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Integrated proteomic platforms for studying pediatric brain tumor diseases

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Introduction: Proteomics can relevantly contribute to the comprehension of the tumorigenesis process and to the identification of potential biomarkers of disease and possible therapeutic targets. Differently from adult brain tumors, very few research is devoted to proteomic studies of the pediatric tumors. Proteins can be analysed in the entire (top-down approach) or digested (bottom-up approach) state. The two approaches are complementary and allow the identification of isoforms and post-translation modifications (PTMs) useful for the elucidation of the molecular mechanisms involved in the disease.

The top-down/bottom-up platforms were integrated for the proteomic characterization of tumor fluids and tissues of different pediatric brain tumors, i.e. adamantinomatous craniopharyngioma, pilocytic astrocytoma and medulloblastoma.

Methods: Proteomic analysis was performed by LC in coupling with high resolution ESI-LTQ-Orbitrap mass spectrometry after simple extraction procedures (top-down approach) and using trypsin as proteolytic enzyme for protein digestion (bottom-up approach). Protein sequencing and characterization was performed manually and with the use of specific bioinformatic tools.

Results: The proteomic analysis of the pre- and post-operative cerebrospinal fluid of pediatric patients affected by posterior cranial fossa brain tumors (ependimoma, medulloblastoma and pilocytic astrocytoma) identified the hemorphins as candidate biomarkers of prognosis.^[1] The analysis of the cystic fluids of pilocytic astrocytoma, adamantinomatous craniopharyngioma and Rathke's cleft cyst identified proteins involved in inflammation, cells growth and differentiation, protein breakdown and degradation, lipid transport and removal.^[2,3,4]

Conclusions: Some proteins resulted specific of different brain tumour types suggesting a probable involvement of oxidative stress in pilocytic astrocytoma and inflammation in craniopharyngioma. The comparative proteomic analysis of pilocytic astrocytoma and medulloblastoma tumor tissues revealed interesting differences for the characterization of the most malignant medulloblastoma.

References:

¹ Desiderio et al, *Proteomics* 12 (2012) 2158

² Pettorini et al., *Child's Nervous System* 26 (2010) 1779

³ Desiderio et al, *Child's Nervous System*, 29 (2013) 951

⁴ Martelli et al., *Electrophoresis*, submitted