Significance of Epithelial-Mesenchymal Transition Markers in Breast Cancer

Palacký University Olomouc

Neria Bitton, Markéta Kolečková

Department of Pathology, Faculty of Medicine and Dentistry, University Hospital in Olomouc, Czech Republic

Faculty of Medicine and Dentistry

Introduction

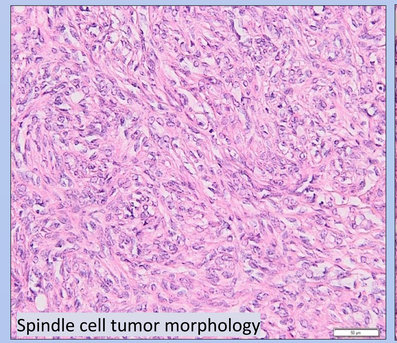
- Breast cancer is the most frequently diagnosed cancer and is the second most common cancer related death in women worldwide[1]. Breast cancer represents the morphologically and genetically heterogenous group of cancers which can be classified into several molecular subtypes (luminal A/B, non-luminal HER2/neu positive and triple-negative – TNBC) differing in prognosis and therapeutic response[2]. TNBC, lacking the hormone receptor (ER, PR) and HER2/neu protein expression, display the vast genetical diversity associated with reduced sensitivity to chemotherapy. Aberrant activation of epithelial – mesenchymal transition (EMT) results in higher metastatic potential and multidrug resistance[3,4,5]. However, the mechanisms of EMT and role of microRNAs (miRNAs) in EMT activation has not been sufficiently clarified yet.

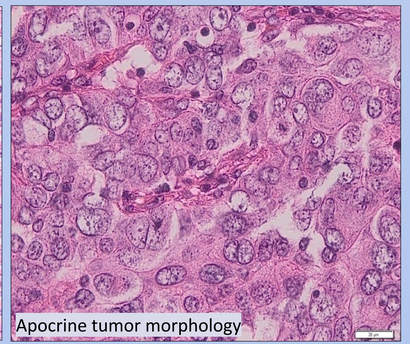
Aim of study

- The purpose of our study was the identification and analysis of EMT – related miRNAs playing a pivotal role in TNBC development, progression and multidrug resistance.

Material and methods

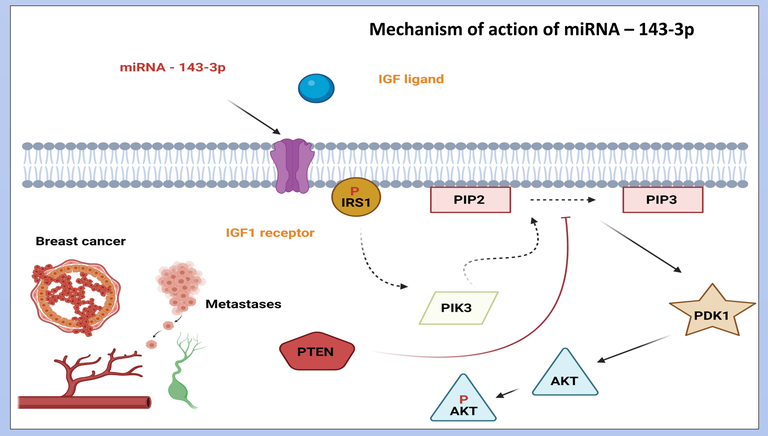
- In the initial phase of our research, we focused on the morphological analysis of 25 non-therapeutically influenced TNBCs. To identify the changes in miRNA expression levels, the laser-capture microdissection technique for the isolation of spindle and apocrine EMT-related tumor cell morphology, RNA extraction, microarray and statistical analysis were used. Verification of the selected miRNAs was performed by qRT-PCR. The results were compared to the recent literature on this topic.


Spindle cell tumor morphology


Apocrine tumor morphology

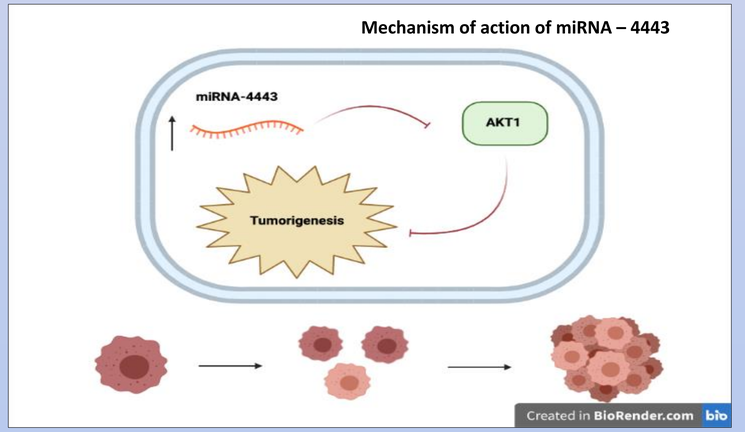
Results

- EMT-related tumor morphology showed the specific miRNA expression profile in comparison to other identifed tumor areas. Down-regulation of miRNA-143-3p expression is seemed to be associated with the stimulation of multidrug resistance in TNBC. The mechanism of action of miRNA-143-3p includes the overexpression of cytokine-induced apoptosis inhibitor protein 1 (CIPIN1) involved in the regulation of P-glycoprotein (P-gp) and p53 expression. Up-regulation of miRNA-4443 is described in relation to the metastatic potential of TNBC which is induced by the phosphatidylethanolamine binding protein 1 (PEBP1) expression and tissue inhibitors of metalloproteinases inhibition and matrix metalloproteinases activation.



Conclusions

- EMT-related tumor morphologies display a specific miRNA expressions profile in TNBC which may reflect the prognosis and multidrug resistance of TNBC.



References

1. Coughlin, S. S. (2019). Epidemiology of Breast Cancer in Women. *Advances in Experimental Medicine and Biology Breast Cancer Metastasis and Drug Resistance*, 9-29.
2. Al-Thoubaity, F. K. (2020). Molecular classification of breast cancer: A retrospective cohort study. *Annals of Medicine and Surgery*, *49*, 44-48.
3. Yao, D., Dai, C., & Peng, S. (2011). Mechanism of the Mesenchymal–Epithelial Transition and Its Relationship with Metastatic Tumor Formation. *Molecular Cancer Research*, *9*(12), 1608-1620.
4. Yin, L., Duan, J., Bian, X., et al (2020). Triple-negative breast cancer molecular subtyping and treatment progress. *Breast Cancer Research*, *22* (1).
5. Vijay, G. V., Zhao, N., Hollander, et al (2019). GSK3β regulates epithelial-mesenchymal transition and cancer stem cell properties in triple-negative breast cancer. *Breast Cancer Research*, *21*(1).

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