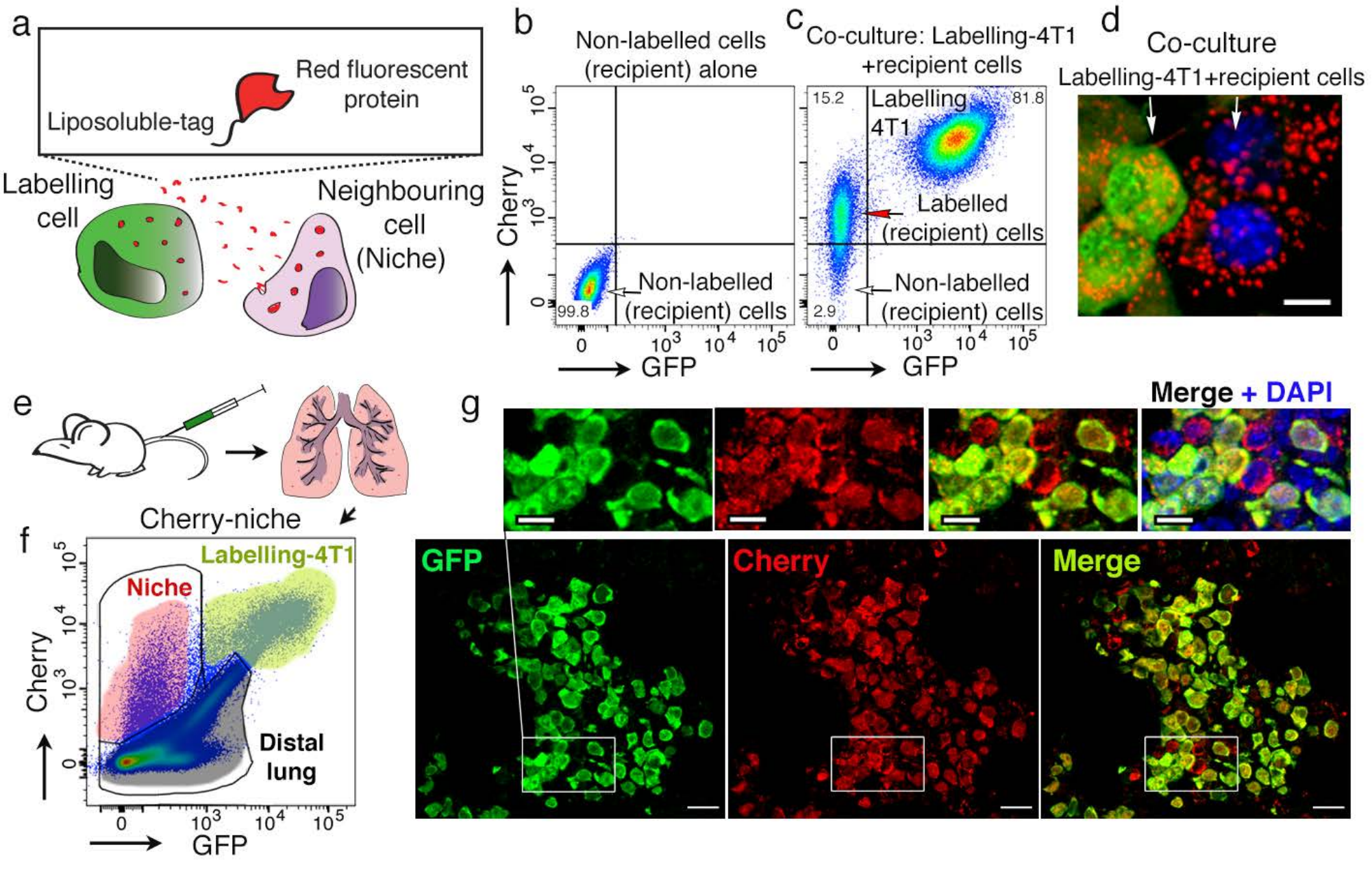
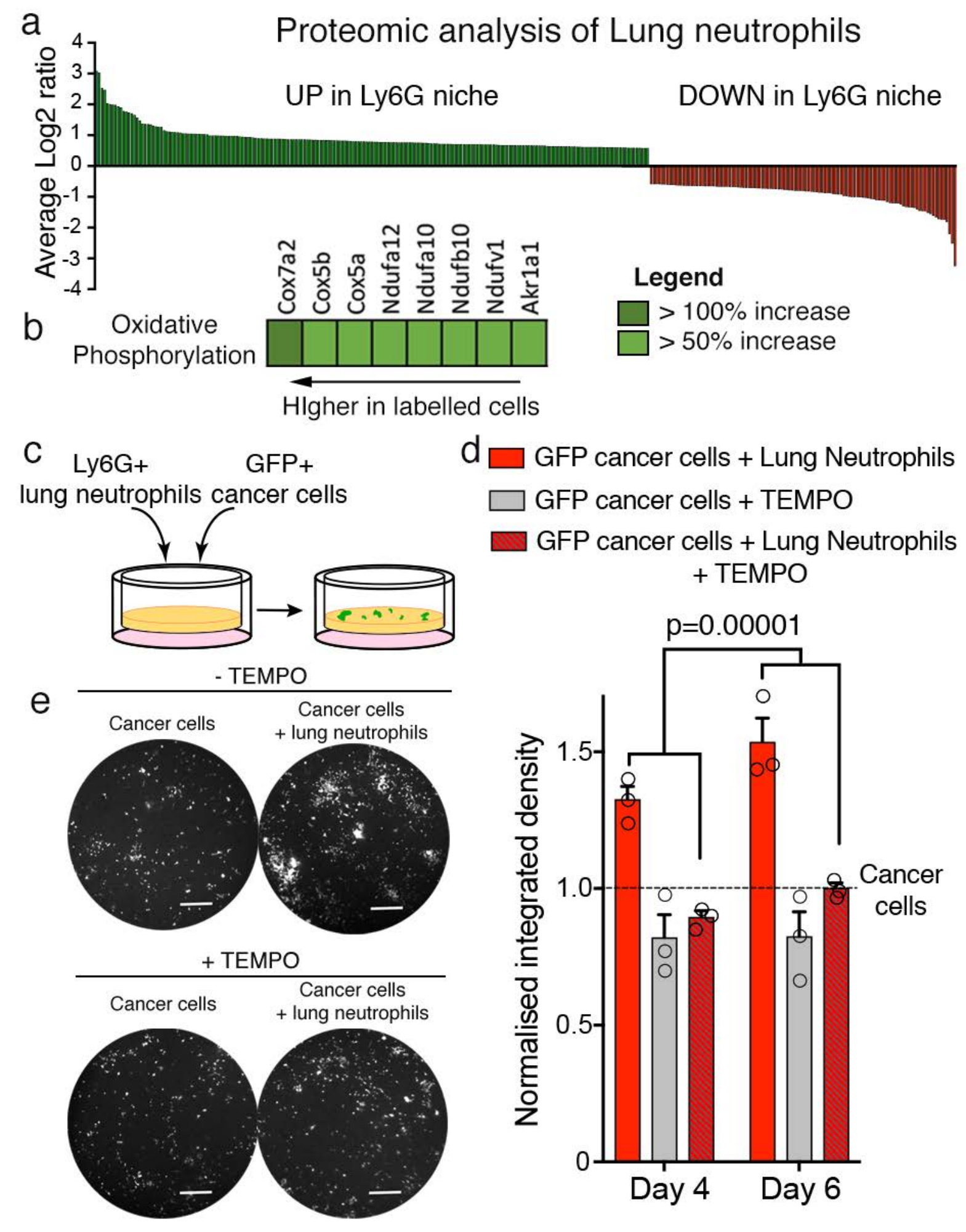
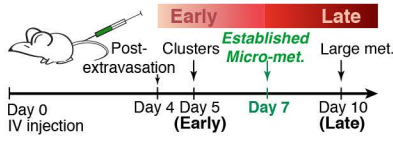
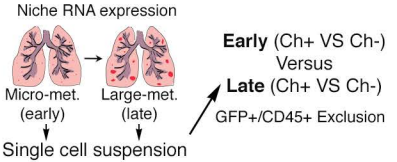
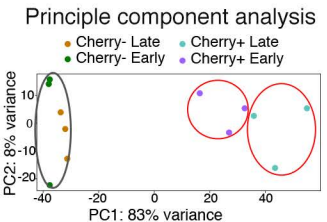
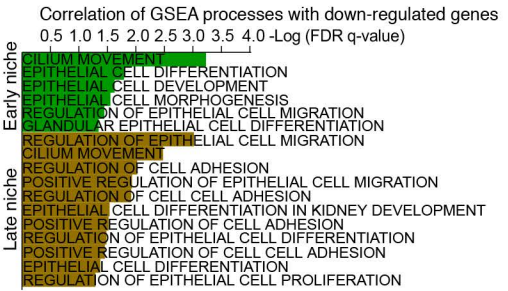

a
Red fluorescent protein
Liposoluble-tag
Labelling cell
Neighbouring cell (Niche)
b
Non-labelled cells (recipient) alone
Cherry
GFP
99.8
Non-labelled (recipient) cells
c
Co-culture: Labelling-4T1 +recipient cells
15.2
81.8
Labelling 4T1
Labelled (recipient) cells
Non-labelled (recipient) cells
2.9
d
Co-culture
Labelling-4T1+recipient cells
e
f
Cherry-niche
Labelling-4T1
Niche
Distal lung
g
Merge + DAPI
GFP
Cherry
Merge

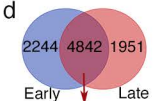

a
Proteomic analysis of Lung neutrophils
Average Log2 ratio
4
3
2
1
0
-1
-2
-3
-4
UP in Ly6G niche
DOWN in Ly6G niche
b
Oxidative Phosphorylation
Cox7a2
Cox5b
Cox5a
Ndufa12
Ndufa10
Ndufb10
Ndufv1
Akr1a1
Legend
> 100% increase
> 50% increase
HIgher in labelled cells
c
Ly6G+ lung neutrophils
GFP+ cancer cells
d
GFP cancer cells + Lung Neutrophils
GFP cancer cells + TEMPO
GFP cancer cells + Lung Neutrophils + TEMPO
p=0.00001
Normalised integrated density
1.5
1.0
0.5
0
Cancer cells
Day 4
Day 6
e
- TEMPO
Cancer cells
Cancer cells + lung neutrophils
+ TEMPO
Cancer cells
Cancer cells + lung neutrophils



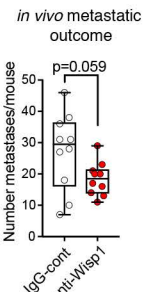


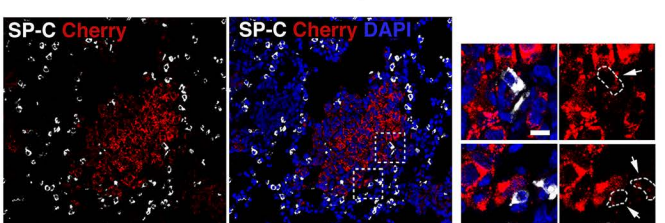


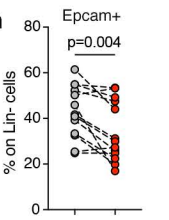


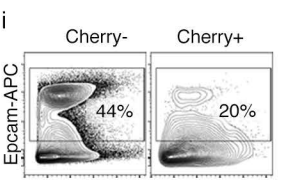


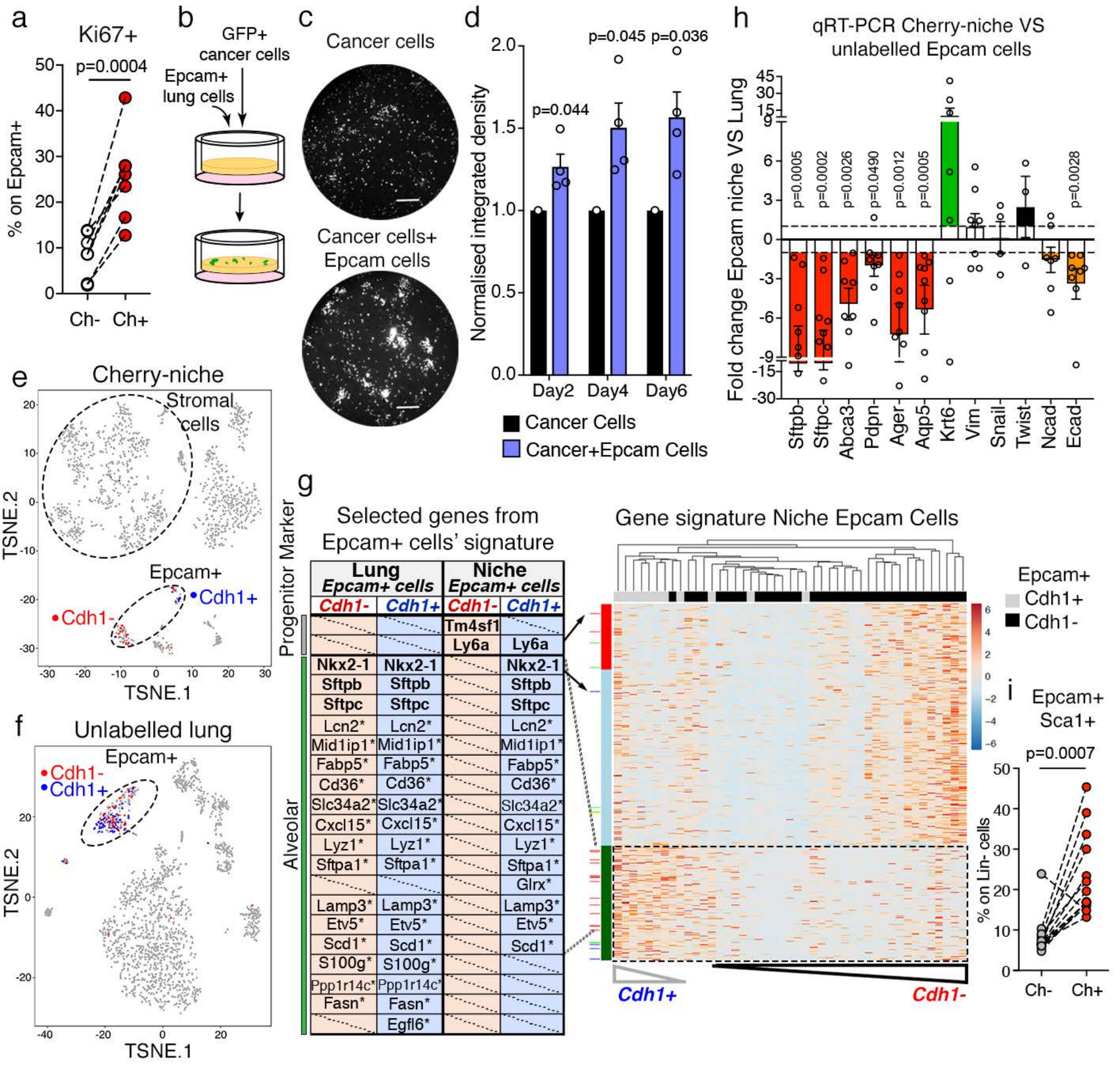
	logFoldChange Ch+vsCh-
Mmp9	6.92
Csf3	6.26
Wnt10a	5.94
Ccl2	4.48
Tnc	4.03
Wisp1	**3.91**
IL11	3.56
Wnt7b	3.55
Cxcl1	2.86
Loxl4	2.25
Loxl3	2.06
Postn	1.87

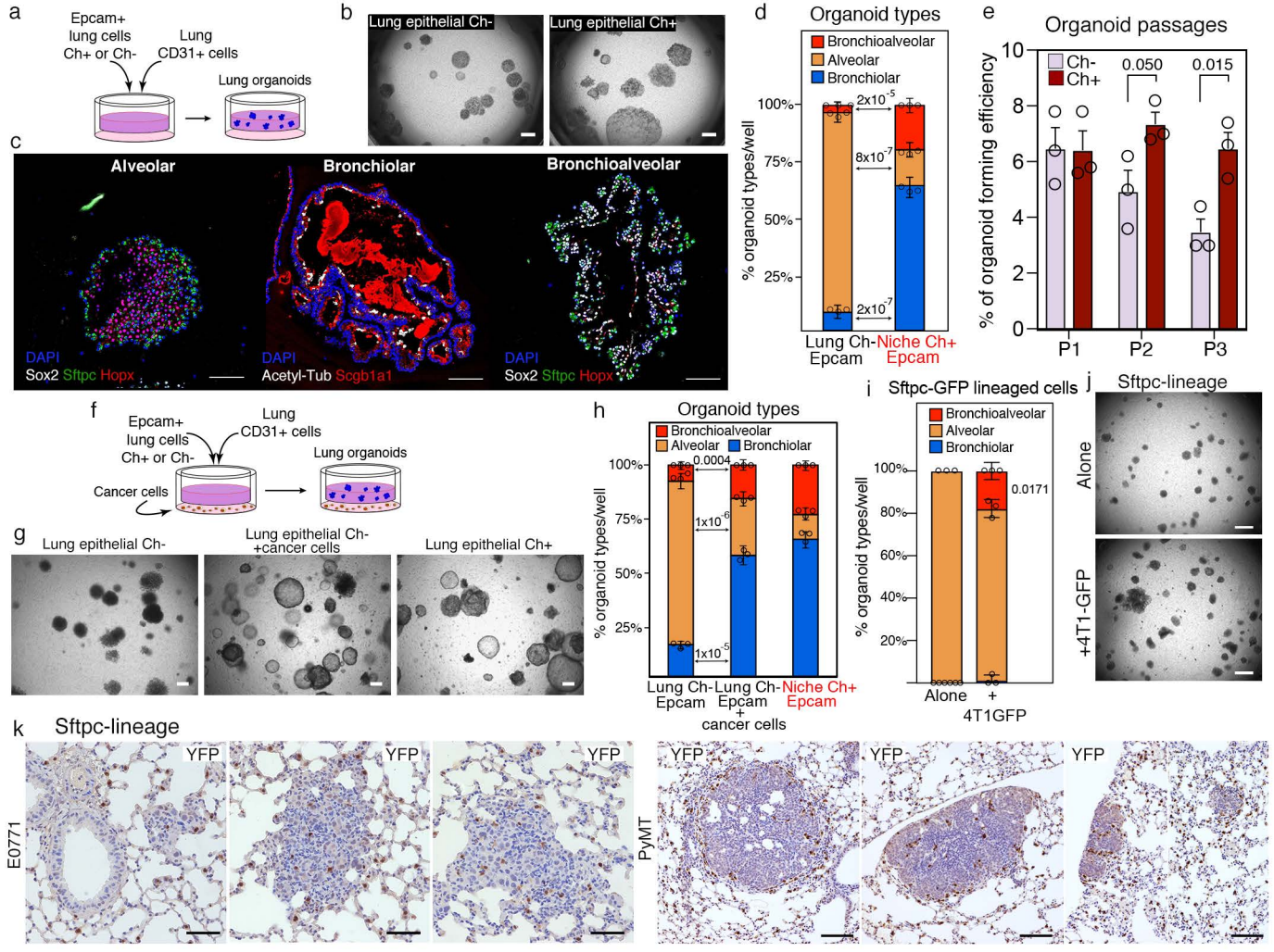









a
Ki67+
p=0.0004
% on Epcam+
Ch-
Ch+
b
GFP+ cancer cells
Epcam+ lung cells
c
Cancer cells
Cancer cells+ Epcam cells
d
p=0.045
p=0.036
p=0.044
Normalised integrated density
Day2
Day4
Day6
Cancer Cells
Cancer+Epcam Cells
h
qRT-PCR Cherry-niche VS unlabelled Epcam cells
Fold change Epcam niche VS Lung
p=0.0005
p=0.0002
p=0.0026
p=0.0490
p=0.0012
p=0.0005
p=0.0028
Sftpb
Sftpc
Abca3
Pdpn
Ager
Aqp5
Krt6
Vim
Snail
Twist
Ncad
Ecad
e
Cherry-niche
Stromal cells
Epcam+
Cdh1+
Cdh1-
TSNE.2
TSNE.1
f
Unlabelled lung
Epcam+
Cdh1-
Cdh1+
TSNE.2
TSNE.1
g
Selected genes from Epcam+ cells' signature
Progenitor Marker
Alveolar
Lung Epcam+ cells
Niche Epcam+ cells
Cdh1-
Cdh1+
Tm4sf1
Ly6a
Nkx2-1
Sftpb
Sftpc
Lcn2*
Mid1ip1*
Fabp5*
Cd36*
Slc34a2*
Cxcl15*
Lyz1*
Sftpa1*
Glrx*
Lamp3*
Etv5*
Scd1*
S100g*
Ppp1r14c*
Fasn*
Egfl6*
Gene signature Niche Epcam Cells
Epcam+
Cdh1+
Cdh1-
i
Epcam+ Sca1+
p=0.0007
% on Lin- cells
Ch-
Ch+


a
Epcam+ lung cells Ch+ or Ch-
Lung CD31+ cells
Lung organoids
b
Lung epithelial Ch-
Lung epithelial Ch+
c
Alveolar
Bronchiolar
Bronchioalveolar
DAPI
Sox2 Sftpc Hopx
DAPI
Acetyl-Tub Scgb1a1
DAPI
Sox2 Sftpc Hopx
d
Organoid types
Bronchioalveolar
Alveolar
Bronchiolar
% organoid types/well
100%
75%
50%
25%
2x10-5
8x10-7
2x10-7
Lung Ch- Epcam
Niche Ch+ Epcam
e
Organoid passages
Ch-
Ch+
0.050
0.015
% of organoid forming efficiency
10
8
6
4
2
0
P1
P2
P3
f
Epcam+ lung cells Ch+ or Ch-
Lung CD31+ cells
Lung organoids
Cancer cells
g
Lung epithelial Ch-
Lung epithelial Ch- +cancer cells
Lung epithelial Ch+
h
Organoid types
Bronchioalveolar
Alveolar
Bronchiolar
0.0004
1x10-6
1x10-5
% organoid types/well
100%
75%
50%
25%
Lung Ch- Epcam
Lung Ch- Epcam + cancer cells
Niche Ch+ Epcam
i
Sftpc-GFP lineaged cells
Bronchioalveolar
Alveolar
Bronchiolar
0.0171
% organoid types/well
100%
80%
60%
40%
20%
Alone
+ 4T1GFP
j
Sftpc-lineage
Alone
+4T1-GFP
k
Sftpc-lineage
E0771
PyMT
YFP