Abstract

SET (TAF-1/I2PP2A) is a protein that participates in cell cycle control, apoptosis, migration and histone acetylation. It has been reported to be increased in head and neck squamous cell carcinoma (HNSCC) and participates in an inhibitory complex of histone acetylation, masking the targets of acetyltransferases, which presumably prevents transcription. The objective of the present study was to identify changes in the levels of miRNAs after knockdown of the protein SET in the HNSCC cell line HN12. The knockdown of protein SET was mediated by short hairpin RNA (shRNA) or small interfering RNA (siRNA) against mRNA coding for SET. Other methods used were: Western Blot, Real time RT-PCR and Transwell®. After the knockdown of SET there was an increase of lysine acetylation and the release of 88 miRNAs detected by real time PCR (PCR array - SYBR-Green®). The levels of miR-21, miR-133b, miR-137, miR-193a-3p, miR-15a, miR-29b, miR-100 and miR-125b, among others, were increased by 2- to 10-fold in HN12shSET cells compared to cells control (HN12shCTRL). These miRNAs act in the regulation of proliferation/viability and/or migration/invasion in various types of cancer, including HNSCC. This increase of miRNAs was also demonstrated in the HNSCC cell line Cal 27 after knockdown of SET using siRNA against SET (Cal 27siSET), measured by real time PCR using TaqMan® assays. Functional assays in Transwell® chambers revealed that the migration and invasion capacity of HN12shSET cells are increased compared to HN12shCTRL. The transfection of HN12shCTRL cells with pre-miR-29b reduced cell migration in 73% and invasion in 65%, while the transfection of the same miRNA in HN12shSET cells, reduced the cell invasion in 82%, decreasing the effect of SET knockdown in invasion capacity. These data suggest that SET, accumulated in malignant cells, is involved in the regulation of the acetylation level of lysine with possible impact on miRNAs levels.

Key Words: I2PP2A/SET; miRNAs; Cancer