MOLECULAR AND CELLULAR EXPRESSION OF THERAPY RESISTANT GENES IN GLIOMAS AND MENINGIOMAS

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CURRENT STATUS OF PROJECT: Ongoing.

RESEARCHERS:

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TRACK RECORD:

1. Molecular genetic analysis and immunohistochemistry of the p53 tumour suppressor gene in brain tumour patients in Malaysia. (2002)
2. Loss of heterozygosity on chromosomes 10q, 9p, 17p and 13q and mutational analysis of PTEN gene in human malignant gliomas. (2003)
3. Analyis of tumour suppressor gene p16 and telomerase activity assay among the central nervous system tumour's patients in Malaysia. (2003)
4. Molecular studies of NF2 gene in malay patients with meningiomas and schwannomas. (2004)
5. Ras, C-Myc and Epidermal Growth Factor Receptor (Egfr) Mutations in Human Gliomas in North East Malaysian Patients. (2004)

INTRODUCTION

Brain tumors are the second most frequently reported cases in Malaysia, after leukemia in children. The brain tumor cases are reported to have increment of about 2000 new cases every year in adults. A total of 21,464 cancer cases were diagnosed among Malaysians in Peninsular Malaysia in the year 2003, comprising 9,400 males and 12,064 females. Accumulation of multiple genetic alterations has been proposed to contribute to various cancer cases including brain tumors.

OBJECTIVES

1. Determine p27 and cyclin D1 genes alteration, which contribute to brain tumor development.
2. Analyze p27 and cyclin D1 protein expressions at cellular and ultrastructural level through immunohistochemistry analysis.

TECHNICAL METHODOLOGY

The diagnoses were carried out using human brain tumor tissues collected from the Hospital University Science Malaysia (HUSM) with ethical approval. To investigate genetic alteration of both genes, p27 (exon 1 and 2) and cyclin D1 gene (exon 4 and 5), Polymerase Chain Reaction (PCR), denaturing High Performance Liquid Chromatography (dHPLC) and DNA sequencing were done. Immunohistochemistry was also performed to determine the level of both protein expressions in human brain tumor tissues.

EXPECTED OUTCOME

We postulate to detect alterations within the hot-spots of both p27 and cyclin D1 genes by the mutation screening using dHPLC technique. The alteration might cause up regulation of cyclin D1 protein level of expression and down regulation of p27 protein level of expression. These can be observed through the immunohistochemistry analysis. By doing immunogold staining of electron microscopy, we will then be able to detect the exact location of protein expression of both p27 and cyclin D1 protein.