ABSTRACT:

Oral cancer, the sixth-most common cancer worldwide, comprises of oral squamous cell carcinoma within the oral cavity. The clinical opinion of the OSCC is mostly indigent owing to delayed diagnosis and lack of appropriate markers to identify the disease. There is, therefore, an urgent need to find early detection markers for diagnosis as well as prognosis of oral cancer. Proteomics is an advanced approach for the detection of protein biomarker. In the present study, we have used high-resolution mass spectrometry combined with iTRAQ labeling technology for the characterization and quantization of the proteins in cancerous and non-cancerous oral tissue. Based on iTRAQ quantification, we found 288 proteins to be differentially expressed in cancerous tissue with comparison to non-cancerous tissue. Among these, 126 proteins were found to be overexpressed (<2-fold) and 162 were found to be down regulated (>2-fold) in the tissue proteome. From these proteins we have chosen three signature molecules S100A7, RAB2A and PRDX1 for our further study based on their significant expression profile. Significant increase in expression levels of RAB2A and PRDX1 was evident from the results of tissue microarray and western blot analysis. In addition, RAB2A was found to be localized in the cytoplasm whereas PRDX1 was expressed in cytoplasm as well as membrane within the cancerous tissue. In addition, co-immunoprecipitation and immunofluorescence analysis elaborates the plausible interaction between S100A7 and RAB2A. Further, RNA interference (RNAi) mediated knockdown of S100A7 inhibited cell growth, proliferation, migration and invasion *in vitro*. It also suppressed the metastasis by altering the expression of EMT regulatory proteins as well as the induction of apoptosis followed by the down regulation of RAB2A mediated p38/MAPK pathway. We also provide new evidence that the S100A7 is responsible for anoikis resistance and tumorigenicity in human oral cancer cells. This result also demonstrated that S100A7 is up-regulated during cell detachment in anoikis resistance cell line, mediated through the PKB survival pathway. Our findings have clearly demonstrated for the first time a potential role of S100A7 as a potential early detection marker for oral cancer.

Key words: Anoikis, Apoptosis, Biomarker, Epithelial to mesenchymal transdifferentiation, Isobaric tags for relative and absolute quantization, MAPK, Oral Cancer, Orthotopic, Proteomics, RAB2A, RNAi (RNA interference), S100A7, Tumorigenesis.