TITLE:
ROLE OF MATRIX METALLOPROTEINASE 3 AND APOPTOTIC GENE BAX IN BRAIN TUMORS

RESEARCH CENTER:
Human Genome Center, School of Medical Sciences, USM
Department of Pathology, School of Medical Sciences, USM

CURRENT STATUS OF PROJECT: Ongoing

RESEARCHERS:
1. Ku Asmarina Binti Ku Ahmad (post-graduate student)
2. Prof. Dr. Jafri Malin Bin Abdullah (main supervisor)
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TRACK RECORDS:
1. Molecular genetic analysis and immunohistochemistry of the p53 tumor suppressor gene in brain tumours patients in Malaysia.
2. Loss of heterozygosity on chromosomes 10q, 9p, 17p and 13q and mutational analysis of PTEN gene in human malignant gliomas.
3. Analysis of tumor suppressor gene p16 and telomerase activity assay among the central nervous system tumor's patients in Malaysia.
4. Molecular studies of NF2 gene in Malay patients with meningiomas and schwannomas
5. Ras, C-Myc and Epidermal Growth Factor Receptor (Egfr) Mutations in Human Gliomas in North East Malaysian Patients.

Introduction

The development of an invasive brain tumor involves a multistep process that has been associated with the altered expression of several oncogenes and tumor-suppressor genes. Pathologic roles of apoptosis have been defined in cancer biology. Previous findings have reported the possibility that BAX functions as a tumor suppressor in a transgenic mouse brain tumor. Matrix Metalloproteinse-3 (MMP-3) is an extracellular matrix-degrading enzyme which acts on type IV collagen that forms basal membrane. Numerous studies have shown that a high expression of MMPs in brain tumors is correlated with an increased aggressiveness of tumors.

Objectives

1) To analyze mutation in the sequence of apoptotic gene (*BAX*) and Matrix Metalloproteinases (*MMP3*) in brain tumors from patients with gliomas and meningiomas using DHPLC and sequencing
2) To observe the expression level of apoptotic protein (*BAX*) and Matrix Metalloproteinase (*MMP3)* in brain tumors from patients with gliomas and meningiomas using immunohistochemistry staining for light microscope
3) To observe the localization of Bax and MMP-3 at ultracellular level using immunogold staining method for electron microscope

Technical methodology

Meningiomas and gliomas tissues were obtained from patients underwent surgery. Genomics DNA were extracted from brain tumor frozen tissues. Mutational screening was then carried out for Bax gene and MMP3 gene by using denaturing High Performance Liquid Chromatography (dHPLC) and direct sequencing using ABI PRISM® 3100 Genetic Analyzer.

For the protein expression analysis, slides were stained by standard immunohistochemistry using polyclonal antibody against Bax (Santa Cruz Biotechnology Inc.) and monoclonal antibody against MMP3 (CHEMICON International Inc.). Independent investigators determined the percentage of positive cells. The localization of these 2 markers will observe under electron microscope by using immunogold staining technique.

EXPECTED OUTCOME

Study of these apoptotic gene and matrix metalloproteinases will not only enhance our understanding of the biology of this process, it will also provide new targets for early diagnosis and facilitate treatment design for example in developing DNA vaccine as an anti-cancer agent and virus therapy which has shown promise as a cancer treatment besides treated with chemotherapy and/or radiotherapy.