Ras-Raf-MEK-ERK Signaling

The Ras-Raf-MEK-MAPK-ERK signaling pathway plays a crucial role in cell differentiation, proliferation, and survival. This pathway transmits extracellular signals through ligands of receptor tyrosine kinases on the membrane, activating nuclear transcription factors that regulate gene expression and product synthesis. Protein mutations in this pathway are prevalent in various cancers, leading to hyperactivation of signaling and inducing uncontrolled cell proliferation. Therefore, proteins and receptors in the Ras-Raf-MEK-MAPK-ERK pathway are important targets for anticancer therapies. Additionally, the Ras signaling pathway is closely associated with aging and metabolism, and research on small molecule targeting of this pathway has garnered attention in neurodegenerative diseases. For example, the Ras/ERK pathway, through activation of amyloid precursor protein (APP), promotes the development of neurodegenerative lesions and formation of dendritic plaques. Future research targeting this key pathway may provide novel therapeutic strategies for various diseases.

MEK

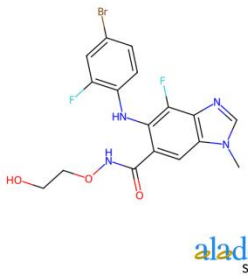

Figure 1 Chemical structure of ARRY-162

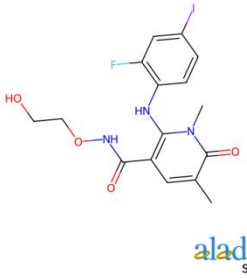

Figure 2 Chemical structure of AZD8330

MEK (mitogen-activated protein kinase kinase, MAP2K) is a class of tyrosine/threonine kinases activated by Raf, responsible for phosphorylating ERK and other MAPK proteins. There are two isoforms of MEK, MEK1 and MEK2. These kinases may undergo mutations in certain

Name	ID
ARRY-162	M126898、B408532
AS-703026	A125227、P408137
AZD8330	A127453、A409124
GDC-0623	G420768、G413780、G610532
GSK1120212	T127461、T407821
PD184352	C125418、P408384
PD325901	M1371702、P125494、M409191

cancer types, leading to sustained and uncontrolled activation.

RDEA119	B426935、B339747
Selumetinib	S125580、S407860

Ras

Ras family proteins are small GTPases, similar to Rho, Ran, and Arf, involved in regulating intracellular processes like nuclear transport, vesicle trafficking, and signal transduction. Ras proteins are activated by receptor tyrosine kinases, such as growth factor and ephrin receptors. Specific Ras proteins, including K-Ras, H-Ras, and N-Ras, transmit growth factor signals by activating Ras family proteins are small GTPases, similar to Rho, Ran, and Arf, involved in regulating intracellular processes like nuclear transport, vesicle trafficking, and signal transduction. Ras proteins are activated by receptor tyrosine kinases, such as growth factor and ephrin receptors. Specific Ras proteins, including K-Ras, H-Ras, and N-Ras, transmit growth factor signals by activating.

Figure 3 Chemical structure of Zoledronic Acid Monohydrate

Name	ID
Deltarasin Hydrochloride	D648580、D655480
(E,Z)-4-Hydroxytamoxifen	H113421、H408276
Kobe0065	K423962、K276196
Kobe2602	K424067、K275031
Manumycin A	M274901
Nobiletin	N130079、N130078、N409132
Zoledronic Acid Hydrate	Z140117

RAF

Raf proteins are serine/threonine kinases responsible for transmitting signals from Ras proteins and amplifying them through the MAPK signaling cascade. The main Raf proteins are A-Raf, B-Raf, and C-Raf. While mutations in A-Raf and C-Raf occur occasionally, mutant B-Raf forms play a significant role in many cancers. In B-Raf, V599 and V600 are part of the activation loop, maintaining the inactive conformation until

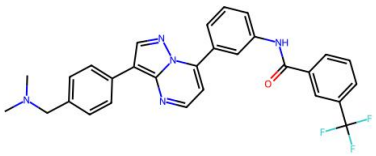

Figure 4 Chemical structure of B-Raf IN1

phosphorylation. Mutations like V599K or V600E disrupt these interactions, induce activation, and lead to uncontrolled signaling and growth. Raf proteins are explored as targets for chemotherapy drugs, like Dabrafenib and Vemurafenib.

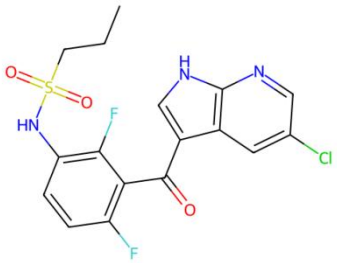

Figure 5 Chemical structure of PLX4720

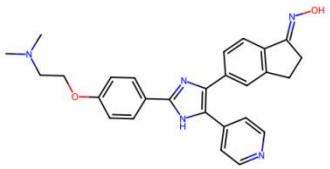

Figure 6 Chemical structure of SB-590885

Name	ID
AZ628	A129605
B-Raf IN1	B413508、B427058
CEP-32496	C126457、A407908
Dabrafenib	D127289、D409111
Dabrafenib Mesylate	D420864、D286637
GDC-0879	G127893、G409101
GW5074	G408888、G129612
MLN2480	M420574、M275976
Pazopanib	P424022、P125184
PD184352 (CI-1040)	C125418、P408384
PD325901	P125494
PLX4720	P127903
RAF265	R409224、R127906
D10137	R420361、R413223
SB-590885	S125513
Sorafenib	S125098、S408543
TAK-632	T413733、T420987
Vemurafenib(PLX4032)	V127521、V409259
ZM-336372	Z614980、Z129624

ERK

ERK (extracellular signal-regulated kinase) is a classic MAP kinase that receives signals from MEK and other proteins involved in the MAPK signaling cascade, thereby activating downstream transcription factors such as c-Fos, c-Myc, and ELK1. These transcription factors regulate the synthesis of gene products associated with meiosis, mitosis, and cell differentiation. ERK1 or ERK2 signaling plays a crucial role in the initiation and progression of cancer, and it is also closely associated with migraines and mood disorders, such as schizophrenia and bipolar disorder.

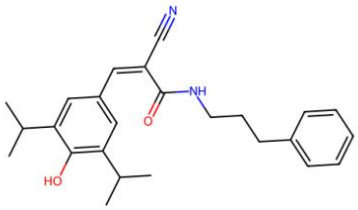

Figure 7 Chemical structure of SU-1498

Name	ID
Apigenin	A106675、A464373、A106676、 A408941
Bisdemethoxycurcumin	B117979、B131602
Canertinib 2HCl	C423017、C169301
CV-65	C276161
Demethoxycurcumin	D117978、D299451
Enniatin B1	E329658
4-O-Methylhonokiol	O648808、O655579
Nitidine Chloride	N421189、N117977
Nobiletin	N130079、N130078、N409132
Olomoucine II	O276007
Pelitinib	P125444、P409066
SU-1498	S422089、S167823
Tangeretin	T123655、T408390
Ulixertinib(BVD-523)	U413857、U409233
VX-11e	V426729、V127492

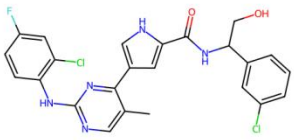

Figure 8 Chemical structure of VX-11e

p38 MAPK

Name	ID
Apigenin	A106675、A464373、A106676、A408941
Bisdemethoxycurcumin	B117979、B131602
Canertinib 2HCl	C423017、C169301
CV-65	C276161
Demethoxycurcumin	D117978、D299451
Enniatin B1	E329658
4-O-Methylhonokiol	O648808、O655579
Nitidine Chloride	N421189、N117977
Nobiletin	N130079、N130078、N409132
Olomoucine II	O276007
Pelitinib	P125444、P409066
SU-1498	S422089、S167823
Tangeretin	T123655、T408390
Ulixertinib(BVD-523)	U413857、U409233
VX-11e	V426729、V127492

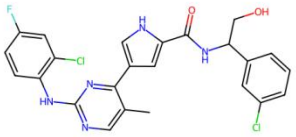

Figure 8 Chemical structure of VX-11e

Aladdin: https://www.aladdinsci.com/