## Supplementary Information

# The drug-induced phenotypic landscape of colorectal cancer organoids

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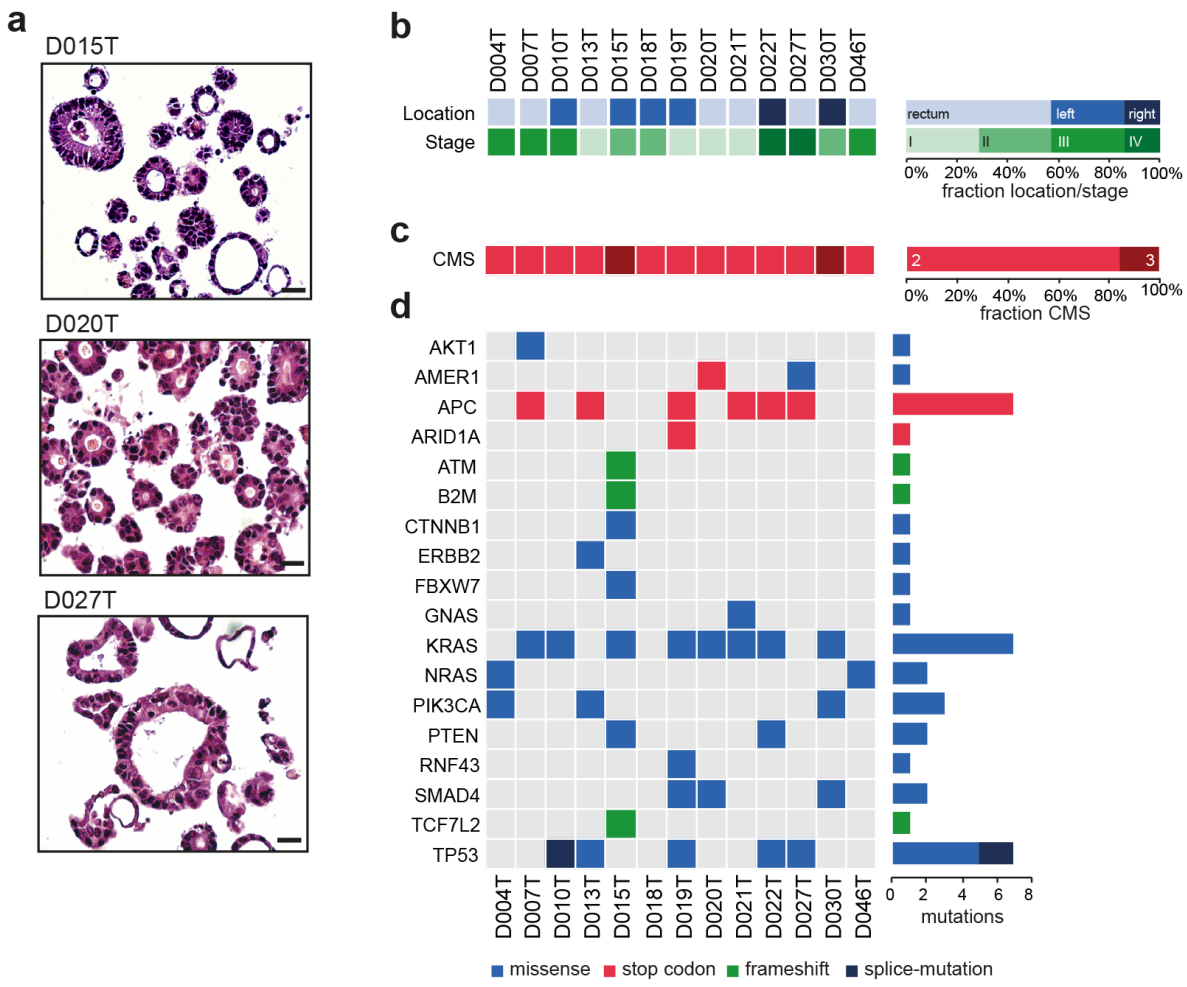
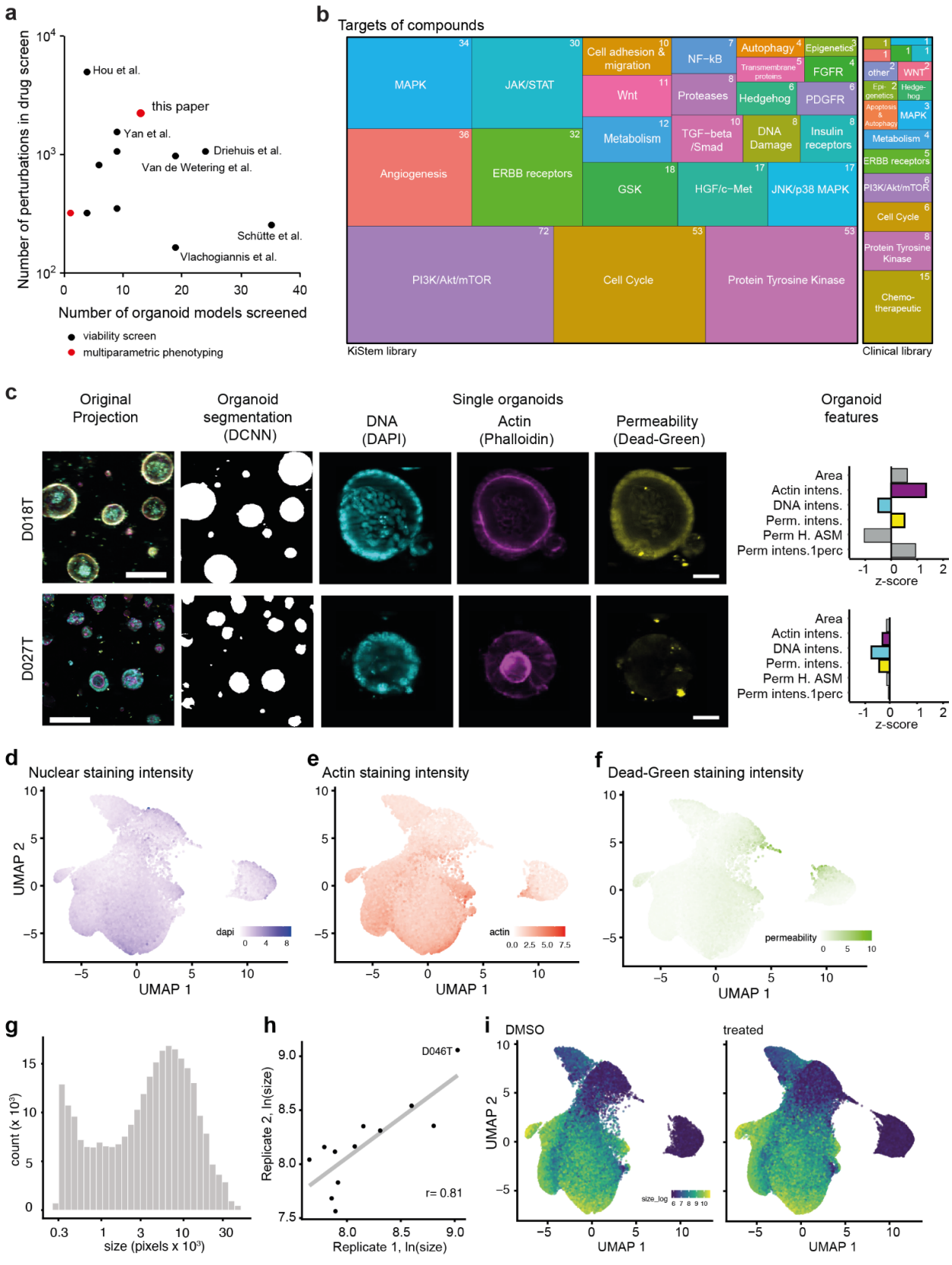
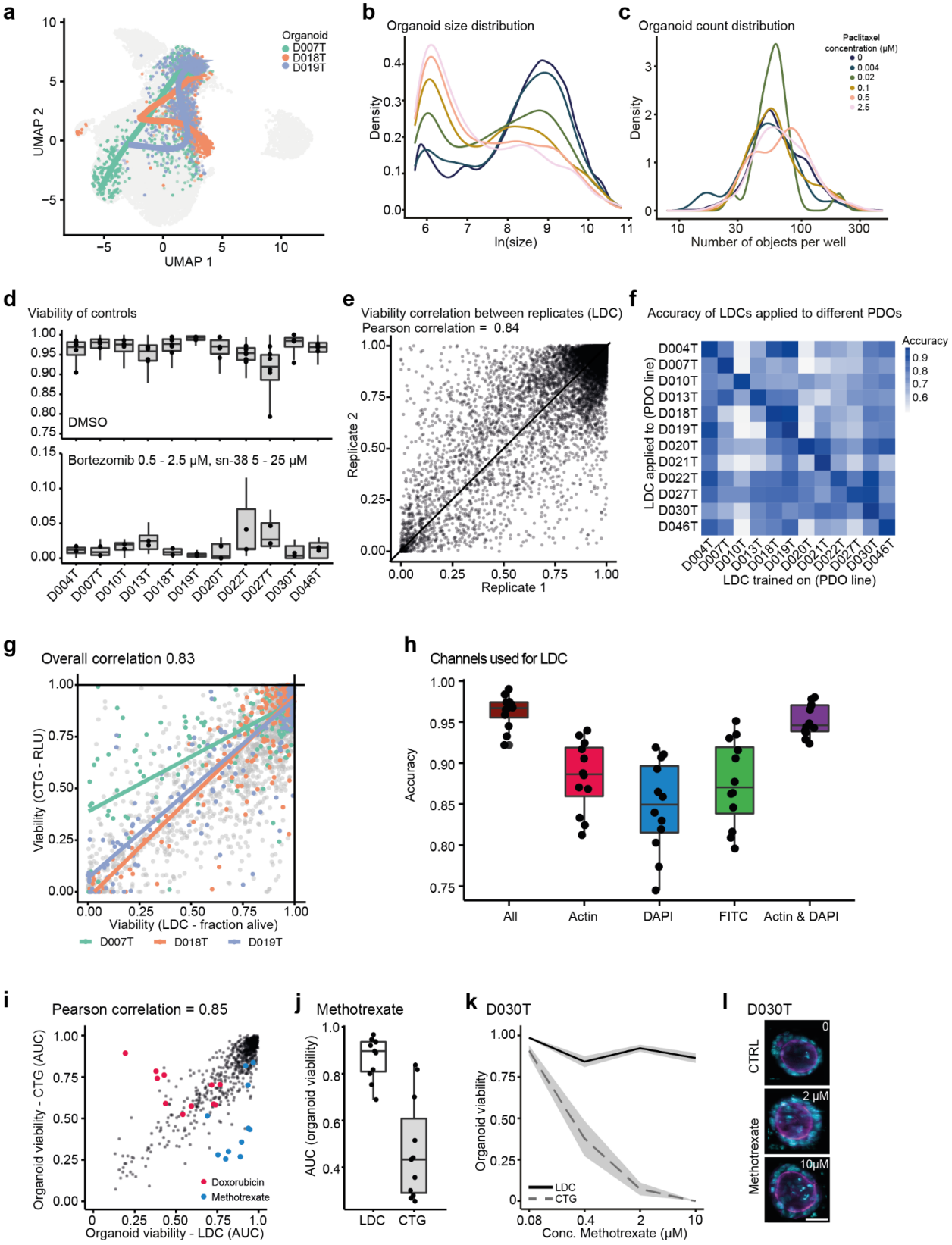
## Supplemental Figures



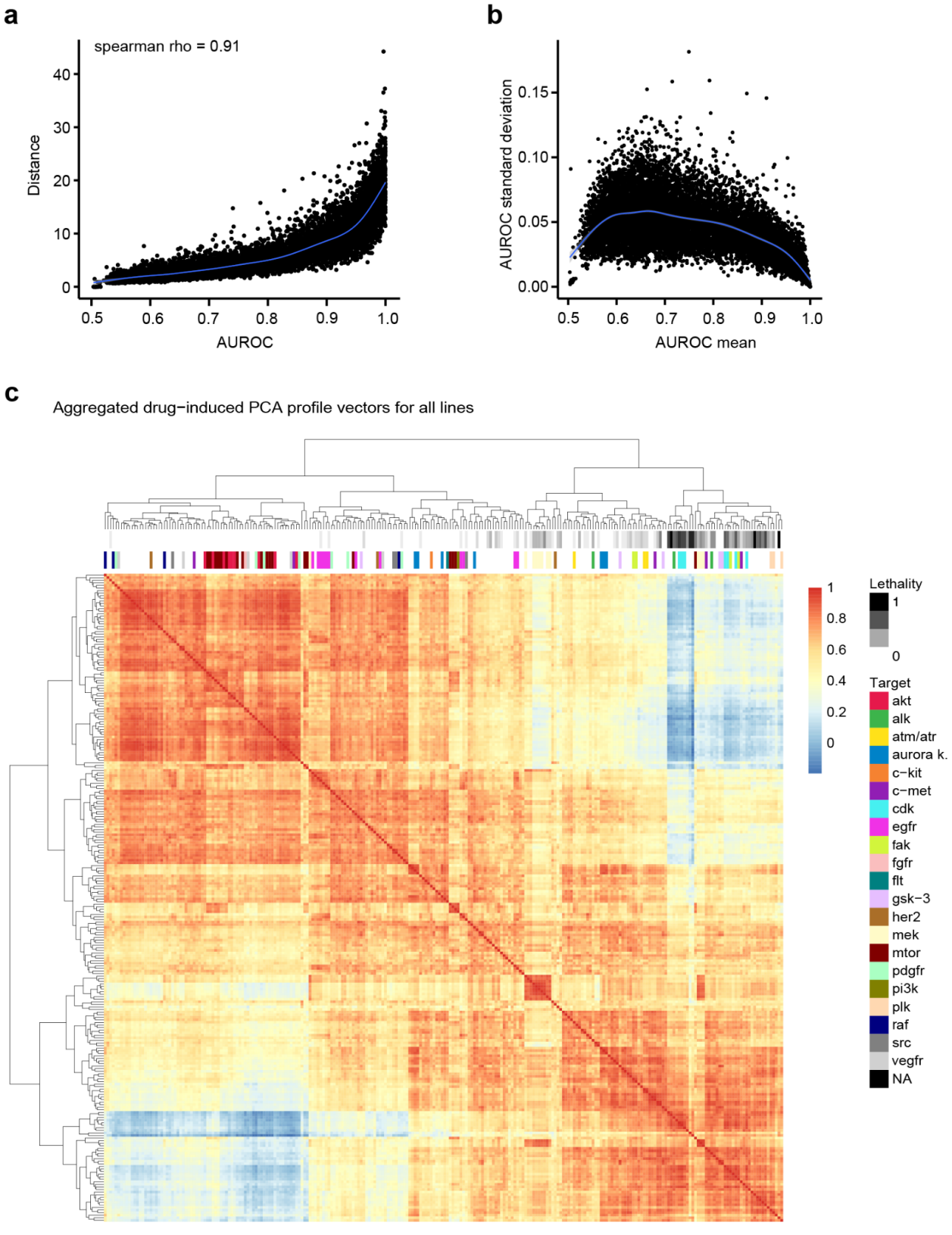

**Supplemental Fig. S1: Establishment of patient derived organoids for high-throughput image-based compound profiling**. **a**, Examples of H&E stained slides of selected representative PDO cultures; scale bar: 25µm. **b**, Tumor location (right/left/rectum) and AJCC/UICC stage of colorectal cancers that PDOs were derived from. **c**, Consensus molecular subtypes of PDOs determined by RNA expression analysis. **d**, Mutation status in PDOs, as analyzed by amplicon sequencing (more information in Supplemental Table S1).


a
Number of perturbations in drug screen
Number of organoid models screened
Hou et al.
this paper
Yan et al.
Driehuis et al.
Van de Wetering et al.
Schütte et al.
Vlachogiannis et al.
viability screen
multiparametric phenotyping
b
Targets of compounds
MAPK
JAK/STAT
Cell adhesion & migration
NF−kB
Autophagy
Epigenetics
Transmembrane proteins
FGFR
Wnt
Proteases
Hedgehog
PDGFR
Metabolism
TGF−beta /Smad
DNA Damage
Insulin receptors
Angiogenesis
ERBB receptors
GSK
HGF/c−Met
JNK/p38 MAPK
PI3K/Akt/mTOR
Cell Cycle
Protein Tyrosine Kinase
KiStem library
other
WNT
Epi- genetics
Hedge- hog
Apoptosis & Autophagy
MAPK
Metabolism
ERBB receptors
PI3K/Akt/mTOR
Cell Cycle
Protein Tyrosine Kinase
Chemo- therapeutic
Clinical library
c
Original Projection
Organoid segmentation (DCNN)
Single organoids
DNA (DAPI)
Actin (Phalloidin)
Permeability (Dead-Green)
Organoid features
D018T
D027T
Area
Actin intens.
DNA intens.
Perm. intens.
Perm H. ASM
Perm intens.1perc
z-score
d
Nuclear staining intensity
dapi
UMAP 1
UMAP 2
e
Actin staining intensity
actin
f
Dead-Green staining intensity
permeability
g
count (x 10³)
size (pixels x 10³)
h
Replicate 2, ln(size)
Replicate 1, ln(size)
D046T
r= 0.81
i
DMSO
treated
size_log

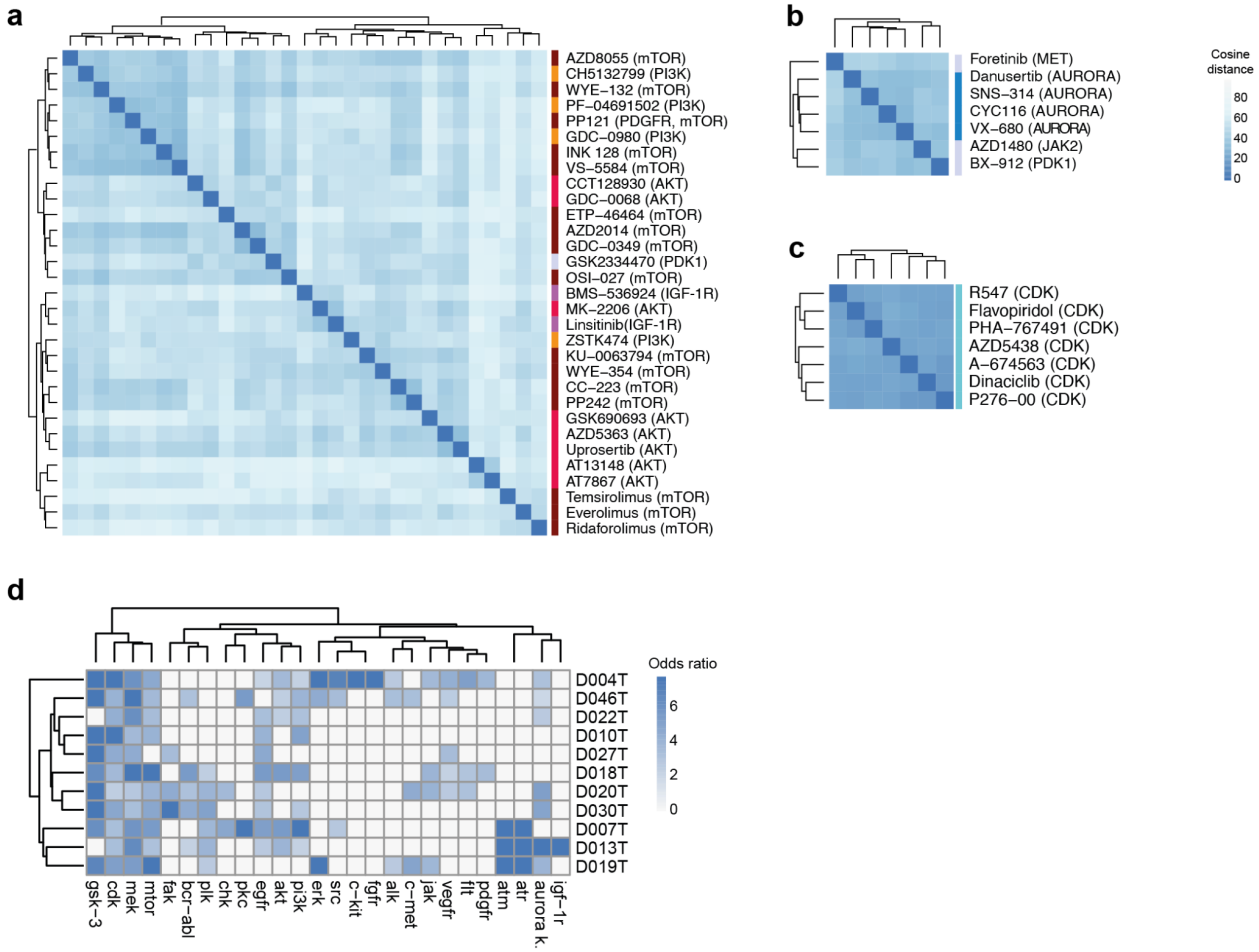
**Supplemental Fig. S2: Automated morphological analysis of patient derived organoids. a**, Number of organoid models and number of perturbations in previous publications reporting high-throughput drug screenings with patient derived cancer organoids **b**, Graphical representation of the compound libraries used for drug screening in this project: A library targeting kinases and stem cell pathways (KiStem library, 464 compounds) and a clinical library with 63 drugs in 5 concentrations. **c**, The image-processing pipeline illustrated with representative example images from 2 organoid lines: The multi-channel (DNA/DAPI, actin/TRITC, permeability/FITC) 3D image stack was projected onto a plane and a deep convolutional neural network subsequently recognized complete foreground organoids. Descriptive features were extracted from all three channels to quantify phenotypes. Feature plots show the median phenotype of unperturbed organoids, six example features (Area, Phalloidin intensity, DAPI intensity, FITC intensity, FITC Haralic angular second moment (ASM) and FITC intensity 1-percentile) and their z-scores relative to all profiled organoid lines are shown. Scale bars: 200µm (left images / projection and segmentation), 50µm (right images / single organoids). **d-f**, Uniform Manifold Approximation and Projection (UMAP) of organoid-level features marked by DNA (DAPI) staining intensity (d), actin (Phalloidi/FITC) staining intensity (e) and permeability (DeadGreen) staining intensity (f). **g**, Distribution of organoid size in control (DMSO) treated organoid lines. **h**, Replicate correlation of organoid size in control treated organoids. **i**, UMAP representation of DMSO treated and drug treated organoids.


a
Organoid
D007T
D018T
D019T
UMAP 2
UMAP 1
b
Organoid size distribution
Density
ln(size)
c
Organoid count distribution
Paclitaxel concentration (µM)
0
0.004
0.02
0.1
0.5
2.5
Density
Number of objects per well
d
Viability of controls
DMSO
Bortezomib 0.5 - 2.5 µM, sn-38 5 - 25 µM
D004T
D007T
D010T
D013T
D018T
D019T
D020T
D022T
D027T
D030T
D046T
e
Viability correlation between replicates (LDC)
Pearson correlation = 0.84
Replicate 2
Replicate 1
f
Accuracy of LDCs applied to different PDOs
Accuracy
LDC applied to (PDO line)
LDC trained on (PDO line)
g
Overall correlation 0.83
Viability (CTG - RLU)
Viability (LDC - fraction alive)
D007T
D018T
D019T
h
Channels used for LDC
Accuracy
All
Actin
DAPI
FITC
Actin & DAPI
i
Pearson correlation = 0.85
Organoid viability - CTG (AUC)
Organoid viability - LDC (AUC)
Doxorubicin
Methotrexate
j
Methotrexate
AUC (organoid viability)
LDC
CTG
k
D030T
Organoid viability
LDC
CTG
Conc. Methotrexate (µM)
l
D030T
CTRL
Methotrexate
0
2 µM
10µM

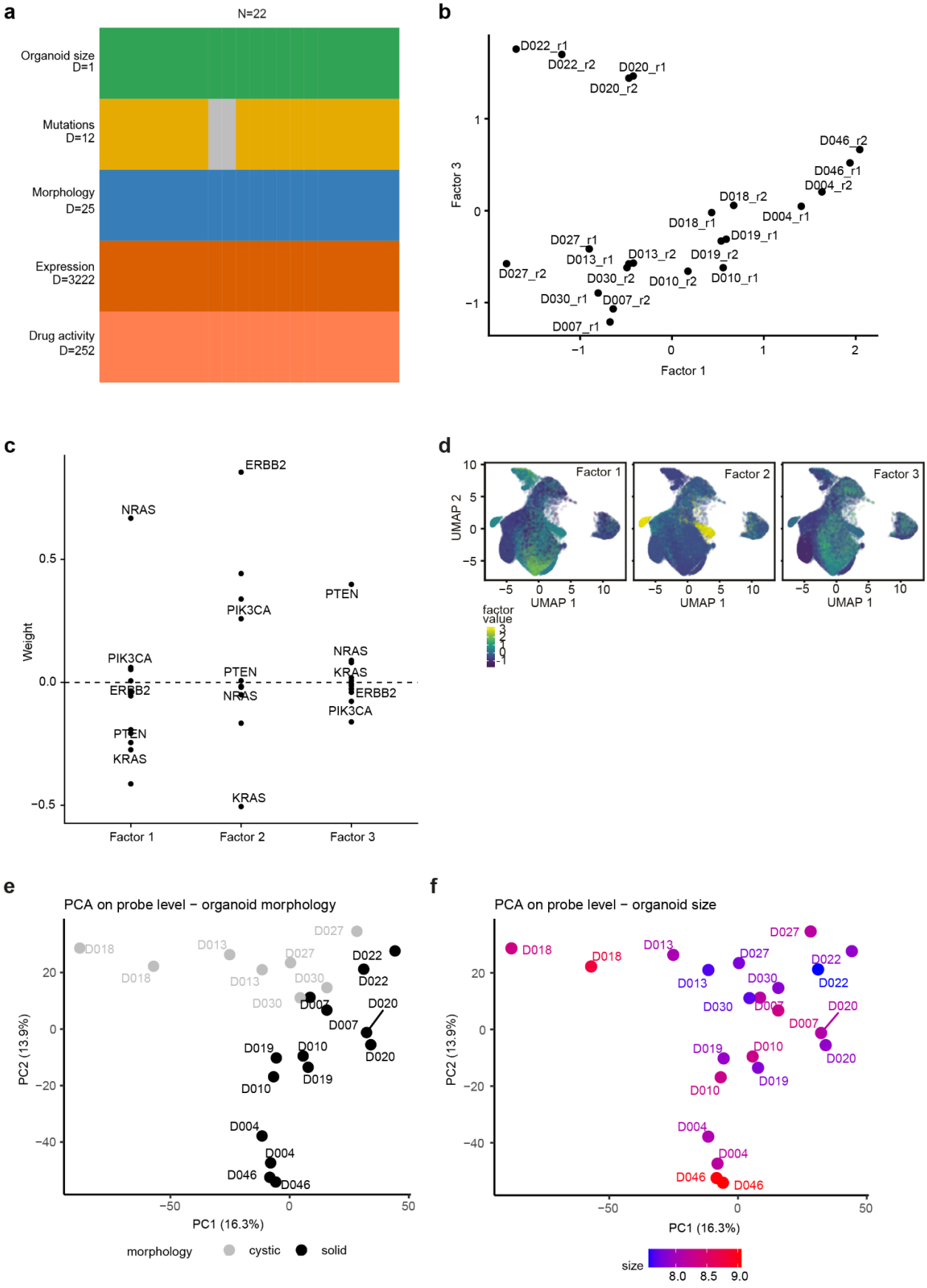
**Supplemental Fig. S3: Analysis of lethal and non-lethal PDO phenotypes. a**, Dose-dependent-trajectory of sn-38 drug effect. UMAP of organoid-level features are shown for example organoid lines D007T, D018T, D019T. For visual purposes, trajectory inference was limited to partition 1, the left-hand set of measurements within the UMAP representing ca. 95% of all imaging data. **b**, Distribution of organoid size at different concentrations of paclitaxel. Shown is a random sample of 30% of all paclitaxel treated organoids for this and the following figures. **c**, Distribution of organoid number per well at different concentrations of paclitaxel. **d-f**, Supervised machine learning of organoid viability. Organoid phenotype based viability classifiers (live-dead classifiers, LDC) were trained on positive- (high-dose bortezomib and SN-38) and negative (DMSO) controls. **d**, Plate-wise depiction of the fraction of DMSO treated (correctly) classified as viable (top) and fraction of organoids classified as dead in positive controls (bottom) for each PDO line. Data points average all organoids of DMSO treated wells (top) or bortezomib 0.5-2.5µM and sn-38 5-25µM treated wells per 384-well plate, respectively (i.e. 2 replicates of 2 plates KiStem library, 2 replicates of 2 plates clinical cancer library per line). Box indicates median, Q1 and Q3, whiskers indicate min and max. **e**, Correlation of viability (fraction of viable organoids per well) between 2 biological replicates classified by LDC. **f**, Transfer learning of organoid viability. LDCs were trained on the feature sets of negative- and positive controls for every PDO line. Receiver operator characteristic curves (ROCs) were analyzed on validation sets of negative- and positive controls of the same lines and other lines. Systematic analysis of the transfer-performance of all LDCs when applied across data from all organoid lines is shown. Classification performance is measured as the AUROC (area under the receiver operating characteristic curve). **g**, Association of organoid viability of selected example lines as determined by LDC vs. luminescence-based, ATP-dependent viability profiling with CellTiter-Glo (CTG). **h**, Accuracy of LDCs trained on image-features of all three available fluorescence channels compared to classifiers trained on single-channel data (actin/TRIC, DNA/DAPI, cell permeability/FITC) and on a combination of actin (TRIC) and DNA (DAPI) data only. All tested organoid lines were included in this analysis (2 replicates each), points depict accuracies of individual lines. Box indicates median, Q1 and Q3, whiskers indicate min and max. **i**, Pearson correlation of areas under the dose-response curve (AUCs) for drugs with multiple tested concentrations. Shown are AUCs for phenotype based viability classification (x-axis) and CTG ground truth ($r = 0.87$). Measurements of methotrexate and doxorubicin are marked in blue and red, respectively. All profiled lines are included. **j**, Methotrexate, an example of a drug that had divergent viability response results between phenotype based and CTG measurements. Data points represent AUCs calculated from dose-response curves generated with LDC or CTG measurement of 11 organoid lines (averages of 2 biological replicates). Box indicates median, Q1 and Q3, whiskers indicate min and max. **k**, Representative example of dose-response curves (organoid line D030T) for methotrexate. The range of min. - max. of LDC-values from two biological replicates are shaded in grey. **l**, Representative images of organoids treated with DMSO (control) and methotrexate 2 and 10 µM.; cyan = DAPI, magenta = Phalloidin, yellow = cell permeability; scale-bar: 50µm.


a
spearman rho = 0.91
Distance
AUROC
b
AUROC standard deviation
AUROC mean
c
Aggregated drug−induced PCA profile vectors for all lines
Lethality
1
0
Target
akt
alk
atm/atr
aurora k.
c−kit
c−met
cdk
egfr
fak
fgfr
flt
gsk−3
her2
mek
mtor
pdgfr
pi3k
plk
raf
src
vegfr
NA

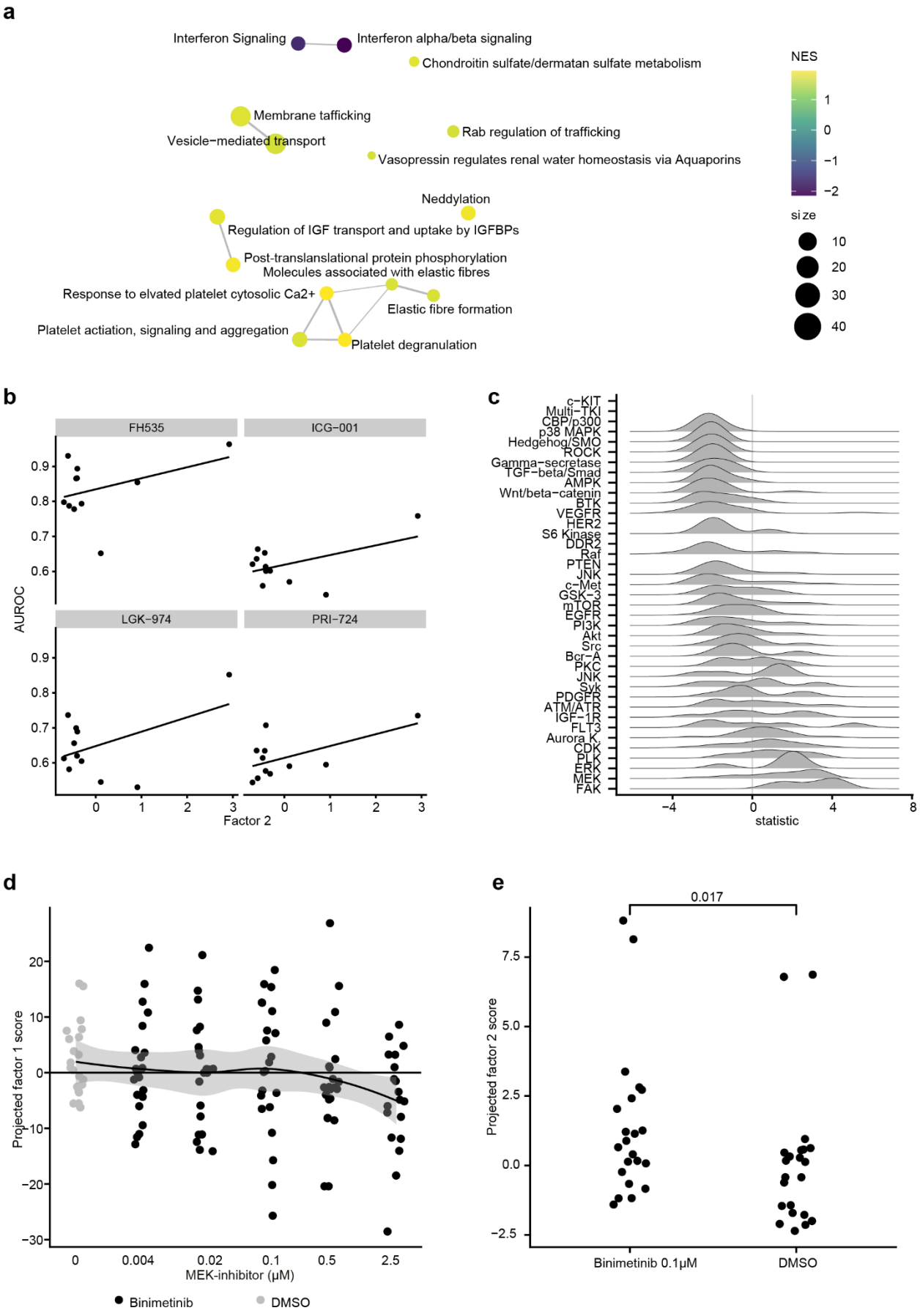
**Supplemental Fig. S4: Comparison of drug activity metrics. a**, comparison of euclidean distance and classifier performance (AUROC) to describe drug activity. **b**, average AUROC observed and standard deviation of AUROC estimates after 10-fold cross validation. **c**. Hierarchical clustering of active compound effects by pearson correlation. Compound effects were determined by concatenating average morphology profiles from all organoid lines (25 principal components).



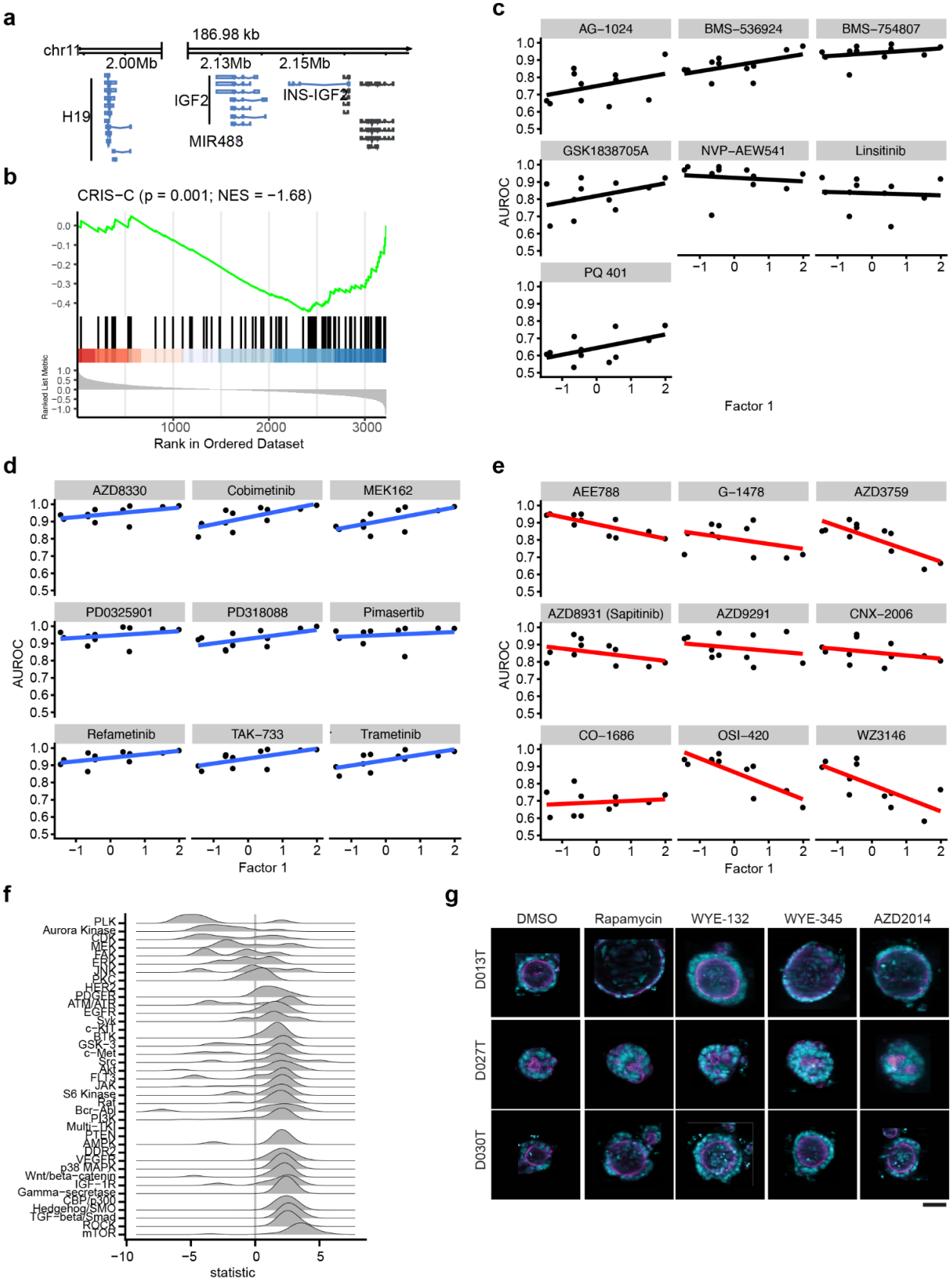

**Supplemental Fig. S5: Selected drug-induced profile clusters** (From Fig. 3d). **a-c**, shown are clusters enriched for PI3K/AKT/mTOR signaling inhibitors, Aurora kinase and CDK inhibitors, respectively. **d**, Significantly enriched targets across profiled PDOs. The cosine distance between drug effect vectors in individual organoid models was clustered, enrichment of annotated molecular targets was tested using Fisher's exact test. Log odds ratios for enriched targets and organoid lines are shown.


a
N=22
Organoid size
D=1
Mutations
D=12
Morphology
D=25
Expression
D=3222
Drug activity
D=252
b
Factor 3
Factor 1
D022_r1
D022_r2
D020_r1
D020_r2
D046_r2
D046_r1
D004_r2
D018_r2
D004_r1
D018_r1
D019_r1
D027_r1
D013_r1
D013_r2
D019_r2
D027_r2
D030_r2
D010_r2
D010_r1
D030_r1
D007_r2
D007_r1
c
Weight
Factor 1
Factor 2
Factor 3
ERBB2
NRAS
PIK3CA
PTEN
KRAS
d
Factor 1
Factor 2
Factor 3
UMAP 1
UMAP 2
factor value
e
PCA on probe level − organoid morphology
PC1 (16.3%)
PC2 (13.9%)
morphology
cystic
solid
f
PCA on probe level − organoid size
PC1 (16.3%)
PC2 (13.9%)
size

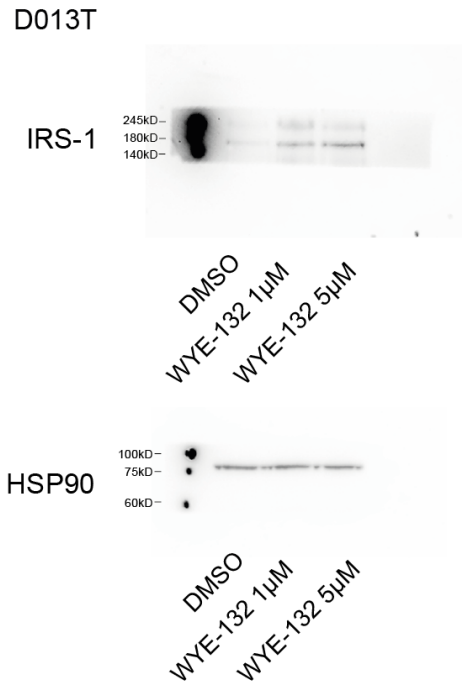
**Supplemental Fig. S6: Multi-omics factor analysis overview. a,** input data matrix showing the five included data modalities and 22 observations (11 lines a' 2 replicates). **b**, Factor 3 scores across unperturbed organoid lines. **c,** Factor loadings for somatic mutations, as identified by amplicon sequencing. **d**, UMAP embedding with organoid lines colored by factor scores. **e-f,** PCA analysis of expression data of unperturbed organoid lines. Two biological replicates were performed of all organoid lines. Colors represent organoid morphology (cystic vs. solid, visual inspection, e) and organoid size (f).


a
Interferon Signaling
Interferon alpha/beta signaling
Chondroitin sulfate/dermatan sulfate metabolism
Membrane tafficking
Vesicle−mediated transport
Rab regulation of trafficking
Vasopressin regulates renal water homeostasis via Aquaporins
Neddylation
Regulation of IGF transport and uptake by IGFBPs
Post-translanslational protein phosphorylation
Molecules associated with elastic fibres
Response to elvated platelet cytosolic Ca2+
Elastic fibre formation
Platelet actiation, signaling and aggregation
Platelet degranulation
NES
1
0
−1
−2
size
10
20
30
40
b
FH535
ICG−001
LGK−974
PRI−724
AUROC
Factor 2
c
c−KIT
Multi−TKI
CBP/p300
p38 MAPK
Hedgehog/SMO
ROCK
Gamma−secretase
TGF−beta/Smad
AMPK
Wnt/beta−catenin
BTK
VEGFR
HER2
S6 Kinase
DDR2
Raf
PTEN
JNK
c−Met
GSK−3
mTOR
EGFR
PI3K
Akt
Src
Bcr−A
PKC
JNK
Syk
PDGFR
ATM/ATR
IGF−1R
FLT3
Aurora K
CDK
PLK
ERK
MEK
FAK
statistic
d
Projected factor 1 score
MEK-inhibitor (μM)
Binimetinib
DMSO
e
0.017
Projected factor 2 score
Binimetinib 0.1μM
DMSO

**Supplemental Fig. S7: Factor 2 defined by organoid LGR5 stem cell identity. a**, Reactome pathway enrichment results for factor 2 gene expression loadings. Colorscale corresponds to normalized enrichment score (NES), where a positive value stands for an enrichment and a negative value for a depletion. Size of the nodes represent gene set size, edges correspond to gene set overlap **b,** Relationship of Wnt pathway inhibitor activity with factor 2 score. **c,** Approximated factor 2 shifts measured in organoids treated with small molecule inhibitors when accounting for line specific differences. Shifts are expressed as t statistics for the model (factor 2 ~ drug + line). **d,** Dose-dependent changes in factor 1 (IGFR1 signaling) scores after treatment with the MEK inhibitor binimitenib across organoid lines. The black line indicates median factor 2 values of 2 replicates from N=11 organoids treated with binimetinib, grey shading indicates the 95% confidence intervals based on the loess regression with default parameters. **e,** Factor 2 scores for organoids treated with 1μM binimetinib and DMSO control, data points shown represent the average factor scores of DMSO and binimetinib 0.1μM treated organoids from 11 lines (2 biological replicates / line) two-sided Wilcoxon rank sum test.


a
chr11
2.00Mb
186.98 kb
2.13Mb
2.15Mb
H19
IGF2
INS-IGF2
MIR488
b
CRIS−C (p = 0.001; NES = −1.68)
Ranked List Metric
Rank in Ordered Dataset
c
AG−1024
BMS−536924
BMS−754807
GSK1838705A
NVP−AEW541
Linsitinib
PQ 401
AUROC
Factor 1
d
AZD8330
Cobimetinib
MEK162
PD0325901
PD318088
Pimasertib
Refametinib
TAK−733
Trametinib
AUROC
Factor 1
e
AEE788
G−1478
AZD3759
AZD8931 (Sapitinib)
AZD9291
CNX−2006
CO−1686
OSI−420
WZ3146
AUROC
Factor 1
f
PLK
Aurora Kinase
CDK
MEK
FAK
ERK
JNK
PKC
HER2
PDGFR
ATM/ATR
EGFR
Syk
c−Kit
BTK
GSK−3
c−Met
Src
Akt
FLT3
JAK
S6 Kinase
Raf
Bcr−Abl
PI3K
Multi−TKI
PTEN
AMPK
DDR2
VEGFR
p38 MAPK
Wnt/beta−catenin
IGF−1R
Gamma−secretase
CBP/p300
Hedgehog/SMO
TGF−beta/Smad
ROCK
mTOR
statistic
g
DMSO
Rapamycin
WYE-132
WYE-345
AZD2014
D013T
D027T
D030T

**Supplemental Fig. S8: Factor 1 defined by IGF1R receptor signaling. a**, Genomic track plot for *IGF2*, *H19* and *INS-IGF2*. **b**, gene set enrichment analysis for CRIS signature C on factor 1 gene expression loadings. **c-e,** Relationship of IGF1R-, MEK- and EGFR-inhibitor activity with factor 1 scores, respectively. Shown are 9 randomly sampled small molecule inhibitors. **f,** Approximated factor 1 shifts measured in organoids treated with small molecule inhibitors when accounting for line specific differences. Shifts are expressed as t statistics for the model (factor 1 ~ drug + line). **g**, Representative images of organois treated with DMSO (left) or selected mTOR inhibitors. Shown are images of organoid lines D013T, D027T and D030T (cyan = DNA, magenta = actin; sampled images were cropped and embedded in black background; scale bar: 50µm).




**Supplemental Fig. S9: Complete scans of Western blot membranes in Fig. 6g**

## Supplemental Tables

## Table S1: Patient and organoid characteristics

| PDO line | PDO medium | PDO growth | Patient sex | Tumor location | Tumor stage (UICC) |
|---|---|---|---|---|---|
| **D004T** | ENA | good | f | rectum | 3 |
| **D007T** | ENA | good | m | rectum | 3 |
| **D010T** | ENA | good | m | sigm | 3 |
| **D013T** | ENAS | good | f | rectum | 1 |
| **D015T** | ENA | good | m | desc | 2 |
| **D018T** | ENA | good | m | sigm | 2 |
| **D019T** | ENA | good | f | sigm | 1 |
| **D020T** | ENA | good | m | rectum | 1 |
| **D021T** | ENA | medium | m | rectum | 1 |
| **D022T** | ENA | good | m | asc | 4 |
| **D027T** | ENA | good | m | rectum | 4 |
| **D030T** | ENA | good | f | asc | 2 |
| **D046T** | ENA | good | f | rectum | 3 |

Abbreviations: f, female; m, male; sigm, sigmoid; desc, descending colon; asc, ascending colon; ENA, basal medium + EGF, Noggin and A83-01 (ALK-inhibitor); ENAS, ENA + SB202190 (p38 inhibitor).

## Table S2: Mutations in organoids detected by amplicon sequencing

| SAMPLE | SYMBOL | Protein_position | Amino_acids | Consequence |
|---|---|---|---|---|
| P004T | NRAS | 61 | Q/L | missense_variant |
| P004T | PIK3CA | 546 | Q/P | missense_variant |
| P007T | AKT1 | 17 | E/K | missense_variant |
| P007T | APC | 564 | R/* | stop_gained |
| P007T | KRAS | 12 | G/D | missense_variant |
| P010T | KRAS | 13 | G/D | missense_variant |
| P010T | TP53 | - | - | splice_acceptor_variant |
| P013T | APC | 876 | R/* | stop_gained |
| P013T | APC | 1450 | R/* | stop_gained |
| P013T | ERBB2 | 310 | S/F | missense_variant |
| P013T | ERBB2 | 769 | D/Y | missense_variant |
| P013T | PIK3CA | 1004 | M/I | missense_variant |
| P013T | TP53 | 273 | R/C | missense_variant |
| P015T | ATM | 2809 | Q/X | frameshift_variant |
| P015T | B2M | 14-15 | SL/X | frameshift_variant |
| P015T | CTNNB1 | 34 | G/V | missense_variant |
| P015T | FBXW7 | 465 | R/C | missense_variant |
| P015T | KRAS | 13 | G/D | missense_variant |
| P015T | PTEN | 160 | T/I | missense_variant |
| P015T | TCF7L2 | 465 | R/X | frameshift_variant |
| P019T | APC | 1378 | Q/* | stop_gained |
| P019T | ARID1A | 1844 | W/* | stop_gained |
| P019T | KRAS | 146 | A/T | missense_variant |
| P019T | RNF43 | 225 | R/C | missense_variant |
| P019T | SMAD4 | 361 | R/C | missense_variant |
| P019T | TP53 | 234 | Y/N | missense_variant |
| P020T | AMER1 | 511 | P/A | missense_variant |
| P020T | KRAS | 12 | G/V | missense_variant |
| P020T | SMAD4 | 102 | P/R | missense_variant |
| P021T | APC | 1356 | S/* | stop_gained |
| P021T | GNAS | 844 | R/H | missense_variant |
| P021T | KRAS | 12 | G/D | missense_variant |
| P022T | APC | 232 | R/* | stop_gained |
| P022T | KRAS | 12 | G/C | missense_variant |
| P022T | PTEN | 137 | A/V | missense_variant |
| P022T | TP53 | 132 | K/R | missense_variant |
| P027T | AMER1 | 373 | A/G | missense_variant |
| P027T | APC | 216 | R/* | stop_gained |
| P027T | TP53 | 282 | R/W | missense_variant |
| P030T | KRAS | 146 | A/T | missense_variant |
| P030T | PIK3CA | 420 | C/R | missense_variant |
| P030T | SMAD4 | 537 | D/A | missense_variant |
| P046T | NRAS | 61 | Q/L | missense_variant |

## Table S3: Clinical cancer compound library

| Compound Name | Target | Category | Phase | Max conc (µM) | Min conc (µM) |
|---|---|---|---|---|---|
| 17AAG | HSP90 | Targeted | Phase III | 12,5 | 0,02 |
| Afatinib | ErbB-Receptors | Targeted | Clinical use | 100 | 0,16 |
| Alisertib | Aurora A | Targeted | Phase II/III | 25 | 0,04 |
| Alpelisib | PIK3a | Targeted | Phase I | 25 | 0,04 |
| Axitinib | PDGFR, KIT, VEGFR | Targeted | Clinical use | 75 | 0,12 |
| AZD 4547 | FGFR | Targeted | Phase II/III | 25 | 0,04 |
| AZD 5363 | AKT | Targeted | Phase II | 25 | 0,04 |
| Bexaroten | Retinoid-Receptor | Targeted | Clinical use | 20 | 0,032 |
| Binimetinib | NRAS, MEK | Targeted | Phase III | 25 | 0,04 |
| Birinapant | SMAC | Targeted | Phase II | 25 | 0,04 |
| Bortezomib | Proteasom | Targeted | Clinical use | 2,5 | 0,004 |
| Cabozantinib | VEGF, MET, RET | Targeted | Clinical use | 100 | 0,16 |
| Crizotinib | ALK | Targeted | Clinical use | 12,5 | 0,02 |
| Dabrafenib | BRAF | Targeted | Clinical use | 50 | 0,08 |
| Dasatinib | DDR2, BCR-ABL, SRC, KIT, PDGFR | Targeted | Clinical use | 100 | 0,16 |
| Defactinib | FAK | Targeted | Phase II | 7,5 | 0,012 |
| Erlotinib | EGFR | Targeted | Clinical use | 100 | 0,16 |
| Everolimus | mTOR | Targeted | Clinical use | 5 | 0,008 |
| Gefitinib | EGFR | Targeted | Clinical use | 100 | 0,16 |
| GSK2636771 | PTEN | Targeted | Phase I/II | 25 | 0,04 |
| Idelalisib | PIK3δ | Targeted | Clinical use | 100 | 0,16 |
| Lapatinib | HER2 and EGFR | Targeted | Clinical use | 100 | 0,16 |
| LGK974 | Porcupine | Targeted | Phase I | 100 | 0,16 |
| MK-1775 | Wee1 | Targeted | Phase II | 25 | 0,04 |
| MK-8776 | Chk1 | Targeted | Phase II | 7,5 | 0,012 |
| Napabucasin | STAT3 | Targeted | Phase III | 25 | 0,04 |
| Nutlin3a | p53 | Targeted | Preclinical | 100 | 0,16 |
| Olaparib | PARP | Targeted | Clinical use | 100 | 0,16 |
| Palbociclib | CDK | Targeted | Clinical use | 5 | 0,008 |
| Panobinostat | HDAC | Targeted | Clinical use | 2,5 | 0,004 |
| Pazopanib | c-KIT, FGFR, PDGFR and VEGFR | Targeted | Clinical use | 100 | 0,16 |
| Ponatinib | BEGFR, PDGFR, FGFR, EPH recep | Targeted | Clinical use | 25 | 0,04 |
| PRI-724 | CBP/p300 | Targeted | Phase I-II | 75 | 0,12 |
| Regorafenib | VEGFR-1/2/3, TIE-2, KIT, RET, RAF | Targeted | Clinical use | 100 | 0,16 |
| Ruxolitinib | JAK1 and JAK2 | Targeted | Clinical use | 100 | 0,16 |
| Sonidegib | SMO | Targeted | Clinical use | 100 | 0,16 |
| Sorafenib | PDGFR, KIT, VEGFR | Targeted | Clinical use | 100 | 0,16 |
| Sunitinib | Multi-TKI | Targeted | Clinical use | 50 | 0,08 |
| Taselisib | PI3K | Targeted | Phase III | 25 | 0,04 |
| Trametinib | Mek1/2 | Targeted | Clinical use | 2,5 | 0,004 |
| Venetoclax | Bcl-2 | Targeted | Clinical use | 25 | 0,04 |
| Vismodegib | SMO | Targeted | Clinical use | 100 | 0,16 |
| Volasertib | PLK1 | Targeted | Phase II | 25 | 0,04 |
| Vorinostat | HDAC | Targeted | Clinical use | 100 | 0,16 |
| VX-702 | p38 MAPK | Targeted | Phase II | 25 | 0,04 |
| YM155 | Survivin | Tagreted | Phase II | 5 | 0,008 |
| 5-FU | Antimetabolite | Chemotherapy | Clinical use | 100 | 0,16 |
| Bleomycin | DNA-Damage | Chemotherapy | Clinical use | 50 | 0,08 |
| Dacarbazine | Alkylating | Chemotherapy | Clinical use | 12,5 | 0,02 |
| Docetaxel | Mikrotubuli | Chemotherapy | Clinical use | 2,5 | 0,004 |
| Doxorubicin | Intercalating, mRNA synthesis | Chemotherapy | Clinical use | 50 | 0,08 |
| Etoposid | Topoisomerase | Chemotherapy | Clinical use | 100 | 0,16 |
| Fludarabine | Antimetabolite | Chemotherapy | Clinical use | 12,5 | 0,02 |
| Gemcitabine | DMA-Synthesis | Chemotherapy | Clinical use | 12,5 | 0,02 |
| Irinotecan / SN-38 | Topoisomerase | Chemotherapy | Clinical use | 25 | 0,04 |
| Methotrexate | Antimetabolite | Chemotherapy | Clinical use | 50 | 0,08 |
| Mitomycin C | Alkylating | Chemotherapy | Clinical use | 12,5 | 0,02 |
| Oxaliplatin | Alkylating | Chemotherapy | Clinical use | 75 | 0,12 |
| Paclitaxel | Mikrotubuli | Chemotherapy | Clinical use | 2,5 | 0,004 |
| Trifluoridin/Tipiracil | Antimetabolite | Chemotherapy | Clinical use | 55 | 0,088 |
| Vinblastin | Mikrotubuli | Chemotherapy | Clinical use | 2,5 | 0,004 |
| Miglitol | Antidiabetic | Metabolism | Clinical use | 12,5 | 0,02 |
| Phenformin | Antidiabetic | Metabolism | Clinical use | 100 | 0,16 |

## Table S4: Kinase-Stemcell (Ki-Stem) compound library

| Compound name | Target | Pathway | conc (uM) |
|---|---|---|---|
| 1-Azakenpaullone | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| 10058-F4 | c-Myc | Cell Cycle | 7,5 |
| 3-Methyladenine | PI3K | PI3K/Akt/mTOR | 7,5 |
| 7,8-Dihydroxyflavone | Trk receptor | Protein Tyrosine Kinase | 7,5 |
| A-674563 | Akt, CDK, PKA | PI3K/Akt/mTOR | 7,5 |
| A-769662 | AMPK | PI3K/Akt/mTOR | 7,5 |
| A66 | PI3K | PI3K/Akt/mTOR | 7,5 |
| AC480 (BMS-599626) | HER2 | Neuronal Signaling | 7,5 |
| Acadesine | AMPK | PI3K/Akt/mTOR | 7,5 |
| AEE788 (NVP-AEE788) | EGFR, Flt, VEGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| Afatinib (BIBW2992) | EGFR | Protein Tyrosine Kinase | 7,5 |
| AG-1024 | IGF-1R | Protein Tyrosine Kinase | 7,5 |
| AG-1478 (Tyrphostin AG-1478) | EGFR | Protein Tyrosine Kinase | 7,5 |
| AG-18 | EGFR | Protein Tyrosine Kinase | 7,5 |
| AG-490 (Tyrphostin B42) | JAK, EGFR | Others | 7,5 |
| Akti-1/2 | Akt | PI3K/Akt/mTOR | 7,5 |
| Alisertib (MLN8237) | Aurora Kinase | Others | 7,5 |
| AMG 337 | c-Met | Protein Tyrosine Kinase | 7,5 |
| AMG-458 | c-Met | Protein Tyrosine Kinase | 7,5 |
| AMG-900 | Aurora Kinase | Cell Cycle | 7,5 |
| AMG319 | PI3K | PI3K/Akt/mTOR | 7,5 |
| Amuvatinib (MP-470) | c-Met, c-Kit, PDGFR, Flt, c-RET | Protein Tyrosine Kinase | 7,5 |
| ANA-12 | Trk receptor | Protein Tyrosine Kinase | 7,5 |
| Anacardic Acid | Histone Acetyltransferase | Epigenetics | 7,5 |
| AP26113 | ALK | Protein Tyrosine Kinase | 7,5 |
| Apatinib | VEGFR | Protein Tyrosine Kinase | 7,5 |
| AR-A014418 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| AR-A014418 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| AS-252424 | PI3K | PI3K/Akt/mTOR | 7,5 |
| AS-604850 | PI3K | PI3K/Akt/mTOR | 7,5 |
| Asiatic Acid | p38 MAPK | MAPK | 7,5 |
| ASP3026 | ALK | Protein Tyrosine Kinase | 7,5 |
| AST-1306 | EGFR | Protein Tyrosine Kinase | 7,5 |
| Astragaloside A | others | TGF-beta/Smad | 7,5 |
| AT13148 | Akt | PI3K/Akt/mTOR | 7,5 |
| AT7519 | CDK | Cell Cycle | 7,5 |
| AT7867 | Akt, S6 kinase | PI3K/Akt/mTOR | 7,5 |
| AT9283 | Bcr-Abl, JAK, Aurora Kinase | Others | 7,5 |
| Aurora A Inhibitor I | Aurora Kinase | Cell Cycle | 7,5 |
| Avagacestat (BMS-708163) | Gamma-secretase | Proteases | 7,5 |
| AVL-292 | BTK | Angiogenesis | 7,5 |
| Axitinib | VEGFR, PDGFR, c-Kit | Protein Tyrosine Kinase | 7,5 |
| AZ 628 | Raf | MAPK | 7,5 |
| AZ 960 | JAK | JAK/STAT | 7,5 |
| AZ20 | ATM/ATR | PI3K/Akt/mTOR | 7,5 |
| AZD1080 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| AZD1208 | Pim | JAK/STAT | 7,5 |
| AZD1480 | JAK | JAK/STAT | 7,5 |
| AZD1480 | JAK | JAK/STAT | 7,5 |
| AZD2014 | mTOR | PI3K/Akt/mTOR | 7,5 |
| AZD2858 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| AZD2932 | PDGFR | Protein Tyrosine Kinase | 7,5 |
| AZD3463 | ALK | Protein Tyrosine Kinase | 7,5 |
| AZD3759 | EGFR | Protein Tyrosine Kinase | 7,5 |
| AZD4547 | FGFR | Angiogenesis | 7,5 |
| AZD5363 | Akt | PI3K/Akt/mTOR | 7,5 |
| AZD5438 | CDK | Cell Cycle | 7,5 |
| AZD6482 | PI3K | PI3K/Akt/mTOR | 7,5 |
| AZD6738 | ATM/ATR | PI3K/Akt/mTOR | 7,5 |
| AZD7762 | Chk | Cell Cycle | 7,5 |
| AZD8055 | mTOR | PI3K/Akt/mTOR | 7,5 |
| AZD8330 | MEK | MAPK | 7,5 |
| AZD8931 (Sapitinib) | EGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| AZD9291 | EGFR | Protein Tyrosine Kinase | 7,5 |
| Barasertib (AZD1152-HQPA) | Aurora Kinase | Others | 7,5 |
| Baricitinib (LY3009104, INCB02 | JAK | Epigenetics | 7,5 |
| BAY 11-7082 | I_B/IKK | NF-_B | 7,5 |
| Bay 11-7085 | I_B/IKK | NF-_B | 7,5 |
| BGT226 (NVP-BGT226) | PI3K, mTOR | PI3K/Akt/mTOR | 7,5 |
| BI 2536 | PLK | Others | 7,5 |
| BI-78D3 | JNK | MAPK | 7,5 |
| BI-D1870 | S6 Kinase | PI3K/Akt/mTOR | 7,5 |
| Bikinin | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| BIO | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| BIRB 796 (Doramapimod) | p38 MAPK | MAPK | 7,5 |

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|---|---|---|---|
| BIX 02188 | MEK | MAPK | 7,5 |
| BKM120 (NVP-BKM120, Buparli | PI3K | PI3K/Akt/mTOR | 7,5 |
| BLZ945 | CSF-1R | Protein Tyrosine Kinase | 7,5 |
| BMS-265246 | CDK | Cell Cycle | 7,5 |
| BMS-345541 | I_B/IKK | NF-_B | 7,5 |
| BMS-536924 | IGF-1R | Protein Tyrosine Kinase | 7,5 |
| BMS-582949 | p38 MAPK | MAPK | 7,5 |
| BMS-754807 | IGF-1R | Others | 7,5 |
| BMS-777607 | c-Met | Protein Tyrosine Kinase | 7,5 |
| BMS-794833 | c-Met, VEGFR | Protein Tyrosine Kinase | 7,5 |
| BMS-833923 | Hedgehog/Smoothened | GPCR & G Protein | 7,5 |
| Bosutinib (SKI-606) | Src | Angiogenesis | 7,5 |
| Brivanib (BMS-540215) | VEGFR, FGFR | GPCR & G Protein | 7,5 |
| Brivanib Alaninate (BMS-582664 | VEGFR, FGFR | Others | 7,5 |
| BS-181 HCl | CDK | Cell Cycle | 7,5 |
| Butein | EGFR | Protein Tyrosine Kinase | 7,5 |
| BX-795 | PDK-1, IKK | PI3K/Akt/mTOR | 7,5 |
| BX-912 | PDK-1 | PI3K/Akt/mTOR | 7,5 |
| BYL719 | PI3K | PI3K/Akt/mTOR | 7,5 |
| Cabozantinib (XL184, BMS-907 | VEGFR, c-Met, Flt, Tie-2, c-Kit | Others | 7,5 |
| CAL-101 (Idelalisib, GS-1101) | PI3K | PI3K/Akt/mTOR | 7,5 |
| CAY10505 | PI3K | PI3K/Akt/mTOR | 7,5 |
| CC-223 | mTOR | PI3K/Akt/mTOR | 7,5 |
| CCT128930 | Akt | PI3K/Akt/mTOR | 7,5 |
| Cediranib (AZD2171) | VEGFR, Flt | Protein Tyrosine Kinase | 7,5 |
| CEP-32496 | Raf | MAPK | 7,5 |
| CEP-33779 | JAK | JAK/STAT | 7,5 |
| CGI1746 | BTK | Angiogenesis | 7,5 |
| CGK 733 | ATM/ATR | DNA Damage | 7,5 |
| CH5132799 | PI3K, mTOR | PI3K/Akt/mTOR | 7,5 |
| CHIR-124 | Chk | Cell Cycle | 7,5 |
| CHIR-98014 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| CHIR-99021 (CT99021) | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| Chrysophanic Acid | EGFR, mTOR | Protein Tyrosine Kinase | 7,5 |
| CNX-2006 | EGFR | Protein Tyrosine Kinase | 7,5 |
| CNX-774 | BTK | Angiogenesis | 7,5 |
| CO-1686 (AVL-301) | EGFR | Protein Tyrosine Kinase | 7,5 |
| Cobimetinib (GDC-0973, RG74 | MEK | MAPK | 7,5 |
| CP-673451 | PDGFR | Protein Tyrosine Kinase | 7,5 |
| CP-724714 | EGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| Crenolanib (CP-868596) | PDGFR | Protein Tyrosine Kinase | 7,5 |
| Crizotinib (PF-02341066) | c-Met, ALK | Others | 7,5 |
| CUDC-101 | HDAC, EGFR, HER2 | Epigenetics | 7,5 |
| CUDC-907 | HDAC, PI3K | Cytoskeletal Signaling | 7,5 |
| CX-6258 HCl | Pim | JAK/STAT | 7,5 |
| CYC116 | Aurora Kinase, VEGFR | Cell Cycle | 7,5 |
| CYT387 | JAK | JAK/STAT | 7,5 |
| CZC24832 | PI3K_ | PI3K/Akt/mTOR | 7,5 |
| D 4476 | CK | Metabolism | 7,5 |
| Dabrafenib (GSK2118436) | Raf | MAPK | 7,5 |
| Dacomitinib (PF299804, PF299) | EGFR | Protein Tyrosine Kinase | 7,5 |
| Danusertib (PHA-739358) | Aurora Kinase, FGFR, Bcr-Abl, | Others | 7,5 |
| Daphnetin | PKA/PKC/EGFR | DNA Damage | 7,5 |
| DAPT (GSI-IX) | Gamma-secretase, Beta Amyloi | Proteases | 7,5 |
| DASA-58 | PKM2 | Others | 7,5 |
| Dasatinib | Src, Bcr-Abl, c-Kit | Angiogenesis | 7,5 |
| DCC-2036 (Rebastinib) | Bcr-Abl | Angiogenesis | 7,5 |
| DDR1-IN-1 | DDR(receptor tyrosine kinase) | Others | 7,5 |
| Decernotinib (VX-509) | JAK | JAK/STAT | 7,5 |
| Degrasyn (WP1130) | DUB, Bcr-Abl | Angiogenesis | 7,5 |
| Dinaciclib (SCH727965) | CDK | Cell Cycle | 7,5 |
| Dovitinib (TKI-258, CHIR-258) | c-Kit, FGFR, Flt, VEGFR, PDGF | Angiogenesis | 7,5 |
| Dovitinib Dilactic Acid | Flt, FGFR, PDGFR, VEGFR, c- | Angiogenesis | 7,5 |
| EHop-016 | Rac | Cell Cycle | 7,5 |
| ENMD-2076 | Flt, Aurora Kinase, VEGFR | Angiogenesis | 7,5 |
| Entrectinib (RXDX-101) | Trk receptor | Protein Tyrosine Kinase | 7,5 |
| Enzastaurin (LY317615) | PKC | Neuronal Signaling | 7,5 |
| ERK5-IN-1 | ERK | MAPK | 7,5 |
| ETC-1002 | AMPK | PI3K/Akt/mTOR | 7,5 |
| ETP-46464 | mTOR | PI3K/Akt/mTOR | 7,5 |
| Everolimus (RAD001) | mTOR | Others | 7,5 |
| Fasudil (HA-1077) HCl | ROCK | Cell Cycle | 7,5 |
| FH535 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| FIIN-2 | FGFR | Protein Tyrosine Kinase | 7,5 |
| Filgotinib (GLPG0634) | JAK | JAK/STAT | 7,5 |
| Fingolimod (FTY720) HCl | S1P Receptor, Bcr-Abl, PKC | GPCR & G Protein | 7,5 |
| Flavopiridol (Alvocidib) | CDK | Cell Cycle | 7,5 |
| Foretinib (GSK1363089) | c-Met, VEGFR | Others | 7,5 |

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|---|---|---|---|
| Fostamatinib (R788) | Syk | Angiogenesis | 7,5 |
| FRAX597 | PAK | Cytoskeletal Signaling | 7,5 |
| G-749 | FLT3 | Angiogenesis | 7,5 |
| GDC-0068 | Akt | PI3K/Akt/mTOR | 7,5 |
| GDC-0349 | mTOR | PI3K/Akt/mTOR | 7,5 |
| GDC-0879 | Raf | Others | 7,5 |
| GDC-0941 | PI3K | Metabolism | 7,5 |
| GDC-0980 (RG7422) | mTOR, PI3K | PI3K/Akt/mTOR | 7,5 |
| Gefitinib (ZD1839) | EGFR | Protein Tyrosine Kinase | 7,5 |
| Genistein | EGFR | Protein Tyrosine Kinase | 7,5 |
| GF109203X | PKC | TGF-beta/Smad | 7,5 |
| GF109203X | PKC | TGF-beta/Smad | 7,5 |
| GNE-0877 | leucine-rich repeat kinase 2 (LR | Autophagy | 7,5 |
| GNE-7915 | LRRK | Autophagy | 7,5 |
| GNE-9605 | LRRK2 | Autophagy | 7,5 |
| GNF-2 | Bcr-Abl | Angiogenesis | 7,5 |
| GNF-5 | Bcr-Abl | Angiogenesis | 7,5 |
| Go 6983 | PKC | TGF-beta/Smad | 7,5 |
| Golvatinib (E7050) | c-Met, VEGFR | Protein Tyrosine Kinase | 7,5 |
| GSK1838705A | IGF-1, ALK | Protein Tyrosine Kinase | 7,5 |
| GSK1904529A | IGF-1R | Others | 7,5 |
| GSK2126458 (GSK458) | PI3K, mTOR | PI3K/Akt/mTOR | 7,5 |
| GSK2292767 | PI3K | PI3K/Akt/mTOR | 7,5 |
| GSK2334470 | PDK-1 | PI3K/Akt/mTOR | 7,5 |
| GSK2578215A | LRRK2 | Autophagy | 7,5 |
| GSK2636771 | PI3K | PI3K/Akt/mTOR | 7,5 |
| GSK429286A | ROCK | Cell Cycle | 7,5 |
| GSK461364 | PLK | Cell Cycle | 7,5 |
| GSK621 | AMPK | PI3K/Akt/mTOR | 7,5 |
| GSK650394 | SGK | Others | 7,5 |
| GSK690693 | Akt | Others | 7,5 |
| GW441756 | Trk Receptor | Protein Tyrosine Kinase | 7,5 |
| GW5074 | Raf | MAPK | 7,5 |
| GW788388 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| GZD824 | Bcr-Abl | Angiogenesis | 7,5 |
| H 89 2HCl | S6 Kinase | PI3K/Akt/mTOR | 7,5 |
| Hesperadin | Aurora Kinase | Cell Cycle | 7,5 |
| Hesperetin | Histamine Receptor | TGF-beta/Smad | 7,5 |
| HMN-214 | PLK | Cell Cycle | 7,5 |
| HO-3867 | STAT | JAK/STAT | 7,5 |
| Honokiol | Akt, MEK | PI3K/Akt/mTOR | 7,5 |
| HS-173 | PI3K | PI3K/Akt/mTOR | 7,5 |
| HTH-01-015 | AMPK | PI3K/Akt/mTOR | 7,5 |
| Ibrutinib (PCI-32765) | Src | Angiogenesis | 7,5 |
| ICG-001 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| Icotinib | EGFR | Protein Tyrosine Kinase | 7,5 |
| IKK-16 (IKK Inhibitor VII) | IKK | NF-_B | 7,5 |
| IM-12 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| Imatinib Mesylate (STI571) | PDGFR, c-Kit, Bcr-Abl | Protein Tyrosine Kinase | 7,5 |
| IMD 0354 | IKK | NF-_B | 7,5 |
| Indirubin | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| INK 128 (MLN0128) | mTOR | PI3K/Akt/mTOR | 7,5 |
| IPA-3 | PAK | Cytoskeletal Signaling | 7,5 |
| IPI-145 (INK1197) | PI3K | Angiogenesis | 7,5 |
| IWP-L6 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| IWR-1-endo | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| JNJ-38877605 | c-Met | Others | 7,5 |
| JNJ-7706621 | CDK, Aurora Kinase | Cell Cycle | 7,5 |
| JNK Inhibitor IX | JNK | MAPK | 7,5 |
| JNK-IN-8 | JNK | MAPK | 7,5 |
| K02288 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| Ki8751 | VEGFR, c-Kit, PDGFR | Protein Tyrosine Kinase | 7,5 |
| KN-62 | Ca2+/calmodulin-dependent pro | Others | 7,5 |
| KN-93 Phosphate | CaMK | Others | 7,5 |
| KRN 633 | VEGFR, PDGFR | Protein Tyrosine Kinase | 7,5 |
| KU-0063794 | mTOR | PI3K/Akt/mTOR | 7,5 |
| KU-55933 (ATM Kinase Inhibitor | ATM | Others | 7,5 |
| KU-60019 | ATM | DNA Damage | 7,5 |
| KW-2449 | Flt, Bcr-Abl, Aurora Kinase | Angiogenesis | 7,5 |
| KX2-391 | Src | Angiogenesis | 7,5 |
| KY02111 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| Lapatinib | EGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| Lapatinib (GW-572016) Ditosyla | EGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| LDC000067 | CDK | Cell Cycle | 7,5 |
| LDE225 (NVP-LDE225,Erismod | Smoothened | Stem Cells & Wnt | 7,5 |
| LDK378 | ALK | Protein Tyrosine Kinase | 7,5 |
| LDN-214117 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| Lenvatinib (E7080) | VEGFR | Protein Tyrosine Kinase | 7,5 |

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|---|---|---|---|
| LFM-A13 | BTK | Angiogenesis | 7,5 |
| LGK-974 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| Linifanib (ABT-869) | PDGFR, VEGFR | Protein Tyrosine Kinase | 7,5 |
| LJH685 | S6 Kinase | PI3K/Akt/mTOR | 7,5 |
| LJI308 | S6 Kinase | PI3K/Akt/mTOR | 7,5 |
| Losmapimod (GW856553X) | p38 MAPK | MAPK | 7,5 |
| LY2090314 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| LY2157299 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| LY2603618 | Chk | Cell Cycle | 7,5 |
| LY2784544 | JAK | JAK/STAT | 7,5 |
| LY2784544 | JAK | JAK/STAT | 7,5 |
| LY2811376 | 5-alpha Reductase | Proteases | 7,5 |
| LY2835219 | CDK | Cell Cycle | 7,5 |
| LY294002 | PI3K | Others | 7,5 |
| LY3023414 | Akt | PI3K/Akt/mTOR | 7,5 |
| LY411575 | Gamma-secretase | Proteases | 7,5 |
| Masitinib (AB1010) | c-Kit, PDGFR, FGFR, FAK | Others | 7,5 |
| MEK162 (ARRY-162, ARRY-43 | MEK | MAPK | 7,5 |
| MGCD-265 | c-Met, VEGFR, Tie-2 | Protein Tyrosine Kinase | 7,5 |
| Milciclib (PHA-848125) | CDK | Cell Cycle | 7,5 |
| MK-0752 | Gamma-secretase | Proteases | 7,5 |
| MK-2206 2HCl | Akt | Others | 7,5 |
| MK-2461 | c-Met, FGFR, PDGFR | Protein Tyrosine Kinase | 7,5 |
| MK-5108 (VX-689) | Aurora Kinase | Cell Cycle | 7,5 |
| MK-8745 | Aurora Kinase | Cell Cycle | 7,5 |
| MLN2480 | Raf | MAPK | 7,5 |
| MLN8054 | Aurora Kinase | Others | 7,5 |
| Motesanib Diphosphate (AMG-7 | VEGFR, PDGFR, c-Kit | Protein Tyrosine Kinase | 7,5 |
| Mubritinib (TAK 165) | HER2 | Protein Tyrosine Kinase | 7,5 |
| Nilotinib (AMN-107) | Bcr-Abl | Angiogenesis | 7,5 |
| Nintedanib (BIBF 1120)_uncerta | VEGFR, PDGFR, FGFR | Protein Tyrosine Kinase | 7,5 |
| NSC 23766 | Rac | Cell Cycle | 7,5 |
| NU6027 | CDK | Cell Cycle | 7,5 |
| NVP-AEW541 | IGF-1R | Protein Tyrosine Kinase | 7,5 |
| NVP-BHG712 | VEGFR, Src, Raf, Bcr-Abl | Protein Tyrosine Kinase | 7,5 |
| NVP-BSK805 2HCl | JAK | JAK/STAT | 7,5 |
| NVP-BVU972 | c-Met | Protein Tyrosine Kinase | 7,5 |
| Oclacitinib | JAK | JAK/STAT | 7,5 |
| Olmutinib (HM61713, BI 148269 | EGFR | Protein Tyrosine Kinase | 7,5 |
| ONO-4059 | BTK | Angiogenesis | 7,5 |
| OSI-027 | mTOR | PI3K/Akt/mTOR | 7,5 |
| OSI-420 | EGFR | Protein Tyrosine Kinase | 7,5 |
| OSI-906 (Linsitinib) | IGF-1R | Others | 7,5 |
| OSI-930 | c-Kit, VEGFR | Protein Tyrosine Kinase | 7,5 |
| OSU-03012 (AR-12) | PDK-1 | Others | 7,5 |
| P276-00 | CDK | Cell Cycle | 7,5 |
| Pacritinib (SB1518) | JAK | JAK/STAT | 7,5 |
| Palomid 529 (P529) | mTOR | PI3K/Akt/mTOR | 7,5 |
| Pazopanib | VEGFR | Protein Tyrosine Kinase | 7,5 |
| Pazopanib HCl | VEGFR, PDGFR, c-Kit | Protein Tyrosine Kinase | 7,5 |
| PD0325901 | MEK | DNA Damage | 7,5 |
| PD168393 | EGFR | Protein Tyrosine Kinase | 7,5 |
| PD173074 | FGFR, VEGFR | Angiogenesis | 7,5 |
| PD173955 | Bcr-Abl | Angiogenesis | 7,5 |
| PD184352 (CI-1040) | MEK | MAPK | 7,5 |
| PD318088 | MEK | MAPK | 7,5 |
| PD98059 | MEK | MAPK | 7,5 |
| Pelitinib (EKB-569) | EGFR | Protein Tyrosine Kinase | 7,5 |
| PF-00562271 | FAK | Angiogenesis | 7,5 |
| PF-04217903 | c-Met | Others | 7,5 |
| PF-04691502 | mTOR, PI3K, Akt | PI3K/Akt/mTOR | 7,5 |
| PF-3758309 | PAK | Cytoskeletal Signaling | 7,5 |
| PF-431396 | FAK | Angiogenesis | 7,5 |
| PF-4708671 | S6 Kinase | PI3K/Akt/mTOR | 7,5 |
| PF-477736 | Chk | Cell Cycle | 7,5 |
| PF-5274857 | Hedgehog/Smoothened | Stem Cells & Wnt | 7,5 |
| PF-543 | SphK1 | GPCR & G Protein | 7,5 |
| PF-562271 | FAK | Angiogenesis | 7,5 |
| PF-573228 | FAK | Angiogenesis | 7,5 |
| PFK15 | 6-phosphofructo-2-kinase (PFK | Others | 7,5 |
| PH-797804 | p38 MAPK | MAPK | 7,5 |
| PHA-665752 | c-Met | Others | 7,5 |
| PHA-680632 | Aurora Kinase | Cell Cycle | 7,5 |
| PHA-767491 | CDK | Cell Cycle | 7,5 |
| PHA-793887 | CDK | Cell Cycle | 7,5 |
| Phenformin HCl | AMPK | PI3K/Akt/mTOR | 7,5 |
| PHT-427 | Akt, PDK-1 | PI3K/Akt/mTOR | 7,5 |
| PI-103 | DNA-PK, PI3K, mTOR | Neuronal Signaling | 7,5 |

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|---|---|---|---|
| Piceatannol | Syk | Angiogenesis | 7,5 |
| PIK-293 | PI3K | PI3K/Akt/mTOR | 7,5 |
| PIK-294 | PI3K | PI3K/Akt/mTOR | 7,5 |
| PIK-93 | PI3K, VEGFR | PI3K/Akt/mTOR | 7,5 |
| Pimasertib (AS-703026) | MEK | MAPK | 7,5 |
| Pirfenidone | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| PLX-4720 | Raf | Others | 7,5 |
| PLX7904 | Raf | MAPK | 7,5 |
| Ponatinib (AP24534) | Bcr-Abl, VEGFR, FGFR, PDGF | Angiogenesis | 7,5 |
| PP1 | Src | Angiogenesis | 7,5 |
| PP121 | DNA-PK, mTOR, PDGF | Protein Tyrosine Kinase | 7,5 |
| PP2 | Src | Angiogenesis | 7,5 |
| PP242 | mTOR | PI3K/Akt/mTOR | 7,5 |
| PQ 401 | IGF-1R | Protein Tyrosine Kinase | 7,5 |
| PRI-724 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| PRT062607 (P505-15, BIIB057) | Syk | Angiogenesis | 7,5 |
| Purvalanol A | CDK | Cell Cycle | 7,5 |
| Quercetin | PI3K, PKC, Src, Sirtuin | Epigenetics | 7,5 |
| Quizartinib (AC220) | Flt | Angiogenesis | 7,5 |
| R406 | Syk, Flt | Angiogenesis | 7,5 |
| R406 (free base) | Syk | Angiogenesis | 7,5 |
| R547 | CDK | Cell Cycle | 7,5 |
| RAF265 (CHIR-265) | Raf, VEGFR | MAPK | 7,5 |
| Rapamycin (Sirolimus) | mTOR | DNA Damage | 7,5 |
| Refametinib (RDEA119, Bay 86- | MEK | Others | 7,5 |
| Regorafenib (BAY 73-4506) | c-Kit, Raf, VEGFR | Protein Tyrosine Kinase | 7,5 |
| RepSox | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| Ridaforolimus (Deforolimus, MK | mTOR | PI3K/Akt/mTOR | 7,5 |
| Rigosertib (ON-01910) | PLK | Cell Cycle | 7,5 |
| RKI-1447 | ROCK | Cell Cycle | 7,5 |
| RN486 | BTK | Angiogenesis | 7,5 |
| Ro 31-8220 Mesylate | PKC | TGF-beta/Smad | 7,5 |
| Ro-3306 | CDK | Cell Cycle | 7,5 |
| Ro3280 | PLK | Cell Cycle | 7,5 |
| RO4929097 | Y-Secretase | Proteases | 7,5 |
| Roscovitine (Seliciclib,CYC202) | CDK | Others | 7,5 |
| Ruxolitinib (INCB018424) | JAK | JAK/STAT | 7,5 |
| S-Ruxolitinib (INCB018424) | JAK | JAK/STAT | 7,5 |
| SANT-1 | Smoothened | Stem Cells & Wnt | 7,5 |
| SAR131675 | VEGFR | Protein Tyrosine Kinase | 7,5 |
| SAR245409 (XL765) | PI3K, mTOR | PI3K/Akt/mTOR | 7,5 |
| Saracatinib (AZD0530) | Src, Bcr-Abl | Angiogenesis | 7,5 |
| SB202190 (FHPI) | p38 MAPK | PI3K/Akt/mTOR | 7,5 |
| SB203580 | p38 MAPK | Transmembrane Transpc | 7,5 |
| SB216763 | GSK-3 | Others | 7,5 |
| SB239063 | p38 MAPK | MAPK | 7,5 |
| SB415286 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| SB431542 | TGF-beta/Smad | Others | 7,5 |
| SB505124 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| SB525334 | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| SB590885 | Raf | MAPK | 7,5 |
| SC-514 | I_B/IKK | NF-_B | 7,5 |
| SC1 | ERK | MAPK | 7,5 |
| Schisandrin B (Sch B) | ATM/ATR | PI3K/Akt/mTOR | 7,5 |
| Selumetinib (AZD6244) | MEK | MAPK | 7,5 |
| Semagacestat (LY450139) | Gamma-secretase | Proteases | 7,5 |
| Semaxanib (SU5416) | VEGFR | Protein Tyrosine Kinase | 7,5 |
| SGI-1776 free base | Pim | JAK/STAT | 7,5 |
| SGI-7079 | VEGFR | Protein Tyrosine Kinase | 7,5 |
| SH-4-54 | STAT | JAK/STAT | 7,5 |
| Skepinone-L | p38 MAPK | MAPK | 7,5 |
| SKI II | sphingosine kinase (SphK) | GPCR & G Protein | 7,5 |
| SL-327 | MEK | Others | 7,5 |
| SMI-4a | Pim | JAK/STAT | 7,5 |
| SNS-032 (BMS-387032) | CDK | Others | 7,5 |
| SNS-314 Mesylate | Aurora Kinase | Others | 7,5 |
| Sorafenib | Raf | MAPK | 7,5 |
| Sotrastaurin | PKC | TGF-beta/Smad | 7,5 |
| SP600125 | JNK | MAPK | 7,5 |
| SSR128129E | FGFR | Angiogenesis | 7,5 |
| STA-21 | STAT | JAK/STAT | 7,5 |
| SU11274 | c-Met | Neuronal Signaling | 7,5 |
| SU6656 | Src | Angiogenesis | 7,5 |
| SU9516 | CDK | Cell Cycle | 7,5 |
| Sunitinib Malate | VEGFR, PDGFR, c-Kit, Flt | Microbiology | 7,5 |
| TAE226 (NVP-TAE226) | FAK | Angiogenesis | 7,5 |
| TAK-285 | EGFR, HER2 | Protein Tyrosine Kinase | 7,5 |
| TAK-632 | Raf | MAPK | 7,5 |

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| TAK-715 | p38 MAPK | MAPK | 7,5 |
| TAK-733 | MEK | MAPK | 7,5 |
| TAK-901 | Aurora Kinase | Cell Cycle | 7,5 |
| Taladegib (LY2940680) | Hedgehog,Hedgehog/Smoothen | Stem Cells & Wnt | 7,5 |
| TCS 359 | FLT3 | Angiogenesis | 7,5 |
| TDZD-8 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| Telatinib | VEGFR, PDGFR, c-Kit | Protein Tyrosine Kinase | 7,5 |
| Temsirolimus (CCI-779, NSC 68 | mTOR | Neuronal Signaling | 7,5 |
| Tepotinib (EMD 1214063) | c-Met | Protein Tyrosine Kinase | 7,5 |
| TG003 | CDK | Cell Cycle | 7,5 |
| TG100-115 | PI3K | PI3K/Akt/mTOR | 7,5 |
| TG101209 | Flt, JAK, c-RET | JAK/STAT | 7,5 |
| TG101348 (SAR302503) | JAK | JAK/STAT | 7,5 |
| TGX-221 | PI3K | PI3K/Akt/mTOR | 7,5 |
| Theophylline | TGF-beta/Smad | TGF-beta/Smad | 7,5 |
| Thiazovivin | ROCK | Cell Cycle | 7,5 |
| TIC10 Analogue | Akt | PI3K/Akt/mTOR | 7,5 |
| Tideglusib | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| Tie2 kinase inhibitor | Tie-2 | Protein Tyrosine Kinase | 7,5 |
| Tivantinib (ARQ 197) | c-Met | Protein Tyrosine Kinase | 7,5 |
| Tivozanib (AV-951) | VEGFR, c-Kit, PDGFR | Protein Tyrosine Kinase | 7,5 |
| Tofacitinib (CP-690550,Tasociti | JAK | JAK/STAT | 7,5 |
| Tofacitinib (CP-690550) Citrate | JAK | JAK/STAT | 7,5 |
| Torin 2 | mTOR | PI3K/Akt/mTOR | 7,5 |
| TPCA-1 | IKK | NF-_B | 7,5 |
| Trametinib (GSK1120212) | MEK | MAPK | 7,5 |
| Triciribine | Akt | Others | 7,5 |
| TSU-68 (SU6668, Orantinib) | VEGFR, PDGFR , FGFR | Protein Tyrosine Kinase | 7,5 |
| TWS119 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| TWS119 | GSK-3 | PI3K/Akt/mTOR | 7,5 |
| Tyrphostin 9 | EGFR | Protein Tyrosine Kinase | 7,5 |
| Tyrphostin AG 1296 | PDGFR | Protein Tyrosine Kinase | 7,5 |
| Tyrphostin AG 879 | HER2 | Protein Tyrosine Kinase | 7,5 |
| U0126-EtOH | MEK | Others | 7,5 |
| Ulixertinib (BVD-523, VRT75227 | ERK | MAPK | 7,5 |
| Uprosertib (GSK2141795) | Akt | PI3K/Akt/mTOR | 7,5 |
| URMC-099 | Abl1; LRRK2; MLK3; MLK1 | Others | 7,5 |
| Vacquinol-1 | JNK | MAPK | 7,5 |
| Varlitinib | EGFR | Protein Tyrosine Kinase | 7,5 |
| Vatalanib (PTK787) 2HCl | VEGFR, c-Kit, Flt | Others | 7,5 |
| VE-821 | ATM/ATR | DNA Damage | 7,5 |
| VE-822 | ATM/ATR | PI3K/Akt/mTOR | 7,5 |
| Vemurafenib (PLX4032, RG720 | Raf | MAPK | 7,5 |
| Vismodegib (GDC-0449) | Hedgehog, P-gp | Neuronal Signaling | 7,5 |
| Volasertib (BI 6727) | PLK | Cell Cycle | 7,5 |
| VPS34-IN1 | PI3K | PI3K/Akt/mTOR | 7,5 |
| VS-5584 (SB2343) | PI3K | PI3K/Akt/mTOR | 7,5 |
| VX-11e | ERK | MAPK | 7,5 |
| VX-680 (Tozasertib, MK-0457) | Aurora Kinase | Endocrinology & Hormone | 7,5 |
| VX-702 | p38 MAPK | MAPK | 7,5 |
| VX-745 | p38 MAPK | MAPK | 7,5 |
| WAY-600 | mTOR | PI3K/Akt/mTOR | 7,5 |
| WH-4-023 | Src | Angiogenesis | 7,5 |
| WHI-P154 | JAK, EGFR | JAK/STAT | 7,5 |
| WIKI4 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| Wnt agonist 1 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| Wnt-C59 (C59) | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| WP1066 | JAK | JAK/STAT | 7,5 |
| WYE-125132 (WYE-132) | mTOR | PI3K/Akt/mTOR | 7,5 |
| WYE-354 | mTOR | PI3K/Akt/mTOR | 7,5 |
| WZ3146 | EGFR | Protein Tyrosine Kinase | 7,5 |
| WZ4002 | EGFR | Protein Tyrosine Kinase | 7,5 |
| WZ4003 | AMPK | PI3K/Akt/mTOR | 7,5 |
| WZ8040 | EGFR | Protein Tyrosine Kinase | 7,5 |
| XAV-939 | Wnt/beta-catenin | Stem Cells & Wnt | 7,5 |
| XL019 | JAK | JAK/STAT | 7,5 |
| XMD8-92 | ERK | MAPK | 7,5 |
| Y-27632 2HCl | ROCK | Others | 7,5 |
| YM201636 | PI3K | PI3K/Akt/mTOR | 7,5 |
| YO-01027 | Gamma-secretase | Proteases | 7,5 |
| ZM 306416 | VEGFR | Protein Tyrosine Kinase | 7,5 |
| ZM 323881 HCl | VEGFR | Protein Tyrosine Kinase | 7,5 |
| ZM 336372 | Raf | MAPK | 7,5 |
| ZM 39923 HCl | JAK | JAK/STAT | 7,5 |
| ZM 447439 | Aurora Kinase | Others | 7,5 |
| Zotarolimus(ABT-578) | mTOR | PI3K/Akt/mTOR | 7,5 |
| ZSTK474 | PI3K | Neuronal Signaling | 7,5 |