JOLANDA SARNO, PHD

PERSONAL INFORMATION

- Date and place of birth: 10/29/1988, Avellino (AV) Italy
- Citizenship: Italian
- Appointment: Junior Group Leader at Tettamanti Research Center IRCCS San Gerardo dei Tintori, Department of Pediatrics.
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CURRENT POSITION

Junior Group Leader at Tettamanti Research Center – IRCCS San Gerardo dei Tintori, Department of Pediatrics. Via Pergolesi 33, 20900 Monza (MB), Italy.

PERSONAL STATEMENT

I am a Junior Group Leader at M. Tettamanti Center, a diagnostic and research laboratory dedicated to the cure, assistance, and research of hematological diseases in children.

In this contest, as a scientist dedicated to the field of cancer biology, I have focused my interest on B-cell acute lymphoblastic leukemias. I am passionate about understanding the molecular basis of leukemia, mechanisms of treatment resistance, and the identification of new therapeutic approaches to further improve patient outcomes. Specifically, my research program focuses on the study of the features associated with resistance by taking advantage of single-cell technologies to unravel inter-patient and intra-tumor heterogeneity.

Throughout my research experience, I worked on different aspects of the disease: identification of patients with poor prognosis (Bugarin C, <u>Sarno J</u> et al. Haematologica 2015), testing of alternative therapeutic approaches using epigenetic drugs (Savino AM, <u>Sarno J</u> et al. Leukemia 2017) or combinations of kinase inhibitors (<u>Sarno J</u> et al. Oncotarget 2018) and prediction of patients at high risk of relapse (Good Z & <u>Sarno J</u> et al. Nat Med 2018). During my PhD and postdoc, I spent about 7 years at Stanford University, where I gained a strong expertise in the use of single-cell mass cytometry (CyTOF), a high throughput technology able to measure up to 45 parameters simultaneously. Leveraging the application of mass cytometry to clinical samples, we identified features of specific subtypes of cells that are predictive of relapse at diagnosis and developed a predictor of relapse named DDPR (Good Z & <u>Sarno J</u> et al. Nat Med 2018). More recently using the tools developed during my postdoc, we identified phenotypic plasticity as a mechanism of glucocorticoid (GC) resistance in B-ALL that can be overcome by the combination of GCs with the dual SRC/ABL kinase, dasatinib (<u>Sarno J</u> et al. Nat Comm 2023). By leveraging the dimensionality of such technology, I decided to apply this tool to answer biological questions related to leukemia diagnosis and resistance to therapy of MRD cell.

The overall goal of my research is to impact clinical decision-making by providing single-cell information of resistant cells that could help in re-define risk stratification of the patients and identify targets of resistant cells that can be therapeutically targeted.

EDUCATION

• **Stanford Ignite Program** – January 2021 to March 2021

Entrepreneur program for scientists offered by Stanford Business School, California, USA.

Professional Accreditation for Biologists in Italy (Esame di Stato) – October 2020

Professional Qualification obtained at the University of Pavia, Italy.

• Ph.D. – November 2012 to June 2016

Ph.D. program in Translational and Molecular Medicine (DIMET) at University of Milano-Bicocca, Milan, Italy. Supervisors: Prof. Andrea Biondi, MD and Giuseppe Gaipa, PhD.

Dissertation title: "*Cell signaling in high-risk childhood B-cell precursor acute lymphoblastic leukemia: high-throughput dissection and targeting strategies*".

Master Degree in Medical Biotechnology – November 2010 to October 2012

University of Milano-Bicocca, Milan, Italy. Supervisors: Prof. Andrea Biondi, MD and Giuseppe Gaipa, Ph.D. Score: 110/110.

Dissertation title: "Study of signal transduction in pediatric CRLF2-rearranged acute lymphoblastic leukemia".

Bachelor Degree in Life Science Biotechnology – October 2007 to October 2010

University of Napoli, Federico II, Naples, Italy. Supervisor: Prof. Giuseppe Tortora, MD. Score: 104/110.

Dissertation title: "Effects of the mTOR inhibitor, everolimus, on signal transduction in human cancer model of kidney tumor".

RESEARCH AND WORKING EXPERIENCES

Junior Group Leader – September 2023 to date

Recipient of AIRC Start-UP grant that will support the development of my research unit at Tettamanti Research Center - IRCSS San Gerardo dei Tintori.

Senior Research Scientist – March 2022 to August 2023

Kara Davis laboratory at Pediatric Department of Stanford University, School of Medicine.

My research activity was divided into the development of specific projects that I lead, and the supervision of projects developed by other lab members. In addition, I have established and maintained several external collaborations with researchers at different institutions.

Postdoctoral Fellow – March 2017 to February 2022

Kara Davis laboratory at Pediatric Department of Stanford University, School of Medicine.

As a postdoctoral fellow, I led several projects related to treatment failure in acute lymphoblastic leukemia and mentored undergraduate, medical and Ph.D. students. I also successfully obtained fellowships to support my academic appointment.

Part-time consultant – May 2021 to July 2021

Factorial Biotechnologies start-up. CEO: John Wells.

Protocol troubleshooting for genomic/proteomic assay development and its application to cancer biology

• Research Scientist – July 2016 to December 2016

Giuseppe Gaipa laboratory at Tettamanti Research Center. Scientific director: Prof. Andrea Biondi.

Finalization of ongoing projects before moving to the United States for postdoctoral training.

Visiting Ph.D. student – June 2014 to November 2014 and June 2015 to August 2015

Garry Nolan Lab at Microbiology and Immunology Department, Stanford University, School of Medicine.

Deep training on mass cytometry (CyTOF) technology: from the sample processing to analysis. The training was supported by a grant from "Fondazione Benedetta è la vita ONLUS".

AWARDS, FELLOWSHIPS, GRANTS

• **Start-UP AIRC 2022** – from 2023 to 2027.

Junior PI recipient of Start-UP reintegration grant sponsored by Italian Association for Cancer Research (AIRC). The program funds a 5-year project (200.000 euro/year) entitled: "Developmental heterogeneity as a key determinant of treatment-resistant cells in childhood acute lymphoblastic leukemia".

• **BD Investigator Sponsored Study** – September 2022 to August 2023.

Co-PI in a research grant to perform transcriptomic profile of minimal residual disease in childhood acute lymphoblastic leukemia using BD Rhapsody system (\$50.000/1-year).

- TRTH scholar awarded in the academic year 2020 but postponed to 2022 due to the pandemic. Translational Research Training in Hematology (TRTH) ASH/EHA joint program. Selected participant for a year-long training mentored by professor scientists in hematology. <u>https://ehaweb.org/research/training-and-mentoring/eha-ash-translational-research-training-inhematology/trth-hall-of-fame/</u>
- Postdoctoral Fellowship September 2019 to September 2021

2-years postdoctoral fellowship granted by Maternal and Child Research Health Institute (MCHRI).

• **Postdoctoral Fellowship** – March 2017 to February 2018

1-year postdoctoral fellowship granted by Italian Association for Cancer Research (AIRC).

 Abstract Achievement Awards – American Society of Hematology (ASH) 2015 and ASH 2021 conferences

EDUCATIONAL WORKSHOPS

- **Intro to R and tidyverse** offered by CCDL (Childhood Cancer Data Lab). Navigate in RStudio environment, R functions and R datatypes. Introduction to ggplot2 and tidyverse documentation.
- Bulk RNA-Seq analysis offered by CCDL (Childhood Cancer Data Lab). Data processing and exploratory analysis using DESeq2 and pathway analysis packages.
- Scientific writing offered by Stanford University. Grant application writing, bio sketch and manuscripts.
- Introduction to programming with R offered by Stanford University. Basic knowledge of R programming.

TEACHING AND MENTORING EXPERIENCE

- **Stanford Immunology course.** Lesson for Ph.D. students in cancer biology program. (January 2022, Stanford, USA).
- DIMET PhD program. Lesson for PhD students about mass cytometry use as a tool to study cancer heterogeneity in acute lymphoblastic leukemia (November 2019, Milan, Italy).

Mentoring activity of undergraduates (n=3), MD students (n=2), and Ph.D. students (n=2) to carry on their scientific projects.

PROFESSIONAL MEMBERSHIP AND EDITOR ROLES

- American Society of Hematology (ASH) since 2018.
- Guest Associate Editor in Frontiers Cell Growth and Division (2023)
- EHA (European Hematology of Association) since 2024
- Reviewer of scientific articles for: *Cancer Reports, Hematology, Pediatric Blood and Cancer, Hematologica, HemaSphere.*

PUBLICATIONS IN PEER-REVIEWED JOURNALS

- Colella P, Sayana R, Suarez-Nieto MV, Sarno J, Nyame K, Xiong J, Pimentel Vera LN, Arozqueta Basurto J, Corbo M, Limaye A, Davis KL, Abu-Remaileh M, Gomez-Ospina N. *CNS-wide repopulation by hematopoietic-derived microglia-like cells corrects progranulin deficiency in mice*. Nat Commun. 2024 Jul 5;15(1):5654. doi: 10.1038/s41467-024-49908-4. PMID: 38969669; PMCID: PMC11226701.
- Pan F, Sarno J, Jeong J, Yang X, Jager A, Gruber TA, Davis KL, Cleary ML. *Genome editing-induced* t(4;11) chromosomal translocations model B cell precursor acute lymphoblastic leukemias with KMT2A-AFF1 fusion. J Clin Invest. 2023 Nov 2:e171030. doi: 10.1172/JCI171030. Epub ahead of print. PMID: 37917159.
- Sarno J*, Domizi P, Liu Y, Merchant M, Pedersen CB, Jedoui D, Jager A, Nolan GP, Gaipa G, Bendall SC, Bava FA, Davis KL*. *Dasatinib overcomes glucocorticoid resistance in B-cell acute lymphoblastic leukemia*. Nat Commun. 2023 May 22;14(1):2935. doi: 10.1038/s41467-023-38456-y. * co-corresponding authors
- Lo YC, Keyes TJ, Jager A, Sarno J, Domizi P, Majeti R, Sakamoto KM, Lacayo N, Mullighan CG, Waters J, Sahaf B, Bendall SC, Davis KL. *CytofIn enables integration of public mass cytometry datasets using generalized anchors*. Nat Commun. 2022 Feb 17;13(1):934. doi: 10.1038/s41467-022-28484-5.
- Geron I, Savino AM, Fishman H, Tal N, Brown J, Turati V, James C, Sarno J, Hameiri-Grossman M, Nee Lee Y, Rein A, Maniriho H, Birger Y, Zemlyansky A, Muler I, Davis KL, Marcu-Malina V, Mattson N, Parnas O, Wagener R, Fischer U, Barata JT, Jamieson CHM, Müschen M, Chen CW, Borkhardt A, Kirsch IR, Nagler A, Enver T, Izraeli S. *An instructive role for interleukin-7 receptor a in the development of human B-cell precursor leukemia*. Nat Commun. 2022 Feb 3;13(1):659. doi: 10.1038/s41467-022-28218-7.
- **Sarno J**, Davis KL. *Single-cell mass cytometry and machine learning predict relapse in childhood leukemia.* Mol Cell Oncol. 2018 Sept 12;5(5):e1472057. doi:10.1080/23723556.2018.1472057.
- Sarno J, Savino AM, Pinto S, Bugarin C, Buracchi C, Jager A, Palmi C, Barber RC, Silvestri D, Israeli S, Dyer MJS, Cazzaniga G, Nolan GP, Biondi A, Davis KL and Gaipa G. SCR/ABL inhibition disrupts CRLF2-

driven signaling to induce cell death in B-cell acute lymphoblastic leukemia. Oncotarget. 2018 May 1;9(33):22872-22885. doi: 10.18632/oncotarget.25089.

- Good Z*, Sarno J*, Jager A, Samusik N, Agaheepour N, Simonds EF, White L, Lacayo NJ, Fantl WJ, Gaipa G, Biondi A, Tibshirani R, Bendall SC, Nolan GP, Davis KL. *Single-cell developmental classification of B-cell precursor acute lymphoblastic leukemia at diagnosis reveals predictor of relapse*. Nat Med. 2018 May;24(4):474-483. doi: 10.1038/nm.4505. Epub 2018 Mar 5. *co-first authors.
- Savino AM, Sarno J, Trentin L, Vieri M, Fazio G, Bardini M, Bugarin C, Fossati G, Davis KL, Gaipa G, Meyer LH, Nolan GP, Biondi A, Te Kronnie G, Palmi and Cazzaniga G. *The histone deacetylase inhibitor Givinostat* (*ITF2357*) has a potent anti-tumor activity against CRLF2 rearranged BCP-ALL. Leukemia 2017 Apr 21. doi: 10.1038/leu.2017.93.
- Bugarin C, Sarno J, Palmi C, Savino AM, te Kronnie G, Dworzak M, Schumich S, Buldini B, Maglia O, Sala S, Bronzini I, Bourquin JP, Mejstrikova, Hrusak O, Luria D, Basso G, Izraeli S, Biondi A, Cazzaniga G and Gaipa G. *Fine tuning of surface CRLF2 expression and its associated signaling profile in childhood B cell precursor acute lymphoblastic leukemia*. Haematologica June 2015 100: e229-e232. doi:10.3324/haematol.2014.114447.
- Gaipa G, Bugarin C, Cianci P, Sarno J, Bonaccorso P, Biondi A, Selicorni A. Peripheral blood cells from children with RASopathies show enhanced spontaneous colonies growth in vitro and hyperactive RAS signaling. Blood Cancer J. 2015 Jul 17;5:e324. doi: 10.1038/bcj.2015.52.

BOOK CHAPTER

 Jager A, Sarno J, Davis KL. Mass Cytometry of hematopoietic cells. Methods Mol Biol. 2021; 2185:65-76. doi: 10.1007/978-1-0716-0810-4_5.

PREPRINTS

 Craig E, Keyes T, Sarno J, Zaslavsky M, Nolan G, Davis K, Hastie T, Tibshirani R. *MMIL: A novel algorithm* for disease associated cell type discovery. ArXiv [Preprint]. 2024 Jun 12:arXiv:2406.08322v1. PMID: 38947923; PMCID: PMC11213120.

PROCEEDING ABSTRACTS

- Vallabhbhai Koladiya A, Jager A, Culos A, Merchant M, Liu Y, Stuani L, Sarno J, Domizi P, Mullighan CG, Nima Aghaeepour, Sean Bendall, Kara L Davis. *Prior Knowledge Integration Improves Relapse Prediction and Identifies Relapse Associated Mechanisms in Childhood B Cell Acute Lymphoblastic Leukemia*. Blood 142, 1603. ASH November 2023.
- Liu Y, Jiang H, Stuani L, Sarno J, Domizi P, Merchant M, Jedoui D, Jager A, Huang M, Lacayo NJ, Sakamoto KM, Ye J, Davis KL. Uridine Synthesis Is the Metabolic Vulnerability in Relapse-Associated B-ALL Cells with Active Pre-BCR Signaling. Blood 142, 4340. ASH November 2023.
- Stuani L, Jager A, Sahal A, Koladiya A, Sarno J, Domizi P, Liu Y, De Mas V, Recher C, Vergez F, Sarry JE, Davis KL. Single-Cell Proteomic Analysis Defines Metabolic Heterogeneity in Response to Venetoclax in AML. Blood 140, 1028-1029. ASH November 2022.
- Domizi P, Sarno J, Jager A, Baskar R, Reynolds WD, Sahaf B, Bendall SC, Mullighan CG, Leahy A, Myers RM, Grupp SA, Sotillo E, Barrett D, Davis KL. *Ikaros Mediates Antigen Escape Following CD19 CAR T Cell Therapy in r/r B-ALL*. Blood 138, 613. Nov 2021.

- Savino AM, Sarno J, Trentin L, Vieri M, Fazio G, Bardini M, Bugarin C, Fossati G, Davis KL, Gaipa G, Meyer LH, Nolan GP, Biondi A, Te Kronnie G, Palmi C, Cazzaniga G. *Role of the histone deacetylase inhibitor givinostat (ITF2357) in treatment of CRLF2 rearranged acute lymphoblastic leukemia.* Blood 126, 23:2534, Nov 2015.
- Sarno J, Pedersen C, Jager A, Burns T, Gaipa G, Nolan GP, Bava AF, Davis KL. *Glucocorticoids exert a dual role in B-cell acute lymphoblastic leukemia: apoptosis and differentiation of early B-cell populations.* Experimental Hematology 64, S100, Elsevier, August 2018.
- Domizi P, Jager A, Sarno J, Mullighan CG, Grupp S, Sotillo E, Barrett DM, Davis KL. Prediction of patients at risk of CD19Neg relapse following CD19-Directed CAR T cell therapy in B cell precursor acute lymphoblastic leukemia. Blood 134, 749. Nov 2019.

SCIENTIFIC PRESENTATION AT INTERNATIONAL MEETINGS

- Italian Society of Cytometry (GIC) annual conference June 2024, Napoli, Italy. Invited speaker.
- Keystone Symposia Single cell biology: pushing new frontiers in the life sciences. April 2022, Florence, Italy. Poster presentation.
- American Society of Hematology (ASH) annual conference December 2021, Atlanta, USA. Oral presentation.
- Pediatric Oncology Experimental Therapeutics Investigators Consortium (POETIC) July 2019, Palo Alto, USA. Oral presentation. *Invited speaker*.
- Leukemia Lymphoma Society (LLS) Research Progress Meeting September 2019, New York, USA. Oral presentation. *Invited speaker*.
- International Society for Advanced cytometry (CyTO) annual conference June 2019, Vancouver, Canada. Oral presentation.
- International Society of Experimental Hematology (ISEH) annual conference August 2018, Los Angeles, USA. Poster presentation.
- International Society of Pediatric Oncology (SIOP) annual conference November 2018, Kyoto, Japan. Poster presentation.
- American Society of Hematology (ASH) annual conference December 2015, Orlando, USA. Oral presentation.
- Italian Association of Pediatric Hemato-Oncology (AIEOP) September 2015, Naples, Italy. Poster presentation.
- Italian Society of Cytometry (GIC) annual conference October 2013, Lucca, Italy. Oral presentation.
- European Society of Clinical Cell Analysis (ESCCA) annual conference September 2013, Luxembourg, Luxembourg. Oral presentation.