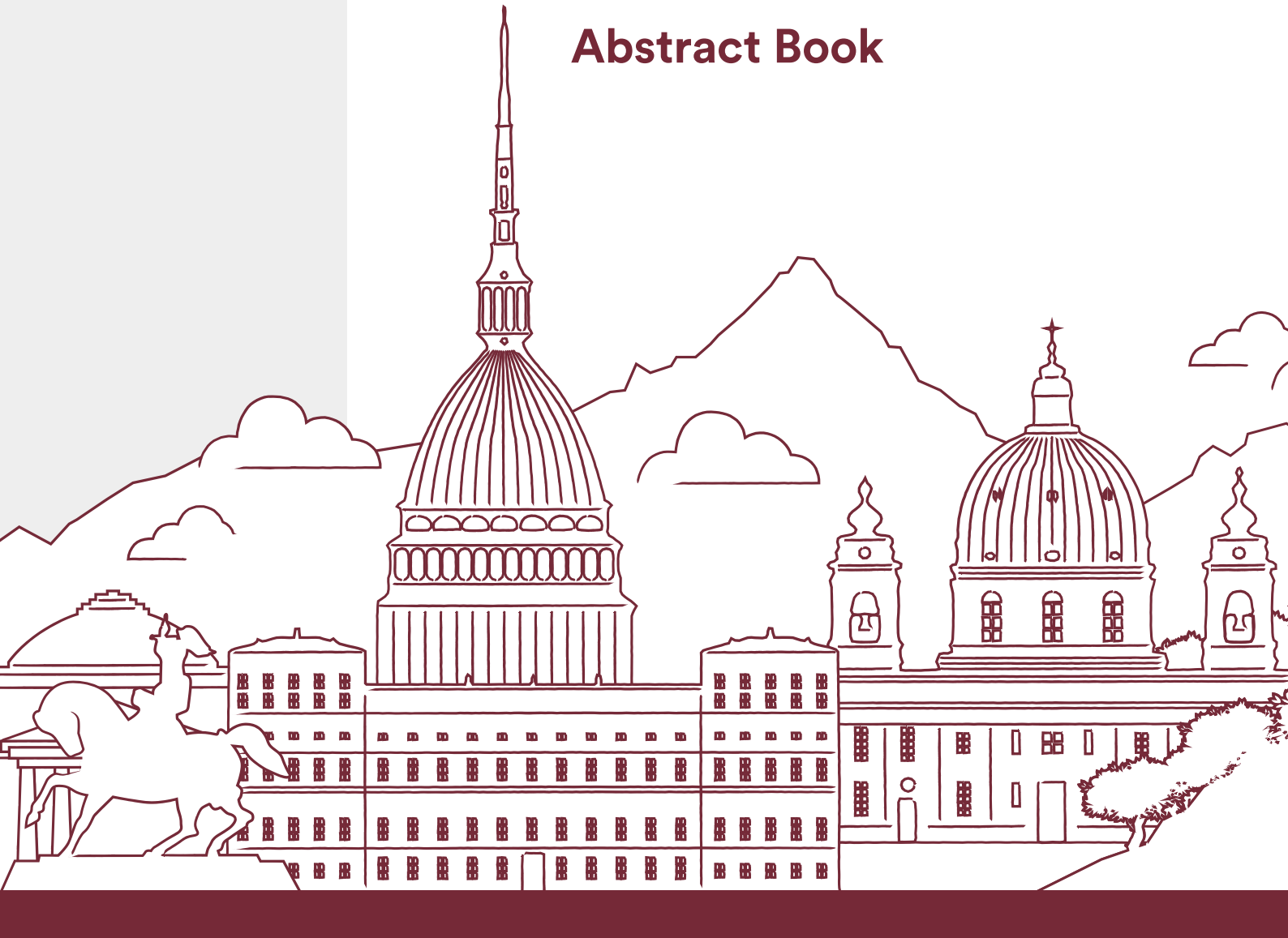
SIC

65th Annual Meeting of the Italian Cancer Society

Targeting Cancer Hallmarks

Abstract Book



Turin, December 3-4-5, 2025

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Topic

F. Novel therapeutic approaches and drug resistance

F16

Modulation of tumor-suppressor ncRNAs in cancer cells via administration of extracellular vesicles released by sorafenibtreated cells.

Grossi I. [1], Pelisenco I.A. [1], Maffezzoni M. [1], Guerra F. [2], Bucci C. [2], D' Agostino V.G. [3], De Petro G. [1], Salvi A. [1]
(1) University of Brescia, Department of Molecular and Translational Medicine, Brescia - Italy, (2) University of Salento, Department of Biological and Environmental Sciences and Technologies, Lecce - Italy, (3) University of Trento, Department of Cellular, Computational and Integrative Biology (CIBIO), Trento - Italy

Extracellular vesicles (EVs) are a heterogeneous group of nanoscale membrane-enclosed structures produced by all cell types. EVs carry a range of molecular cargo, including RNA, proteins, and lipids, and play a crucial role in mediating intercellular communication. Given their natural ability to deliver biologically active molecules into the cytoplasm of recipient cells, EVs have received growing interest as delivery vehicles of therapeutic molecules that can be used in different disease contexts, including cancer.
The aim of this work is to explore an innovative cell-based approach to vehicle non-coding RNAs (ncRNAs) with tumor-suppressive functions in cancer cells. We specifically selected three ncRNAs that act mainly as tumor-suppressors and are down-modulated in many cancer types: miR-23b-3p, miR-126-3p and the long ncRNA GAS5. We previously demonstrated that these ncRNAs were dis-regulated in cancer cells treated with the multi-kinase inhibitor sorafenib. Here, we isolated the EVs from 4 breast cancer (BC) and 2 hepatocellular carcinoma (HCC) cell lines after sorafenib treatment. The EVs were characterized for size, particle concentration, and protein markers. Then, we quantified the levels of miR-23b-3p, miR-126-3p, and GAS5 encapsulated within the EVs using droplet digital PCR (ddPCR). The results showed increased levels of the selected ncRNAs in EVs derived from cancer cells after sorafenib treatment. To assess the ability of the enriched EVs as carriers of the three ncRNAs, we verified the uptake of EVs by recipient cells using fluorescence microscopy analysis with labelled EVs. Notably, the levels of cellular miR-23b-3p, miR-126-3p and GAS5 increased in target cells after the treatment with enriched EVs. Concurrently, the cell proliferation was reduced by the EVs-based treatment. We also used EVs released by HCC cells resistant to sorafenib (SKHep1C3-SR) which contained higher levels of the selected ncRNAs compared to EVs obtained from the sensitive cells. The uptake of these EVs by SKHep1C3 cells was verified and the increased levels of the selected ncRNAs in recipient cells were confirmed. In conclusion, this study presents a feasible and innovative approach to generate EVs enriched with specific tumor-suppressor ncRNAs and demonstrates their potential as delivery vehicles capable of modulating the expression of miR-23b-3p, miR-126-3p and GAS5 in different *in vitro* cancer models.

F17

Effects of natural compounds on colorectal cancer cell lines

Bianchini S. [1], Bovio F. [1], Cristani F. [1], Guzzo F. [2], Forcella M. [1], Fusi P. [1]
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Colorectal carcinoma (CRC) is one of the most common types of cancer worldwide, with a worrying rise in patients younger than 50 years. To treat such a heterogeneous disease, many drugs have been developed, but mortality remains high especially for metastatic CRC. Looking for new therapeutic options, natural compounds can represent an interesting opportunity, considering that clinically approved drugs such as irinotecan have been isolated from molecules present in plant species.
Therefore, we tested the extract derived from *Diospyros kaki* and *Gratiola officinalis* on the E705 and SW480 CRC cell lines to evaluate their possible anticancer properties. We observed that treatment with *D. kaki* increases oxidative stress and induces mitochondrial dysfunction in both cell lines, leading to apoptotic death[1]. Treatment with *G. officinalis* also determines apoptosis in the E705 cell line, while it blocks cell-cycle progression in the SW480 cell line. Moreover, taking advantage of the Seahorse Technology, we demonstrated that *G. officinalis* administration disrupts the glycolytic metabolism in the E705 cell line[2]. These observations prompt us to further test and characterize the effects verbascoside[3], a molecule present in *G. officinalis*, on a wider platform of CRC cell lines.

[1]Bianchini S, Bovio F, Negri S, et al. Methanolic Extract of the Nutritional Plant (*Diospyros kaki* Thunb.) Exhibits Anticancer Activity by Inducing Mitochondrial Dysfunction in Colorectal Cancer Cells. *Nutrients*. 2024;16(21):3742. Published 2024 Oct 31. doi:10.3390/nu16213742 [2]Bianchini S, Bovio F, Negri S, Guzzo F, Forcella M, Fusi P. *Gratiola officinalis* Alcoholic Extract Targets Warburg Effect, Apoptosis and Cell Cycle Progression in Colorectal Cancer Cell Lines. *Int J Mol Sci*. 2025;26(5):2220. Published 2025 Feb 28. doi:10.3390/ijms26052220

[3]Attia YM, El-Kersh DM, Wagdy HA, Elmazar MM. Verbascoside: Identification, Quantification, and Potential Sensitization of Colorectal Cancer Cells to 5-FU by Targeting PI3K/AKT Pathway. *Sci Rep*. 2018;8(1):16939. Published 2018 Nov 16. doi:10.1038/s41598-018-35083-2