

ORESTES MICROARRAY REVEALS A NOVEL GENE PROBABLY SILENCED BY METHYLATION DURING HUMAN MELANOMA PROGRESSION

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Melanoma progression occurs through three major stages: radial growth phase (RGP), vertical growth phase (VGP) and metastasis. RGP cells are confined to the epidermis, in contrast with VGP cells that acquired the ability to invade deeply into the dermis and have competence to metastasis. In order to identify novel genes involved in melanoma progression we selected, *in silico*, Open Reading Frame ESTs (ORESTES) mapping to chromosome regions associated to melanoma development. The fragments were spotted onto nylon membranes and the cDNA microarrays were used to compare gene expression profiles among melanoma cell lines from RGP, VPG and metastatic stages. Microarray analysis indicated a small, but statistically significant group of genes presenting differential expression. A gene of unknown function (C6ORF51) had its decreased expression in a metastatic cell line, as compared to RGP and VGP cells, further validated by Northern blotting analysis. *In silico* analysis showed the presence of CpG islands in the promoter region of this gene and treatment with the methylation inhibitor 5-aza-2'-deoxycytidine restored its expression levels in the metastatic cells, suggesting that C6ORF51 may represent a novel tumor suppressor candidate, silenced by promoter hypermethylation during melanoma progression.

Supported by: FAPESP, CNPq and CAPES

Key words: melanoma progression, microarray, tumor suppressor gene.