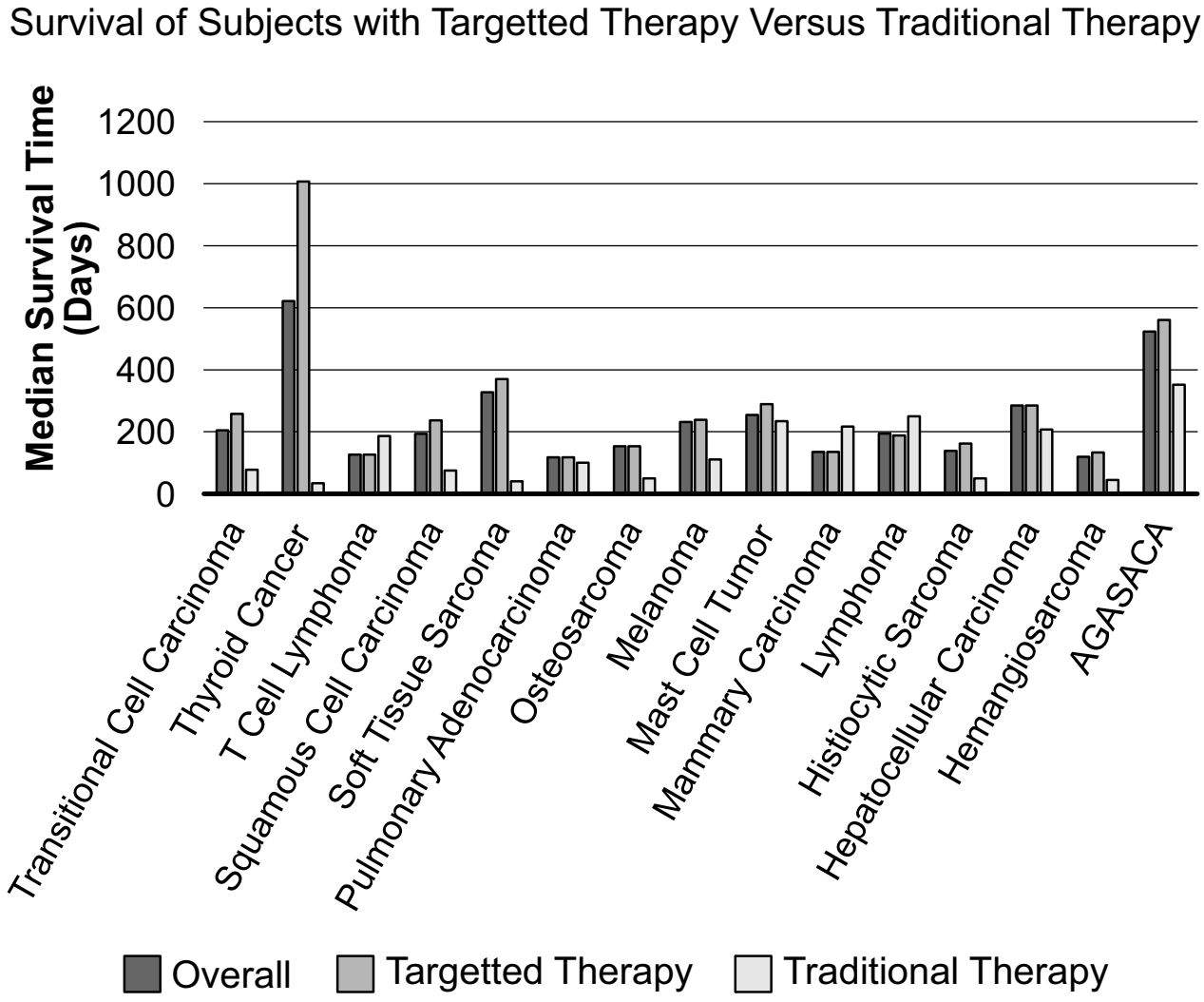
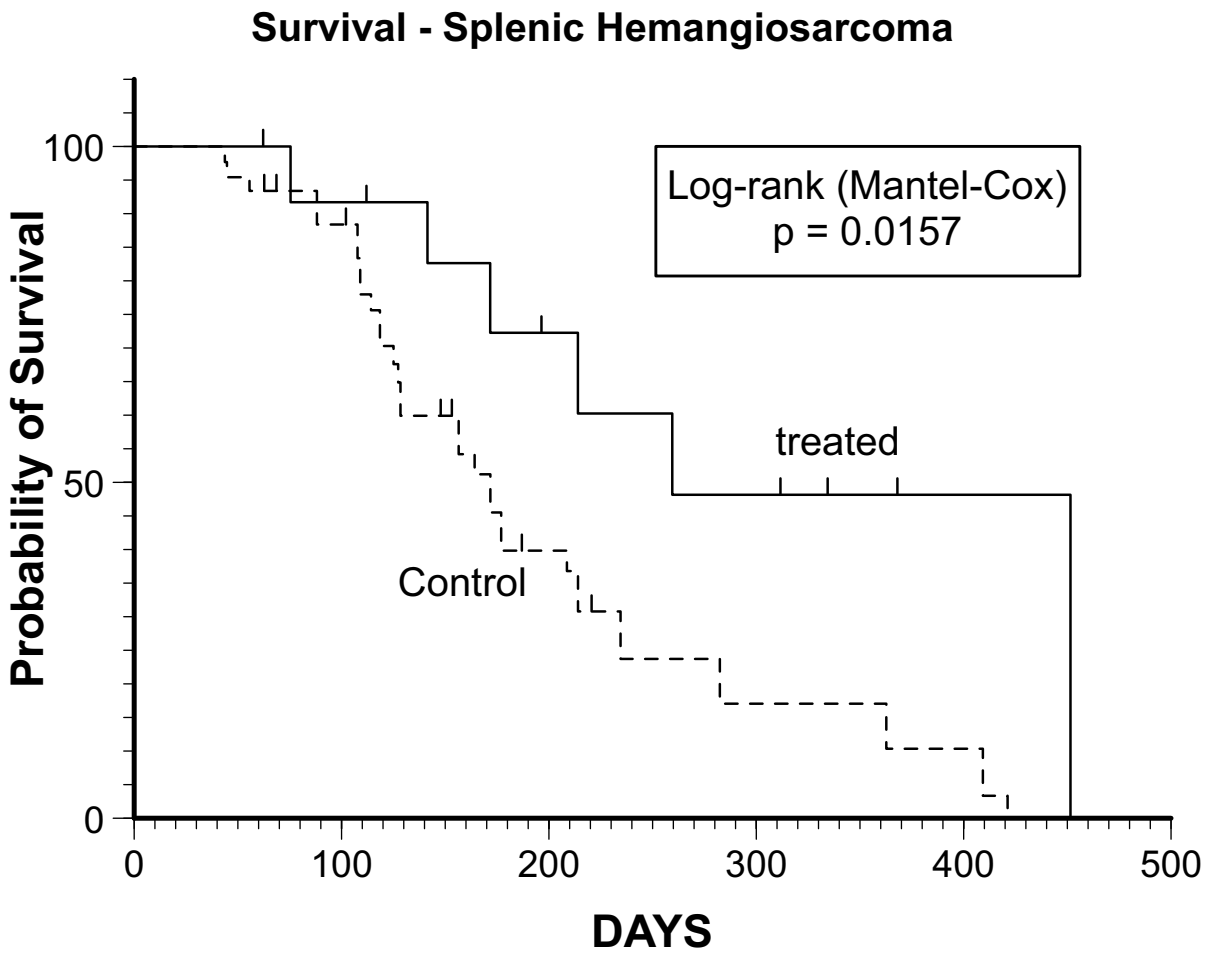

Survival of Subjects with Targetted Therapy Versus Traditional Therapy
Median Survival Time (Days)
1200
1000
800
600
400
200
0
Transitional Cell Carcinoma
Thyroid Cancer
T Cell Lymphoma
Squamous Cell Carcinoma
Soft Tissue Sarcoma
Pulmonary Adenocarcinoma
Osteosarcoma
Melanoma
Mast Cell Tumor
Mammary Carcinoma
Lymphoma
Histiocytic Sarcoma
Hepatocellular Carcinoma
Hemangiosarcoma
AGASACA
Overall
Targetted Therapy
Traditional Therapy

Figure 1



Control (Splenectomy + IV Chemotherapy
n = 44

Treated (Splenectomy + IV Chemotherapy + Targeted Therapy
n =13

Figure 2

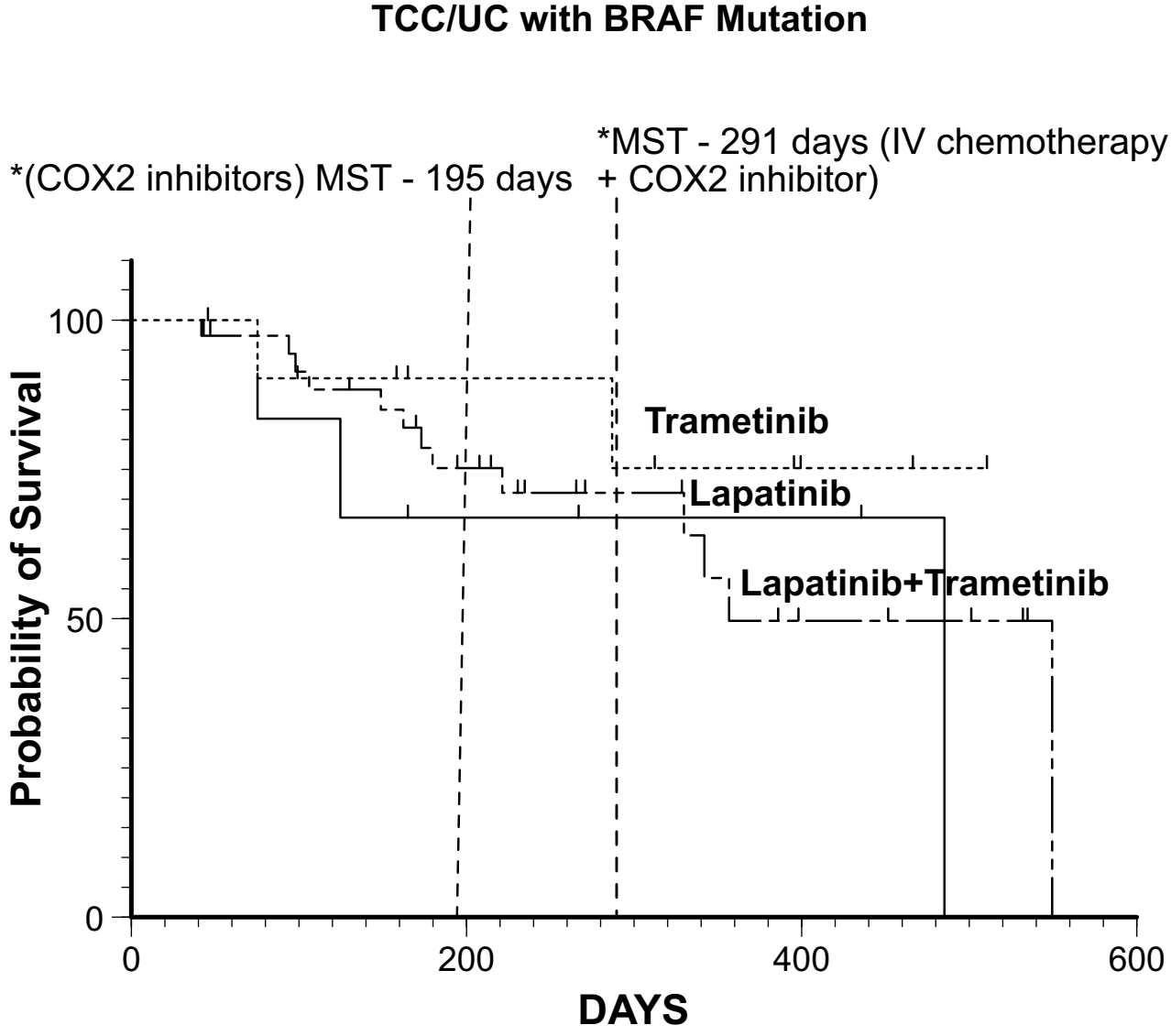

TCC/UC with BRAF Mutation
*(COX2 inhibitors) MST - 195 days
*MST - 291 days (IV chemotherapy + COX2 inhibitor)
Trametinib
Lapatinib
Lapatinib+Trametinib
Probability of Survival
100
50
0
0
200
400
600
DAYS
Trametinib +/- Chemotherapy/COX2 inhibitor (n=11)
Lapatinib +/- Chemotherapy/COX2 inhibitor (n=6)
Lapatinib and Trametinib +/- Chemotherapy/COX2 inhibitor (n=35)

Figure 3

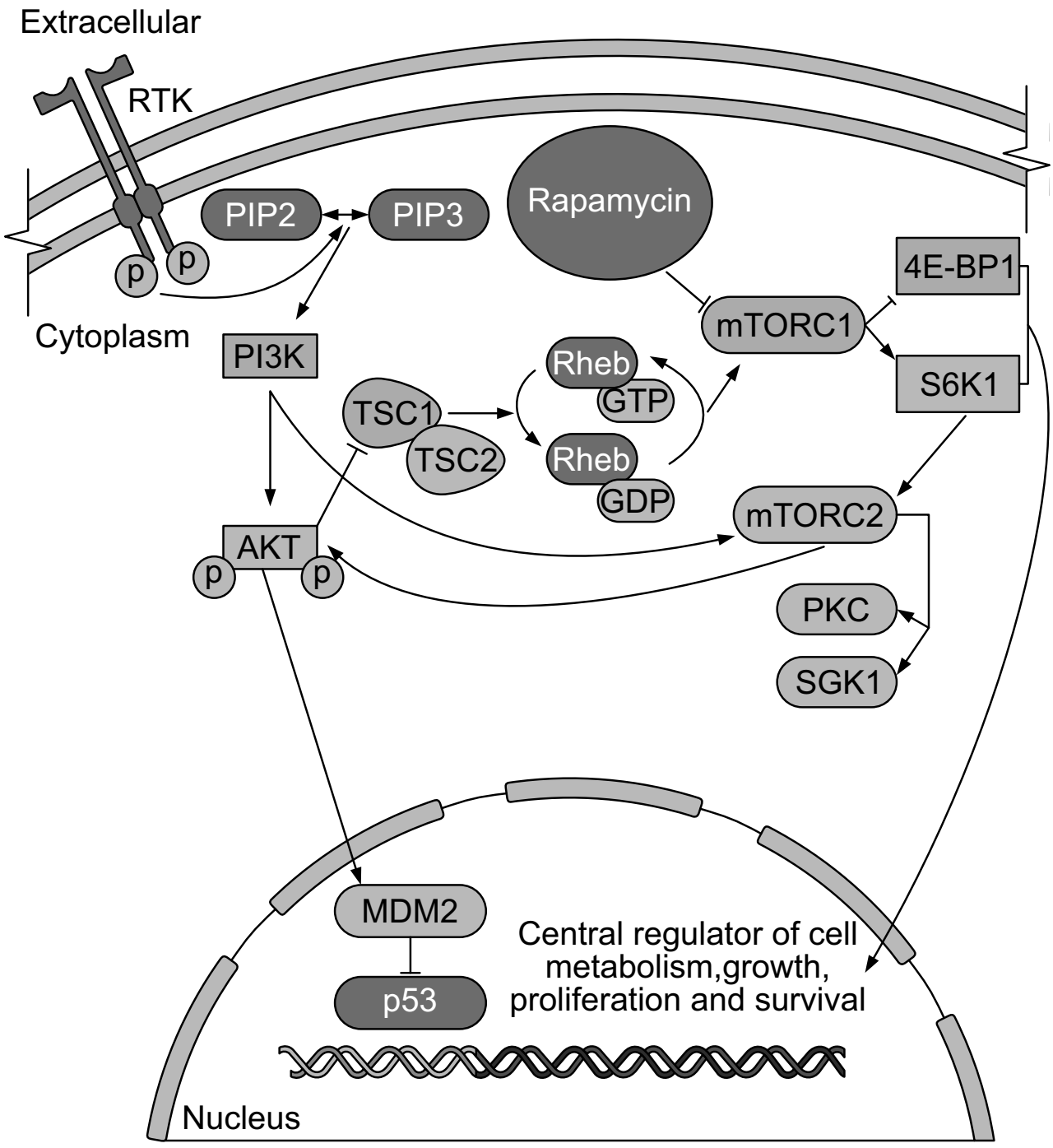

Extracellular
RTK
PIP2
PIP3
Rapamycin
4E-BP1
p
p
Cytoplasm
PI3K
mTORC1
Rheb
GTP
S6K1
TSC1
TSC2
Rheb
GDP
mTORC2
AKT
p
p
PKC
SGK1
MDM2
Central regulator of cell
metabolism,growth,
proliferation and survival
p53
Nucleus

Figure 4

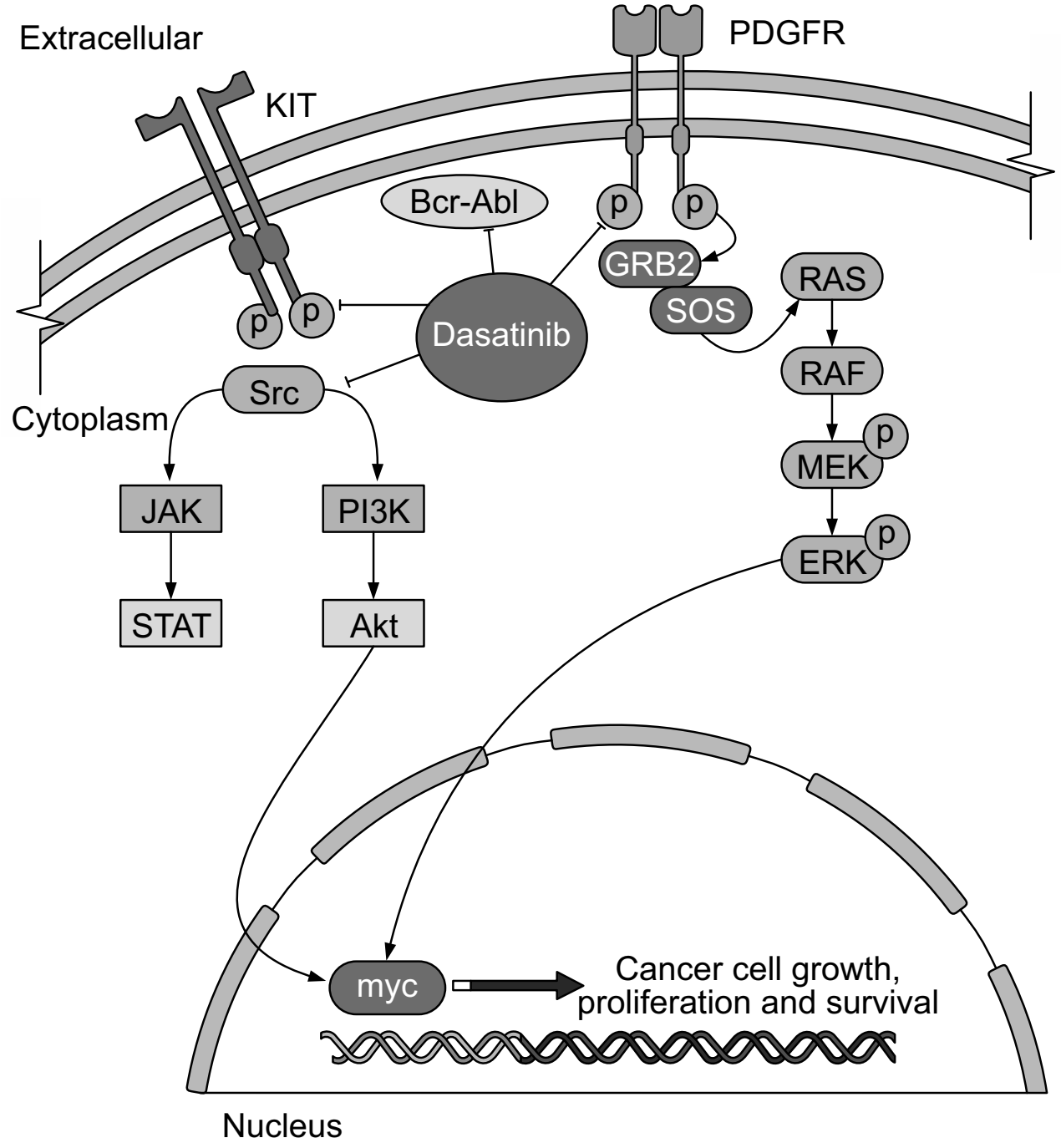

Extracellular
PDGFR
KIT
Bcr-Abl
p
p
GRB2
SOS
RAS
p
p
Dasatinib
RAF
Src
Cytoplasm
p
MEK
JAK
PI3K
p
ERK
STAT
Akt
myc
Cancer cell growth,
proliferation and survival
Nucleus

Figure 5

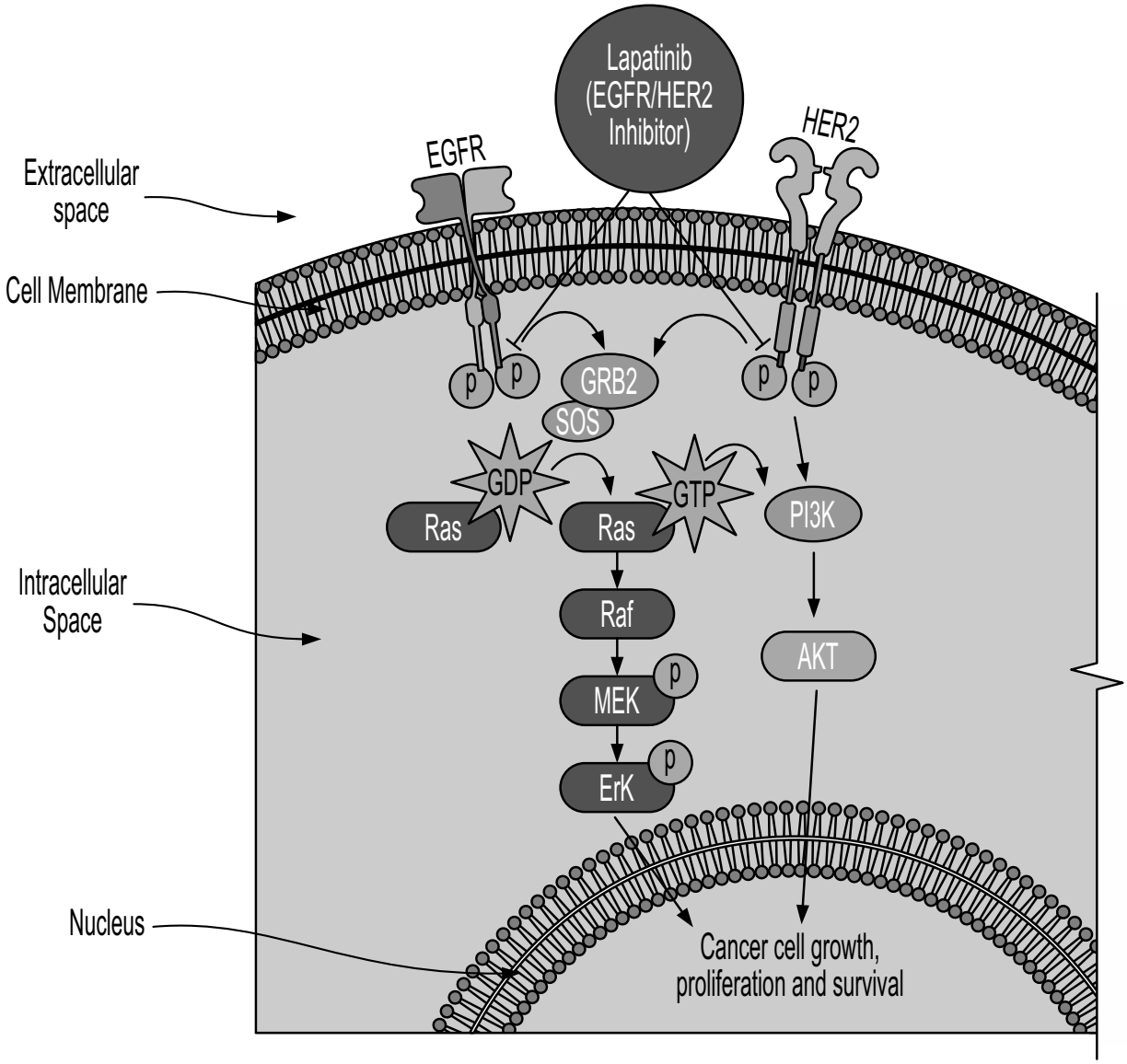

Lapatinib
(EGFR/HER2
Inhibitor)
EGFR
HER2
Extracellular
space
Cell Membrane
p
p
GRB2
SOS
p
p
GDP
Ras
Ras
GTP
PI3K
Intracellular
Space
Raf
AKT
MEK
p
ErK
p
Nucleus
Cancer cell growth,
proliferation and survival

Figure 6

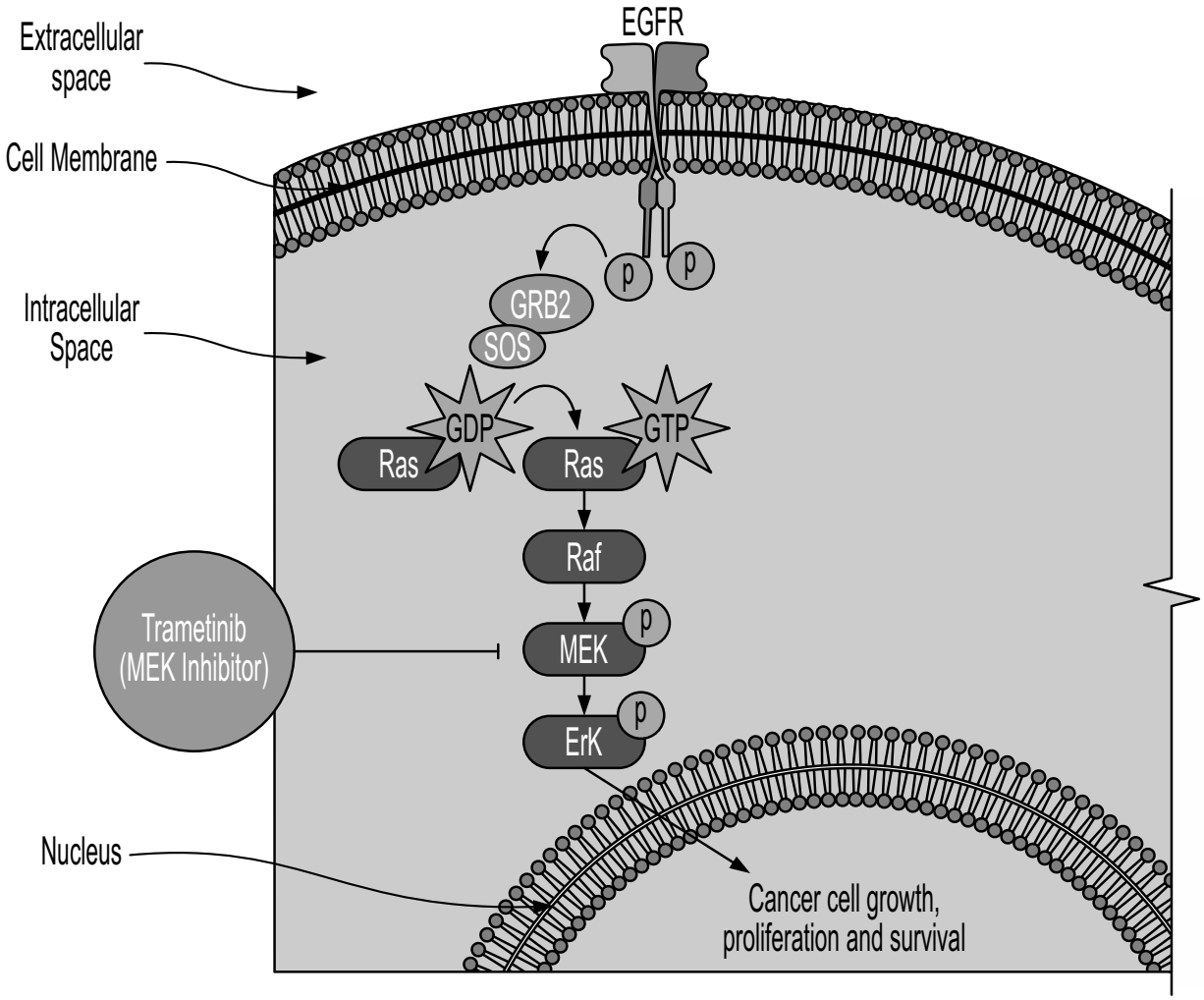

Extracellular space
Cell Membrane
Intracellular Space
Nucleus
EGFR
p
p
GRB2
SOS
GDP
GTP
Ras
Ras
Raf
MEK
p
ErK
p
Trametinib (MEK Inhibitor)
Cancer cell growth, proliferation and survival

Figure 7

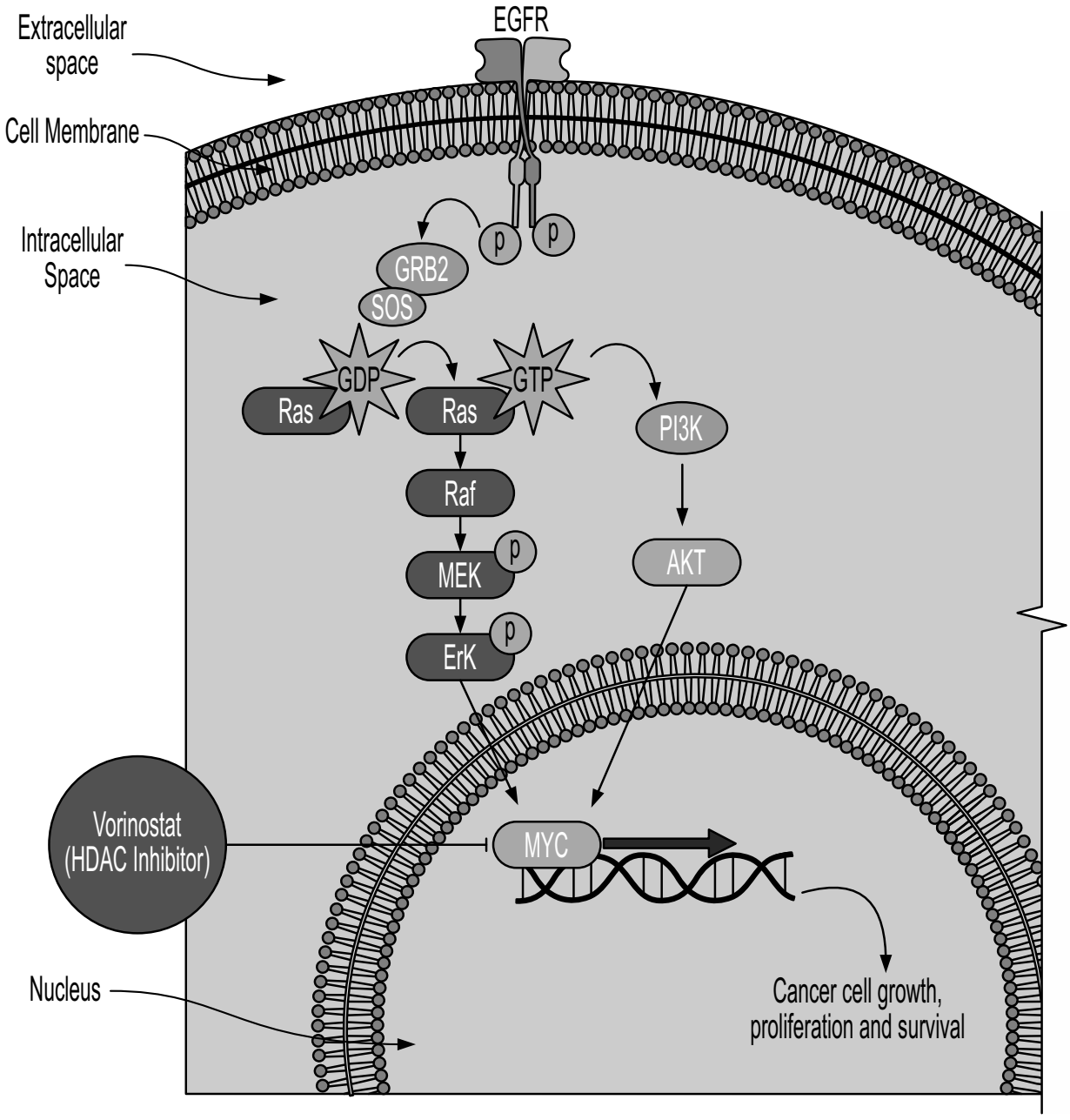

Extracellular space
EGFR
Cell Membrane
Intracellular Space
p
p
GRB2
SOS
GDP
GTP
Ras
Ras
PI3K
Raf
MEK
p
AKT
ErK
p
Vorinostat (HDAC Inhibitor)
MYC
Nucleus
Cancer cell growth, proliferation and survival

Figure 8

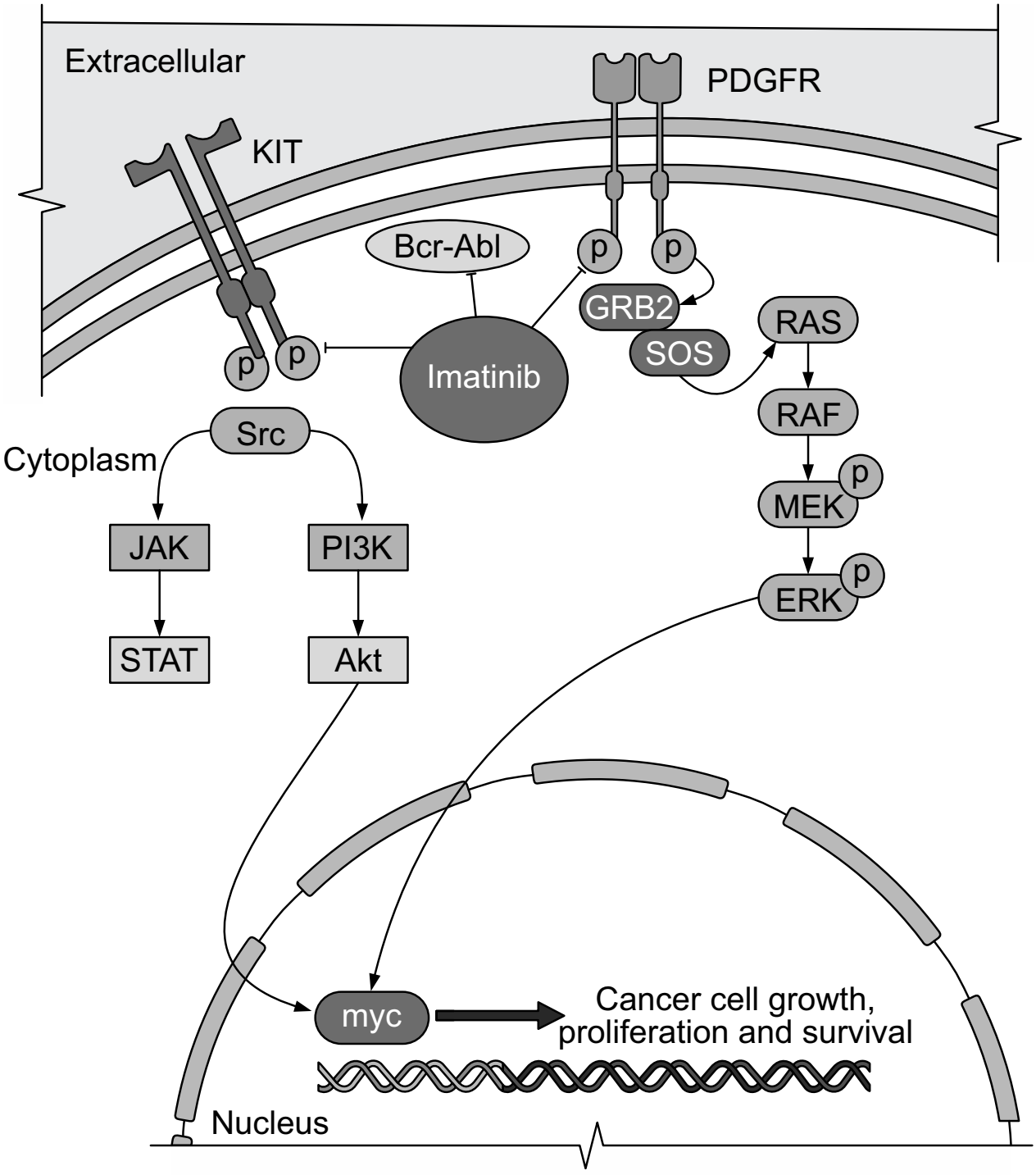

Extracellular
PDGFR
KIT
Bcr-Abl
p
p
GRB2
SOS
RAS
p
p
Imatinib
RAF
Src
Cytoplasm
MEK
p
JAK
PI3K
ERK
p
STAT
Akt
myc
Cancer cell growth,
proliferation and survival
Nucleus

Figure 9

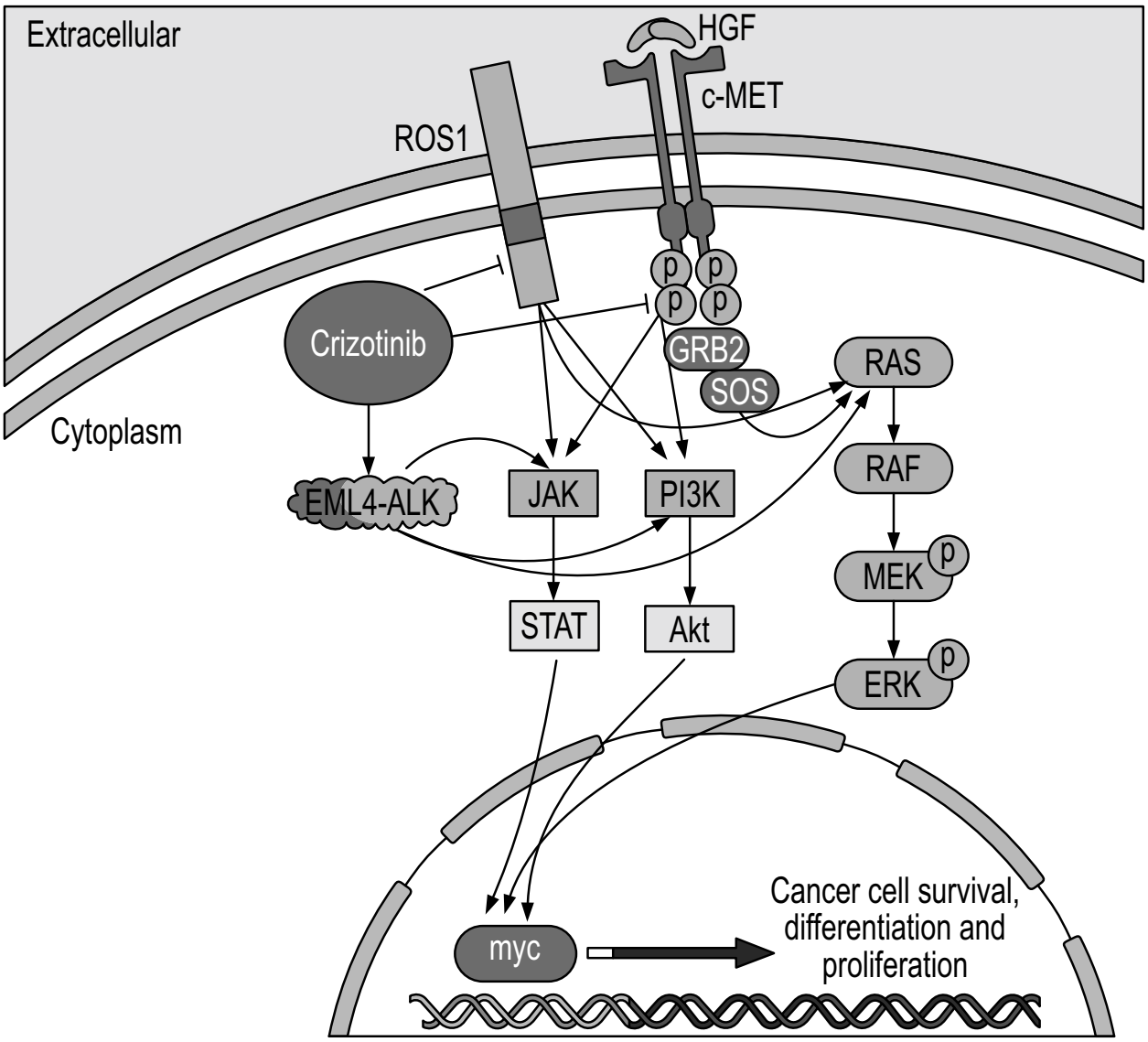

Extracellular
HGF
c-MET
ROS1
p
p
p
p
Crizotinib
GRB2
SOS
RAS
Cytoplasm
RAF
EML4-ALK
JAK
PI3K
MEK
p
STAT
Akt
ERK
p
Cancer cell survival,
differentiation and
proliferation
myc

Figure 10

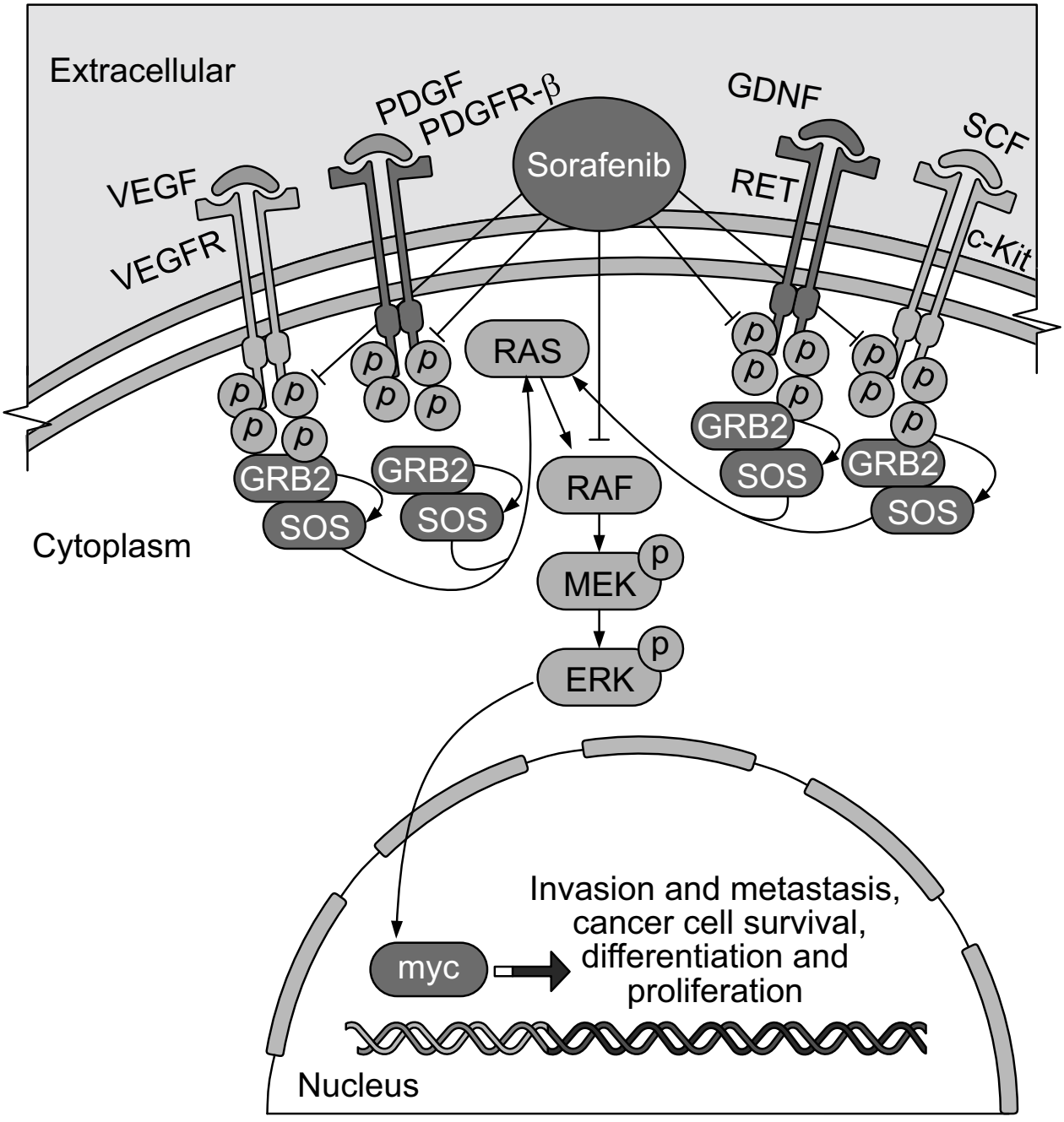

Extracellular
PDGF
PDGFR-β
GDNF
SCF
VEGF
VEGFR
Sorafenib
RET
c-Kit
RAS
GRB2
SOS
RAF
MEK
ERK
p
Cytoplasm
Invasion and metastasis,
cancer cell survival,
differentiation and
proliferation
myc
Nucleus

Figure 11

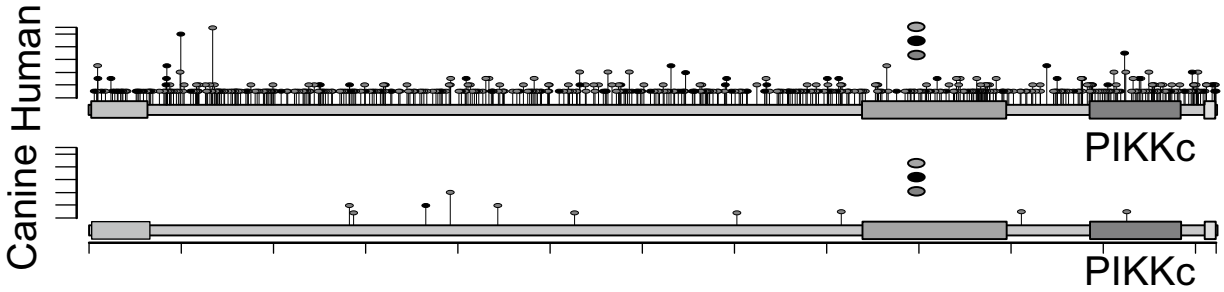


Figure 12