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Dark Sweet Cherry (DSC) phenolics enriched in anthocyanins suppressed the expression of genes associated with metastasis in a triple-negative breast cancer (TNBC) BALB/c mouse syngeneic model.

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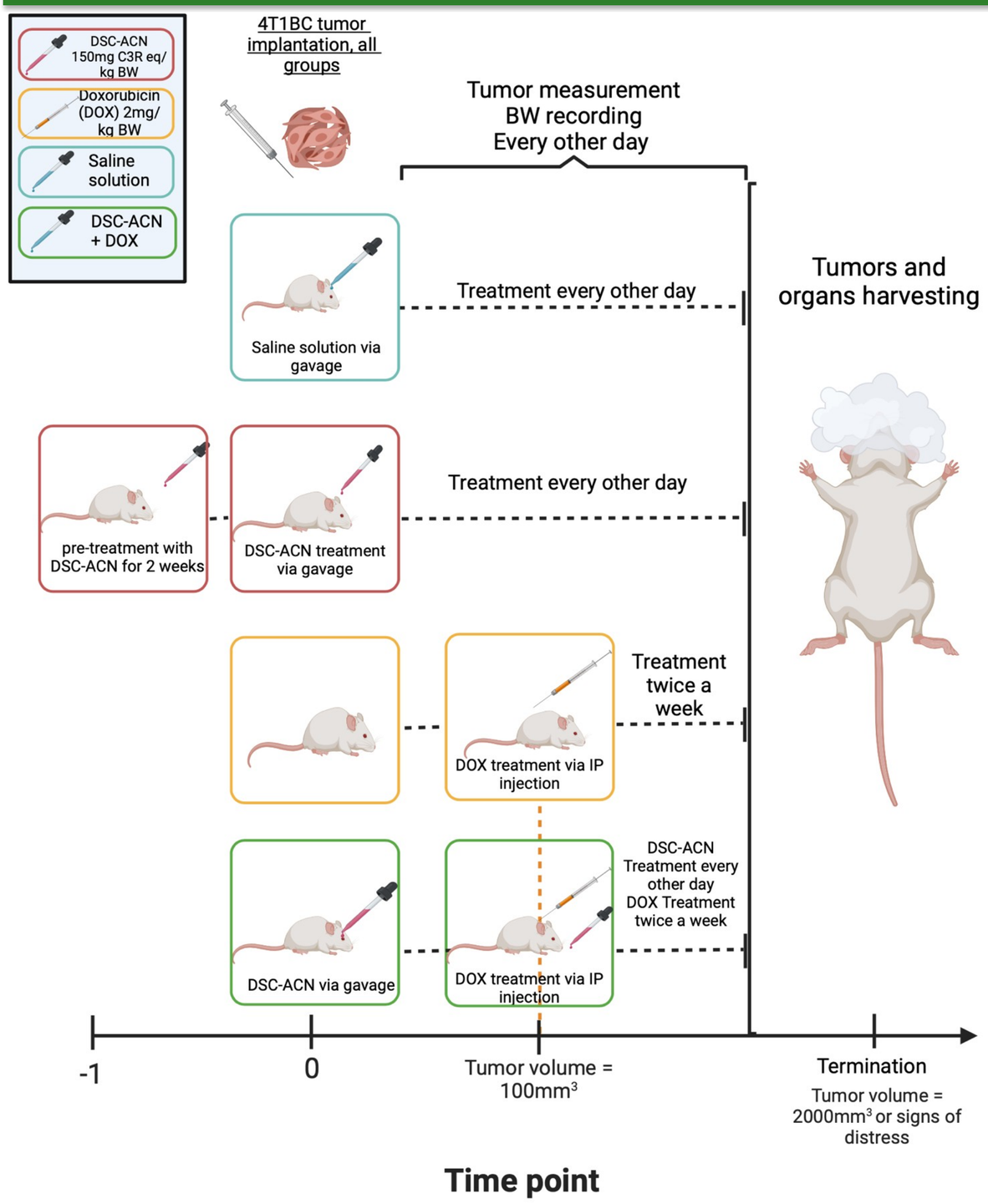
INTRODUCTION & AIM

DSCs are a source of anthocyanins (ACNs) that have been proven to suppress tumor growth and metastasis *in vitro* and *in vivo*. TNBC metastasis is linked to genes associated with cell growth, stemness, hypoxia, and epithelial–mesenchymal transition (EMT), where epithelial cells acquire enhanced motility and invasiveness.

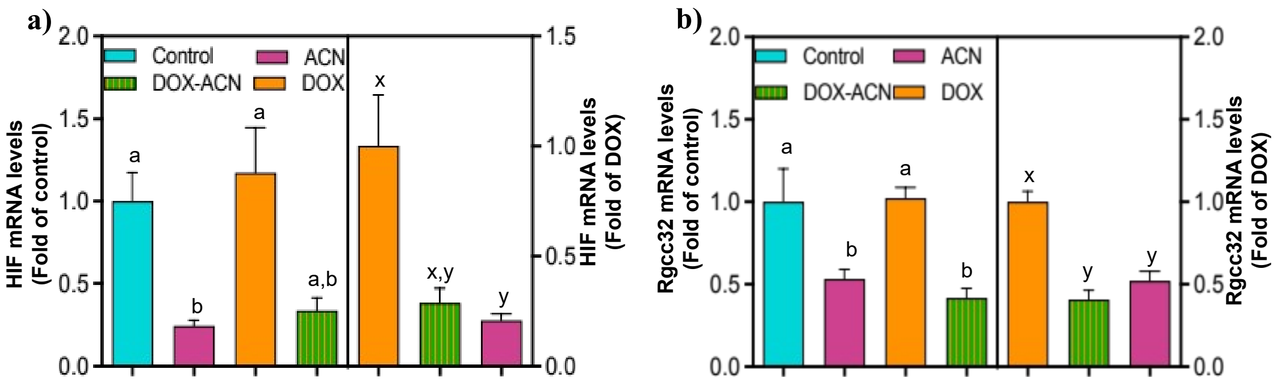
This study assessed ACN's role in TNBC tumors from an animal model mimicking stage-IV human BC.

METHODS



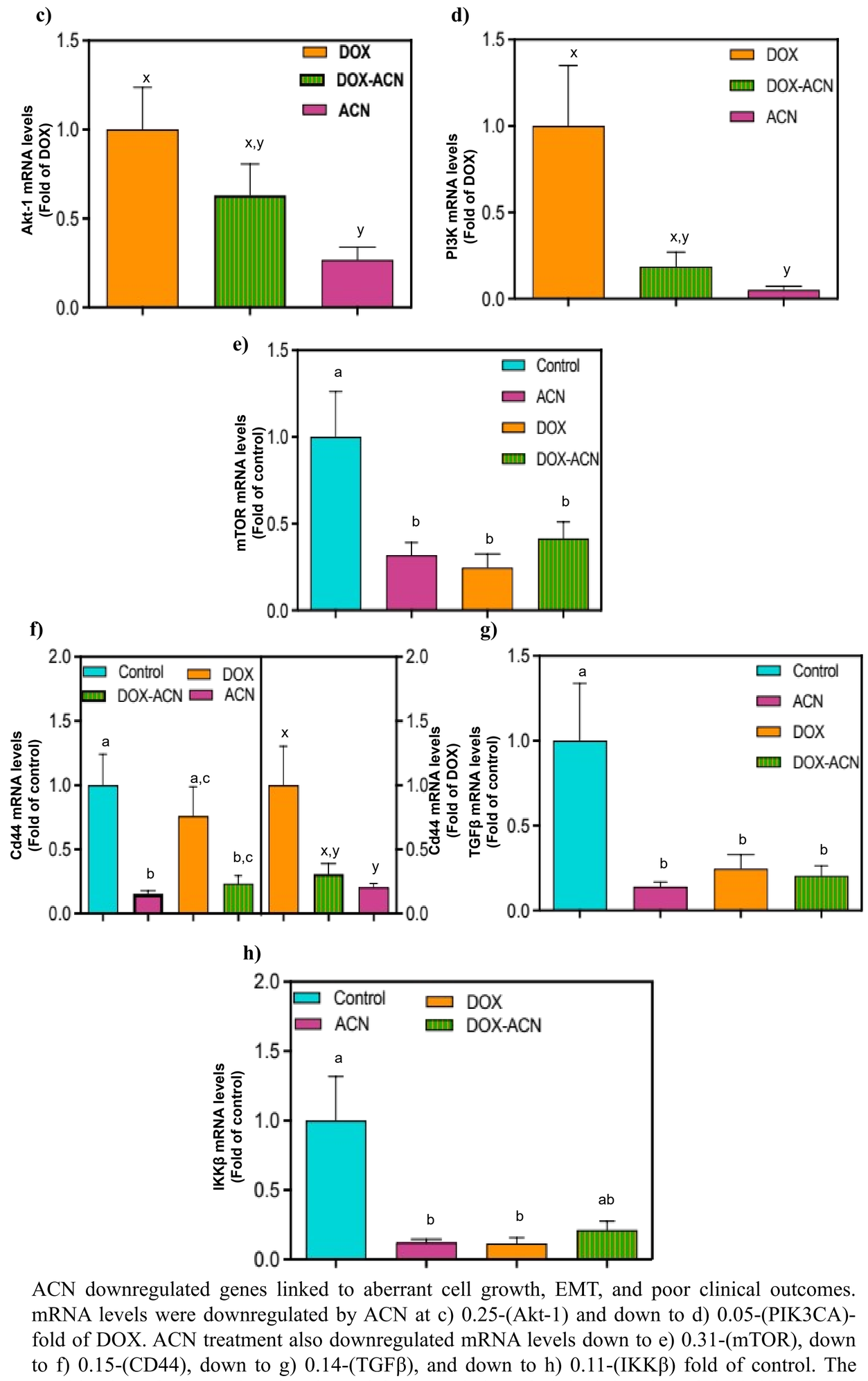
Tumors were analyzed for mRNA levels of genes associated with invasion and metastasis.

RESULTS



ACN treatment downregulated mRNA levels down to a) 0.24-(HIF-1a)- and down to b) 0.53-(Rgcc-32)-fold of control. Furthermore, DOX alone failed to suppress g) Rgcc-32, but DOX-ACN showed downregulation to 0.4-fold of DOX, suggesting a role of ACNs in enhancing the therapeutic efficacy of DOX.

RESULTS & DISCUSSION



ACN downregulated genes linked to aberrant cell growth, EMT, and poor clinical outcomes. mRNA levels were downregulated by ACN at c) 0.25-(Akt-1) and down to d) 0.05-(PIK3CA)-fold of DOX. ACN treatment also downregulated mRNA levels down to e) 0.31-(mTOR), down to f) 0.15-(CD44), down to g) 0.14-(TGFβ), and down to h) 0.11-(IKKβ) fold of control. The combination of DOX-ACN also showed downregulation of e) 0.41-(mTOR), f) 0.23-(CD44) and g) 0.20-(TGFβ) fold of control.

CONCLUSION

Analysis of gene expression in tumor tissues revealed that ACN as chemopreventive treatment suppressed the PI3K/Akt-1/mTOR pathway as one of the underlying mechanisms to prevent lung metastasis. ACN also targeted TGFβ, IKKβ and Cd44 as chemopreventive treatment and as a complementary treatment to DOX suggesting a role in suppressing inflammation and stem cell properties. The mRNA levels of Rgcc32 and HIF were suppressed by ACN as chemopreventive and as complementary to DOX treatment.