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ABOUT THE COVER

Vitamin D3 and metformin are widely used in humans for regulating mineral metabolism and as an anti-diabetic drug respectively; and both of them have been shown to have chemopreventive effects against various tumors. Potential synergistic chemopreventive effects of vitamin D3 and metformin against the development of early colon neoplasia was investigated in two models: DMH-induced colon cancer rat model and DMH-DSS-induced colitis-associated colon neoplasia mouse model. The combination of vitamin D3 and metformin showed a more pronounced effect in reducing the numbers of aberrant crypt foci and tumor in the colon when compared to vitamin D3 or metformin alone (shown: macroscopic image of mucosal hyperplasia in rat colon). Results from this study showed that enhancement of metformin's chemopreventive effects by vitamin D3 was associated with down-regulation of S6P expression, via the AMPK (IGF-1)/mTOR pathway. Furthermore, enhancement of vitamin D3's chemopreventive effects by metformin was associated with inhibition of the protein expressions of c-Myc and Cyclin D1, via the vitamin D receptor/β-catenin pathway. These findings suggest that combined use of vitamin D3 and metformin exhibits synergistic effects against the development of early colon neoplasia and that its use may represent a novel strategy for chemoprevention of colorectal cancer. See article by Li et al. (beginning on page 139) for more information.