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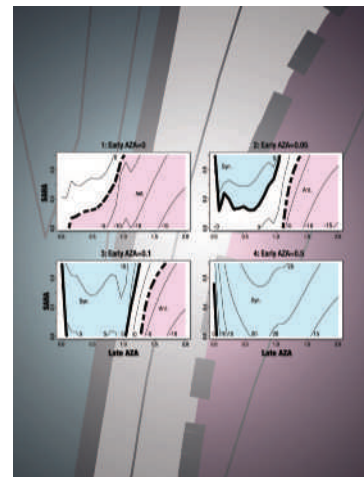
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Conference Report: Eighth Annual AACR International Conference on Frontiers in Cancer Prevention Research

Abenaa M. Brewster, Sherri L. Patterson, Michele R. Forman, Chanita Hughes-Halbert, Paul J. Limburg, Frank G. Ondrey, Electra D. Paskett, David W. Wetter, and Ernest T. Hawk

ABOUT THE COVER

The cover image of four contour plots reflects a novel statistical methodology for assessing the chemopreventive synergy of combined agents (epigenetic modulators in this case). Standard statistics for two-drug combinations are limited for addressing complex dose-response patterns of chemopreventive combinations, which can involve nonmonotonic, or nonlinear, relationships with a plateau effect or U-shaped curve. The Emax and recently developed semiparametric statistical models can address such complexities. Each contour plot shows the growth-inhibition effects of a demethylating agent (AZA) plus a histone deacetylase inhibitor (SAHA) at different doses and/or schedules in tumorigenic human bronchial epithelial cells without serum. AZA was added to cells at an early (Early AZA) and late (Late AZA) time point, whereas SAHA was added only at the late time point. The *x* axis (AZA) and *y* axis (SAHA) show doses in $\mu\text{mol/L}$. The complex dose-response relationships included only an additive (white area) or antagonistic (Ant., pink area) relationship of late AZA plus SAHA with no early AZA (top-left panel) and increasingly synergistic effects (Syn.) when adding low doses of late AZA to SAHA plus increasing doses of early AZA (light-blue areas in the top-right, lower-left, and lower-right panels). Numbers adjacent to the contour lines indicate beyond-additive growth inhibition, i.e., differences between the observed and predicted growth inhibition. The graph data were generated via the Emax and Loewe-additivity models (predicted additive growth inhibition) and the semiparametric model (beyond-additive growth inhibition and confidence bands). These results are part of a comprehensive set of experiments and analyses that validated this novel statistical approach for assessing the synergy of combined chemopreventive drugs. See article by Fujimoto et al. (beginning on page 917) for more information.



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