

Supplemental Table 1

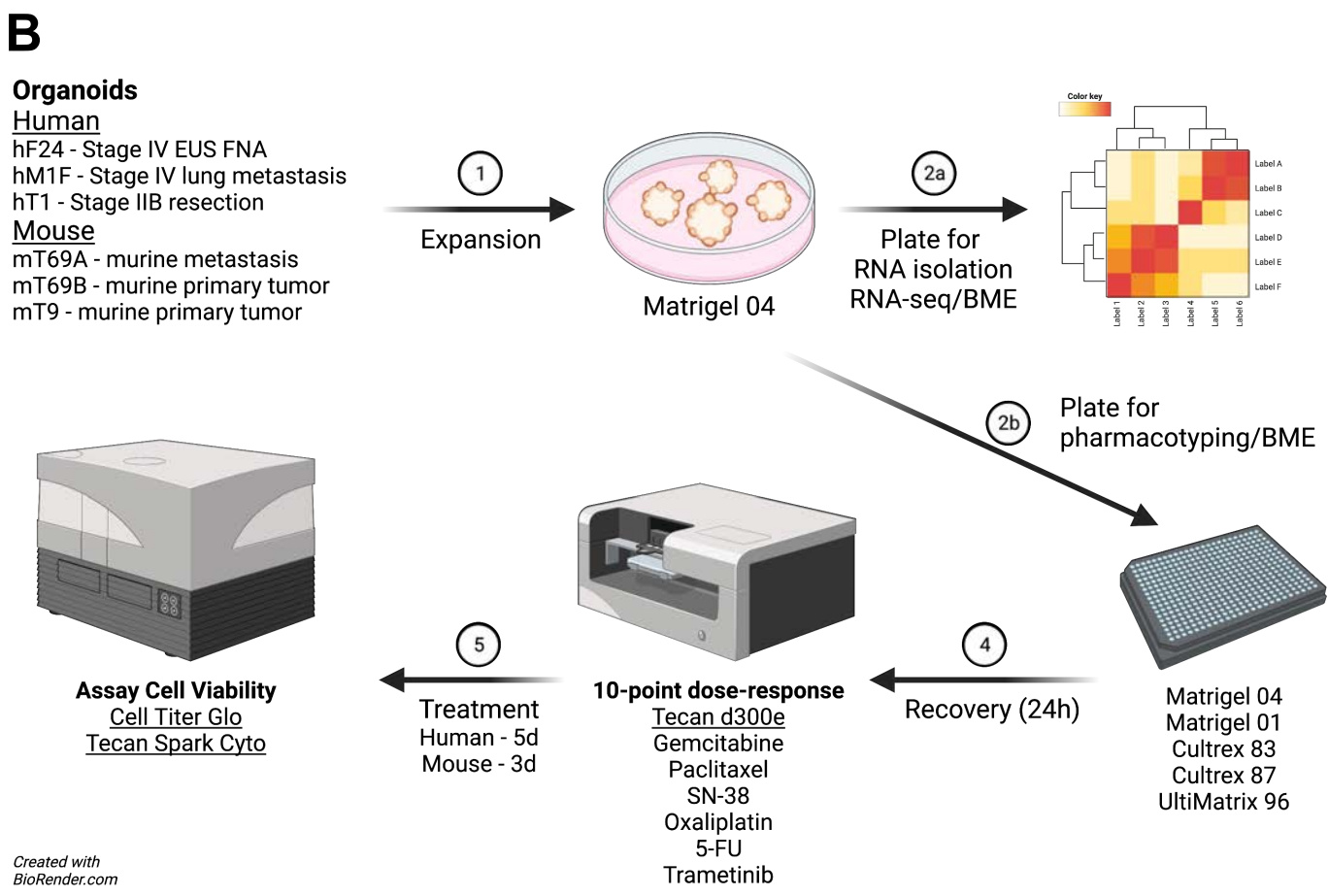
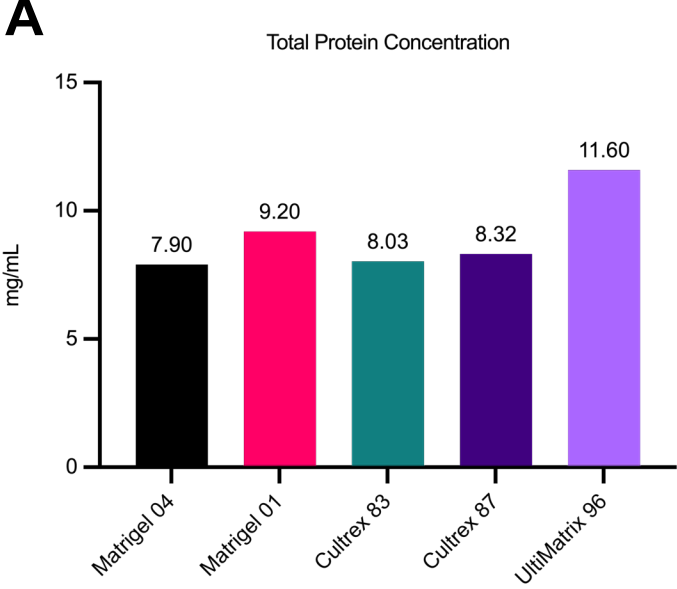
PDO	Origin	Site	Type of sample	Sex	Age	Race	Stage	KRAS (allele frequencies)	TP53 (allele frequencies)	SMAD4 (allele frequencies)	CDKN2A (allele frequencies)	Treatment prior to organoid
hF24*	H. sapiens	Pancreas	EUS FNA	F	57	Caucasian	4	G12V 82%	F113V (100%)	LOSS (N/A)	DEEP LOSS (N/A)	NO
hM1F*	H. sapiens	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.

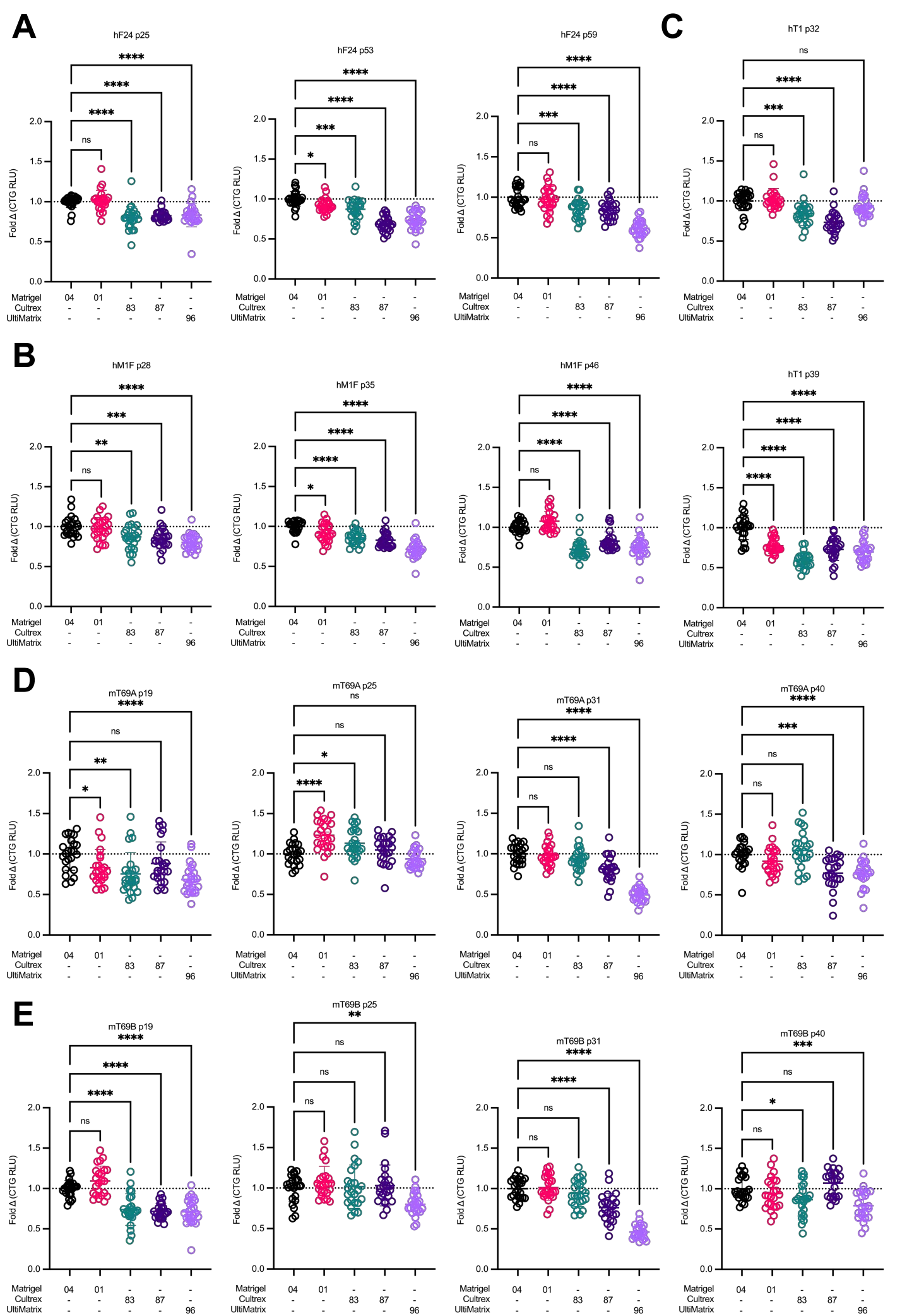
Supplemental Table 2

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



Created with BioRender.com

Supplemental Figure 1

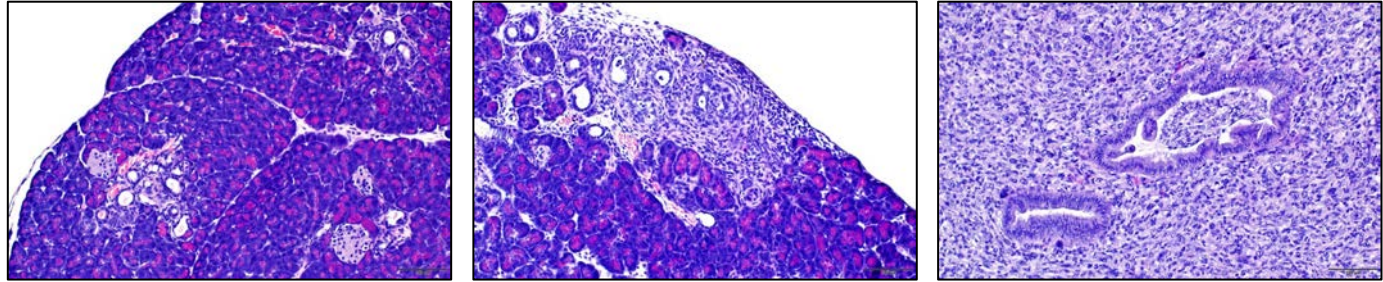


A

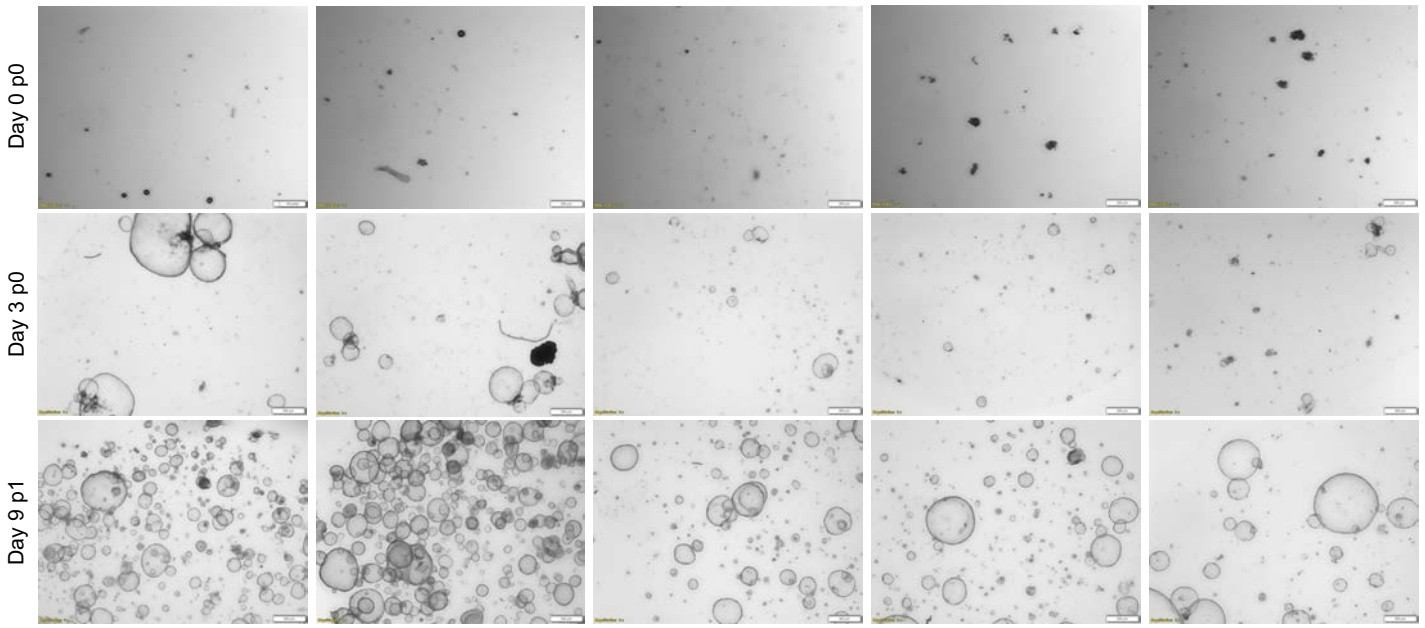
A5462

A5504

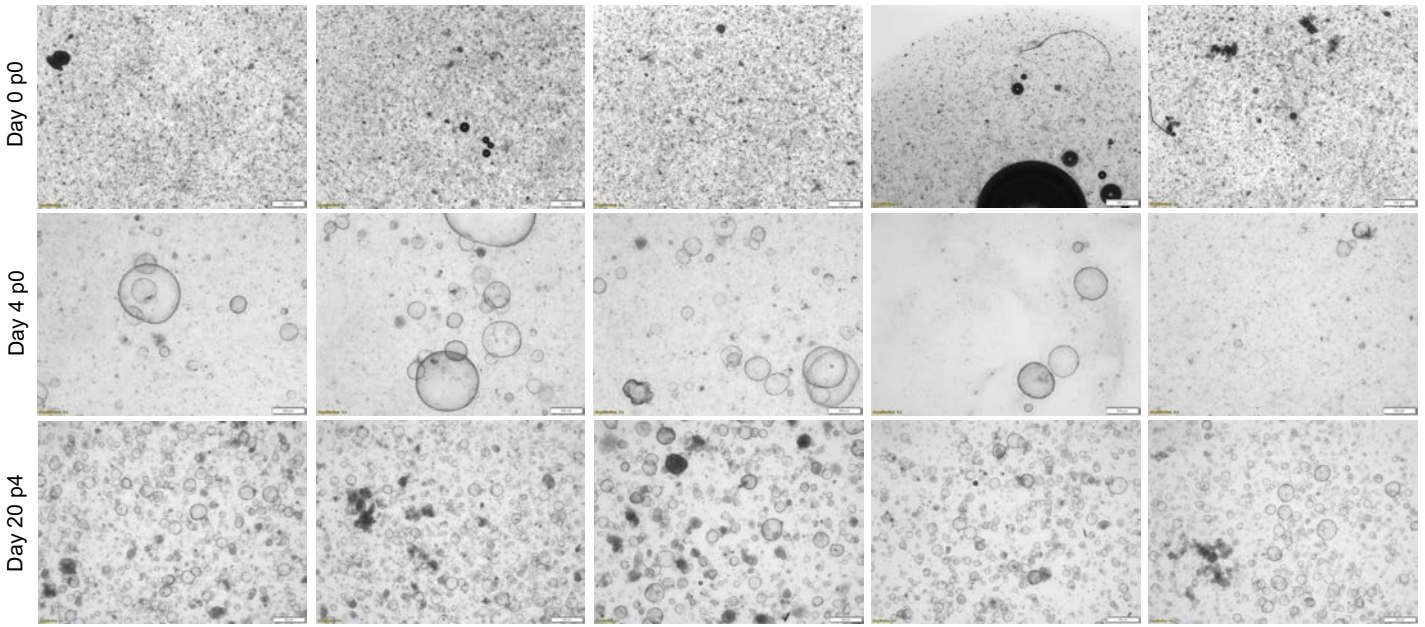
A5505

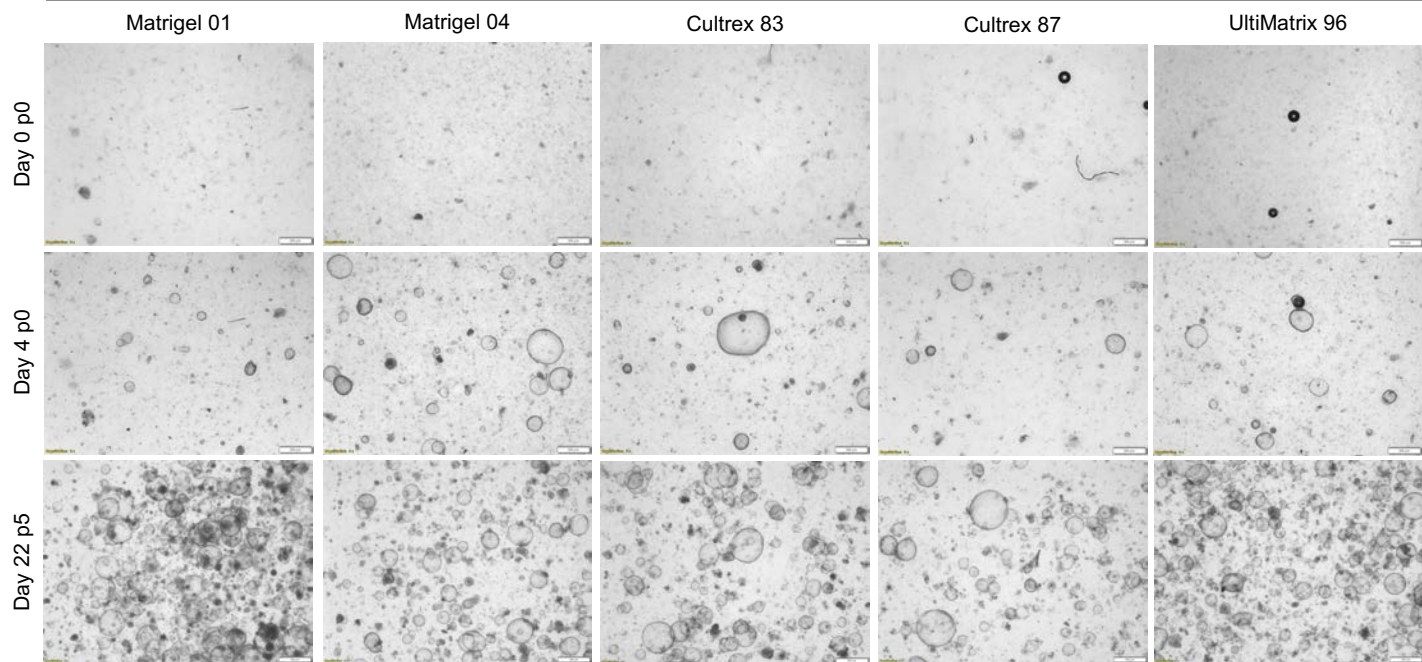
**B**A5462 – *LSL-Kras^{G12D/+};LSL-Trp53^{R172H/+};Pdx-1-Cre* (KPC)

Matrigel 01 Matrigel 04 Cultrex 83 Cultrex 87 UltiMatrix 96

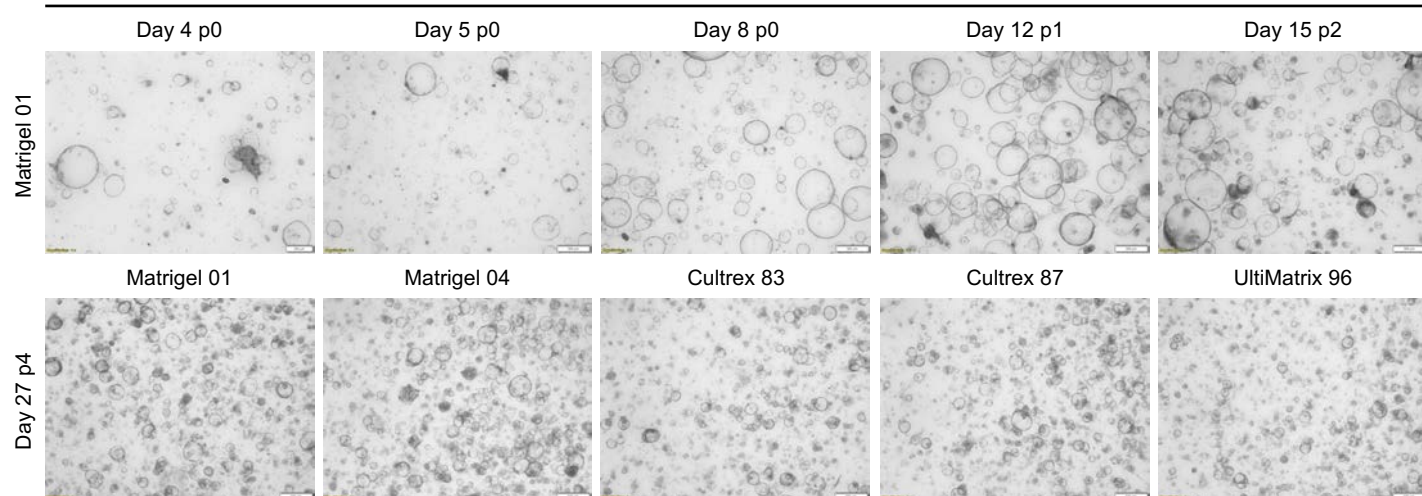
**C**A5504 – *LSL-Kras^{G12D/+};LSL-Trp53^{R172H/+};Pdx-1-Cre* (KPC)

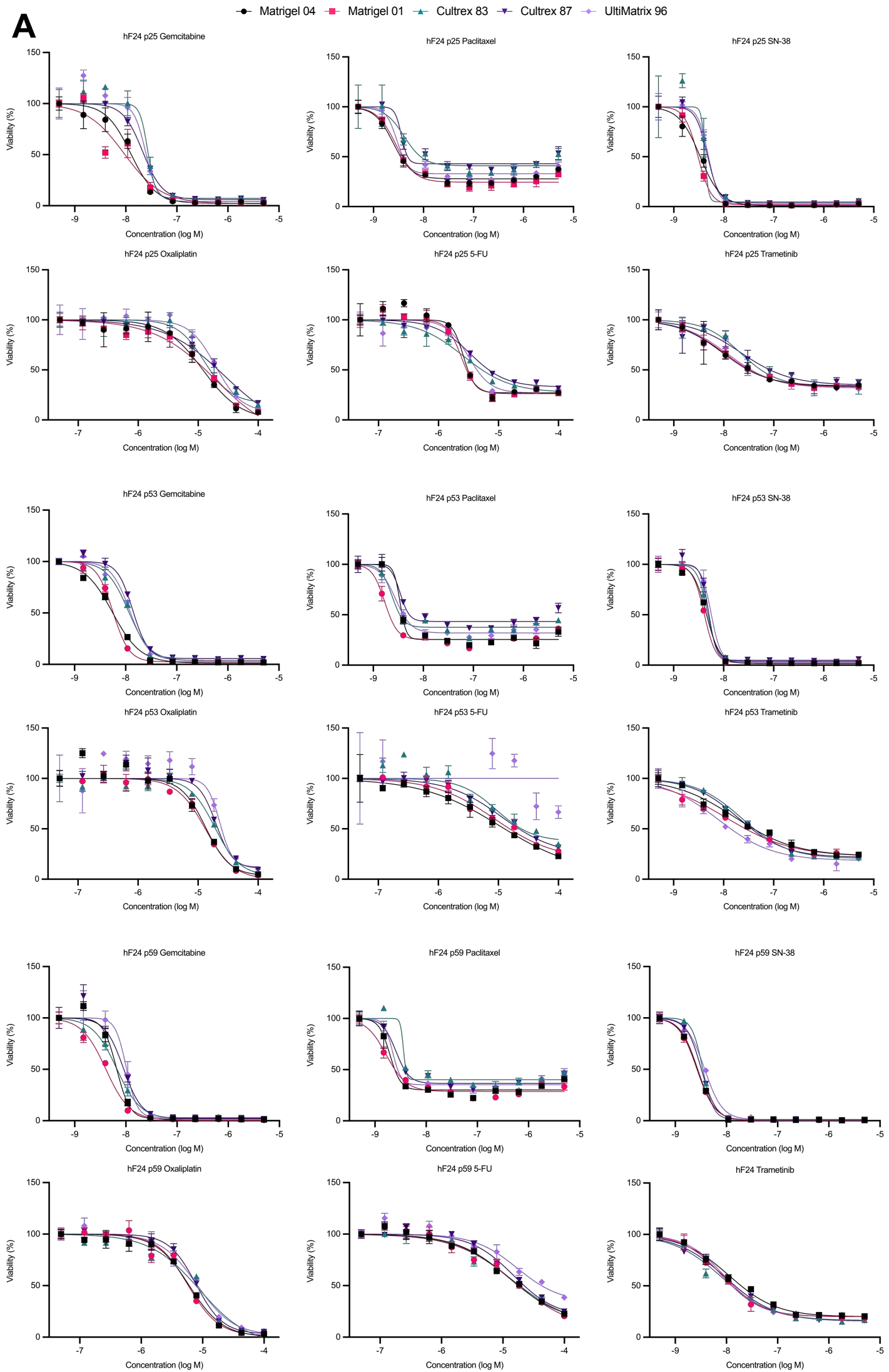
Matrigel 01 Matrigel 04 Cultrex 83 Cultrex 87 UltiMatrix 96



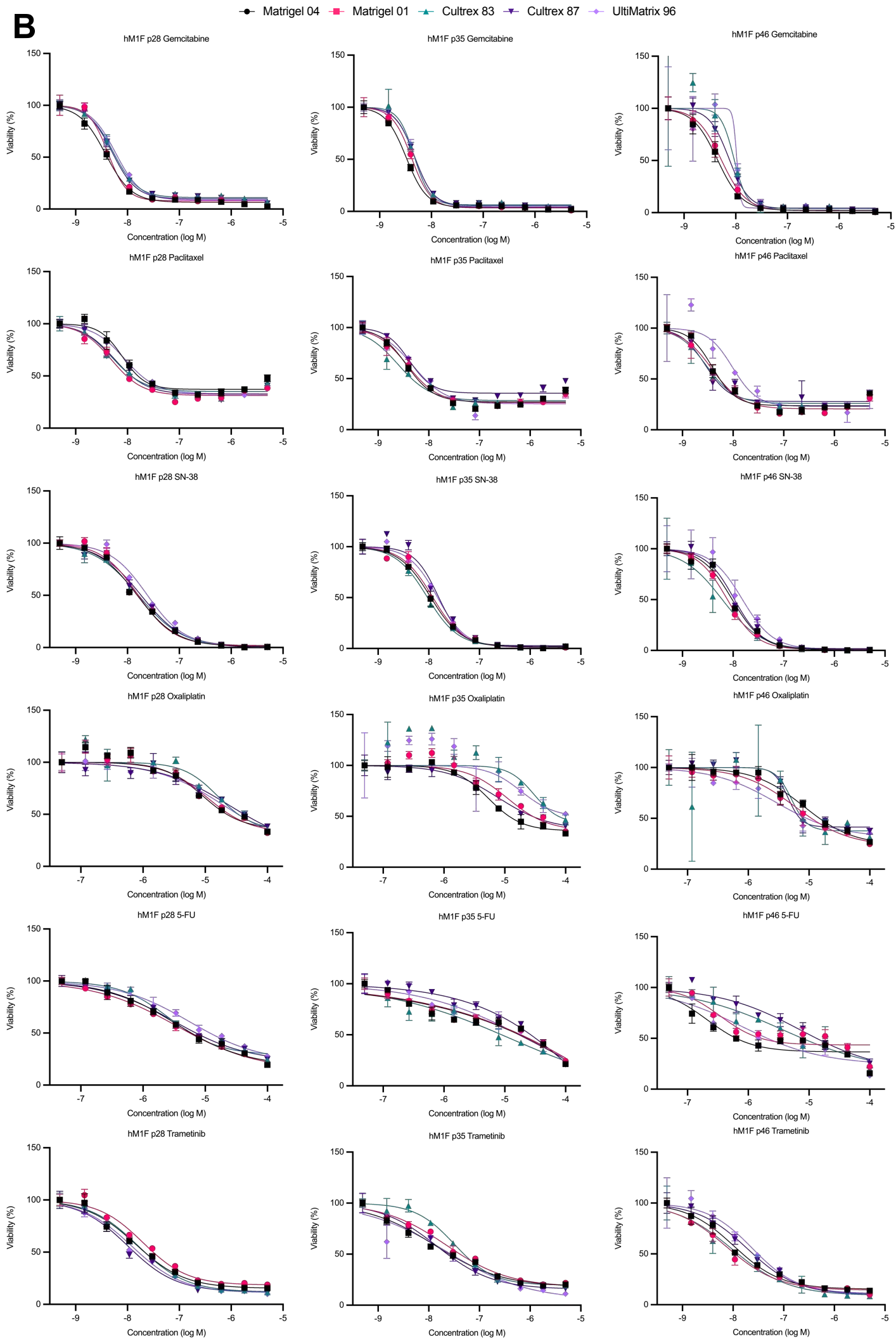
DA5505 – *LSL-Kras^{G12D/+};LSL-Trp53^{R172H/+};Pdx-1-Cre* (KPC)**E**

Human liver metastasis (449)



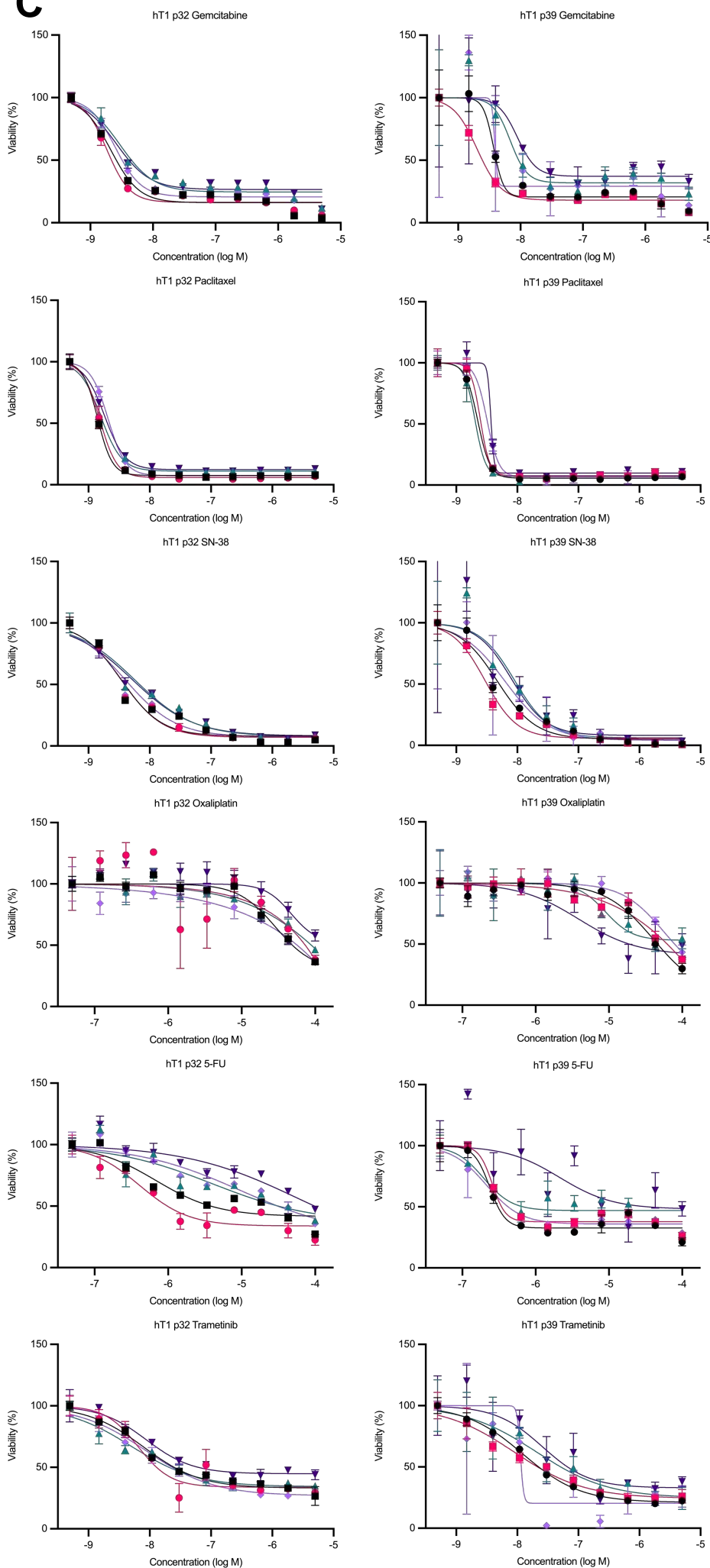


Supplemental Figure 4A

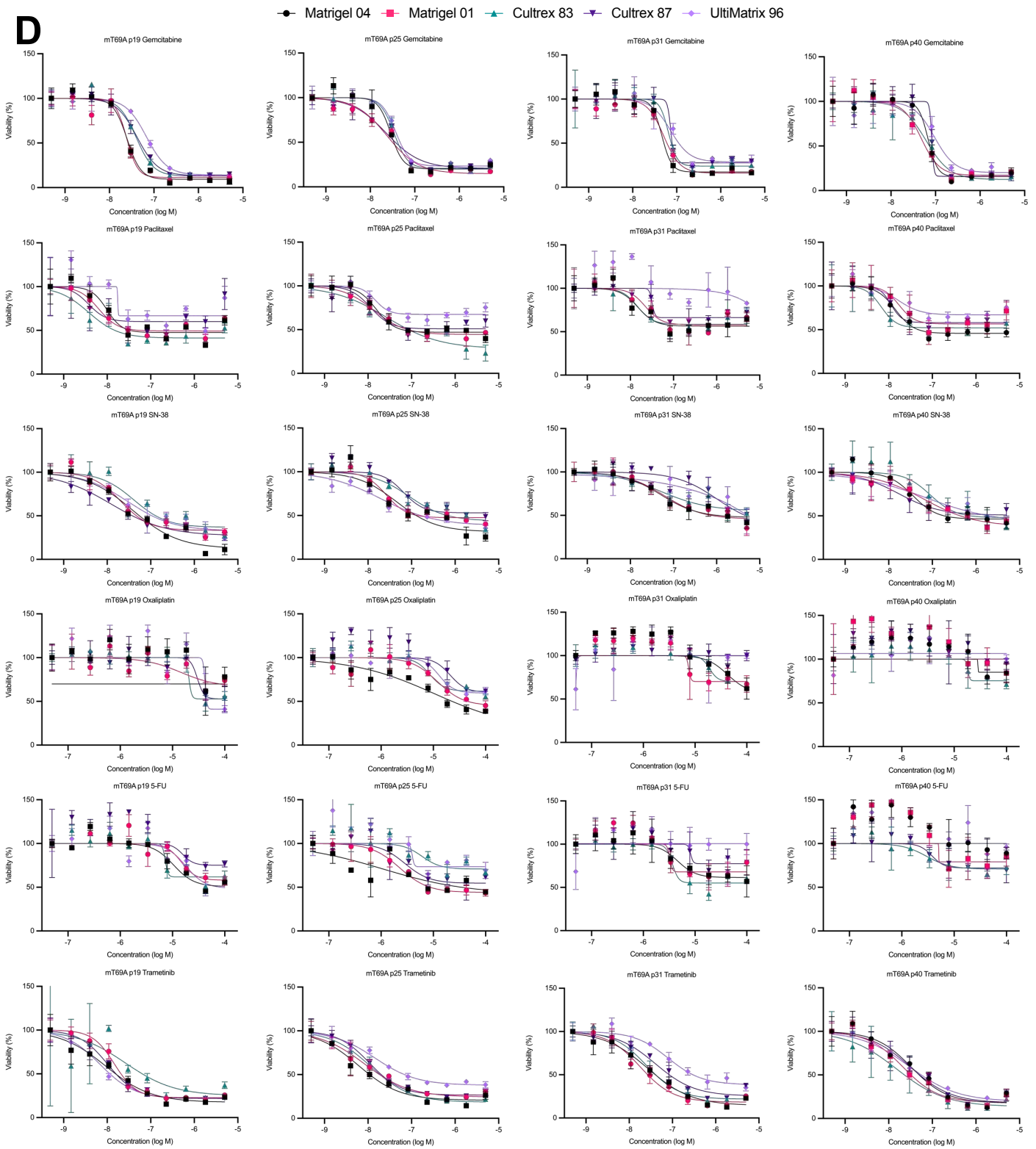


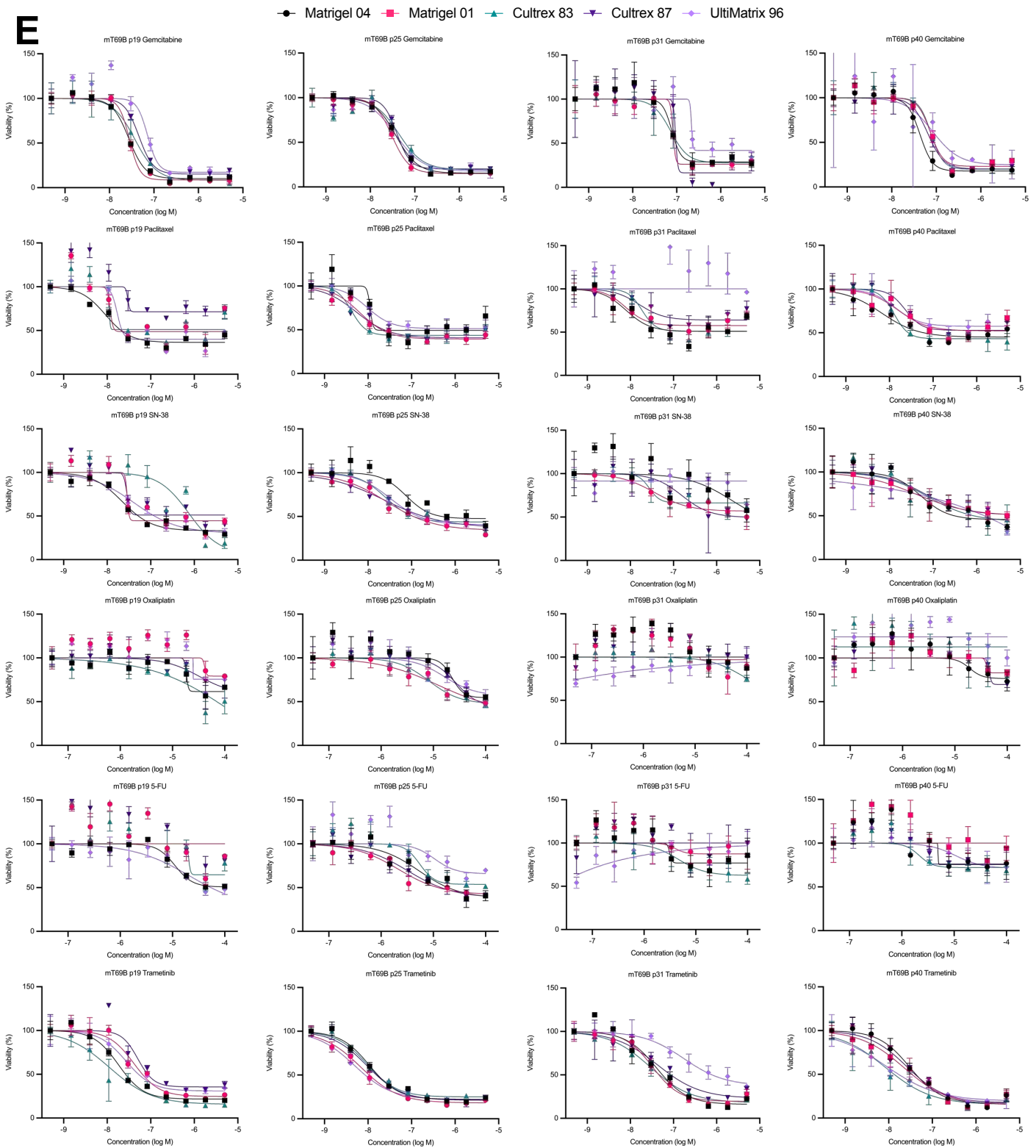
Supplemental Figure 4B

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



Supplemental Figure 4C

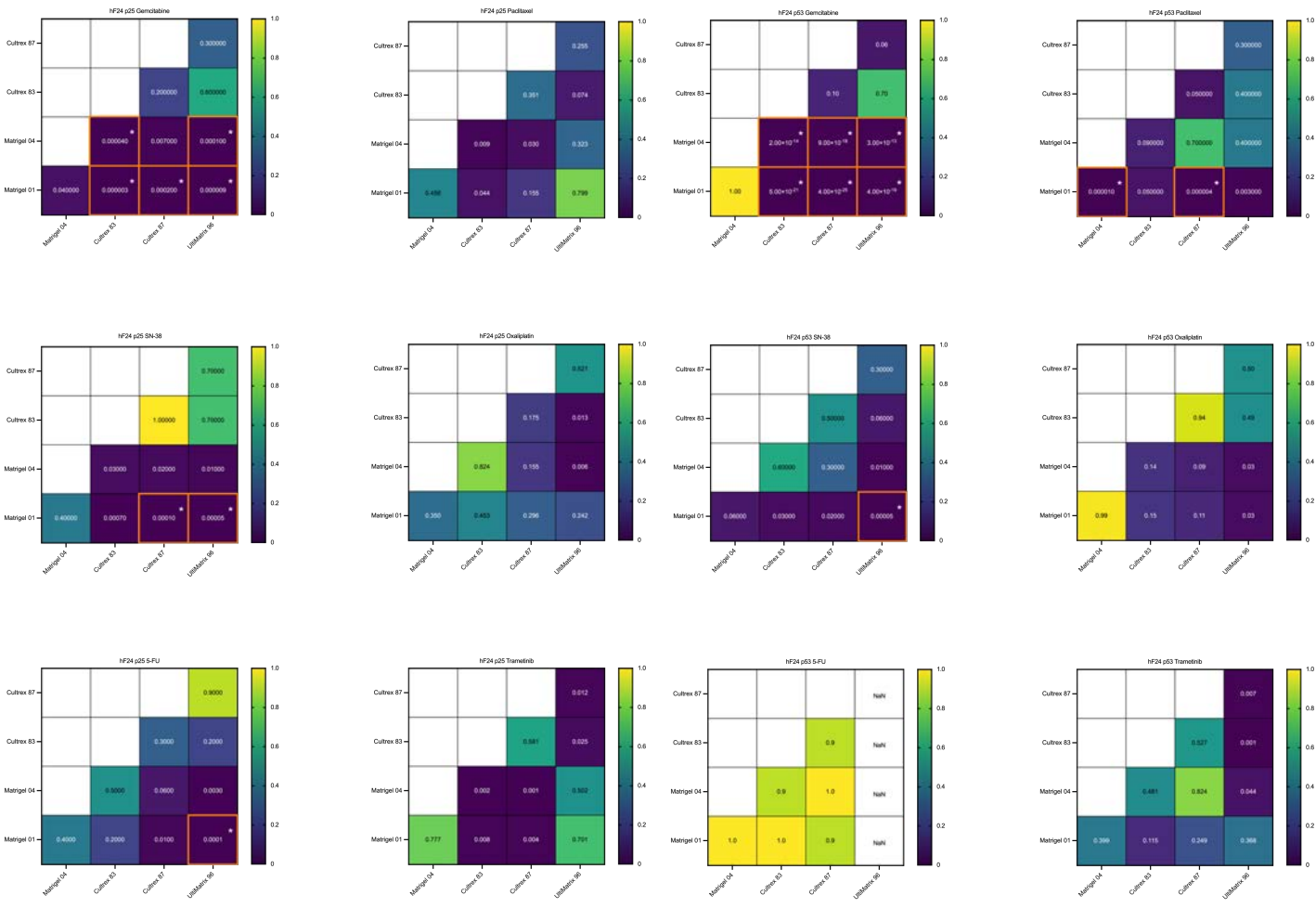




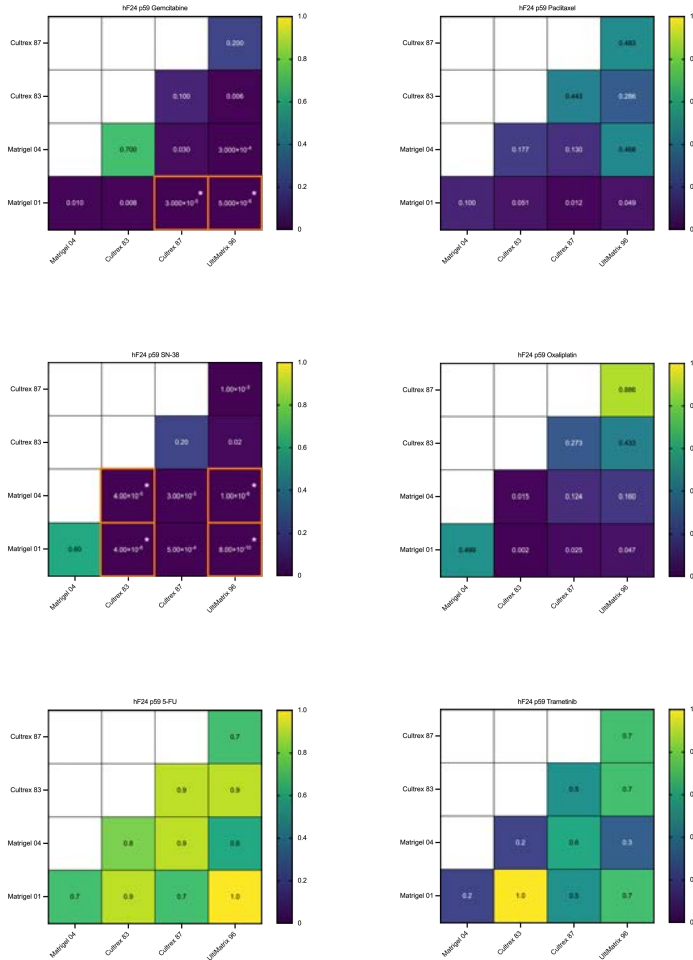
A

hF24 p25

hF24 p53

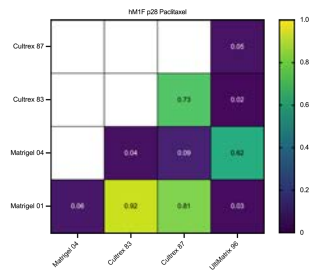
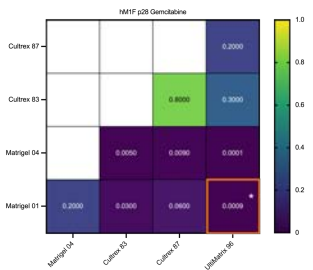


hF24 p59

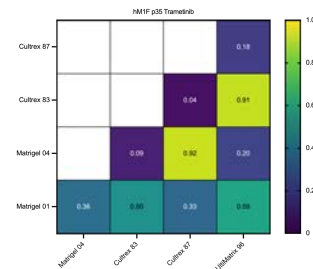
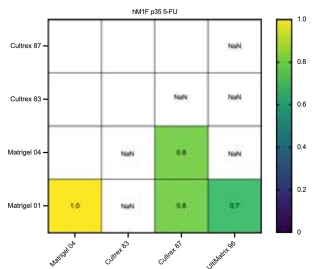
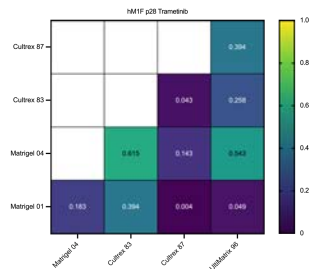
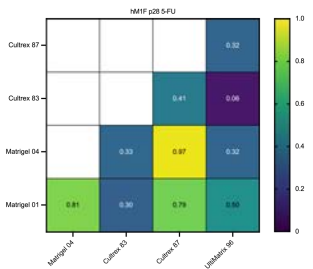
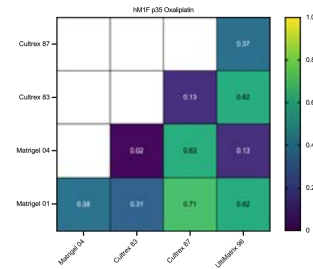
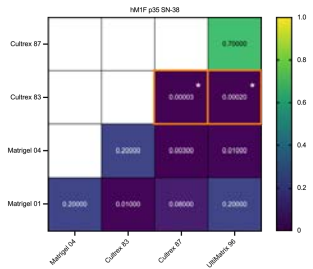
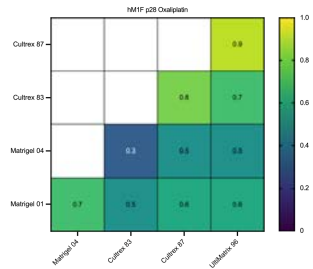
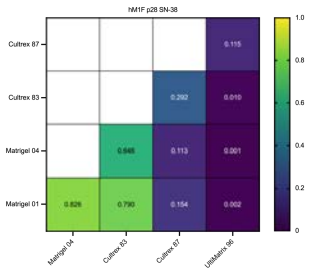
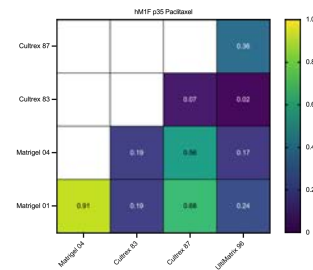
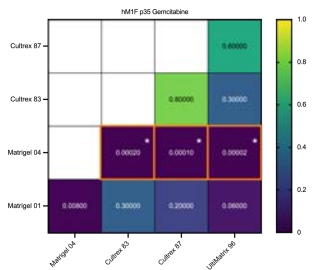


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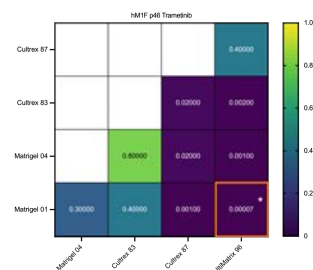
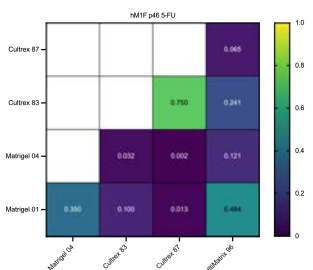
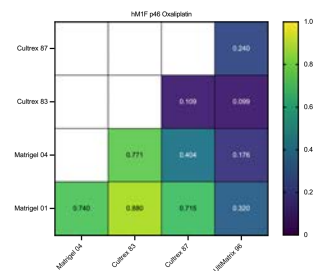
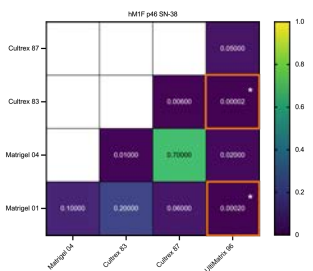
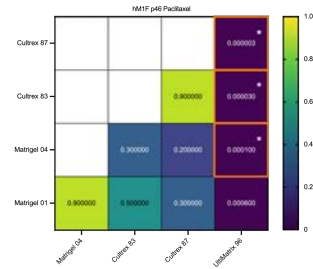
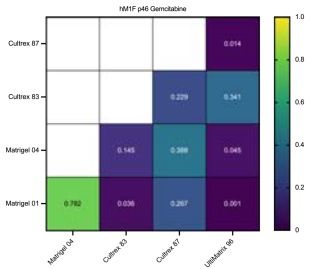
hM1F p28



hM1F p35



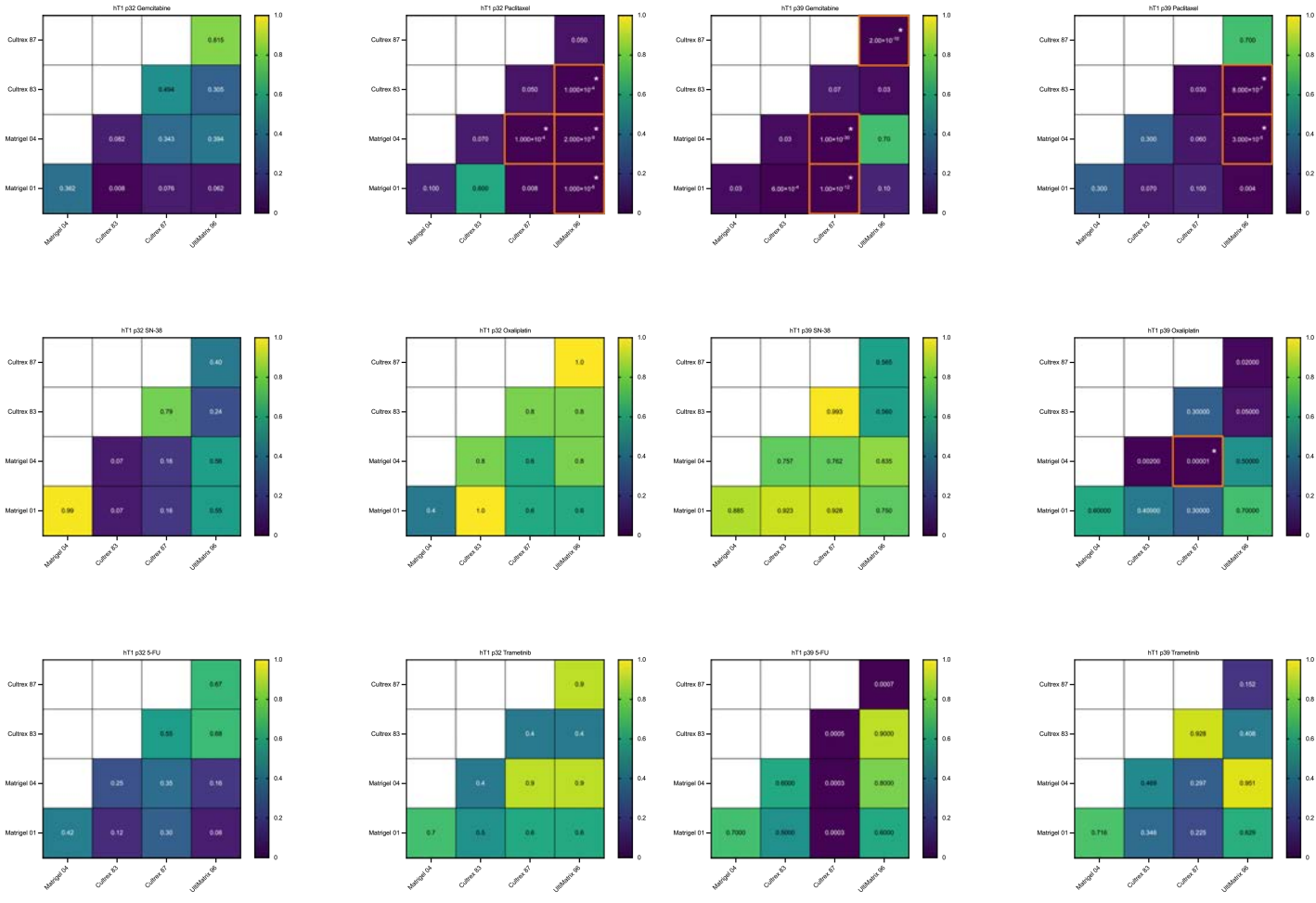
hM1F p46



C

hT1 p32

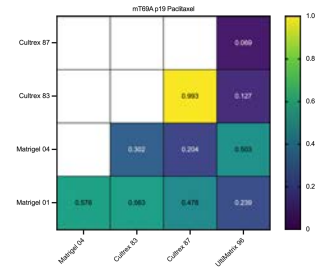
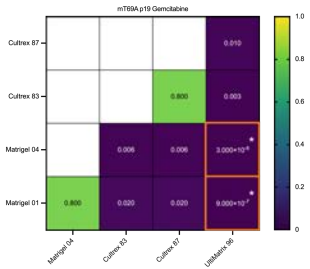
hT1 p39



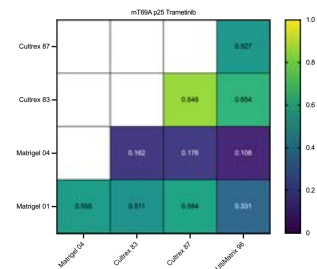
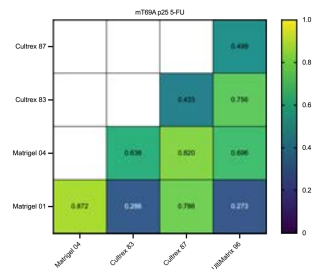
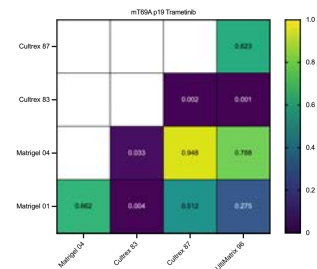
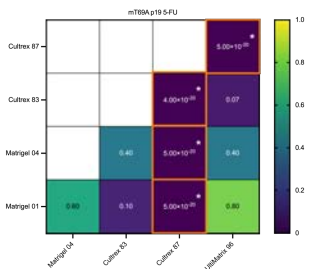
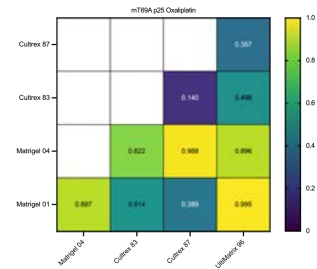
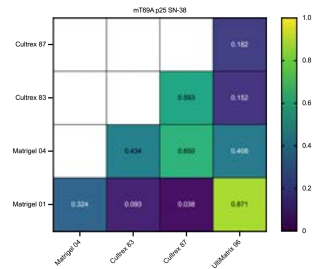
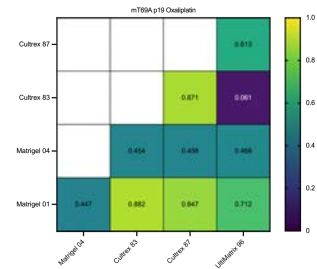
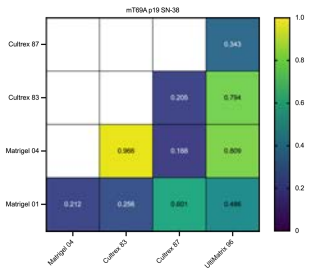
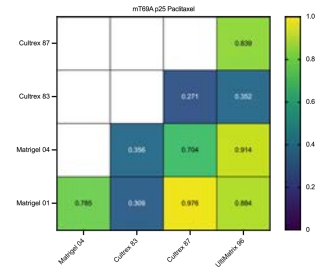
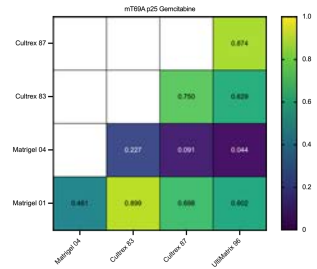
Supplemental Figure 5C – IC50

D

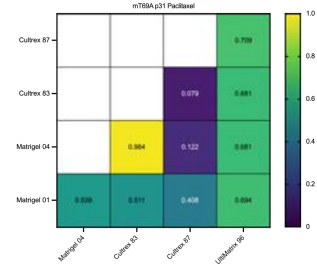
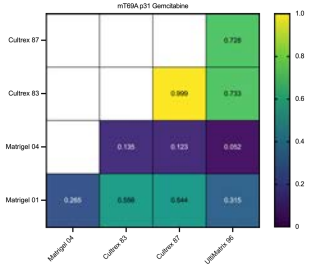
mT69A p19



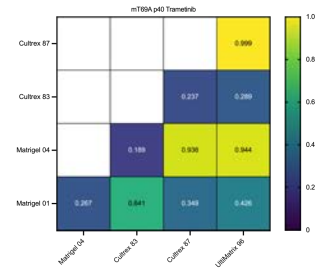
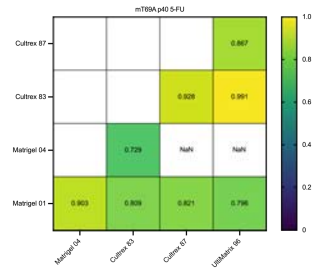
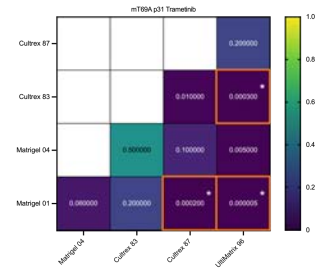
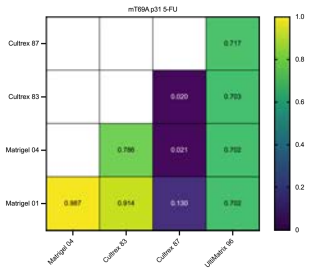
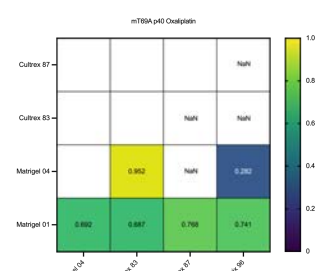
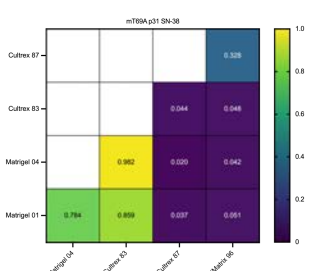
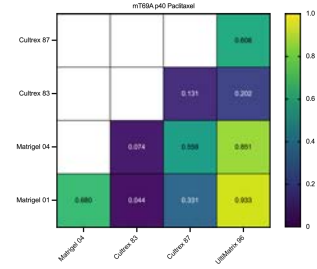
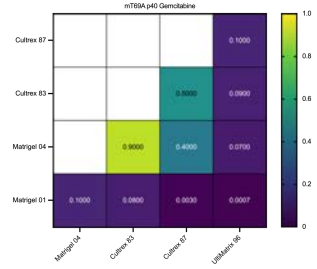
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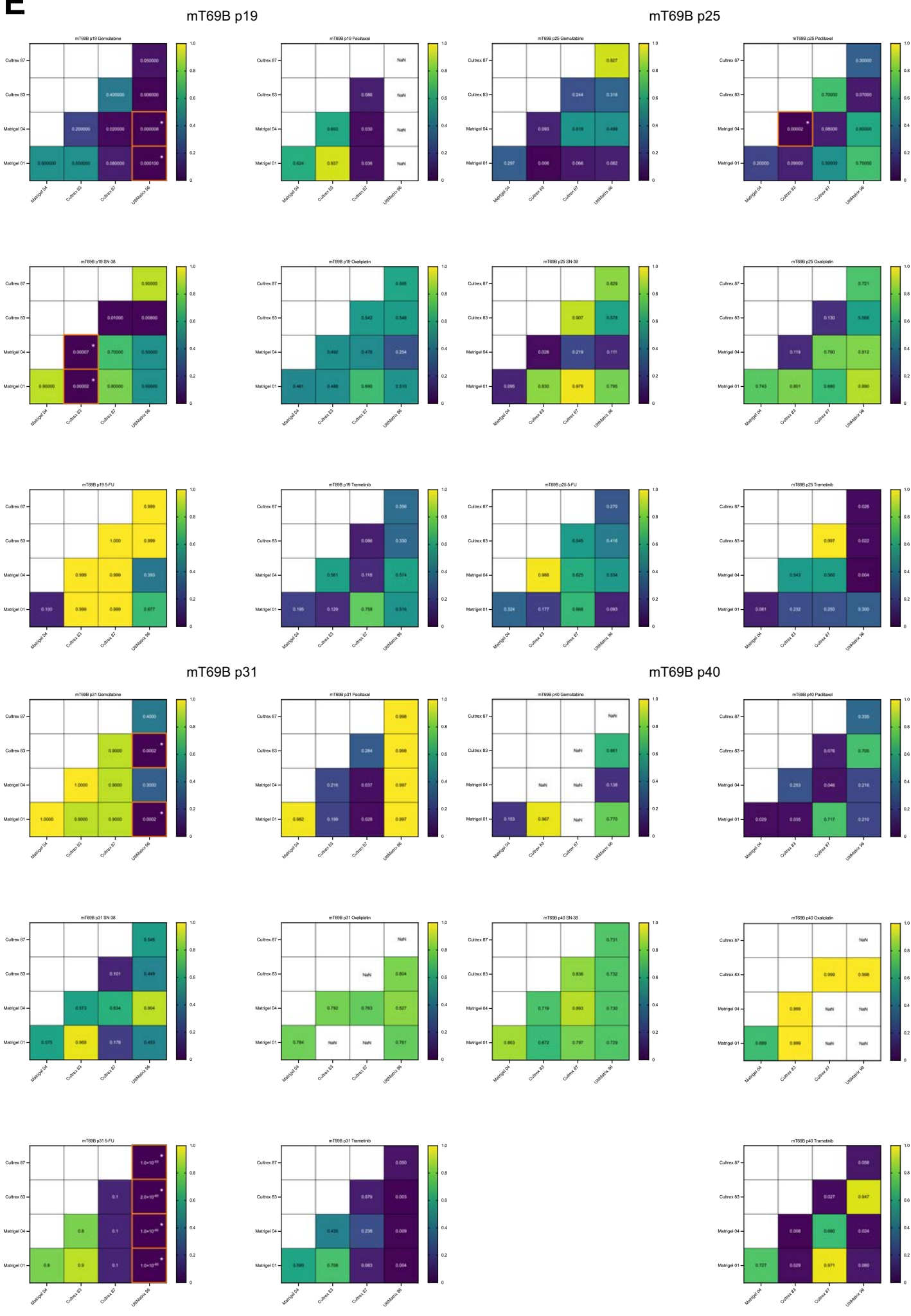


mT69A p31



mT69A p40



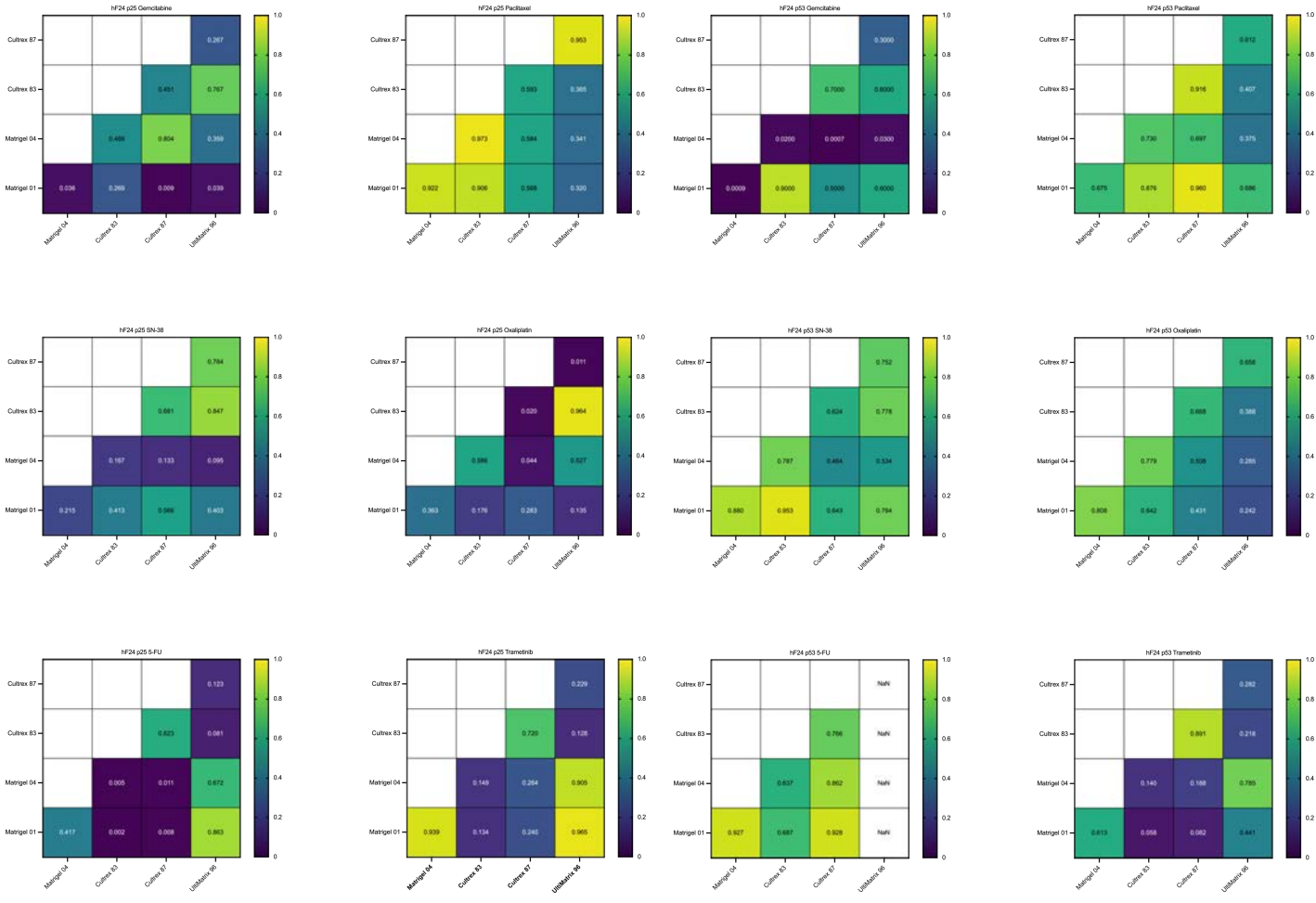
E

Supplemental Figure 5E – IC50

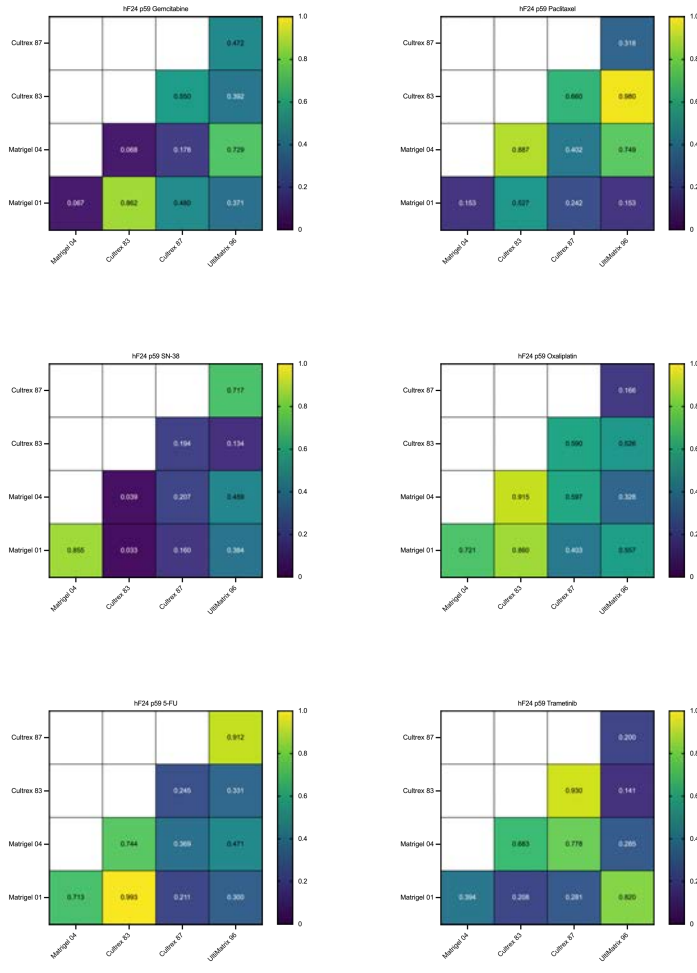
A

hF24 p25

hF24 p53



hF24 p59

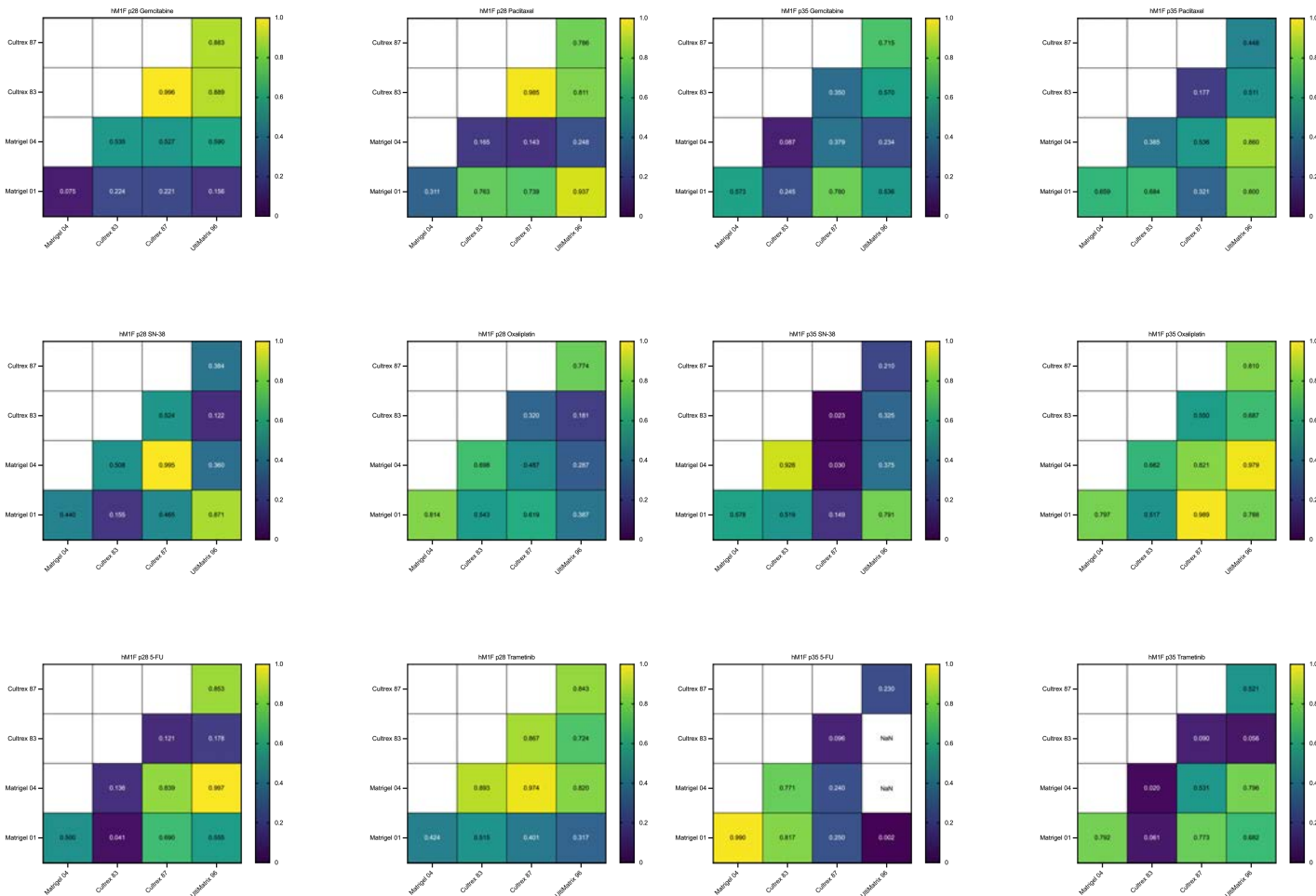


Supplemental Figure 6A – Hill Slope

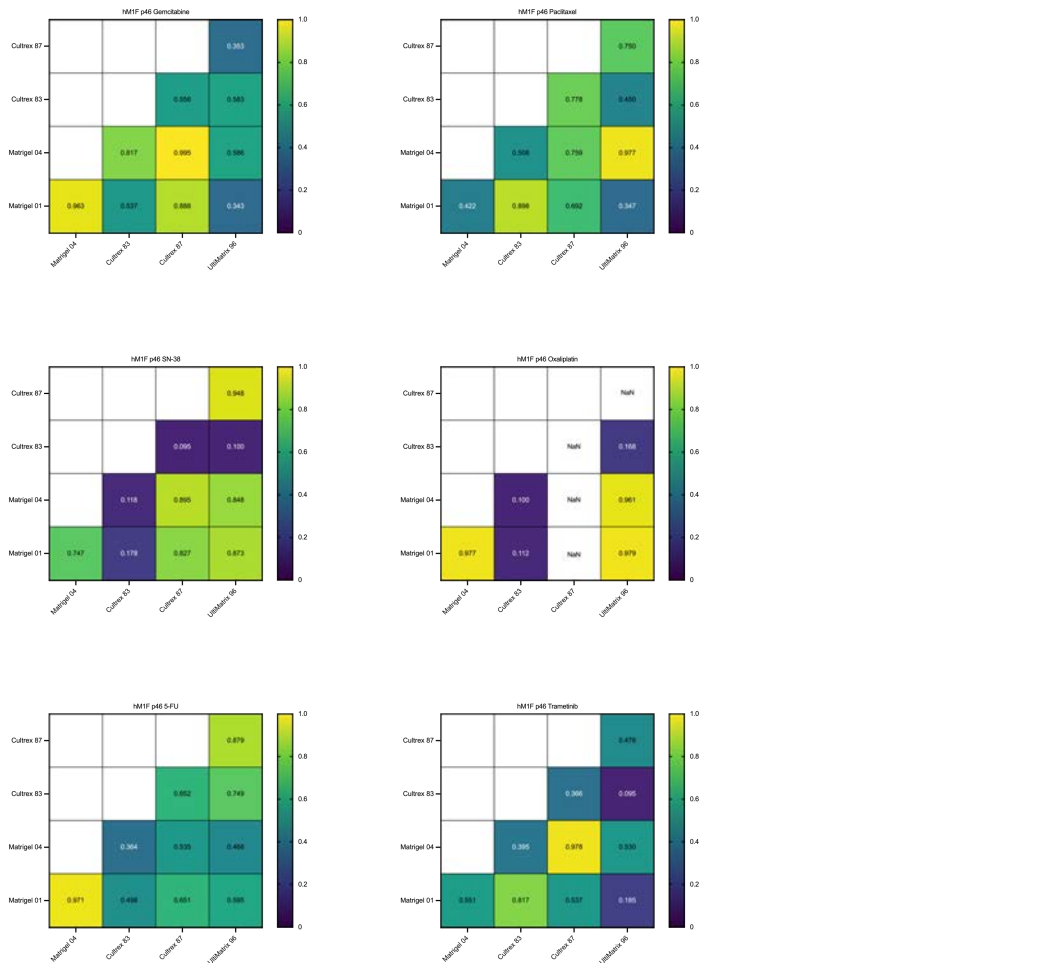
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hM1F p28

hM1F p35



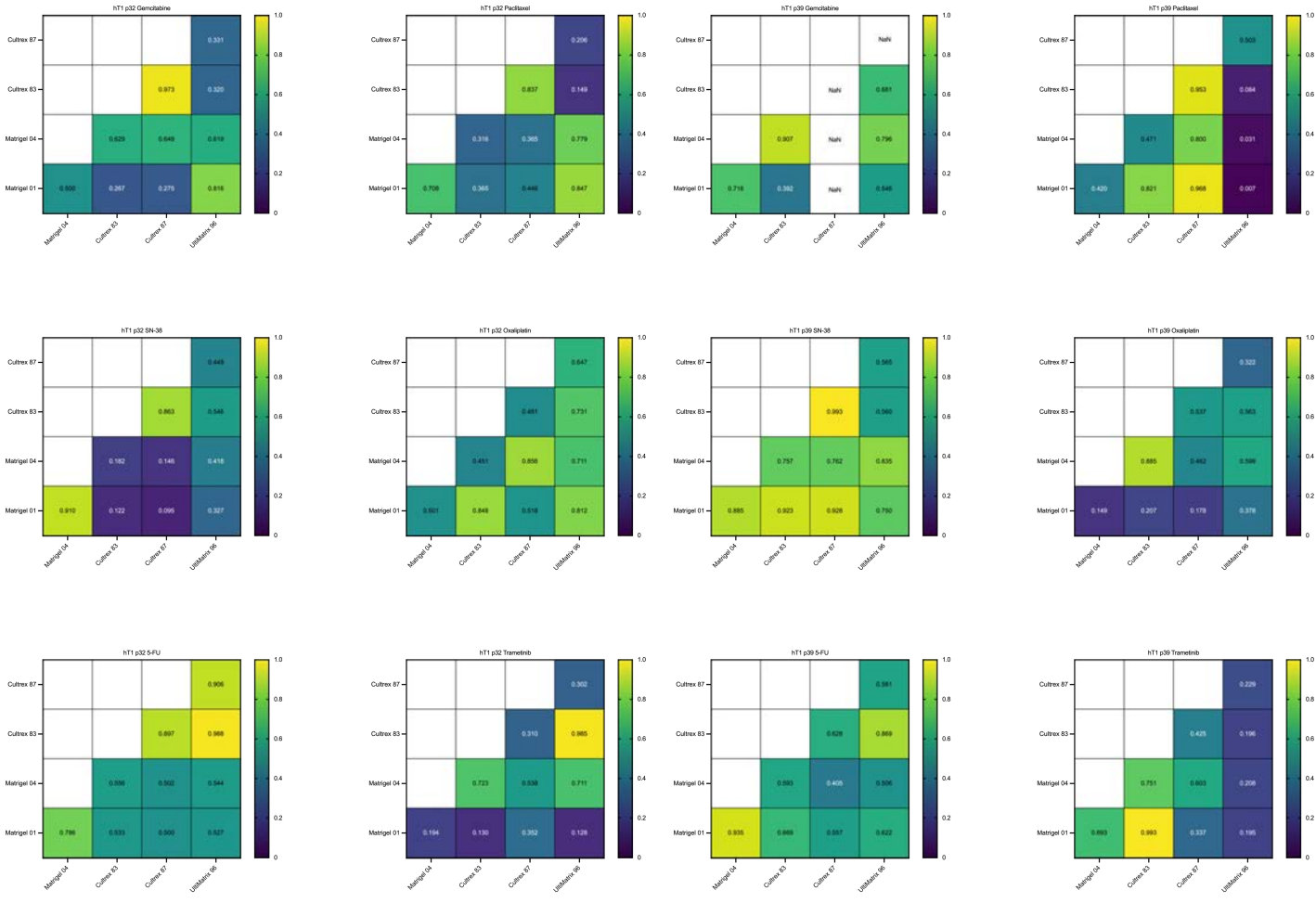
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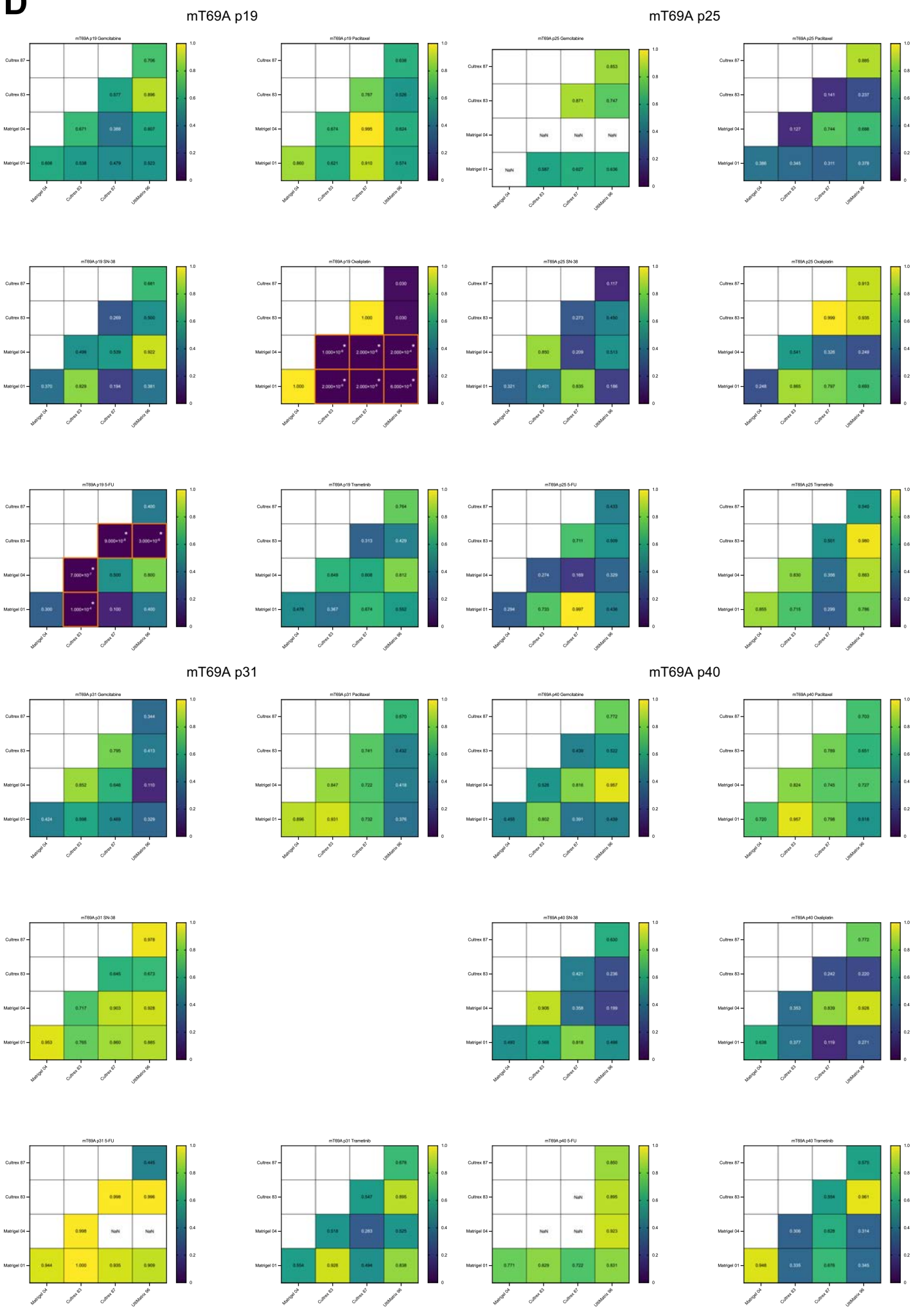
C

hT1 p32

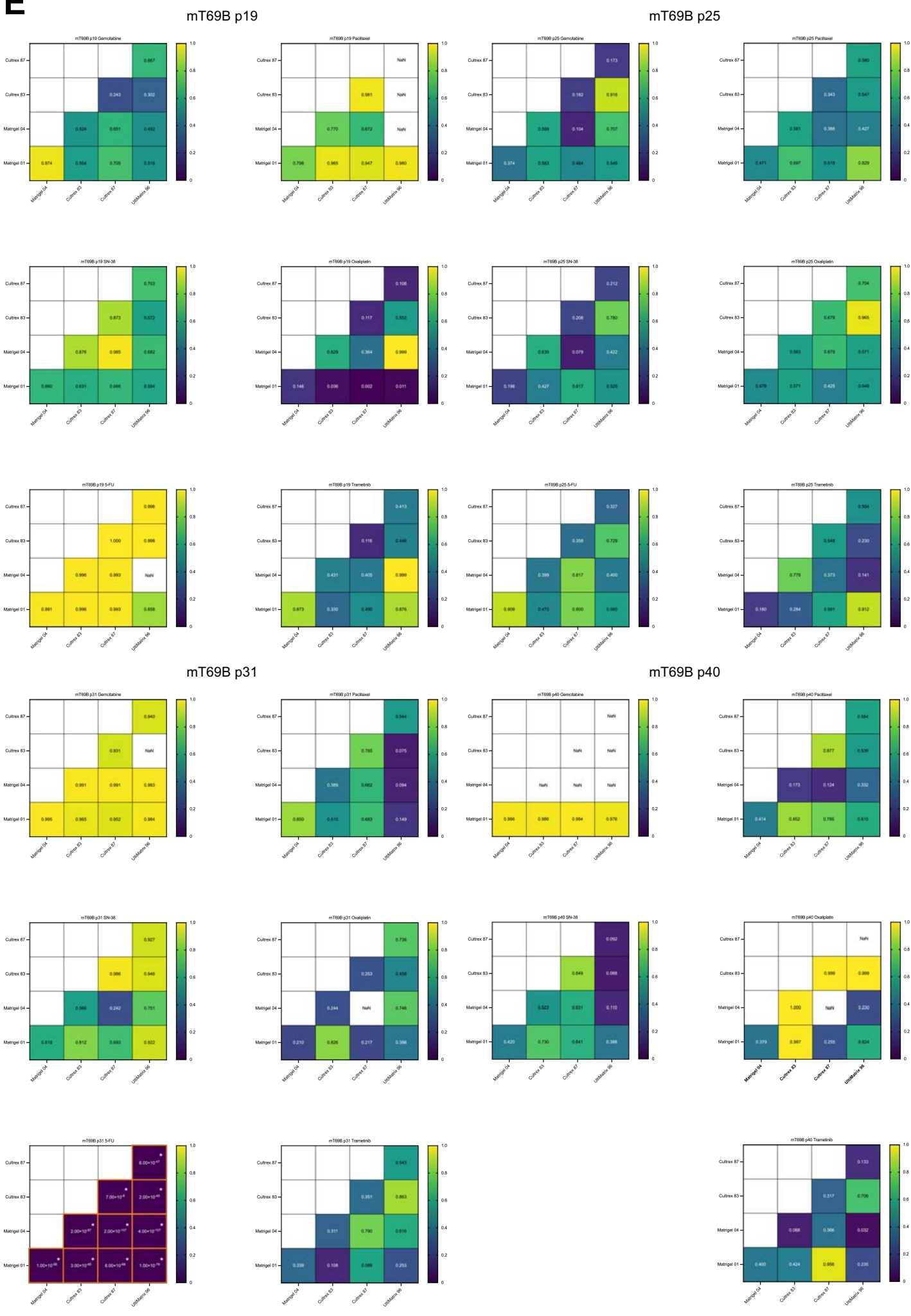
hT1 p39



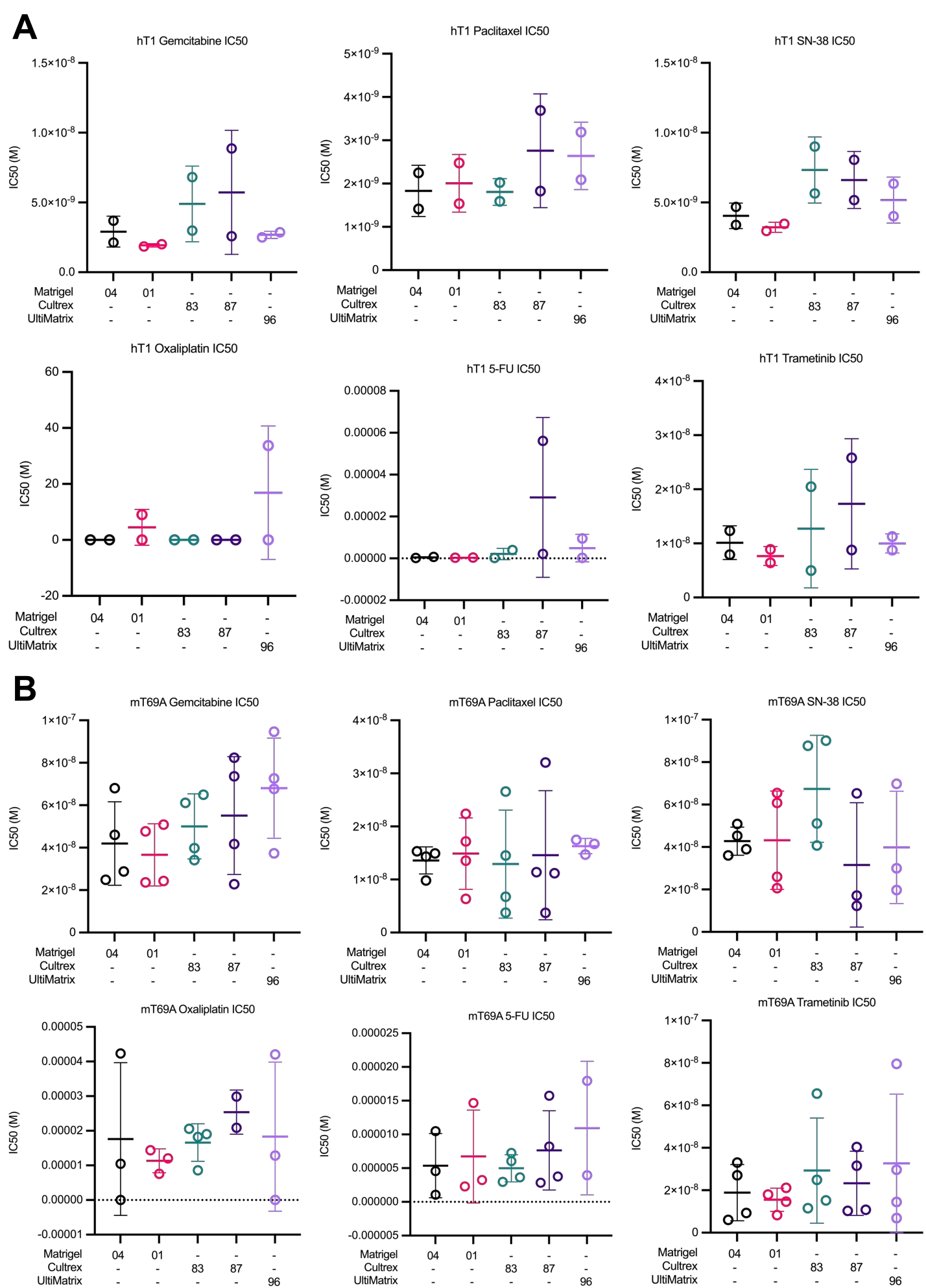
Supplemental Figure 6C – Hill Slope

D**Supplemental Figure 6D – Hill Slope**

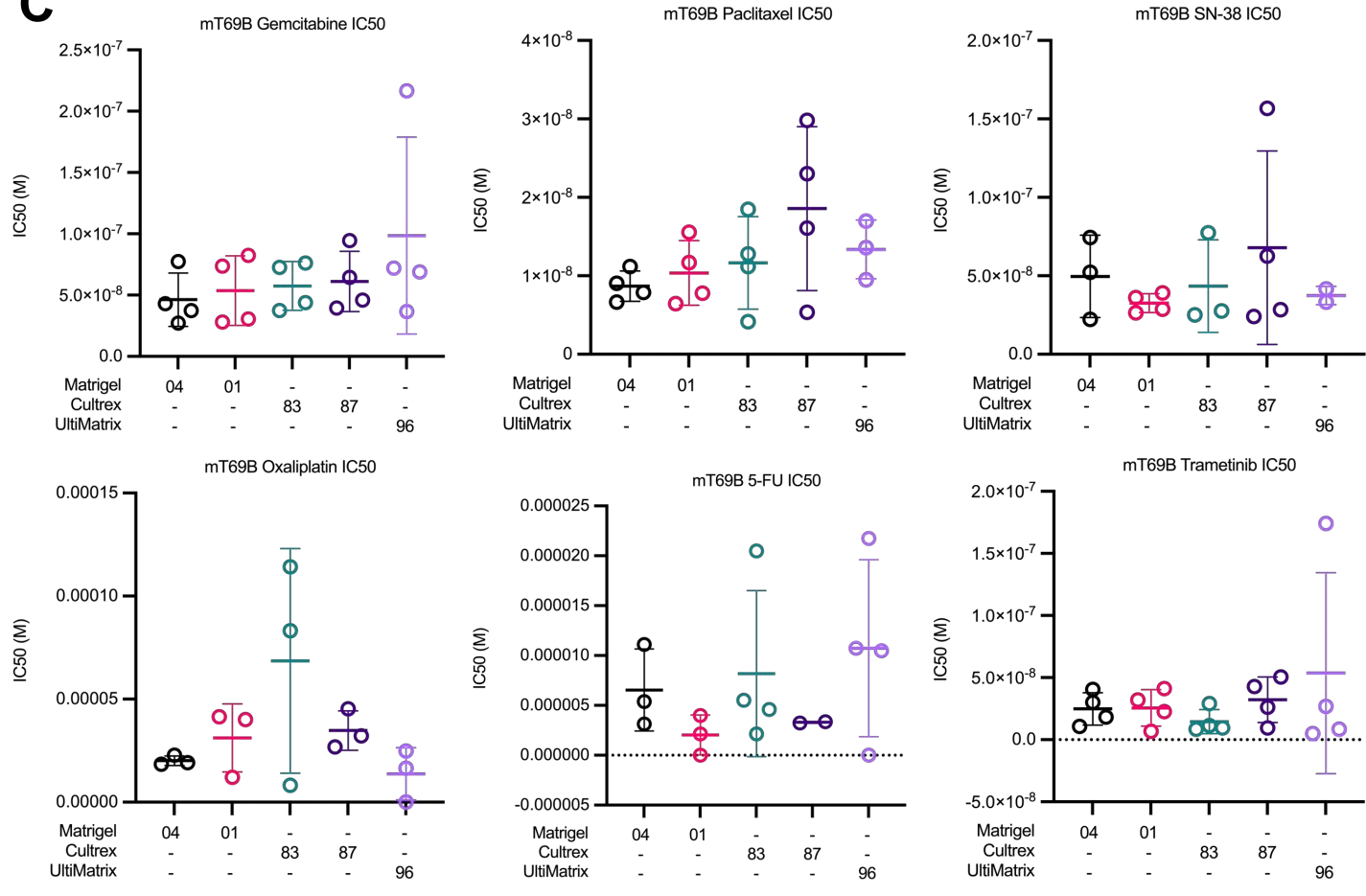
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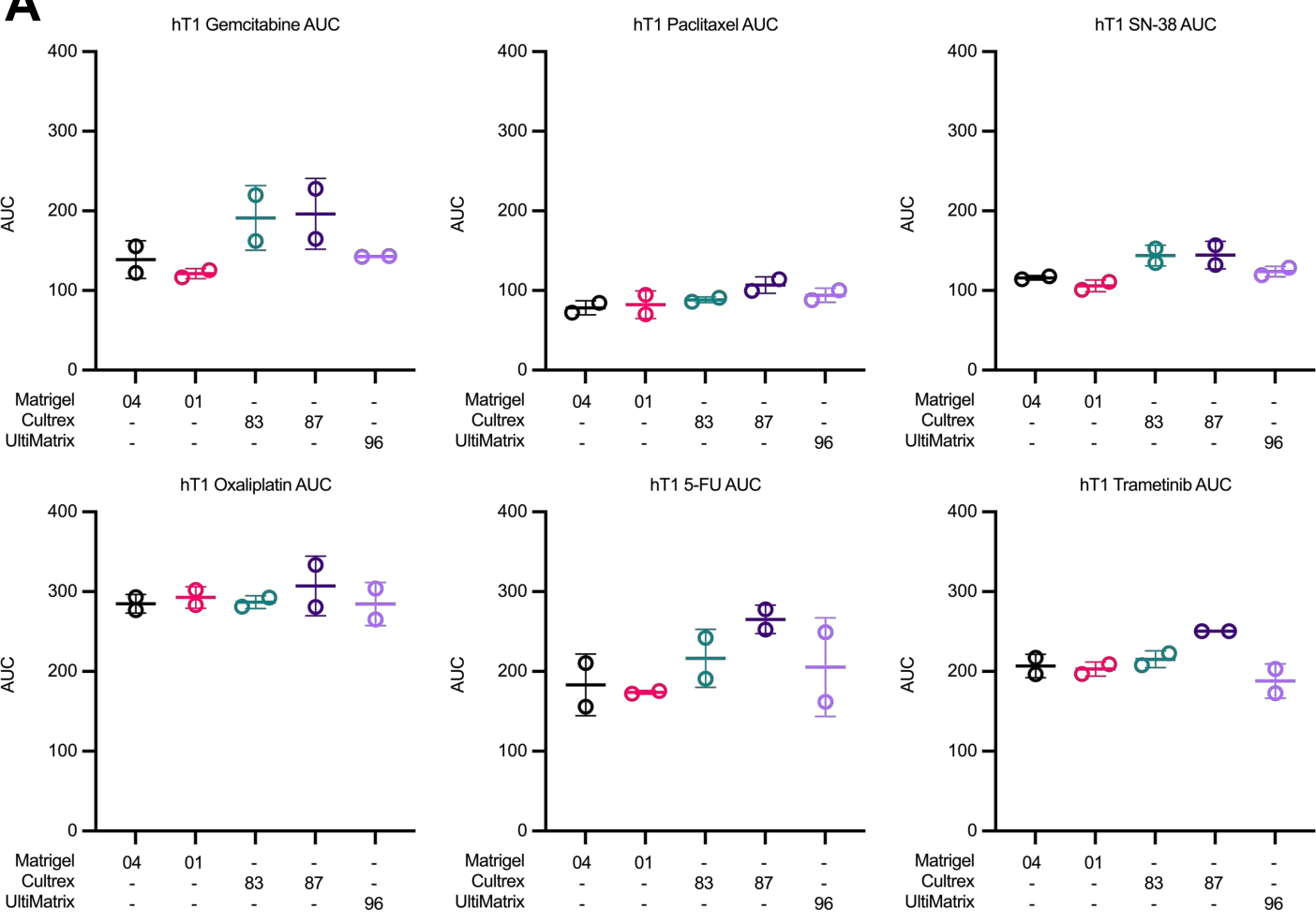
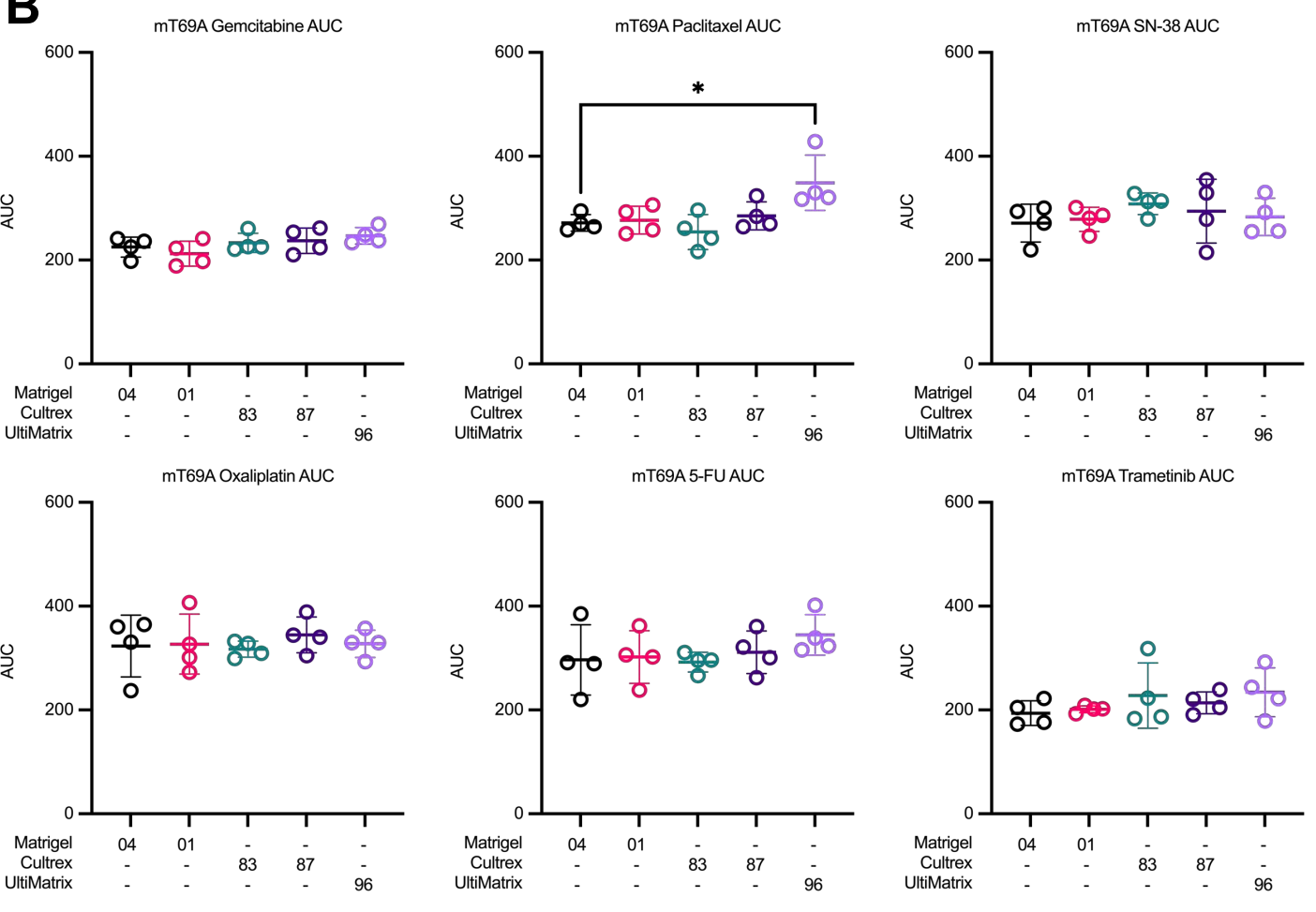


Supplemental Figure 6E – Hill Slope

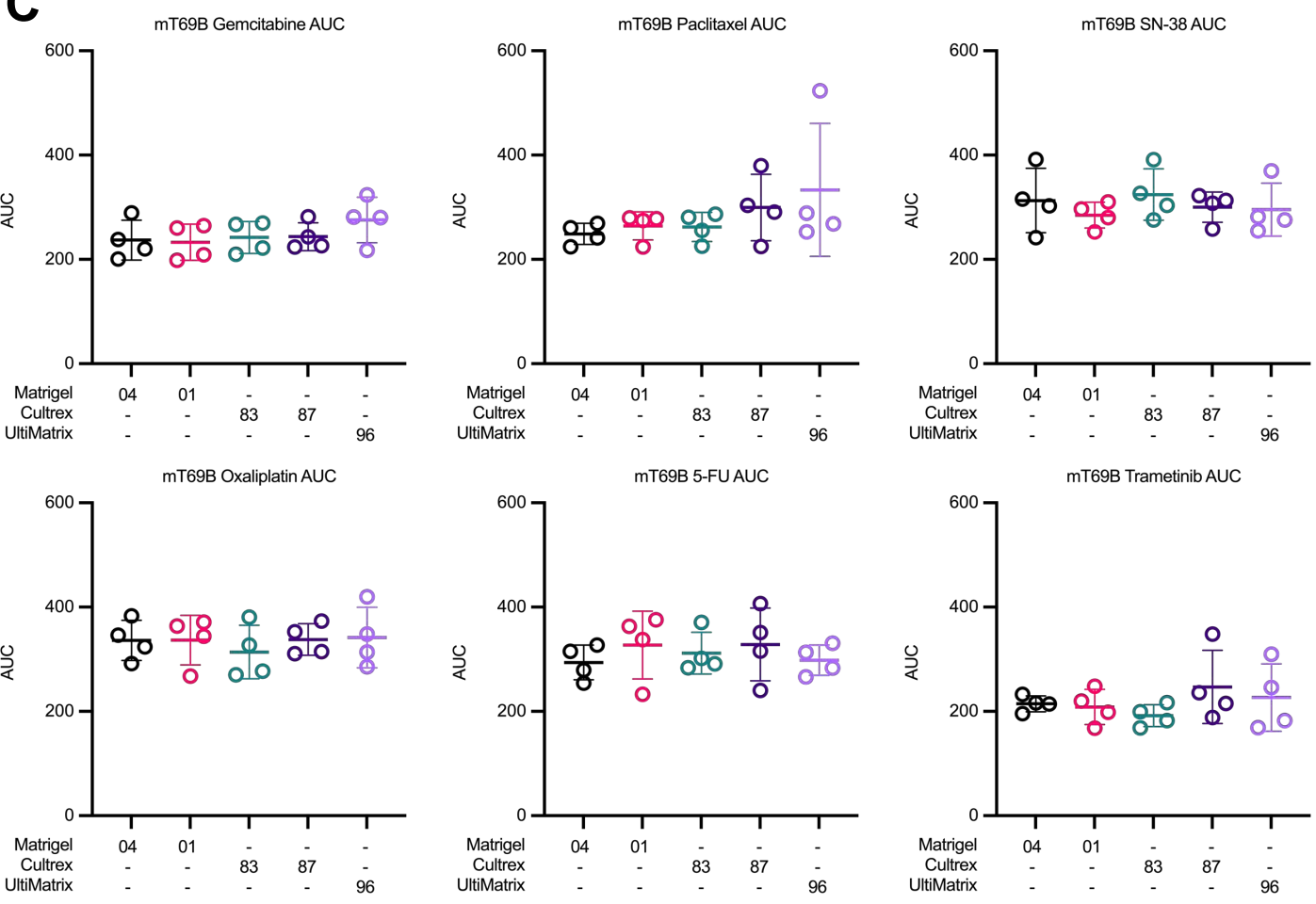


Supplemental Figure 7A-B

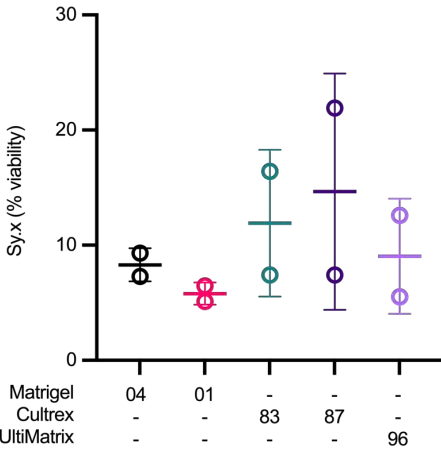
C**Supplemental Figure 7C**

A**B**

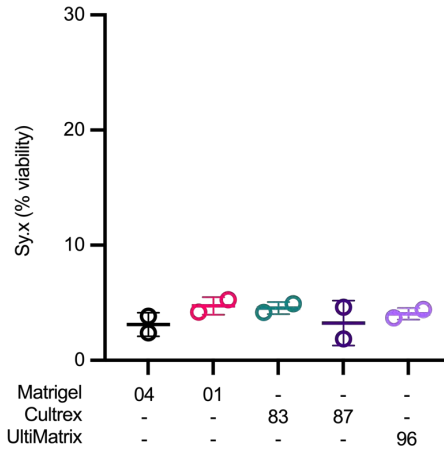
Supplemental Figure 8A-B

C

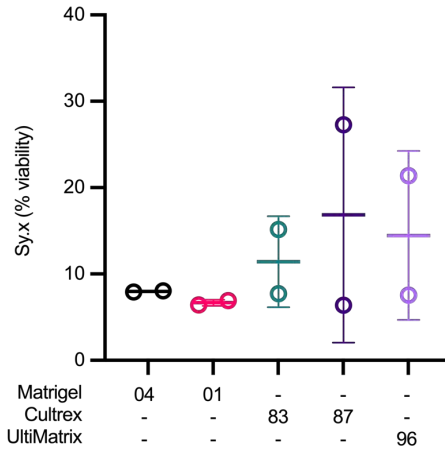
hT1 Gemcitabine Sy.x



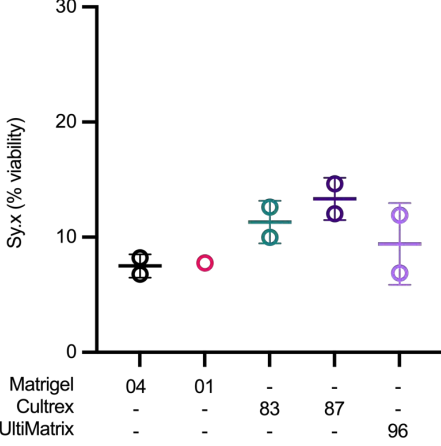
hT1 Paclitaxel Sy.x



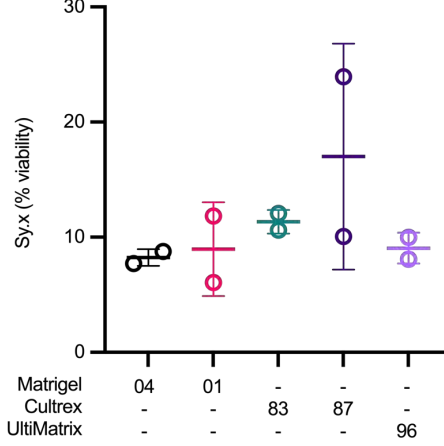
hT1 SN-38 Sy.x



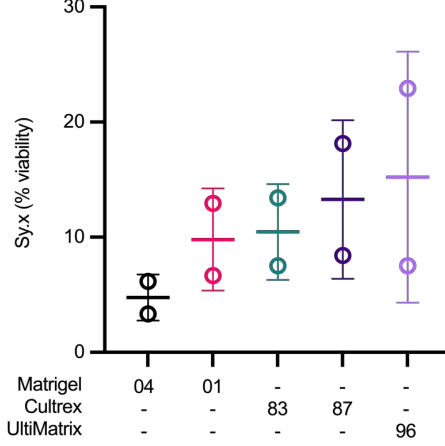
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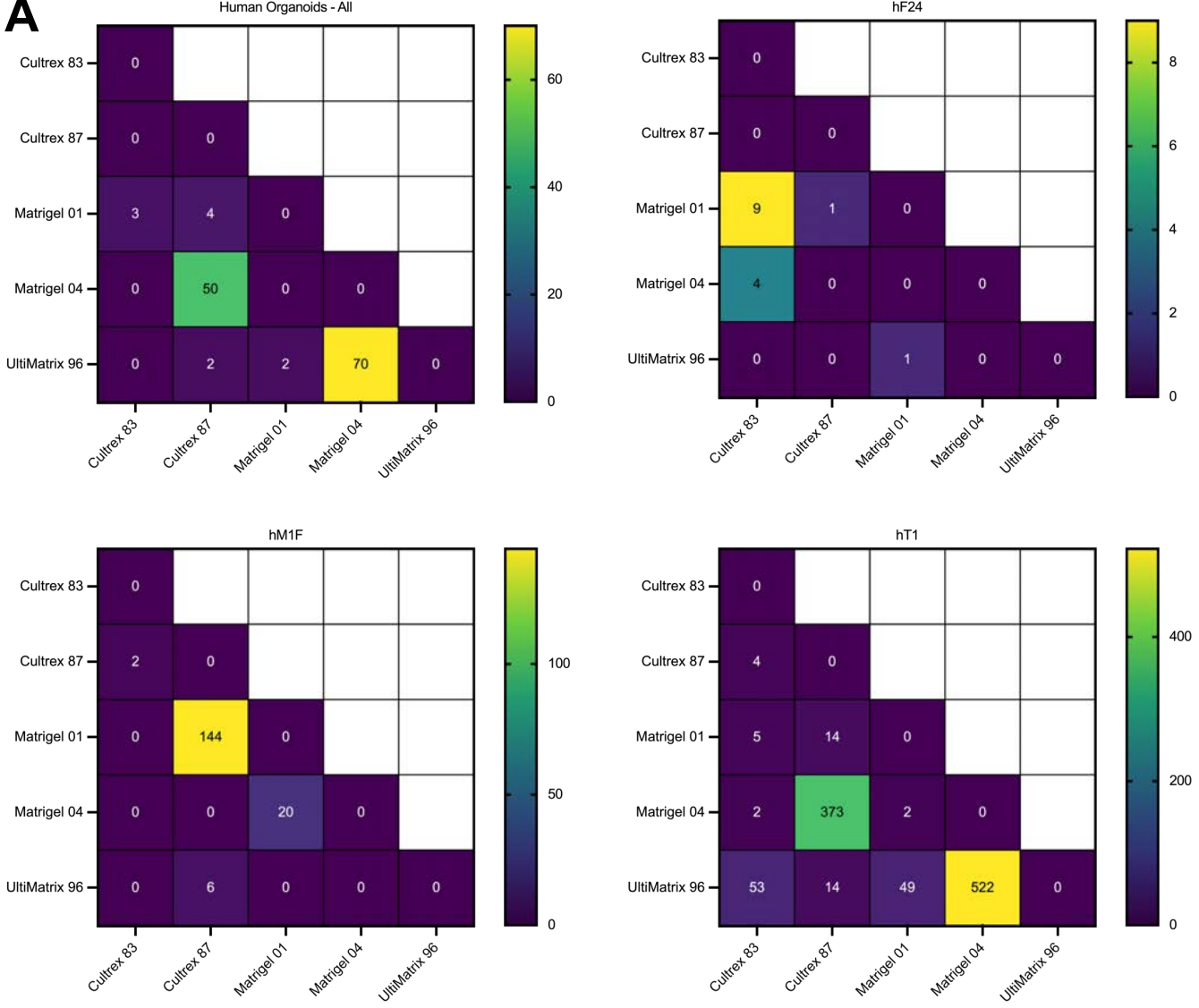
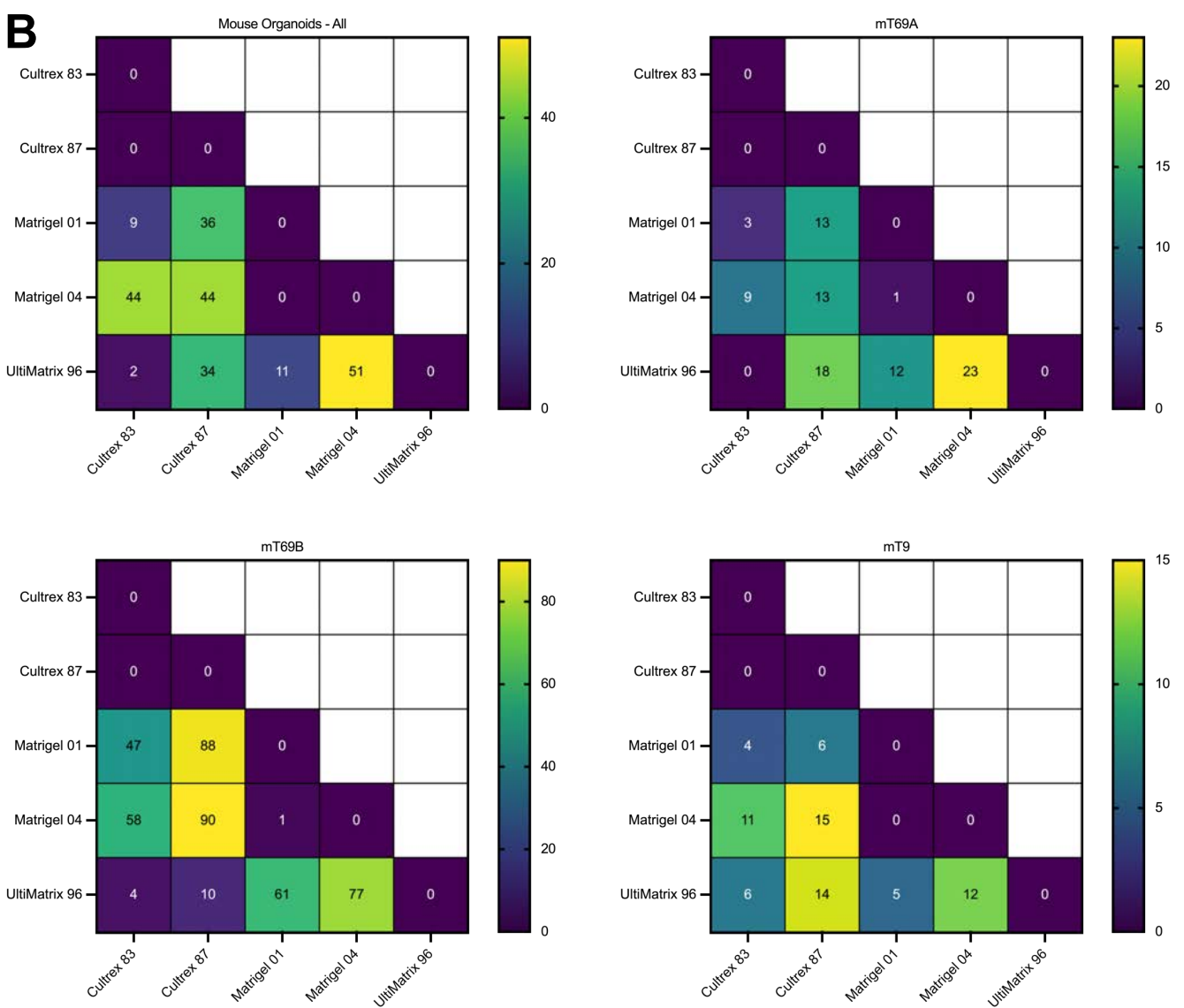


hT1 5-FU Sy.x

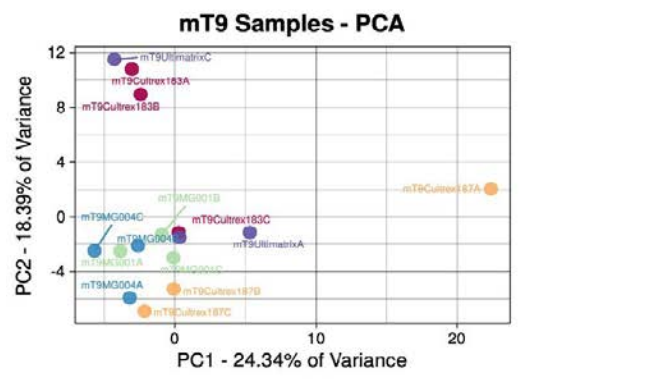
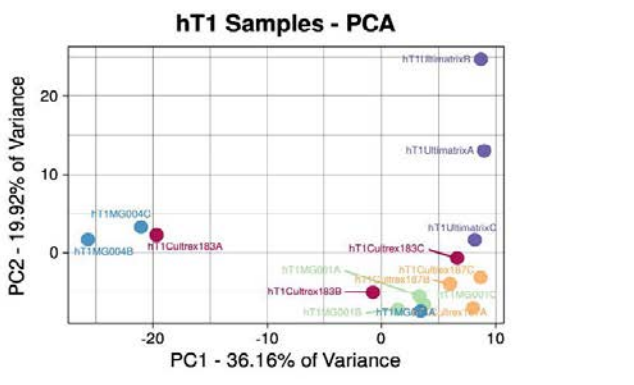
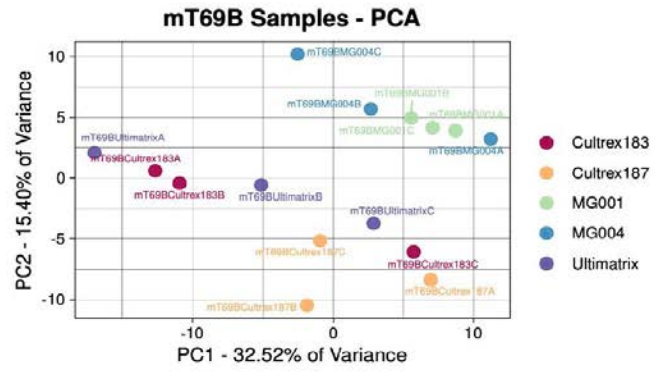
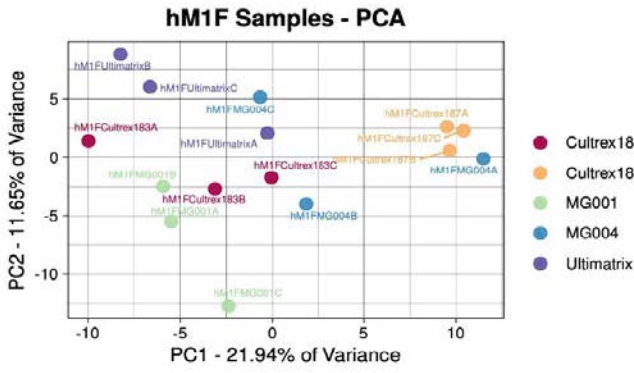
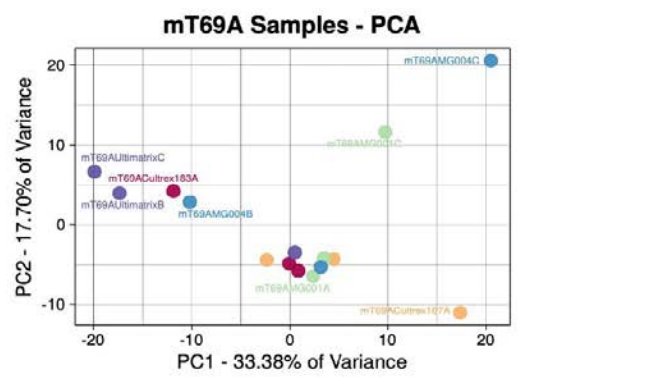
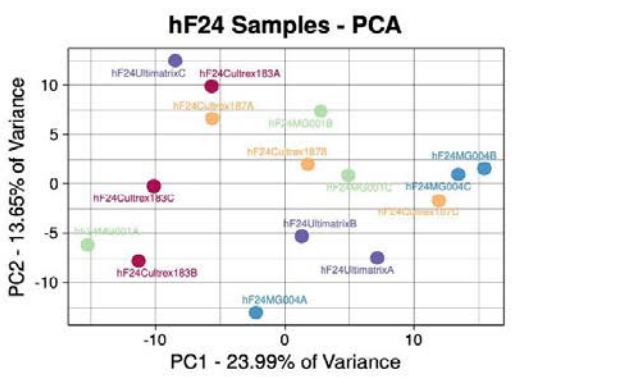
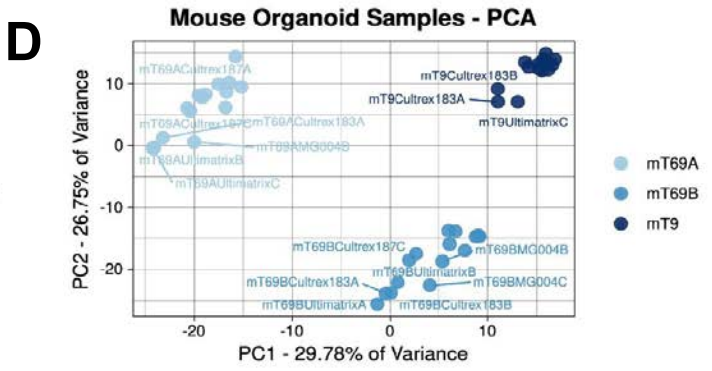
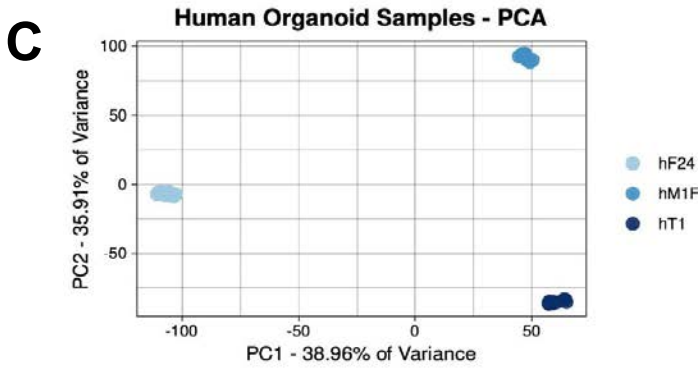


hT1 Trametinib Sy.x



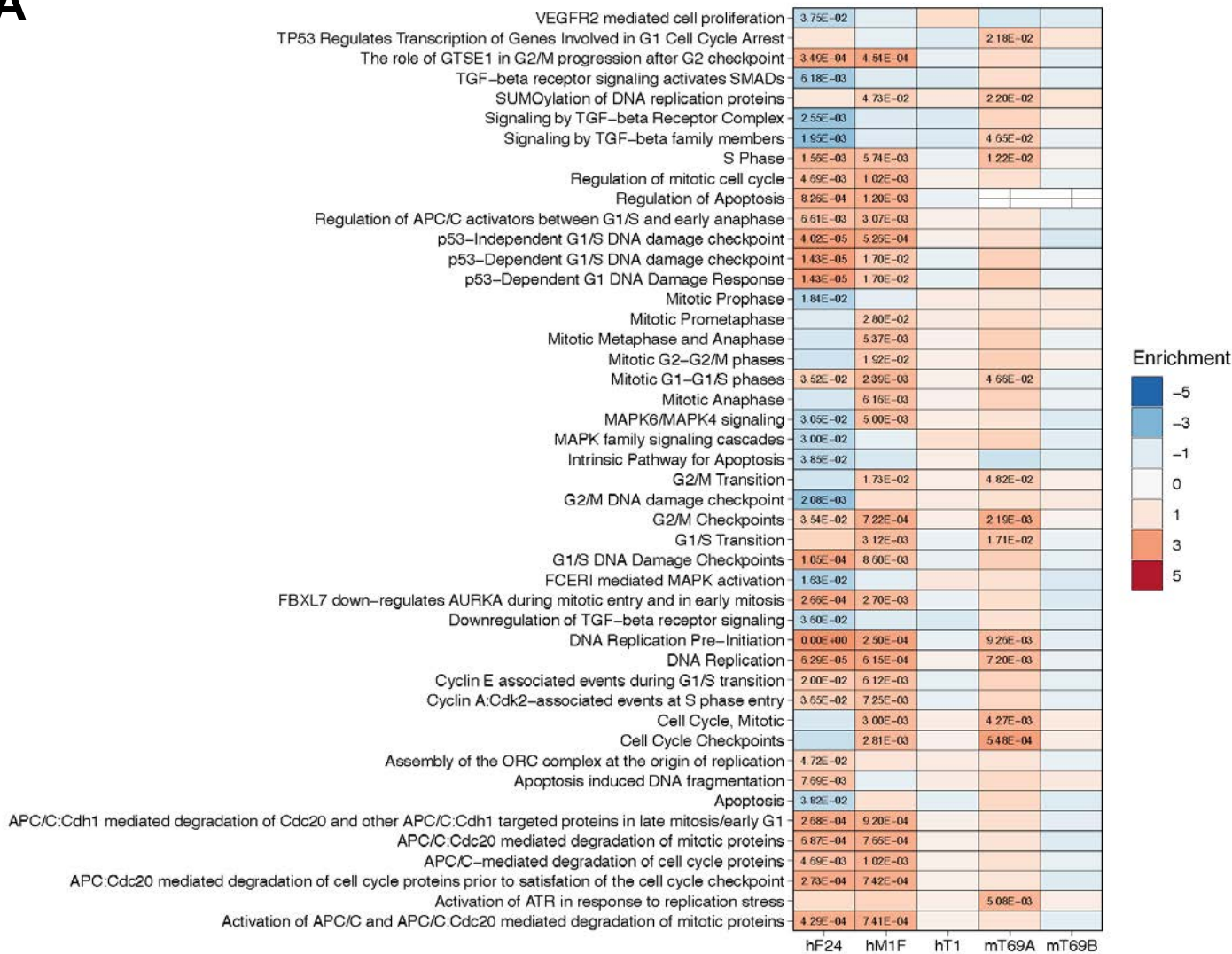
A**B**

Supplemental Figure 10A-B

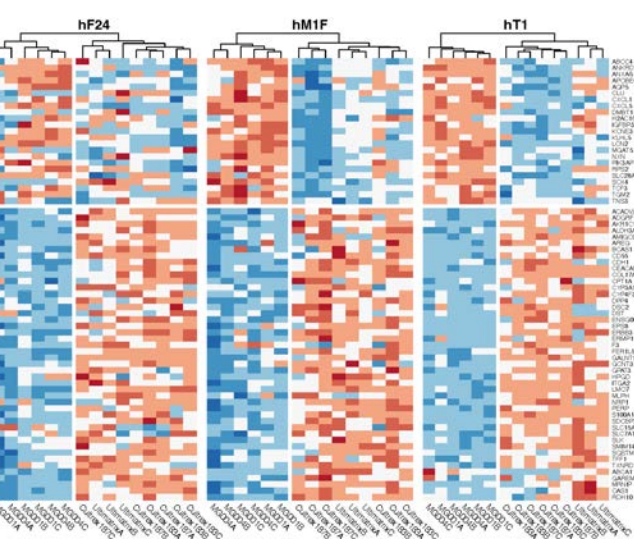


Supplemental Figure 10C-D

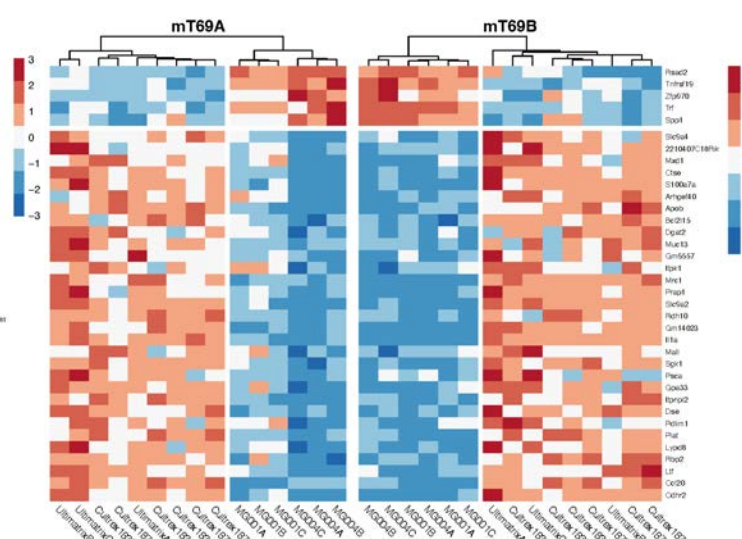
A



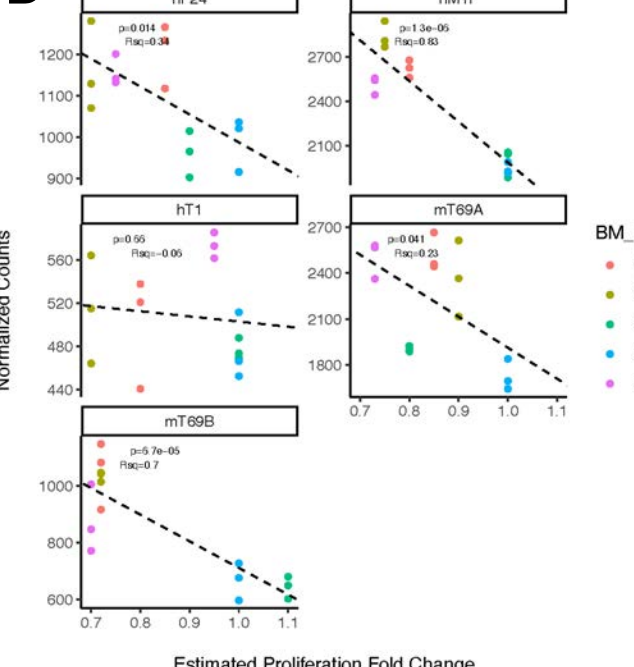
B



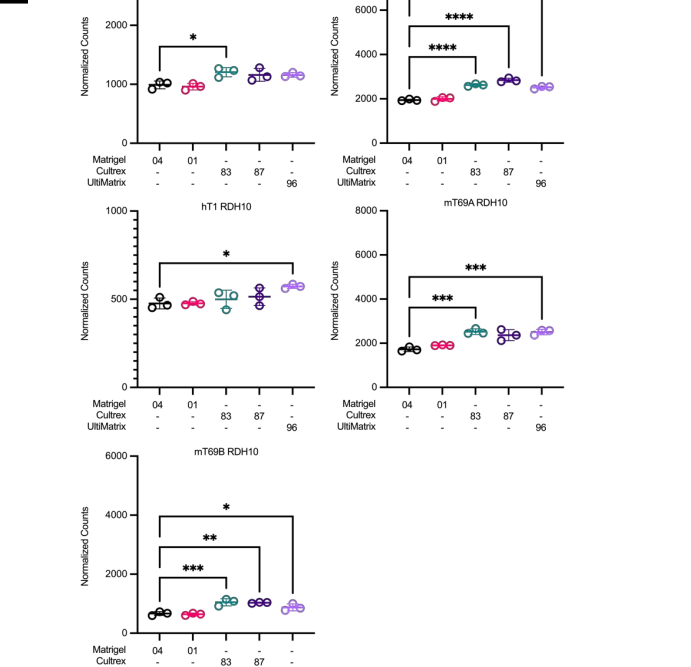
C

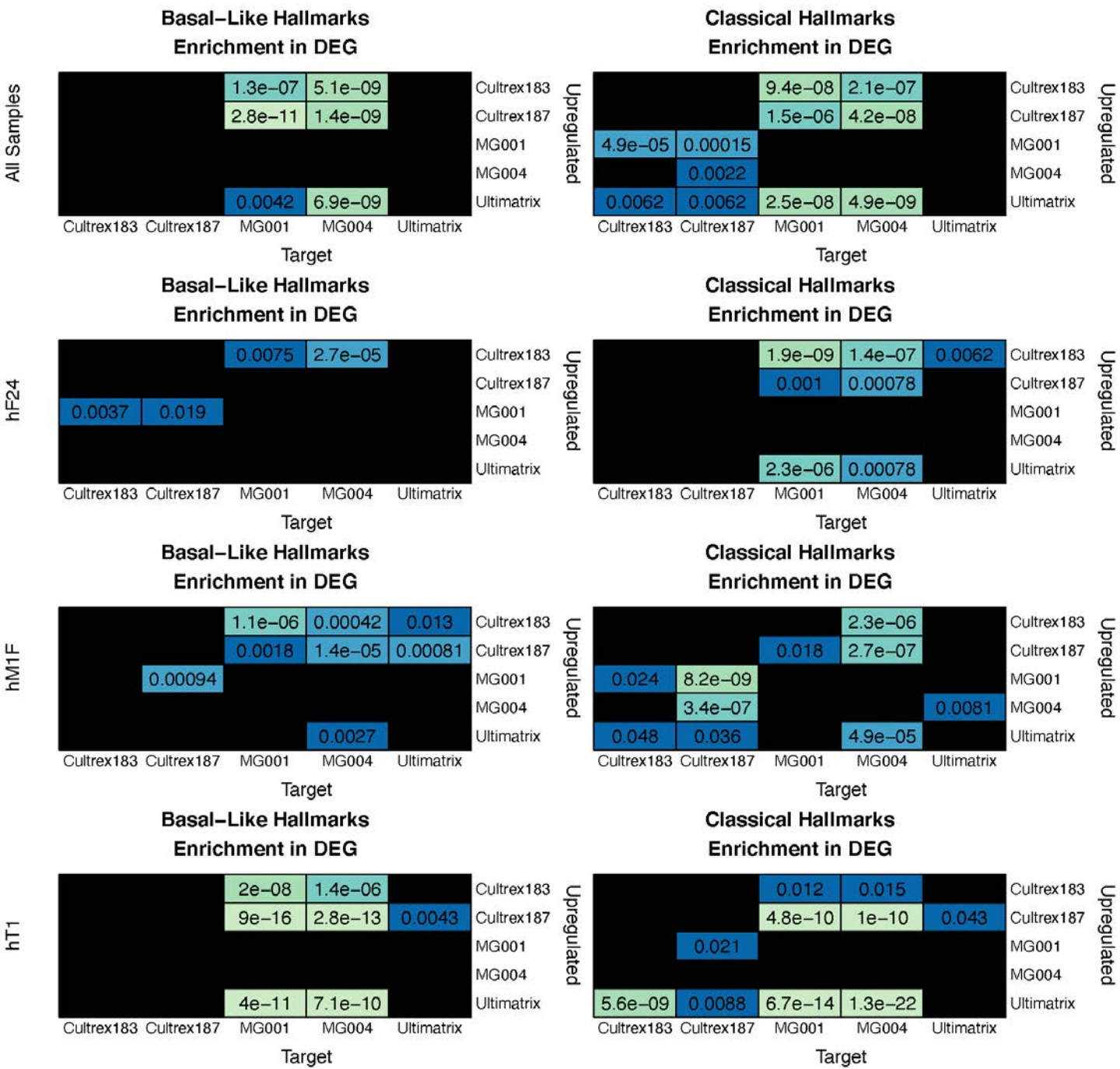


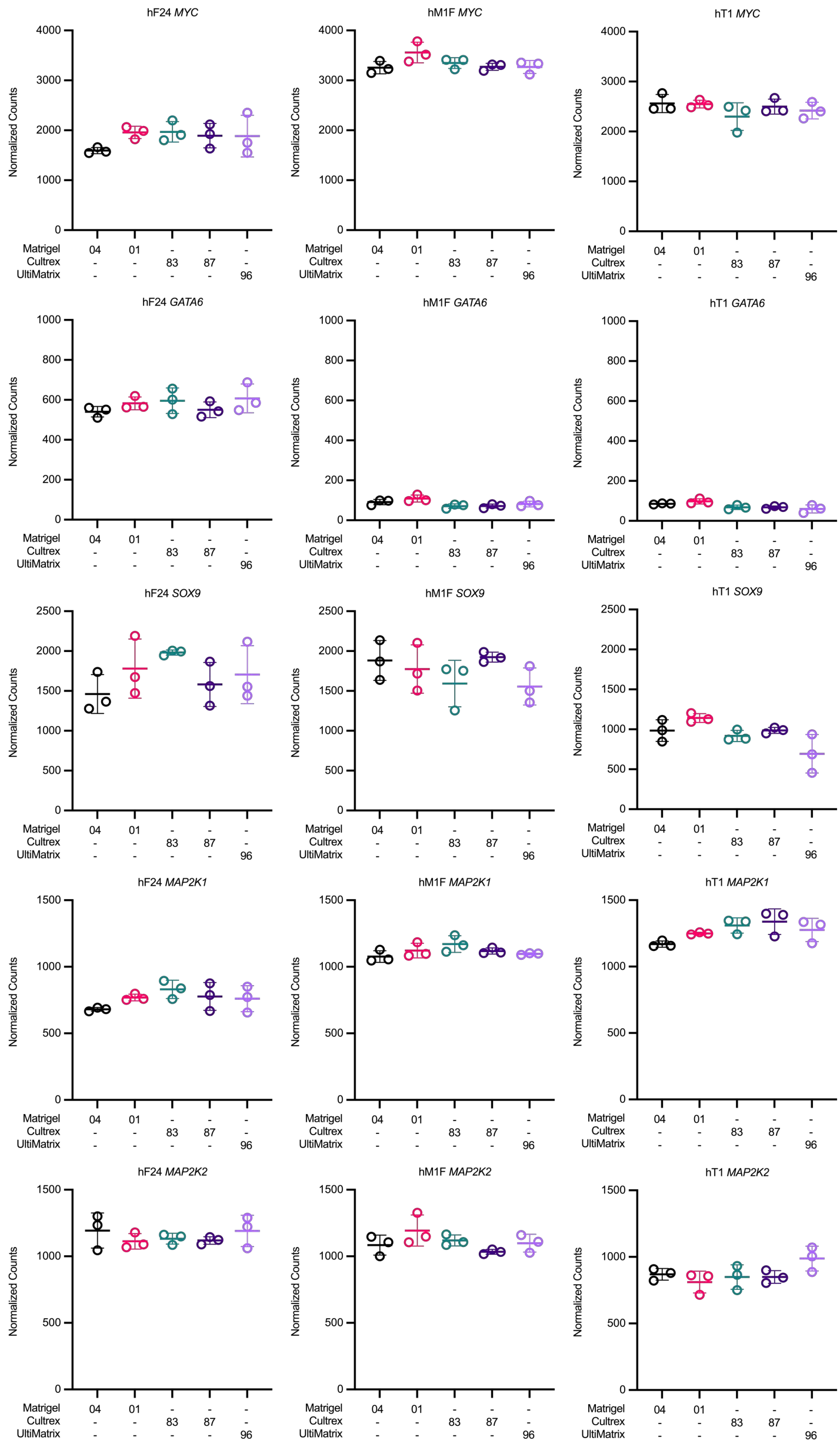
D



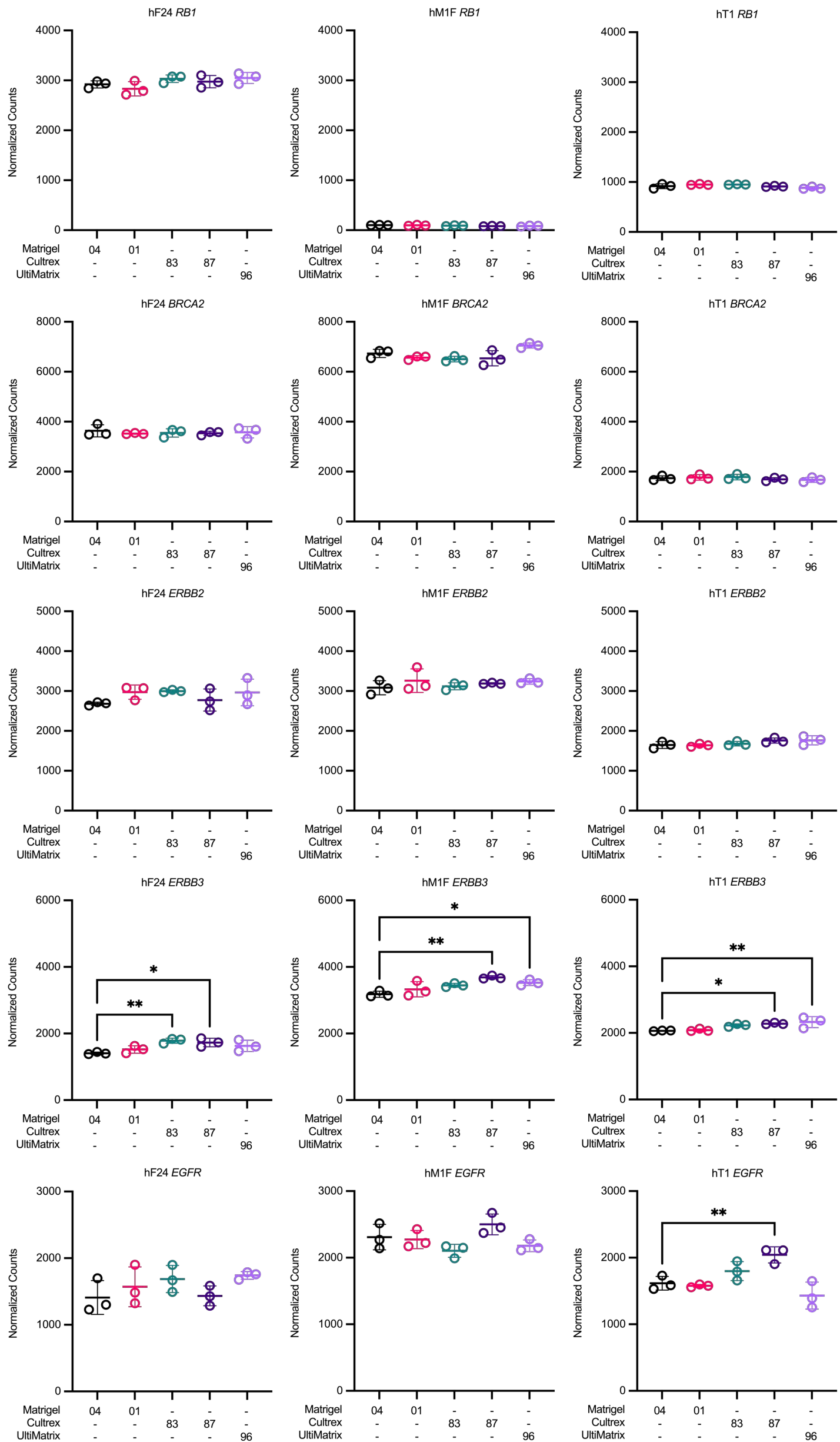
E



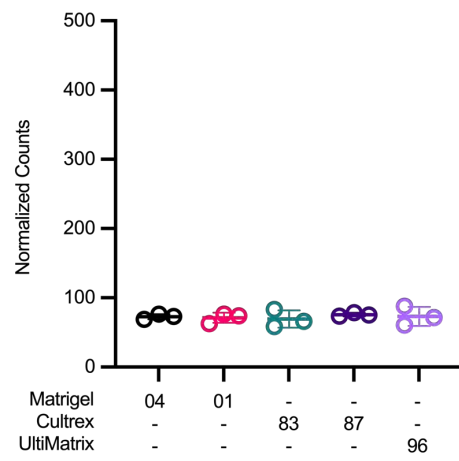
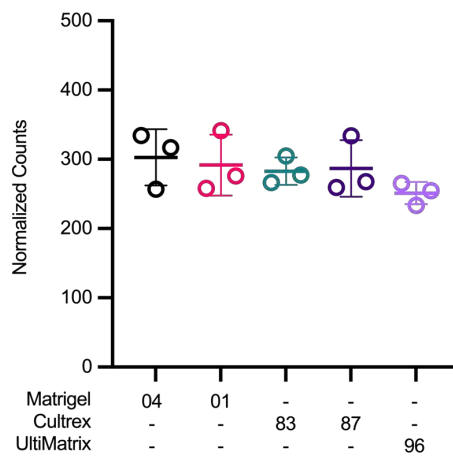
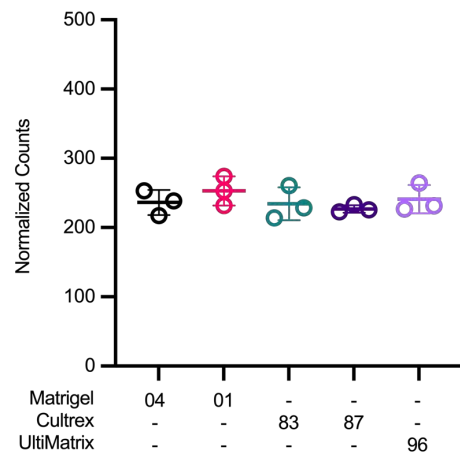
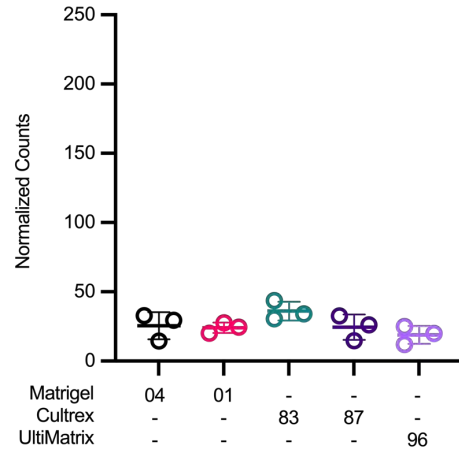
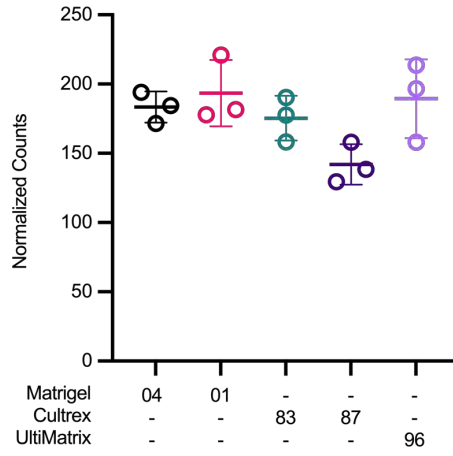




Supplemental Figure 13



Supplemental Figure 13

hF24 *HNF1A*hM1F *HNF1A*hT1 *HNF1A*hF24 *ABCB1*hM1F *ABCB1*hT1 *ABCB1*