

BIOGRAPHICAL SKETCH

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NAME: Sivori, Simona

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

POSITION TITLE: Full Professor of Human Histology and Embryology, University of Genova (Italy)

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 (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Genova, Italy	BS	11/1991	Biology
University of Genova, Italy	Three-year research fellowship	12/1995	Immunology
University of Genova, Italy	Ph.D.	01/2000	Immunology
University of Genova, Italy	Four-year postdoctoral fellowship	05/2003	Immunology
IRCCS-Istituto G. Gaslini	Contract for research projects	12/2003	Immunology

A. Personal Statement

I am a Full Professor of Human Histology and Embryology and Coordinator of the PhD Program in Clinical and Experimental Immunology at University of Genova (Italy), and my research activity has been consistently focused on the biology of human natural killer (NK) cells and their role in antitumor immune responses. Over the years, my work has aimed to elucidate the molecular and cellular mechanisms regulating NK cell activation, differentiation, and interaction with tumor cells, with the goal of translating fundamental discoveries into innovative immunotherapeutic strategies. My research has combined basic, translational, and preclinical approaches to define how NK cells recognize and eliminate tumor cells and how these processes can be exploited for the development of NK cell-based immunotherapies.

I have led competitive, nationally and internationally funded research projects, serving as Principal Investigator and group leader. Through these studies, I have contributed to a detailed characterization of NK cell receptor repertoires, intracellular signaling pathways, immune surveillance, and tumor immune evasion mechanisms, as well as the impact of the tumor microenvironment on NK cell function.

As head of research units, I have provided scientific leadership in project design, execution, and dissemination of results. I have supervised PhD students, postdoctoral fellows, and junior faculty, promoting their professional development and fostering an environment of scientific rigor, collaboration, and innovation.

In parallel with my research leadership, I have been actively engaged in teaching and institutional service, contributing to curriculum development, academic governance, peer review, and evaluation panels. Overall, my career reflects a long-term commitment to advancing NK cell-based tumor immunology, with the ultimate goal of improving antitumor immune responses and contributing to the development of innovative NK cell-centered cancer immunotherapies.

Ongoing and completed projects that I would like to highlight include:

- 2018 – present: AIRC 5x1000 – Group Leader
Immunity in Cancer Spreading and Metastasis (ISM) - n. 21147
Associazione Italiana per la Ricerca sul Cancro (AIRC)
- 2019 – 2023: PRIN2017 - Group Leader
Innovative approaches with genetically modified immune cells to target hematological malignancies - Prot. 2017WC8499_004
MUR – IT
- 2018 – 2022: AIRC-IG 2017 - Principal Investigator
Checkpoint inhibitors regulate anti-tumor responses by human NK cells - n. 20312
Associazione Italiana per la Ricerca sul Cancro (AIRC)
- 2014 – 2015: Progetto di ricerca di Ateneo 2013 - Principal Investigator
The role of KIR-activating receptors in anti-tumor and anti-viral NK-mediated response -
Prot. N°9563 – 28/4/2014
University of Genova - Genova
- 2009 – 2011: My First AIRC grant - 2008 - Principal Investigator
Analysis of NK cell function in tumor microenvironment - n. 6383
Associazione Italiana per la Ricerca sul Cancro (AIRC)

B. Positions, Scientific Appointments, and Honors

- 2024 – Present Deputy Director of the Department of Experimental Medicine (DIMES), School of Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy
- 2023 – Present President of the Scientific Committee of CDIE, Human Histology and Embryology Teaching Board (Scientific Society recognized by the Italian Ministry of Health)
- 2022 – Present Associate Editor for NK and Innate Lymphoid Cell Biology, *Frontiers in Immunology*
- 2021 – Present Section Editor for Immunology Letters, published by Elsevier as the official journal of the European Federation of Immunological Societies (EFIS)
- 2021 – Present Member of the Council of the Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy
- 2020 – Present Coordinator of the PhD Program in Clinical and Experimental Immunology, University of Genova, Genova, Italy
- 2018 – Present Full Professor, Department of Experimental Medicine (DIMES), School of Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy
- 2018 – Present Head of the Histology Section, Department of Experimental Medicine (DIMES), School of Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy
- 2018 – 2021 Consultant, Sandhill Therapeutics Inc, Dallas, Texas, USA
- 2014 – 2018 Associate Professor, Department of Experimental Medicine (DIMES), School of Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy
- 2014 – 2020 Member of the Board, Center of Excellence for Biomedical Research (CEBR), University of Genova, Genova, Italy
- 2014 – Present Member of the Committee for Animal Welfare, University of Genova, Genova, Italy
- 2013 – 2022 Guest Editor for NK and Innate Lymphoid Cell Biology, *Frontiers in Immunology*
- 2004 – 2014 Assistant Professor, Department of Experimental Medicine (DIMES), School of Medical and Pharmaceuticals Sciences, University of Genova, Genova, Italy

C. Contributions to Science

My research activity has been directed towards the understanding of human Natural Killer (NK) cells effector functions and has helped define important molecular mechanisms that regulate the activity of these lymphocytes against tumors. In particular:

1) I contributed to the discovery and characterization of numerous activating and inhibitory (HLA class I-specific and non-specific) receptors critically regulating anti-tumor activity of human NK cells:

- Moretta A, **Sivori S**, Vitale M, Pende D, Morelli L, Augugliaro R, Bottino C, Moretta L. *Existence of both inhibitory (p58) and activatory (p50) receptors for HLA-C molecules in human natural killer cells*. J Exp Med. 1995, 182(3):875-84
- **Sivori S**, Vitale M, Bottino C, Marcenaro E, Sanseverino L, Parolini S, Moretta L, Moretta A. *CD94 functions as a natural killer cell inhibitory receptor for different HLA class I alleles: identification of the inhibitory form of CD94 by the use of novel monoclonal antibodies*. Eur J Immunol. 1996, 26(10):2487-92
- Costello RT, **Sivori S**, Marcenaro E, Lafage-Pochitaloff M, Mozziconacci MJ, Revirion D, Gastaut JA, Pende D, Olive D, Moretta A. *Defective expression and function of natural killer cell-triggering receptors in patients with acute myeloid leukemia*. Blood. 2002, 99(10):3661-7
- **Sivori S**, Carlomagno S, Falco M, Romeo E, Moretta L, Moretta A. *Natural killer cells expressing the KIR2DS1-activating receptor efficiently kill T-cell blasts and dendritic cells: implications in haploidentical HSCT*. Blood. 2011, 117(16):4284-92

2) I played a fundamental role in studies that led to the discovery and characterization of NKp46, the prototype of the NCR activating receptors involved in NK cytotoxicity against tumors:

- **Sivori S**, Vitale M, Morelli L, Sanseverino L, Augugliaro R, Bottino C, Moretta L, Moretta A. *p46, a novel natural killer cell-specific surface molecule that mediates cell activation*. J Exp Med. 1997, 186(7):1129-36
- Pessino A, **Sivori S**, Bottino C, Malaspina A, Morelli L, Moretta L, Biassoni R, Moretta A. *Molecular cloning of NKp46: a novel member of the immunoglobulin superfamily involved in triggering of natural cytotoxicity*. J Exp Med. 1998, 188(5):953-60

3) I provided full evidence of Toll-like receptors expression and function on human NK cells and identified a new function of the receptor KIR3DL2 that, in addition to recognizing HLA-I molecules, is able to transfer CpG-DNA from the cell membrane to the endosome, where it can stimulate TLR9 suggesting the potential of TLR adjuvants in triggering NK-mediated anti-tumor responses:

- **Sivori S**, Falco M, Della Chiesa M, Carlomagno S, Vitale M, Moretta L, Moretta A. *CpG and double-stranded RNA trigger human NK cells by Toll-like receptors: induction of cytokine release and cytotoxicity against tumors and dendritic cells*. PNAS 2004, 101(27):10116-21
- **Sivori S**, Falco M, Carlomagno S, Romeo E, Soldani C, Bensussan A, Viola A, Moretta L, Moretta A. *A novel KIR-associated function: evidence that CpG DNA uptake and shuttling to early endosomes is mediated by KIR3DL2*. Blood. 2010, 116(10):1637-47

4) I contributed to the characterization of the human NK cell precursors subjected to in vitro differentiation helping to design NK-based precision immunotherapies based on the generation of specialized effector NK cell subsets:

- **Sivori S**, Falco M, Marcenaro E, Parolini S, Biassoni R, Bottino C, Moretta L, Moretta A. *Early expression of triggering receptors and regulatory role of 2B4 in human natural killer cell precursors undergoing in vitro differentiation*. PNAS 2002, 99(7):4526-31

5) I played a fundamental role in the phenotypic and functional characterization of peripheral blood NK cells engineered with chimeric antigen receptor (CAR) in order to provide a powerful cell therapy tool against high-risk leukaemias:

- Quintarelli C*, **Sivori S***, Caruso S*, Carlomagno S*, Falco M, Boffa I, Orlando D, Guercio M, Abbaszadeh Z, Sinibaldi M, Di Cecca S, Camera A, Cembrola B, Pitisci A, Andreani M, Vinti L, Gattari S, Del Bufalo F, Algeri M, Li Pira G, Moseley A, De Angelis B, Moretta L, Locatelli F. *Efficacy of third-party chimeric antigen receptor modified peripheral blood natural killer cells for adoptive cell therapy of B-cell precursor acute lymphoblastic leukemia*. Leukemia. 2020 Apr;34(4):1102-1115

6) I contributed to the characterization of tumor-associated NK cells in colorectal cancer:

- Obino V, Giordano C, Carlomagno S, Setti C, Greppi M, Bozzo M, Pesce S, Ferretti E, Candiani S, Muccio L, Ciferri E, Buttiron Webber T, Solari A, Ortolani F, Paleari L, Clavarezza M, Barberis A, Filairo M, Provinciali N, Rutigliani M, Marcenaro E, DeCensi A, Della Chiesa M, **Sivori S**. *Colorectal cancer-*

infiltrating NK cell landscape analysis unravels tissue-resident PD-1+ NK cells in microsatellite instability tumors. Front Immunol. 2025 Jun 18;16:1578444.

- Rebuffet L, Melsen JE, Escalière B, Basurto-Lozada D, Bhandoola A, Björkström NK, Bryceson YT, Castriconi R, Cichocki F, Colonna M, Davis DM, Diefenbach A, Ding Y, Haniffa M, Horowitz A, Lanier LL, Malmberg KJ, Miller JS, Moretta L, Narni-Mancinelli E, O'Neill LAJ, Romagnani C, Ryan DG, **Sivori S**, Sun D, Vagne C, Vivier E. High-dimensional single-cell analysis of human natural killer cell heterogeneity. Nat Immunol. 2024 Aug;25(8):1474-1488.

Complete List of Published Work:

<https://scholar.google.com/citations?user=0wplLr0AAAAJ&hl=it>

<https://www.scopus.com/authid/detail.uri?authorId=7003599900>

Patents:

Title: *New monoclonal antibody for the selective expansion of NKG2C+ NKG2A- adaptive NK lymphocytes and method thereof*

Inventors: Sivori Simona, Della Chiesa Mariella, Giordano Chiara, Carlomagno Simona, Chiara Setti

Applicant: Università degli Studi di Genova

Priority: IT202300026241A.2023-12-07

Application: IB2024061837W.2024-11-26

Publication: WO2025120448A1.2025-06-12

License agreements with Companies:

7 May 2021 – 18 May 2023 License agreement with Ansun Biopharma Inc (San Diego, CA)

1 March 2020 – 06 May 2021 License agreement with Sandhill Therapeutics Inc (Dallas, Texas)

Organization of scientific meetings:

- Genova, 12-14 September 2024
77° Congresso SIAI
Organizers: Davide Bagnara, Katia Cortese, Franco Fais, Emanuela Marcenaro, **Simona Sivori**
- Roma, 18-19 June 2019
Ospedale Pediatrico Bambino Gesù
Science in the city: Highlights in immunology and oncohaematology
Presidents: Lorenzo Moretta, Enrico Maggi, Franco Locatelli
Scientific Committee: Genny Del Zotto, Maria Cristina Mingari, Concetta Quintarelli, **Simona Sivori**, Paola Vacca
- Camogli, 25-27 October 2018
KIR workshop 2018
Organizers: Daniela Pende, Michela Falco, **Simona Sivori**, Alessandro Moretta