



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

DIPARTIMENTO
DI FARMACIA
E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno **23 luglio 2025**
alle ore **14.30**

Prof.ssa Sara Sigismund

Associate Professor, Dept. of Oncology and Hemato-Oncology - University of Milan
Head of the Organelle Communication, Trafficking and Cancer Lab, Dept. of
Experimental Oncology - IEO
(ospite della Prof.ssa A.M. Porcelli)

terrà un seminario in lingua inglese dal titolo:

Below the Surface: Endocytic Control of Cell Plasticity in Cancer

Area tematica: Cancer Biology

in presenza:

Aula B, Via Irnerio 42, Bologna

L'evento è organizzato nell'ambito del Corso di Dottorato in Biologia
Cellulare e Molecolare

ABSTRACT

Endocytosis serves as a regulatory mechanism influencing multiple aspects of cell physiology, and our evidence suggests that disruptions in this process may play a causal and targetable role in cancer. Using the EGFR model system, we confirmed that the dual functions of endocytosis – signal propagation and attenuation – can be integrated, at least in part, at the plasma membrane (PM) through the activation of distinct endocytic mechanisms. Specifically, a form of EGFR endocytosis known as non-clathrin endocytosis (NCE), which is triggered only at high ligand concentrations and directs the receptor toward degradation, requires a tripartite organelle platform involving the PM, endoplasmic reticulum (ER), and mitochondria. This platform enables direct communication between active EGFR and mitochondrial metabolism, thereby shutting down proliferative signals while promoting collective cell motility.

In parallel, our research has established the causal role of the endocytic protein Epsin3 (EPN3) in breast cancer progression, particularly in connection with partial epithelial-to-mesenchymal transition (pEMT) and invasive phenotypes. Notably, increased endocytosis of E-cadherin is the initiating event in EPN3-driven pEMT, enhancing cellular plasticity and facilitating metastatic dissemination. Crucially, blocking this elevated E-cadherin endocytosis can reverse EPN3-dependent invasiveness. Given its limited expression in adult tissues and its overexpression in breast cancer, EPN3 – and the endocytic processes it governs – emerges as a promising target for therapeutic intervention.

BIOGRAPHICAL SKETCH

Sara Sigismund is Associate Professor at the University of Milan and leads the Endocytosis Research team at the Department of Experimental Oncology, IEO, Milan. Her long-standing research goal is to understand the role of endocytosis in the regulation of growth factor receptor signaling in physiology and cancer.

Prof. Sigismund has contributed to the elucidation of molecular mechanisms governing epidermal growth factor receptor (EGFR) ubiquitination and endocytosis, showing that monoubiquitination is a critical signal in EGFR internalization through the establishment of a network of ubiquitin-mediated interactions with specific adaptor proteins that possess ubiquitin-interacting motifs (UIMs) and that are themselves ubiquitinated upon EGF stimulation (Polo S et al., *Nature* 2002; Haglund K*, Sigismund S* et al., *Nature Cell Biology* 2003). The importance of this work was recognized through a number of prizes awarded to Prof. Sigismund in 2004, including the Cecilia Cioffrese Award (Carlo Erba, Italy, assigned for the best Italian research on cancer and viral disease) and the Upstate Young Cell Signaller Award (Upstate, Dundee, UK, assigned for the best international research on signalling). For her discoveries in the endocytic field, in 2022, Prof. Sigismund was elected EMBO member.

Her 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).

Prof. Sigismund is 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 she is the President.