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• 中文關鍵字	自由基；細胞分化；氧化壓力；重金屬；肝癌
• 英文關鍵字	Free radical；Cell differentiation；Oxidative stress；Heavy metal；Hepatoma
• 中文摘要	自由基,尤其是指活性氧分子(ROS),是細胞正常代謝過程所產生的高活性代謝物,ROS 可經由直接與生物分子作用導致細胞傷害,或者經由訊息傳遞過程促使細胞分化、增生、癌化甚至凋亡(Apoptosis)。抗氧化酵素爲細胞內活性氧分子的重要代謝系統,爲了瞭解抗氧化酵素活性與細胞分化間的關聯性,本論文選用不同分化程度肝癌細胞進行系列性研究,包括分化程度較高的 Hep G2、Hep 3B,以及分化程度較低的 SK-Hep-1、HA22T/VGH、HA55T/VGH,分別比較不同分化程度的肝癌細胞,其內生性抗氧化酵素的活性,包括 Catalase(CAT)、Manganeses superoxide dismutase(MnSOD)、Copper-zinc superoxide dismutase(CuZnSOD)、Glutathione peroxidase(GPx)以及 Glutathione reductase(GRx)等。實驗結果指出,分化程度較高的肝癌細胞株中,其 CAT、MnSOD、GRx 之活性明顯較分化程度低的肝癌細胞株高出許多,其平均值分別差了 5.1 倍、2.8 倍及 6.9 倍;而 GPx 與 CuZnSOD 則在不同分化程度的肝癌細胞株未出現明顯差異。以西方墨漬、放射線免疫沈澱及北方墨漬法進行分析,發現 MnSOD 及 CAT 的蛋白質及 RNA 表現量在分化程度較高的肝癌細胞株中亦被提升,爲了解釋不同分化程度肝癌細胞株之抗氧化能力,實驗中以 50.mu.M H/sub 2/ O/sub 2/處理細胞,作爲氧化壓力的來源,數據顯示,與控制組相比較,分化程度較低的肝癌細胞株 MnSOD 活性可被誘導增加約 1-2 倍,而分化程度較高的肝癌細胞株則無此情形。這結果顯示分化程度較低的肝癌細胞有較佳的氧化壓力耐受性,推測 MnSOD 的增加可能與訊息傳遞因子 NF.kappa.B 的活化有關,此假設需進一步證實。除此之外,在臨床上,CAT 以及 GRx 活性的差異應可用於肝癌細胞分化的指標。
• 英文摘要	Free radicals, especially the reactive oxygen species (ROS) are highly reactive metabolites that are generated during normal cell metabolism. The ROS can cause cellular damages by direct interaction with bio-molecules or regulate the process of differentiation, proliferation, carcinogenesis and apoptosis through the signaling pathway. In order to reveal the correlation of scavenging enzymes activities and cell differentiation, a panel of human hepatocellular carcinoma

(HCC) cell lines, including three poor-differentiated (HA22T, HA55T and SK-Hep-1) and three well-differentiated (Hep 3B, Hep G2 and Chang liver cell) were used to examine the expression pattern of superoxide dismutase (MnSOD and CuZnSOD), catalase (CAT), glutathione reductase (GRx) and glutathione peroxidase (GPx). Results showed that the well-differentiated cells exhibited higher activities of antioxidant enzymes (MnSOD, CAT and GRx) than poor-differentiated ones for about 2.8, 5.1 and 6.9 folds in average, respectively. However, the activities of CuZnSOD and GPx were only minor differences in the HCC cell lines used. By immunoblotting, radio-immunoprecipitation and northern blot analysis, the protein and RNA level of CAT and MnSOD were also elevated in the well-differentiated cells. To elucidate the antioxidation ability of different differentiated HCC cells, we investigated the antioxidant enzyme activities after treatment with H/sub 2/O/sub 2/. The activity of MnSOD could be induced significantly in poor differentiated HCC cells (SK-Hep-1). However, the other scavenging enzymes show only minor differences compared with the control cells. These results suggested that poor-differentiated HCC cells might have better antioxidative ability than well-differentiated ones. It is possible that the inducible activity of MnSOD might be contributed by NF-.kappa.B signaling pathway. Thereby, such phenomena could participate to the high metastasis frequency of poor-differentiated HCC cells clinically. This hypothesis will be investigated in future study. In clinical, the activities of CAT and GRx might be potential differentiation makers of human hepatocellular carcinoma.