

# Concordant Genomic Vulnerabilities of Patient-Derived Cell Line and Matched Xenograft-Derived Cell Line through Whole Exome Sequencing in Breast-Brain Metastatic Cancer

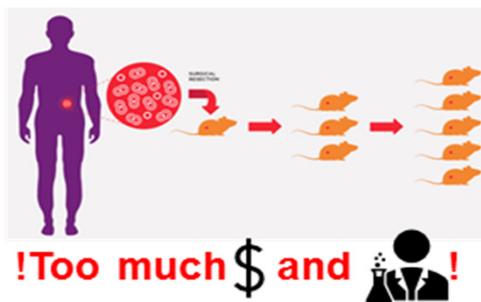
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## BACKGROUND

Brains metastasis (mets) is often associated with the worse prognosis and options of treatment are very limited, which becomes a major limitation of life expectancy. Therefore, developing a cost-efficient, robust model that could precisely recapitulate the features of tumor origin will be beneficial to discovery of novel therapeutic strategies to further improve outcomes.

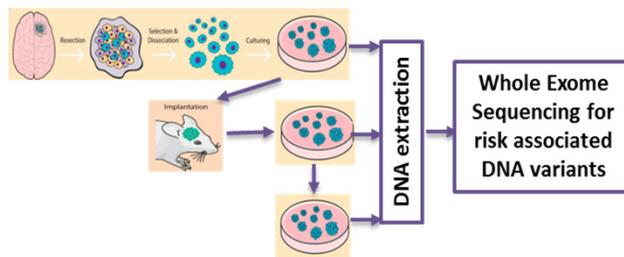
Patient-derived xenografts (PDXs) often accurately recapitulate the tumor of origin in terms of genomic landscape, histopathology, and therapeutic response, however, restrictions such as cost, high maintenance and limited amenability for large-scale screening for potential therapies remain a challenge.



## OBJECTIVE

To develop a cost-efficient, robust model that could precisely recapitulate the features of tumor origin will be beneficial to discovery of novel therapeutic strategies.

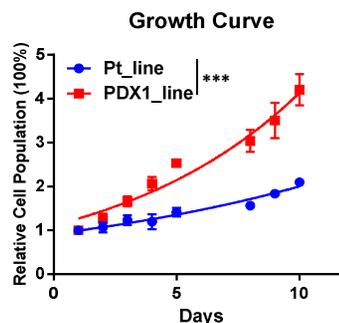
## METHODS



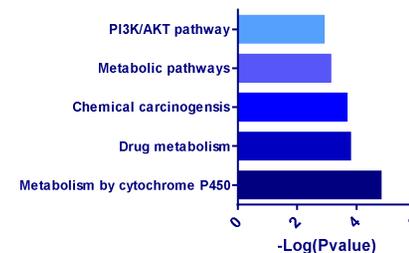
DNAs from the first passage of cells derived from a patient tumor along with two different passages of cells derived from a matched PDX were extracted, followed by the whole exome sequencing analysis. Raw FASTQ files were quality controlled using FASTQC and then aligned to hg38 using BWA-MEM without trimming. The aligned BAM files were processed using GATK4 following best practice. Mutations were called using mutect2 without normal control. Classification (benign vs. pathogenic) of variants was finally referred to ClinVar.

## RESULTS

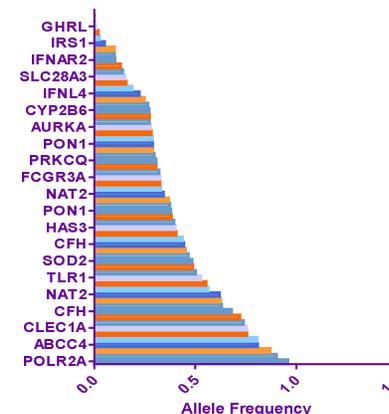
Cells derived from PDXs (PDXL) has a significantly shorter doubling time than cells derived from patient tumor (PTL).



## Consistent pathways of genes with risky variants



## Consistent allele frequency of risky variants



## CONCLUSIONS

Our PT-PDX cell line platform represents a preclinical tool for functional gene validation and proof of concept studies to identify novel druggable vulnerabilities in BBM, which could be further applied to other types of brain mets.

## REFERENCES

Choisat BB, Leyton CK, Legras XD et al., *Journal of Hepatology*, 2016  
 Kuwta T, Yanagihara K, Iino Y et al., *Cells*, 2019