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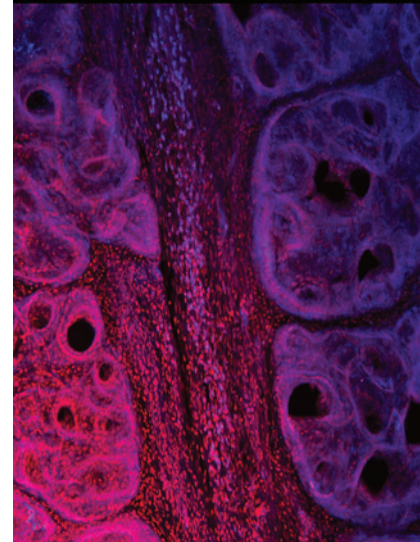
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## ABOUT THE COVER

Interest in the use of metformin as a potential chemopreventive/therapeutic agent has increased over the last few years based on epidemiologic studies suggesting that diabetics taking this drug compared with those taking sulfonylurea or insulin have a lower incidence of cancer. Metformin acts by increasing levels of activated AMP-activated protein kinase (AMPK) and decreasing circulating insulin growth factor-1, which suggests efficacy in cancer prevention and therapy. In this study, two different animal models were used to evaluate the effects of metformin administration on mammary cancer growth. Metformin was ineffective in decreasing mammary cancer multiplicity, latency, or weight in either ER<sup>+</sup> or ER<sup>-</sup> animal models. Metformin induced increases in phosphorylated AMPK and p53 but had little effect on any other biomarker, including phosphorylated Akt (cover image) and failed to reduce the proliferation index or expression of proliferation-related genes. This lack of efficacy in commonly used mammary cancer models is somewhat disconcerting. Overall, metformin did not prevent mammary cancer development in these two models, which raises questions about metformin efficacy in breast cancer in nondiabetic populations. See the article by Thompson et al. (beginning on page 231) for more information. (Staining was performed by Alyssa Langfald, The Hormel Institute, University of Minnesota.)



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