

BIOGRAPHICAL SKETCH

NAME Jolanda Sarno, PhD	POSITION TITLE Junior Group Leader at Fondazione Tettamanti Tenure-track researcher at University of Milano-Bicocca (RTD-A)		
ORCID – ID 0000-0003-3488-0248			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Naples, Federico II Naples, Italy	BSc	10/2010	Biotechnology
University of Milano-Bicocca Milan, Italy	MSc	10/2012	Medical Biotechnology
University of Milano-Bicocca Milan, Italy	PhD	06/2016	Molecular and Translational Medicine

A. Personal Statement (Briefly describe how your experience and qualifies you to undertake the role assigned (e.g., PI, researcher, etc.) in the project proposed in the current application).

I am a Junior Group Leader at M. Tettamanti Center, a diagnostic and research laboratory located at IRCCS San Gerardo Hospital. The center is part of the M.L. Verga children hospital dedicated to the cure, assistance, and research of hematological disease. In this contest, as a scientist dedicated to the field of cancer biology, I have focused my interest on the understanding of the molecular basis of B-cell acute lymphoblastic leukemia. Specifically, my research program focuses on performing a high throughput profiling of clinical samples by using single cell technologies in order to identify tumor intrinsic characteristics associated with resistance with the final goal to identify actionable therapeutic approaches that can be used to prevent the relapse and improve outcomes. Throughout my training during my Ph.D. in Molecular and Translational Medicine and during my postdoc at Stanford University in Kara Davis Laboratory I have worked to unravel inter-patient and intra-tumor heterogeneity. I first worked on a multicentric collaborative project aimed at developing a diagnostic flow cytometry panel able to identify a specific poor prognosis subgroup of children patients with B-cell acute lymphoblastic leukemia (Bugarin C, Sarno J et al. Haematologica 2015). On the same subtype of patients, B-ALL CRLF2-rearranged, I worked on two different projects aimed at identifying alternative approaches to target this type of leukemia either with epigenetic drugs (Savino AM, Sarno J et al. Leukemia 2017) or combinations of kinase inhibitors (Sarno J et al. Oncotarget 2018).

Thanks to a collaborative research project, I then had the unique chance to join Garry Nolan laboratory at Stanford University as PhD visiting student for 9 months. Throughout my training at Stanford University as visiting PhD student first in Nolan Laboratory and as a postdoctoral researcher in Kara Davis Laboratory, I gained a strong expertise in the use of single-cell technologies to study cancer heterogeneity. Specifically, I specialized in the use of mass cytometry (CyTOF), a high-throughput technology that allows a multiparametric proteomic analysis at a single cell level. Applying this technology to clinical samples, we identified features of specific subtypes of cells that are present at diagnosis and predictive of relapse (Good Z & Sarno J et al. Nat Med 2018). More recently using the tools developed in Kara Davis's lab, 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 (Sarno J et al. Nat Comm 2023). In the CAR-T field, we recently identified a early progenitor subpopulation bearing low levels of IKAROS protein being associated with CD19neg relapses following CAR-T cell therapy (Domizi P et al. Nat Comm in press).

Thus, the overall goal of my research is to impact clinical decisions by providing single-cell information of resistant cells that could help in re-define risk stratification of the patients and identify features of resistant cells that can be therapeutically targeted. In my pursuit of progress, I have recently started my own research team where I plan to apply multiparametric high throughput analysis of primary samples to identify MRD (minimal residual disease) resistant features with the final goal to deliver actionable options to clinicians to better treat high-risk patients.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	END DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Undergraduate internship	06/10	10/10	Oncology	University of Naples, Federico II, Italy	Prof. Gianpaolo Tortora
Master degree internship	01/12	10/12	Medical Biotechnology	M.Tettamanti Research Center, University of Milano-Bicocca, Italy	Dr. Giuseppe Gaipa
Doctoral fellow	11/12	06/16	Molecular and Translational Medicine	M.Tettamanti Research Center, University of Milano-Bicocca, Italy	Prof. Andrea Biondi
Fellow	07/16	12/16	Hemato-oncology Pediatrics	M.Tettamanti Research Center, University of Milano-Bicocca, Italy	Prof. Andrea Biondi
Postdoctoral fellow	03/17	02/22	Hemato-oncology Pediatrics	Bass Center for Childhood Cancer and Blood Disorder, Stanford University, USA	Dr. Kara Davis
Senior Research Scientist	03/22	08/23	Hemato-oncology Pediatrics	Bass Center for Childhood Cancer and Blood Disorder, Stanford University, USA	Dr. Kara Davis
Junior Group Leader	09/23	to date	Hemato-oncology Pediatrics	M.Tettamanti Research Center, IRCCS San Gerardo, Monza, Italy	Prof. Andrea Biondi

Professional Membership

- ASH 2019/2022
- EHA 2023 to date

Honors

11/2012	PhD fellowship, PhD program in Molecular and Translational Medicine, University of Milano-Bicocca, Milan, Italy
06/2014	Fellowship for research abroad by "Benedetta è la vita ONLUS" Foundation
10/2015	Abstract Achievement Award at ASH Annual Meeting, Orlando, USA
03/2017	Postdoctoral Fellowship by Italian Association for Cancer Research (AIRC)
06/2019	Postdoctoral Fellowship granted by Maternal & Child Health Research Institute (MCHRI)
02/2022	TRTH (Translational Research Training in Hematology) ASH/EHA

C. Contribution to Science (List selected peer-reviewed publications or manuscripts in press. Mark the 5 most relevant articles for the research proposal).

List of publications:

- Capelletti MM, Montini O, Ruini E, Tettamanti S, Savino AM, **Sarno J**. Unlocking the Heterogeneity in Acute Leukaemia: Dissection of Clonal Architecture and Metabolic Properties for Clinical Interventions. *Int J Mol Sci*. 2024 Dec 24;26(1):45. doi: 10.3390/ijms26010045. PMID: 39795903; PMCID: PMC11719665.
- 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.
- Geron I, Savino AM, Fishman H, Tal N, Brown J, Turati V, James C, **Sarno J**, Hameiri-Grossman M, Nee Lee Y, Rein A, Manirihio 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 α in the development of human B-cell precursor leukemia*. *Nat Commun*. 2022 Feb 3;13(1):659.
- **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.
- **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.. 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.

D. Research Support

Ongoing

- *Italian Association for Cancer Research (AIRC)* 09/2023 – 09/2028
Start-UP reintegration grant (200,000 euro/year, 5 years)
Project: Developmental heterogeneity as a key determinant of treatment-resistant cells in childhood acute lymphoblastic leukemia
- *European Hematology Association (EHA)* estimated 01/2026 – 01/2028
EHA Bilateral Grant 2025 (80,000 euro/year, 2 years)
Project: Understanding how AML interacts with the immune system through CCR1 signalling pathway: a step toward the development of novel immunotherapeutic approaches.

Completed

- *BD (Becton/Dickinson) Sponsored Program* 08/2022 – 08/2023
\$ 50,000 to perform scRNA-Seq using BD platform Rhapsody to study MRD
- *MCHRI (Maternal and Child Health Research Institute)* 09/2019 – 08/2021
Two years post-doctoral fellowship for abroad (\$ 120,000)
Project: *Glucocorticoid resistance in childhood ALL*
- *Italian Association for Cancer Research (AIRC)* 03/2017 – 02/2018
One year post-doctoral fellowship for abroad (51,500 euro)
Project: *Single-cell analysis of chemo-resistant childhood ALL cells: signaling dissection and discovery of therapeutic approaches*

E. Available resources and an inventory of relevant equipment:

The host institution, Tettamanti Research Center, is a hemato-oncology center part of the Pediatric Clinic of University of Milano-Bicocca. The pediatric department is the largest Italian center for the treatment of acute lymphoblastic leukemia, also leading Italian and European clinical trials for the last 25 years. The presence of a diagnostic unit within the research center allows researchers to have full access to primary patients' samples from the Pediatric Hematology Department. Furthermore, as part of AIEOP clinical trials, the molecular screening of all Italian children diagnosed with leukemia is performed in our center where we centralized and bank all the samples. The research center is equipped with state-of-art technologies currently shared between 6 research groups. Specifically, the flow cytometry unit is equipped with a cell sorter (BD FACS Aria), and four modern multi-parametric flow cytometry analyzers (BD FACSCantoII, BD Fortessa X20, BDFACSLyric and Cytex Aurora). The single cell unit, headed by Dr. Sarno Jolanda, has a CyTOF XT mass cytometer (Standard Biotech). The sequencing facility provides Illumina MiSeq for targeted sequencing. In addition to that, there are three labs for molecular biology equipped with ultracentrifuges, electrophoresis, machine for qPCR, Agilent Bioanalyzer and Affimetrix gene chip platform and two labs for cell biology with 5 laminar flow cabins, centrifuges, incubators, ELISA machine, Luminex MagPix, liquid nitrogen room for sample banking, biosafety level 2 (BSL-2) laboratory for manipulation of genetically modified microorganisms and bioinformatic stations for data analysis.