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A study on the effects of chitosan on tumor growth and metastasis.

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Chitin and chitosan have been shown to accelerate wound healing through its granulation tissue promotion, analgesic and hemostatic actions, and boosting resistance against infection. Chitosan particles are engulfed by macrophages, which become activated to promote systemic immune responses. On the other hand, activated macrophages play an important role on the suppression of neoplastic growth. The purpose of this study was to investigate the efficacy of chitosan to inhibit the growth *in vitro* and *in vivo*, and metastasis *in vivo* of these tumor cells : Sarcoma-180 ; Dunn osteosarcoma ; B16F1 melanoma ; P815 mast cell tumor and KLN205 pulmonary squamous cell tumor. These tumor cells were subcutaneously injected into the back of syngenic mice. Chitosan was administered by intratumor injection every 2 weeks.

Intratumor injection of 10mg/kg or 100mg/kg chitosan decreased the volume of the tumors, especially strongest with B16F1 melanoma, except for the P815 mast cell tumor. The chitosan and the culture media of macrophages stimulated by the addition of chitosan, have also shown inhibition of cell prolifera-

tion of tumor cells *in vitro*. However, treatment on mice bearing KLN205 pulmonary squamous cell tumor increased the rate of lung metastasis and treatment on mice bearing P815 mast cell tumor promoted tumor growth and liver metastasis. The number of capillaries formed also increased in both tumor tissues.

From these results, it is thought that chitosan may exert its antitumor effects *in vivo* by activating macrophages. However, its stimulatory effects on the metastasis of P815 and KLN205 tumors *in vivo* may be due to its induction of angiogenic factors IL-8 and MIP-2. More study is needed to clarify these effects.

In conclusion, this study demonstrated that the activation of macrophages by chitosan is suggested to mediate its antitumor effects *in vivo*, while its angiogenic inducing properties may likewise promote tumor growth and metastasis *in vivo*. It is thus important to mention about the harmful effects of chitosan, such as promotion of tumor growth and invasion, prior to chitosan administration.