UNIVERSITY of WASHINGTON TACOMA

Origins for breast cancer development in association with epithelial-mesenchymal transitions (EMTs) and essential signaling pathways

Kaitlin Nguyen and Marc Nahmani

INTRODUCTION

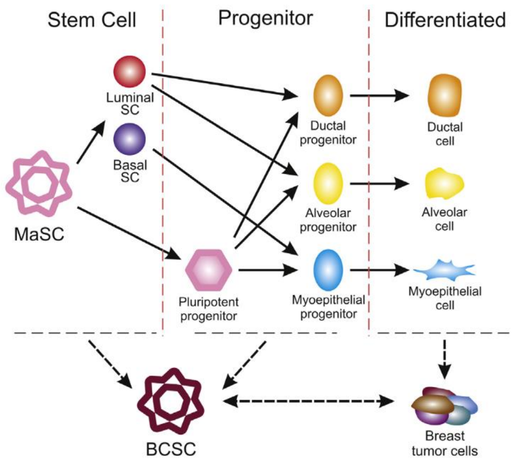
- There are an estimated 43,000 U.S. deaths from breast cancer every year with prostate, lung, and colorectal cancers tolling close behind it. Recent evidence suggests that a process known as the epithelial-mesenchymal transitions (EMTs) during embryonic growth have a role in giving rise to migratory carcinoma, contributing to breast cancer development.

Cancer Type	Estimated New Cases	Estimated Deaths
Bladder	81,180	17,100
Breast (Female – Male)	287,850 – 2,710	43,250 – 530
Colon and Rectal (Combined)	151,030	52,580
Endometrial	65,950	12,550
Kidney (Renal Cell and Renal Pelvis)	79,000	13,920

National Cancer Institute, 2021.

Table 1. A table of the estimated cases and death tolls for the top 5 most common cancer types collected for 2022. (5)

- EMT has been associated with the generation of metastatic cells, as other neighboring epithelial cells couple with migrating EMT cells to target sites prior to replicating into cancerous tissue.



Feng et al., 2018.

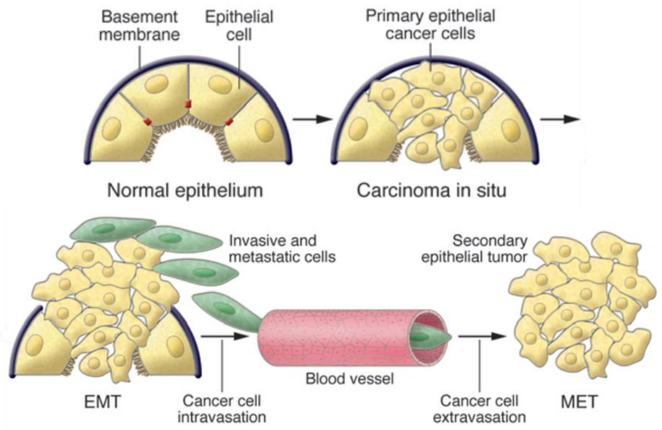
Figure 1. Hierarchy of breast cell stem cells and its differentiation into breast cancer stem cells. (2)

OBJECTIVE

- In this literature review, I investigated the significance of EMTs and their role in contributing to the generation of breast cancer through signaling pathways.

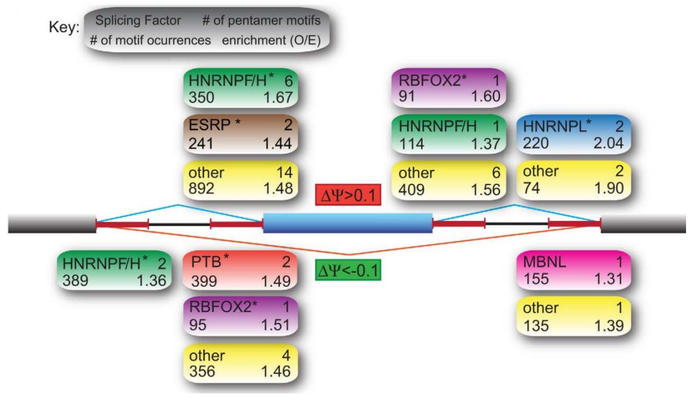
METHODS AND MATERIALS

- 6 peer-review articles
- 4 statistical websites (American Cancer Society, National Cancer Institute, SEER Cancer, World Cancer Research Fund International)



Kalluri and Weinberg, 2009.

Figure 2. The Formation of metastatic epithelial cells via EMT. (3)



Shapiro et al., 2011.

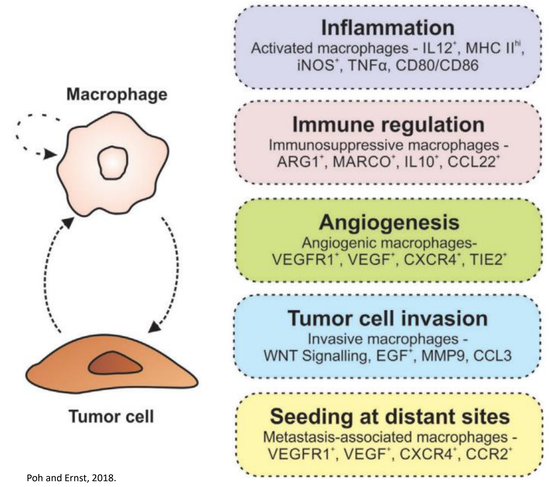
Figure 3. Pentamer motif analysis revealing splicing factors involved with EMT-specific splicing within intronic regions. (8)

RESULTS & FUTURE WORK

- Although contributing factors such as genetics and external environments influence the body and its tissues, the relation of EMTs to breast cancer development can provide more insight to the prevention of metastatic cells for future studies

- Malignant non-EMT cell lines observed in tissue lining
- EMT capacity to generate throughout several networks and signaling pathways
- BRCA1/2 primary gene subsets held the greatest probability of creating metastatic cells
- Mutated genes responsible for DNA repair and tumor suppression

- EMT research should focus on identifying the significance of specific gene-splicing events on cancer development
- Future research could benefit from exploring macrophage stimulation and sensitivity to increase efficiency in cancer breakdown
- The development of breast cancer could also be explored by examining varying microbiome diversity



Poh and Ernst, 2018.

Figure 4. The influence of macrophages on tumorigenesis within the microenvironment. Autocrine and paracrine loops promote pro-tumorigenic properties. (6)

REFERENCES

1) American Cancer Society. "Breast Cancer: Breast Cancer Information & Overview." *American Cancer Society*, 2021. https://www.cancer.org/cancer/breast-cancer.html.
2) Feng, Yixiao, Mia Spezia, Shifeng Huang, Chengfu Yuan, Zongyue Zeng, Linghuan Zhang, Xiaojuan Ji, et al. 2018. "Breast Cancer Development and Progression: Risk Factors, Cancer Stem Cells, Signaling Pathways, Genomics, and Molecular Pathogenesis." *Genes & Diseases* 5 (2): 77–106. https://doi.org/10.1016/j.gendis.2018.05.001.
3) Kalluri, Raghu, and Robert A Weinberg. "The basics of epithelial-mesenchymal transition." *The Journal of clinical investigation* vol. 119,6 (2009): 1420-8. doi:10.1172/JCI39104
4) Kotiyal, & Bhattacharya, S. (2014). Breast cancer stem cells, EMT and therapeutic targets. *Biochemical and Biophysical Research Communications.*, *453*(1), 112–116. https://doi.org/10.1016/j.bbrc.2014.09.069
5) National Cancer Institute. "Common Cancer Types." *National Cancer Institute*, 22 Apr. 2021, https://www.cancer.gov/types/common-cancers#:~:text=The%20 most%20 common%20type%20of,are%20combined%20for%20the%20list.
6) Poh, Ashleigh R., and Matthias Ernst. "Targeting Macrophages in Cancer: From Bench to Bedside." *Frontiers*, Frontiers, 12 March. 2018, https://doi.org/10.3389/fonc.2018.00049
7) SEER Cancer Stat Facts: Female Breast Cancer. *National Cancer Institute*, 2021. Bethesda, MD, https://seer.cancer.gov/statfacts/html/breast.html
8) Shapiro IM, Cheng AW, Flytzanis NC, Balsamo M, Condeelis JS, Oktay MH, et al. (2011) An EMT–Driven Alternative Splicing Program Occurs in Human Breast Cancer and Modulates Cellular Phenotype. PLoS Genet 7(8): e1002218. https://doi.org/10.1371/journal.pgen.1002218
9) Vincent-Salomon, A., Thiery, J.P. Host microenvironment in breast cancer development: Epithelial–mesenchymal transition in breast cancer development. *Breast Cancer Res* 5, 101 (2003). https://doi.org/10.1186/bcr578.
10) WCRF International. "Breast Cancer Statistics: World Cancer Research Fund International." *WCRF International*, 25 May 2021, https://www.wcrf.org/dietandcancer/breast-cancer-statistics/.

ACKNOWLEDGEMENTS

- Thanks to the University of Washington Tacoma for providing the resources and references needed to assemble this project.

- Special thanks to Dr. Marc Nahmani and Dr. John Finke for mentoring me and guiding the creation of this project.