

Supplemental Table 1

PDO	Origin	Site	Type of sample	Sex	Age	Race	Stage	KRAS (allele frequencies)	TP53 (allele frequencies)	SMAD4 (allele frequencies)	CDKN2A (allele frequencies)	Treatment prior to organoid
hF24*	H. sapiens	Pancreas	EUS FNA	F	57	Caucasian	4	G12V 82%	F113V (100%)	LOSS (N/A)	DEEP LOSS (N/A)	NO
hM1F*	H. sapiens	Lung	RAP	M	55	Caucasian	4	G12D 73%	R175H (100%)	WT (N/A)	WT (N/A)	YES
hT1*	H. sapiens	Pancreas	Resection	M	65	Caucasian	2B	G12V 39%	R213* (100%)	WT (N/A)	DEEP LOSS (N/A)	NO
449**	H. sapiens	Liver	Wedge biopsy	M	73	Caucasian	4	--	WT**	--	--	YES

*H. Tiriac *et al.*, Organoid Profiling Identifies Common Responders to Chemotherapy in Pancreatic Cancer. *Cancer Discov* **8**, 1112-1129 (2018).

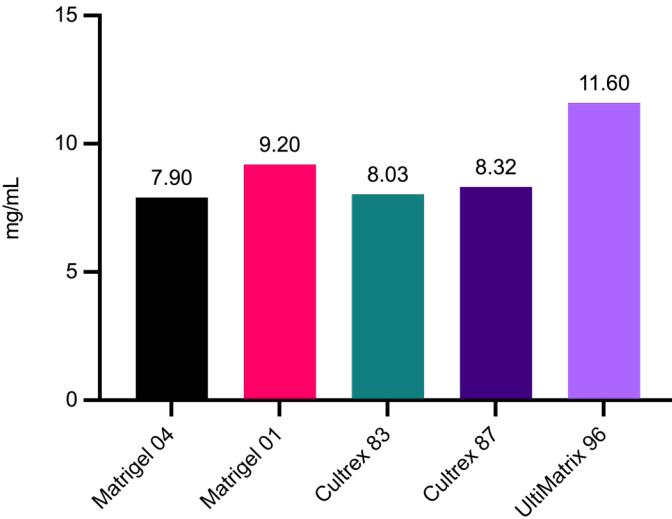
**UCSD Moores Cancer Center Biorepository and Tissue Technology Shared Resource.

Supplemental Table 2

PDO	Origin	Sex	Site	Type of sample
mT69A	M. musculus	F	Pancreas	KPC B6, PDAC local pancreatic metastasis
mT69B	M. musculus	F	Pancreas	KPC B6, PDAC primary tumor
mT9	M. musculus	F	Pancreas	KPC PDAC primary tumor
A5462	M. musculus	F	Pancreas	KPC B6, pancreas harboring premalignant lesions
A5504	M. musculus	M	Pancreas	KPC B6, pancreas harboring premalignant
A5505	M. musculus	M	Pancreas	KPC B6, pancreatic tumor with mixed adenocarcinoma and sarcomatoid histopathology

A

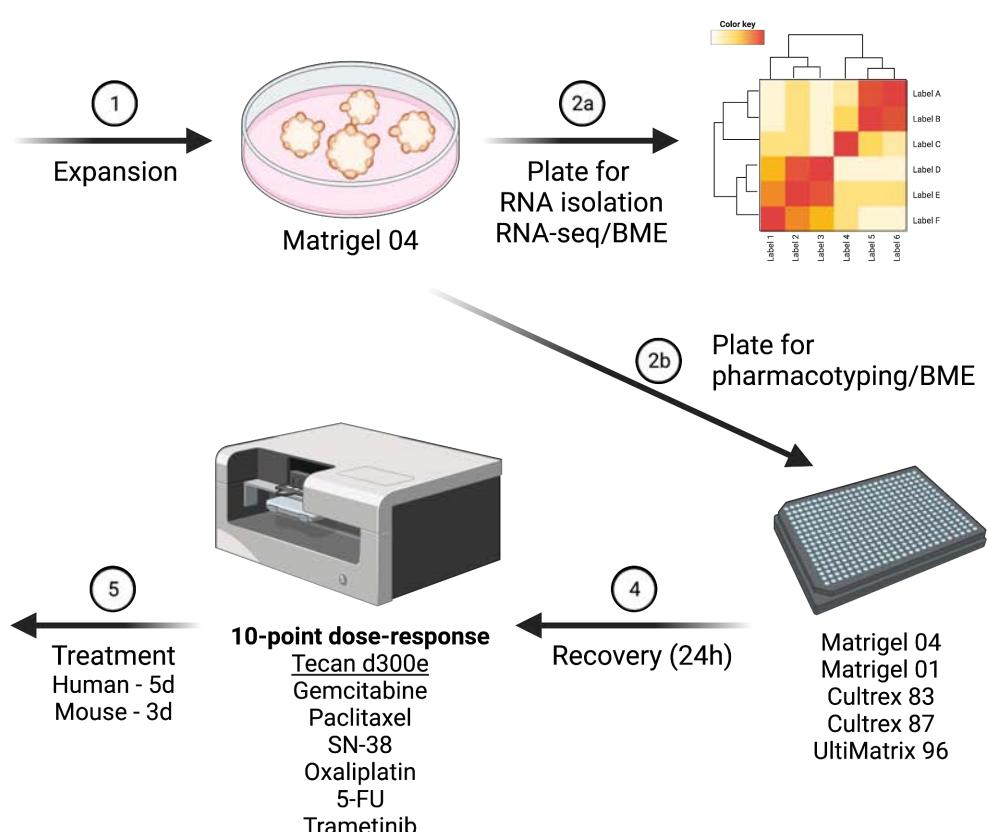
Total Protein Concentration

**B****Organoids****Human**

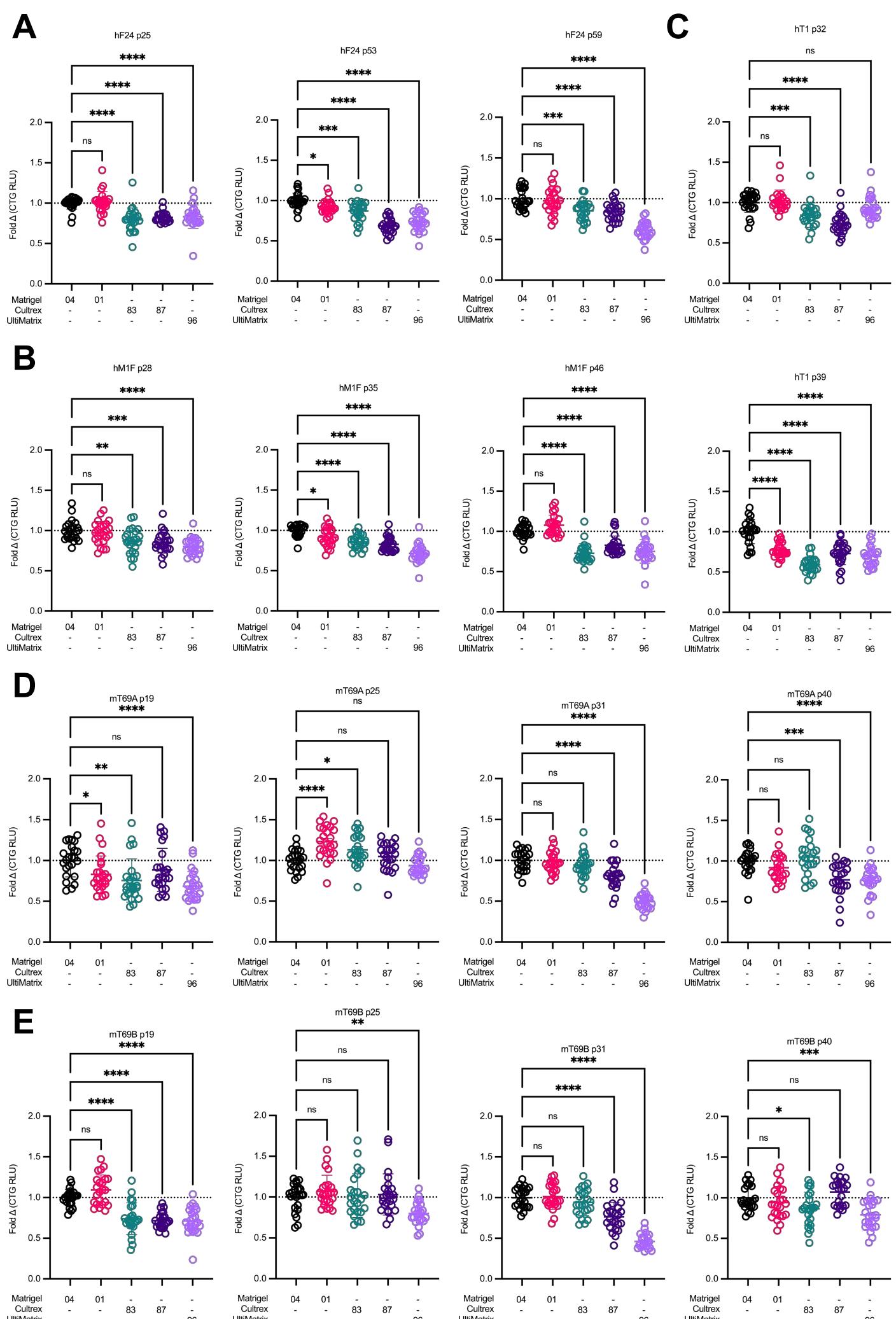
hF24 - Stage IV EUS FNA
 hM1F - Stage IV lung metastasis
 hT1 - Stage IIB resection

Mouse

mT69A - murine metastasis
 mT69B - murine primary tumor
 mT9 - murine primary tumor



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[BioRender.com](https://biorender.com)



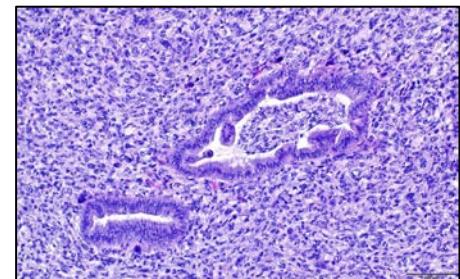
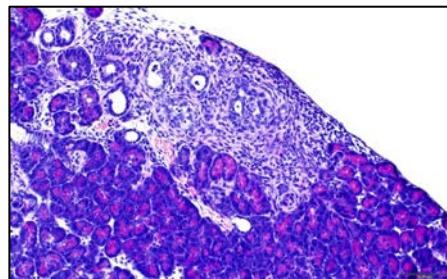
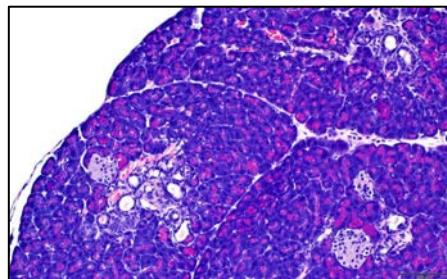
Supplemental Figure 2

A

A5462

A5504

A5505

**B**A5462 – *LSL-Kras^{G12D/+};LSL-Trp53R172H/+;Pdx-1-Cre* (KPC)

Matrigel 01

Matrigel 04

Cultrex 83

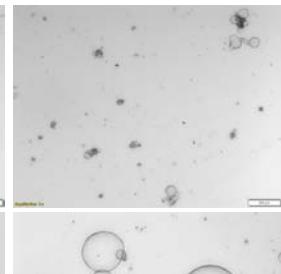
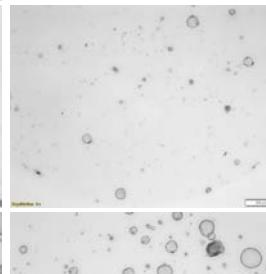
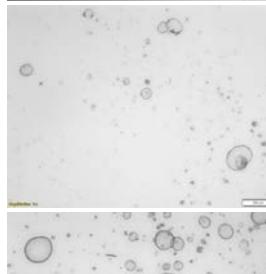
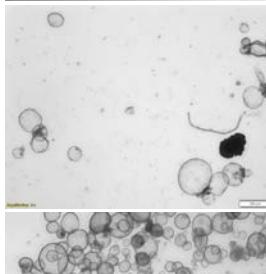
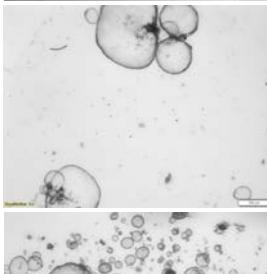
Cultrex 87

UltiMatrix 96

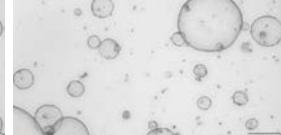
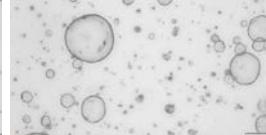
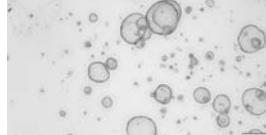
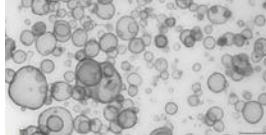
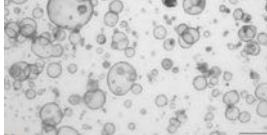
Day 0 p0



Day 3 p0



Day 9 p1

**C**A5504 – *LSL-Kras^{G12D/+};LSL-Trp53R172H/+;Pdx-1-Cre* (KPC)

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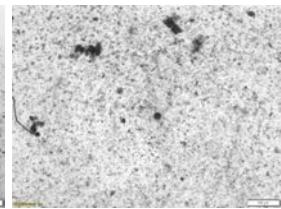
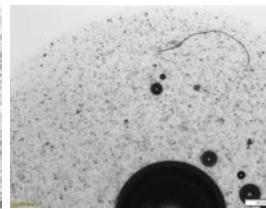
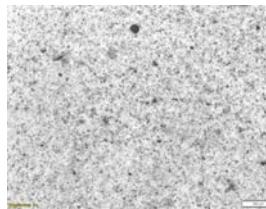
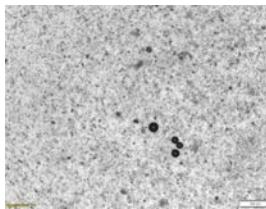
Matrigel 04

Cultrex 83

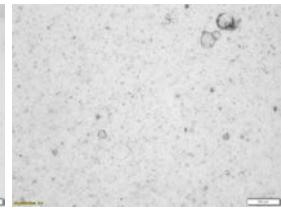
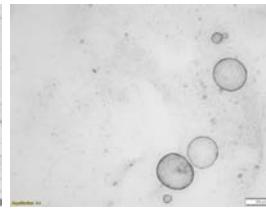
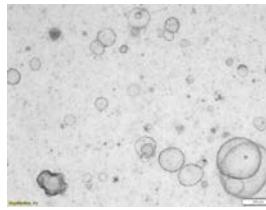
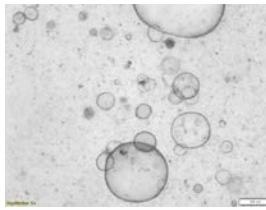
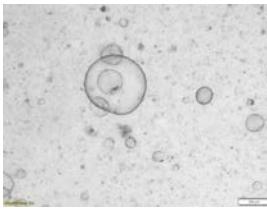
Cultrex 87

UltiMatrix 96

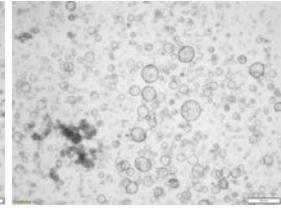
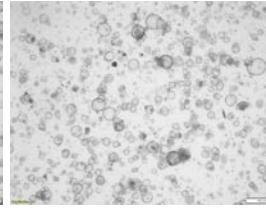
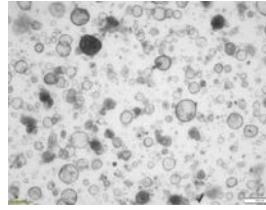
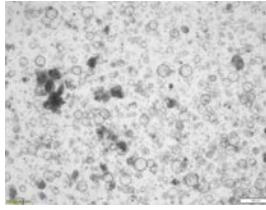
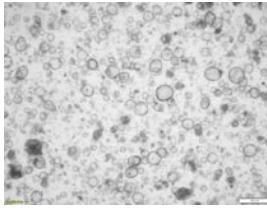
Day 0 p0

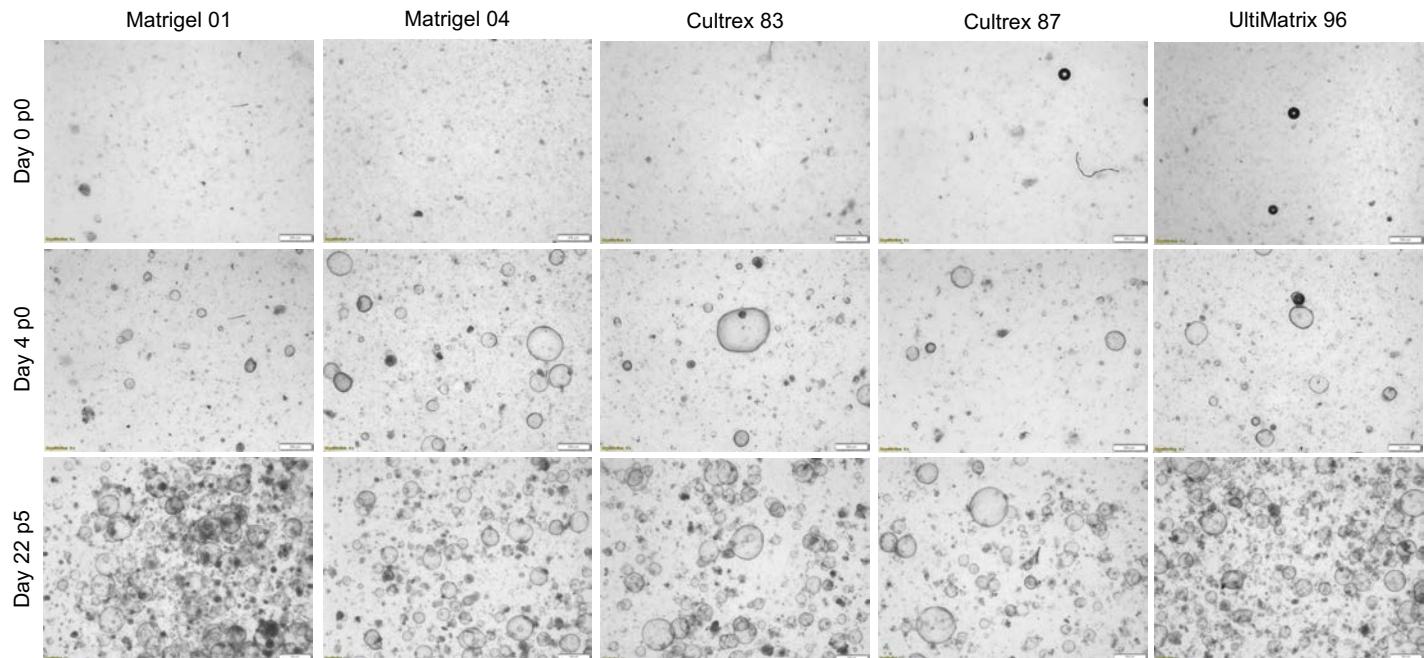


Day 4 p0

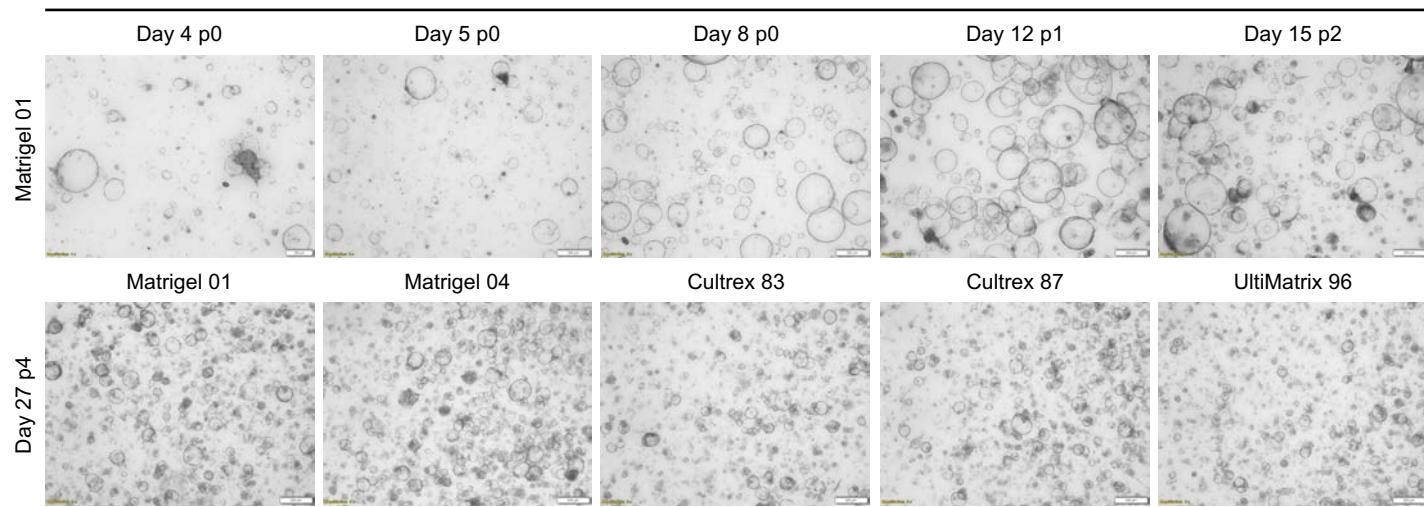


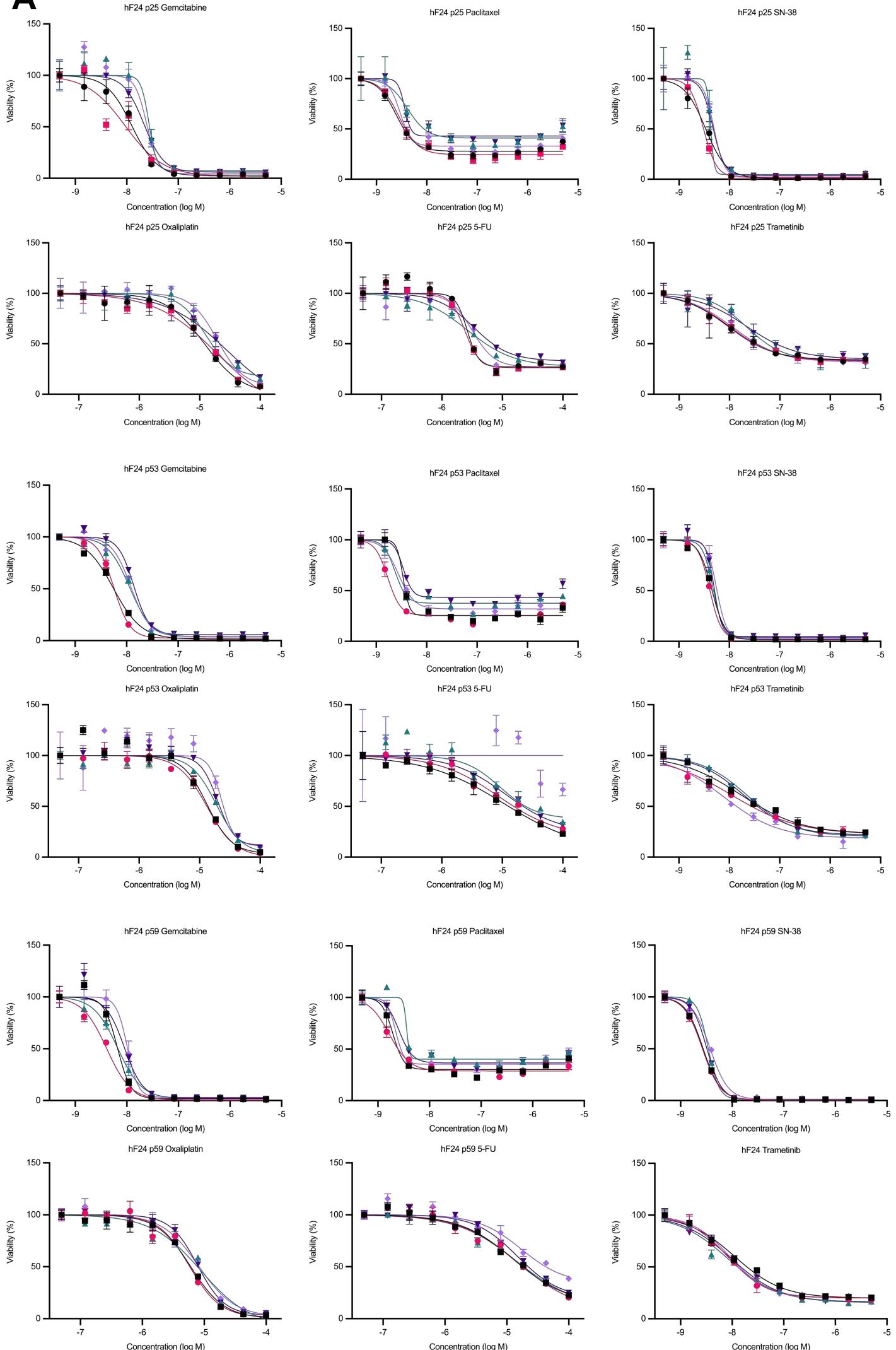
Day 20 p4

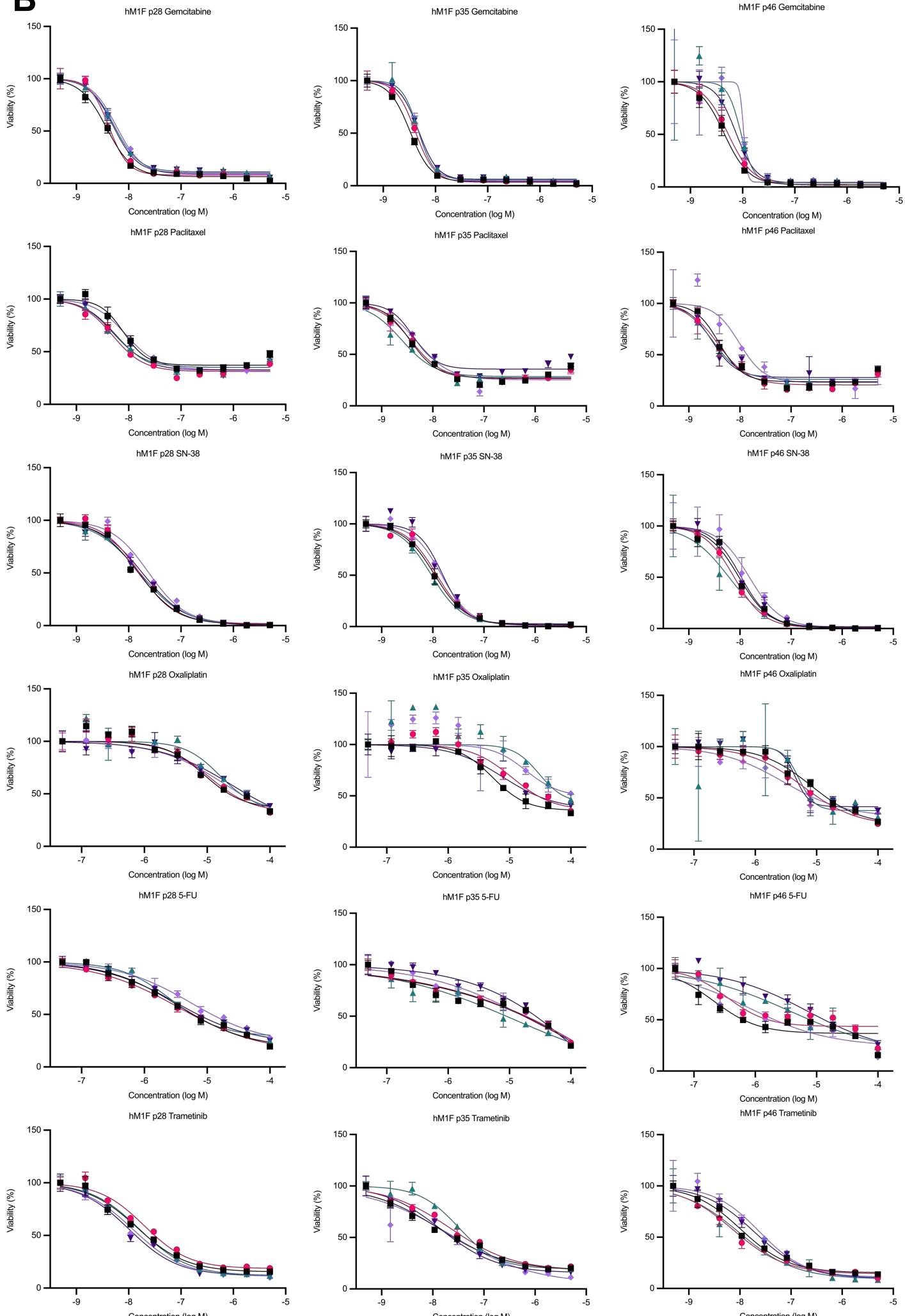
**Supplemental Figure 3A-C**

DA5505 – *LSL-Kras^{G12D/+}; LSL-Trp53R172H/+; Pdx-1-Cre* (KPC)**E**

Human liver metastasis (449)

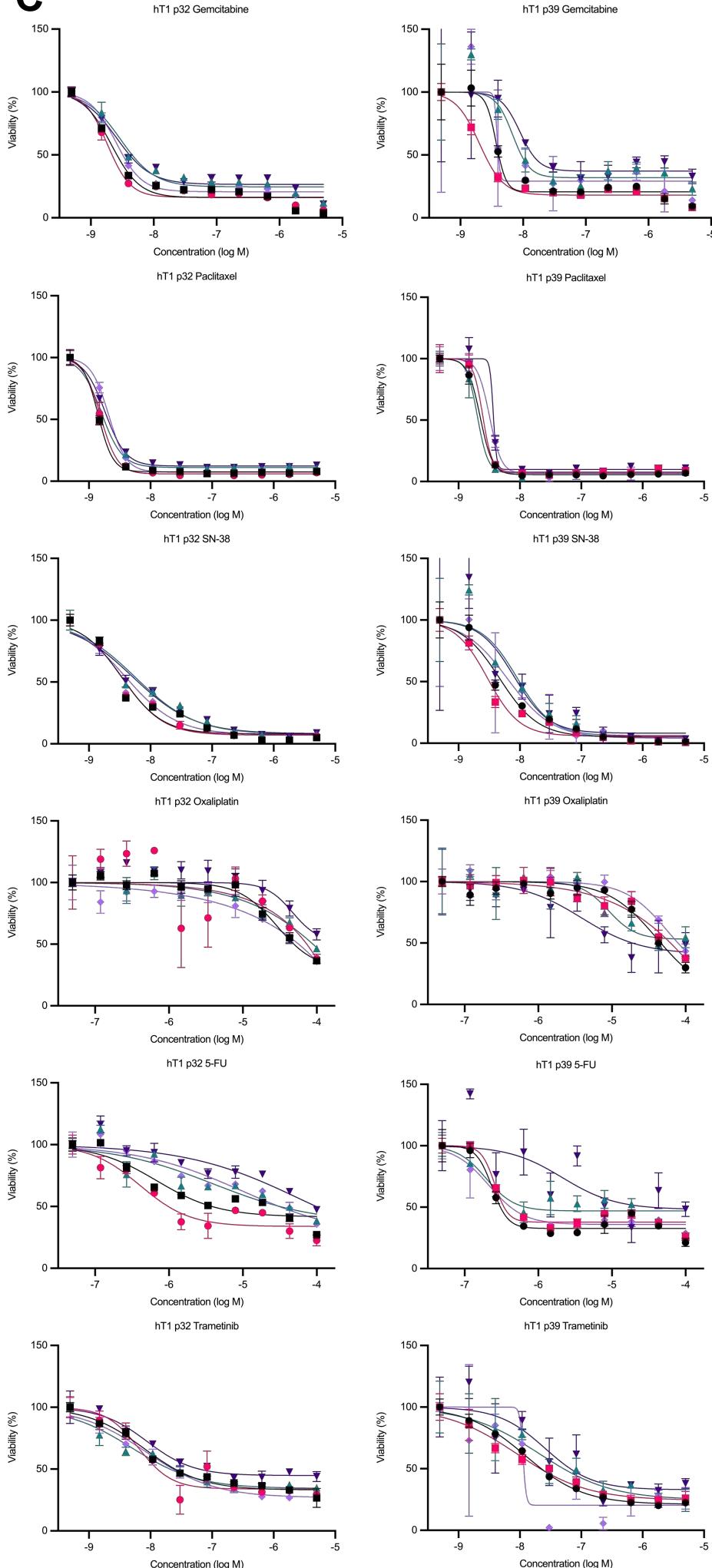
**Supplemental Figure 3D-E**

A**Supplemental Figure 4A**

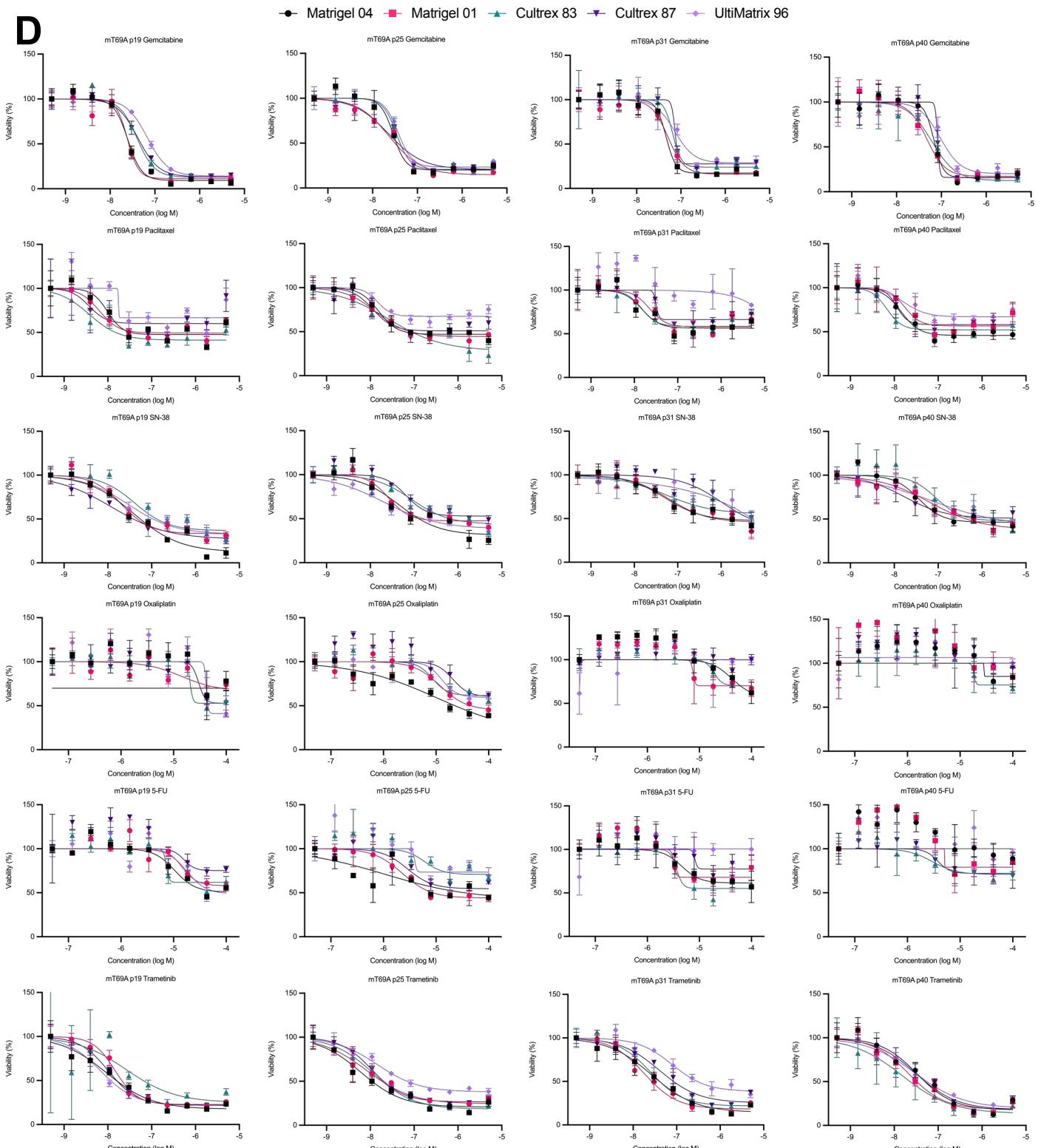
B**Supplemental Figure 4B**

C

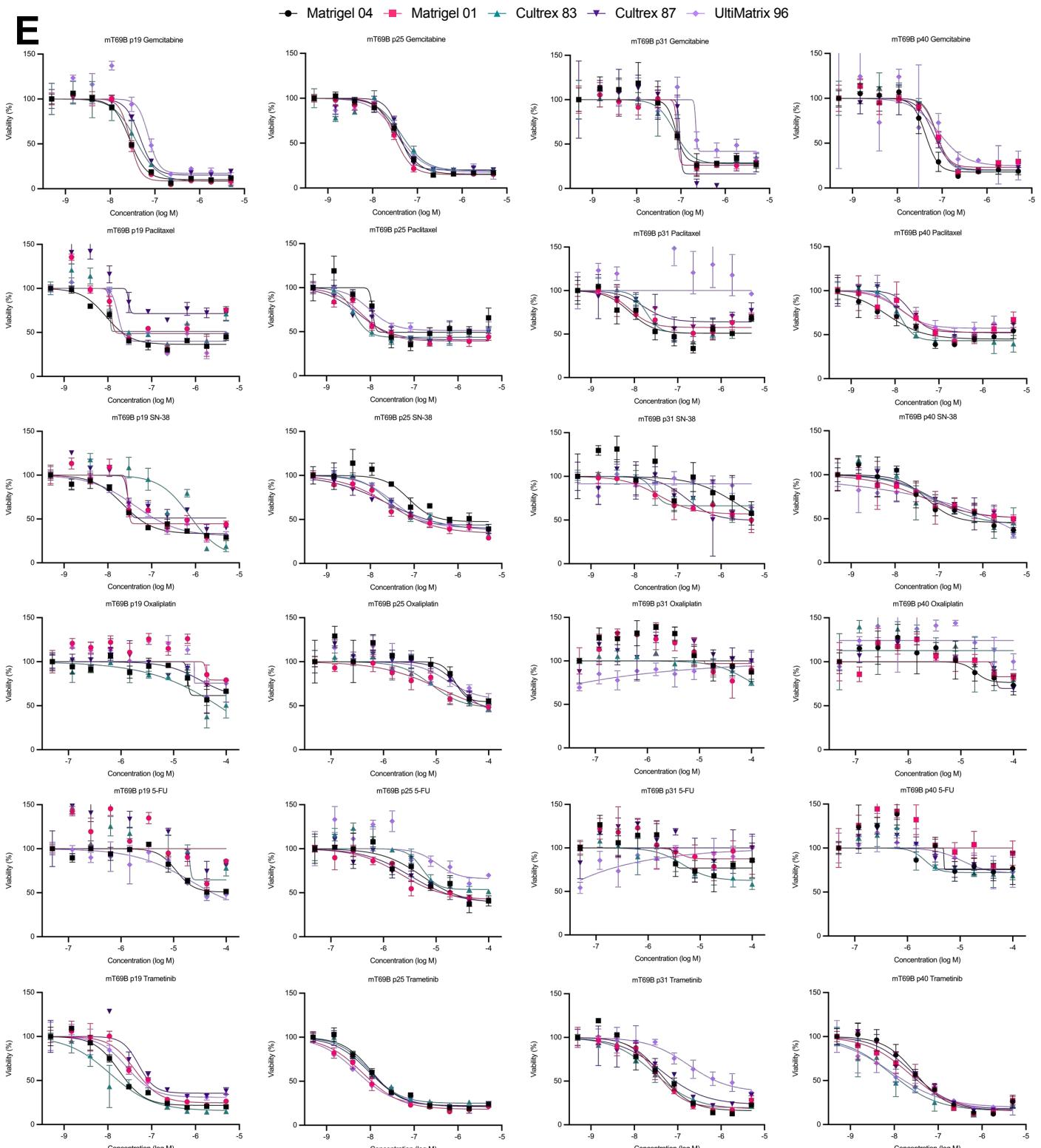
● Matrigel 04 ■ Matrigel 01 ▲ Cultrex 83 ▼ Cultrex 87 △ UltiMatrix 96



Supplemental Figure 4C



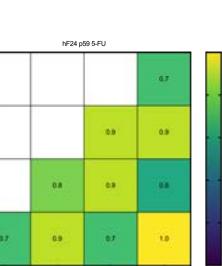
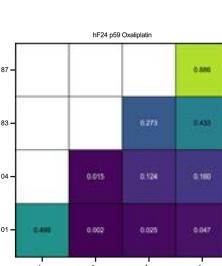
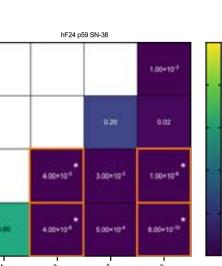
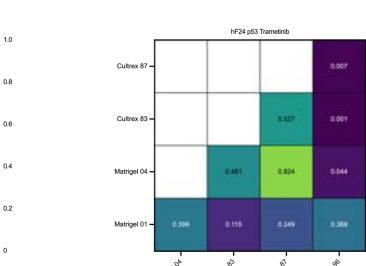
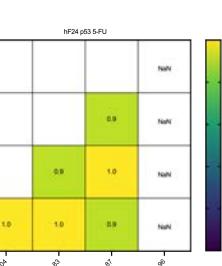
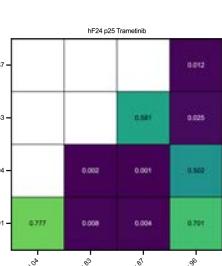
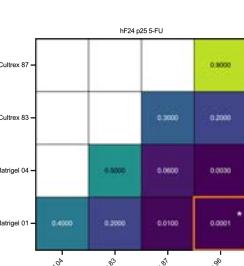
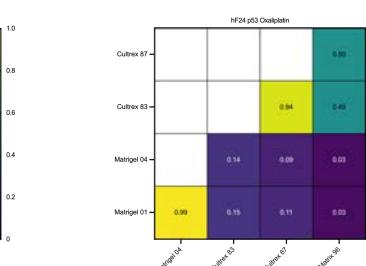
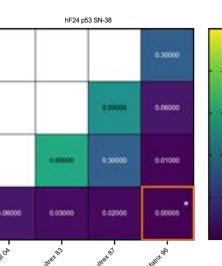
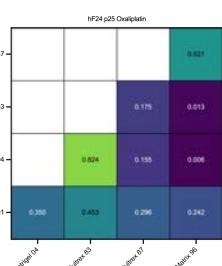
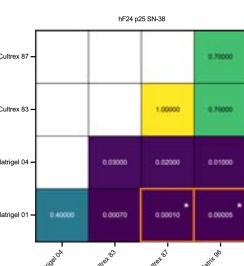
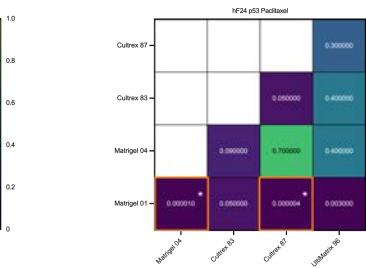
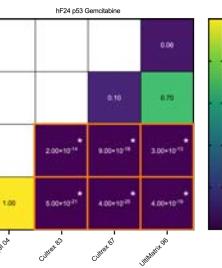
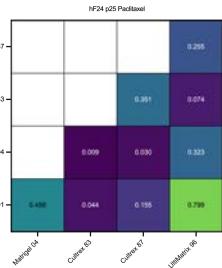
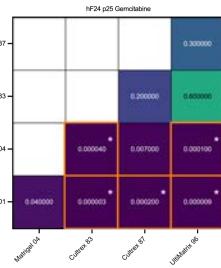
Supplemental Figure 4D



Supplemental Figure 4E

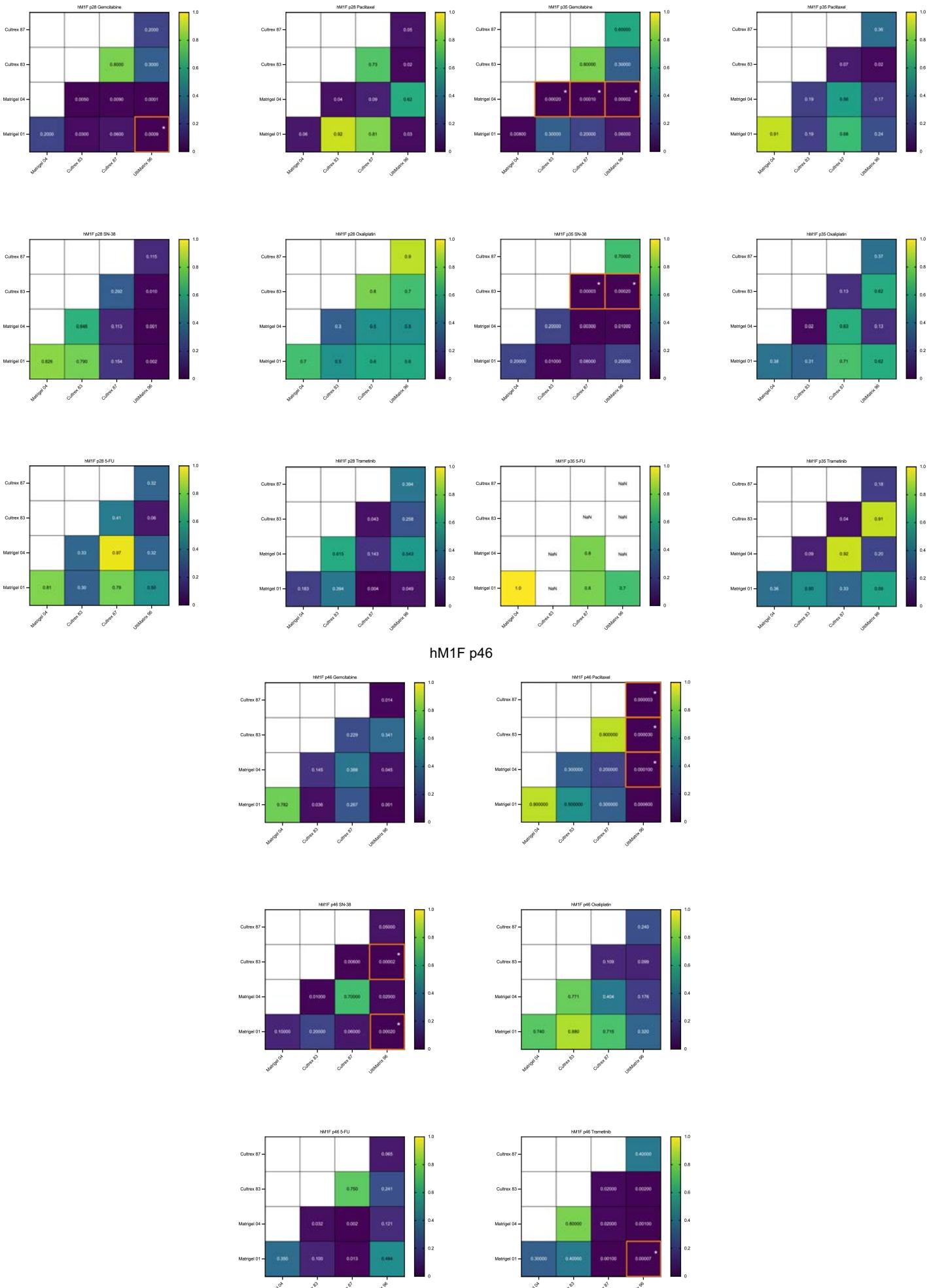
A

hF24 p25



B

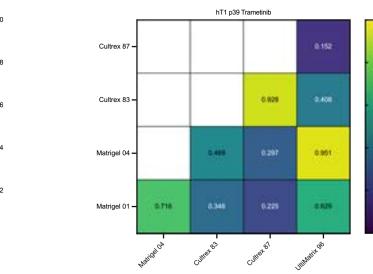
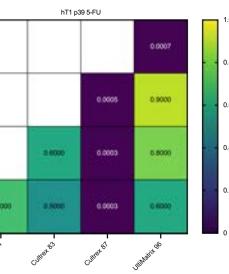
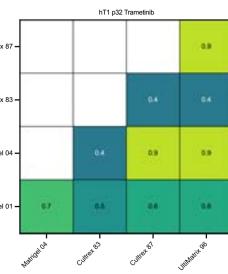
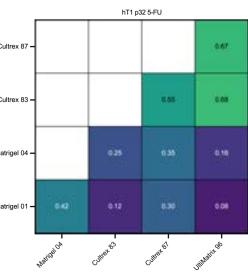
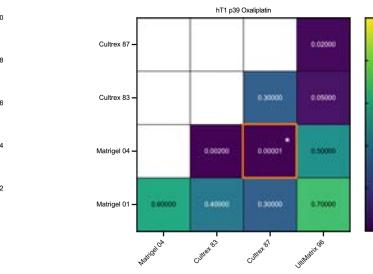
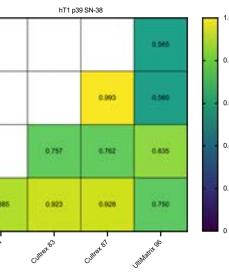
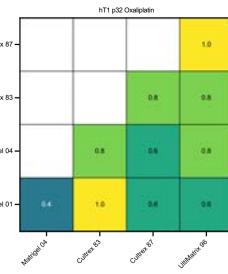
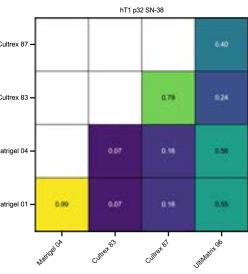
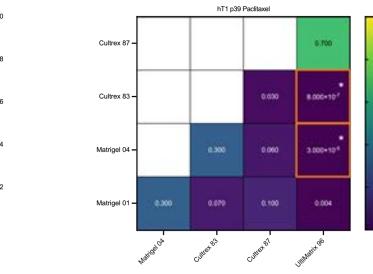
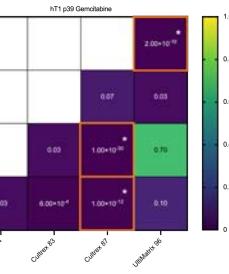
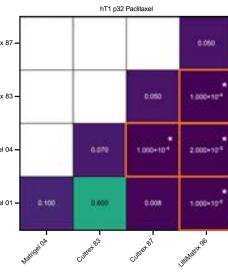
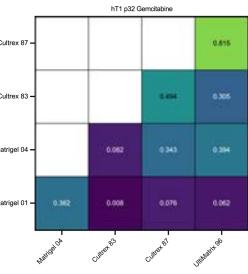
hM1F p28



Supplemental Figure 5B – IC50

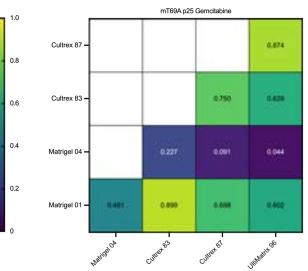
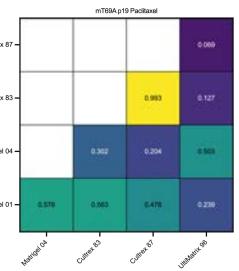
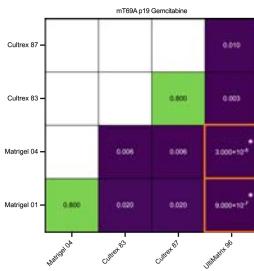
C

hT1 p32

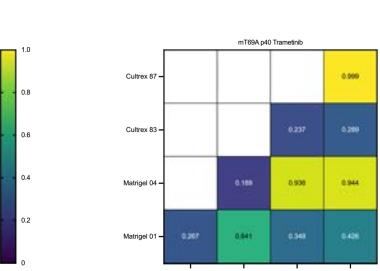
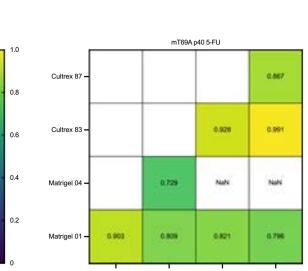
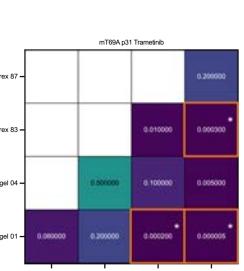
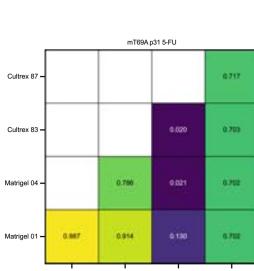
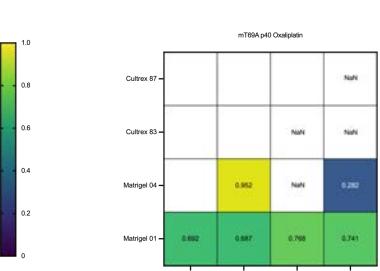
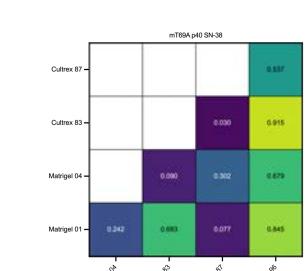
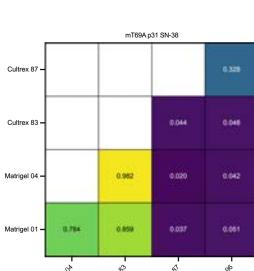
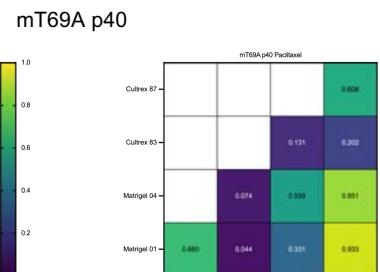
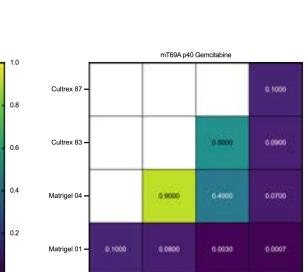
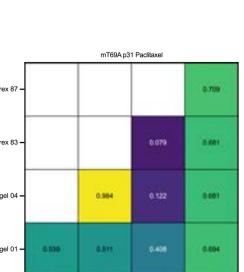
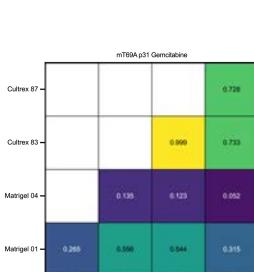
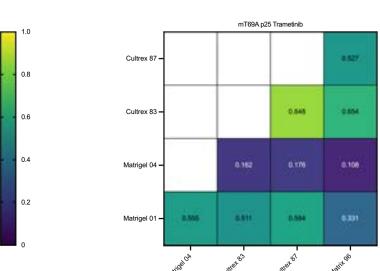
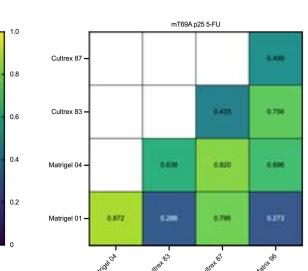
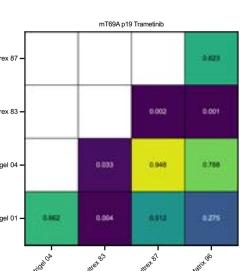
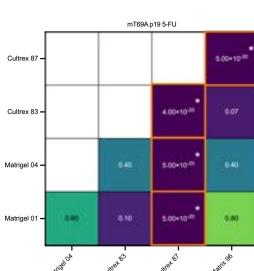
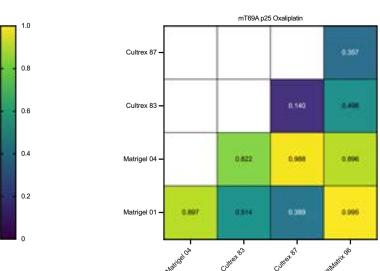
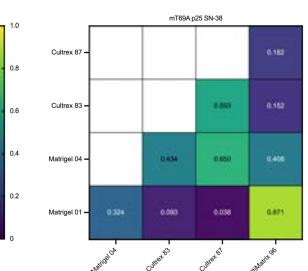
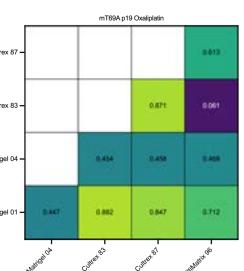
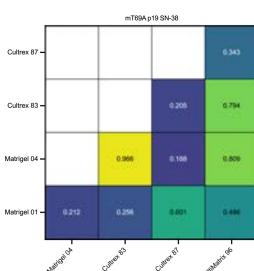
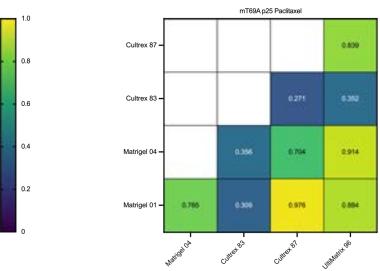


D

mT69A p19



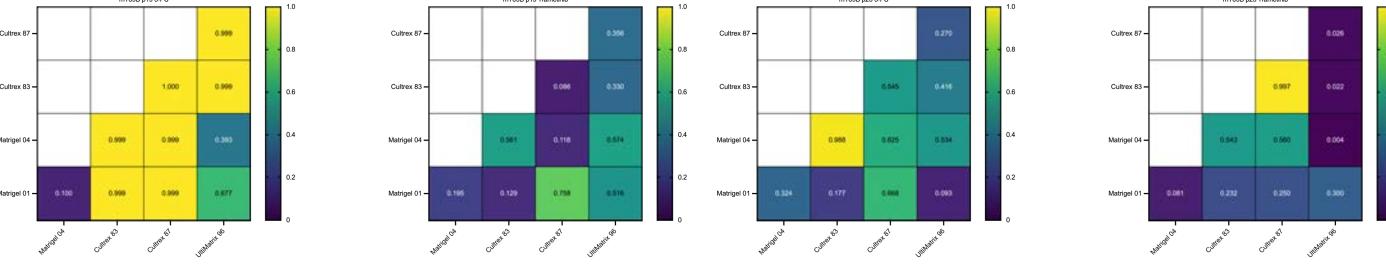
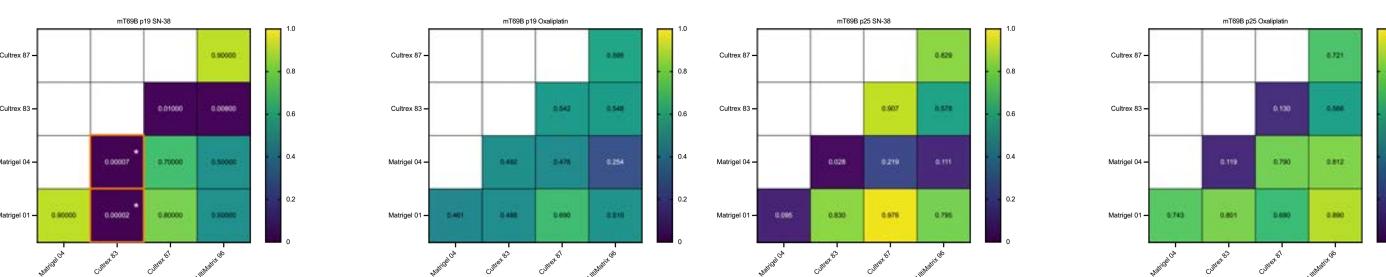
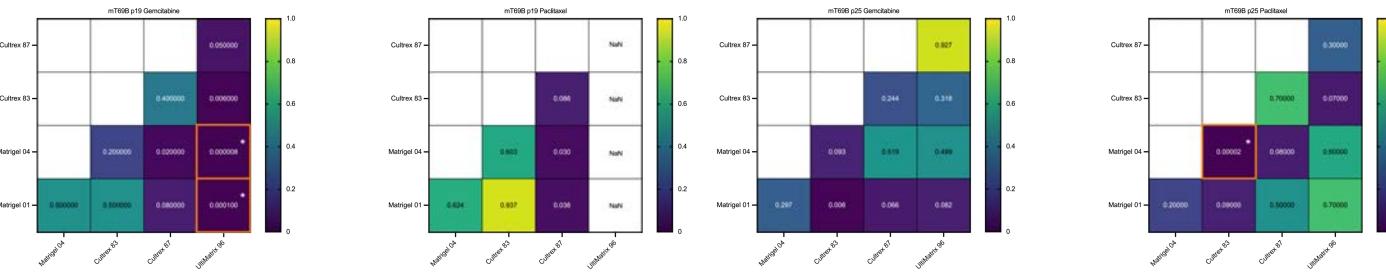
mT69A p25



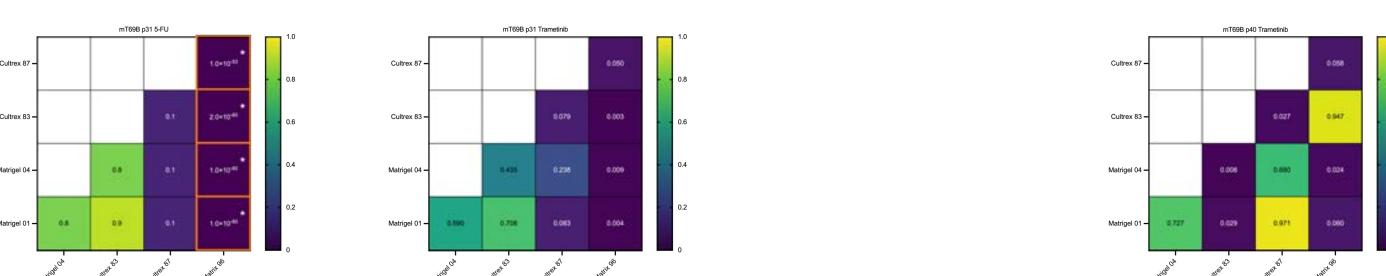
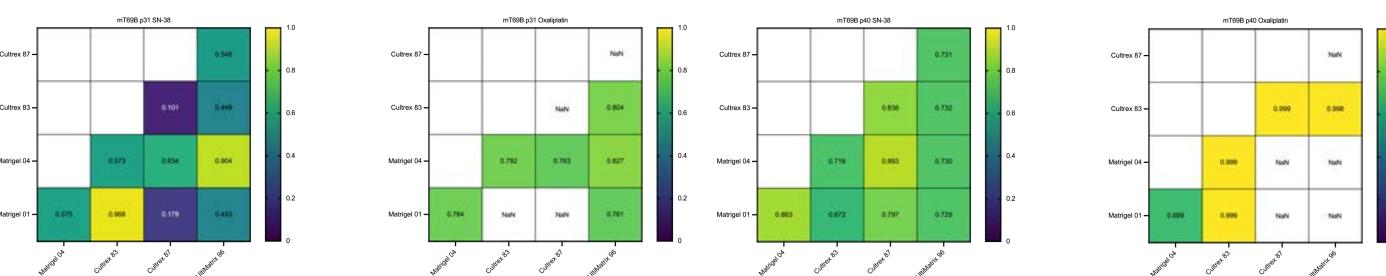
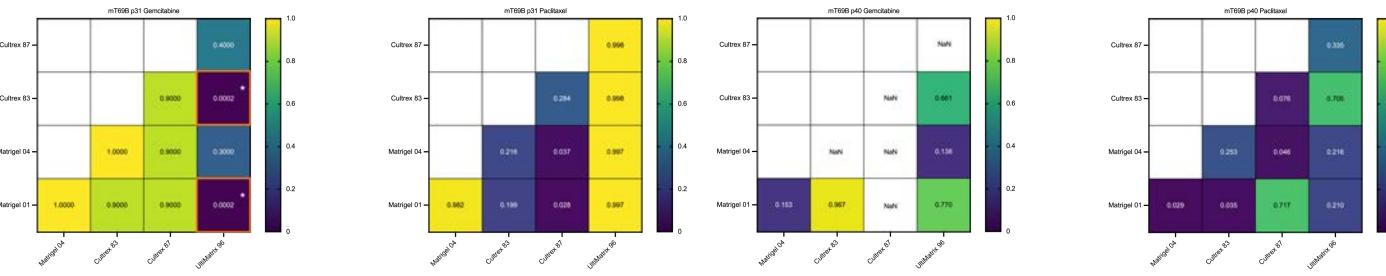
Supplemental Figure 5D – IC50

E

mT69B p19



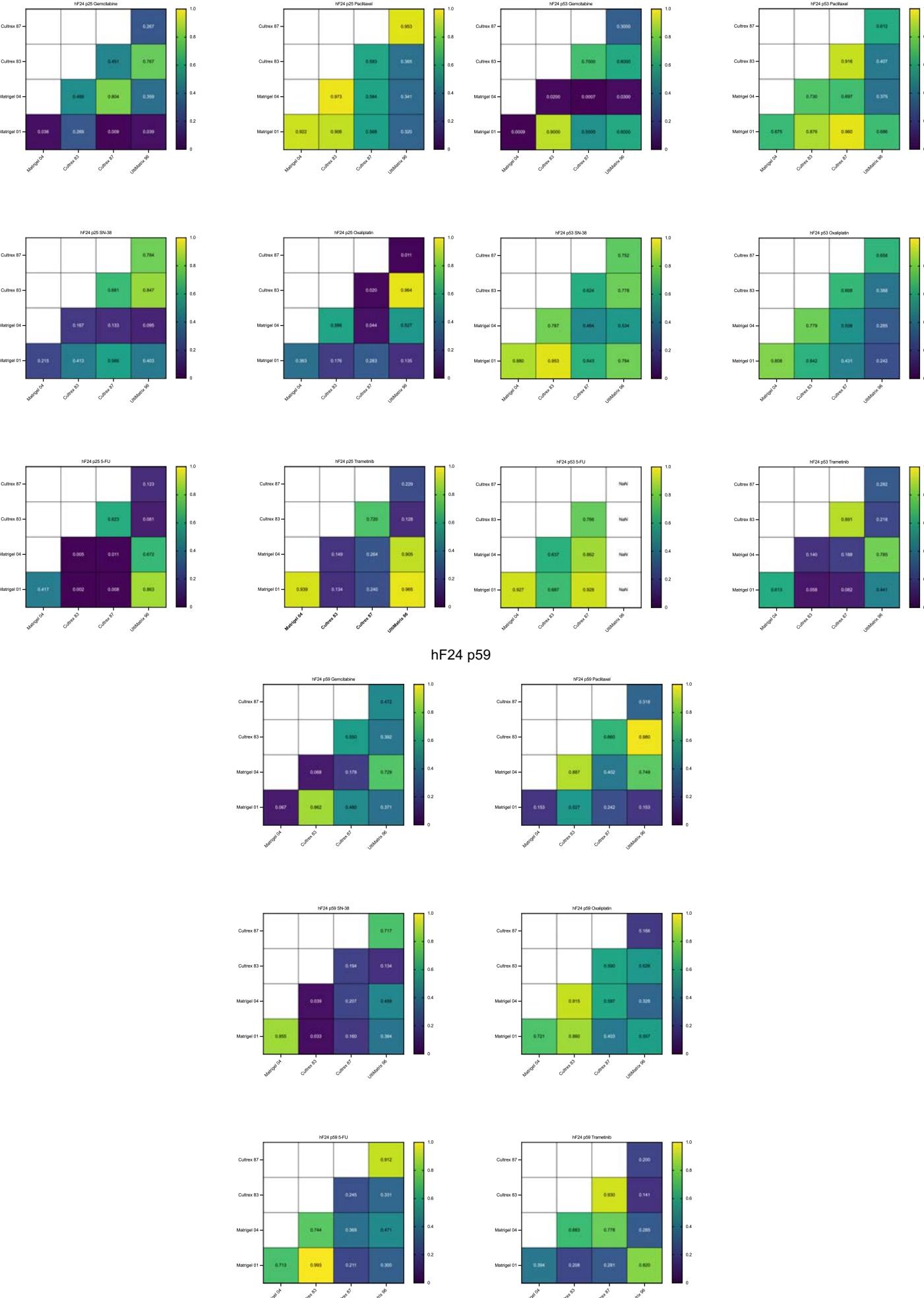
mT69B p31



Supplemental Figure 5E – IC50

A

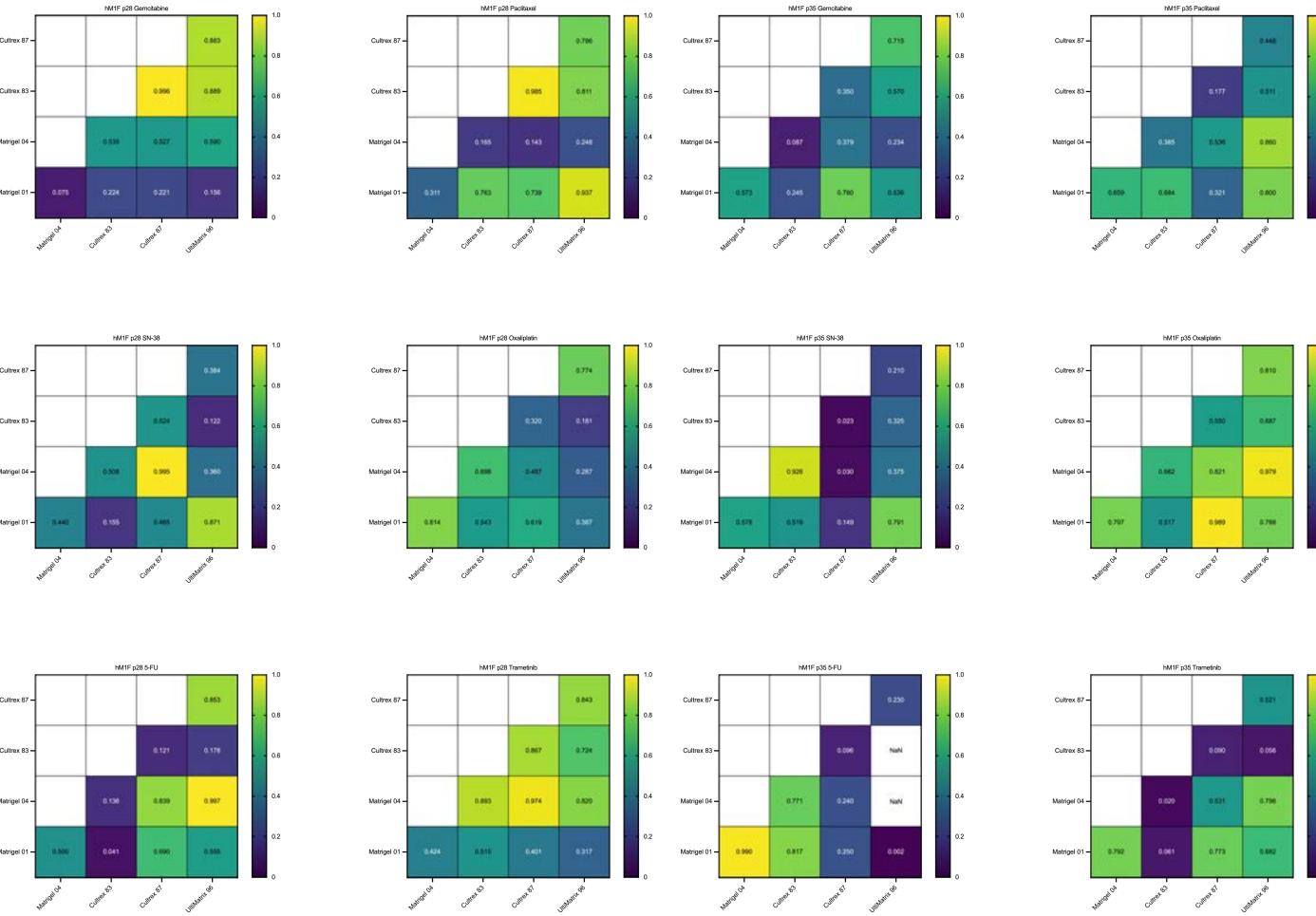
hF24 p25



Supplemental Figure 6A – Hill Slope

B

hM1F p28



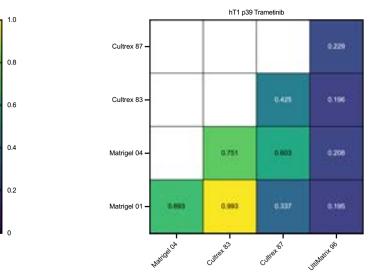
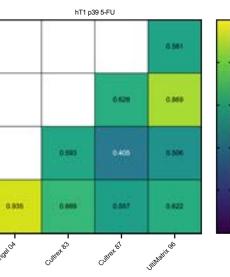
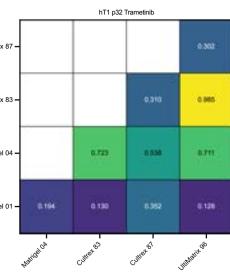
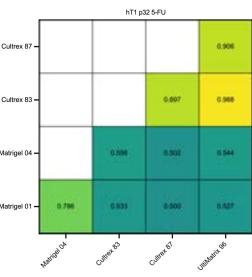
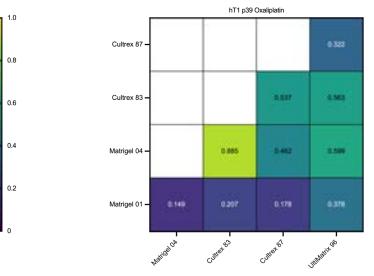
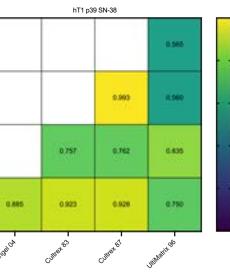
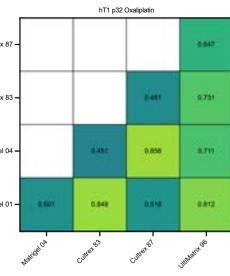
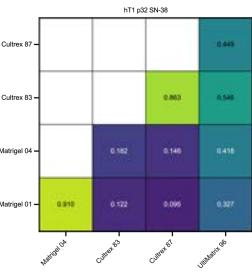
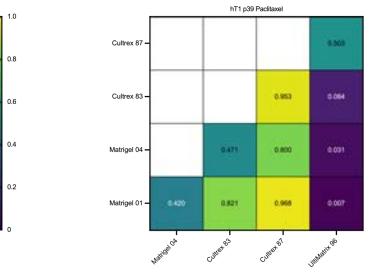
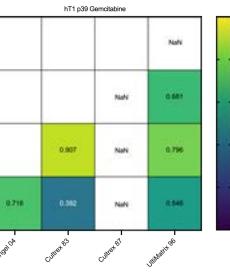
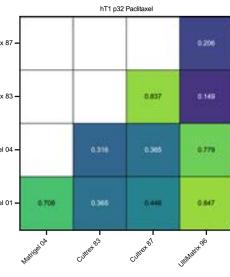
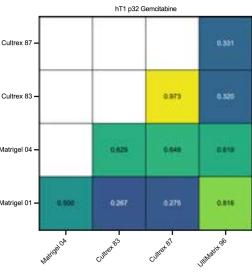
hM1F p46



Supplemental Figure 6B – Hill Slope

C

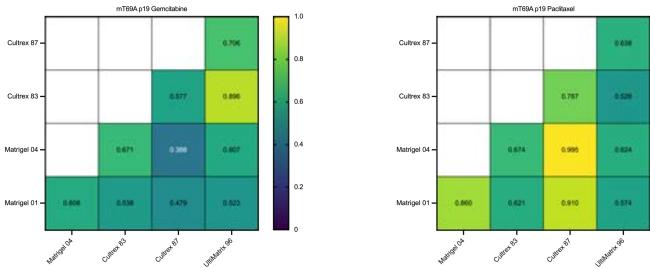
hT1 p32



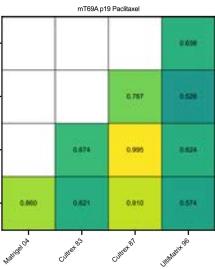
Supplemental Figure 6C – Hill Slope

D

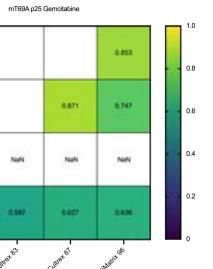
mT69A p19



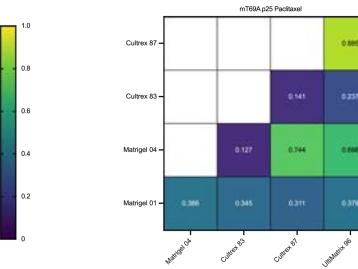
mT69A p19



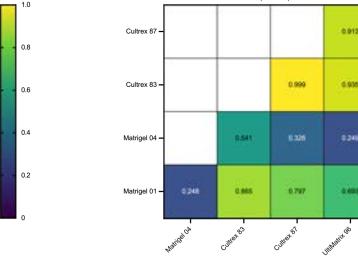
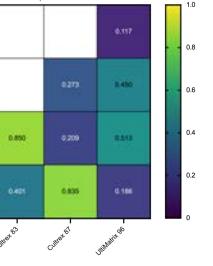
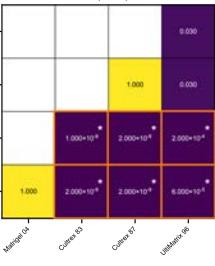
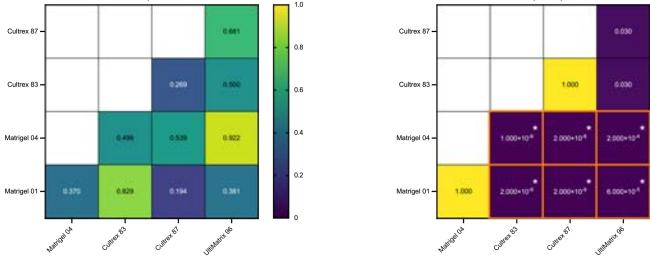
mT69A p25



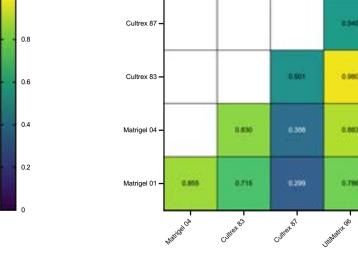
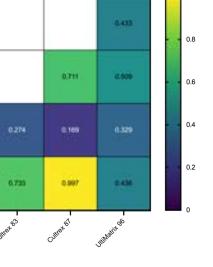
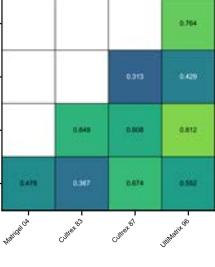
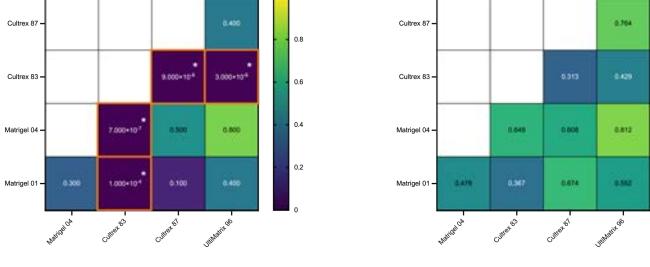
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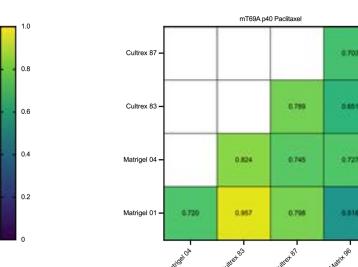
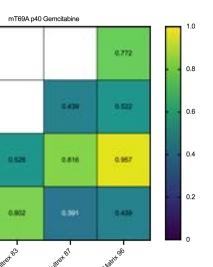
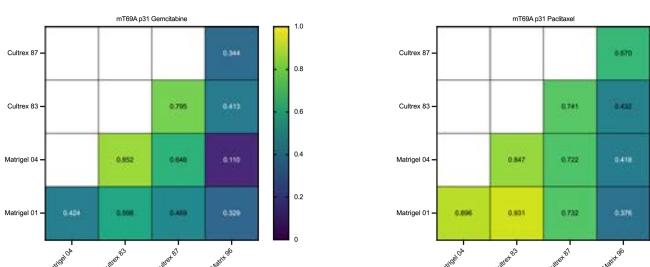
mT69A p19 SN-38



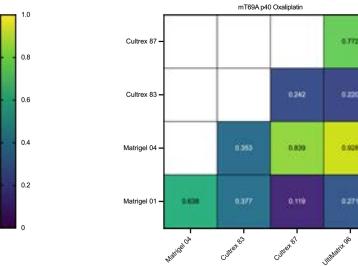
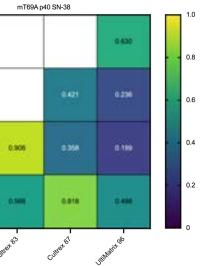
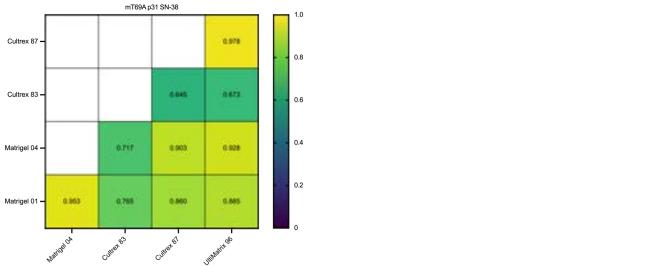
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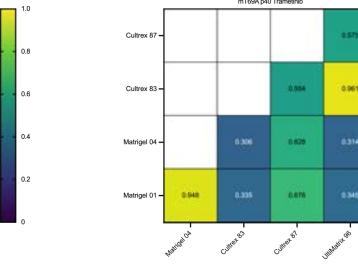
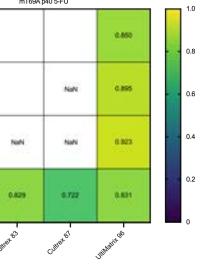
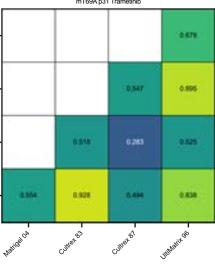
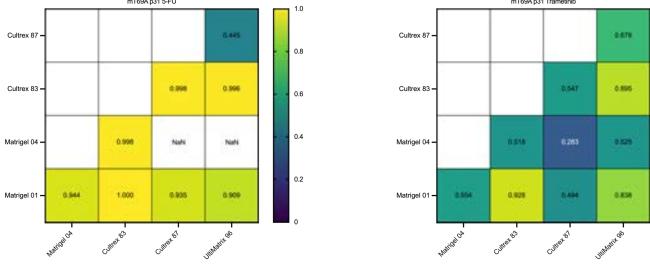
mT69A p31



mT69A p31 SN-38



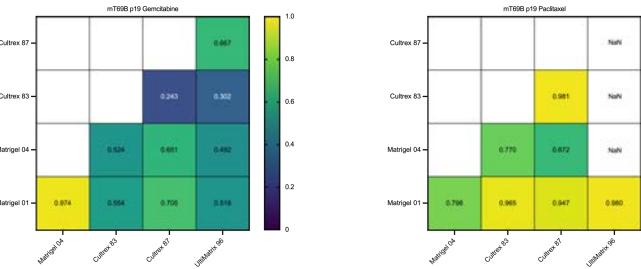
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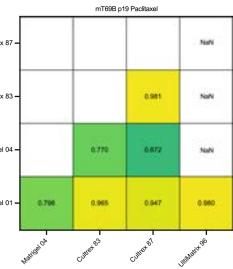
Supplemental Figure 6D – Hill Slope

E

mT69B p19

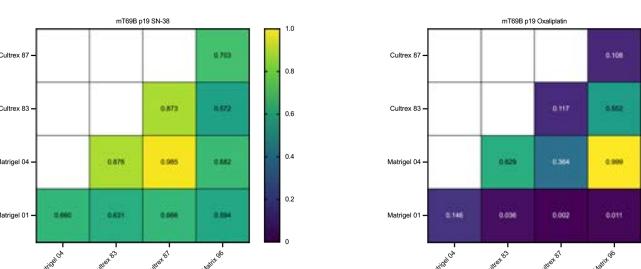


mT69B p19

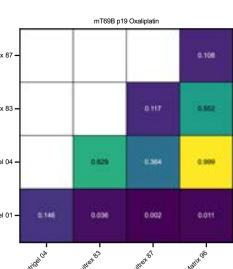


mT69B p25

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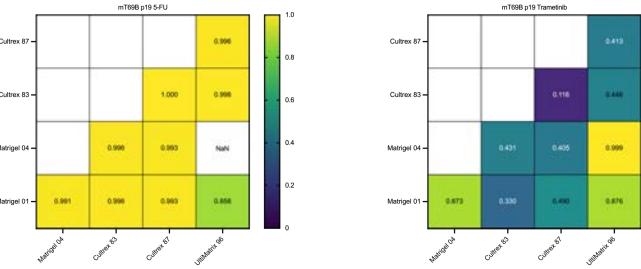


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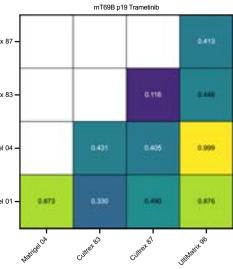


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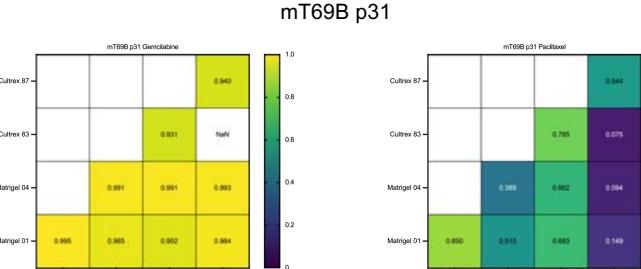


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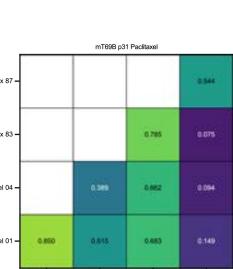


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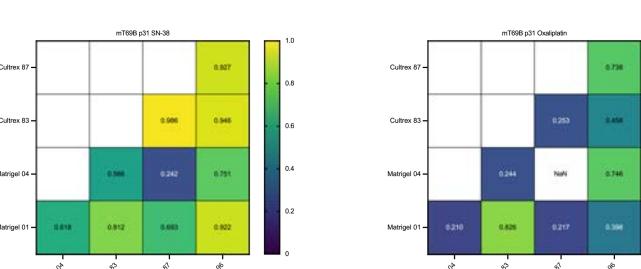


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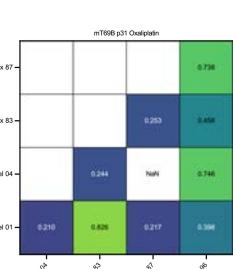


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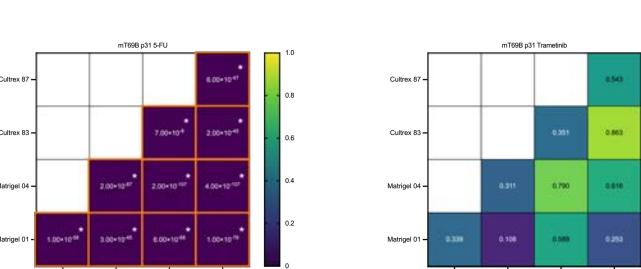


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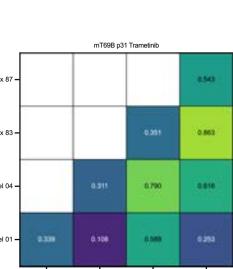


mT69B p40

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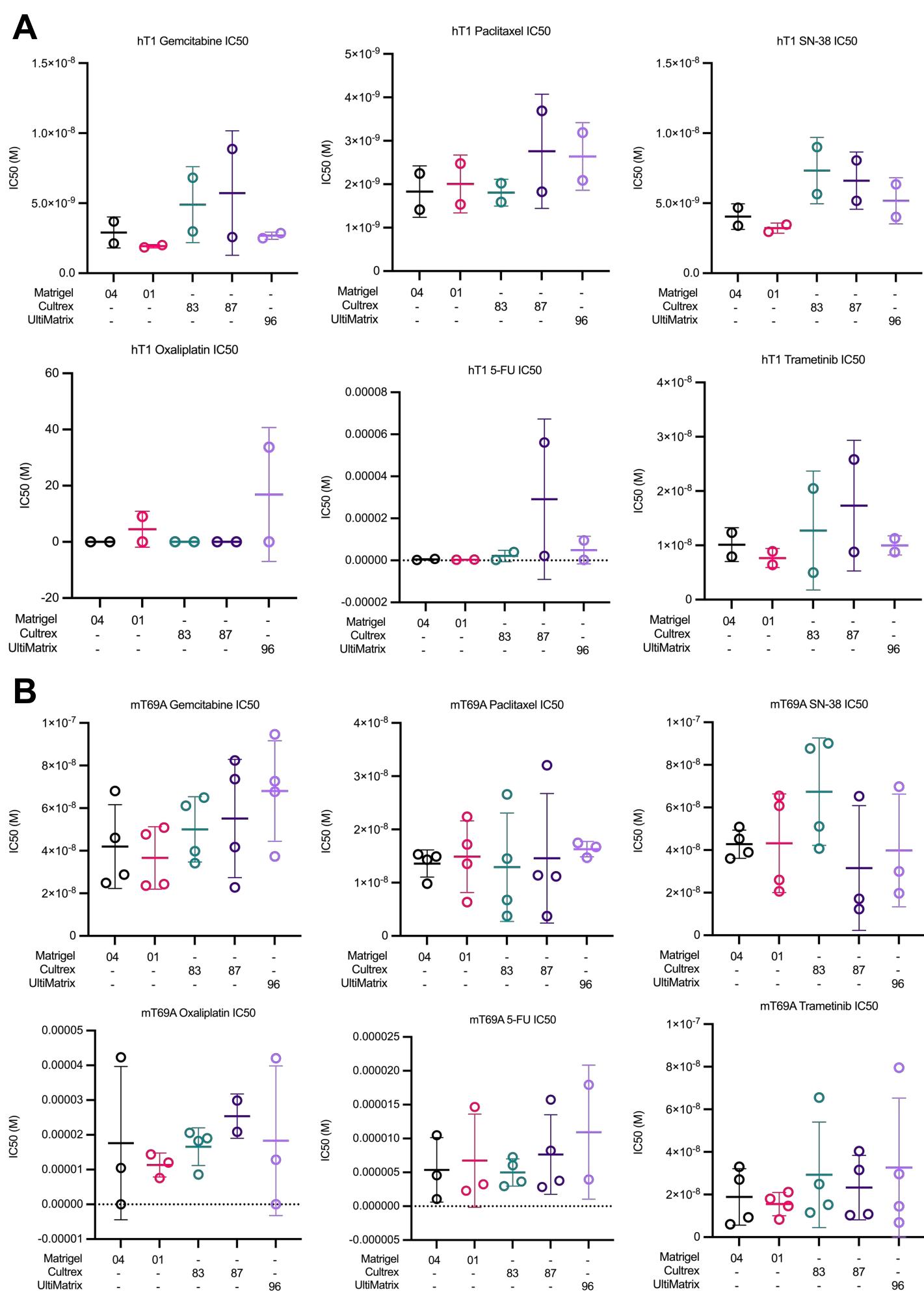


mT69B p31



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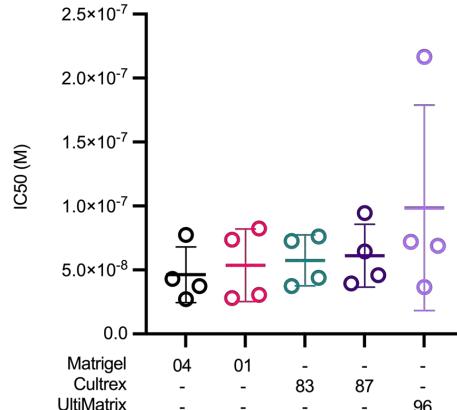
Supplemental Figure 6E – Hill Slope



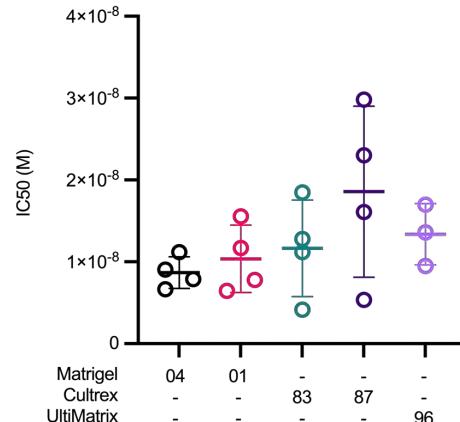
Supplemental Figure 7A-B

C

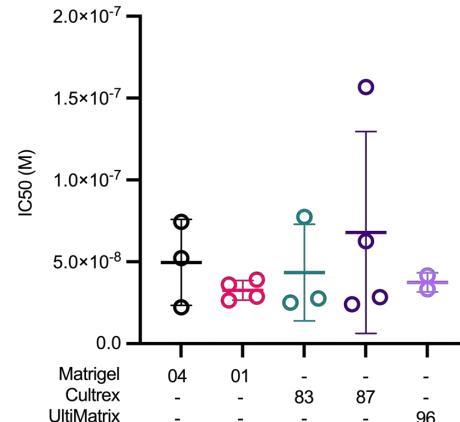
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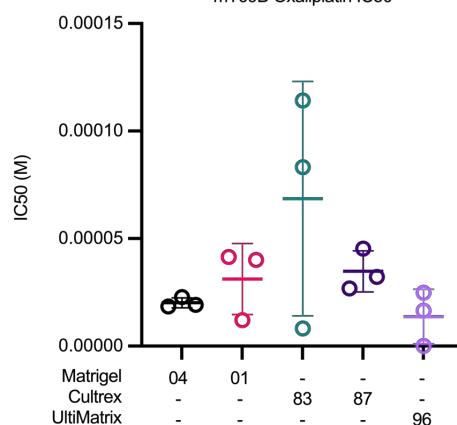
mT69B Paclitaxel IC50



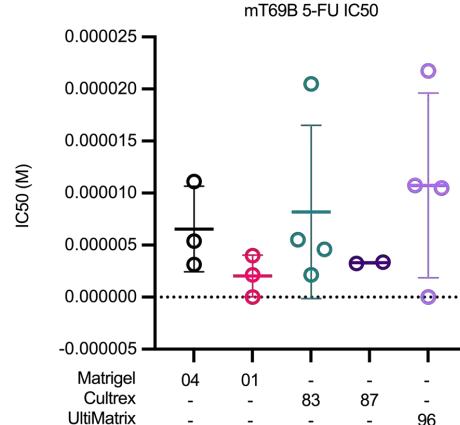
mT69B SN-38 IC50



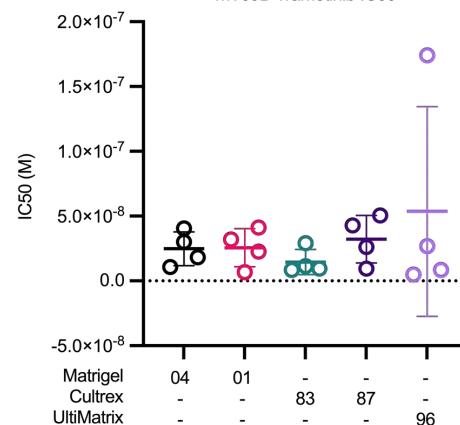
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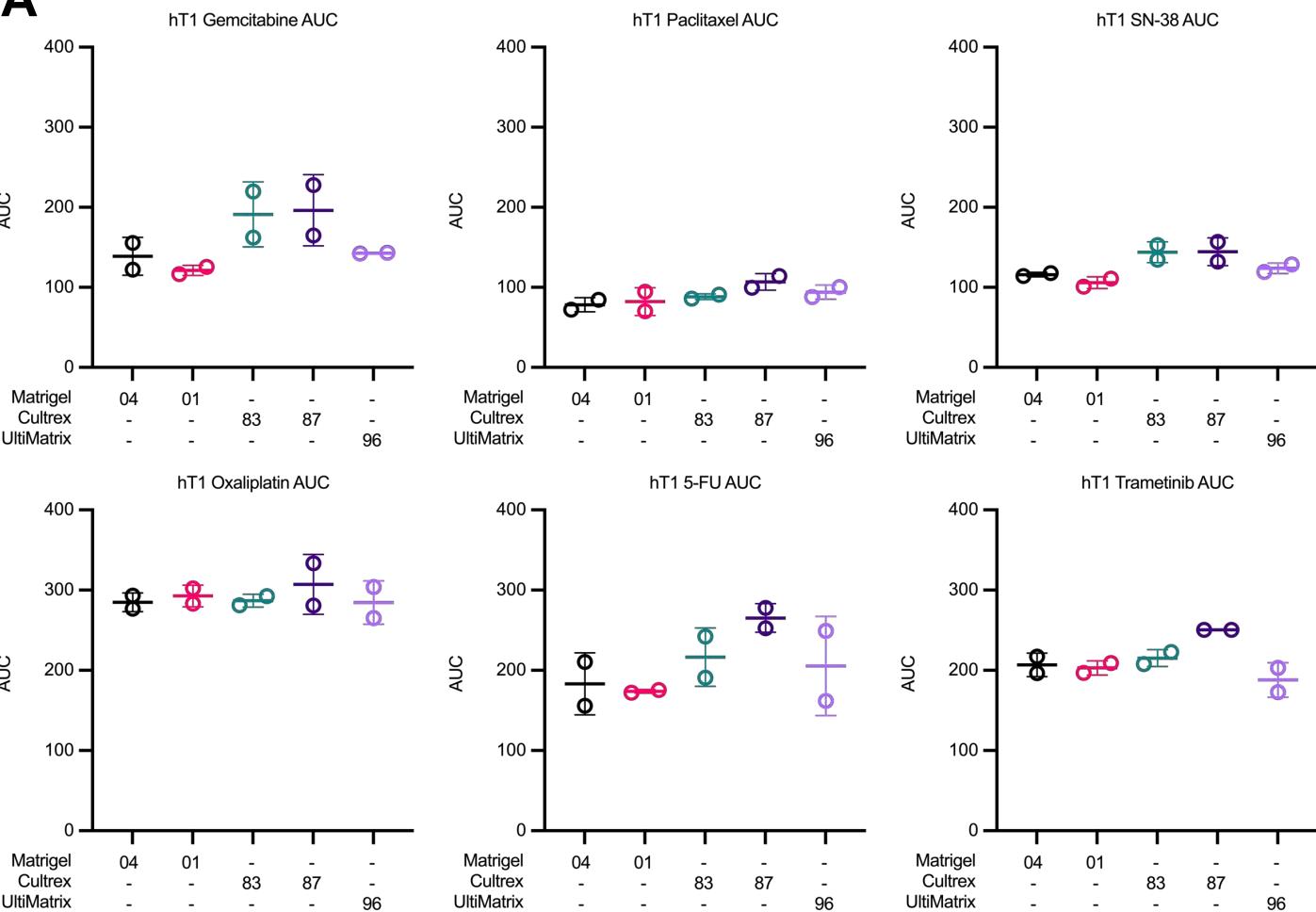
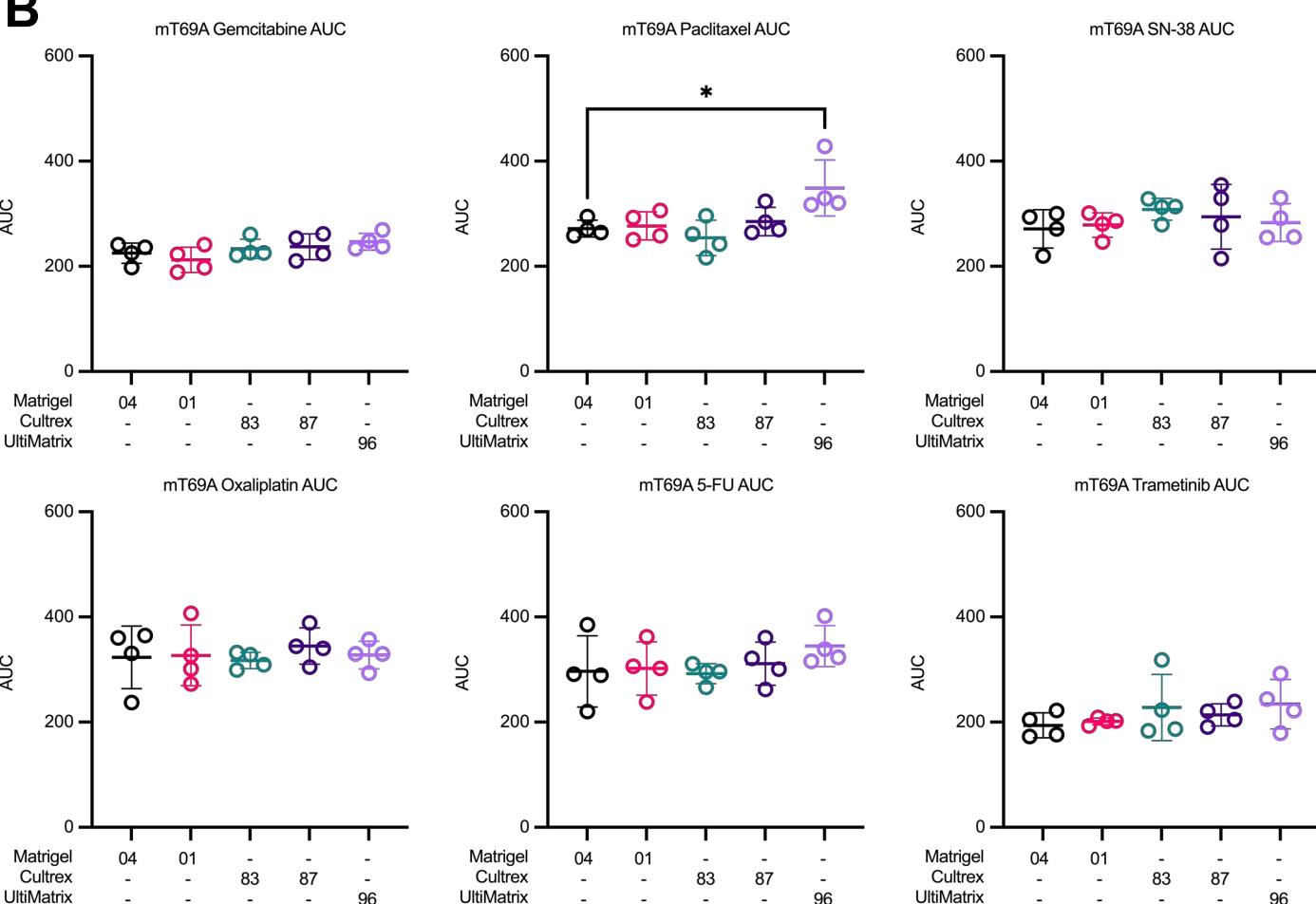


mT69B 5-FU IC50



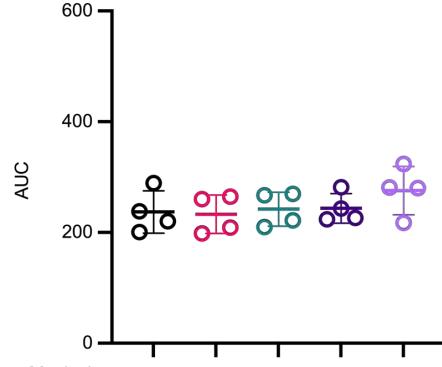
mT69B Trametinib IC50



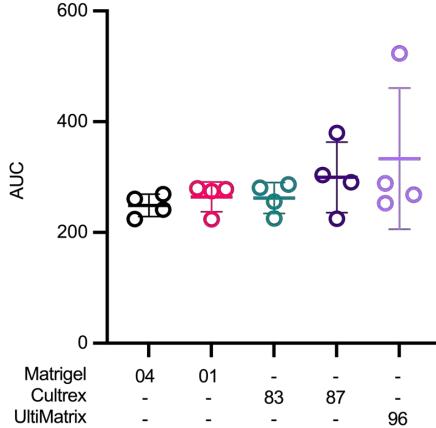
A**B****Supplemental Figure 8A-B**

C

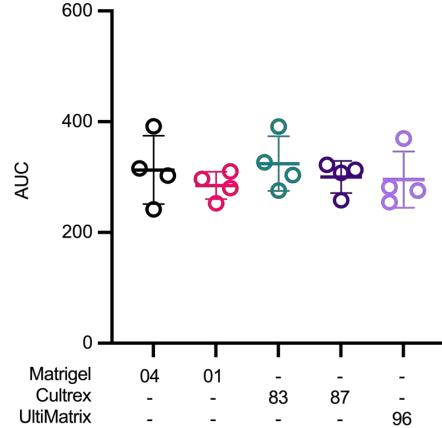
mT69B Gemcitabine AUC



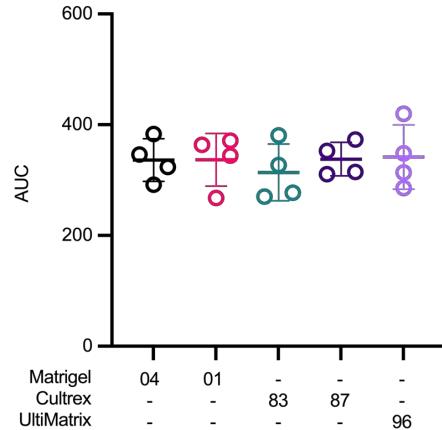
mT69B Paclitaxel AUC



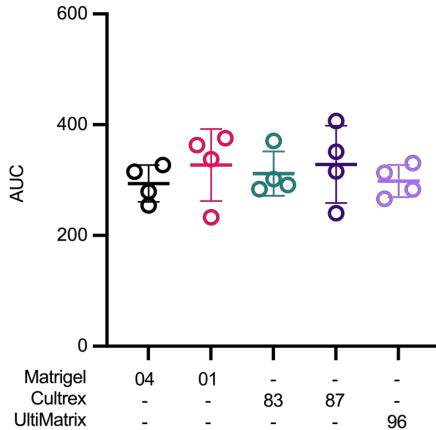
mT69B SN-38 AUC



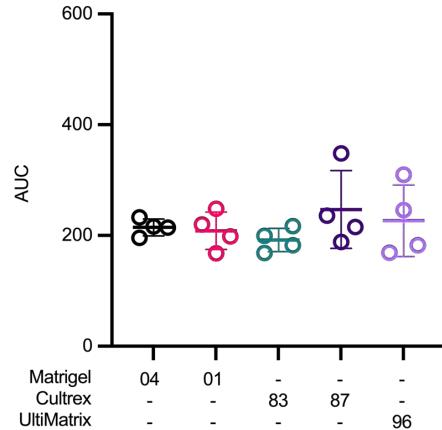
mT69B Oxaliplatin AUC

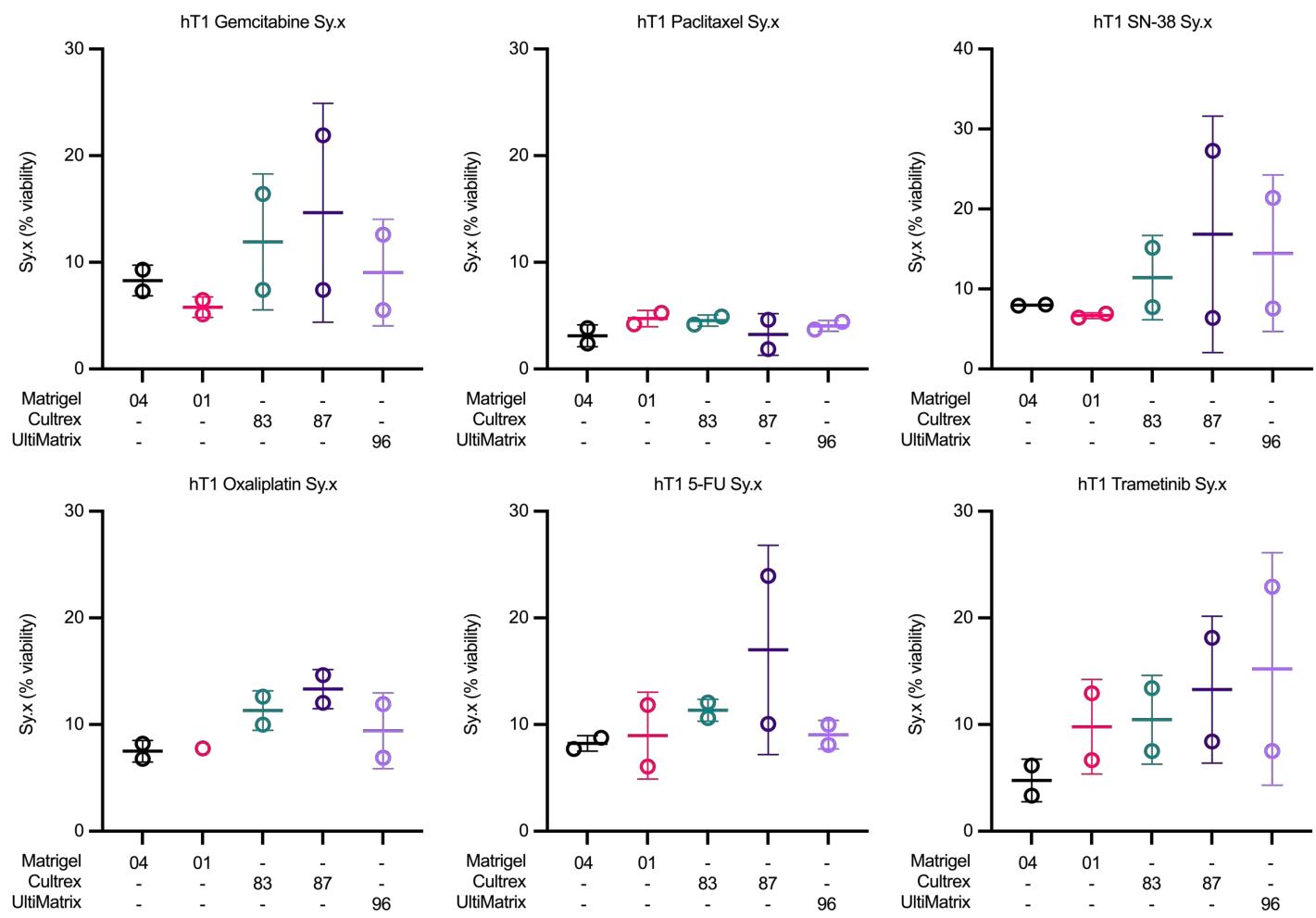


mT69B 5-FU AUC

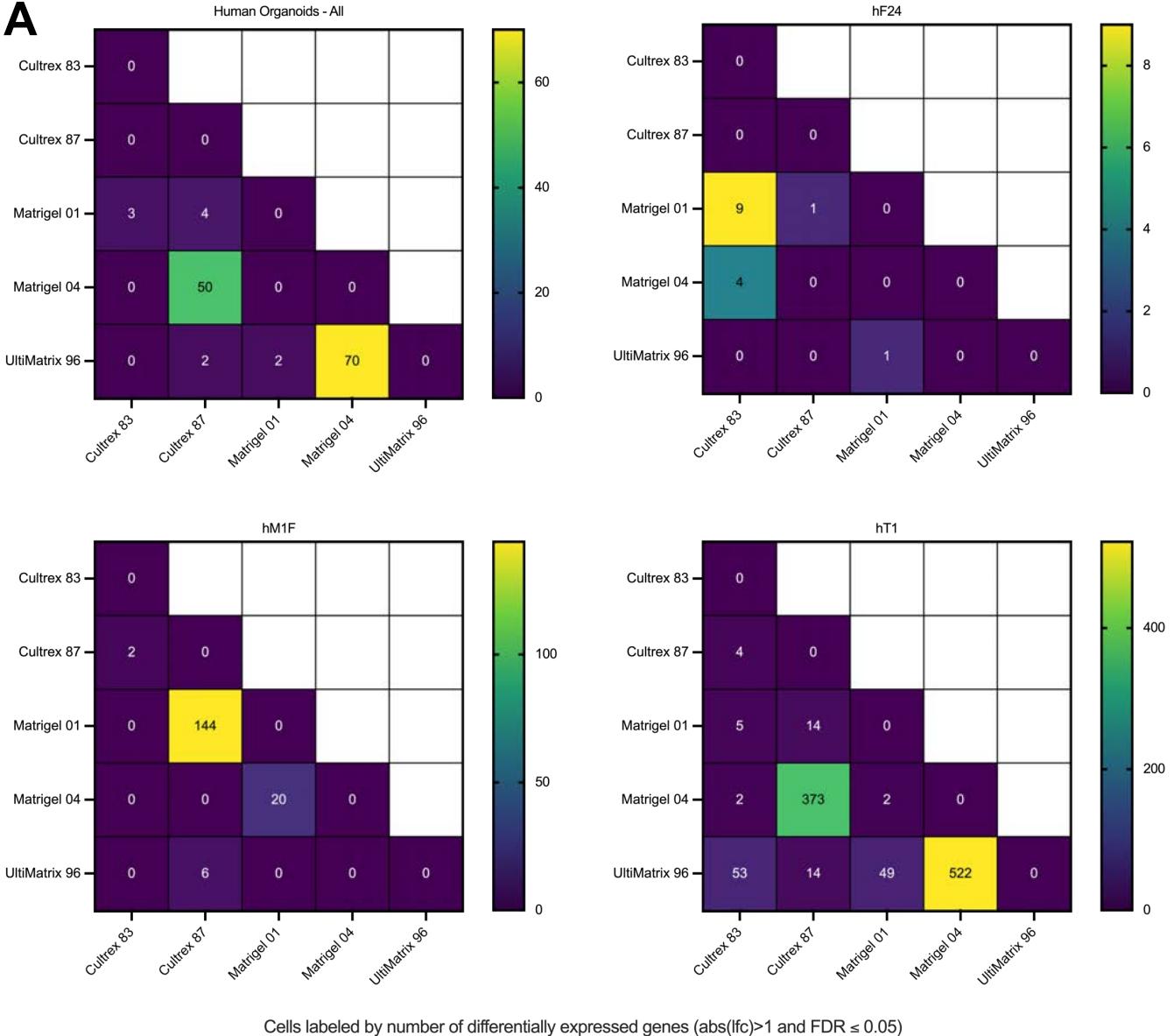
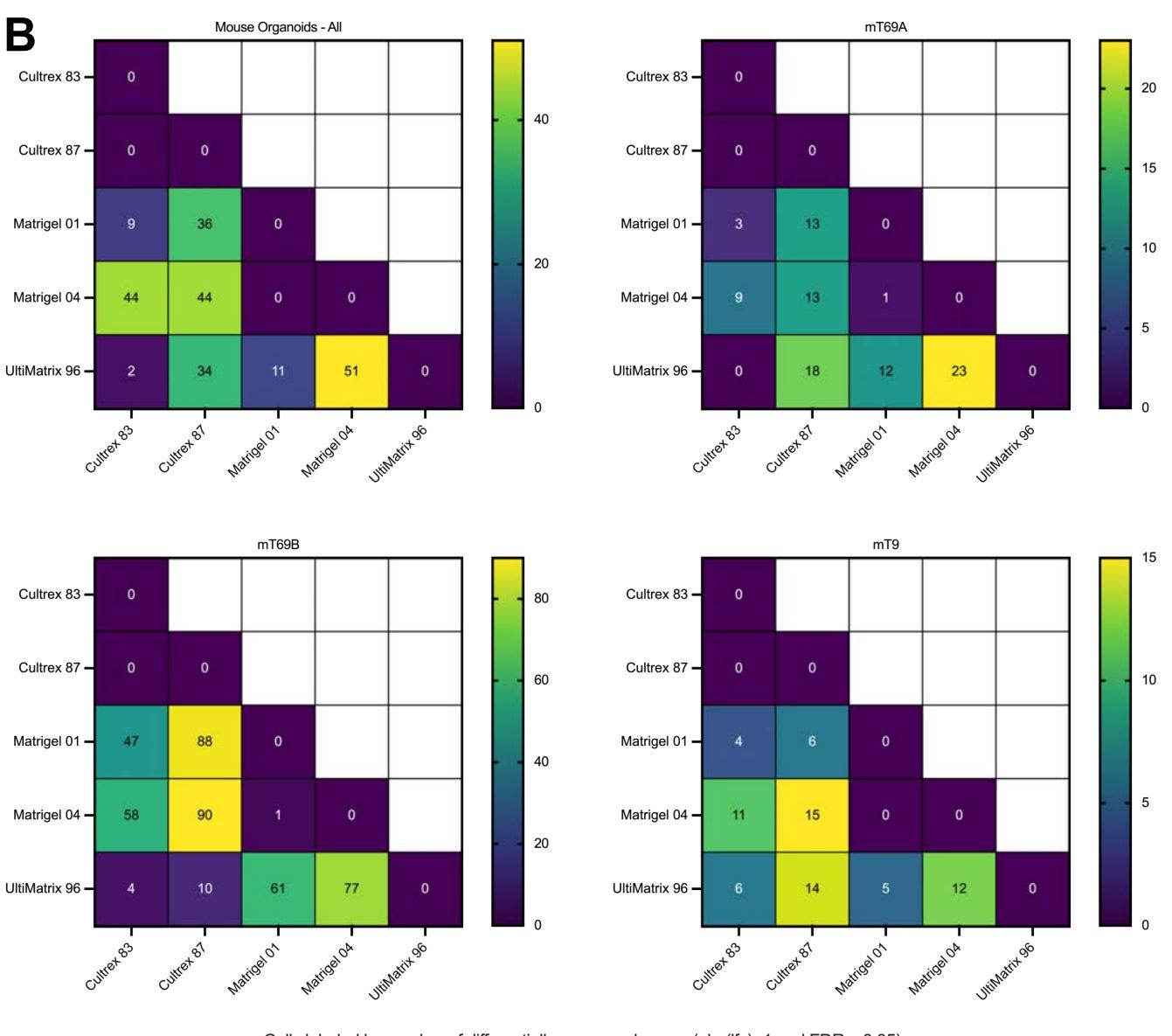


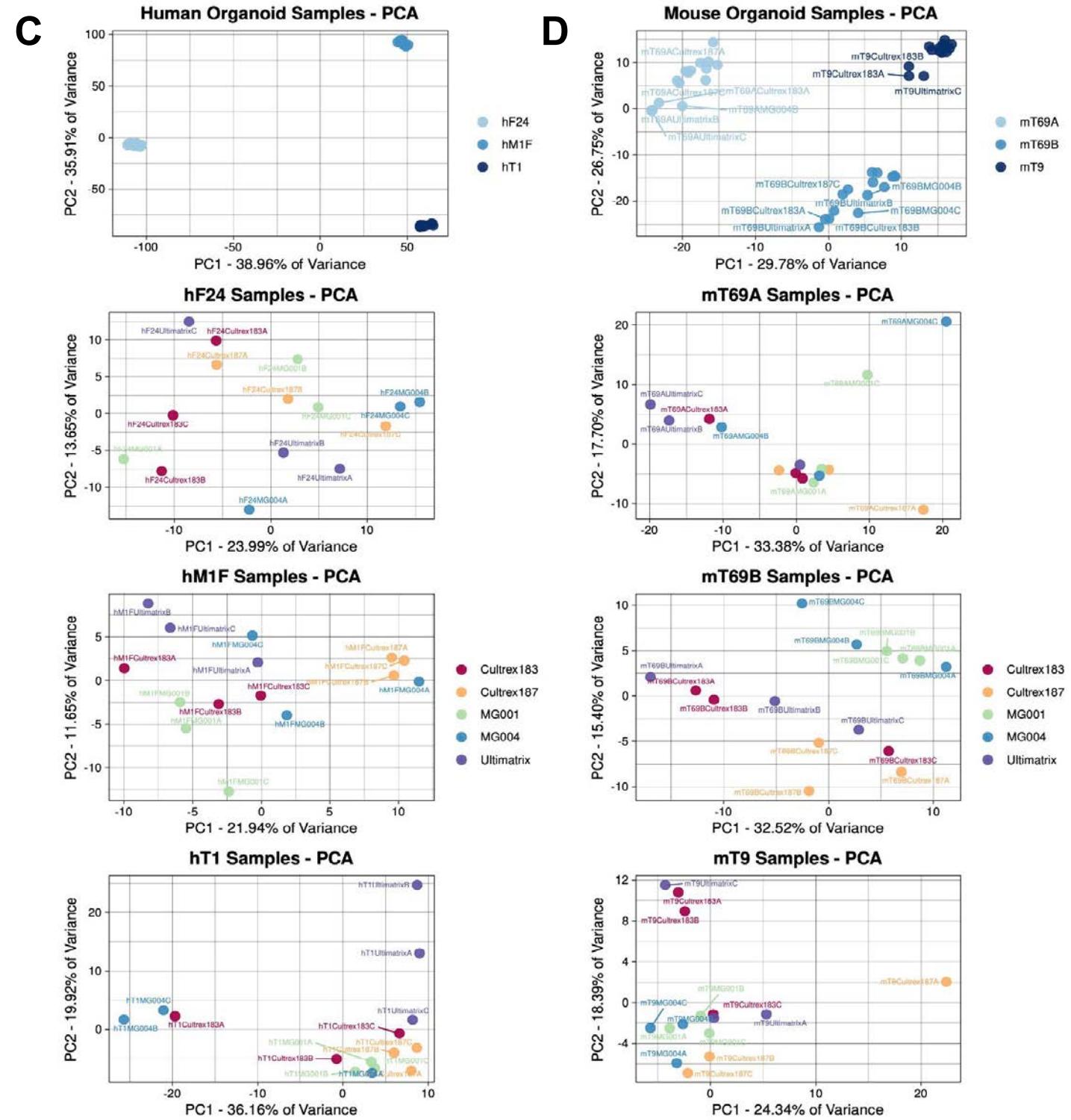
mT69B Trametinib AUC





Supplemental Figure 9

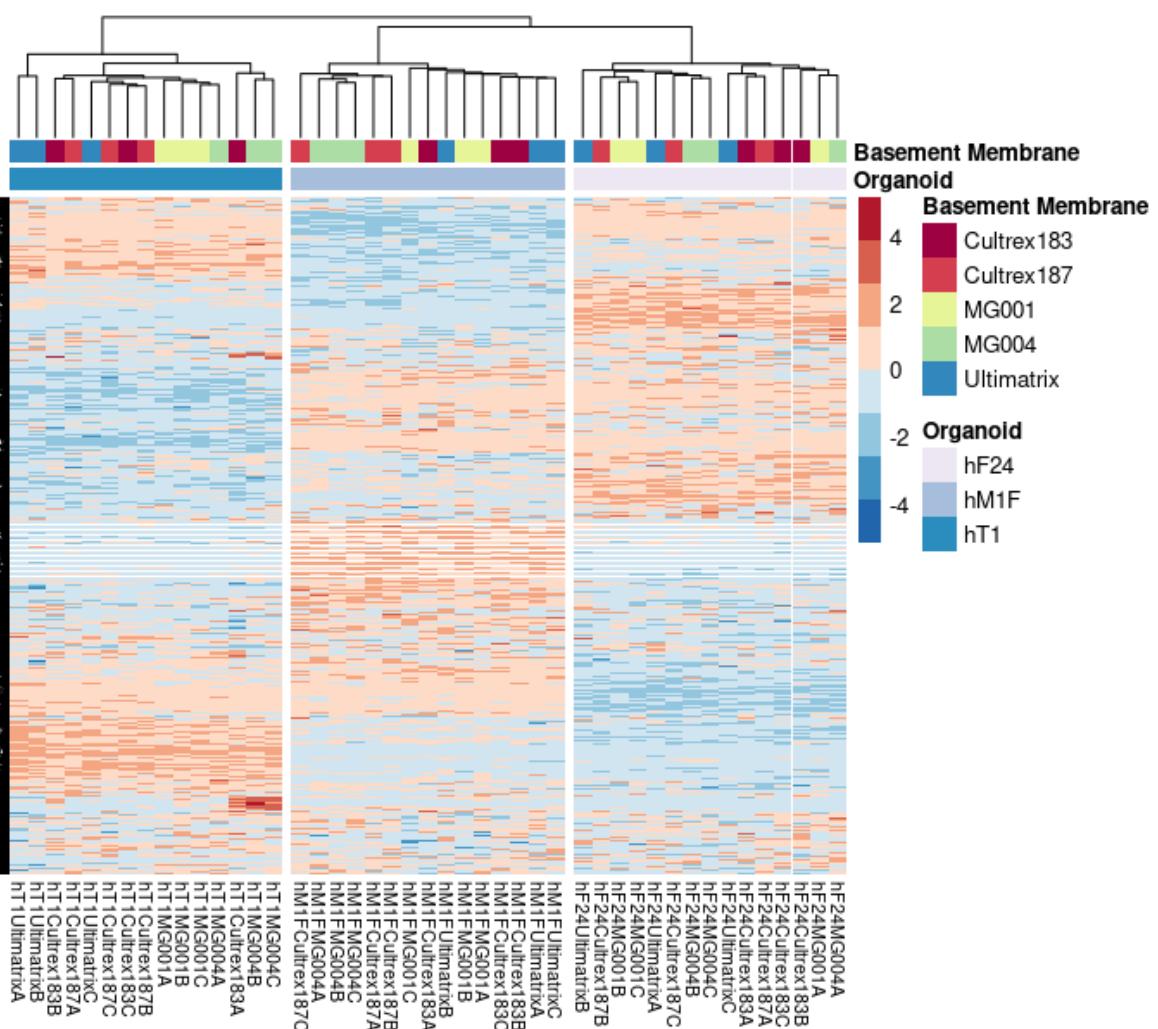
A**B****Supplemental Figure 10A-B**



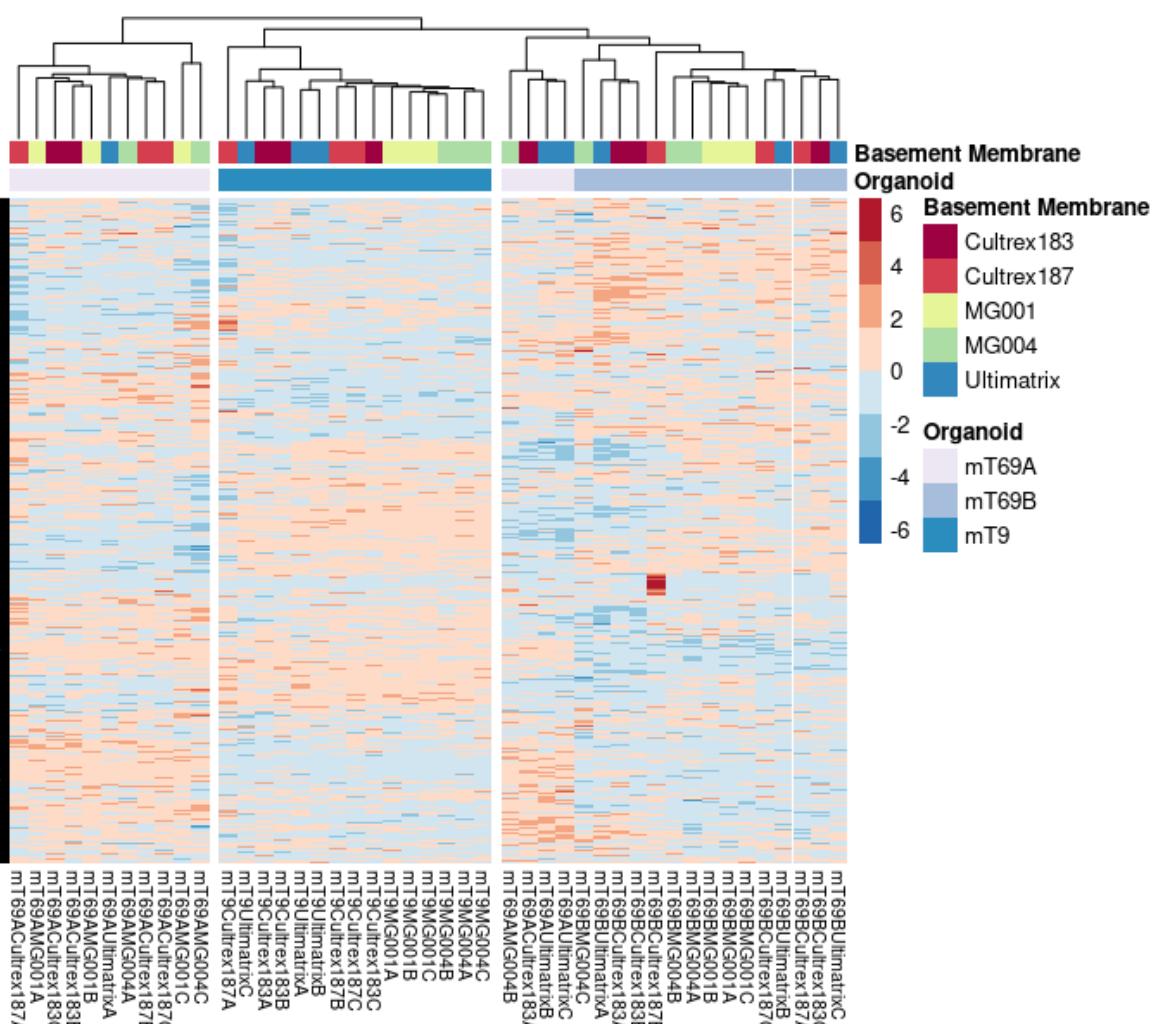
Supplemental Figure 10C-D

E

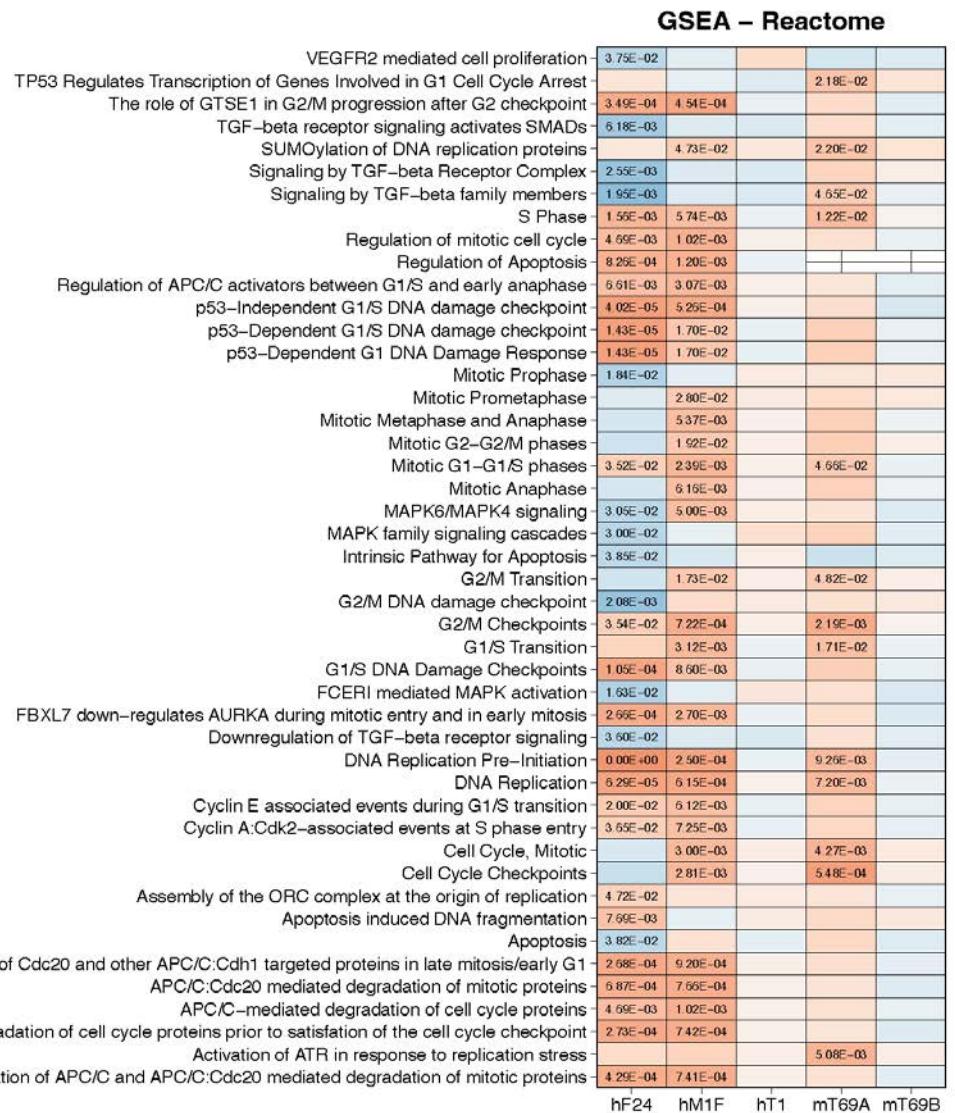
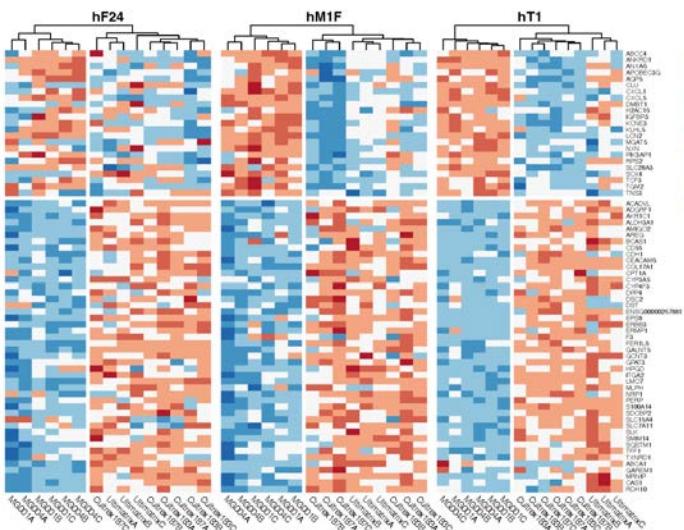
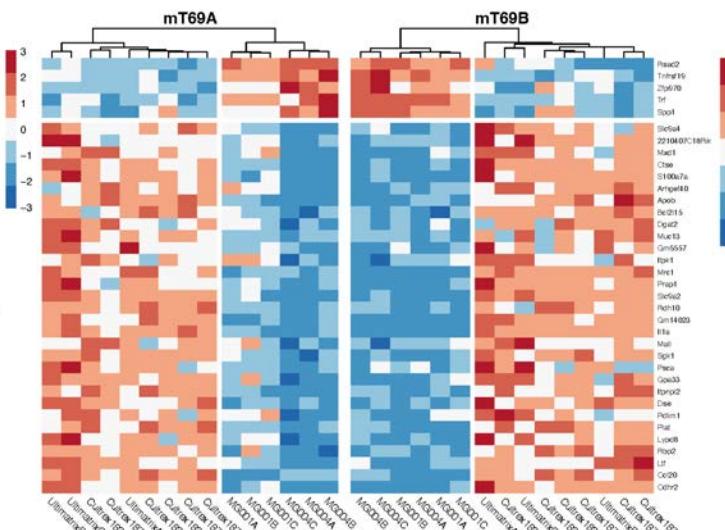
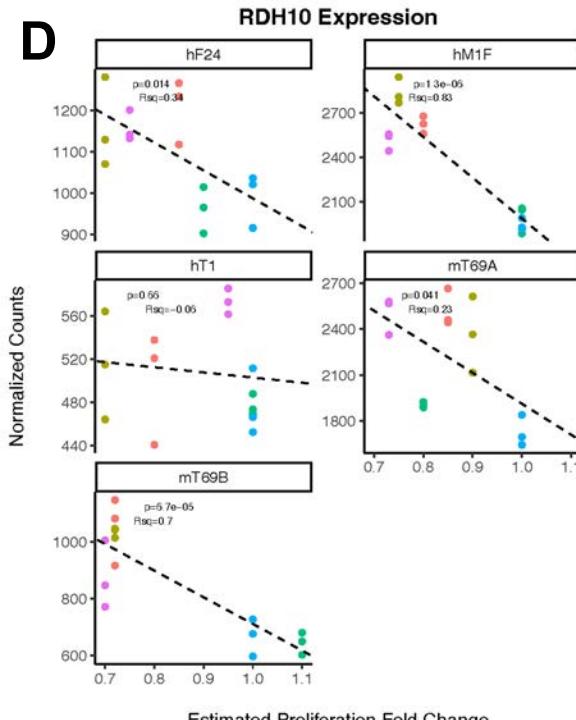
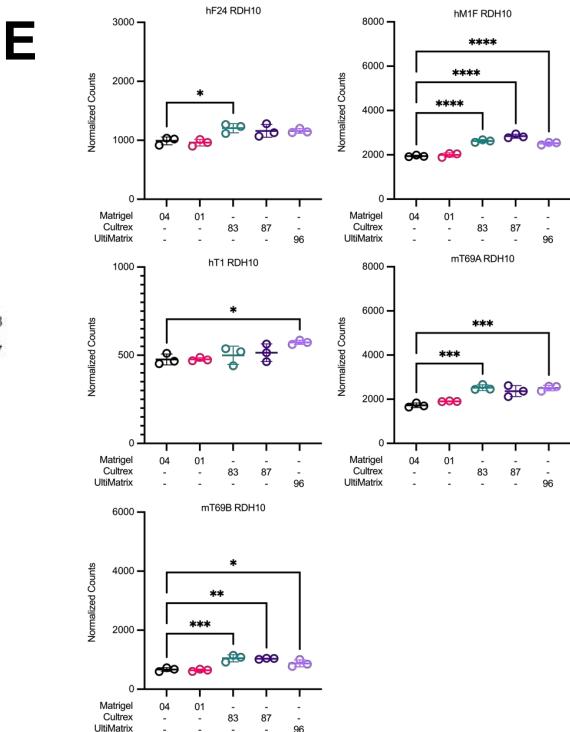
Expression Heatmap of All Genes Z-Scores of Human Organoid Normalized Counts

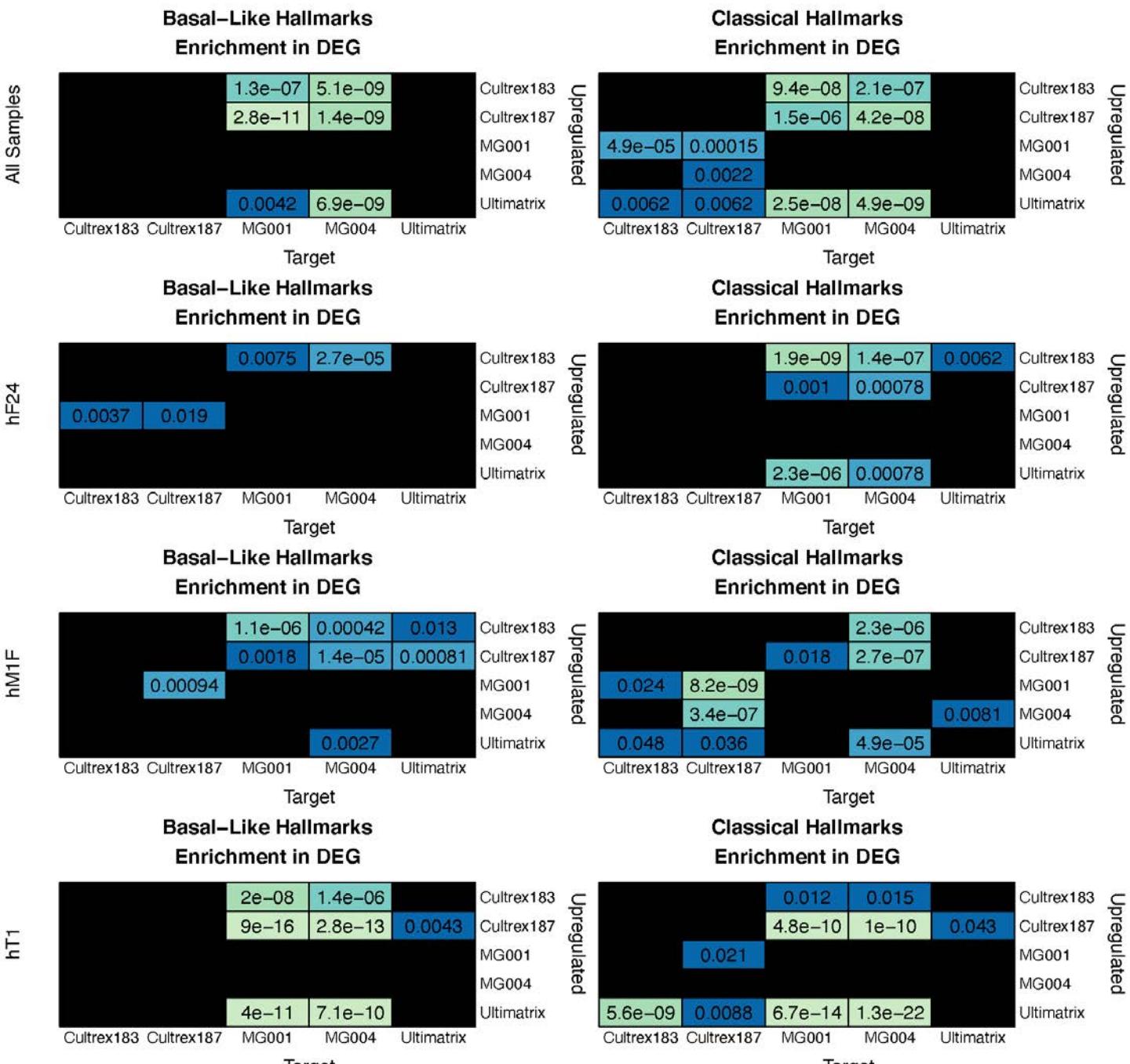
**F**

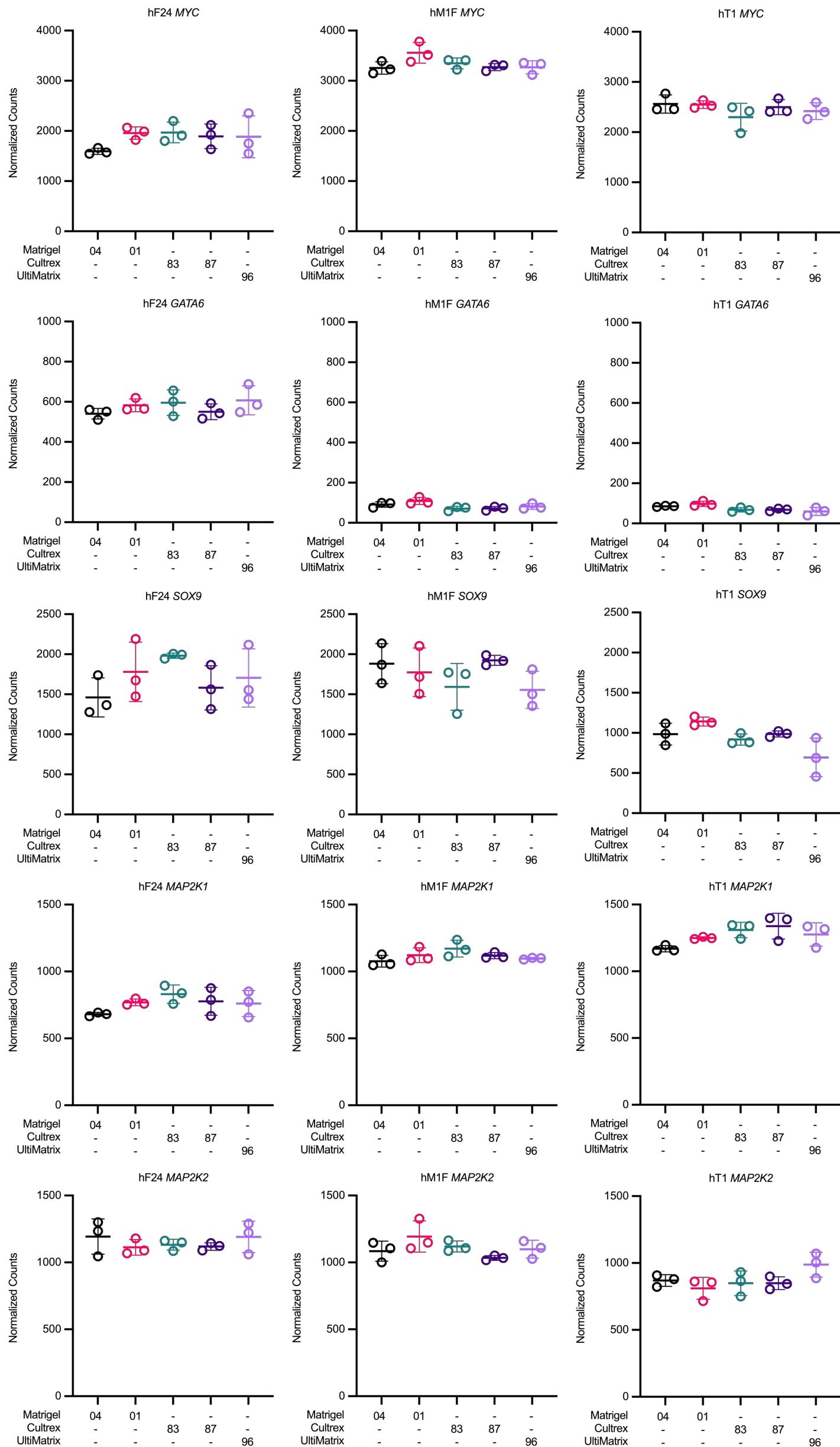
Expression Heatmap of All Genes Z-Scores of Mouse Organoid Normalized Counts



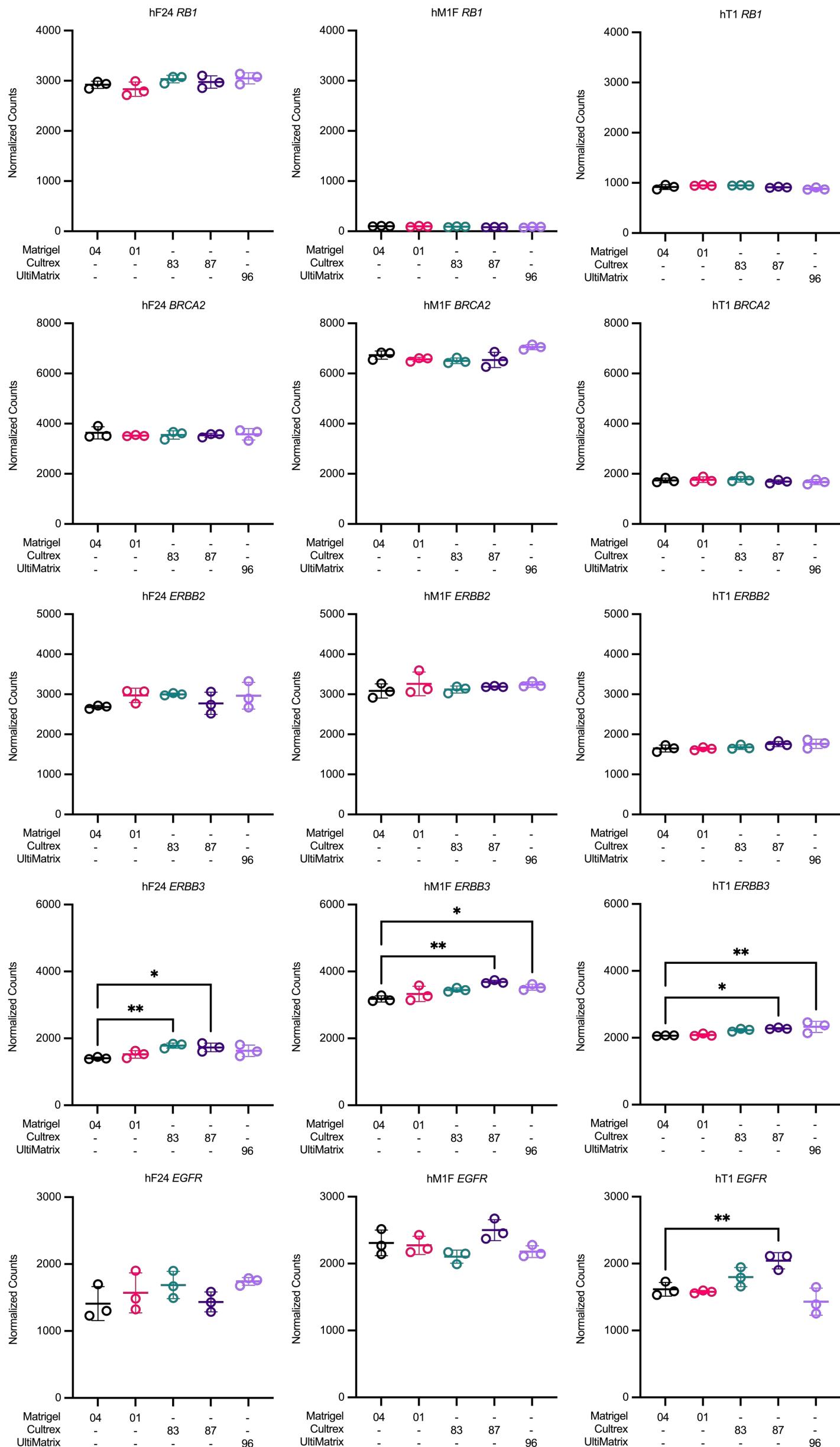
Supplemental Figure 10E-F

A**B****C****D****E****Supplemental Figure 11**



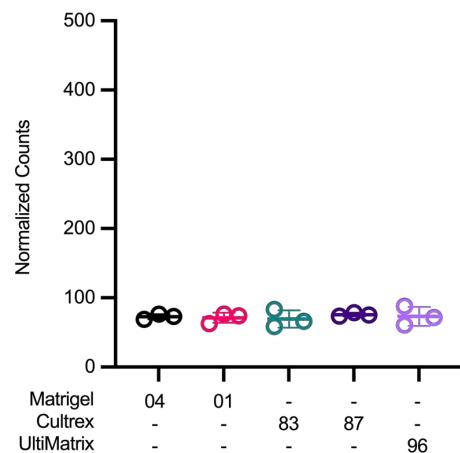


Supplemental Figure 13

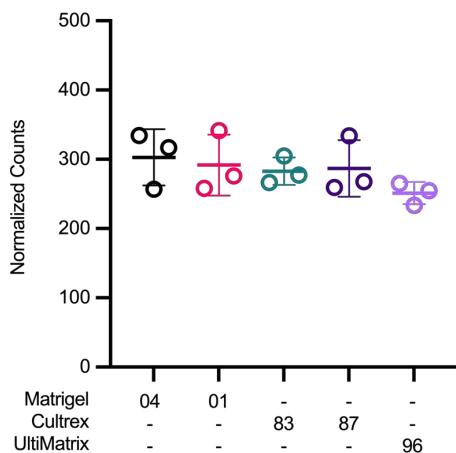


Supplemental Figure 13

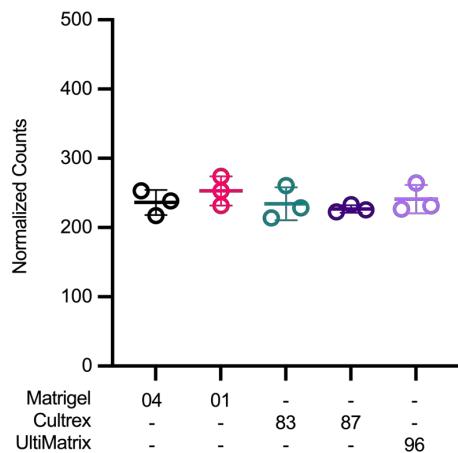
hF24 HNF1A



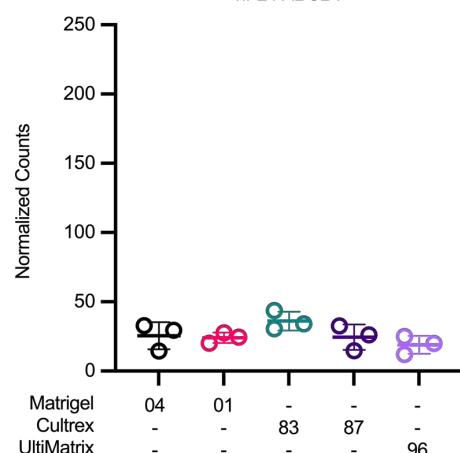
hM1F HNF1A



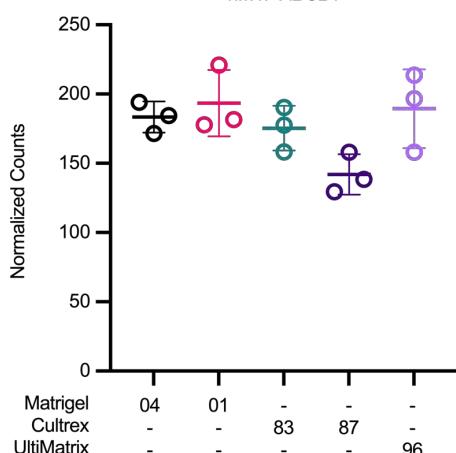
hT1 HNF1A



hF24 ABCB1



hM1F ABCB1



hT1 ABCB1

