METHYLATION-SPECIFIC PCR REVEALED ABERRANT PROMOTER GENE METHYLATION OF p16, MGMT AND SPOCK2 IN DIFFUSE LARGE B CELL LYMPHOMA

1Lailatul Jalliah Mohd Ridah, 2Norafiza Zainuddin, 3Norlelawati A. Talib, 4Faenzahtul Arbaeyah Hussain

1Department of Biomedical Science, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Kuantan, Pahang
2Department of Basic Medical Sciences, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang.
3Department of Histopathology, Hospital UniversitiSains Malaysia, Kubang Kerian, Kelantan

DNA methylation silences the gene through addition of methyl group. p16, a tumor suppressor gene that inhibits cyclin-dependent kinase, inactivates the Rb protein and blocks G1 phase in a normal cell cycle. A DNA repair gene, MGMT removes alkyl adduct to a cysteine residue within the protein, thus preventing lethal cross-links. p16 and MGMT methylation has been reported to associate with DLBCL. A member of the extracellular chondroitin and heparinsulfate proteoglycans, SPOCK2 functions mainly in extracellular matrix for cell adhesion. Uniquely, SPOCK2 (testican 2) abolishes the inhibition of membrane-type 1-matrix metalloproteinase by other testican family which might enhance the angiogenesis. In this study, we aimed to screen for aberrantly methylated genes which might contribute to the pathogenesis of DLBCL using methylation specific PCR (MSP). p16 methylation was identified in 64 (73%) of 88 samples. On the other hand, SPOCK2 was found to be unmethylated in 30 (34%) samples. Interestingly, MGMT methylation was detected in all cases. We also found an association between p16 methylation status with patients aged >50 years old (p= 0.023). This finding is parallel with an animal study showing that aging increases p16 methylation. No association was found between the methylation of other genes with age. Unmethylation of SPOCK2 might cause testican 2 expressions, which has been suggested to contribute toward malignant behaviour. MGMT was reported to be methylated among cancer patients who smoke, drink and are non-vegetarian. Thus, it is hypothesized that lifestyle might affect MGMT methylation in this study population.