MOLECULAR PROFILE OF SALIVARY GLAND TUMORS USING MASS SPECTROMETRY

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INTRODUCTION

Pleomorphic Adenoma (PA) is a benign neoplasm and Adenoid Cystic Carcinoma (ACC) is a malignant neoplasm of the salivary glands. These tumors originate from the intercalated duct of the salivary gland and the diagnosis remains a challenge due to the high variation in histological subtypes and overlapping features. Molecular signatures might help to improve early diagnosis and treatment of these patients. Mass spectrometry approaches provide molecular information on tissue composition and this investigation may contribute to understanding of the pathogenesis of salivary gland cancers.

MATERIALS AND METHODS

Proteomics analyses of 14 tissues from tumors and normal paired samples were performed. The mass spectrometry analyses were carried out using the nanoElute nanoflow chromatographic system, from Bruker Daltonics, Bremen, Germany, coupled online to a hybrid trapped ion mobility spectrometry-quadrupole time-of-flight mass spectrometer-timsTof Pro, from Bruker Daltonics. The raw files were processed in the MaxQuant software, version 2.4.0.0. The search engine integrated with MaxQuant is Andromeda. The Perseus analysis software, version 2.0.9.0, was used to filter the proteomic results. We used MetaboAnalyst 6.0 software to identify differentially expressed proteins. PANTHER.db.org platform was used in data enrichment.

RESULTS AND DISCUSSION

The proteomic analysis revealed 7164 proteins and 19 proteins differentially expressed between the paired normal and tumor samples: 3 proteins were down regulated in the tumor tissues and 16 were up regulated. Considering the Molecular Function in the Gene Ontology, down regulated proteins in tumor samples were predominantly from the binding category whereas up regulated proteins are from the catalytic and structural molecule activity category. For Biological Process, the downregulated and upregulated proteins demonstrated an involvement in the cellular process. Furthermore, Gene Ontology for Cellular Component analysis demonstrated that proteins were active in the cellular anatomical entity, in both groups (up and down regulated proteins). The analysis of the Protein Class revealed that the most predominant proteins in the down regulated group were the cytoskeletal protein, while the up regulated group are represented by proteins involved in the cell adhesion molecule, cytoskeletal protein and metabolite interconversion enzyme category. The pathway demonstrated the protein Actin, cytoplasmic 1 in the down regulated proteins group. This protein is involved in diverse categories, such as cadherin, integrin and Wnt signaling pathways. In summary, the differentially expressed proteins in the salivary gland tumors exhibited different molecular function and protein class compared with healthy tissue samples. The similarity of some categories in both benign and malignant tumors may reflect the histological

origin of the tumors.

CONCLUSIONS

In conclusion, we have described a proteomic profile able to distinguish the tumor and normal tissue that might be used for diagnosis and /or prognosis of salivary gland tumors. The evaluation of this comprehensive molecular profile is important to understand the pathogenesis of these tumors and might be helpful in medical decisions.

Agradecimentos: