

Selective Enrichment of Circular RNAs in Extracellular Vesicles released by Ovarian Cancer Cells: A New Frontier in Liquid Biopsy

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Background

Ovarian cancer (OC) remains one of the most lethal gynecological malignancies. Liquid biopsy represents an alternative source for investigating tumor-related alterations. This method allows the analysis of various analytes, including the extracellular vesicles (EVs). EVs carry bioactive molecules such as Circular RNAs (circRNAs). CircRNAs are an emerging class of covalently closed ncRNAs with increasing relevance in cancer research due to their stability and regulatory functions. While recent studies have elucidated the roles of circRNAs in tumor biology, their presence and potential functions within EVs released by cancer cells remain poorly characterized. in this study we aimed to identify circRNAs selectively packaged into EVs derived from OC cells.

Method

EVs were isolated from the conditioned media of OC cell lines and the plasma of OC patients by ultracentrifugation or size exclusion chromatography and were characterized in accordance with MISEV guidelines. To analyze circRNAs, total RNA was extracted from OC cells and EVs and treated with RNase R. Complementary DNA was synthesized by reverse transcription, and circRNA expression was assessed using divergent primers by RT-qPCR.

Results

We identified a specific profile of circRNAs selectively packaged into EVs released from OC cells, including circ-MUC16, derived from MUC16 gene (CA125), a well-known but limited biomarker for OC. Circ-MUC16 is aberrantly expressed in OC cells compared to normal ovarian epithelial cells and has been shown to promote autophagy and tumor progression, while its silencing suppresses the oncogenic phenotype.

Conclusion

Due to their stability and specificity, circRNAs like circ-MUC16 may offer more reliable biomarkers than their linear counterparts. Further studies are needed to assess their functional roles and clinical potential in liquid biopsy applications, as well as their relevance in OC therapy. This work is part of NARCISUS project, funded by PRIN 2022 Program under grant agreement No. 20224XB79P, Next-generation EU, PNRR, M.4-C2-1.1.