十字花科蔬菜衍生物對腫瘤轉移暨相關黏附及分化之影響

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

中文摘要

本研究主要以黑色素瘤細胞誘導轉移之動物及黑色素瘤細胞探討十字花科蔬菜衍生物 indole-3-carbinol (I3C)、phenylethylisothiocyanate (PEITC)對黑色素瘤誘發轉移的影響。動物實驗結果顯示，給予 I3C 及 I3C 與 PEITC 混合，雖與控制組無統計上的差異但肺臟上黑色素瘤結節平均數有降低的情形，且組織切片發現黑色素瘤(foci)較小；PEITC 的給予，黑色素瘤結節數與控制組亦無統計上的差異，且 foci大小也與控制組相近。細胞實驗結果顯示 I3C 組可隨濃度及培養天數增加而顯著抑制癌細胞增殖作用，且發現於培養第六天，細胞培養液中黑色素含量顯著增加及細胞型態較膨大表示細胞有分化的現象產生；而 PEITC 則無顯著抑制細胞增殖作用；coated 玻尿酸(hyaluronan, HA)黏附作用上，添加 I3C、PEITC 及兩種混合於 1-2 小時內，皆可顯著抑制細胞與 HA 的黏附，但經過 24 小時後，PEITC 組則無法持續作用。於 coated Matrigel 實驗，發現 I3C (125 μM 及 150 μM)及混合組有輕微抑制細胞黏附且與控制組有顯著差異。由以上得知，I3C 具有抑制癌症轉移的潛力，而 PEITC 抑制轉移效果有限，不過當兩種物質的混合較 I3C 單獨抑制作用稍佳，顯示著具加成或協同作用，更貼近由天然食物攝取營養素的原則。

英文摘要

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.