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THESES

TRANSCRIPTION ANALYSIS OF TIMP-1 AND NM23 GENES IN GLIOMA CELL INVASION (ABSTRACT)*. **THESIS. SÃO PAULO, 2005.**

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Purpose: To evaluate using transcription analysis the presence and importance of two genes: NM23-H1 and TIMP-1 on control of tumor cell invasion in diffuse astrocytomas (WHO II) and glioblastoma multiforme (WHO IV).

Method: Northern Blot analysis of NM23-H1 and TIMP-1 was performed. Eight diffuse astrocytomas and nineteen glioblastomas (WHO IV) were analyzed to determine if TIMP-1 and NM23-H1 were candidates to inhibition of tumor cell invasion quantitated RNA levels. The samples were collected directly from operating room. Total cellular RNA was extracted from frozen tissue samples using guanidinium-isothiocyanate and cesium chloride gradients. Total RNA (10μl per sample) from tumor tissue were size fractionated through 1% agarose-formaldehyde gels and transferred to nylon filters and then hybridized to ^{32}P-labeled DNA probes and placed for autoradiography. Levels of specific RNAs were determined by computer-assisted laser densitometry. Blot filters were sequentially hybridized to nm23 and TIMP-1 probes in addition to GAPDH, as a control. Statistical analyses were carried out according to t-test for equality of means.

Results: NM23-H1 was detected in each sample, however it was not correlate malignancy and invasiveness with NM23-H1 expression. On the other side TIMP-1 gene expression showed a clear correlation between low expression and invasiveness.

Conclusion: The data suggest that TIMP-1 is an inhibitor of high grade gliomas invasion. NM23-H1 was present in the entire gliomas sample, but it did not vary in diffuse astrocytomas and glioblastomas.

KEY WORDS: tumor cell invasion, TIMP-1, NM23, RNA levels, gliomas.

*Análise transcricional dos genes TIMP-1 e NM23 na invasão celular em astrocitoma difuso e glioblastoma multiforme (Resumo). Tese de Doutorado. Universidade Federal de São Paulo, EPM/UNIFESP (Área: Ciências, Neurocirurgia). Orientador: Fernando Patriani Ferraz.

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CLINICAL AND GENETIC EVALUATION OF EIGHT BRAZILIAN FAMILIES WITH SPINOCEREBELLAR ATAXIA TYPE 10 (ABSTRACT)*. **THESIS. CURITIBA, 2004.**

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Spinocerebellar ataxia type 10 (SCA10) is an autosomal dominant ataxia caused by an expansion of a pentanucleotide (ATTCT) repeat in an intron of the SCA10 gene on chromosome 22. SCA10 has been previously reported only in Mexican families, in which the disease presented with a unique combination of pure cerebellar ataxia and epilepsy. So far, SCA 10 has not been reported in a non-Mexican population. Thus, this may very well be the first description of SCA 10 series outside Mexico.

We report on 47 patients with the SCA10 mutation on 8 new Brazilian families. All patients showed pure cerebellar ataxia without epilepsy, suggesting a different phenotype of the SCA 10 mutation in Brazilian families, when compared to their Mexican counterparts.

Cerebellar ataxia (gait ataxia, dysarthria and nystagmus) was seen in all Brazilian patients, whereas saccadic eye movement dysmetria was present in 76.6% of this population. Brisk deep tendon reflexes and lower limbs spasticity were observed in 10.63% and 6.38%, respectively. Peripheral neuropathy was not diagnosed in the Brazilian series.

Patients became symptomatic at the mean age of 35 years old and their illness last an average of 13.59 years.

Neuroimaging studies displayed signs of cerebellar atrophy in all cases. Molecular genetic studies showed an expansion repeat (ATTCT) on gene SCA 10, between 1350 and 2370, with an average of 1820. A correlation between age of clinical onset and type of expansion could be clearly established, as follows: the earlier the clinical onset, the longer the expansion (r=0,44, t=2,5). There is a difference between the average size of expansions in Brazilian (1820) and Mexican (2838) families.

Comparison between SCA 10, SCA 3 and other SCA