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Global proteome and phosphoproteome analysis of meningiomas

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INTRODUCTION

Meningiomas are common brain tumours arising from meningeal tissue. Despite the majority of them displaying benign features, they can cause mild to severe morbidity. The current main therapeutic approach is complete tumour resection commonly with adjunct radiation therapy. However, tumour location can hamper complete resection and chemotherapies are ineffective. In this study we aim to elucidate dysregulated pathways in meningioma pathogenesis and identify novel molecular targets by deciphering the proteome and phosphoproteome of different grades of meningiomas.

METHODS

Tumour lysates were collected from grade I, II and III frozen meningioma specimens and three normal healthy human meninges. Phosphoprotein purification was performed using Qiagen® PhosphoProtein Purification Kit. Proteins were separated by SDS-PAGE followed by in-gel tryptic digestion. Extracted peptides were purified and analysed by electrospray ionization LC-MS/MS. Raw mass spectrometry files were analysed using MaxQuantTM. Expression data was validated by Western blot and functionally annotated using Ingenuity® Pathway Analysis (IPA®) and DAVID 6.8.

RESULTS

We have quantified 3888 proteins and 3074 phosphoproteins across all grades of meningioma and normal meninges. Comparative analysis confirmed 181 proteins and 338 phosphoproteins to be commonly significantly upregulated (log2 fold-change$\geqslant$1.5; $p<0.05$) among all grades vs. normal meninges. We have successfully validated the expression data of several upregulated proteins and phosphoproteins. Gene Ontology revealed biological processes including EFGR and VEGFR signalling to be enriched in the phosphoproteome. Grade-wise comparisons identified 667 proteins and 769 phosphoproteins to be differentially expressed ($p<0.05$) between grade III meningiomas compared to grade II and I.

CONCLUSION

We have performed a comparative proteomic analysis across all meningioma grades and identified changes in proteomic profiles between these tumours and normal healthy meninges. We will use this data to define novel targets common to all grades and specific to a grade of meningioma for future therapies.