MicroRNA profiles in metastatic versus non-metastatic salivary mucoepidermoid carcinoma

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BACKGROUND: Mucoepidermoid carcinoma (MEC) is the most common malignant tumor of the salivary glands, especially affecting the parotids. MEC derives from the main duct segment and it is composed of mucous, intermediate, and epidermoid cells in varying combinations. Histological grading (low, intermediate, and high) is of recognized prognostic importance. This is based on the architectural formation, cytological features, perineural invasion, and the presence of necrosis. Metastatic spread occurs in up to 80% of high-grade tumors and it is a strong predictor of poor outcome, however, the mechanisms underlying this process are largely unknown. Large-scale microRNA expression profiling studies of human cancers have demonstrated that dysregulation of miRNA is frequently associated with many cancer types. MicroRNAs (miRNAs) are approximately 22 nucleotide non-coding RNA molecules that regulate gene expression post-transcriptionally and are involved in various biological processes.

HYPOTHESIS: microRNA profiles could discriminate the metastatic potential of salivary MECs and might be helpful in diagnostic and prognostic evaluation of patients.

METHODS: Using Real Time RT-PCR we have analyzed the expression of 762 miRNAs and controls using the TaqMan Array Human MicroRNA A+B Cards in FFPE samples from 2 metastatic MEC, 2 non-metastatic MEC and 2 non-neoplastic human salivary glands. For the identification of differentially expressed microRNAs between tumor samples versus normal samples and between metastatic versus non-metastatic samples, bioinformatics analysis was performed using hierarchical cluster analysis and the *t* test with Bonferroni correction was applied.

RESULTS: Among the 762 microRNAs and controls contained in the array panel, 353 showed an expression level below the detection limit (Ct >38) and were excluded from downstream analyses. The microRNA profile was able to discriminate between normal and tumor samples and between metastatic and non-metastatic tumors. Considering tumor and normal samples, 29 microRNAs were differentially expressed. The metastatic versus non-metastatic analysis demonstrated that 62 microRNAs were differentially expressed. Among the differentially expressed microRNAs, some have already been described as associated with the metastatic process (hsa-miR-9, hsa-miR-125, hsa-miR-145, hsa-miR-494, hsa-miR-140, hsa-miR-212, hsa-miR-146, hsa-miR-183, hsa-miR-21, hsa-miR-200, hsa-miR-638, and hsa-miR-141). Financial Support: FAPESP 11/02051-6