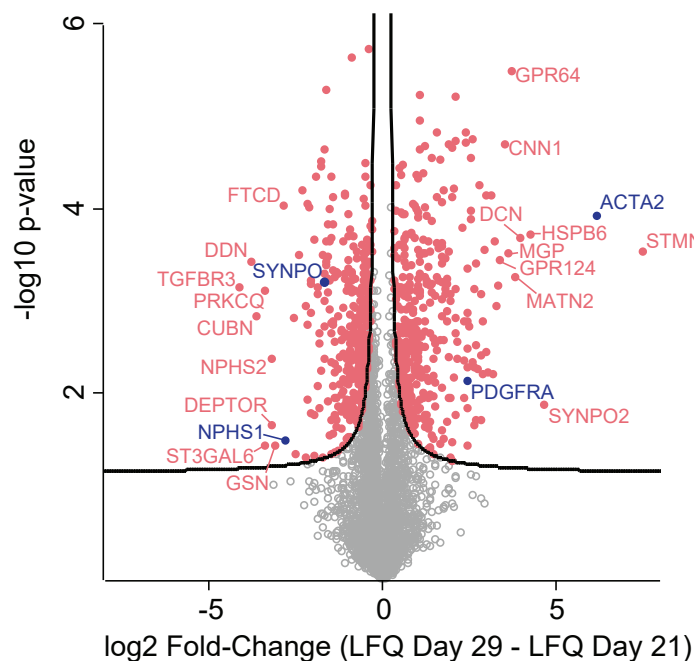
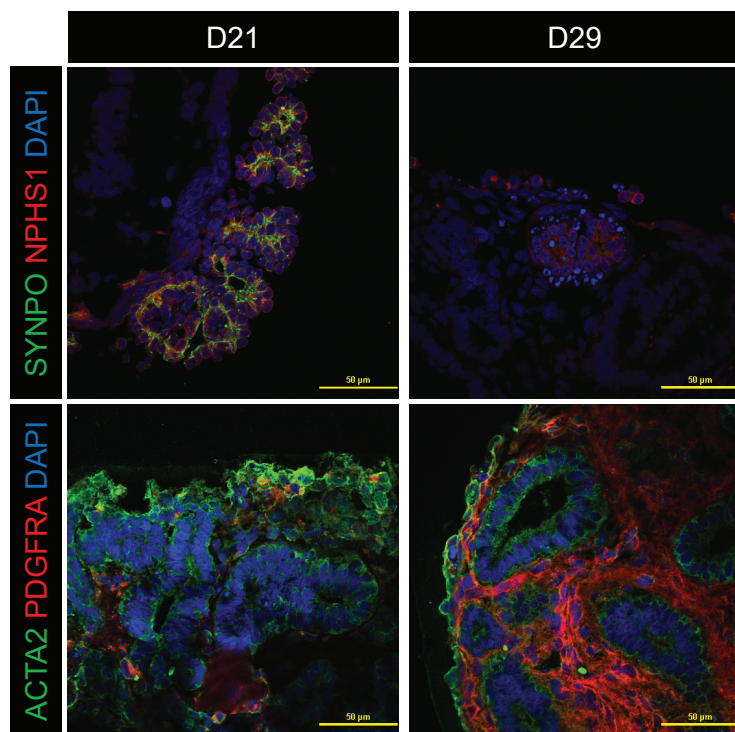
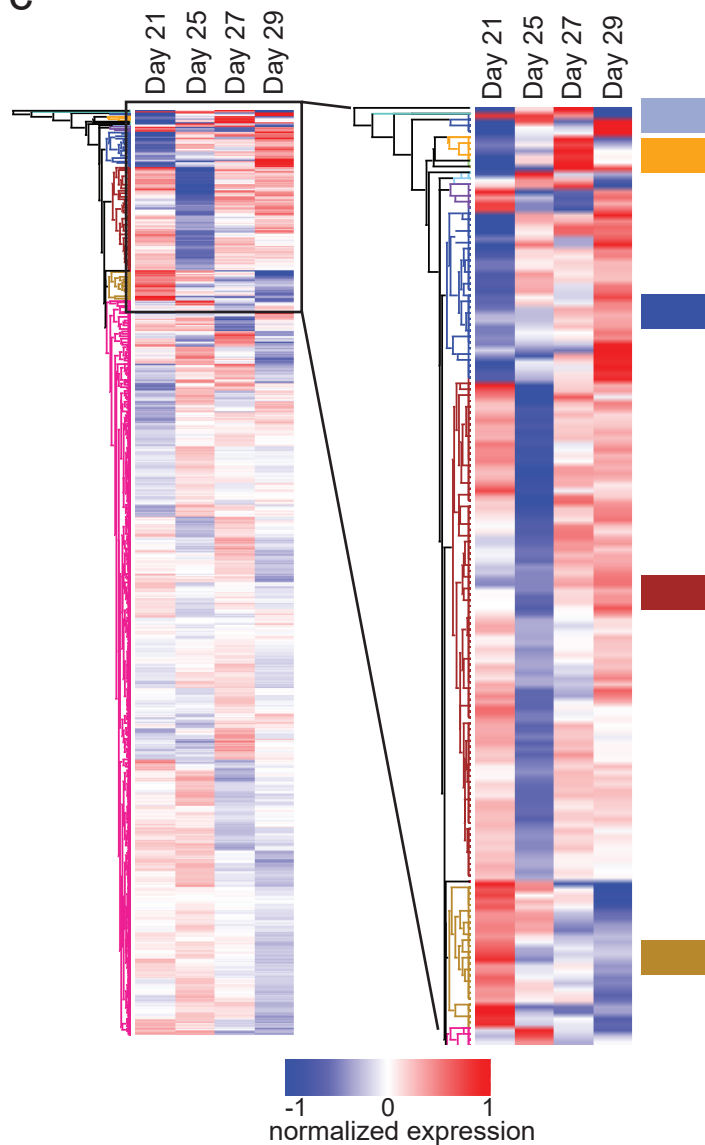
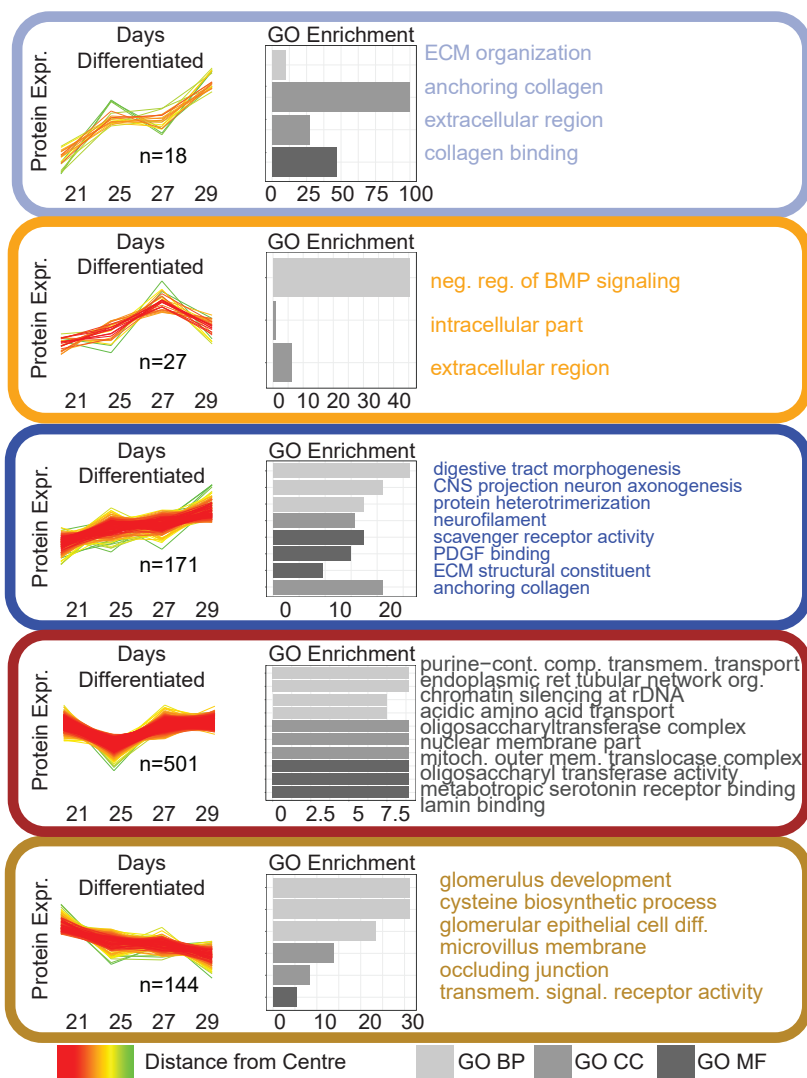
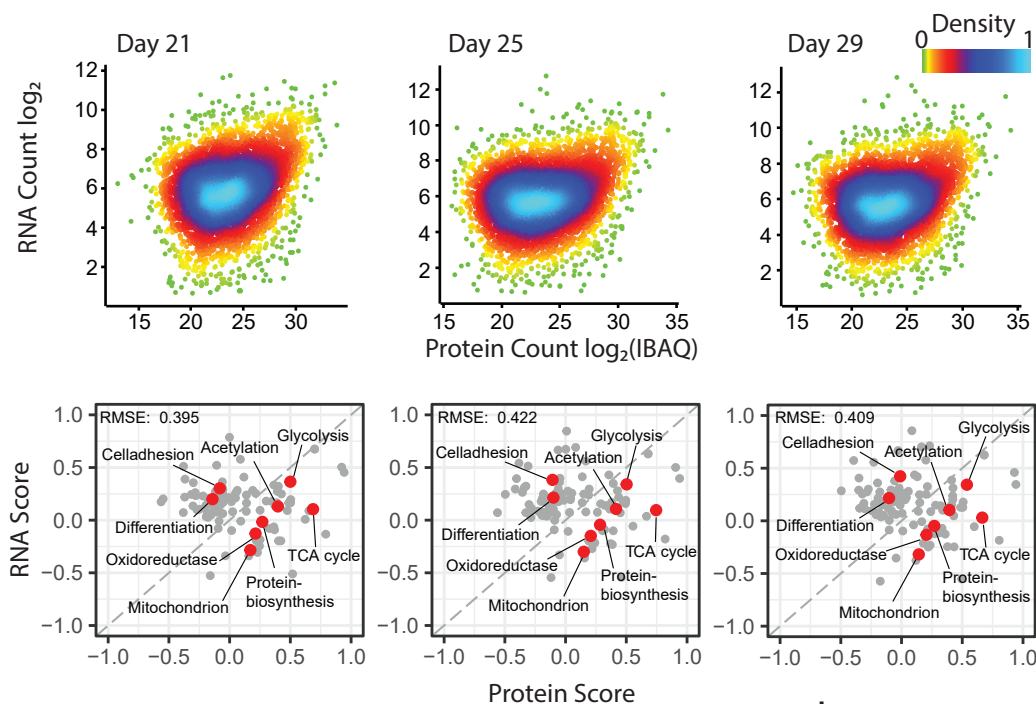
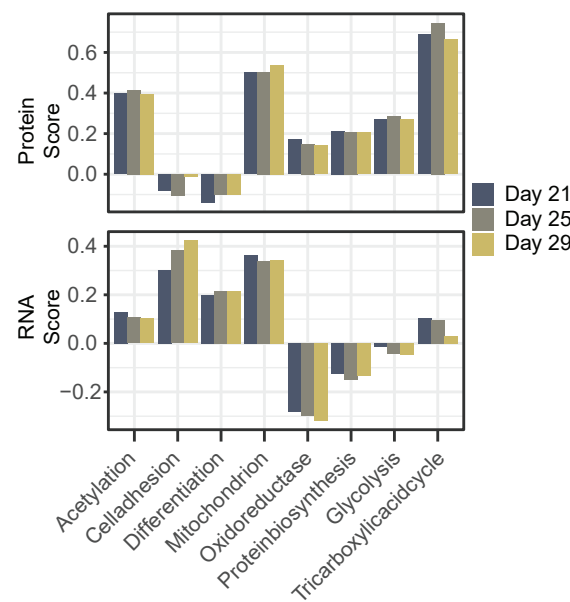


a**b****c****d**

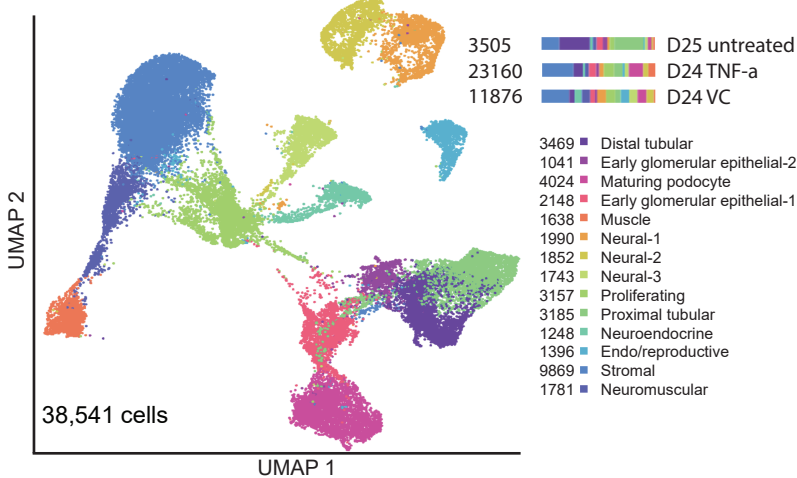
a



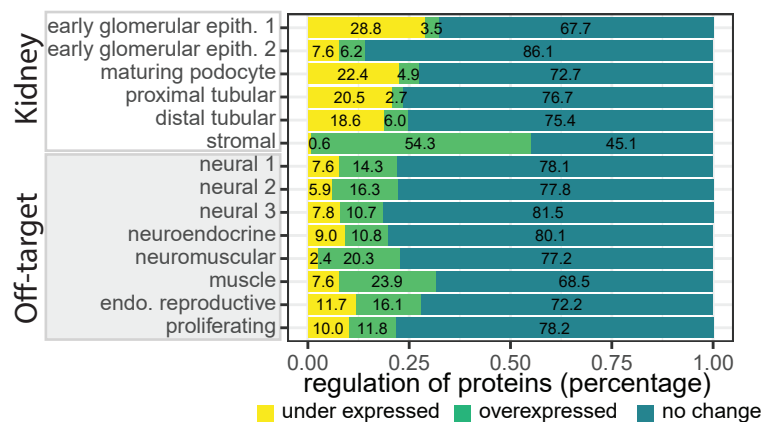
b



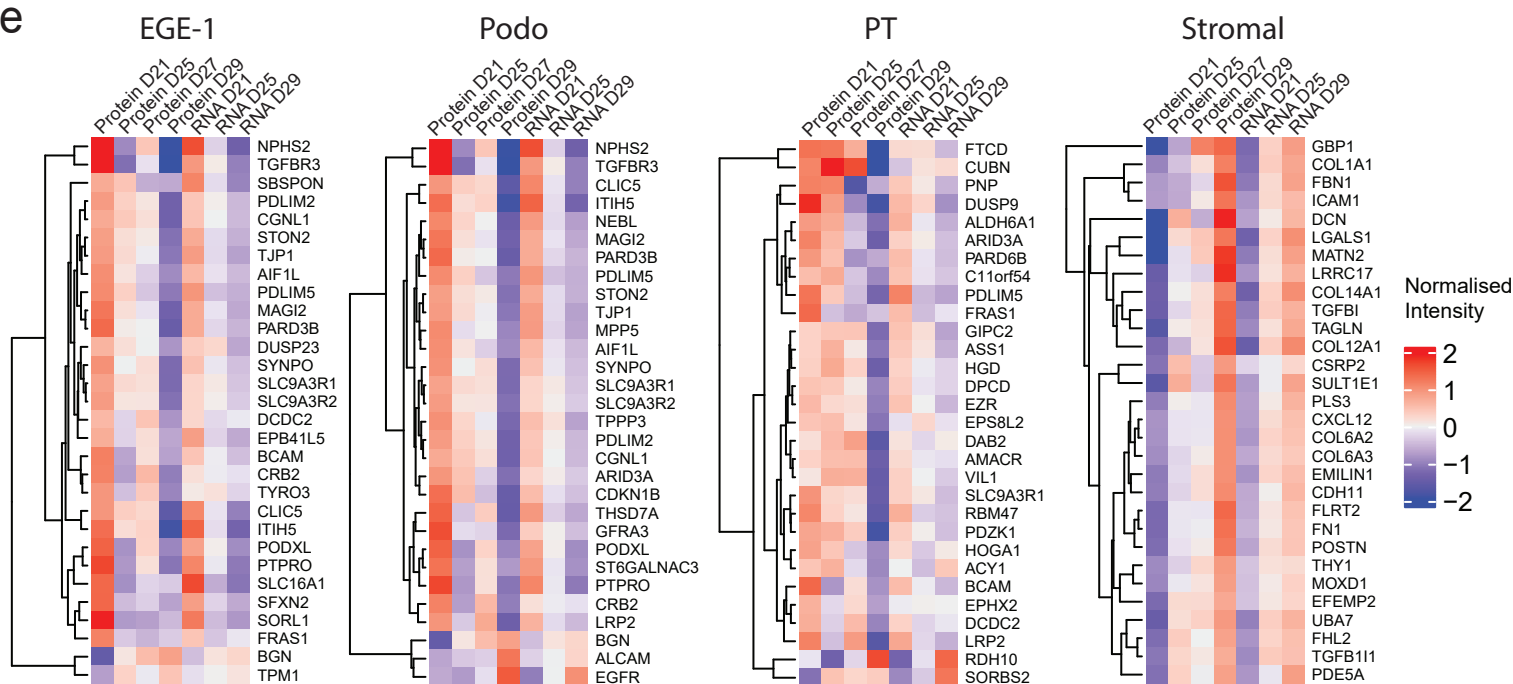
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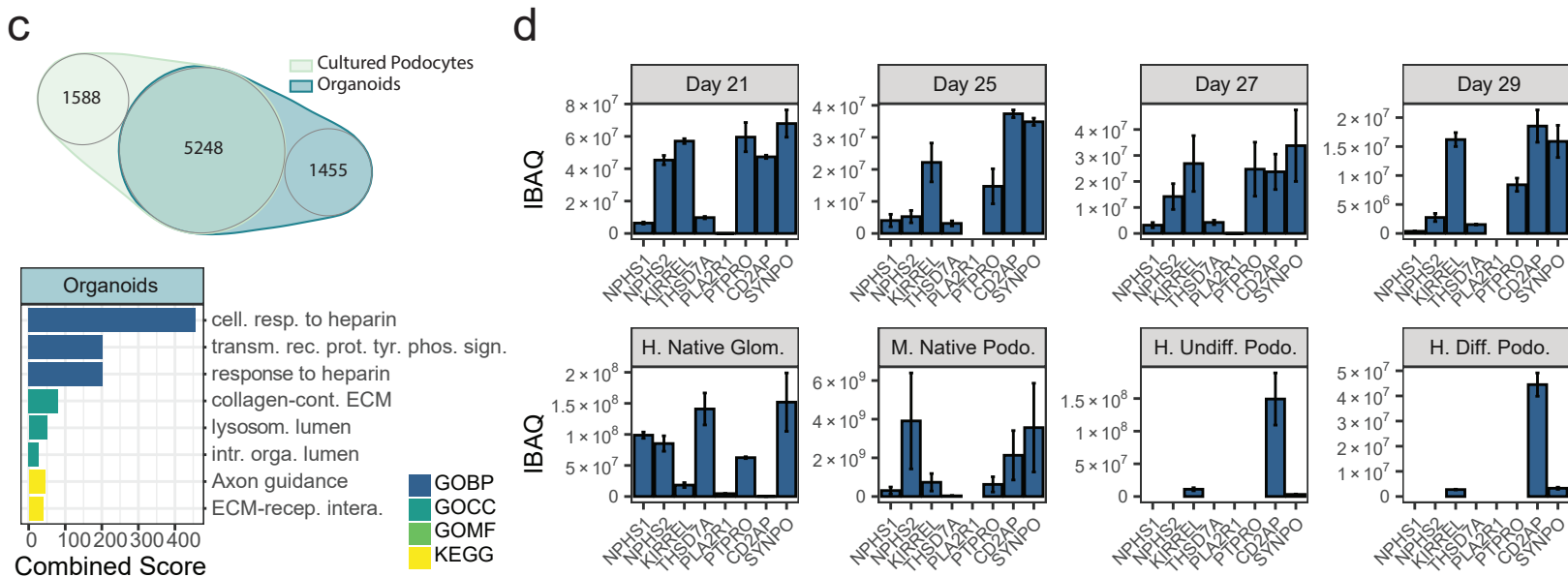
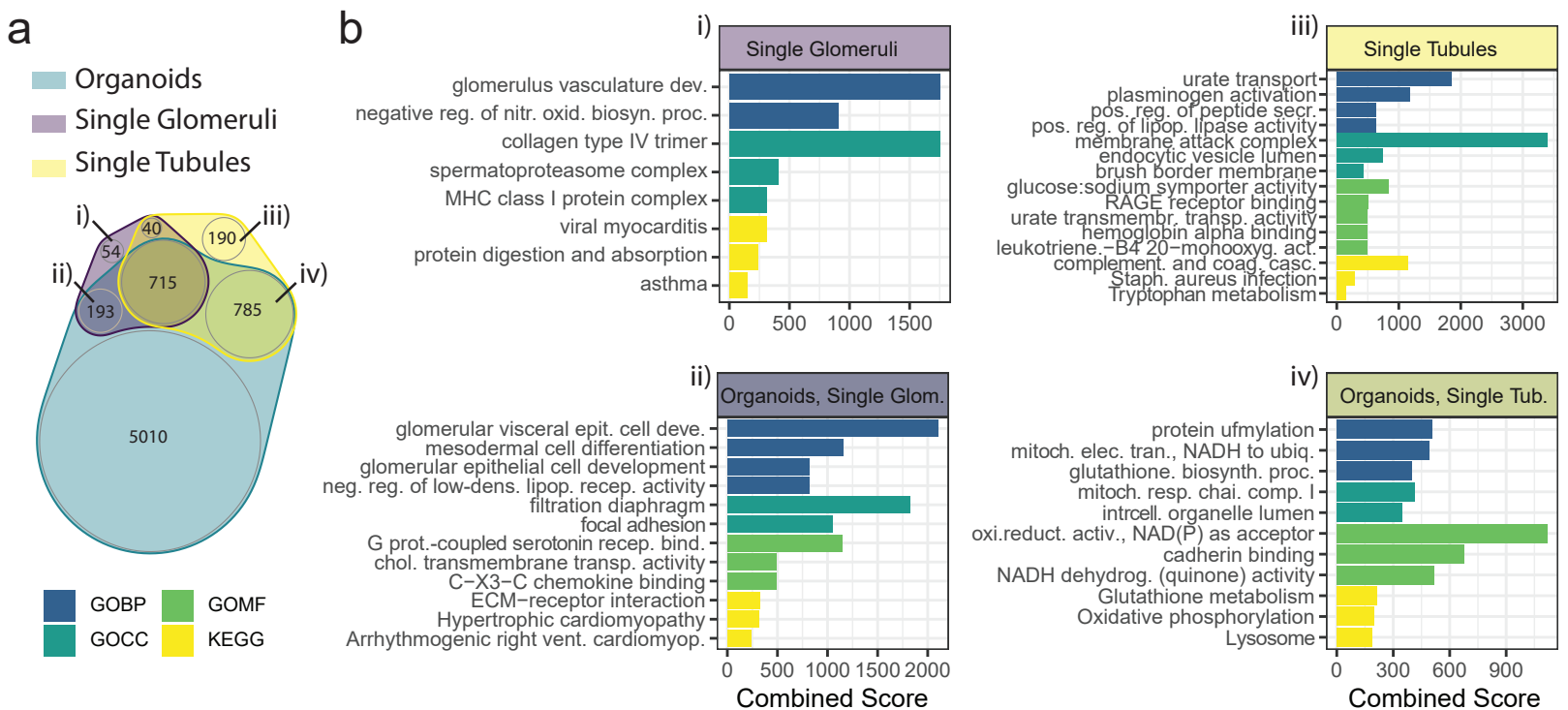


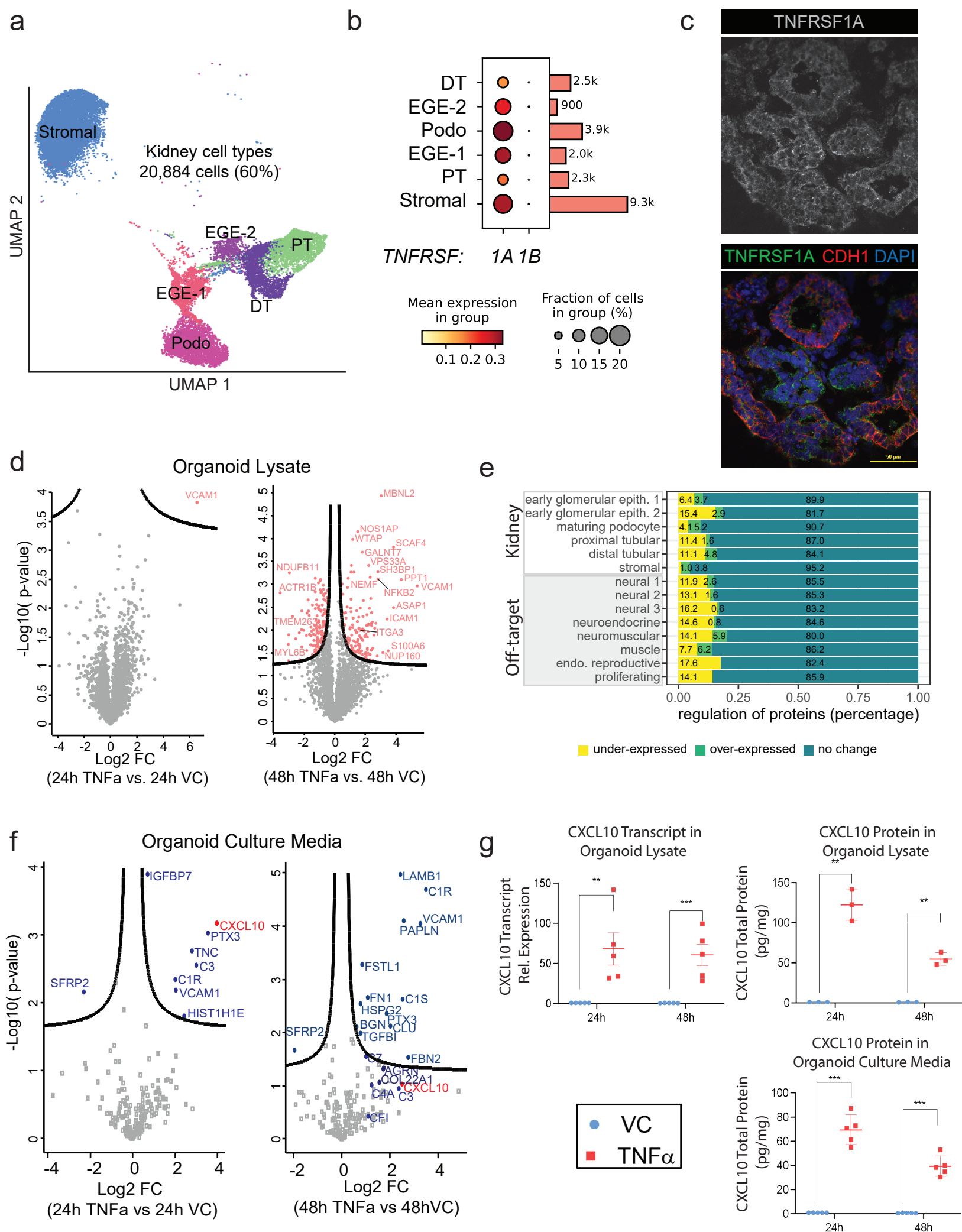
d



e







Transcriptional profiling

220 NEPTUNE biopsies

Consensus clustering

Cluster

1 2 3

ESRD or 40% decline in eGFR

Probability

Years

TNF Z-score

Cluster

1 2 3

Organoid TNF Z-score

[TNF]

0 0

● 3 hours

● 20 hours

TNF signatures

Kidney tissue transcriptomes
272 genes

TNF treated organoids
320 genes

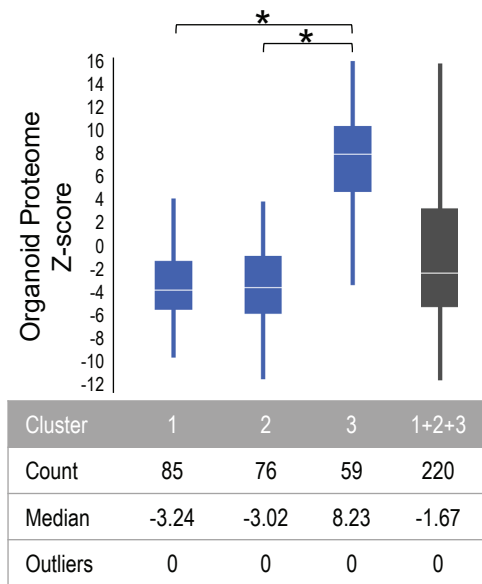
262 10 310

BGN
C3
CXCL10
HSP90B1
ICAM1

MAP4K4
NFKB2
OPTN
PTX3
VCAM1

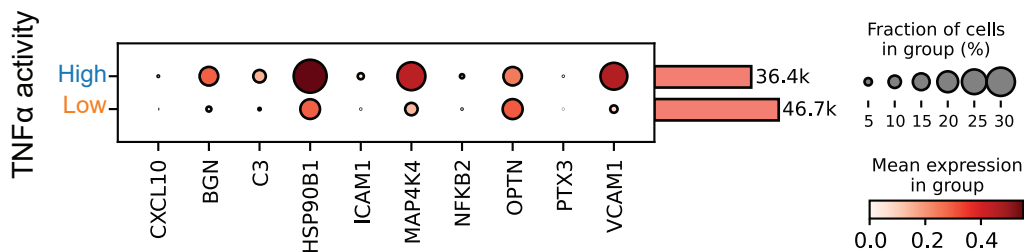
Org. Tissue
Org. Medium
Both

Genes of all 320 proteins differentially expressed in TNF-treated organoids



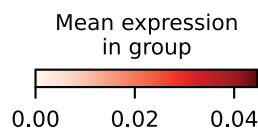
Organoid lysate proteins
only (n = 302)

snRNA-seq of diseased human kidney tissue
n = 10 individuals (5 each TNF α status)

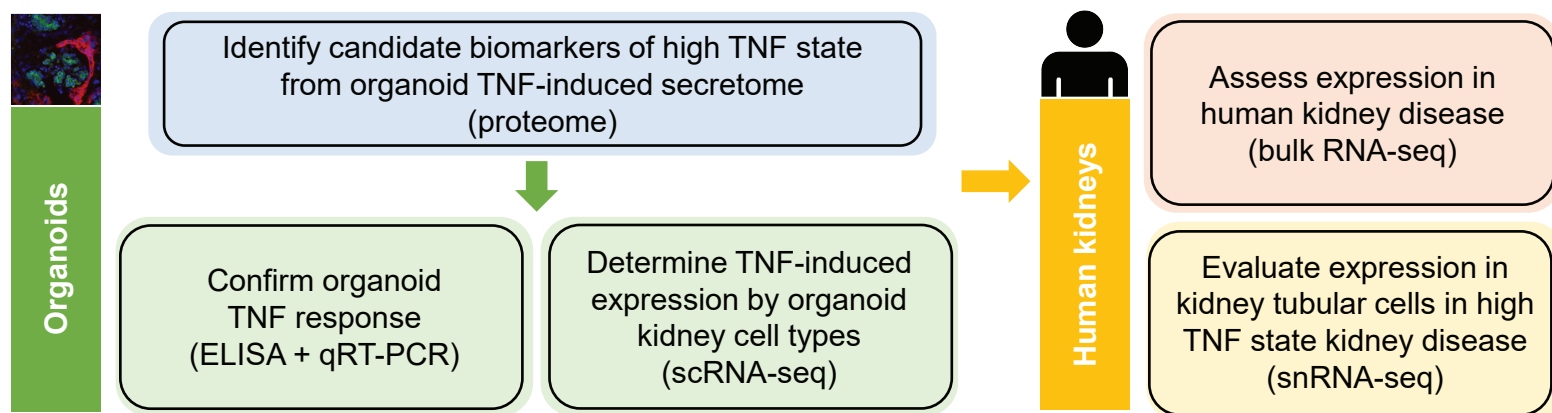


Kidney tissue TNF α activity

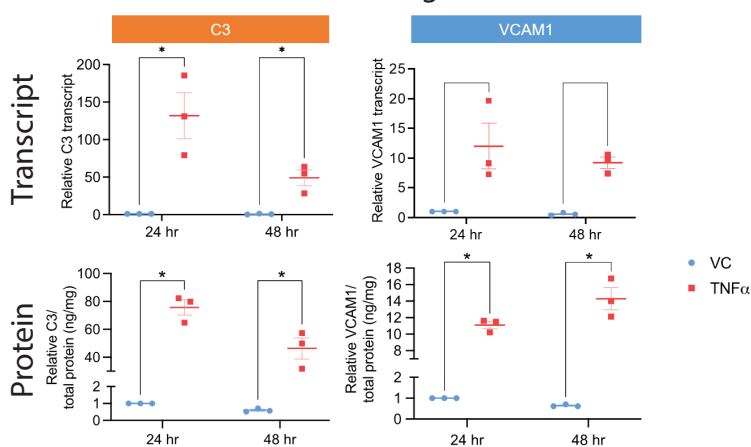
Cell Type	TNF α Activity	CXCL10
ATL	High (1.7k)	12
DCT	High (239)	664
DTL	High (2.5k)	120
EC	High (1.5k)	351
FIB	High (4.8k)	277
Immune	High (2.6k)	30
PC/IC	High (1.5k)	2.6k
POD	High (49)	649
PT	High (18.8k)	38.8k
TAL	High (2.7k)	3.2k



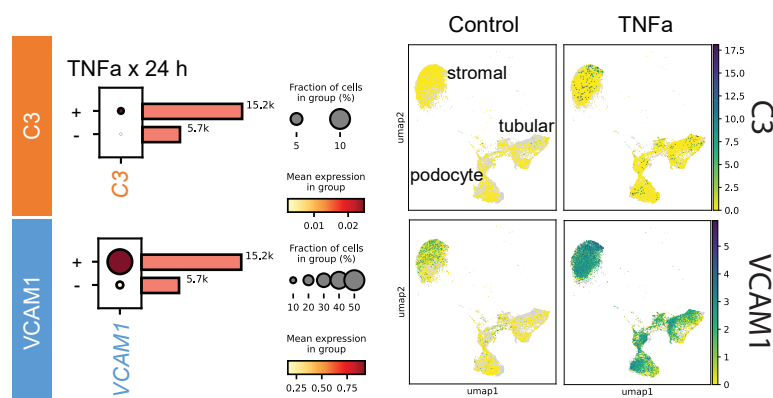
a



b

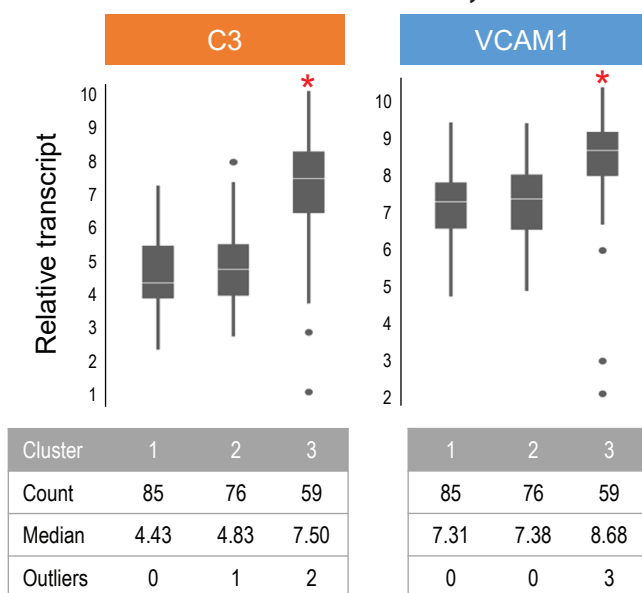
TNF α -treated Organoids

c

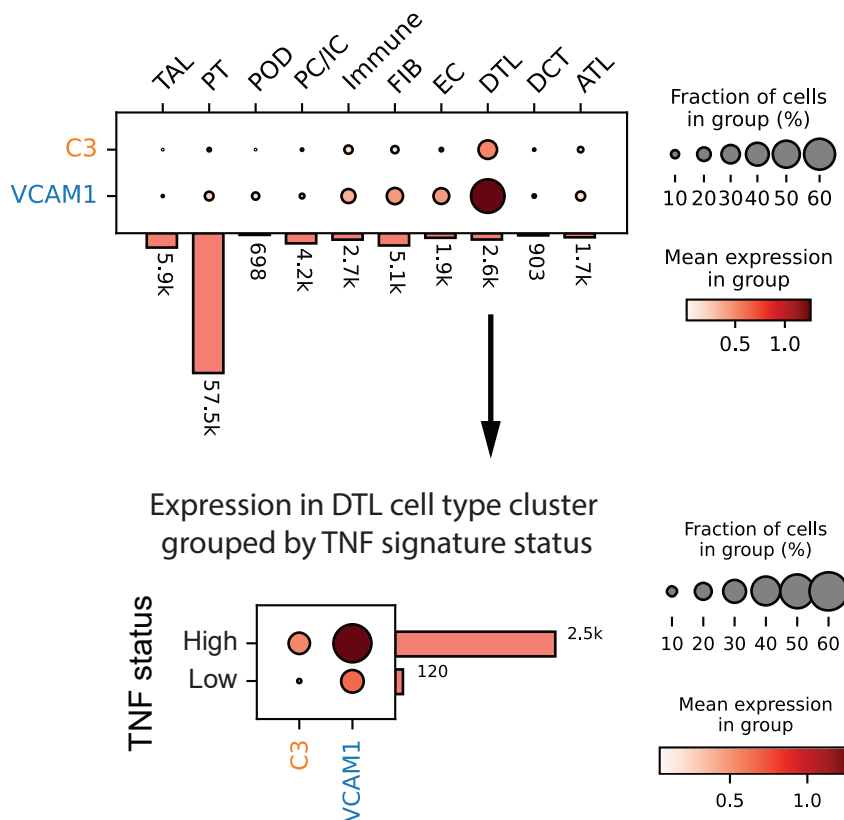
TNF α -treated Organoids

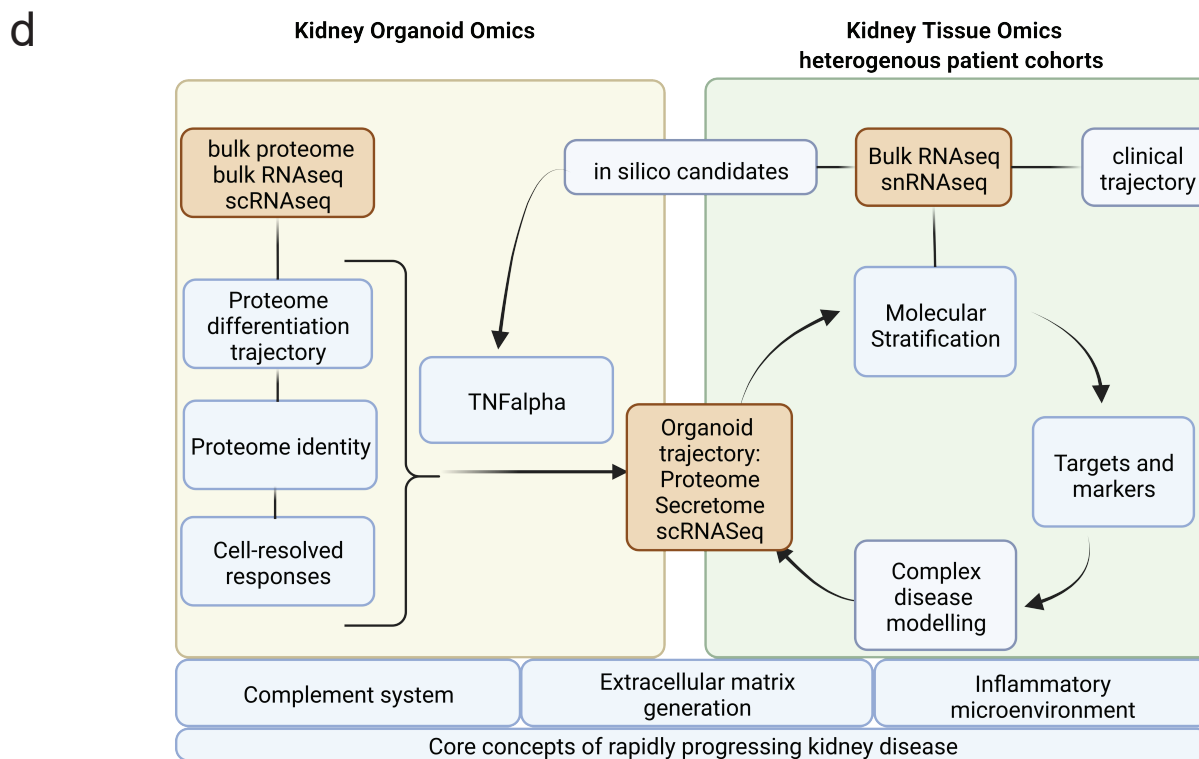
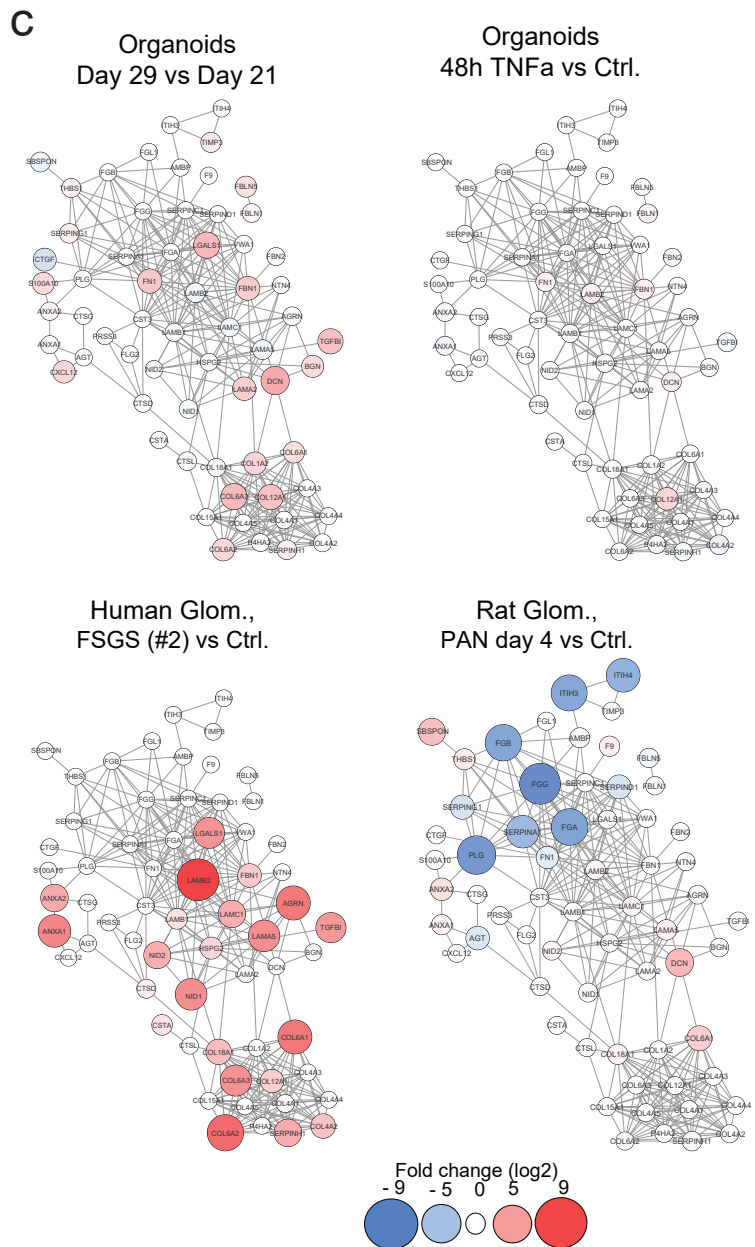
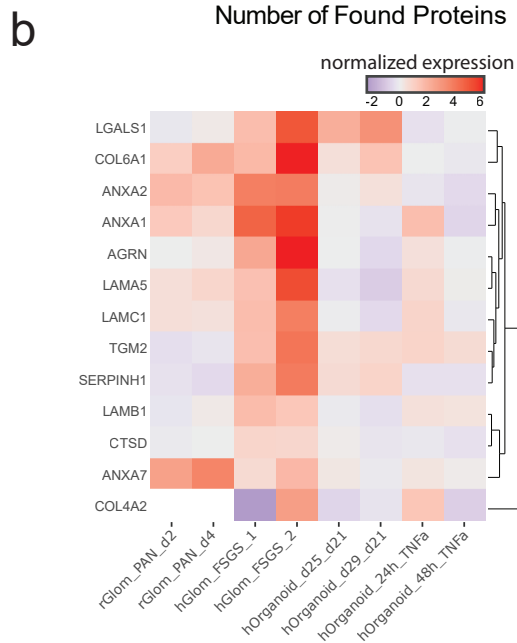
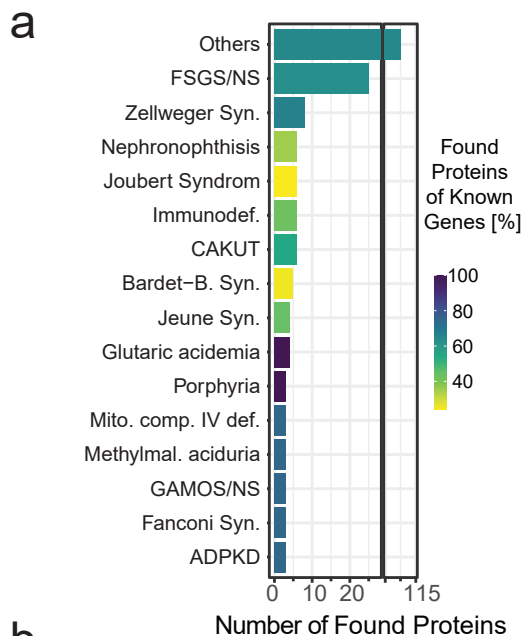
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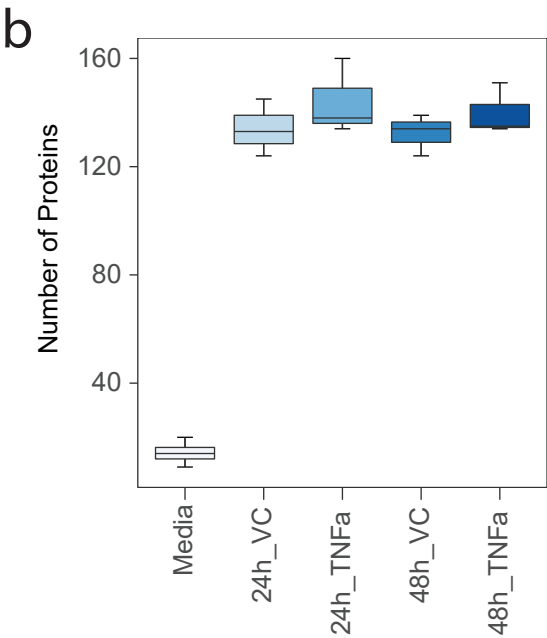
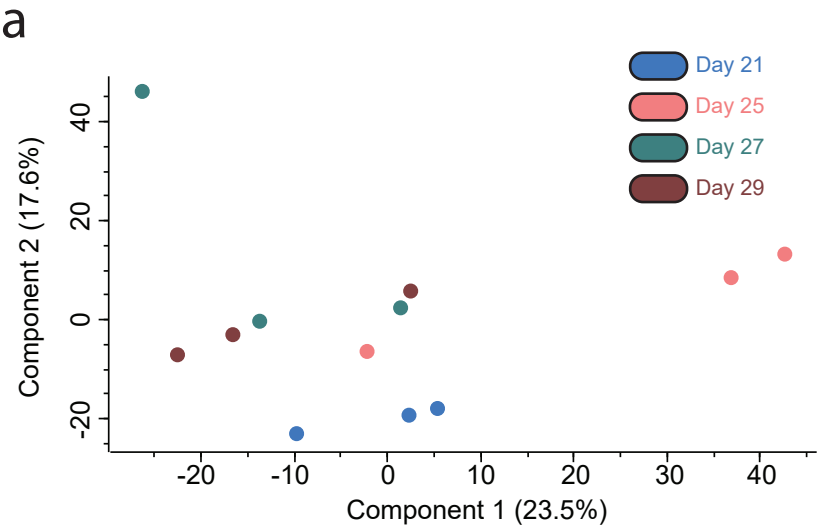
NEPTUNE human kidney



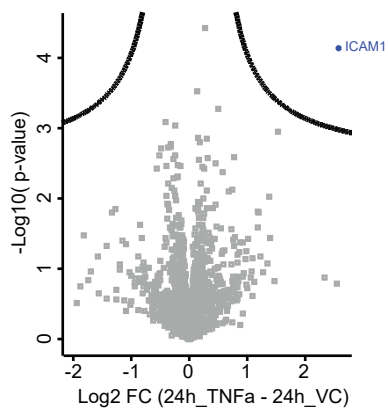
e

NEPTUNE human kidney
snRNA-seq of diseased human kidney tissue

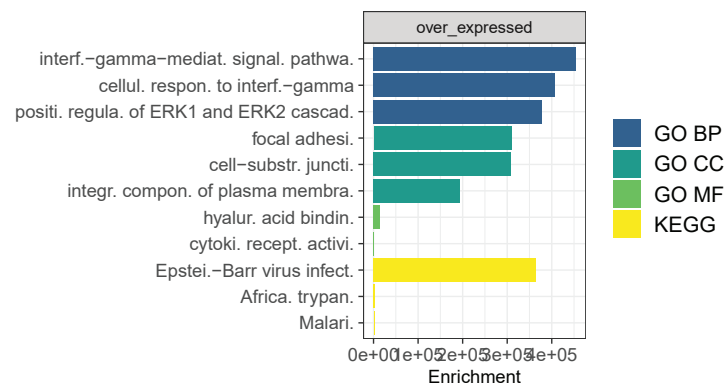




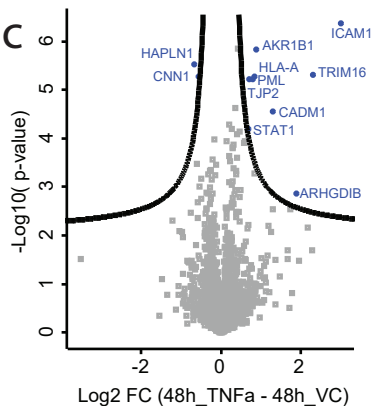
a



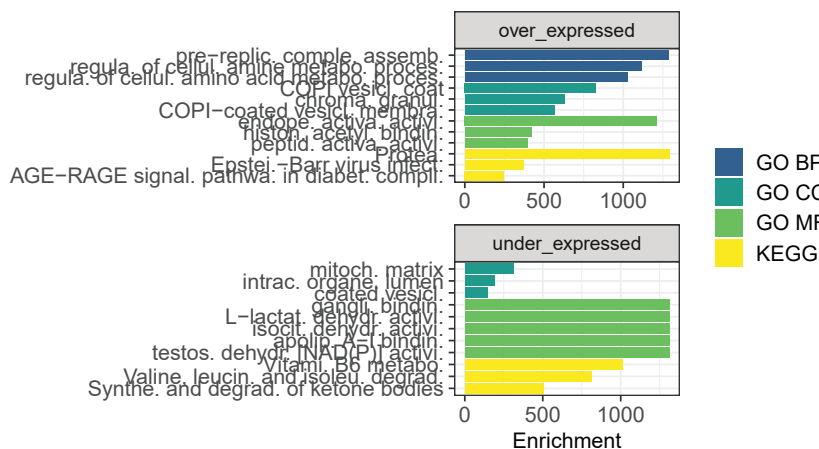
b



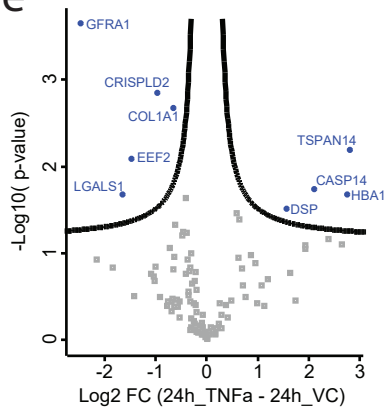
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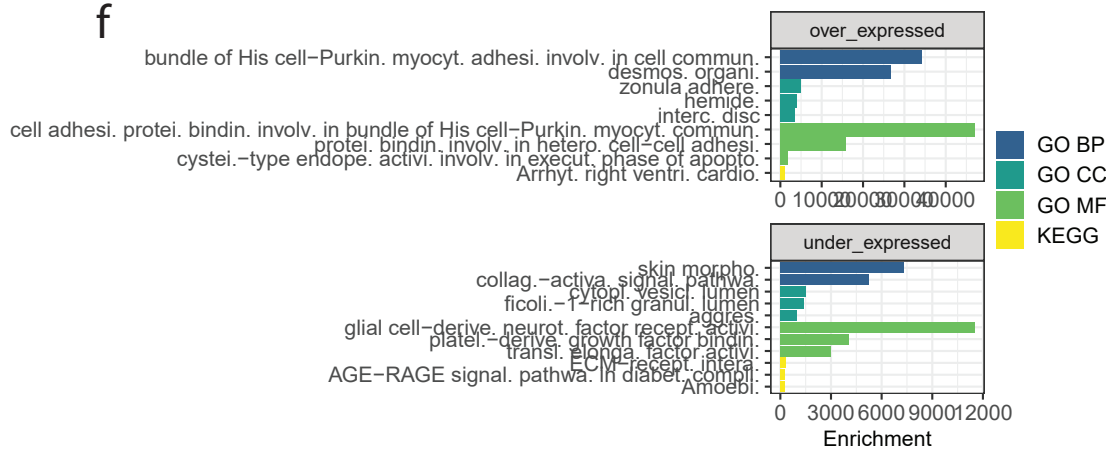
d



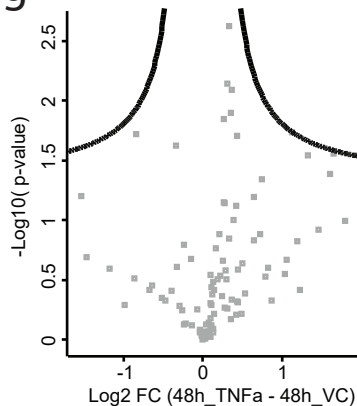
e



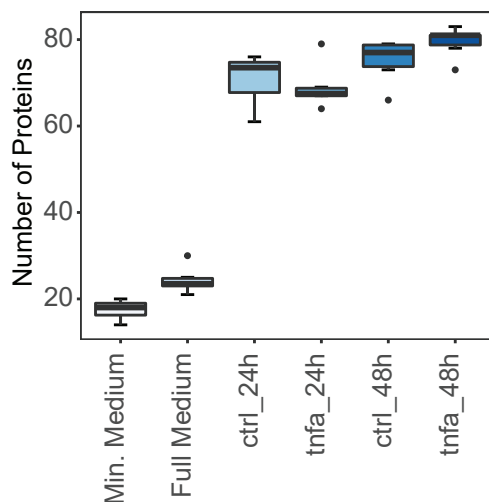
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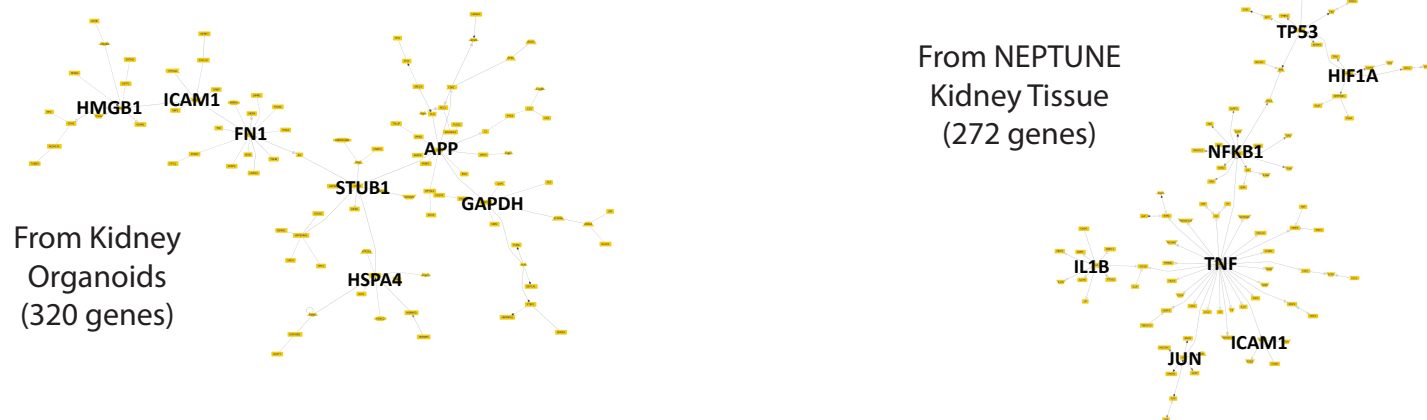
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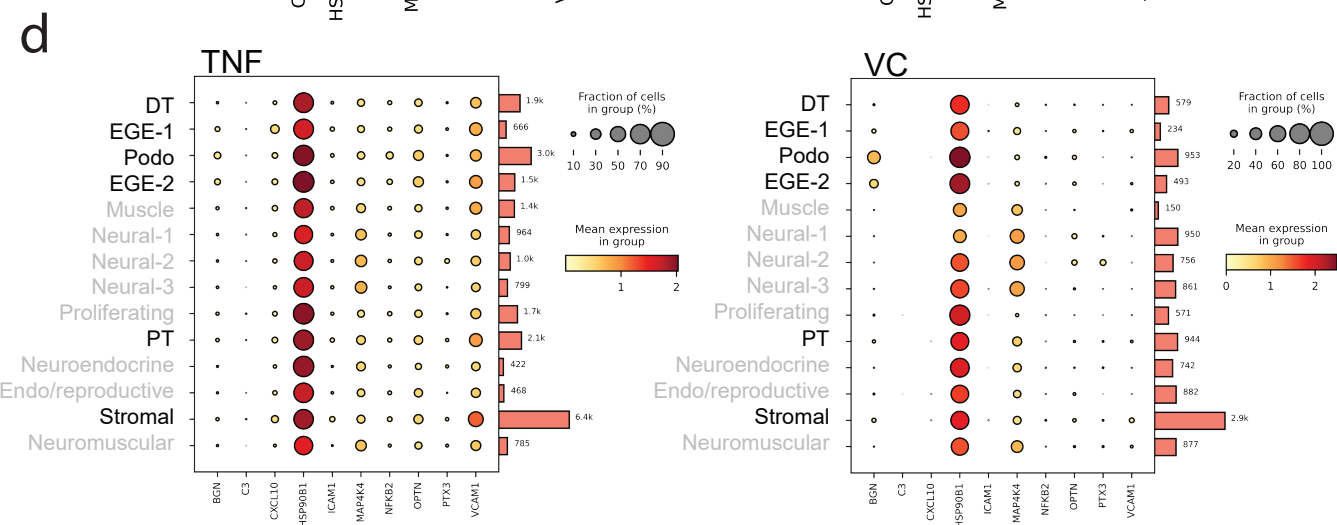
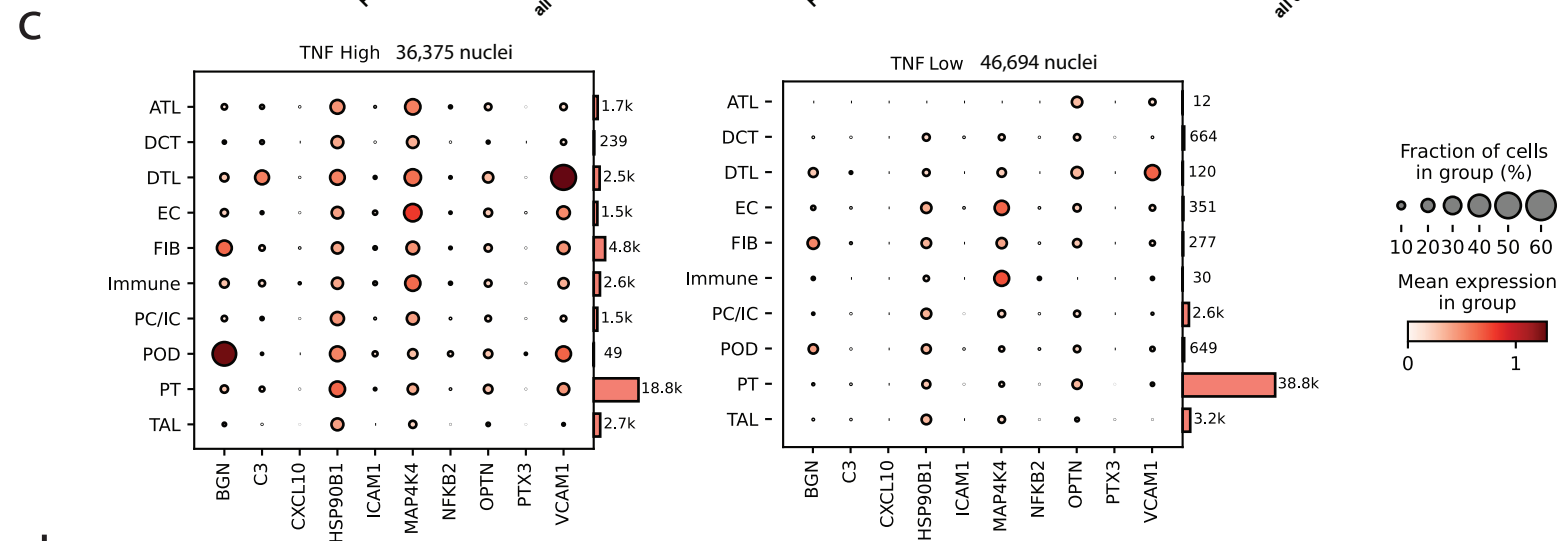
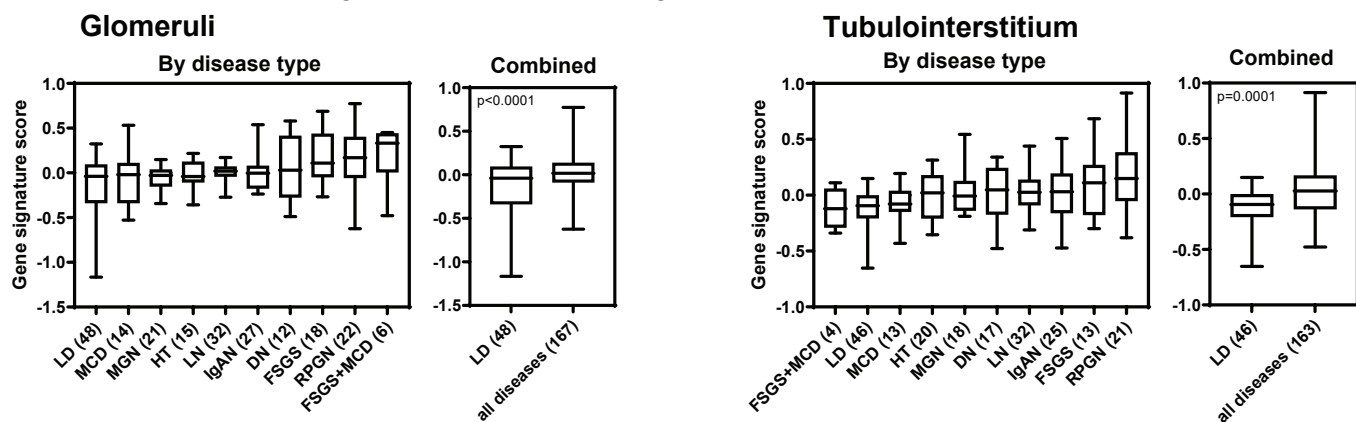
h



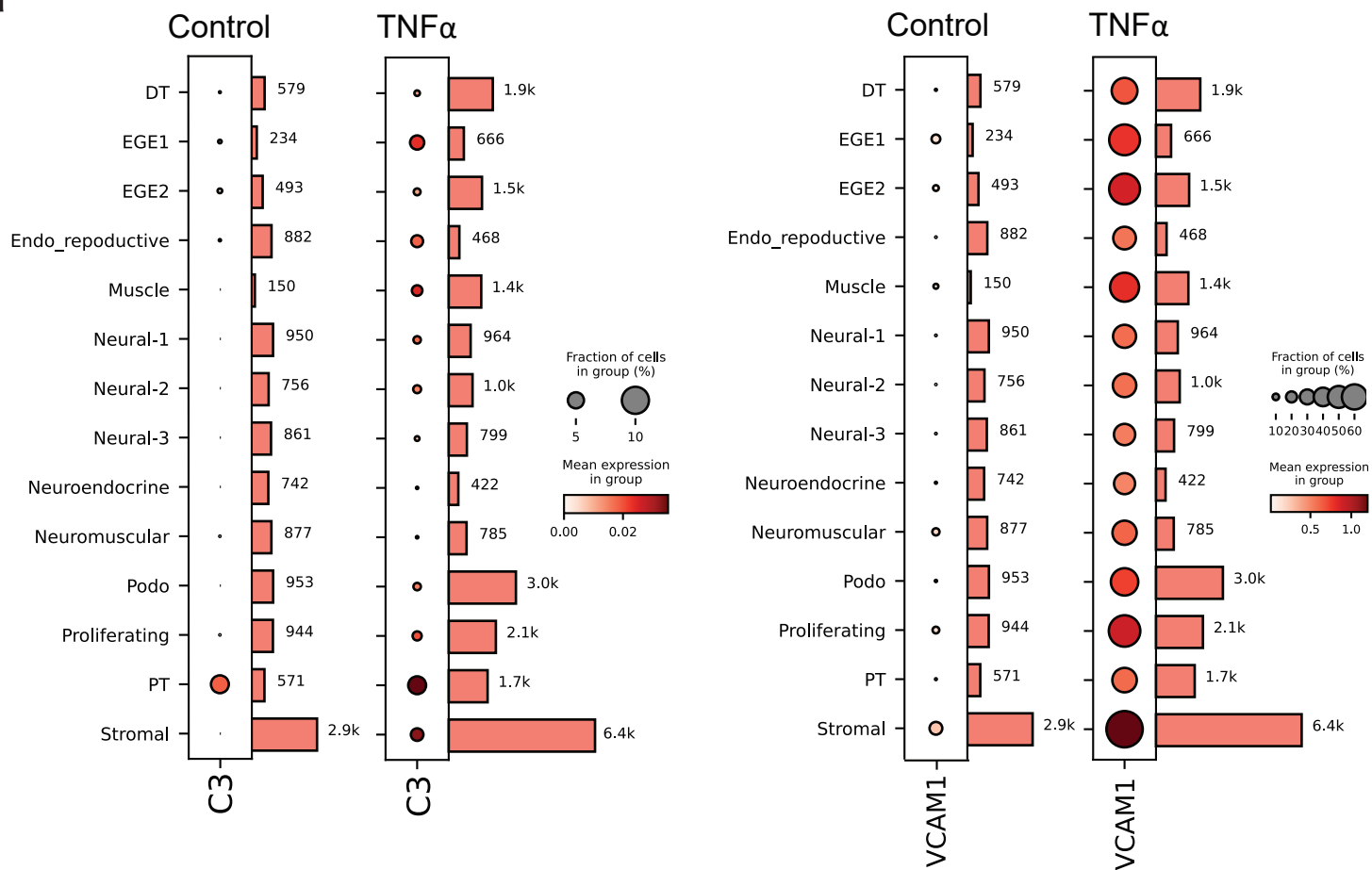
a GePS: Literature-based networks (“by-default” networks from top 100 best-connected genes; function-word filter)



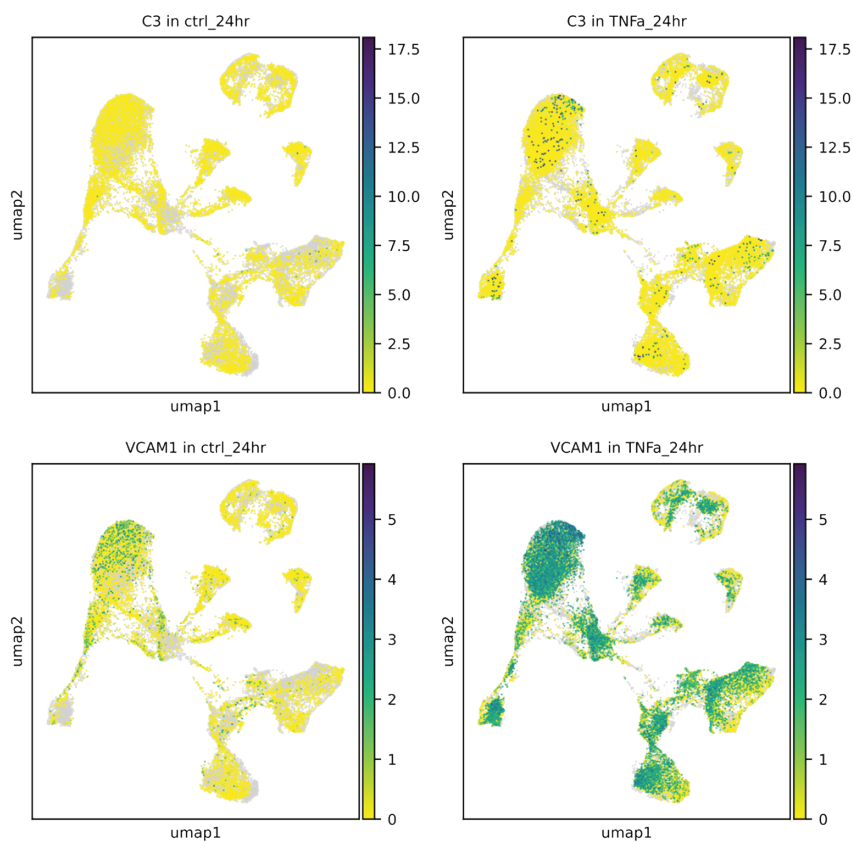
b Organoid proteome TNF signature score in ERCB



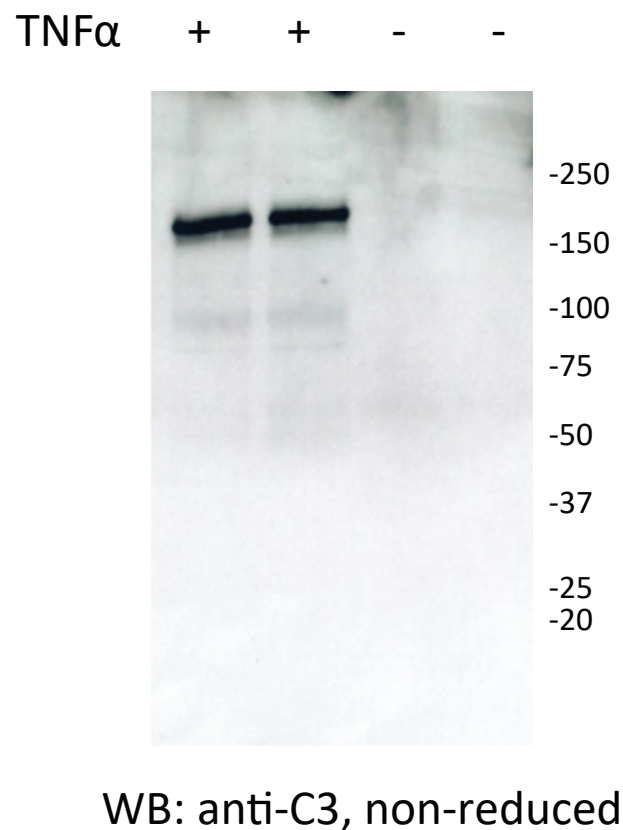
a



b



c



a

