**ATP synthasome contributes to efficient energy flux in malignant breast cancer**

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**Purpose**

This study investigates the metabolic alterations associated with breast cancer progression and elucidates the underlying mechanisms. Adenine nucleotide translocase 2 (ANT2), a mitochondrial protein essential for cellular energy metabolism, facilitates the exchange of ADP and ATP across the inner mitochondrial membrane. The role of ANT2, particularly its interaction with the ATP synthasome, in breast cancer metastasis remains poorly understood.

**Materials and Methods**

We analyzed ANT2 in breast cancer using genetic and clinical methods, validating its expression in human tissues. Gene enrichment studies and functional assays assessed ANT2's role in mitochondrial function and cancer metabolism. Knockdown experiments and pharmacogenomic screening evaluated ANT2's impact on metastasis and identified potential inhibitors in 3D cultures.

**Results**

Our analysis revealed that ANT2 expression is significantly elevated in breast cancer patients with lymph node metastasis, correlating with decreased survival rates. ANT2 was found to enhance energy flux and metastasis in breast cancer by promoting ATP production through oxidative phosphorylation. Inhibition of ANT2 effectively reduced breast cancer cell growth and metastasis, attributed to the disrupted binding of transcription factors CREB1 and Zeb1 to the ANT2 promoter. Pharmacogenomic analysis identified cymarin as a potential small molecule inhibitor, which effectively reduced spheroid formation by breast cancer cells in a 3D culture system and showed similar efficacy in orthotopic breast cancer models in mice.

**Conclusion**

ANT2 plays a critical role in breast cancer progression and metastasis through CREB1/Zeb1 regulation. ANT2 could serve as a diagnostic biomarker and therapeutic target in breast cancer treatment.