

P3.061-175: Transcriptome of NSCLC Associated Tumour Educated Platelets Correlate With Tumour Stage

Joshua Flynn^{1,2}, Myron G. Best³, Sjors G.J.G. In 't Veld³, Stephen P. Finn¹, Orla Sheils^{1,4}, Anne-Marie Baird^{2,4}

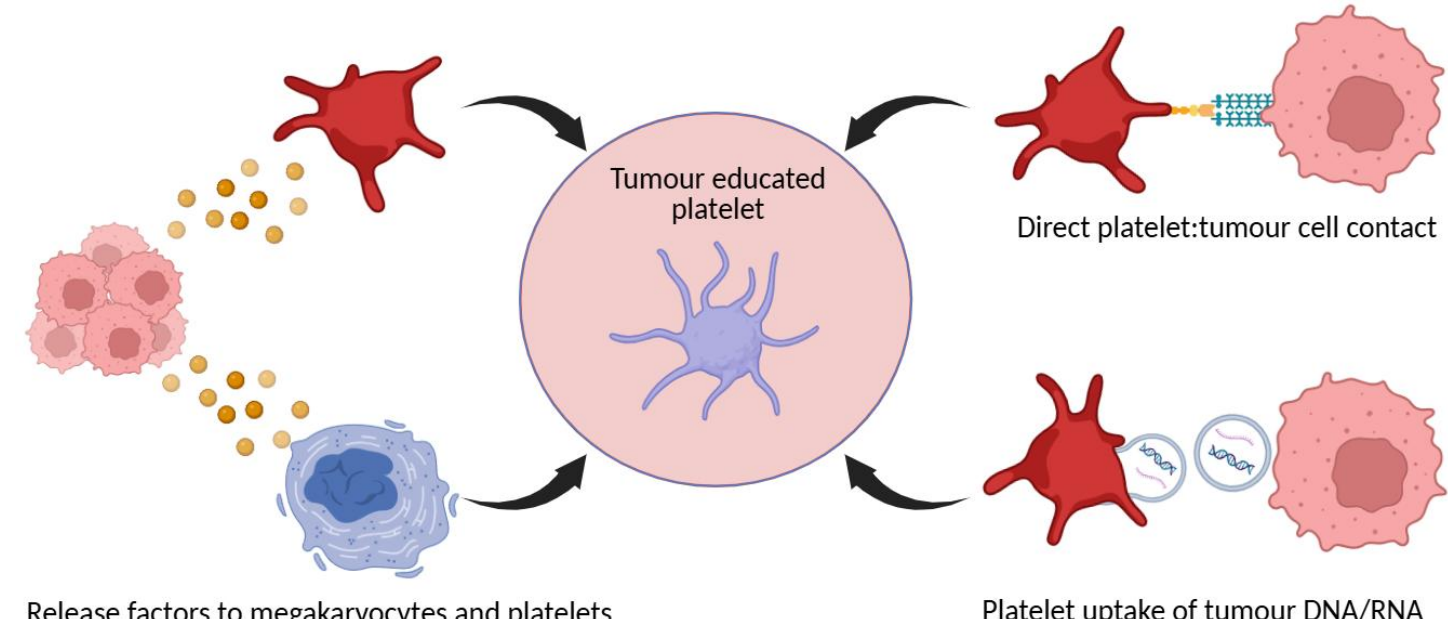
¹Department of Histopathology and Morbid Anatomy, Trinity Translational Medicine Institute, Trinity College Dublin, Ireland, ²Trinity St. James's Cancer Institute, St. James's Hospital, Dublin, Ireland ³Department of Neurosurgery, Brain Tumour Centre Amsterdam, Cancer Centre Amsterdam, Amsterdam UMC, VU University Medical Centre, Amsterdam, Netherlands, ⁴School of Medicine, Trinity Translational Medicine Institute, Trinity College Dublin, Ireland

Correspondence: jfflynn6@tcd.ie

INTRODUCTION

Clinical Need: Metastatic progression is a major determinant of poor survival in NSCLC¹.

Platelets: Platelets are central to metastasis². Platelet behaviour can change upon contact with tumour cells.



How these tumour educated platelets (TEPs) contribute to metastasis is not fully understood.

Study Goal: Examine changes in TEP signatures in NSCLC with different metastatic site patterns and compare these signatures from primary and metastatic NSCLC tissue samples.

METHODS

TEP Dataset: The GSE183635 dataset³ was downloaded from the GEO and contains RNA expression data from TEPs from participants with early stage (stage I/II, n = 33) and stage IV (n = 399) disease, and asymptomatic controls (n = 390).

Single-Cell RNA Seq Dataset: The Chan *et al.* 2021⁴ dataset was downloaded from the Human Tumor Atlas Network. The dataset contains 22 samples from NSCLC including samples from brain metastases (n = 3).

Data Analysis: Differentially expressed genes were identified using edgeR with significance denoted as an FDR < 0.01. Gene set enrichment analysis was performed using clusterProfiler (v4.16.0). Single-cell data was processed using Seurat (v5).

REFERENCES & ACKNOWLEDGEMENTS

- Dillekås, H., Rogers, M.S., & Straume, O. Are 90% of deaths from cancer caused by metastases? *Cancer Med.* 2019 8:5574-5576
- Li, S., Lu, Z., Wu, S., *et al.* The dynamic role of platelets in cancer progression and their therapeutic implications. *Nat Rev Cancer.* 2024 24:72-87
- Best, M.G., Sol, N., In 't Veld, S.G.J.G., *et al.* Swarm Intelligence-Enhanced Detection of Non-Small-Cell Lung Cancer Using Tumour-Educated Platelets. *Cancer Cell.* 2017 32(2):238-52
- Chan, J.M., Quintanal-Villalonga, A., Gao, V.R., *et al.* Signatures of plasticity, metastasis, and immunosuppression in an atlas of human small cell lung cancer. *Cancer Cell.* 2021 39(11):1479-96

Claude Code was used as a support for code review.

This study was supported by the Dr. Joan McCormick Cancer Research Scholarship.

We thank our PPI panel: Mr. Seamus Cotter and Mrs. Kate Sinclair for their valuable project input.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Profiling of TEPs can help us understand how they contribute to metastasis in NSCLC
- Cross-validation with single-cell RNA seq data demonstrate that TEPs can reflect tumour biology
- TEPs represent an exciting potential bioresource for liquid biopsy
- Identified fructose 6-phosphate and GDP-mannose metabolism as clinically relevant

Future Direction for Research

- Validate these results in matched platelets and tumour samples
- Investigate the impact of fructose 6-phosphate and GDP-mannose metabolism in NSCLC cell survival
- Expand analyses into SCLC

RESULTS

1. TEPs from people with stage IV NSCLC show enhanced extracellular matrix and tissue remodelling alongside reduced immune signalling vs. early stage NSCLC

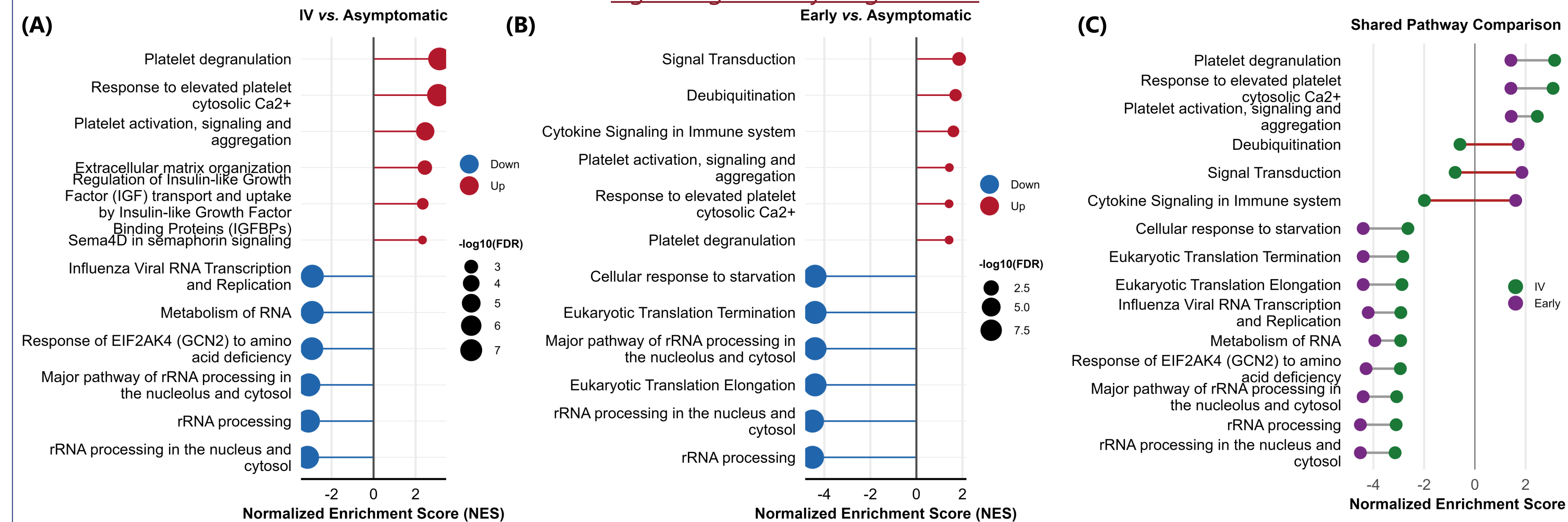


Figure 1. Increased extracellular remodelling, IGF and SEMA4D signalling pathways in TEPs from metastatic samples compared to non-metastatic TEPs. Altered Reactome pathways identified in differentially expressed genes (DEGs) from TEPs from people with stage IV NSCLC (A) and TEPs from people with early stage disease compared to asymptomatic controls (B). Comparison of common pathways identified in stage IV and early stage TEPs (C).

2. TEPs display a metastatic site specific signature highlighting differential immune and cell division capabilities

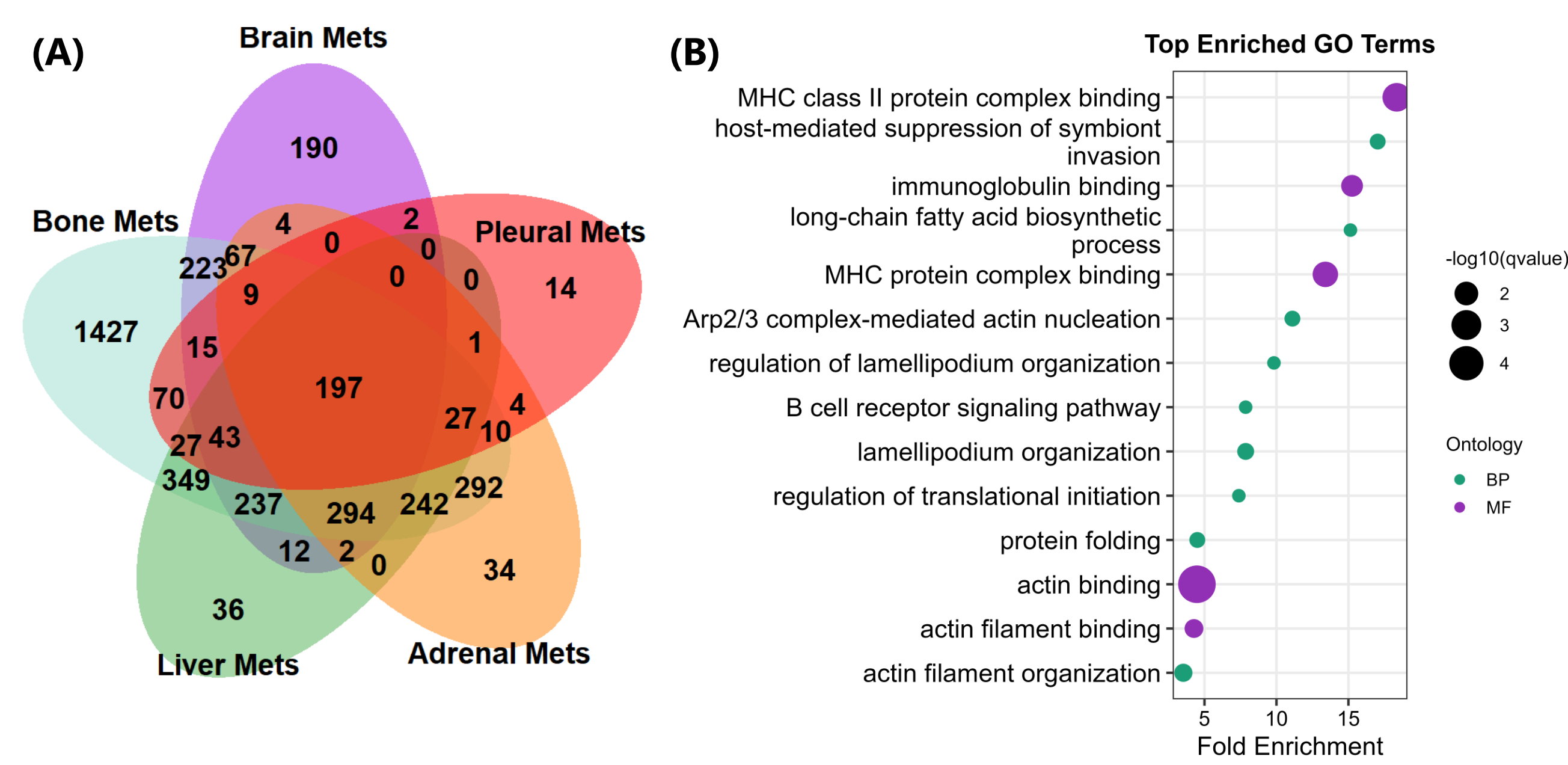


Figure 2. TEPs from people with stage IV NSCLC display increased invasive capability signalling and metastatic specific signatures.

Overlapping and metastatic site specific DEGs identified in TEPs (A). The top enriched gene ontology (GO) terms identified from the 197 genes common to all metastatic sites (B). Comparison of significantly altered GO terms from metastatic site specific DEGs identified in TEPs from people with different metastatic profiles vs. asymptomatic controls (C).

3. TEPs can reflect metastatic tumour biology and highlight metabolic pathways significantly associated with survival in NSCLC

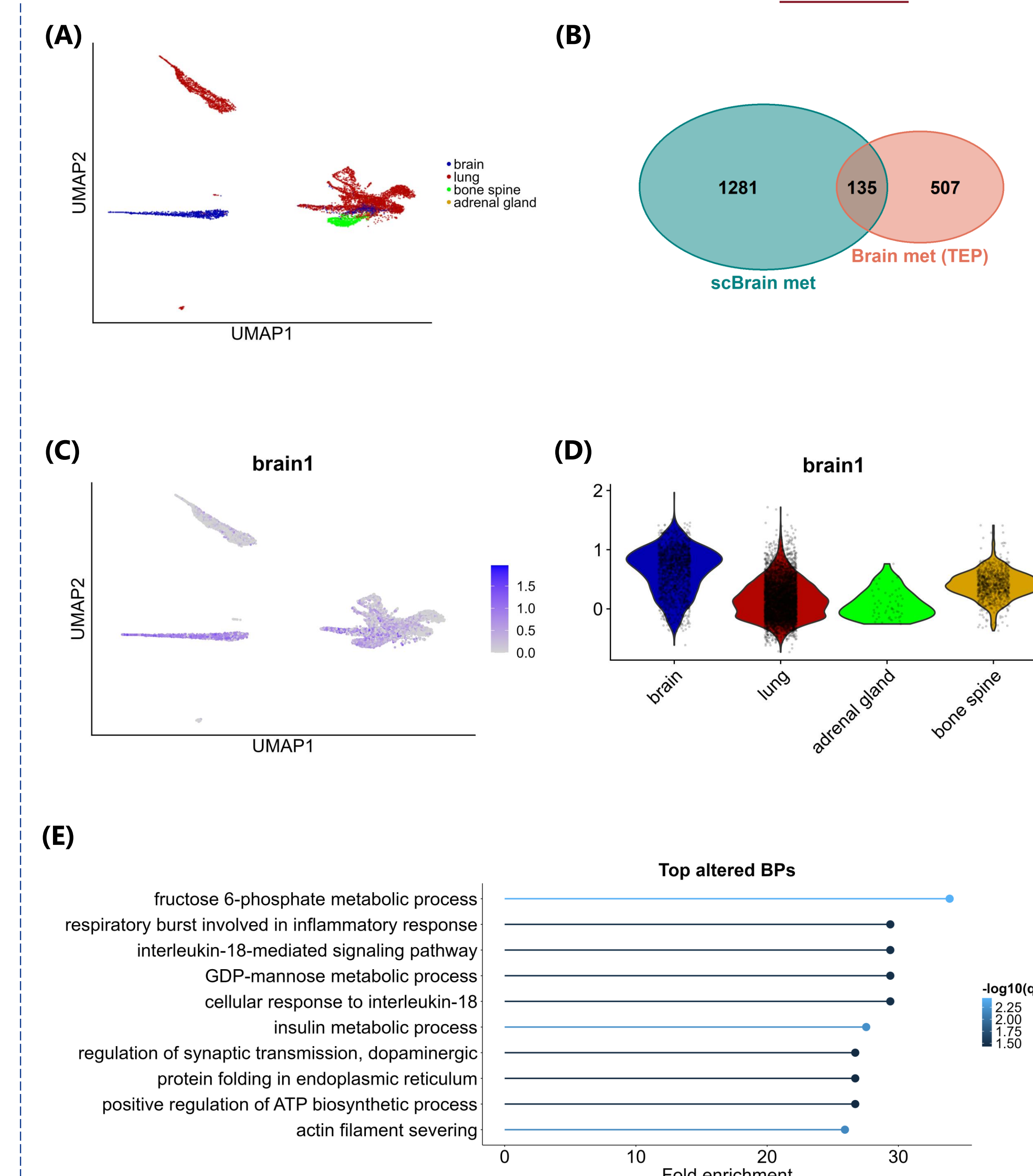


Figure 3. TEP signatures reflect that of lung and metastatic tissue.

UAMP of Chan *et al.* dataset (A). Venn diagram showing overlapping DEGs from TEPs and brain tissue from Chan *et al.* dataset (B). Module scoring using the overlapping brain signature gene set on the Chen *et al.* dataset visualised in UMAP (C) and violin plot (D). Significantly altered biological processes (BPs) identified using the overlapping gene set (E). KM plots of combined expression of genes involved in altered BPs using the TCGA_LUAD dataset (F-G).