Inhibiting prostaglandin decreases proliferation rates of estrogen receptor positive breast cancer over triple-negative breast cancer

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INTRODUCTION:

- Breast cancer (BC) is the uncontrolled growth of glandular or ductular breast cells.[1]
- Estrogen receptor (ER) positive and triple negative (TN) BC are two of the most common BC subtypes.[2]
- In other diseases, ER can increase prostaglandin synthesis.[3]
- Prolonged use of prostaglandin inhibitors (aspirin) can lower the occurrence of BC.[3]

HYPOTHESIS:

Does inhibiting prostaglandin synthesis in ERBC decrease growth compared to TNBC.

METHODS:

- **Cells**: Bone tropic, TN 4T1.2 BC cells were transduced to express ER
- **RNA sequencing**: Total RNA from TN and ER 4T1.2 cells were collected and sequenced through Novogene, Gene Set Enrichment Analysis were performed
- **Proliferation Rates**: 2000 cells per well were seeded in a 96-well plate and were treated with vehicle control or aspirin (1 mM and 10 mM), proliferation rates were measured for 72 hours using the Incucyte.

RESULTS:

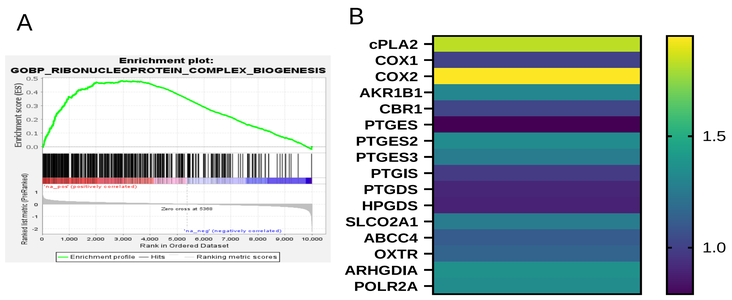

Figure 1. Transcription of prostaglandin synthesis genes were upregulated in ERBC compared to TNBC. A. Gene set enrichment analysis for ER and TN 4T1.2 cells. Ribonucleoprotein complex biogenesis transcription, including genes associated with prostaglandin synthesis, were significantly upregulated in ERBC. B. Fold change of prostaglandin synthesis gene transcription in ERBC compared with TNBC.

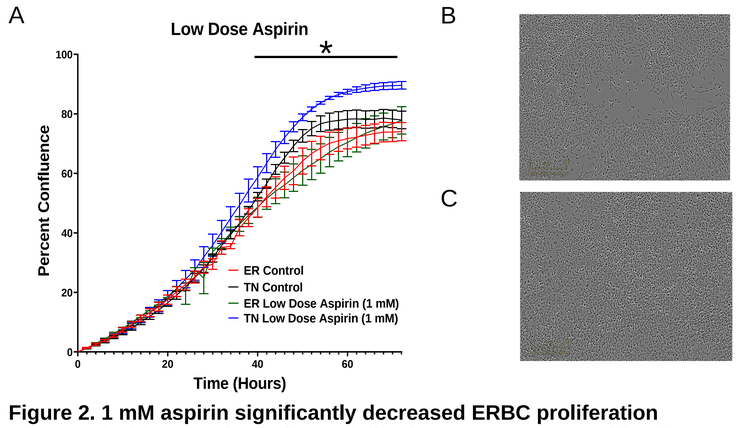

Figure 2. 1 mM aspirin significantly decreased ERBC proliferation compared with TNBC by 40 hours following treatment. A. Proliferation rates of ERBC and TNBC over 72 hours, measured by confluence. ERBC proliferation was significantly decreased from 40-72 hours compared with TNBC following 1 mM aspirin treatment (n=4, two-way ANOVA, p<0.05). B. Representative phase contrast image of ERBC 72 hours following 1 mM aspirin treatment (10x magnification). C. Representative phase contrast image of TNBC 72 hours following 1 mM aspirin treatment (10x magnificiation).

RESULTS:

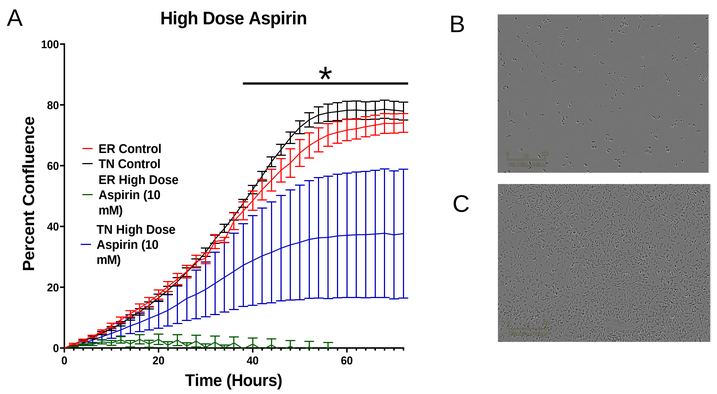

Figure 3. 10 mM aspirin significantly decreased ERBC proliferation compared with TNBC by 38 hours following treatment. A. Proliferation rates of ERBC and TNBC over 72 hours, measured by confluence. ERBC proliferation was significantly decreased from 38-72 hours compared with TNBC following 10 mM aspirin treatment (n=4, two-way ANOVA, p<0.05). B. Representative phase contrast image of ERBC 72 hours following 10 mM aspirin treatment (10x magnification). C. Representative phase contrast image of TNBC 72 hours following 10 mM aspirin treatment (10x magnification).

DISCUSSION

- ERBC had increased prostaglandin transcriptional activity compared with TNBC and 1 and 10 mM aspirin significantly decreased ERBC proliferation rates compared with TNBC
- Aspirin alone or combined with antiestrogen treatments may be a useful treatment option for women with ERBC

SOURCES:

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2. Shaw, Gina. "Types of Breast Cancer: Triple Negative, ER-Positive, HER2-Positive." *WebMD*, WebMD, https://www.webmd.com/breast-cancer/breast-cancer-types-er-positive-her2-positive
3. . Wang, D, and R N Dubois. "Prostaglandins and Cancer." *Gut*, BMJ Group, Jan. 2006, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1856377/.

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