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1183 Pioglitazone, a PPARγ Agonist, Suppresses CYP19 Transcription: Evidence for Involvement of 15-Hydroxyprostaglandin Dehydrogenase and BRCA1 Kotha Subbaramaiah, Louise R. Howe, Xi Kathy Zhou, Peiying Yang, Clifford A. Hudis, Levy Kopelovich, and Andrew J. Dannenberg

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A Randomized Clinical Trial of the Effects of Supplemental Calcium and Vitamin D₃ on the APC/β-Catenin Pathway in the Normal Mucosa of Colorectal Adenoma Patients
Thomas U. Ahearn, Aasma Shaukat, W. Dana Flanders, Robin E. Rutherford, and Roberd M. Bostick
ABOUT THE COVER

Obesity, an established risk factor for epithelial cancers, remains prevalent in the U.S. and many other countries. Calorie restriction has been shown to act as a universal inhibitor of tumorigenesis in multiple animal models of human cancer. The effect of dietary energy balance on tumor promotion was evaluated using diet-induced changes in the epidermal proliferative response in mice following TPA treatment. ICR female mice (maintained on four diets [lean, normal, overweight, obese] for 15 weeks) were treated with either acetone or TPA, twice weekly for 2 weeks. The micropictogram featured on the cover (400 x magnification) shows a representative TPA-treated, BrdU-stained (brown) skin section excised from overweight mice. Epidermal hyperplasia (skin thickness) and BrdU incorporation were significantly greater in the overweight and obese groups when compared with the lean and normal groups (P < 0.05, Mann-Whitney U test; not shown), demonstrating that dietary energy balance modulates TPA-induced epidermal hyperproliferation. These diet-induced changes were accompanied by increased levels of cell cycle proteins that favored enhanced epidermal proliferation during tumor promotion. See article by Moore et al. (beginning on page 1236) for more information.