
Funding Source and Program: Italian Ministry of Health, PNRR: M6/C2_CALL 2022
Period: 7/2020 - 6/2023
Amount: 1,000,000 (Euro)
Role: Collaborator
Research focus: This project aims to characterize immunological and genetic landscape of patients with Alzheimer's disease in response to immunonutrients and personalized diets.
4. *Proposal Title*: "Hub Scienze della Vita Regione Puglia"
Funding Source and Program: Italian Ministry of Health, T4-AN-01
Period: 2022 - 2027
Total Amount: 1,330,000 (Euro)
Role: Collaborator
Research focus: The POS4 project aims to identify novel cell markers associated with cancer stem cells and compatible with the clinical application of CAR-T cells in human T-cell acute lymphoblastic leukemia and glioblastoma.