ORAL COMMUNICATIONS

EXPLORING THE FUNCTIONAL ROLE OF THE PROTEOGLYCAN ESM1 IN THE BREAST CANCER TUMOR MICROENVIRONMENT

E. Peri[1], S. Feo[1|2], E. Roz[3], A. D'Ascola[4], P. Cancemi[1|2]

[1]Department of Biological Chemical and Pharmaceutical Sciences and Technologies (STEBICEF), University of Palermo, Italy; [2]Experimental Center of Onco Biology (COBS), Palermo, Italy; [3]La Maddalena Hospital III Level Oncological Department, Palermo, Italy; [4]Department of Clinical and Experimental Medicine, University of Messina, Italy

Breast cancer (BC) progression is strongly influenced by the tumor microenvironment (TME), where dynamic interactions between cancer cells, stromal components, and secreted factors drive tumor heterogeneity and aggressiveness. Among these factors, endothelial cell-specific molecule 1 (ESM1), a soluble dermatan sulfate proteoglycan, has emerged as a key regulator of tumor–microenvironment crosstalk. ESM1 promotes angiogenesis, inflammation, and cancer cell proliferation and migration, and is frequently overexpressed in multiple malignancies. However, its role in modulating the TME in breast cancer remains poorly defined. In this study, we evaluated serum and tissues ESM1 levels in BC patients and found that HER2-negative cases exhibit higher and more heterogeneous ESM1 levels. Based on these findings, we investigated the functional role of ESM1 silencing in the triple-negative breast cancer (TNBC) cell line MDA-MB-231. ESM1 silencing led to significant modulation of pathways involved in extracellular matrix remodeling and epithelial--to-mesenchymal transition (EMT). Collectively, our findings indicate that ESM1 acts as a critical mediator of tumor–TME interactions, contributing to the aggressive phenotype of TNBC, and identify ESM1 as a promising biomarker and potential therapeutic target in breast cancer, supporting its possible integration into precision medicine strategies for patient stratification and targeted intervention.

Acknowledgments: This research was supported by the Italian Ministry of Education, University, and Research (MIUR) through the PRIN PNRR 2022 project P2022WZXRP_002 (PRJ-1560) and the INTERREG NEXT Italia Tunisia project BIOGEN4MED - Discovering novel Biomarkers through Pharmaco-Genomics for Precision Medicine - B73C25000310002