Cellular barcoding of pancreatic cancer cells, supports the tracking of metastatic clones

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) has a dismal 5-year survival rate of only 13% and despite chemotherapy marginally improving outcome for patients, metastatic PDAC is the leading cause of death due to late diagnosis[1]. Therefore, to better treat metastatic PDAC we need a more comprehensive understanding of the mechanisms that govern metastasis. It is well established that primary and metastatic tumors are frequently genetically heterogenous. This potentially diverse clonality within tumors can variably affect adaption to different tumour microenvironments, immune evasion, and therapy resistance. Therefore, understanding the clonal composition and their dynamics within primary and secondary tumours may enable more specific targeting of malignant clones and thus prevent further cancer spread.

Methods

To study this, we are utilizing cellular barcoding which efficiently labels individual cancer cells to support tracking of metastatic clones after dissemination from the primary tumour[2]. By cellular barcoding of murine PDAC KC ($Kras^{G12D}$), KPC ($Kras^{G12D}$, $p53^{R172H}$) and KPflC ($Kras^{G12D}$, $p53^{KO}$) cells, we are tracking *in vivo* cancer cell metastasis to distant sites (liver and lungs) and have isolated these metastatic cancer clones for sequencing analysis.

Results

Within the primary tumour we have established diverse clonal composition and have identified clonal dominance that governs primary tumour growth. We show dissemination of specific malignant clones to secondary sites, are present within the primary tumour, while also observing further clonal evolution of metastatic clones.

Conclusion

This study highlights PDAC cell dissemination to secondary sites is driven by malignant clones present within the primary tumour, with new, potential avenues for therapeutic intervention.

References

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