Molecular Characterization of the Solid Component of Pediatric Adamantinomatous Craniopharyngioma by Integrated Proteomic Strategies

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Introduction

Adamantinomatous Craniopharyngioma (AC), the most common sellar tumor in children, represents around 5-11% of all the intracranial tumors in pediatric patients (1). A top-down/bottom-up nanoLC-MS integrated platform was applied to proteomic characterization of the solid component of seven ACs. This benign tumor shows in fact a peculiarly aggressive behavior associated with liquid cysts, frequent recurrencies and neurological impairment. Proteomic characterization is therefore important to elucidate the molecular mechanisms involved in its pathogenesis and progression (2).

Methods

Characterization of the solid component was carried out by means of LC-MS proteomic platform. Samples were collected from patients, extracted and analyzed by nano-LC-nanoESI Orbitrap Elite Mass Spectrometer. Both bottom-up and the top-down strategies were adopted for protein characterization. Results were ultimately evaluated by manual inspection of the MS/MS spectra and using specific software and proteomics tools for data analysis and elaboration.

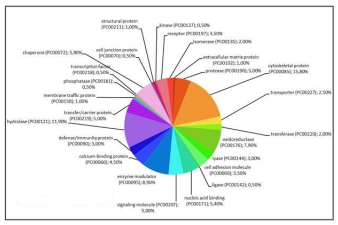
Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of proteomic characterization of the solid component of Adamantinomatous Craniopharyngioma, 2) Discuss, in small groups of the role of inflammation in its pathogenesis, 3) Identify an effective treatment that would involve the suppression of inflammatory mediators from the tumor mass.

Results

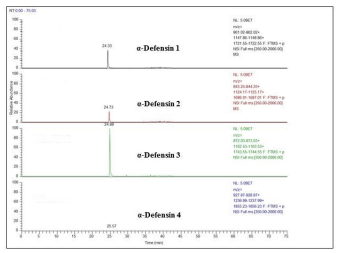
Bottom-up characterization of the AC's solid component achieved numerous shared proteins. Furthermore, the vast majority of them has a pivotal role in cell adhesion and proliferation: a number of filamentous and cytoskeletal proteins were in fact characterized together with proteins related to the ß-catenin pathway, as supported by other preclinical studies. Top-down strategy identified peptide members of ß-thymosins and a-defensins families, together with calcium binding proteins and naturally occurring protein fragments, also allowing to investigate on PTMs and presence of isoforms.

Bottom Up characterization of ACP proteins



Gene Ontology (GO) analysis of the proteins identied by the bottom-up platform.

Top-Down characterization of alpha-defensins in ACP



Total ion current (TIC) profile of the extracted ACP intracystic fluid sample relative to patient 7 analyzed by HPLC-ESI -IT-MS in top-down approach.

Conclusions

This study, representing to the best of our knowledge the first proteomic investigation on the AC solid component, contributes to deepen the knowledge on tumor molecular features also outlining the possible role of inflammation in its pathogenesis and clinical behavior.

References

(1) Pettorini BL et al., Molecular pathogenesis of craniopharyngioma: switching from a surgical approach to a biological one. Neurosurg Focus, 28:E1, (2010).

(2) Massimi L et al., Proteomics in pediatric cystic craniopharyngioma. Brain Pathol. (3):370-376, (2017).