

BIOGRAPHICAL SKETCH

NAME: Sara Lucia Giustina Sigismund

POSITION TITLE: Associate Professor of Applied Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
IFOM Istituto Fondazione di Oncologia Molecolare, Milan	PhD	04/2004	Life Science
Dept. of Genetics and Microbiology, University of Milan	Master Degree	07/200	Molecular and Cellular Biology

A. Personal Statement

I am an Associate Professor at the University of Milan and I lead the Organelle Communication, Trafficking and Cancer at the Department of Experimental Oncology, IEO, Milan. My long-standing research goal is to understand the role of endocytosis in the regulation of growth factor receptor signaling in physiology and cancer.

Within the field of endocytosis, my work has helped establish the concept that **integration of distinct endocytic pathways and communication among different cellular organelles is critical for determining the final signaling output**. My current research interests include the elucidation of the molecular mechanism of EGFR-non-clathrin endocytosis, its interplay with mitochondrial functions, its relevance in different cellular contexts and for different growth factor receptors, and its functional significance in normal physiology and cancer.

My work has received **funding support** from the European Research Council (**ERC** Consolidator Grant 2020), The Worldwide Cancer Research (**WCR** 2015 and 2020), the Italian Association of Cancer Research (**AIRC** Investigator Grant 2020), and the Italian Ministry of Education, University and Research (**PRIN** 2017, 2022).

Finally, I am actively involved in **promoting Science in Italy** by organizing events and courses and establishing networks for students and Post Docs, and between the different Italian Laboratories through the **Italian Association for Cell Biology and Differentiation** (ABCD), of which I am the President.

B. Positions, Scientific Appointments, and Honors**• POSITIONS**

2025 – present	Group Leader, Organelle Communication, Trafficking and Cancer, IEO, Milan
2021 – present	Associate Professor of Applied Biology, Dept. of Oncology and Hemato-Oncology, University of Milan, Milan, Italy c/o IEO, European Institute of Oncology, Milan, Italy
2018 – 2020	Assistant Professor (RTD-B), Dept. of Oncology and Hemato-Oncology, University of Milan, Milan, Italy c/o IEO, European Institute of Oncology, Milan, Italy
2010 – 2017	Head of the Endocytosis Research Team, Laboratory of Cellular Logistics of Cancer directed by Prof. Pier Paolo Di Fiore, IFOM, The FIRC Institute of Molecular Oncology, Milan, Italy
2004 – 2010	Post-doc, Laboratory of Prof. Pier Paolo Di Fiore, IFOM, The FIRC Institute of Molecular Oncology, Milan, Italy
2000 – 2004	Ph.D. student, IFOM-IEO Campus, Milan, Italy

1998 – 2000

Master's thesis student, Laboratory of Prof. Marco E. Bianchi, Dept. of Genetics and Microbiology, University of Milan, Milan, Italy

• AWARDS AND HONORS

- 2022 EMBO Member
- 2007 Keystone Scholarship, Ubiquitin and Signaling, Big Sky, Montana, USA
- 2005 Cecilia Cioffrese Award, Carlo Erba, Italy, assigned for the best Italian research on cancer and viral disease
- 2004 Upstate Young Cell Signaller Award, Upstate, Dundee, UK
- 2004 SIBBM Award, Italian Society of Biophysics and Molecular Biology

C. Contributions to Science

Through the study of EGFR post-translational modifications and their role in endocytosis, my work led to the discovery of a novel mechanism of **non-clathrin endocytosis (NCE)**, which is activated at high doses of EGF and targets EGFRs to lysosomes for degradation, leading to signal attenuation. This mechanism protects cells from overstimulation under conditions of high receptor occupancy and it might represent a novel tumor suppressor pathway whose alterations could contribute to aberrant signaling in cancer (*Sigismund S et al., PNAS 2005; Sigismund S et al., Dev Cell 2008; Sigismund S et al., EMBO J 2013; Capuani et al., Nat Comm 2015; Pascolutti et al Cell Rep 2019; Sigismund S, Nat Rev Mol Cell Biol. 2021*). My work has also revealed that NCE is mediated by a novel endocytic mechanism involving the formation of **interorganelle contact sites** between the plasma membrane (PM), the endoplasmic reticulum (ER) and the mitochondria, and localized calcium signaling directly linking growth factor receptor signaling with mitochondrial metabolism (*Caldieri et al., Science 2017, Mesa et al., Nat Comm 2024*).

In a parallel but related line of research, I investigated the role of endocytosis in epithelial-to-mesenchymal transition (EMT) and cancer cell invasion and metastasis. Through the study of the endocytic protein Epsin 3, whose overexpression in breast cancer correlates with poor prognosis and metastasis, I contributed to the discovery that breast epithelial cells are capable of acquiring a **plastic, hybrid EMT phenotype**, through the establishment of an **endocytic-based circuitry**, which renders them prone to perform *in situ*-to-invasive transition, typical of invasive breast carcinomas (*Schiano Lomoriello et al., Nat Comm 2020; Green BJ et al., Small 2022*).

Complete List of Published Work: <https://pubmed.ncbi.nlm.nih.gov/?term=Sigismund+Sara&sort=date>