Cancer Model Evaluation for Metastatic Prostate Cancer

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MOTIVATION

- As metastasis is the most common cause of cancer-related death , there is an urgent need to discover new therapies for treating metastasized cancers .
- Cancer cell lines are widely-used for studying cancer biology and testing drug candidates. However, many drugs with promising preclinical results fail in clinical settings.
- Thus, it is necessary to understand how adequately cancer cell lines imitate the tumor in patients .
- The recent accumulation of large-scale genomic data in cell lines, patient derived xenografts and organoids have a great potential to evaluate the suitability of cell lines as metastatic cancer research model.

OBJECTIVE

- To evaluate the suitability of available prostate cancer models for studying metastatic prostate cancer.
- To determine the extent of resemblance between prostate cancer cell lines and prostate cancer samples in terms of gene mutation frequency and copy number variation.
- To compare the transcriptome of prostate cancer cell lines, organoids and patient-derived xenografts (PDX).

PROJECT DESIGN

DATA SOURCES

Cell Lines	Primary Tumor	Metastatic Tumor	Patient Derived Xenogrfts	Organoids
Broad institute Cancer Cell Line Encyclopedia (CCLE)	The Cancer Genome Atlas Prostate Adenocarcinoma (TCGA-ORAD)	MET500	SRP084270	SRP137893

R ANALYSIS

1. **Comparision of Genomic profiles in terms of Genetic mutations and Copy Number Variation**
2. **Transcriptome Analysis**

RESULTS

	TCGA	MET500	CCLE
TP53	0.12224449	0.3902439	0.5
TTN	0.12625251	0.19512195	0.875
AR	0.00601202	0.17073171	0.375
KMT2C	0.06012024	0.12195122	0.5
PRKDC	0.02004008	0.08536585	0.875
DNAH8	0.01402806	0.07317073	0.125
NYNRIN	0.01402806	0.07317073	0.25
PIK3CA	0.02805611	0.07317073	0.125
CHD1	0.01603206	0.06097561	0.625
GLI2	0.00601202	0.06097561	0
OBSCN	0.03206413	0.06097561	0.625
RB1	0.00601202	0.06097561	0.125

Table 1 : Top mutated gene frequencies across Primary Cancer Samples, Metastatic Cancer Samples and CCLE cell lines for prostate cancer

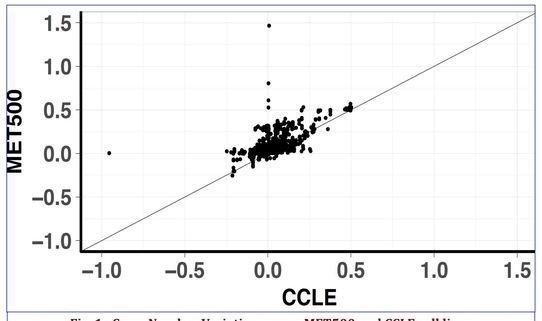

Fig 1 : Copy Number Variation across MET500 and CCLE cell lines

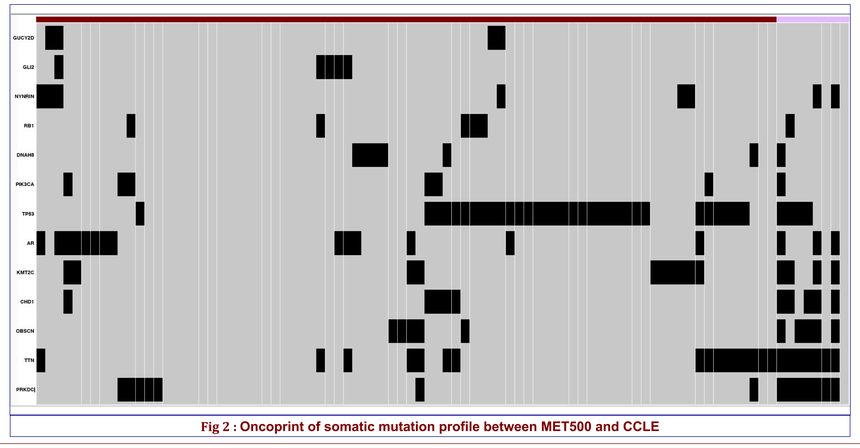

Fig 2 : Oncoprint of somatic mutation profile between MET500 and CCLE

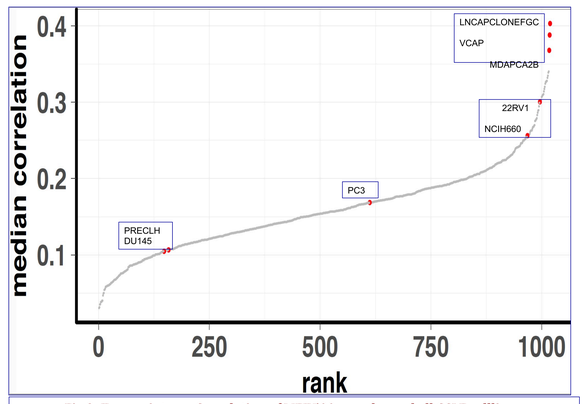

Fig 3 :Transcriptome Correlation of MET500 samples and all CCLE celllines.

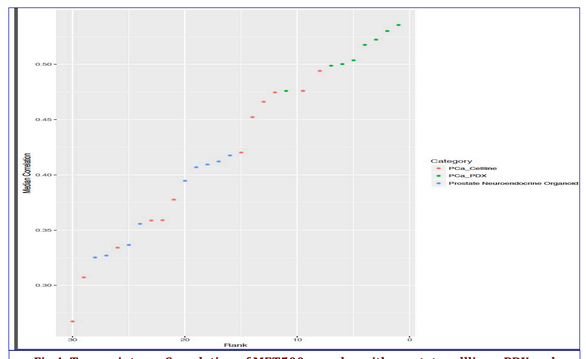

Fig 4: Transcriptome Correlation of MET500 samples with prostate celllines, PDX and organoids

- Highly mutated GUCY2D and GLI2 of MET500 prostate adenocarcinoma sample did not mutated in CCLE prostate cancer cell lines.
- The median CNV profiles of CCLE cell lines and MET500 prostate cancer samples were highly correlated except for genes AR, HEPH, MSN, AMER1 and PRKY.
- Prostate cancer PDX shown more correlation than prostate cancer cell lines in transcriptome analysis.

PRIMARY REFERENCE

Liu, K., Newbury, P., Glicksberg, B., Zeng, W. Z., Andrechek, E., & Chen, B. (2018). Evaluating cell lines as models for metastatic cancer through integrative analysis of open genomic data. doi:10.1101/337287