Abstract citation ID: bvac150.1075

Neuroendocrinology and Pituitary

ODP368

Hyper-phosphorylation of β-catenin at Serine552: predictive marker of invasion and recurrence of Non-Functioning Pituitary Tumours (NFPTs)

Ashutosh Rai, PhD, Soujanya D Yelamanchi, PhD, Bishan D Radotra, MD, PhD, Sunil K Gupta, MCh, Rajesh Chhabra, MCh, Akhilesh Pandey, MD, PhD, Mãrta Korbonits, MD, PhD, Carles Gaston-Massuet, PhD, and Pinaki Dutta, DM

Background: NFPTs are the most common operated pituitary tumours and can present with visual field defects, hormone deficiencies and headache. Surgery is treatment of choice but recurrence rate is high ranging from 10-50%, depending on the extent of tumour removal. No confirmed predictive biomarkers for NFPT recurrence have been identified, apart from Ki-67. We applied high-throughput mass spectrometry-based phosphoproteomic approach to explore the phosphorylation pattern of proteins in NFPTs in order to identify predictive markers of invasion and recurrence. **Methods:** Based on radiological, histopathological, and surgical features, NFPTs were sub-grouped into three groups: non-invasive (n=5), invasive (n=10) and recurrent (n=5) subtypes. Invasiveness was determined by radiology (Knosp classification 3&4), histopathological invasion (bone, dura and mucosa) and intraoperative findings. Tumour recurrence was based on radiological data for a mean±SD follow-up of112±39 months. Fresh-frozen pituitary tumour tissues were used for protein extraction and phosphopeptides were enriched using TiO 2 and labelled with tandem mass tags and subjected tomass spectrometry (Orbitrap)for quantification. Candidate hyper-phosphorylated proteins were validated by immunohistochemistry in 200 additional tumour samples by immunoblotting (n=36). **Results:** In total, we identified 3185 phosphopeptides and observed significant difference in phosphorylation levels of invasive and recurrent groups. Compared to non-invasive cases, in invasive group we found, 452 hyper and 93 hypo phosphorylated proteins, while in the recurrent group there were 790 hyper and 307 hypo phosphorylated proteins. Phospho-serine showed the highest level of difference (90.3%) among the groups, followed by threonine (8.9%) and tyrosine (0.8%). One of the top differentially phosphorylated proteins was Ser552 of β-catenin showing significant hyper-phosphorylation in recurrent (p<0. 001) and invasive (p<0. 001) NFPTs. We also observed hyper-phosphorylation in tumours with suprasellar (p<0. 05) and cavernous sinus extension (p<0. 01). There was no correlation with tumour diameter and volume. Receiver operating characteristics curve analysis was performed to find the optimal cut-off value of β-catenin pSer552 immunohistochemical H-score in patients who had recurrence (n=44) or non-recurrence (n=156)and observed an area under curve of 0.717 (95% CI: 0.61-0.80),indicating a good prognostic ability for theβ-catenin pSer552H-score. A cut-off value of 160 for theβ-catenin pSer552H-score gives a sensitivity of 69% and a specificity of 73% for tumour recurrence. Kaplan-Meier survival curve analysis shows strong statistical correlation in the recurrence free survival (p<0. 0001) and the nuclear positive staining of β-catenin pSer552 with a hazard ratio of 3.1 (95% CI 1.5-6.3). **Conclusions:** our study has identified hyper-phosphorylation of β-catenin at the Ser552 in recurrent and invasive NFPT subgroups. The H-score of β-catenin p552 correlates with tumour recurrence free survival in a large cohort of NFPT patients, which supports that β-catenin pSer552 could be used as predictive biomarker for NFPT recurrence.

Presentation: No date and time listed