

## **Inhibition of glycogen synthase kinase 3 $\beta$ activity attenuates proliferation of human colon cancer cells in rodents**

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The authors' recent discovery that glycogen synthase kinase 3 $\beta$  (GSK3 $\beta$ ) participates in colon cancer cells' survival and proliferation prompted us to investigate whether GSK3 $\beta$  inhibition alters proliferation of colon cancer cells in vivo. Groups of four or five athymic mice (Balb/c, nu/nu) with subcutaneous xenografts of SW480 human colon cancer cells were treated with dimethyl sulfoxide (DMSO) or different doses (1, 2 and 5 mg/kg body weight) of either small-molecule GSK3 $\beta$  inhibitor (SB-216763 and AR-A014418) by intraperitoneal injection three times per week for 5 weeks. Compared with DMSO (a diluent of the GSK3 $\beta$  inhibitors) as a control, either GSK3 $\beta$  inhibitor significantly inhibited proliferation of cancer cell xenografts in the rodents in a dose-dependent manner. Histochemical and immunohistochemical analysis of tumor xenografts demonstrated a significant, dose-dependent decrease in fractions of proliferating cells and an increase in the incidence of apoptosis of cancer cells in mice treated with either GSK3 $\beta$  inhibitor. No adverse events or effects were observed in the rodents during the course of treatment, except for rare lethal accidents due to intraperitoneal injection. Morphological examination showed no apparent pathologic changes in major organs including the lungs, liver, pancreas, kidneys, spleen and large bowel of rodents treated with DMSO and the GSK3 $\beta$  inhibitors. The results indicate that the GSK3 $\beta$  inhibitors would be a novel class of therapeutic agent for colon cancer.

### [Reference]

Shakoori A, Mai W, Miyashita K, Yasumoto K, Takahashi Y, Ooi A, Kawakami K, Minamoto T. Inhibition of GSK-3 $\beta$  activity attenuates proliferation of human colon cancer cells in rodents. *Cancer Sci* 2007;98(9):1388-1393.