

Gene Amplification and Epigenetics are Associated with Increased ABCB1 Expression in Acquired Taxane Resistant Esophageal Squamous Cancer Cells

著者	Anton Sumarpo
学位授与機関	Tohoku University
学位授与番号	11301甲第17380号
URL	http://hdl.handle.net/10097/00122056

学 位 論 文 要 約

博士論文題目 Gene Amplification and Epigenetics are Associated with Increased ABCB1
Expression in Acquired Taxane Resistant Esophageal Squamous Cancer Cells

..... 東北大学大学院医学系研究科 医科学 専攻

..... 病理病態学 講座 分子病理学 分野

学籍番号 B3MD5007 氏名 Anton Sumarpo

The taxanes are applied as potent chemotherapy agents in the treatment of esophageal cancer; however, their therapeutic usefulness is limited by acquired chemoresistance, which is a common drawback to most anti-cancer drugs. In our previous study, to elucidate possible causes for acquisition of resistance, we established three taxane resistance esophageal cancer cell lines and found that *ABCB1* was upregulated in these cells. However, the responsible mechanisms remain unclear. In this study, I explored possible mechanisms that might contribute to upregulated *ABCB1* expression in taxane resistant cells. *ABCB1* amplification was present in taxane resistant cells as shown by significant increases of gene copy number. In addition, after treatment with 5-Aza and/or TSA in parental cell TE1, the *ABCB1* expression was activated, suggesting the involvement of epigenetic mechanism. Moreover, I demonstrated that *ABCB1* downstream promoter was the dominant promoter in taxane resistant esophageal cancer cell lines and the CpG islands were mostly unmethylated in taxane resistant cells when compared to dominantly methylated pattern in parental cells.

In conclusion, I propose that *ABCB1* gene amplification alongside with alteration in epigenetic mechanism could be responsible for acquisition of taxane resistance in esophageal cancer cells.