人類尿液萃取物對於大鼠神經膠質瘤細胞株之生長抑制與凋亡作用

The Growth-Inhibitory and Apoptotic Effects of Human Urine Extracts on C6 Rat Glioma Cells

中文摘要

傳統的西方醫學認為癌細胞的發生，主要肇因於基因突變導致癌基因的活化或是抑癌基因的去活化。對於癌症治療的主流意見則多半傾向於以外科手術的方式完全清除病灶。毀滅性的細胞毒性療法，如化學治療，放射治療或是免疫療法等，均是朝向對癌細胞「毋枉毋縱，斬草除根」的治療方向作努力。

另一方面，由於分化促進劑或凋亡促進劑的發現，有些學者隨之提出輔助的癌化機轉假說。他們認為細胞的癌化或正常分化等行為之改變，也可能是在ＤＮＡ轉錄成 RNA，或 RNA 製造蛋白質產物的過程中，產生了阻斷或變異的結果。此一假說也提供了臨床治療上的另一思考方向。

自從１９７６年，美國德州休士頓 Stanislaw Burzynski醫師發表了第一篇人尿萃取物與癌症治療觀念的文獻以來，目前已經證實，人尿萃取物確實可以抑制某些人類癌細胞株培養菌落的形成，或者是促進分化現象。對於致癌基因或 p53、pRb 及 TGF-β 之表現與作用以及癌症轉移所需要的細胞間黏著分子 ICAM−I，也有不同程度的影響。在與其他抗癌藥物的協同作用方面，研究結果也顯示人尿萃取物可以增進其他抗癌藥物之抗癌效果。

本文嘗試針對人尿萃取物所造成的分化誘導現象，作定性與定量方面的確認。在藥物導致細胞型態改變的觀察過程中，我們發現神經膠質瘤細胞有因為人尿萃取物而逐漸改變外表型態的現象。經過抑制生長試驗與分化標誌麩胺酸生成酵素定量等試驗之後，我們相信人尿萃取物確實可以引起神經膠質瘤細胞的生長抑制與分化現象。利用染色體片斷階梯檢測法測試人尿萃取物處理後的細胞，並沒有出現明顯的染色體片斷化現象。流式細胞儀針對處理後的細胞做細胞週期檢驗，則發現Ｇ０/Ｇ１期之細胞比率增加，SubＧ１期細胞比例則沒有明顯變化，顯示細胞應該是趨向分化狀態，並且沒有可見的細胞凋亡產生。最後的細胞螢光凋亡染色步驟，也顯示出人尿萃取物並不會造成細胞趨向凋亡過程。

因此我們認為，人尿萃取物確實可以引起大鼠神經膠質瘤細胞的生長抑制現象，且該現象之產生應該是細胞逐漸趨向分化的結果，詳細機轉則尚待查明。

英文摘要

In traditional western medicine field, we have proposed thoughts about the mechanisms and therapies of cancer. Because the difficulty of altering genes, most therapeutics'' suggests for cancer are radical excision as early as possible, followed by cytotoxic drugs or radiotherapy or immune therapy to eradicate the residues, if any.

On the other hand, the existence of differentiative or apoptotic inducers showed us the other face of cancer research. A new though was given as "epigenetic effect" which means the material may cause some changes without altering the gene or DNA level, but on the RNA level or even later, protein level. By changing the RNA or protein product as new methylation pathway, the cell behaviors such as un-limited proliferation and phenotypic changes may stop. These gave us new approaches for cancer treatment, especially on terminal patients.

Dr. Stanislaw Burzynski found that plenty of mall peptides naturally existed in human urine might play the role of cell growth inhibitor on multiple cultured cancer cell line in 1976. Since then, continuous studies revealed the possible inhibitory effects and cell types could be treated. Combinative therapeutic protocols also were presented as well.

Our study tried to demonstrate the effect of human urine extracts as differentiation induction on C6 glioma cells, and also the growth inhibitory phenomenon we found. By observing drug-induced phenotypic change, growth inhibitory test and quantitative assay of differentiation marker, glutamine synthetase, we believe that the drug does induce growth inhibitory and differential effects on C6 glioma cells. By DNA ladder test and Hoechst 33258 florescence apoptotic examination, we concluded that the drug would not cause any apoptotic effect on the cell. Flow-cytometry of primary cell cycle observation also confirmed the result with extra evidences on differentiation side.

The conclusions are the human urinary extracts, CDA-II, may cause cancer cell differentiation without apoptotic effect, and mechanisms to be determined.