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Aberrant DNA methylation as a predictive marker for disease progression of LSIL in uterine cervix

In the present study, 113 patients were classified into four groups according to their cervical cytology, HPV infection and follow up. Cytology samples were examined for aberrant DNA methylation (abMet) of *DLX4* and *SIM1* genes and their protein expressions. CaSki cells were treated with 5-Aza-2′-deoxycytidine (5-aza-dC). Of 113 samples, 40 in Group-1 were negative for intraepithelial lesion or malignancy. 21 low-grade squamous intraepithelial lesions (LSILs) in Group-2 showed a continuance of LSIL for longer than 365 days and 12 LSILs in Group-3 showed an up-grading to high-grade (H) SIL+ within 365 days after the diagnosis of LSIL. 40 in Group-4 were squamous cell carcinoma. All but Group-1 was infected with high-risk HPV. Significant difference existed in frequency of abMet between groups 2 and 3 ($p=0.044$), between groups-3 and 4 ($p=0.020$) for *DLX4* and between Groups-1 and 3 ($p=0.0003$), as well as between Groups-2 and 3 ($p=0.005$) for *SIM1* gene. *DLX4* protein expression was significantly reduced in the *DLX4* abMet positive tissues as compared to the negative tissues ($p=0.008$) and 5-aza-dC treatment extracted *DLX4* protein expression of CaSki cells in a dose-dependent manner ($p<0.005$). The LSIL cases with abMet of *SIM1* gene or both genes progressed faster to HSIL+ than others ($p=0.033$ or $p=0.048$). Therefore, AbMet of *DLX4* and *SIM1* genes should be a useful and novel progression marker of uterine cervical LSIL with HPV infection.

Biography

Kiyomi Taniyama has completed his PhD in Pathology at the Hiroshima University School of Medicine in Japan in 1985 and he learnt molecular techniques and laser capture microdissection at the University of California, San Diego Cancer Center. He has joined the National Hospital Organization (NHO), Kure Medical Center and Chugoku Cancer Center in 2002 and became the President in July 2014.

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