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ABOUT THE COVER

Ultraviolet (UV) B radiation (280–320 nm) induces squamous cell carcinoma (SCC) both in human and murine skin. WNT signaling is associated with the pathogenesis of these cancers as well as a decrease in estrogen receptor β (ERβ) expression. Using the SKH-1 hairless mouse model, topical administration of an ERβ-agonist, Erb-041, augments ERβ expression and effectively attenuates UVB-induced skin tumor number, size, and incidence with a concomitant decrease in proliferative (PCNA, cyclin D1) and angiogenic (CD31/VEGF) biomarkers. In SCCs, Erb-041 treatment downregulated the WNT/β-catenin signaling pathway as well as the phosphorylation of PI3K and AKT. The cover immunofluorescent micrograph (40×) depicts the co-localization (yellow) of WNT7b (red) and β-catenin (green) in the plasma membrane of UVB-induced, Erb-041-treated SCCs (nuclei in blue). Erb-041 treatment considerably reduced the nuclear localization of β-catenin in SCCs compared to control (not shown). Results from this study suggest a role of WNT signaling in regulating ERβ-dependent attenuation of tumor proliferation, migration, and invasiveness and that an ERβ-agonist, Erb-041, may be effective in the chemoprevention of non-melanoma skin cancers. See article by Chaudhary and colleagues (beginning on page 186) for more information.