Medical Research Symposium & Pacific Partnership in conjunction with Kuantan Research Day 2016

International Research Network: The Way Forward

ABSTRACTS

Organized by:

Kulliyyah of Medicine, IIUM
Research Management Centre, Kuantan

In collaboration:
Basic Health Sciences

Abstract ID: 34

Epigenetic methylation status of P16, MGMT and SPOCK2 in diffuse Large B cell lymphoma

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Introduction: Epigenetic methylation has been implicated in the pathogenesis of diffuse large B cell lymphoma (DLBCL). This study investigated the methylation status of p16, MGMT and SPOCK2. Aberrantly methylated p16 and MGMT have been linked to DLBCL, but not SPOCK2. p16 inhibits cyclin-dependent kinase, which results in retinoblastoma phosphorylation and blockage of cell cycle at G1 phase. MGMT removes alkyl adduct at O2- guanine, thus preventing lethal cross-links. SPOCK2, an extracellular chondroitin and heparin sulfate proteoglycans, abolishes the inhibition of membrane-type 1-matrix metalloproteinase which might enhance the angiogenesis. The absence of SPOCK2 methylation was therefore hypothesized in the majority of cases in this study.

Methods: Extracted DNA from 88 formalin-fixed paraffin-embedded (FFPE) tissues of DLBCL were subjected to bisulfite conversion followed by methylation-specific PCR (MSP) analysis for p16, MGMT and SPOCK2 methylation. p16 methylation was also quantified in 16 samples through pyrosequencing assay.

Results: p16 methylation was observed in 65/88 (74%) samples by MSP. Pyrosequencing detected p16 methylation in all 16 samples ranging from 18% to 81%. MGMT methylation was detected in all 88 (100%) cases. Methylated SPOCK2 was found in 83 (94.3%) samples. There was a significant association between p16 methylation status with patients above 50 years of age (p = 0.04).

Conclusions: These preliminary discoveries may serve as a good platform in order to gain a comprehensive overview on the epigenetics contribution in the pathogenesis of DLBCL. Pyrosequencing is a robust tool in detecting and quantifying methylation.

KEYWORDS: DLBCL, epigenetics, MSP, pyrosequencing