miR-200 FAMILY AND EPITHELIAL-MESENCHYMAL TRANSITION IN MAMMARY GLANDS

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INTRODUCTION

Epithelial to mesenchymal transition endows malignant epithelial cells with the capacity to break free from one another and invade the surrounding stroma. On the other hand, MicroRNAs are small non-coding single-stranded RNAs that influence gene expression networks by inhibiting target messenger RNAs. So, the objective of this study is the down-regulation of miR-200 in EMT in order to use it as a target in metastasis breast cancer.

MATERIALS AND METHODS

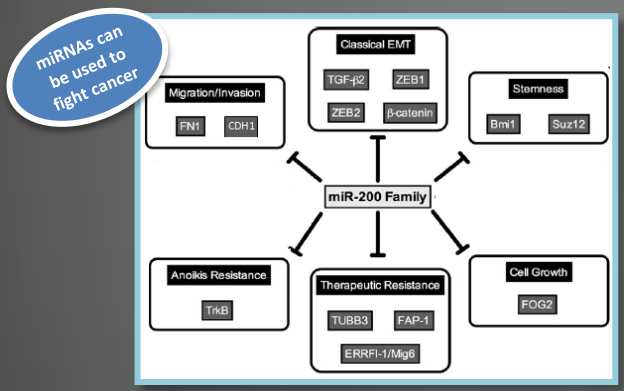
Item introduction by searching Pubmed → Focus on the link between EMT and miRs → Take a closer look at miR's regulation

RESULTS

What are miRNAs functions in mammary glands?

1. **Regulation of intracellular processes.**
2. **They are important during malignant transformation and metastasis**.
3. They act as **oncogenes (oncomiRs) or tumor suppressors.**
4. They have a role in the **mammary involution**: ↑TGFβ ↓E-cadherin

Invasion and metastasis (aberrant EMT) are the hallmarks of malignant tumour progression.



Members of the miR-200 family directly target and down-regulate genes involved in a variety of processes that contribute to tumorigenesis and metastasis.
Figure modified from Howe (2012)

CONCLUSIONS

Statistics

1 out of 8 women develops breast cancer

- Identification of miRs as regulators or biomarkers in both normal mammary and breast cancer
- Targets of miRNA: E-cadh, TGF-β, β-catenina, BMI1, ZEB1/2, SUZ12 or FOG2.

Research

Trials

We can develop novel miRNA therapeutics, like antagomirs or miRNA replacement therapy

21 miRNA in breast
↓
Profile miRNAs
↓
Personalize medicine

Future

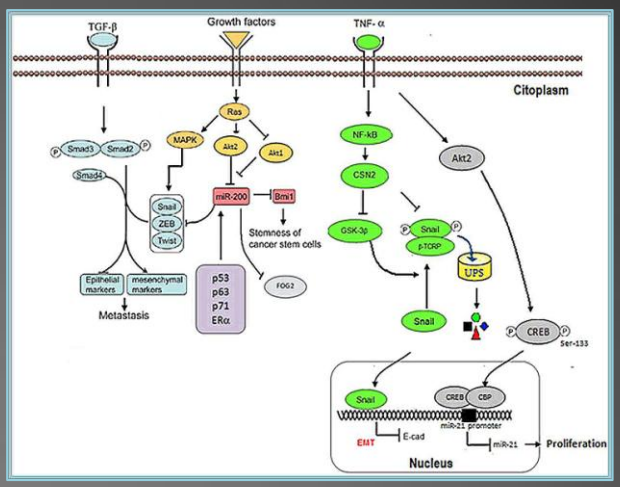
BIBLIOGRAPHY

1.Gregory PA, Bracken CP, Smith E, et al. (2011) An autocrine TGF-beta/ZEB/miR-200 signaling network regulates establishment and maintenance of epithelial-mesenchymal transition. *Mol Biol Cell*. 22(10):1686-1698

2.Iorio MV, Casalini P, Piovan C, Braccioli L, Tagliabue E. (2011) Breast cancer and microRNAs: Therapeutic impact. *Breast*. 20 Suppl 3:S63-70.

3. Liu H. (2012) MicroRNAs in breast cancer initiation and progression. *Cell Mol Life Sci*. 69(21):3587-3599.

The miR-200 and miR-221 families are differentially expressed in carcinomas, particularly in breast cancer. Specifically, the miR-200 family is high in the luminal breast cancer subtypes.



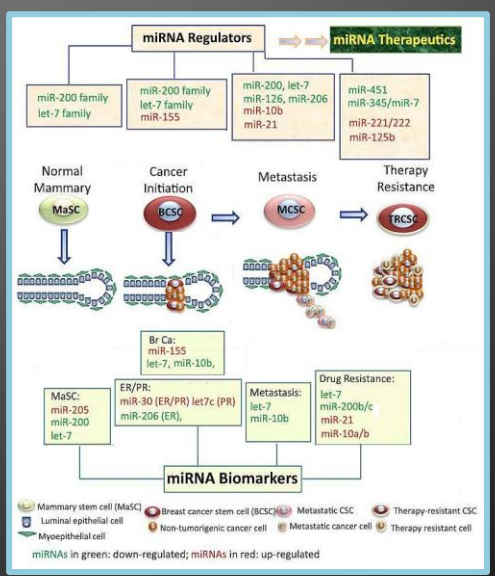
Pathways of reciprocal negative feedback mediated by the miR-200 family in regulating epithelial–mesenchymal transition

MIR-200 FAMILY

Built of of two polycistronic clusters—miR-200c and miR-141 on chromosome 12 and miR-200b, miR-200a and miR-429 on chromosome 1.

They lead to restoration of an epithelial phenotype in breast cancer cell lines, characterized by an increase in E-cadherin expression, and decreased migration and invasion. The miR-200 family has got several targets genes involved in cell cycle control. But it could be influenced by Akt or tumor suppressors.

The **TGF-β/ZEB/miR-200** signalling regulate the EMT, so their study is crucial. Moreover, prolonged activation of this signalling network affects dynamic and reversible DNA methylation of the miR-200 family loci which may contribute to stability of the mesenchymal state.



A summary of miRNA regulators and biomarkers in the development of the normal mammary gland, breast cancer initiation, metastasis, and therapy resistance.
Figure modified from Liu (2012)