Effects of cruciferous vegetable derivetives on metastasis and its adhesion and differentiation

indole-3-carbinol (I3C) phenylethyl isothiocyanate (PEITC)
I3C I3C PEITC
(foci) PEITC
foci I3C

PEITC
coated (hyaluronan, HA) I3C PEITC
1-2 HA 24 PEITC
coated Matrigel I3C (125 μM 150 μM)
I3C PEITC
I3C

This study investigated the effects of indole-3-carbinol (I3C) and/or phenylethyl isothiocyanate (PEITC), two major bioactive compounds derived from cruciferous vegetable on melanoma-induced pulmonary metastasis in both C57BL/6 mice and B16F10 melanoma cells. In animal studies, B16F10 cells (1×105/mouse) were injected via the tail vein to induce metastasis, and the mice were then randomly assigned into four groups, control (vehicle), I3C (50 mg/kg), PEITC (1 mg/kg), and the mixture of I3C (50 mg/kg) and PEITC (1 mg/kg). The treatments were intraperitoneally injected twice a week. After 3 wks treatment, the animals were sacrificed, the number of lung colonies was counted, and the blood was collected for analysis. To understand the mechanisms of these compounds on metastasis, B16F10 cells were treated with I3C, PEITC, and I3C plus PEITC, and the proliferation of the cells was determined. Additionally, adhesion behavior of the cells was analyzed by hyaluronic acid (HA) and matrigel coated plates. The results of the animal experiment showed no significantly difference on metastasized colonies in lung among group, although I3C and I3C plus PEITC groups had lower numbers of colonies, and PEITC had higher numbers. H & E stain indicated smaller foci of tumors in I3C and I3C

puls PEITC groups comparing to the controls. In cultured cells, I3C suppressed the proliferation of B16F10 cells. Unexpectedly, we found that I3C increased melanin concentration in the cultured medium, and the cells were expanded, suggesting I3C may increased the differentiation of the melanoma cells. On the other hand, PEITC showed no effect on proliferation, and the I3C plused PEITC possessed similar results to the I3C group. Additionally, both I3C and PEITC inhibited the adhesion of B16F10 cells to HA after 2 hr treatments, but only I3C inhibited the adhesion after 24 hr. Furthermore, both I3C and the mixture slightly suppressed the adhesion of B16F10 cells to metrigel after 2 hr.

In summary, anti-metastasis of I3C and I3C plus PEITC, but not PEITC, was demonstrated in the present study, and inhibition of adhesion of melanoma cells to ECM was observed. Application of I3C for anti-metastasis is inhibition of tumor cell adhesion, differentiation, and proliferation.