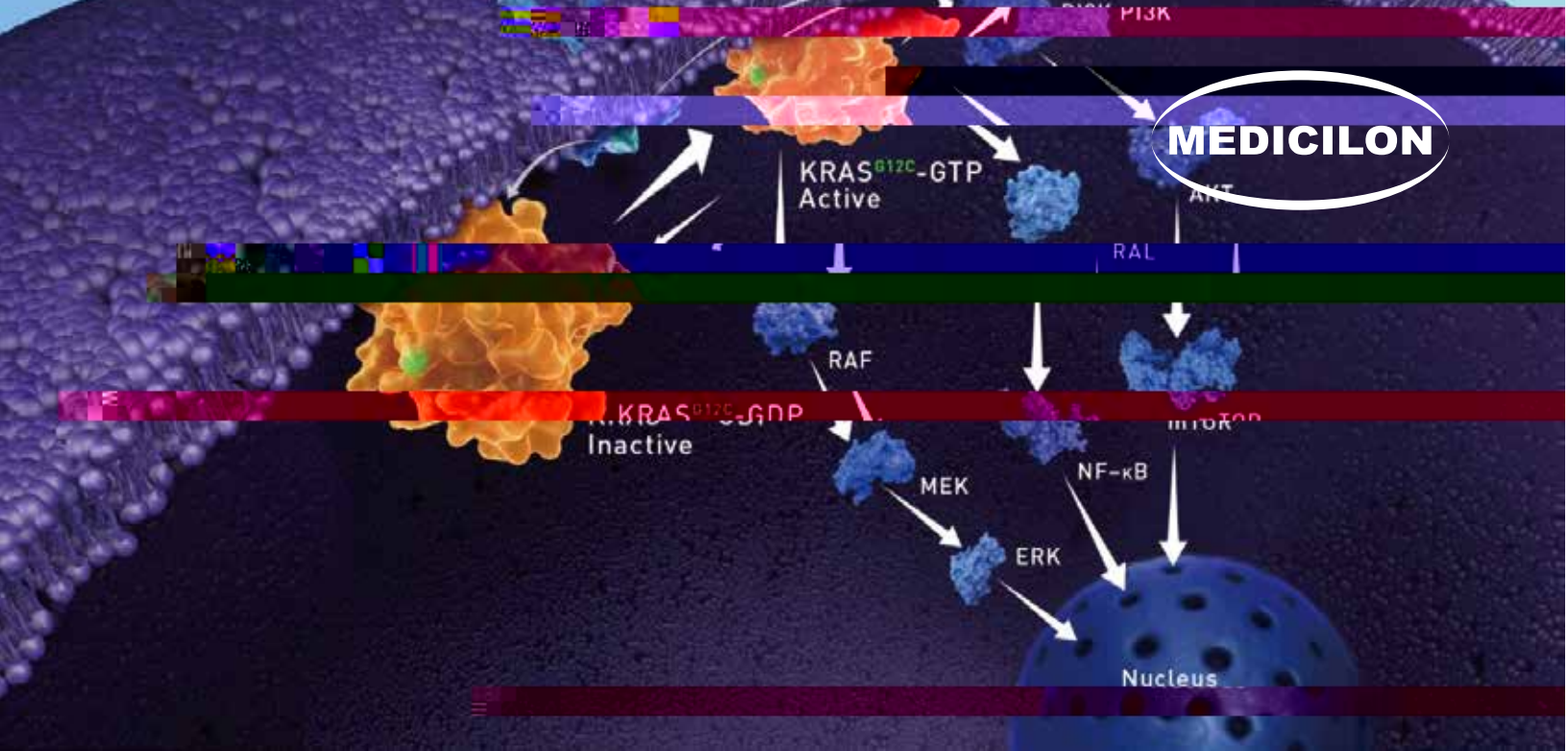
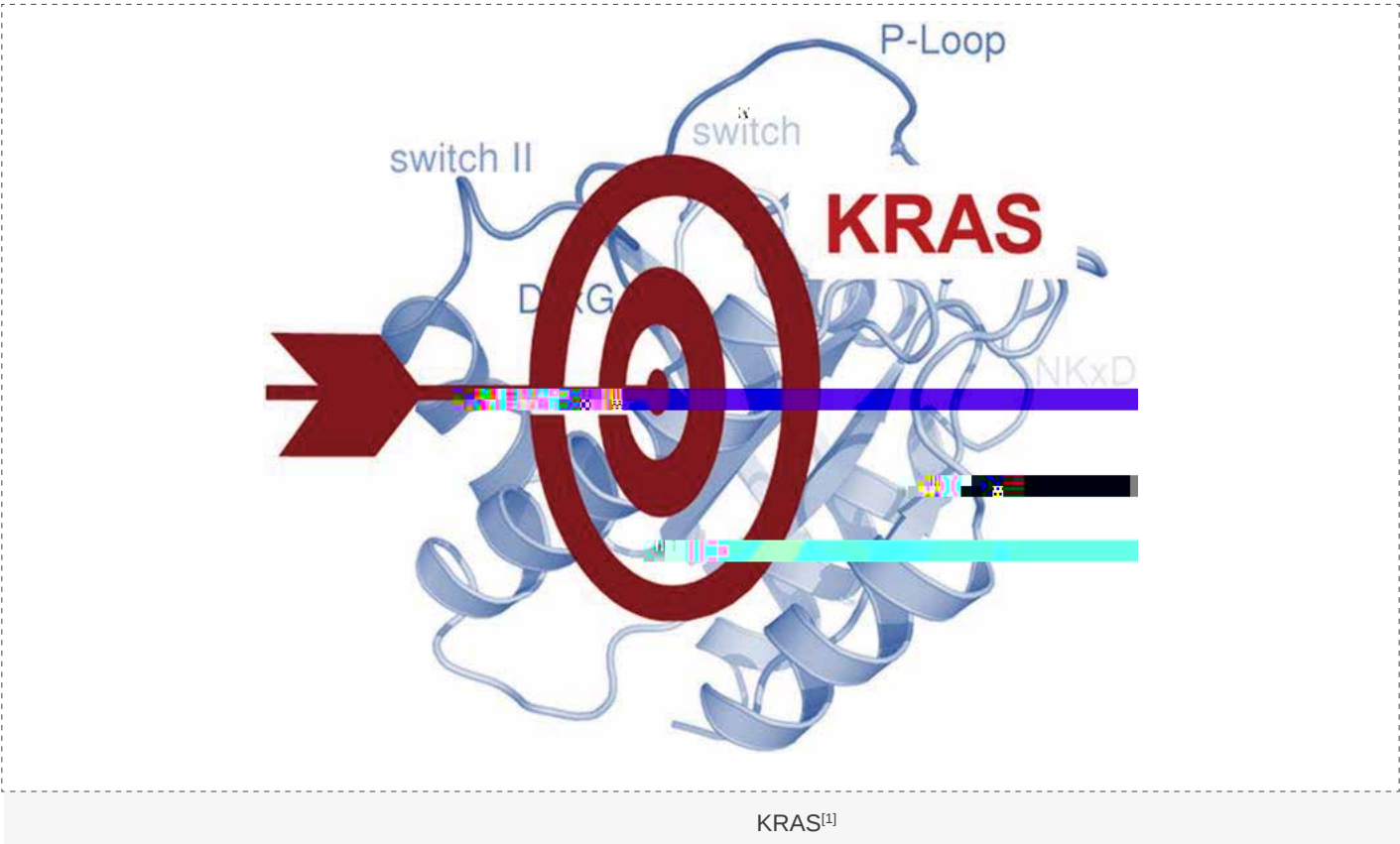




RAS	KRAS	RAS	85% KRAS
RAS			
KRAS		KRAS	CMC (API+)
PK			



RAS GTPase

RAS HRAS KRAS NRAS RAS
KRAS NRAS HRAS KRAS

G12 G13 Q61 KRAS
KRAS4A KRAS4B KRAS4B

KRAS(Kirsten rat sarcoma 2 viral oncogene homolog
Kirsten) GTP/GDP
GTPase RAS

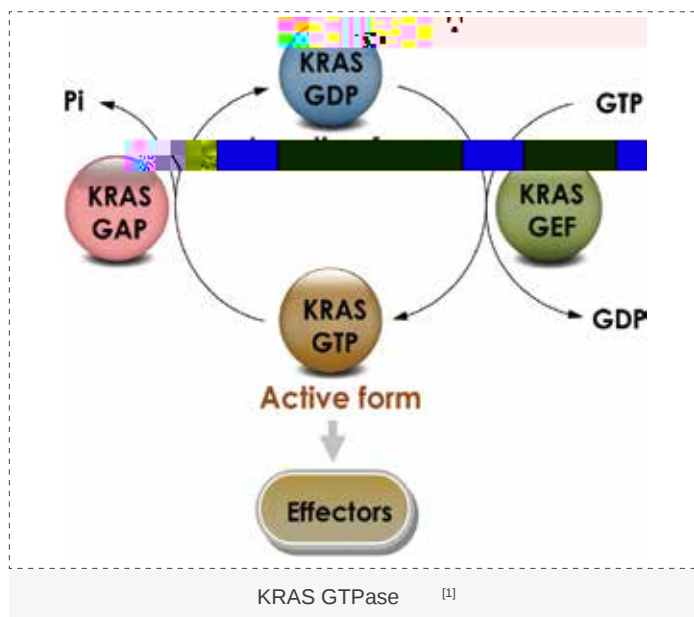
KRAS GDP GTP
KRAS GTP

GDP

KRAS

GTP
(GEFs)

GTP SOS(son of sevenless) Ras
GTP p120GAP (NF1)



GTPase (GAPs)

KRAS

RAS

N

KRAS

G-

KRAS

21

kDa

6

β -

(

) 5 α

G

C

KRAS

G

1-166

GTP

GTPase

(GAPs)

G

GDP-GTP

switch I

switch II

C

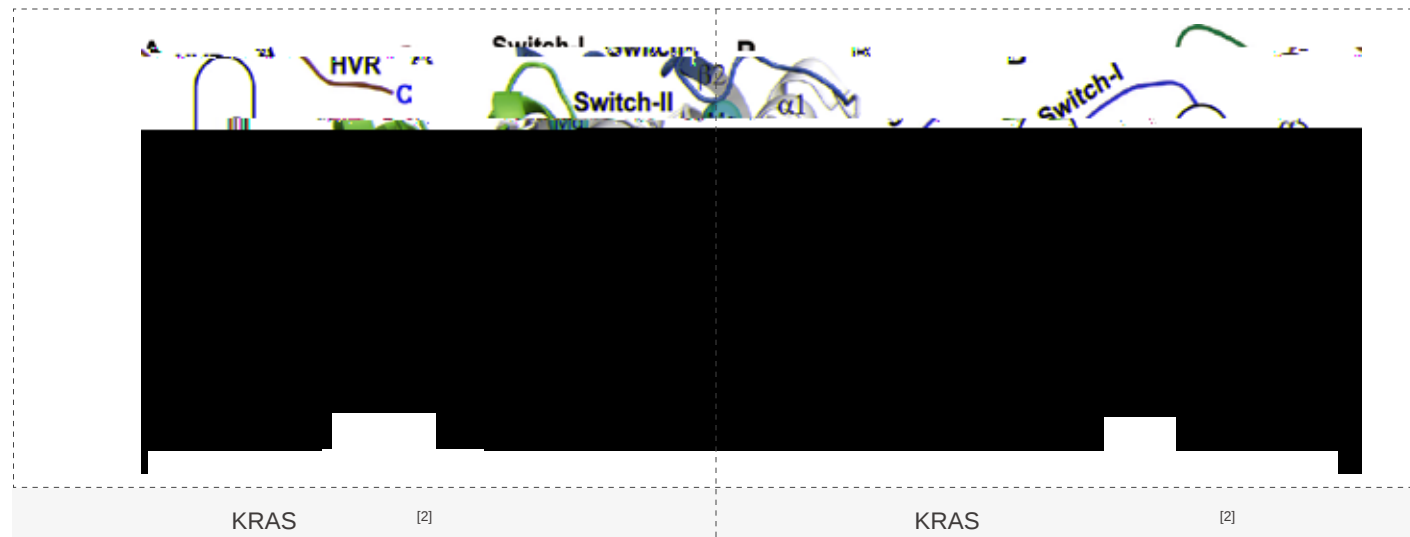
CAAX (C=

A=

X=

)

RAS



KRAS

GTP/GDP

KRAS

KRAS

KRAS

KRAS

()

RAS-GDP
MAPK

RAS-GTP
RAF

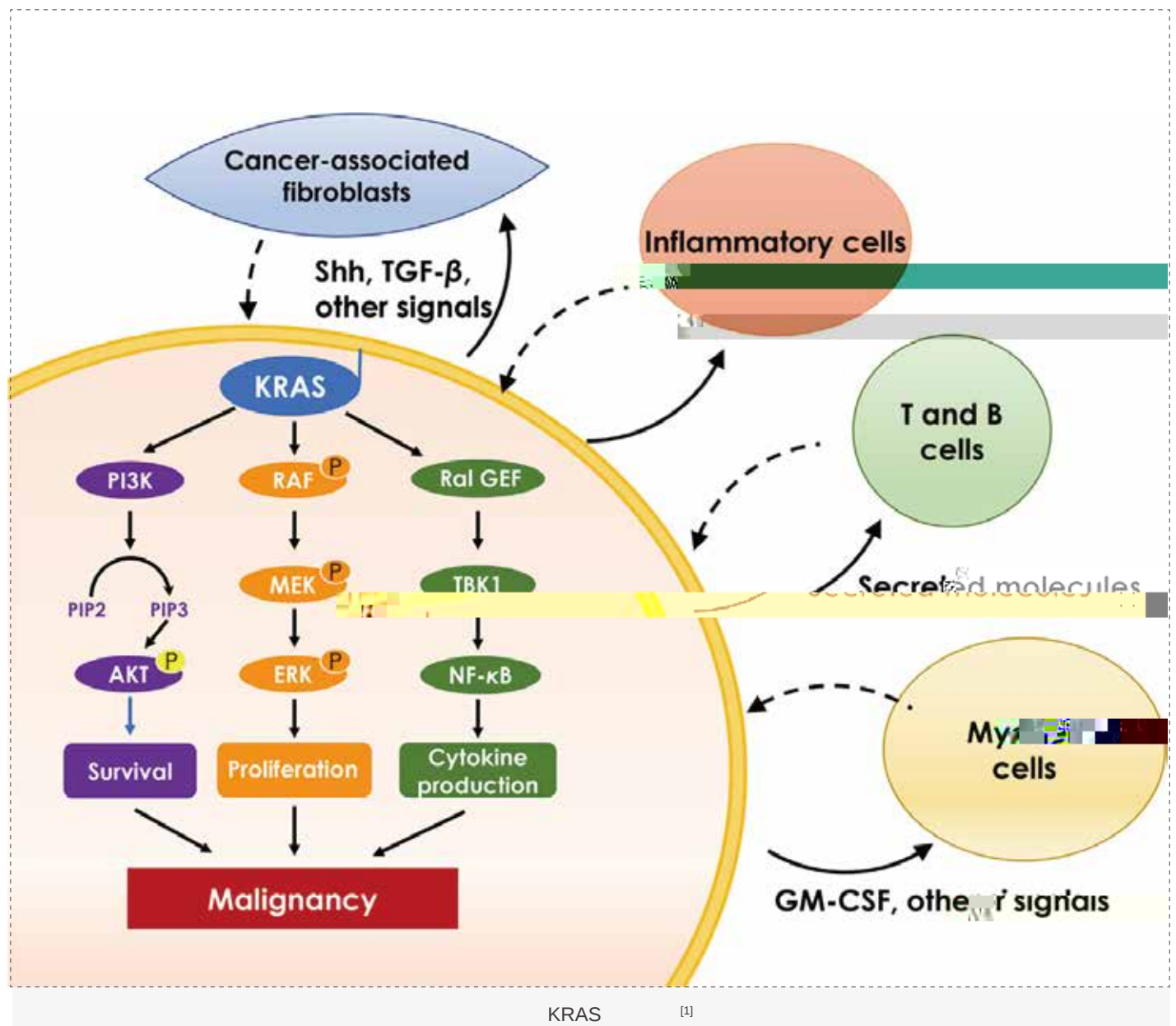
RAS-GTP
MEK

RAF
ERK

MAPK
RAF

PI3K

Ral-GEFs





1000+



Hampton research HT Kits



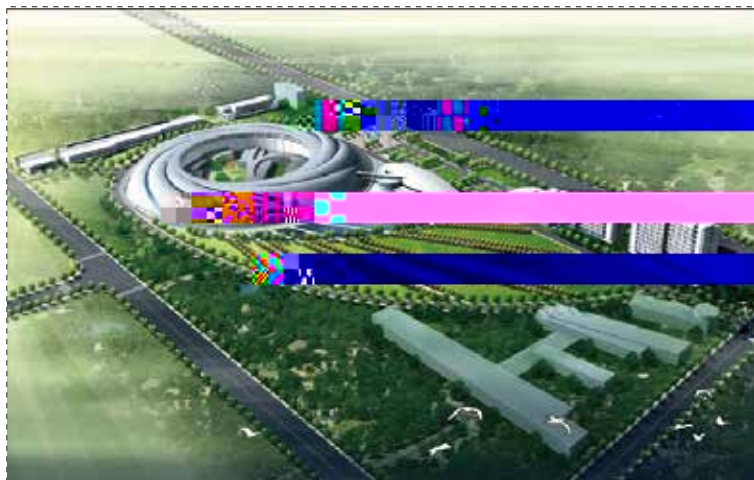
QIAGEN HT Classics Suite



Mosquito



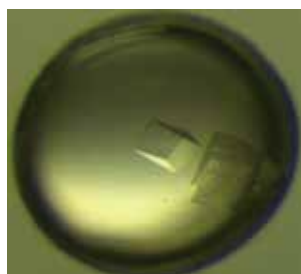
2009 7



-
-
- 3.5 GeV
-
-

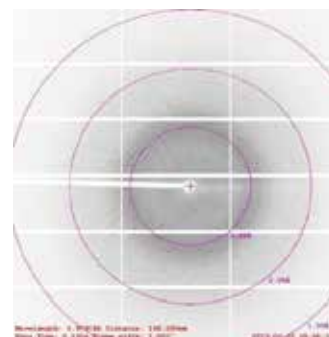


0.17 M
0.085 M pH 4.6
15% (v/v)
25.5% (w/v) PEG 4000



0.2 M
0.1 M Tris-HCl pH 8.5
30% (w/v) PEG 4000

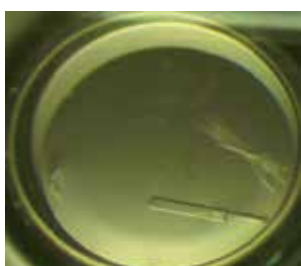
KRAS^{G12D}



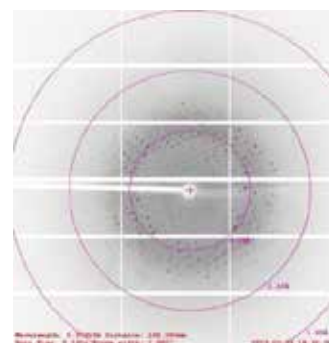
KRAS^{G12D} X



0.17 M
15% (v/v)
25.5% (w/v) PEG 4000



0.2 M
0.1 M pH 4.6
25 % (w/v) PEG 4000

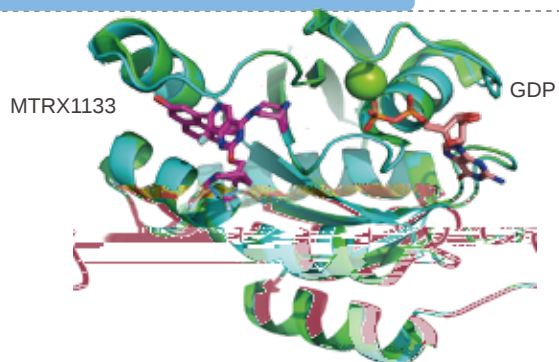


X



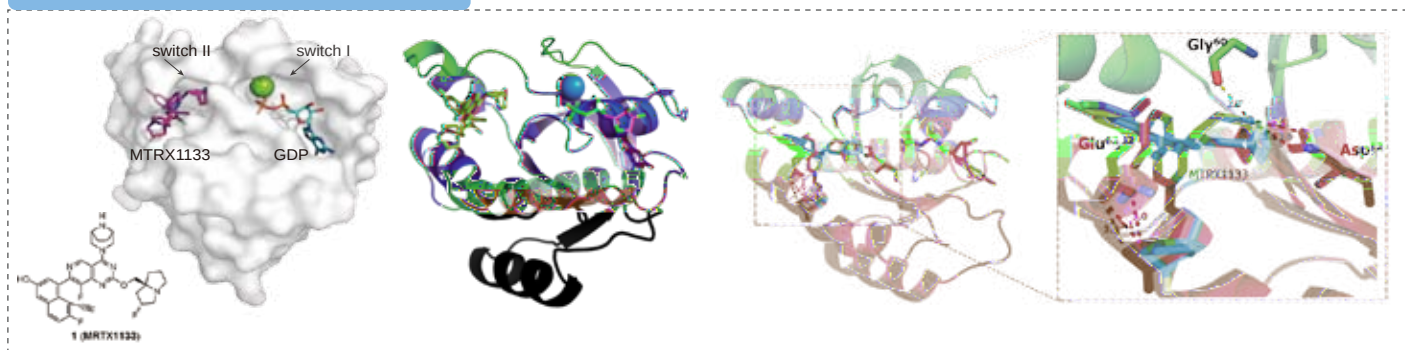
KRAS^{G12D} 7RPZ

PDB ID 7RPZ



KRAS^{G12D} MRTX1133
PDB ID 7RPZ

(7RPZ, PDB)



GDP KRAS^{G12D} MTRX1133

KRAS

KRAS

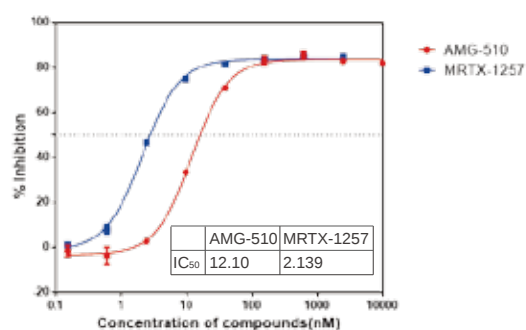
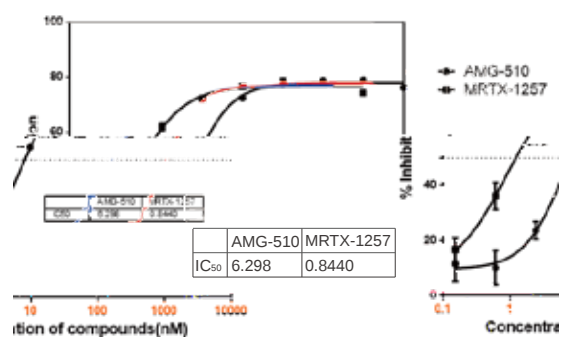
KRAS



KRAS

2D 3D

KRAS



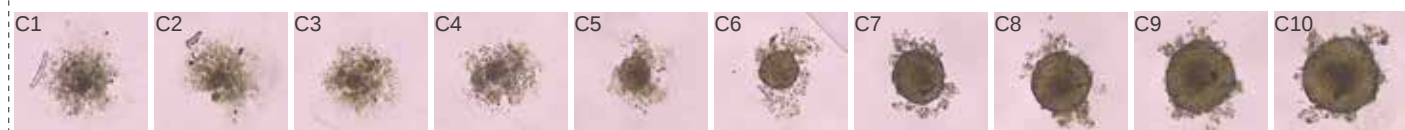
AsPC-1	pancreas	G12D
Capan-1	pancreas	G12V
Capan-2	pancreas	G12V
CFPAC-1	pancreas	G12V
HPAF-II	pancreas	G12D
MIAPaCa-2	pancreas	G12C
Panc 10.05	pancreas	G12D
SU.86.86	pancreas	G12D
HCT116	large_intestine	G13D
HCT15	large_intestine	G13D
LoVo	large_intestine	G13D
T84	large_intestine	G13D
Calu-1	lung	G12C
NCI-H2122	lung	G12C
NCI-H23	lung	G12C
NCI-H358	lung	G12C
NCI-H441	lung	G12V
SW1463	large_intestine	G12C
SW480	large_intestine	G12V
SW620	large_intestine	G12V
SW837	large_intestine	G12C

CellTiter-Glo 2D

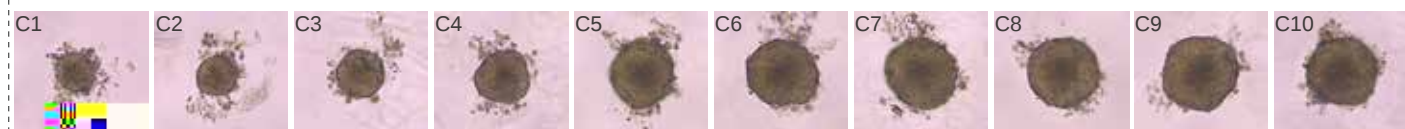


	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
	1000	333.3	111.1	37.04	12.35	4.115	1.372	0.457	0.152	0

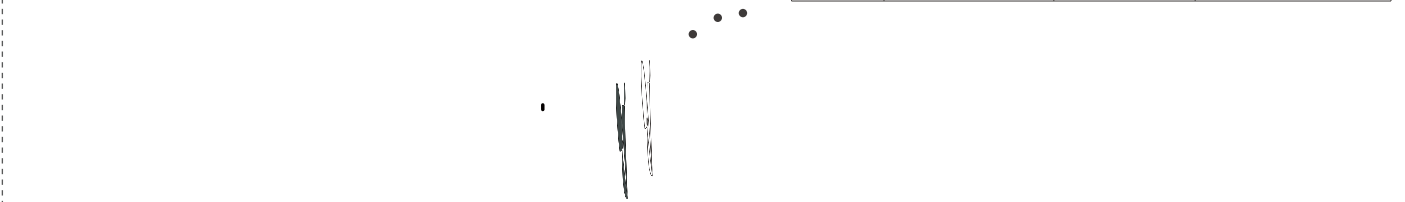
Compound	Cell line	Incubation time (Day)	Start conc	Dilution fold
AMG510	NCI-H358	12	1 μ M	3-fold diluted



Compound	Cell line	Incubation time (Day)	Start conc	Dilution fold
BI3406	NCI-H358	12	1 μ M	3-fold diluted



Compound	CTG-IC ₅₀ S on NCI-H358 cells (nM)	Top Inhibition(%)	Start conc	Dilution fold
AMG510	1.386	99.52	1 μ M	3-fold diluted
BI3406	48.23	71.53	1 μ M	3-fold diluted



1 μ M

1:3

NCI-H358

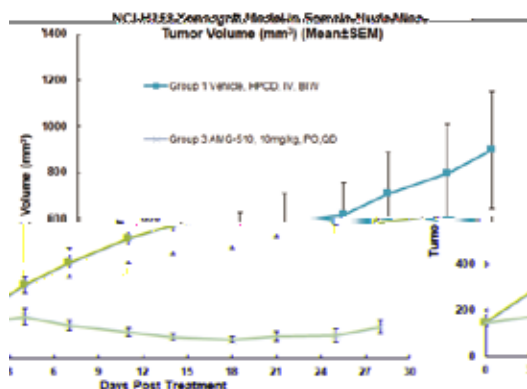
288 h





KRAS G12C	MIA PaCa-2, NCI-H358, UM-UC-3, Calu-1	KRAS G12V	SW480, CAPAN-1, NCI-H727
KRAS G12D	GP2D, SW1990, AsPC-1	KRAS G13D	LoVo, HCT-116, HT15

NCI-H358 Xenograft Model in Female BALB/c Nude Mice



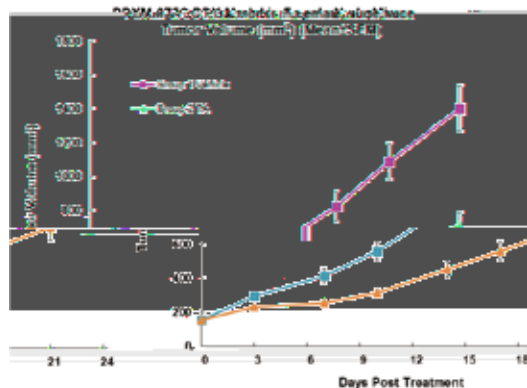
- **Animals:**
Female BALB/c Nude mice
- **Cells:**
NCI-H358
- **Model Establishment:**
Right flank, SC



KRAS Mutation	PDXM-060C (p.G12V), PDXM-069C (p.G12V), PDXM-075C (p.G12D), PDXM-076C (p.G13D), PDXM-212Li (p.G12D)	BCR-ABL Fusion	PDXM-242Le
TP53 Mutation	PDXM-060C (p.R273H), PDXM-072C(p.Y234H)	ERBB2	PDXM-069C, PDXM-016C, PDXM-060C, Overexpression
PIK3CA Mutation	PDXM-075C (p.H1047L), PDXM-092Ga (p.E545G)	...	...

Docetaxel + Cisplatin	PDXM-271O (Ovarian cancer)	Radiation	PDXM-311(H&N)
VDLP + MA + CVAD	PDXM-293Le (Leukemia)	...	...

PDXM-072C PDX Model in Female BALB/c Nude Mice



- **Animals:**
Female BALB/c Nude mice
- **Tissue:**
PDX Colon Cancer
- **Model Establishment:**
Right flank SC Trocar

KRAS

PK

KRAS-PDEδ

-

Compound 17f

KRAS

PROTAC PDEδ

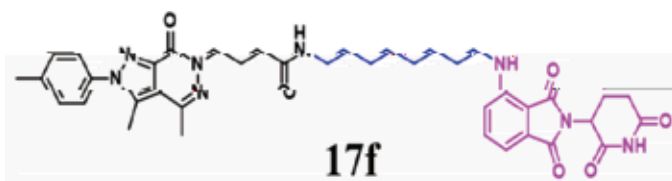
Compound 17f SW480

PROTAC PDEδ

Compound 17f KRAS-PDEδ

KRAS-PDEδ

KRAS



PROTAC

KRAS-PDEδ

Compound 17f^[3]

