Resvseratrol誘導人類血癌細胞之分化與凋亡

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摘 要

近年來誘導腫瘤細胞凋亡與分化作用已成為白血病治療的重要課題，許多誘導細胞凋亡與分化之誘導劑相繼被發現。白藜蘆醇（Reveratrol，簡稱RES）為一多酚類化合物，存在於紅酒、中藥虎杖及多種植物之中，研究顯示RES具有抗氧化活性，並且能調節腫瘤細胞之凋亡作用。然而，對於RES調控細胞凋亡之作用機制為何，目前仍未有明確的證據。此外，在於RES誘導K562細胞分化作用方面亦尚無文獻報導，因此，在本研究中我們將探討RES對於人類白血病細胞之分化與凋亡作用。在本實驗中，我們分別以四種不同特性的人類白血病細胞株HL-60（Acute promyelocytic leukemic cell line, APL）、U937（Histiocytic lymphoma cell line）、K562 （Chronic myeloid leukemic cell line, CML）、以及NB4 （APL）做為研究模式，比較Reveratrol對於不同的白血病細胞之生長調控與分化誘導的活性及其作用機轉。 在我們的實驗結果發現，RES具有抑制上述四細胞株之增生 (proliferation) 作用。並能誘導HL-60、U937、NB4細胞朝向凋亡 (apoptosis) 之途徑，具有dose- and time-dependent 的關係。然而，對於K562細胞，即使添加高劑量 (100 ?M) 的RES，既無凋亡小體 (apoptotic body) 的產生，亦無細胞sub-G1期之凋亡現象，因此針對K562關於RES誘導細胞分化作用方面，我們發現經RES處理的K562細胞，可誘導細胞表面抗原GPA之表現，亦具有劑量與濃度的依存關係。因此，經由型態觀察、Hb染色與細胞表面抗原的評估，推論其分化成熟途徑可能是朝向紅血球分化路徑(Erythrocyte pathway)。而在HL-60、U937以及NB4細胞方面，RES則具有誘導NBT還原表現以及吞噬酵母菌的能力，其分化成熟路徑可能與單核球 (monocyte) 之分化有關。

關鍵詞 : 白藜蘆醇 ; 白血病 ; 細胞凋亡 ; 分化作用

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