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**The triple angiokinase inhibitor nintedanib directly inhibits tumor cell growth and induces tumor shrinkage via blocking oncogenic receptor tyrosine kinases**

Frank Hilberg, Ulrike Tontsch-Grunt, Anke Baum, Anh T. Le, Robert C. Doebele, Simone Lieb, Davide Gianni, Tilman Voss, Pilar Garin-Chesa, Christian Haslinger and Norbert Kraut

Boehringer Ingelheim RCV GmbH Co KG, Dr. Boehringer-Gasse 5-11, A-1121 Vienna, Austria (F.H., U.T-G, A.B., S.L., D.G., P.G-C, C.H., N.K.)

University of Colorado, School of Medicine, Division of Medical Oncology, 12801 E. 17th Ave., MS 8117, Aurora, CO 80045 (A.T.L., R.C.D.)

AstraZeneca - Innovative Medicines and Early Development | Discovery Sciences, 310 Unit Darwin Building - Cambridge Science Park - Milton Rd - CB4 0WG (D.G.)

## Hilberg et al., Supplementary Tables:

<b>Table S1a</b>					
<b>Sensitive cell lines: sensitivity, tumor type, altered genes</b>					
<b>Cell Line</b>	<b>GI50 (nmol/l)</b>	<b>tumortype</b>	<b>histology_type</b>	<b>histology_subtype</b>	<b>altered gene</b>
A-204	21,79	rhabdomyosarcoma	rhabdomyosarcoma		FLT4, NTRK1
A-427	311,8	NSCLC	adenocarcinoma		418 mutated genes
BV-173	405,3	hematopoietic/leukemia	myeloid leukemia	CML, chronic myelogenous leukemia	FLT4, KIT, PDGFRB
CGTH-W-1	8,883	thyroid carcinoma	carcinoma	follicular	KDR, KIT
CML-T1	155,2	hematopoietic/leukemia	myeloid leukemia	CML, chronic myelogenous leukemia	BTK, FLT1, FYN, NTRK1
EM-2	174,8	hematopoietic/leukemia	myeloid leukemia	CML, chronic myelogenous leukemia	MAP3K3
G-402	7,712	renal cancer other	leiomyoblastoma		311 mutated genes
KATO III	209,2	gastric carcinoma	carcinoma	gastric	DDR2, FGFR2, FLT1
MEG-01	420,5	hematopoietic/leukemia	myeloid leukemia	CML, chronic myelogenous leukemia	FGFR1, KDR, KIT, NTRK1
MV-4-11	52,88	hematopoietic/leukemia	lymphoid leukemia	AML, biphenotypic B myelomonocytic leukemia	FLT3-ITD, CSF1R, NUA1
SJCRH30	219,6	rhabdomyosarcoma	rhabdomyosarcoma		PDGFRA, PDGFRB
SW579	21,98	thyroid carcinoma	squamous cell carcinoma		KIT

<b>Table S1b</b>			
<b>Sensitive cell lines and their respective indications</b>			
<b>tumortype</b>	<b>sensitive</b>	<b>insensitive</b>	<b>total</b>
gastric carcinoma	1	5	6
NSCLC	1	14	15
renal cancer other	1	2	3
rhabdomyosarcoma	2	2	4
thyroid carcinoma	2	2	4
hematopoietic/leukemia	5	12	17
	12		

<b>Table S2</b>																	
<b>Distribution of alterations in sensitive cell lines (m: mutation; a: amplification; e: overexpression)</b>																	
<b>cell line</b>	<b>BTK</b>	<b>CSF1R</b>	<b>DDR2</b>	<b>FGFR1</b>	<b>FGFR2</b>	<b>FLT1</b>	<b>FLT3</b>	<b>FLT4</b>	<b>FYN</b>	<b>KDR</b>	<b>KIT</b>	<b>MAP3K3</b>	<b>NTRK1</b>	<b>NTRK3</b>	<b>NUAK1</b>	<b>PDGFRA</b>	<b>PDGFRB</b>
A-204								m						m			
BV-173								e			m						e
CGTH-W-1										a	a						
CML-T1	m					m			m				m				
EM-2												e					
KATO III			m		a	m											
MEG-01				m						e	e		e				
MV-4-11		e					m								e		
SJCRH30																m	m
SW579											a						

<b>Table S3</b>		
cellline name	TumorType	EC50 [nM]
22Rv1	prostate carcinoma	2727
5637	bladder carcinoma	5594
639-V	bladder carcinoma	1886
647-V	bladder carcinoma	3775
769-P	renal carcinoma	5475
786-O	renal carcinoma	3848
A101D	melanoma	8008
A-172	astrocytoma/glioblastoma	2742
A-204	rhabdomyosarcoma	10,02
A-375	melanoma	3429
A-427	NSCLC	409,1
A-431	skin/SCC	454
A-498	renal carcinoma	6413
A549	NSCLC	4230
A-673	sarcoma/soft tissue	4123
A7	melanoma	4291
ACHN	renal carcinoma	5856
AGS	gastric carcinoma	2731
AN3 CA	uterus carcinoma	1529
ARH-77	hematopoietic/leukemia	4489
AsPC-1	pancreas carcinoma	4449
AU565	breast carcinoma	3872
BC-1	hematopoietic/lymphoma	3064
BE(2)-C	neuroblastoma	622,2
BeWo	placenta carcinoma	4249
BFTC-905	bladder carcinoma	3370
BHT-101	thyroid carcinoma	3895
BM-1604	prostate carcinoma	10000

BPH-1	prostate benign hyperplasia	1497
BT-20	breast carcinoma	6384
BT-474	breast carcinoma	3173
BT-483	breast carcinoma	3590
BT-549	breast carcinoma	3544
BV-173	hematopoietic/leukemia	429,8
BxPC-3	pancreas carcinoma	4234
C32	melanoma	7793
C32TG	melanoma	4033
C-33 A	cervix carcinoma	2956
C-4 I	cervix carcinoma	3782
C-4 II	cervix carcinoma	4226
Caki-1	renal carcinoma	3847
Caki-2	renal carcinoma	3895
CAL-27	HNSCC	4049
CAL-62	thyroid carcinoma	3616
Calu-1	NSCLC	5363
Calu-6	NSCLC	3329
CAMA-1	breast carcinoma	4163
Caov-3	ovarian carcinoma	9140
Capan-1	pancreas carcinoma	5267
Capan-2	pancreas carcinoma	4573
CCF-STTG1	astrocytoma/glioblastoma	9512
CCRF-CEM	hematopoietic/leukemia	3645
CEM/C1	hematopoietic/leukemia	3076
CFPAC-1	pancreas carcinoma	4936
CGTH-W-1	thyroid carcinoma	8,969
ChaGo-K-1	NSCLC	8175
CHL-1	melanoma	1122
CHP-212	neuroblastoma	1039

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CML-T1	hematopoietic/leukemia	186,2
COLO 201	colon carcinoma	8177
COLO 205	colon carcinoma	4257
COLO 320DM	colon carcinoma	5102
COLO 320HSR	colon carcinoma	8096
COLO 829	melanoma	8817
COR-L105	NSCLC	1657
COR-L23	NSCLC	10000
CRO-AP2	hematopoietic/lymphoma	1353
D283 Med	medulloblastoma	2370
Daoy	medulloblastoma	4256
Daudi	hematopoietic/lymphoma	2288
DB	hematopoietic/lymphoma	3384
DBTRG-05MG	astrocytoma/glioblastoma	10000
Detroit 562	HNSCC	3775
DK-MG	astrocytoma/glioblastoma	7927
DLD-1	colon carcinoma	6002
DMS 114	SCLC	1743
DMS 273	SCLC	3777
DMS 53	SCLC	4126
DOHH-2	hematopoietic/lymphoma	1081
DoTc2 4510	cervix carcinoma	5299
DU 145	prostate carcinoma	5052
EB-3	hematopoietic/lymphoma	2444
EFM-19	breast carcinoma	3344
EM-2	hematopoietic/leukemia	182,5
ES-2	ovarian carcinoma	3225
FaDu	HNSCC	5048
G-401	renal cancer other	1269
G-402	renal cancer other	12,67

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H4	astrocytoma/glioblastoma	7826
HCT 116	colon carcinoma	1828
HCT-15	colon carcinoma	3911
HCT-8	colon carcinoma	1937
HEC-1-A	uterus carcinoma	4791
HEL 92.1.7	hematopoietic/leukemia	9434
HeLa S3	cervix carcinoma	4509
Hep G2	liver carcinoma	2133
HL-60/MX1	hematopoietic/leukemia	2120
HLE	liver carcinoma	1143
HLF	liver carcinoma	1284
HMCB	melanoma	657,8
HOS	bone sarcoma	1623
HPAF-II	pancreas carcinoma	3583
Hs 578T	breast carcinoma	2274
Hs 695T	melanoma	10000
Hs 746T	gastric carcinoma	8615
Hs 766T	pancreas carcinoma	4519
HT	hematopoietic/lymphoma	10000
HT-1080	sarcoma/soft tissue	3468
HT-1197	bladder carcinoma	6441
HT-1376	bladder carcinoma	5296
HT-29	colon carcinoma	2262
HT-3	cervix carcinoma	2927
HuCC1	liver carcinoma	3363
HUH-6 Clone 5	liver carcinoma	1049
HuP-T4	pancreas carcinoma	4448
IMR-32	neuroblastoma	2558
J82	bladder carcinoma	5762
JAR	placenta carcinoma	3672



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JEG-3	placenta carcinoma	3729
J.RT3-T3.5	hematopoietic/leukemia	3716
Jurkat, Clone E6-1	hematopoietic/leukemia	4023
K-562	hematopoietic/leukemia	782,6
KATO III	gastric carcinoma	204,6
KHOS-240S	bone sarcoma	1391
KLE	uterus carcinoma	10000
KPL-1	breast carcinoma	1331
L-428	hematopoietic/lymphoma	10000
LNCap.FGC	prostate carcinoma	1398
LS1034	colon carcinoma	4265
LS 174T	colon carcinoma	2743
Malme-3M	melanoma	4699
MCF7	breast carcinoma	2247
MC-IXC	neuroblastoma	3420
MDA-MB-231	breast carcinoma	5668
MDA-MB-436	breast carcinoma	10000
MDA-MB-453	breast carcinoma	5119
MDA-MB-468	breast carcinoma	3618
MEG-01	hematopoietic/leukemia	434,6
MES-SA	sarcoma/soft tissue	3417
MeWo	melanoma	3932
MG-63	bone sarcoma	1520
MHH-PREB-1	hematopoietic/lymphoma	4923
MIA PaCa-2	pancreas carcinoma	1750
MOLT-16	hematopoietic/leukemia	3518
MOLT-3	hematopoietic/leukemia	10000
MT-3	breast carcinoma	2375
MV-4-11	hematopoietic/leukemia	57,56
NALM-6	hematopoietic/leukemia	1898

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NCI-H292	NSCLC	1184
NCI-H295R	adrenal gland carcinoma	10000
NCI-H441	NSCLC	10000
NCI-H446	SCLC	3023
NCI-H460	NSCLC	4793
NCI-H508	colon carcinoma	4754
NCI-H520	NSCLC	1303
NCI-H596	NSCLC	10000
NCI-H661	NSCLC	3206
NCI-H69	SCLC	3230
NCI-H747	colon carcinoma	3545
OCUG-1	gallbladder carcinoma	10000
OE19	esophagus carcinoma	3271
OE21	esophagus carcinoma	3661
OVCAR-3	ovarian carcinoma	10000
PANC-1	pancreas carcinoma	3014
PC-3	prostate carcinoma	5636
Raji	hematopoietic/lymphoma	4860
Ramos (RA1)	hematopoietic/lymphoma	4731
RD	rhabdomyosarcoma	1443
RKO	colon carcinoma	3640
RKO-AS45-1	colon carcinoma	3226
RKO-E6	colon carcinoma	3062
RL	hematopoietic/lymphoma	2189
RL95-2	uterus carcinoma	8985
RPMI 6666	hematopoietic/lymphoma	2312
RPMI-7951	melanoma	3411
RPMI 8226	hematopoietic/myeloma	4407
SCaBER	bladder carcinoma	4313
SCC-25	HNSCC	2397

SCC-4	HNSCC	3814
SCC-9	HNSCC	7757
SH-4	melanoma	2683
SHP-77	SCLC	3219
SiHa	cervix carcinoma	5374
SJCRH30	rhabdomyosarcoma	356,8
SJSA-1	bone sarcoma	1721
SK-BR-3	breast carcinoma	3365
SK-LMS-1	sarcoma/soft tissue	3711
SK-MEL-1	melanoma	9207
SK-MEL-28	melanoma	5050
SK-MEL-3	melanoma	3589
SK-MES-1	NSCLC	3515
SK-N-AS	neuroblastoma	4309
SK-N-DZ	neuroblastoma	2478
SK-NEP-1	renal cancer other	9579
SK-N-FI	neuroblastoma	3122
SKO-007	hematopoietic/myeloma	4041
SK-OV-3	ovarian carcinoma	8807
SK-UT-1	sarcoma/soft tissue	5058
SNB-19	astrocytoma/glioblastoma	3974
SNU-1	gastric carcinoma	1092
SNU-16	gastric carcinoma	565,2
SNU-423	liver carcinoma	3450
SNU-5	gastric carcinoma	10000
SR	hematopoietic/lymphoma	975,8
ST486	hematopoietic/lymphoma	3600
SU.86.86	pancreas carcinoma	7573
SW 1088	astrocytoma/glioblastoma	3754
SW1116	colon carcinoma	10000

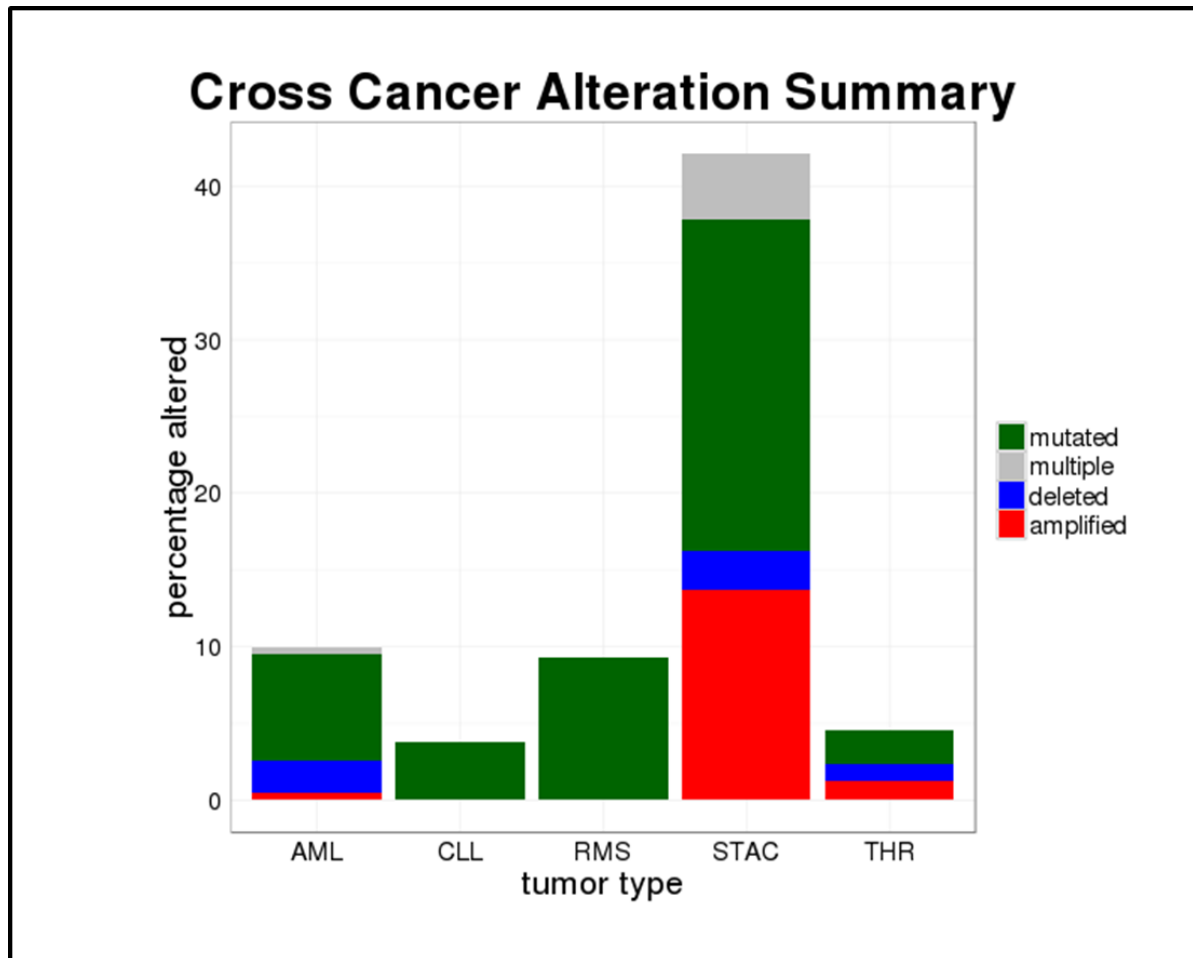
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SW-13	adrenal gland carcinoma	3403
SW 1353	bone sarcoma	1683
SW1417	colon carcinoma	4910
SW1463	colon carcinoma	5000
SW 1783	astrocytoma/glioblastoma	10000
SW403	colon carcinoma	6510
SW48	colon carcinoma	2028
SW480	colon carcinoma	10000
SW579	thyroid carcinoma	38,81
SW620	colon carcinoma	4589
SW 684	sarcoma/soft tissue	6832
SW837	colon carcinoma	3587
SW 872	sarcoma/soft tissue	3898
SW 900	NSCLC	926,8
SW948	colon carcinoma	4082
SW 954	vulva carcinoma	2655
SW962	vulva carcinoma	1688
SW 982	sarcoma/soft tissue	8450
T24	bladder carcinoma	4738
T-47D	breast carcinoma	8031
T84	colon carcinoma	9000
T98G	astrocytoma/glioblastoma	962,5
TCCSUP	bladder carcinoma	2225
TE 381.T	rhabdomyosarcoma	1023
THP-1	hematopoietic/leukemia	7485
U-138 MG	astrocytoma/glioblastoma	3673
U266B1	hematopoietic/myeloma	1740
U-2 OS	bone sarcoma	1394
U-87 MG	astrocytoma/glioblastoma	5485
UM-UC-3	bladder carcinoma	3303

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WI-38	normal	1730
WiDr	colon carcinoma	1549
Y79	retinoblastoma	5808
YAPC	pancreas carcinoma	4421

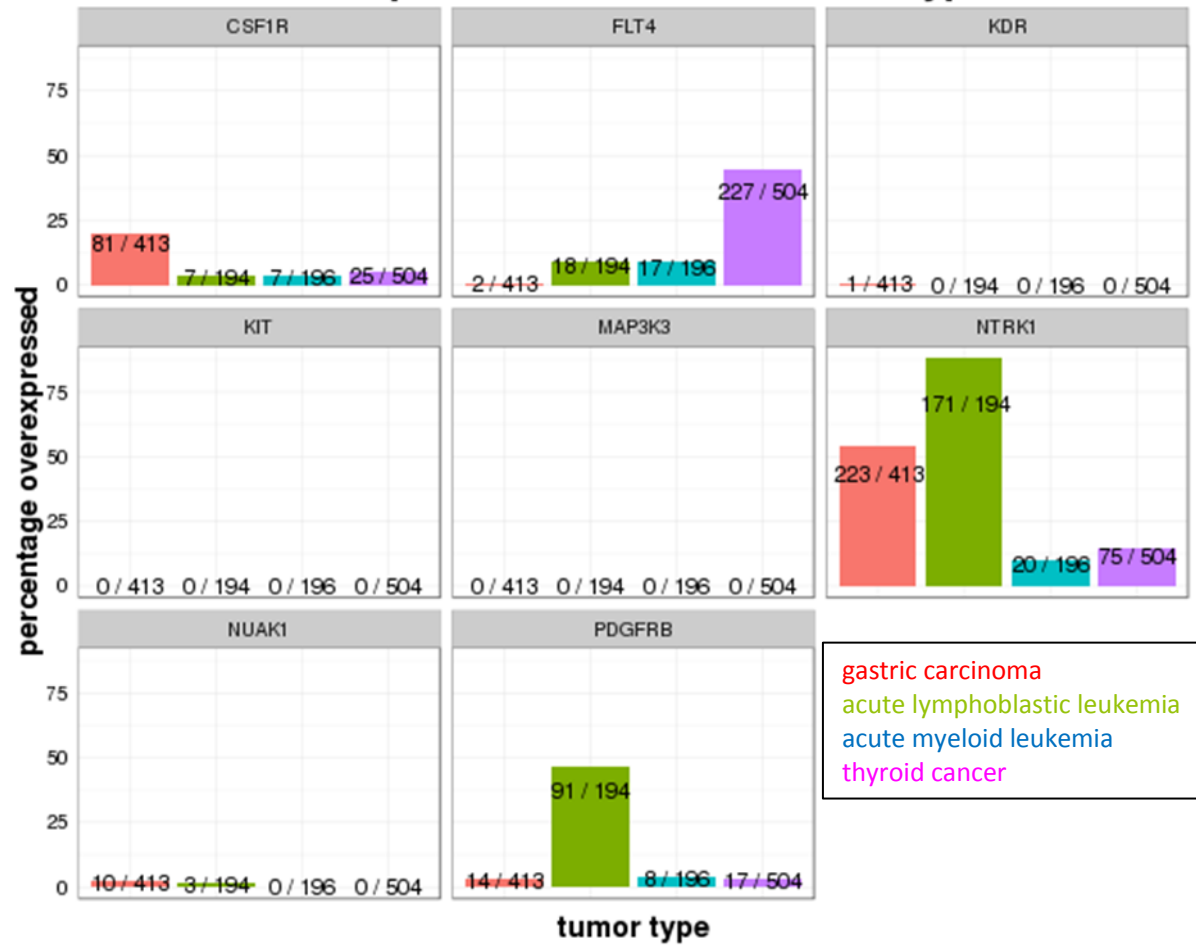
Hilberg et al.: Supplementary Figures:



**Supplementary Figure S1**

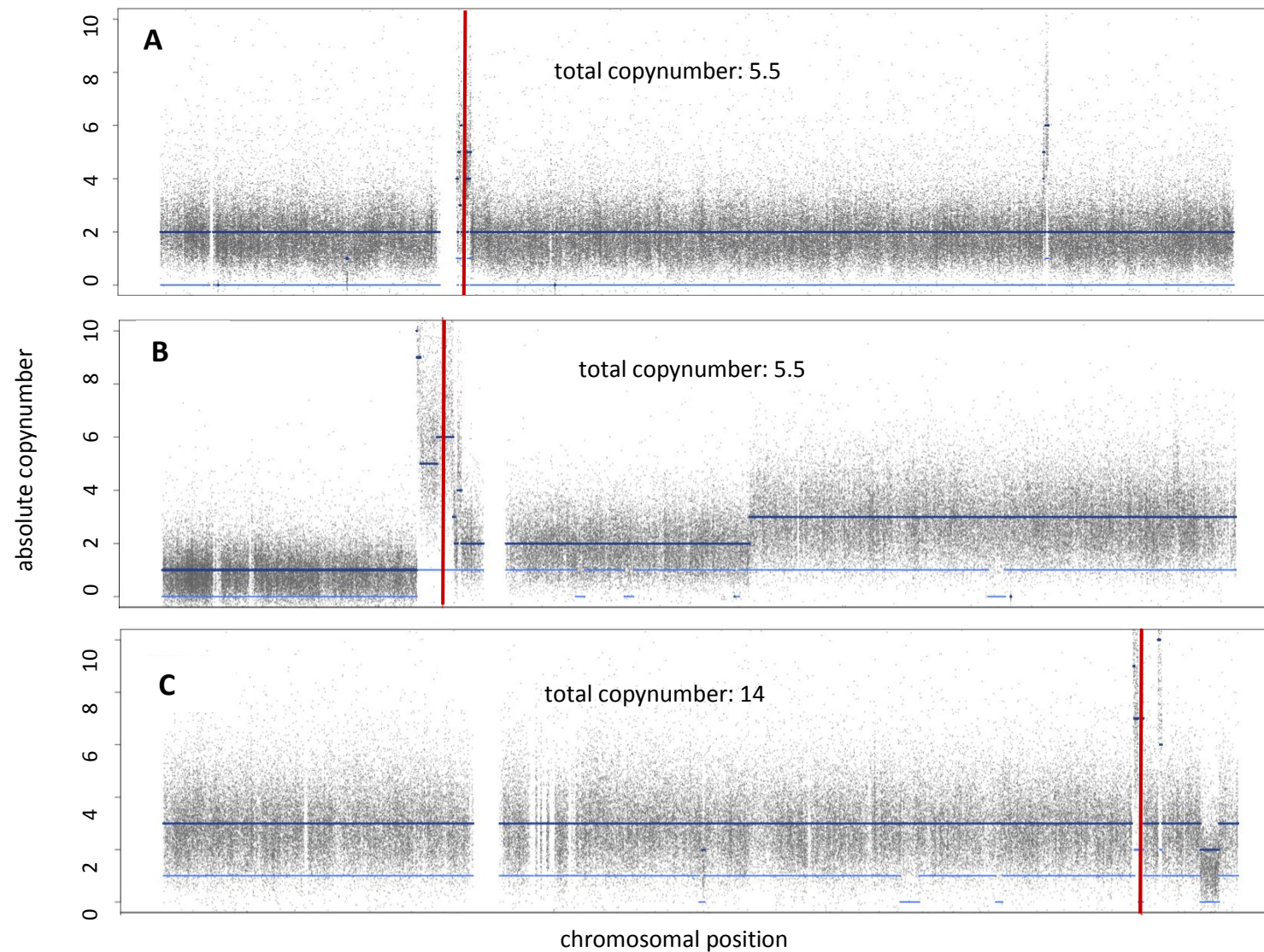
Cross cancer alteration summary of all 16 kinases with alterations in the screened cell lines, AML: Acute Myeloid Leukemia, ALL: Acute Lymphoblastic Leukemia, RMS: Rhabdomyosarcoma, STAC: Stomach Adenocarcinoma, THR: Thyroid Cancer

### Overexpression in Human Tumor Types



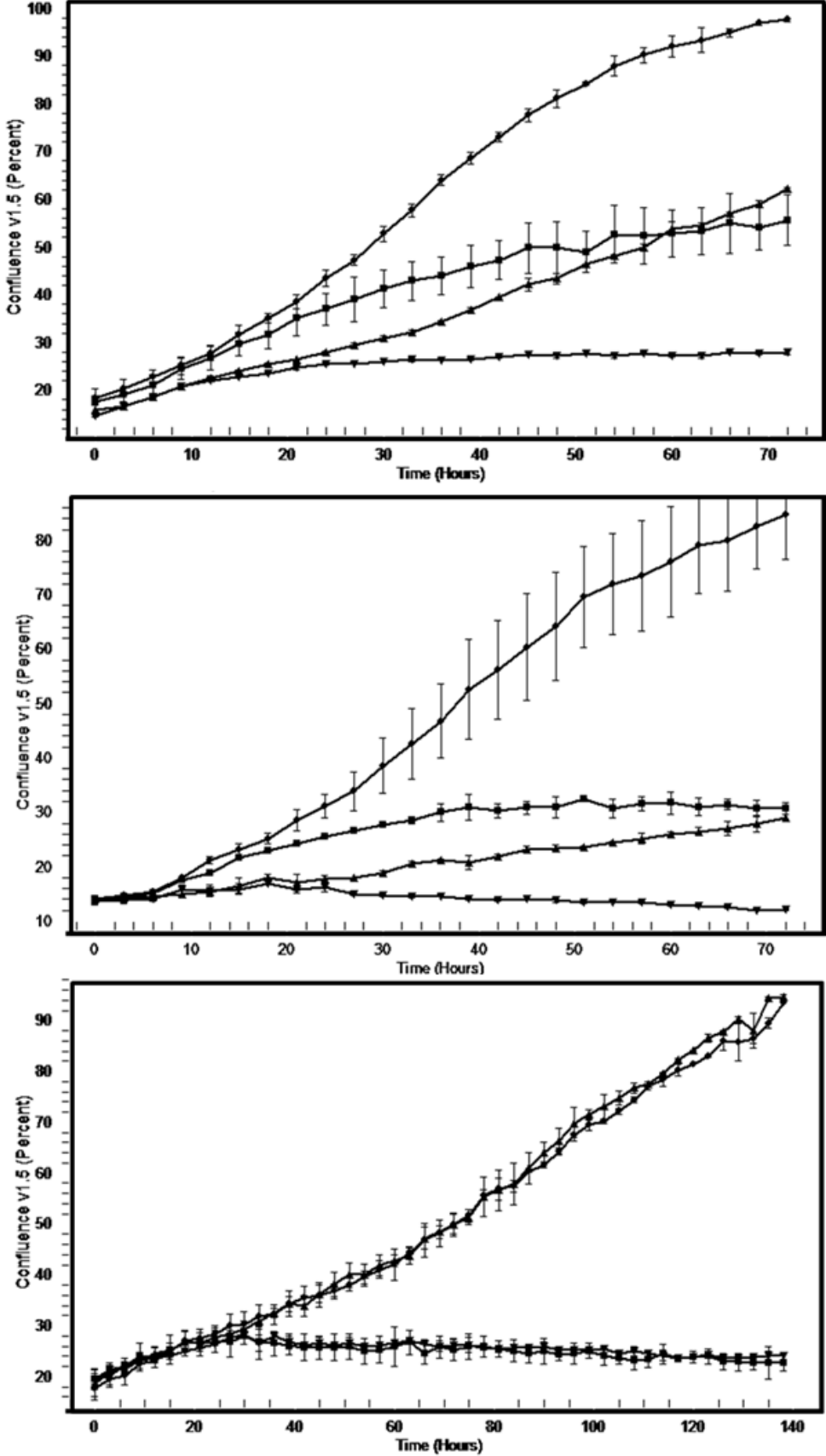
**Supplementary Figure S2**

Expression of selected genes in human tumor types corresponding to the respective tumor types of the sensitive cell lines. The numbers indicate numbers of samples with over expression versus all samples in the respective tumor type. Overexpression threshold is defined as :  $\text{mean}(\text{normal tissue}) + 3 * \text{stddev}(\text{normal tissue})$

**Supplementary Figure S3**

**A:** focal amplification of PDGFRA in NCI-H1703 cells. **B:** focal amplification of FGFR1 in NCI-H1703 cells. **C:** focal amplification of FGFR2 in tetraploid KATO III cells. The red line marks the position of the respective gene.





**Supplementary Figure S4**

Visualization and measurement of cell growth in AML cell lines: A) MOLM13, B) MV-4-11-B and C) THP1 by IncuCyte ZOOM® live cell imaging. Filled circles, DMSO @ 0.1%; filled upward triangles, Nintedanib @ 33 nM; filled squares, BI 894999 @ 10 nM; filled downward triangles, combination of BIBF1120 @ 33 nM and BI 894999 @ 10 nM.

**Hilberg et al.: Supplementary Method information:**



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Customer Protocol an



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