Development of a Pan-Cancer 15 Gene Expression Signature to Detect a Subgroup Driven by MAPK Signalling

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Background

- Unsupervised hierarchical clustering of gene expression data from 265 high grade serous ovarian cancer (HGSOC) tumors identified 3 molecular subgroups.
- These were characterised by upregulation of angiogenesis (Angio subgroup), immune (Immune subgroup) and both angiogenesis and immune (Angioimmune subgroup) genes, respectively.
- Further characterisation of the Angioimmune subgroup reveals it to be driven by MAPK pathway activation and is associated with an EMT (Epithelial to Mesenchymal Transition) like phenotype.
- The aim of this study was to develop a gene signature which could detect the MAPK/EMT subgroup across multiple cancer types.
- Using our datasets and publically available gene expression datasets we have demonstrated that the MAPK/EMT subgroup (as defined by EMT assay) exists in other cancer types and is associated with poor prognosis.
- A positive result for the EMT assay is associated with higher sensitivity to drugs which target components of the MAPK and EMT pathways.

Conclusions

- A 15 gene signature has been developed from formalin fixed paraffin embedded samples to detect a molecular subgroup driven by MAPK/EMT signalling across multiple diseases.
- This assay predicts sensitivity to MEK inhibitors in pre-clinical model systems.
- Further work aims to validate the EMT assay in clinical samples from patients treated with a MEK or EMT inhibitor.
- This assay may be helpful for clinical trial enrichment to select patients that are likely to benefit from MAPK or EMT targeted therapies.

Acknowledgements

This work was supported by Invest NI through the European Sustainable Competitiveness Programme 2007-2013, European Regional Development Fund (ERDF). The samples used in this research were received from the Edinburgh Cancer Research Centre - Ethical approval was obtained from Lothian Local Research Ethics Committee (Ref: 07/S112/33).