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About the Cover
Double-strand DNA damage stimulates an activin-A–dependent response in human mammary epithelial cells with a compromised p16/Rb pathway, as depicted in the cover illustration (courtesy of Colleen Fordyce). DNA damage and telomere malfunction result in the p53-dependent induction of activin A (top left, light tan, mammary epithelial cell), a member of the transforming growth factor β (TGF-β) superfamily. Secreted activin A binds to its receptor, resulting in the p38-dependent expression of cyclooxygenase 2 (COX-2) in an autocrine and paracrine fashion (top right, light tan, mammary epithelial cell). COX-2 catalyzes the rate-limiting step in the synthesis of prostaglandins by converting arachidonic acid (AA) into several prostaglandins, including prostaglandin E2 (PGE2). Secreted prostaglandins induce a number of tumor-promoting phenotypes, including resistance to apoptosis and enhanced cell motility in adjacent cells. Two mammary fibroblasts (beige) appear at the very top of the cover illustration. The consequences of DNA damage extend beyond the cell where the damage occurs, inducing effects that may promote tumorigenesis in the human mammary gland. See article by Fordyce et al. (beginning on page 190) for more information.