

## **Adjuvant immunochemotherapy with protein-bound polysaccharide K for colon cancer in relation to oncogenic $\beta$ -catenin activation.**

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**PURPOSE:** Protein-bound polysaccharide K (PSK) is an immunotherapeutic agent that promotes apoptosis by inhibiting nuclear factor (NF)- $\kappa$ B activation in cancer cells. We previously showed that oncogenic  $\beta$ -catenin activates NF- $\kappa$ B and inhibits apoptosis by up-regulating  $\beta$ -transducin repeat-containing protein. We investigated whether the activation state of  $\beta$ -catenin in the primary tumor is associated with differences in survival rates of patients with colon cancer undergoing immunochemotherapy with 5-fluorouracil (5-FU) plus PSK vs. chemotherapy with 5-FU alone. **METHODS:** We assessed the activation states of  $\beta$ -catenin and NF- $\kappa$ B in the primary tumors of 202 colon cancer patients, and analyzed the data in terms of the clinicopathologic characteristics and survival of patients undergoing the two forms of adjuvant therapy. **RESULTS:** We found two distinct patterns of nuclear accumulation of activated  $\beta$ -catenin in the tumor cells: diffuse nuclear accumulation (NAd) in 89 cases (44 percent) and selective nuclear accumulation at the tumor invasion front (NAinv) in 18 cases (9 percent). NF- $\kappa$ B activation was found in 64 cases (32 percent). In patients with NAd-type  $\beta$ -catenin activation, immunochemotherapy significantly improved recurrence-free survival, cancer death survival, and overall survival rates compared with patients receiving chemotherapy alone. No survival benefit was found in cases with NAinv-type  $\beta$ -catenin activation or no activation. Similarly, immunochemotherapy favored the survival of patients with NF- $\kappa$ B activation. Multivariate analysis established the TNM stage and administration of PSK as independent prognostic factors in the patients with NAd-type  $\beta$ -catenin activation. **CONCLUSIONS:** The presence of NAd-type  $\beta$ -catenin activation identifies patients with colon cancer who respond better to immunotherapy with PSK.

### [Reference]

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