Curcumin induces the differentiation of myeloid-derived suppressor cells and inhibits their interaction with cancer cells and related tumor growth.

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Myeloid-derived suppressor cells (MDSCs) are heterogeneous population of immature myeloid cells, which regulates innate immune responses and suppress T-cell activation in both human and animals. These cells are known to promote tumor growth, angiogenesis, and metastasis. In IL-1β-induced gastric carcinogenesis, one of the initial events is mobilization and activation of MDSCs, which occurs through NF-κB pathway, resulting in enhanced IL-6 production in MDSCs. Hence, inhibition of MDSC activation may be an effective approach for gastric cancer prevention.

Curcumin has been shown to be an antitumor agent, which acts by modulating multiple targets, including suppressing the activity of NF-κB and JAK2/Stat3 signaling in tumor cells and immune cells.

Objective:

To examine the effects of Curcumin on the activation and differentiation of MDSCs, their interaction with human cancer cells, and related tumor growth.

Study Design:

Athymic nude mice (4-week old) were injected with gastric cancer cells MKN-45, whereas BALB/c mice (4-week old) were injected with mouse CT26 colonic cancer cells to induce tumors

Starting on the same day until 4 weeks, the athymic nude or BALB/c mice were fed with 2% Curcumin diet

In another study, once the tumor size reached 100 mm^3, mice were treated with Curcumin (50 mg/kg; i.p.) for 3 weeks

Tumor volume was measured once every 3 days

At the end of the study, spleens, blood and tumor tissues were harvested

Levels of murine IL-6 in the supernatant, serum and xenograft tumor tissues were determined by using an ELISA kit

Splenocytes isolated from tumor-bearing mice were used to detect in vivo apoptosis of MDSCs

Results and Discussion:

In a MKN-45 cell xenograft model, 4-week feeding with Curcumin-rich diet delayed tumor growth as well as reduced the tumor weight by 46.3% at the end of the experiment ($p<0.05$)

Similarly, at the end of the experiment, i.p. injection of Curcumin significantly inhibited the established tumor growth and decreased the tumor weight by 49.2% when compared with the control group

Curcumin significantly inhibited the mobilization and accumulation of MDSCs as percentages of MDSCs in the spleen and blood were significantly decreased in the tumor-bearing mice that were on 14-day Curcumin-rich or given intraperitoneal injection of Curcumin for 5 days, when compared with the control groups

Similar results were witnessed in an allograft model, where BALB/c mice injected with CT26 cells fed with Curcumin or by daily intraperitoneal injection of Crcumin for 3 weeks showed significantly decreased tumor volume, tumor weight and the percentages of MDSCs in the spleens and tumor tissues compared with the control groups

Curcumin significantly inhibited IL-1β–stimulated production of IL-6 by MDSCs as well as the activation of the NF-κB promoter

Conclusion:

Curcumin significantly inhibited the activation of MDSCs, induced the differentiation of MDSCs and suppressed tumor growth. Hence, antitumerigenic activity of Curcumin may be a promising strategy for cancer prevention and therapy.