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Intervenolin, a New Antitumor Compound with Anti-Helicobacter pylori Activity, from

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Nocardia sp. ML96-86F2

precise mechanism of its action.

Tumor tissues are composed of not only tumor cells but also the surrounding stroma. While the stroma consists of various kinds of cells, among them fibroblasts-like stromal cells can regulate the growth and metastasis of tumor cells positively or negatively. Thus, the modulation of the tumor-stromal cell interactions can be a new antitumor

strategy. We have been searching for compounds that modulate the interactions using coculture systems of tumor cells and stromal cells. In the course of our screening, we have isolated a novel compound, intervenolin, from the culture broth of *Nocardia* sp. ML96-86F2. Intervenolin inhibits the growth of human gastric and colorectal cancer cell lines when cocultured with the respective organ-derived stromal cells more strongly than that of the cancer cells cultured alone. To improve low yield of intervenolin from the bacterial culture and to create more potent compounds, we have synthesized intervenolin and its derivatives. Some of the derivatives also show the same effect as intervenolin *in vitro*. Intervenolin shows antitumor effects against xenograft models of human gastric cancer cells and also MDR-expressing colorectal cancer cells *in vivo*. Furthermore, intervenolin and its derivatives exert selective anti-*Helicobacter pylori* activity. Thus, intervenolin and its derivatives are unique compounds possessing both aniturmor and anti-*H. pylori* activities. While our preliminary results suggest that intervenolin inhibits the

tumor growth through the modulation of secreted factors from the stromal cells, we are now investigating the