

Mutational, epigenetic and expressional analyses of caveolin-1 gene in breast cancers

林時宜

**Chen ST;Lin SY;Yeh KT;Kuo SJ;Chan WL;Chu
YP;Chang JG**

摘要

Abstract

Caveolin-1, an integral membrane protein of caveolae found in many cell types, has been suggested as a candidate tumor suppressor. However, the mechanism underlying caveolin-1 decreased expression is not fully understood. The purpose of this study is to investigate the role of aberrant promoter methylation in the regulation of caveolin-1 gene in breast cancer correlated with clinical findings. We used methylation specific PCR, direct sequencing and immunohistochemistry stain methods to explore the role of caveolin-1 gene in the development of breast cancer. We demonstrated that 14 of 55 cases (25.5%) and 4 of 55 cases (7.3%) had methylated CpG-island on caveolin-1 promoter in cancerous and non-cancerous cells, respectively. The frequency of aberrant promoter methylation of breast cancer tissues was significant higher than non-cancerous tissues ($p < 0.05$). There were four types of methylation pattern of caveolin-1 gene in the breast cancer tissues. No mutation but one polymorphism GAC→GAT at codon 82 was found in the whole exonic sequences of caveolin-1 gene. The methylation status of caveolin-1 gene had no clear relationship with age, cell grade, stage of tumor, and status of estrogen receptor, p53 and c-erbB2 in the breast cancer tissues. However, in breast tissue with aberrant promoter methylation of caveolin-1 gene, the presence of progesterone receptor showed borderline statistic difference compared to unmethylated promoter ($p = 0.11$). Immunohistochemistry demonstrated that expression of caveolin-1 gene correlated with aberrant promoter methylation status in sporadic breast cancer tissues. Our findings suggest that aberrant promoter methylation of caveolin-1 gene is associated with inactivation of expression. This process occurs in the precancerous stage and may play an important role in the development of breast cancer.