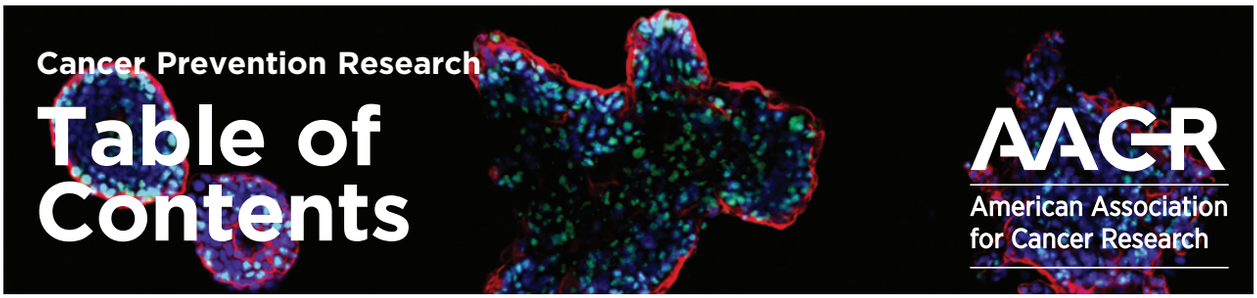
Cancer Prevention Research

Table of Contents



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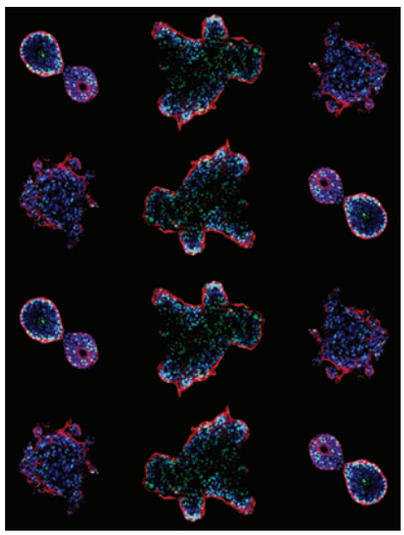
EDITORIALS

RESEARCH ARTICLES

Table of Contents

ABOUT THE COVER



While estrogen receptor (ER) negative (ER−) breast cancer remains a major challenge in the cancer prevention field, ER modulators and aromatase inhibitors have shown adequate efficacy in the prevention of ER+ breast cancer. The activation of Akt signaling pathway has been detected in atypical hyperplasic early stage lesions of patients. In the current study, Akt and the downstream aberrantly activated 70 kDa ribosomal protein S6 (p70S6K) and MAP kinase pathways were identified to confer targeting advantages of premalignant breast lesions in progression to ER− breast cancer using small molecule kinase inhibitors. The micrograph images show human mammary epithelial cells (hMECs) under 3D culture conditions stained for polarity (Laminin V, red) and proliferation (Ki-67, green) markers. The third row of cells: left, normal hMEC acini in a rounded shape with defined boundary and limited cell proliferation (growth arrested); middle, ErbB2-transformed hMEC acini showing increased cell proliferation, which resulted in a disorganized "grape-like" shape with intact boundary; and right, targeting aberrant Akt/p70S6K activation with Phase I–tested dual inhibitor LY2780301 in ErbB2-transformed hMEC acini drastically suppressed cell proliferation and partially reversed the disorganized acini shape, suggesting that p70S6K may potentially be an effective target for the prevention of ER− breast cancer. See the article by Wang et al. (beginning on page 641) for more information.

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10 (11)

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