Licochalcone A is a candidate for breast cancer prevention through its reprogramming of metabolic and antioxidant pathways

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BACKGROUND

- Less than 5% of women who could benefit from breast cancer risk reduction drugs report taking them, mainly due to the adverse effects of these medications.[1] There is no drug for preventing ER- cancer.
- **Prevention strategies with optimal efficacy, less toxicity, and greater acceptance are needed.**
- Natural products with significantly lower toxicity and sufficient efficacy to shift the breast microenvironment to a tumor preventive milieu are ideal candidates.[2]
- Previously, we have shown that licochalconeA (LicA) from licorice inhibits aromatase activity and has antioxidant potential.[3,4,5]
- We now report on the response of high-risk postmenopausal human breast tissue, breast pre-malignant and malignant cells to LicA treatment *in vitro* and *in vivo.*

OBJECTIVE

LicA modulates metabolic and antioxidant pathways in the breast leading to a tumor preventive environment.

METHODS

- Contralateral unaffected breast tissue of 6 postmenopausal women, who had bilateral mastectomy due to unilateral breast cancer were obtained and processed to microstructures.
- Microstructures were treated with DMSO and LicA (5 uM) for 24 h, prior to RNA extraction and total RNA sequencing.
- Differential gene expression was determined. Gene ontology (GO) pathway analysis was performed. The enriched pathways with combined enrichment scores > 4 and FDR < 0.05 were considered statistically significant. The differential gene expression results were further analyzed with computational metabolic flux analysis and NanoString metabolism panel. Modulated pathways with P < 0.05 were considered significant.
- Live cell imaging/proliferation was analyzed in DCIS.COM/ER+ PR+, DCIS.COM, MCF-7, and MDA-MB-231 cells treated with single and repeated doses of LicA.
- Female athymic nude mice inoculated with luminal or triple negative breast cancer cells, received LicA or vehicle for 28 days at the dose of 80 mg/kg.day and tumor volume was evaluated.

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Can a natural product protect high risk women from breast cancer?

Licochalcone A is a good candidate

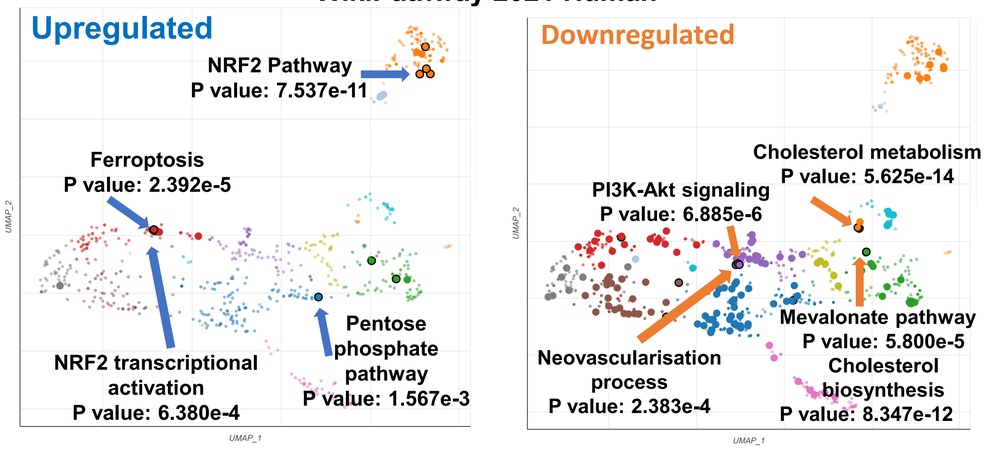
✓In high-risk women's breast microstructures

✓In ER+ and ER- pre-malignant and malignant breast cells

✓In xenograft mouse models of luminal BC and TNBC

RESULTS

WikiPathway 2021 Human



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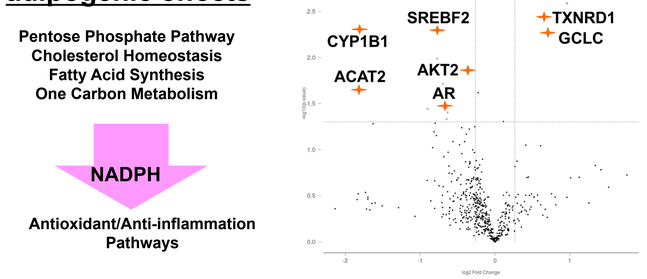
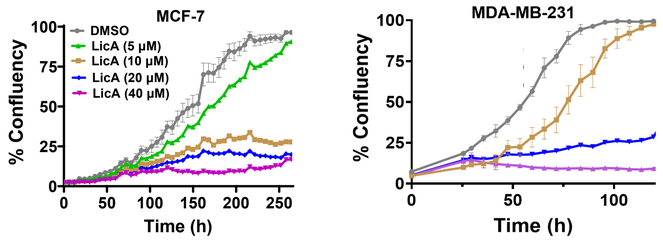
Metabolic flux (left) and NanoString metabolism analysis (right) support antioxidant and anti-adipogenic effects

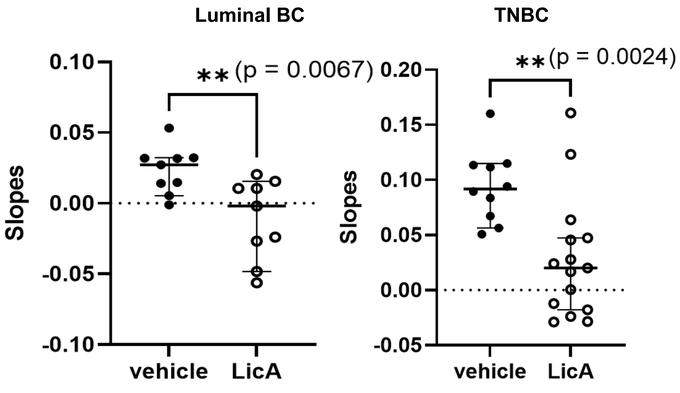


LicA retards *in vitro* proliferation



Representative live cell imaging data using IncuCyte showing that LicA can retard proliferation of MCF-7 (ER+), MDA-MB-231 (ER-) breast cancer cells.

LicA reduces the growth of mammary tumors



The slopes of tumor growth for every animal was generated using linear regression. The differences in tumor growth was statistically compared using unpaired t-test (two tailed). Data presented as median with 95% CI.