癌細胞生理活性之電阻抗感測晶片檢測

Detection of Cancer Cells Viability Using Electric Impedance Sensing Chips

中文摘要

Electrochemical impedance spectroscopy (EIS)之原理爲當細胞貼附於電極上，可利用細胞對於電流具有高阻抗的特性來不間斷量測阻抗值。本實驗使用Indium Tin Oxide (ITO)當電極材料，分析NIH3T3、MG63和HL60於晶片上之電阻抗參數(電阻抗值、電阻抗比值)或電容抗參數(電容抗值、電容抗比值)的生長曲線。分別使用從綠膿桿菌萃取的脂多醣(Lipopolysaccharides，LPS)以及一般性抗癌藥物mitoxantrone (MX)當作毒殺物質，並對本晶片應用在懸浮與貼附細胞之毒殺作用進行一連串動態分析。由電阻抗值生長曲線實驗結果，發現本晶片確實可以觀察到貼附型細胞生長情況，並可偵測到細胞在包括懸浮、貼附及生長、死亡之完整過程，NIH3T3在48小時之內於實驗晶片上細胞活性與電阻抗參數具高度相關性(R2 = 0.8916，P < 0.01)，而MG63於24小時之內達0.6519。在細胞毒殺實驗方面，NIH3T3在3小時內電阻抗比值與細胞活性之間有高度相關(R2 = 0.822，P < 0.05)，顯示本實驗晶片在毒殺初期階段也具有高的靈敏度，MG63在24小時時，與傳統方法比較，其相關性可達0.9709，故以標準化之實驗參數(電阻抗比值)來描述細胞生長及毒殺過程皆可有一良好相關性。而本研究另以100% 小牛血清當偵測培養基觀察電容抗值變化，但由於背景值干擾影響過大，故未來要量測懸浮型細胞之電學特性可改變實驗設計形式，如量測細胞膜之電容、導電率變化。由結果可知，本研究所使用的實驗晶片裝置在特定的實驗條件下，可提供一種連續性之動態量測細胞生長情況，且不需要額外生化檢測。

英文摘要

The principle of electrochemical impedance spectroscopy (EIS) assay is that cell has high resistance for current when they attach to the electrode surface. In this study, indium tin oxide (ITO)-based electrodes were made on a chip for detecting the growth curves of NIH3T3, MG63 and HL60 cells. In addition, the ITO-chip was also used for cytotoxicity experiment. Changes in cellular behavior, including suspension, attachment, growth and deattachment, of NIH3T3, MG63 and HL60 cells were monitored by the chip when they were challenged with lipopolysaccharides (LPS) and mitoxantrone (MX), respectively. Our results showed that, in the proliferation detection of NIH3T3 cell, high correlation was found within 48 hrs when comparing the results obtained from MTT tests and our ITO-chip (R2 = 0.8916，P < 0.01). Similar results were also found for MG63 experiments at 24 hrs (R2 = 0.6519, P >

0.05). In the cytotoxicity tests, our ITO-chip demonstrated high sensitive results at early experimental stage. For NIH3T3 cell high correlations between impedance ratio value (IRV) and cell viability was found ($R2 = 0.822$, $P > 0.05$). For MG63 cell, such a high correlation can be found within 24 hrs of experiment ($R2 = 0.9709$, $P > 0.05$). In this study, IRV, a standardized value of measured impedance ratio value, was used as a parameter to describe cell growth and cytotoxicity on ITO-chip. We found it is sensitive for EIS detection of attachment cell. However, by using capacitance ratio value (CRV), we failed to detect the cell behavior of HL60 cultured in 100% fetal bovine serum (FBS). This is because a high background in CRV was detected when FBS was used to culture medium. In conclusion, the biochip developed in our lab can monitor cellular behavior of attachment cell without additional biochemical and immune-labeling kits.