

Finding new ways to improve the treatment of neuro-oncological diseases

Author: Geza Mezey

Department of Neurosurgery, University of Debrecen

Supervisor: Laszlo Bognar

University of Debrecen, Doctoral School of Neurosciences, Clinical Medicine

Summary

In the thesis I present the collected evidences that we successfully combined the modified surgical bipolar forceps and ultrasonic aspirator with a mobile mass spectrometer. In this manner we created a tool not only for real time but also for in situ tissue analysis. Moreover this method has the fundamental advantage of mass spectrometry by analysing the molecular constitution of tissues. This kind of molecular description may open further gates to compare the mass spectrum with the presence of classic genetic and immunohistochemic markers.

In our experiments with the bipolar forceps and the ultrasound aspirator we have revealed that the discrimination between tumorous and healthy neural tissues is possible. Both instruments were successfully coupled to neuronavigation. These possibilities, especially the ultrasound based method significantly could help the neurosurgeon who operates gliomas or glioblastoma by improving the extent of safe resection.

Our experiments proved if an appropriate database is available, fast and intraoperative histology can be obtained by both of our instruments and even grade level histologic discrimination can be performed. The real time tissue analysis can be useful in the analysis of rare, macroscopically unidentifiable tumors, especially when the operated tumour needs different treatment strategy in the aware of the histology. Therefore in this thesis we showed that retrospective analysis of a rare entity could reveal the importance of real-time intra-operative histology.

Moreover in this thesis I presented our expression results of GHRH, pGHRHR, its splicing variants, PTEN and EGFR genes in human glioblastoma samples. Our study provides the first evidence that GHRH and SV1 are present in a substantial part of human GB tissues. We pointed out that expression pattern of GHRH and its SV1 receptors could predict prognosis. Namely GHRH positive, SV1 negative cases showed better overall survival. These results showed that we have moved towards finding the GHRH pathway suitable as a molecular target and a useful prognostic factor in human glioblastomas.

Keywords

neuro-oncology, micro-neurosurgery, mass spectrometry, real time in situ tissue analysis, splicing variant receptors