β-catenin and ras oncogenes detect most human colorectal cancer *

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PURPOSE AND STUDY DESIGN: Recent studies have shown that β-catenin translocated into the cell nucleus functions like an oncogene. Accumulating evidence suggests that activation of the β-catenin oncogenic signaling cascade along with its twin, the K-ras cascade, may exert syngeneic or synergistic effects on tumor development and progression. In the study reported here, we analyzed oncogenic β-catenin activation on the basis of its nuclear accumulation (NA) and compared the results with those of mutational activation of K-ras in 74 patients with colorectal cancer to determine whether the two oncogene-mediated signaling cascades interact.

RESULTS: We found two distinct patterns of β-catenin activation, i.e., diffuse NA in 20 cases (27%) and selective NA at the tumor invasion front (NAinv) in 19 cases (26%). The presence of the NAinv pattern was significantly correlated with advanced Dukes' stage tumor (P = 0.0005) and the presence of distant metastases (P = 0.0064). K-ras proto-oncogene was mutated in the tumors of 31 cases (42%). Activated β-catenin or K-ras was detected in most (78%) colorectal cancers analyzed, although a weak inverse correlation was found between the activities of the two oncogenes in the tumors. Importantly, most (7 of 8) patients with tumor showing both K-ras activation and the NAinv pattern of β-catenin activation were in Dukes' stage C at surgery, and half of them developed distant metastases to the liver and lungs.

CONCLUSION: The results suggest that although oncogenic activation of β-catenin and K-ras is independent in the process of clinical cancer development, combined analysis of the two major oncogenes can detect most colorectal cancers and identify a subset of patients with poorer outcomes. Consequently, activation of either or both of these oncogenes may serve as a genetic marker for molecular diagnosis.

*Reference:

Zhang B, Ougolkov A, Yamashita K, Takahashi Y, Mai M, Minamoto T. *β-catenin* and *ras* oncogenes detect most human colorectal cancers. Clin Cancer Res 9: 3073-3079, 2003.