IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF NEW GENES WITH DIFFERENTIAL EXPRESSION IN MELANOMA TUMOR PROGRESSION.

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Tumor progression is a complex process involving changes in several cellular pathways. The aim of this work was to compare gene expression profiles between two paired human melanoma cell lines derived from primary (WM278) and metastatic (WM1617) tumors. Using nude immunossupressed mice, we confirmed the tumorigenic and metastatic potential of WM1617 in contrast with no tumorigenic capacity of WM278. Microarray analysis using a selected collection of ORESTES cDNAs matching 1,207 RefSeqs of genes with little or no functional characterization identified a number of up-regulated and down-regulated genes in the metastatic cell line. Based on Northern blotting analysis four of these genes, CYR61, BUB3, HMGN2 and TMEM106C, showing reduced expression in the metastatic cells, were selected for further characterization. In silico analysis showed the presence of CpG island in the promoter region of these genes, so to investigate whether this repression is caused by epigenetic inactivation, we are performing experiments with the methylation inhibitor, 5-aza-2´-deoxycytidine. The full open reading frame of these genes were cloned and are currently being used for functional studies in the melanoma cell lines.

Supported by: FAPESP, CAPES, CNPq and FAEPA