Cancer Research

Product Guide | Edition 2

TOCRIS bioscience

High Performance Life Science Reagents

Autumn Crocus
Colchicum autumnale
A source of Colchicine

Contents by Research Area:

Cancer Research

Contents

Introduction

Cancer is a major focus of research activity throughout the world. Often defined as a multifactorial disease, with genetic, epigenetic and environmental factors influencing its progression, cancers usually develop over many decades from relatively benign collections of cells into malignant tumors. This development usually includes the accumulation of genetic alterations and acquisition of a specific set of properties that permits uncontrolled growth. These consistently observed characteristics displayed by cancer cells have been termed the 'Hallmarks of Cancer' in seminal papers by Hanahan and Weinberg. These hallmarks are: sustained proliferative signaling; evasion and growth suppression; genomic instability; resistance to cell death; and the ability to induce angiogenesis and to metastasize.

Cancer research over the last decade has broadened the concept of primary tumors as a collection of abnormally proliferating cells to include important elements of the host tissue architecture and tumor microenvironment, the influence of the immune system and the presence of tumor stem cells. In addition, the mechanism by which energy metabolism is subverted in tumor cells is beginning to be elucidated. It is with these established and emerging hallmarks of cancer in mind that we have updated the Tocris Cancer Research product guide.

As these cancer hallmarks are established, the mechanisms behind malignancy are more clearly understood and additional mechanisms continue to come to light. Cancer researchers require an ever changing set of pharmacological tools to identify and study targets involved in these processes. Tocris provides a range of high performance life science reagents for use in cancer research; featured in each section are our key products for that area.

Key Cancer Research Products

Receptor Signaling

Receptor Signaling

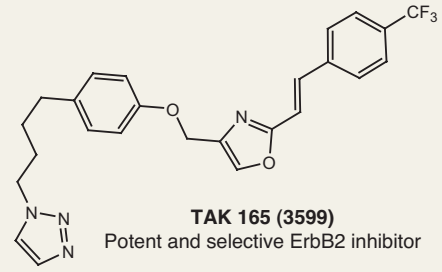
Cellular signaling pathways control normal proliferation, differentiation, survival and migration. Their dysregulation is a key factor in tumor formation. The altered regulation of signaling through overexpressed or mutated receptors at the cell surface, or altered expression of growth factors, cytokines or steroid hormones, are key elements for driving the proliferation of cancer cells and recruiting parenchymal cells to support the formation of tumors. Alternatively, mutated forms of intracellular signaling components can result in activated pathways that are insensitive to external antiproliferative/proapoptotic signals.

Growth Factor Receptors

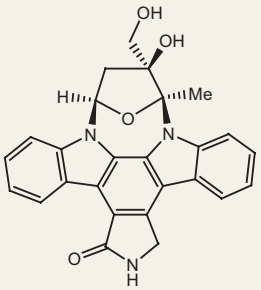
Under normal physiological conditions, growth factor availability dictates the balance between proliferation and cell death. This role in cellular homeostasis is often subverted in cancer. Tumor cells can secrete growth factors to ensure their own survival, and recruit non-malignant cells to the tumor in order to support its growth or to evade detection by the immune system. In many human cancers, receptor tyrosine kinases (RTKs) are

Box 1: Growth Factor Receptor Inhibitors

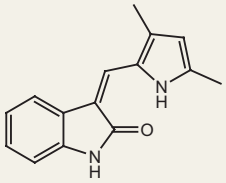
A full list of targets and related products are listed on pages 19-37



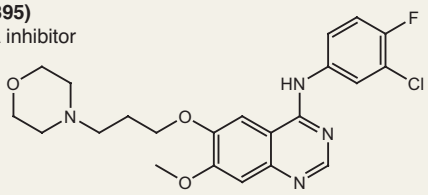
TAK 165 (3599)
Potent and selective ErbB2 inhibitor



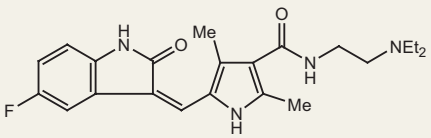
Lestaurtinib (3395)
JAK2, FLT3 and TrkA inhibitor



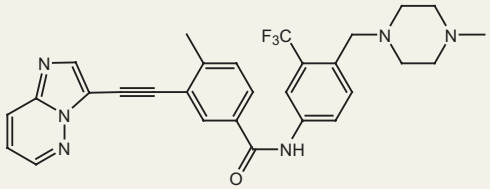
SU 5416 (3037)
VEGFR inhibitor. Also inhibits KIT, RET, MET and FLT3



Iressa (3000)
Orally active, selective EGFR inhibitor



Sunitinib (3768)
Potent VEGFR, PDGFRβ and KIT inhibitor



AP 24534 (4274)
Potent multi-kinase and pan-BCR-ABL inhibitor

commonly affected by mutations and/or alterations resulting in upregulation of their signaling output. For example, the amplification or overexpression of the HER2/Neu/*ERBB2* gene is commonly evident in breast cancer (Figure 2).

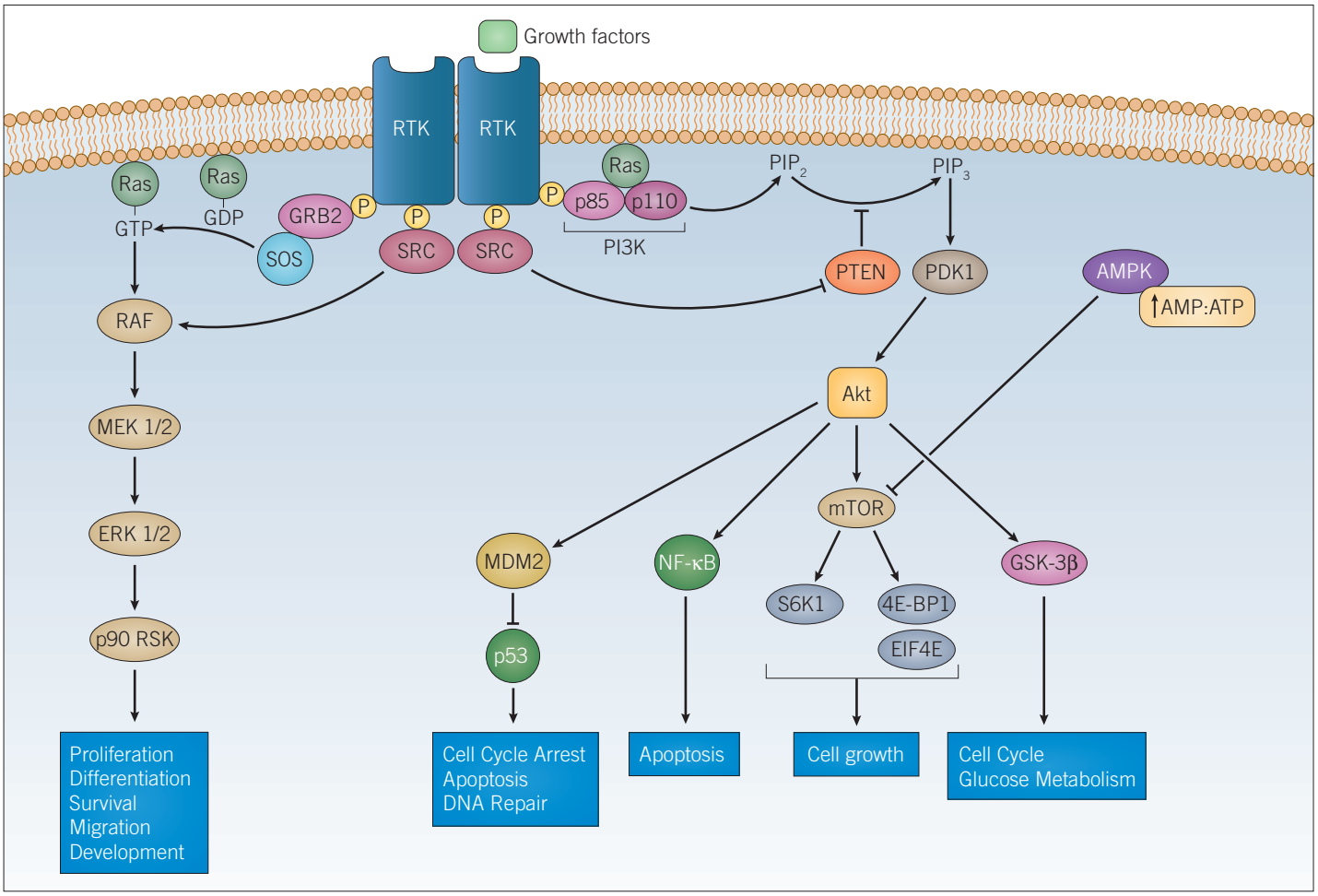
HER2 is part of the ErbB family of RTKs, which consists of four members: epidermal growth factor receptor (EGFR or ErbB1), HER2 (ErbB2), ErbB3 and ErbB4. In addition to EGF, EGFR also binds a number of other growth factors, whilst HER2 has no soluble ligand. However, HER2 is the heterodimerization partner for the other ligand-bound receptors. Intracellular signaling from ErbB homo- and heterodimers occurs through the PI3K and MAPK signaling pathways (Figure 1). Agents that selectively target EGFR (e.g. Iressa, Cat. No. 3000) or ErbB2 (e.g. TAK 165, Cat. No. 3599) are both clinically relevant and are important tool compounds used to study ErbB family signaling (Box 1). By combining ErbB inhibitors with inhibitors for receptors such as insulin-like growth factor receptor (IGF1R) or hepatocyte growth factor receptor (c-MET), it may be possible to overcome resistance to selectively targeted agents that occurs in some cancers.

Whilst some clinically relevant inhibitors are selective for individual RTKs or RTK families, others have proven to be effective by targeting multiple receptors, e.g. sunitinib (Cat. No. 3768), which targets, amongst others, PDGFRβ, VEGFR, FLT3 and RET. Other compounds, such as lestaurtinib (Cat. No. 3395), are more broad-spectrum inhibitors that target both receptor and intracellular kinases (Box 1).

Intracellular Signaling

One of the first intracellular kinases to be elucidated as a proto-oncogene was c-Src, an upstream mediator of both the PI3K and MAPK pathways. Increased c-Src activity has been linked to a number of gastrointestinal cancers, including pancreatic cancer. The Src family of kinases (Src, Fyn, Yes, Lck, Lyn, Hck, Fgr and Blk) are non-receptor tyrosine kinases that interact with the intracellular domains of growth factor receptors,

Figure 1 | Intracellular signaling pathways that are important in tumorigenesis



Dimerization of receptor tyrosine kinases occurs upon ligand binding, enabling activation of the tyrosine kinase on each receptor leading to autophosphorylation. The phosphorylated residues on the cytoplasmic domain of the RTK bind adaptor proteins such as GRB2, or directly to the p85 subunit of PI3K to initiate PI3K signaling. Activation of SOS and Ras mediates the induction of MAPK signaling. Both pathways influence a range of cellular processes and encompass many of the major targets studied in cancer research.

cytokine receptors, G protein-coupled receptors (GPCRs) and integrins. Src kinase activity is regulated by phosphatases, by binding to adaptor proteins, and by proteasomal degradation.

The PI3K pathway is integral to cell growth and survival in many cell types. It is frequently activated in cancer, often as a result of the inactivation of the tumor suppressor PTEN, which is mutated with high frequency. Recently, mutations in the catalytic subunit p110α of PI3K (PIK3CA) have been shown to induce a gain-of-function of PI3K activity. Of the known PI3K catalytic subunit genes, PIK3CA is the only one mutated in cancer. Aberrant PI3K activation from mutations in the genes encoding downstream components of the PI3K pathway have been linked to the development of malignancies such as lymphoma (p85 PI3K regulatory subunit), glioma (PTEN), breast cancer (S6K1) and gastric cancer (Akt1).

Signaling through the PI3K pathway is particularly important in tumor metabolism. Akt1 (protein kinase B) is a key mediator of PI3K signaling. It stimulates glycolysis, promoting cell growth and inhibiting autophagy. AMPK functions in contrast to Akt1 – it acts as an energy sensor and is activated under energetic stress, when the ratio of AMP:ATP is increased, or in hypoxic conditions. AMPK activation inhibits mTOR, inducing autophagy. Tumor cells often suppress AMPK signaling, subverting the shift to oxidative metabolism normally implemented by AMPK.

mTOR acts downstream of both Akt and AMPK, and plays a key role in coordinating the signals for a number of pathways, including insulin signaling, nutrient sensing and mitogenic signaling. New ATP-competitive mTOR inhibitors such as Torin 1 (Cat. No. 4247) and Torin 2 (Cat. No. 4248) are proving useful in elucidating the function of the mTOR/PI3K axis in cancer cell biology (Box 2).

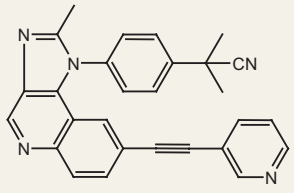
As mentioned above, cancer cells frequently exhibit a shift in metabolism. Rapid ATP production is achieved by switching from oxidative phosphorylation to glycolysis; this is known as the Warburg effect. By serving as a major signaling mediator linked to tumor metabolism, the PI3K pathway thus perpetuates both growth/proliferation signals and metabolic changes in cancer cells.

The other major pathway that has been extensively studied for therapeutic intervention in cancer is the MAPK pathway. MAPKs are serine-threonine kinases that regulate a wide variety of cellular functions. There are 4 major mammalian MAP kinase cascades, involving: ERK1/2, p38, JNK and ERK5/BMK1. MAPK pathways including ERK transduce signals from growth factors and are key in regulating differentiation and proliferation in many cell types. Mutations in key components of these cascades have been linked to various cancers. Consequently, inhibitors targeting the molecules involved in the Ras-Raf-MEK-ERK cascade are of potential therapeutic significance.

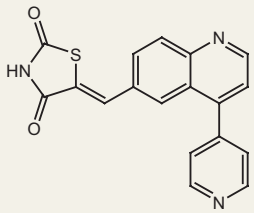
Ras is a small GTPase that is subject to activating mutations in a large proportion of cancers. K-Ras mutations are common in colon and pancreatic cancer; N-Ras mutations in melanomas; and H-Ras mutations in cervival and bladder cancers. These mutations enable Ras activation in the absence of ligand-RTK binding and elicit cellular responses as a consequence of the absence of initiating factors. Prenyltransferases upstream of

Box 2: PI3K/mTOR Inhibitors

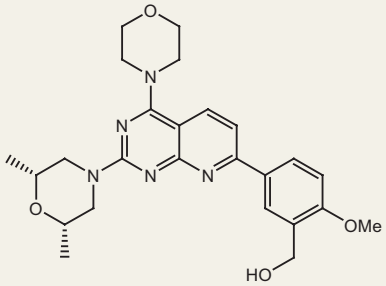
A full list of targets and related products are listed on pages 19-37



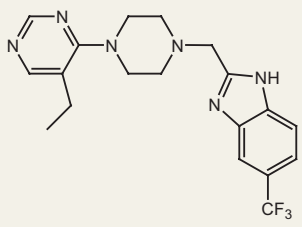
BAG 956 (3606)
Dual PI3-kinase and PDK1 inhibitor



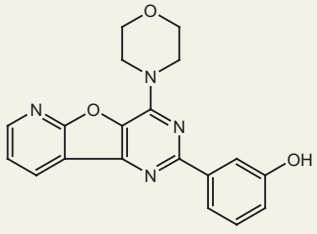
GSK 1059615 (4026)
Potent PI3-kinase inhibitor



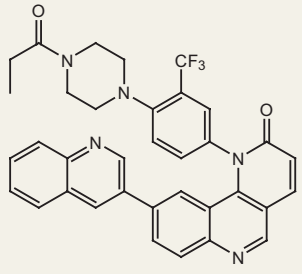
KU 0063794 (3725)
Selective mTOR inhibitor



PF 4708671 (4032)
S6K1 inhibitor



PI 103 (2930)
Inhibitor of PI3-kinase, mTOR and DNA-PK



Torin 1 (4247)
Potent and selective mTOR inhibitor

Ras – FTase and GGTase I – are involved in the association of Ras with the plasma membrane and have been targeted by small molecules reducing their activity.

Raf kinases are activated by GTP-bound Ras and recruited to the cell membrane upon growth factor stimulation. There are three Raf family members – A-Raf, B-Raf and c-Raf. Activating mutations in the B-Raf proteins have been linked to a range of cancers including skin, thyroid, ovarian and pancreatic cancer. In melanomas, *BRAF* is the most commonly mutated gene, with *BRAF* mutations evident in over 65% of malignant melanomas. A high proportion of these *BRAF* mutations contain a missense substitution which generates the B-Raf^{V600E} protein – a constitutively active kinase.

Signal transduction through Raf is also dependent on a number of proteins that are important in cancer research, such as 14-3-3 and Hsp90. Hsp90 (90 kDa heat shock protein) is a molecular chaperone that aids protein folding and quality control for a large number of 'client' proteins, and acts in concert with other chaperones such as Hsp70. Other notable tumor-associated clients include estrogen receptors and p53. Hsp90 plays an important role in some tumor cell types by stabilizing mutated oncogenic proteins.

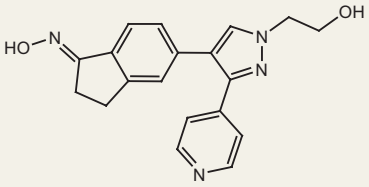
MEK, also known as mitogen-activated protein kinase kinase or MAP2K, is a dual specificity kinase that phosphorylates both the tyrosine and threonine residues required for the activation of the mitogen activated protein kinases, ERK. Although there have been few oncogenic mutations for this kinase reported, the frequent activation of the MAPK pathway in cancer has meant that MEK has been extensively studied as a therapeutic target. The first small-molecule MEK inhibitor to enter clinical trials was PD 184352 (Cat. No. 4237). A more potent analog, PD 0325901 (Cat. No. 4192) has since been developed (Box 3). Both of these compounds target an allosteric site on MEK adjacent to the ATP binding pocket; this mechanism of inhibition provides these compounds with a high degree of selectivity.

As the downstream effector of MEK, there are a limited number of inhibitors that target ERK family members. FR 180204 (Cat. No. 3706) is one of the few commercially available ERK1 and 2 inhibitors. In a related MAPK pathway, XMD 8-92 (Cat. No. 4132) is an inhibitor that exhibits high selectivity for ERK5. ERK5 is selectively activated by MEK5, and has been shown to block tumor cell proliferation *in vitro* and tumor-associated angiogenesis *in vivo*. There is a growing body of evidence which shows that inhibitors of other MAP kinase pathways, involving p38 MAP kinases and JNK, may prove to be useful in cancer therapy. In some cancers, activation of both of these kinases is associated with suppression of apoptosis. For example, correlations have been found between increased phosphorylation of p38α and the malignancy of cancers including lymphoma, glioma, lung, breast and thyroid cancers. Similarly, activation of the JNK pathway by the leukemia-associated Bcr-Abl protein has been observed in hematopoietic cells.

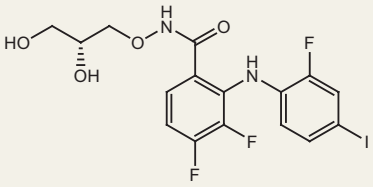
The oncogenic Bcr-Abl fusion protein (caused by a t(9,22) translocation) is linked to the development of chronic myeloid leukemia and has been successfully targeted by tyrosine kinase inhibitors. The majority of patients respond to the frontline

Box 3: Raf-MEK-ERK Pathway Inhibitors

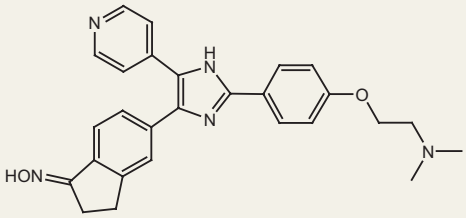
A full list of targets and related products are listed on pages 19-37



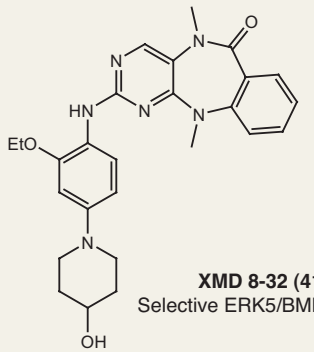
GDC 0879 (4453)
Potent B-Raf inhibitor



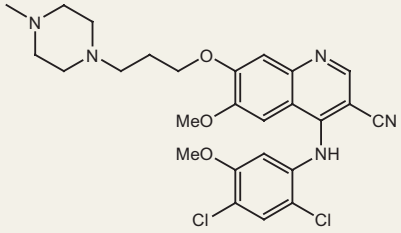
PD 0325901 (4192)
Selective inhibitor of MEK1/2



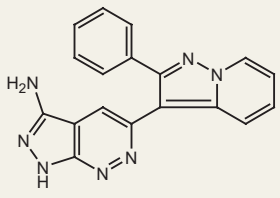
SB 590885 (2650)
Potent B-Raf inhibitor



XMD 8-32 (4132)
Selective ERK5/BMK1 inhibitor

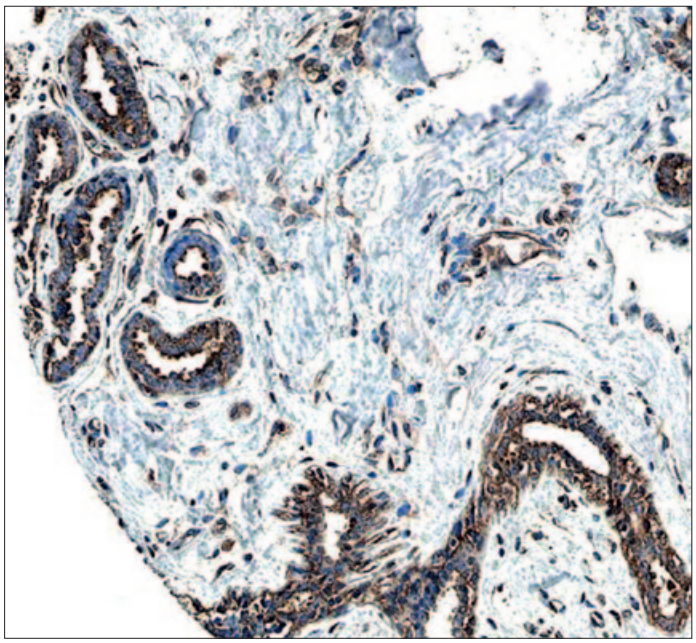


Bosutinib (4361)
Dual Src-Abl inhibitor; antiproliferative



FR 180204 (3706)
Selective ERK inhibitor

Figure 2 | ErbB2/Her2 in human breast cancer tissue



ErbB2 expression detected in paraffin-embedded sections of human breast cancer tissue. The *ERBB2*/HER2 gene is commonly amplified or overexpressed in breast cancer. The receptor is visualized here as brown staining using a Rabbit Anti-Human Phospho-ErbB2 Affinity-purified Polyclonal Antibody (R&D Systems, Catalog #AF4438). Hematoxylin counterstain in blue.

therapies of imatinib, dasatinib or nilotinib. More recent broad spectrum inhibitors with Abl kinase activity, such as ponatinib (AP 24534, Cat. No. 4274) may offer insights into overcoming mutated forms of Bcr-Abl, e.g. BCR-ABL^{T3151}; whilst bosutinib (Cat. No. 4361), the dual Src and Abl kinase inhibitor, has been shown to control the proliferation and migration of breast and colon cancer cells.

In addition to PI3K and MAPK signaling, several other signaling pathways have been found to be involved in the progression of cancer, particularly those involved in cell growth and proliferation. Wnt proteins are secreted glycoproteins that regulate diverse developmental processes such as differentiation, cell migration and proliferation during embryogenesis and in adult tissues. Wnt is known to be proto-oncogenic and promotes tumorigenesis and metastasis. TGF-β is a signaling molecule involved in several pathways leading to cell adhesion, differentiation, motility and death. Disruption of the TGF-β/SMAD pathway has been implicated in a multitude of human cancers, typically involving an inactivation mutation of TGF-β receptor II.

Sphingosine kinase and sphingosine-1-phosphate (S1P) have also been linked to cell growth. Sphingosine kinase exists as two isoforms – SPHK1 and SPHK2 – and mediates the conversion of sphingosine to S1P, a key sphingolipid. Numerous interactions exist between S1P and growth factor signaling pathways, linking S1P to the regulation of tumorigenesis and angiogenesis. For example, VEGFR binding to VEGFR-2 induces PKC-mediated activation of SPHK1, resulting in S1P-mediated Ras activation; angiogenesis occurs as a consequence of activated Ras-Raf-MEK-ERK1/2 signaling. Agents that inhibit sphingosine kinase or antagonize S1P receptors are of interest in the attenuation of hyperproliferative, migratory and inflammatory phenotypes observed in cancer cells.

Histone deacetylases (HDACs) are a group of enzymes that catalyze the removal of acetyl groups from lysine residues in histones and non-histone proteins, resulting in transcriptional repression. In general, they do not act autonomously but as components of large multiprotein complexes, such as pRb-E2F and mSin3A. These complexes mediate important transcription regulatory pathways along with other signaling mechanisms, including the nuclear hormone receptors.

Nuclear Hormone Receptors

Nuclear receptors bind sequence-specific promoter elements on target genes and upregulate gene expression. Altered expression patterns in these receptors have been linked to different cancers.

Androgen receptors (AR) are nuclear hormone receptors that are commonly expressed in prostate cancer – approximately 80-90% of prostate cancers are dependent on androgen. AR activation promotes the growth and differentiation of prostate cancer cells, and AR signaling has also been implicated in breast cancer. In addition, the transcriptional activity of androgen receptors can be influenced by growth factors, prompting prostate cancer cell proliferation in the absence of androgens. Antiandrogens may be used in prostate cancer therapy.

Estrogen also plays an essential role in the growth of breast cancer, and estrogen signal transduction pathways often become dysregulated in this disease. The mechanisms behind estrogen-related development of breast cancer are also being targeted for cancer therapies. For example, aromatase is a CYP450 enzyme which is involved in estrogen biosynthesis. Since estrogen is required for the growth of breast and ovarian cancers, inhibitors of aromatase exhibit anticancer activity by reducing estrogen levels.

Aryl hydrocarbon receptors (AHRs) are cytosolic transcription factors that induce changes in gene expression upon ligand binding. AHR signaling has been implicated in cancer since binding of tumor-derived ligands to AHR suppresses anti-tumor immune responses and is associated with malignant growth.

Clearly, there are various signaling mechanisms that can be dysregulated in cancer cells. By targeting these key receptors and signaling molecules using selective pathway inhibitors, cancer researchers can study one of the major hallmarks of cancer and its impact on tumorigenesis.

Cell Cycle and DNA Damage Repair

Cell Cycle and DNA Damage Repair

In addition to sustaining proliferative signaling, the cancer cell must be able to evade tumor suppression mechanisms that inhibit cell proliferation. Normally, cell division is a tightly controlled process that only occurs under specific conditions. The cell cycle is integral to cell division and as such, the molecules governing its progression have been a subject of great interest for cancer researchers.

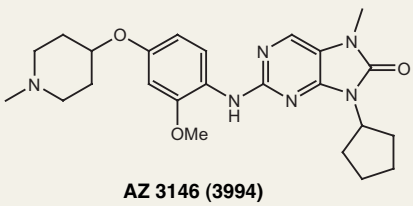
Cell Cycle and Mitosis

Cyclin-dependent kinases (cdks) act in concert with their regulatory subunits, the cyclins, to control cell cycle progression through its 4 phases: G_1, S, G_2 and mitosis (M) (Figure 3). Cdks are constitutively expressed and are regulated by several kinases and phosphatases, including Wee1 and Cdc25 phosphatase. Such controls are necessary, since misregulation of cdk activity can induce unscheduled proliferation, and genomic and chromosomal instability. Cdk inhibitors can induce cell cycle arrest at major transition points such as G_2/M, which is mediated by CDK1/Cyclin B.

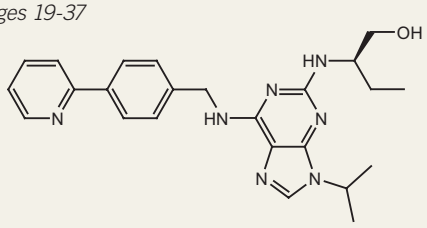
During mitosis, a small number of kinases coordinate a complex series of events. In particular, Aurora kinases, cdks and Polo-like kinases (Plks) work in concert to ensure chromosomes are segregated to daughter cells with high fidelity. Improper chromosome segregation has significant effects on cellular function. It can contribute not only to decreased viability, but also to malignant transformation through the generation of genomic instability and aberrant cell division. A process known as mitotic catastrophe – a form of cell death which is initiated by disturbances in mitotic machinery – helps limit the risk of malignancy by eliminating potentially tumorigenic cells, thereby reducing the damaging effects of genetic instability.

Box 4: Cell Cycle and Mitotic Checkpoint Inhibitors

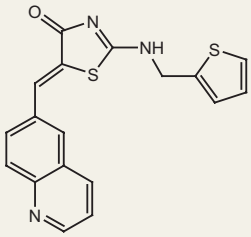
A full list of targets and related products are listed on pages 19-37



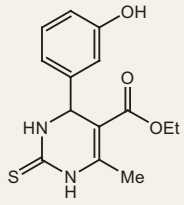
AZ 3146 (3994)
Potent and selective Mps1 inhibitor



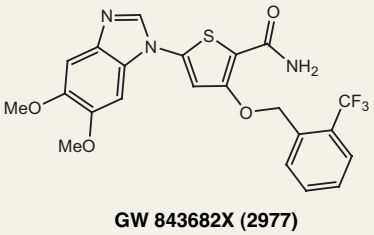
(*R*)-CR8 (3605)
Dual cdk1/cdk5 inhibitor. Also inhibits CK1



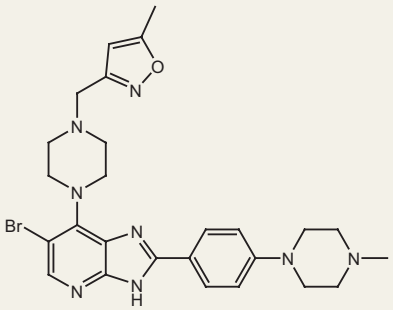
Ro 3306 (4181)
Cyclin-dependent kinase (cdk) 1 inhibitor



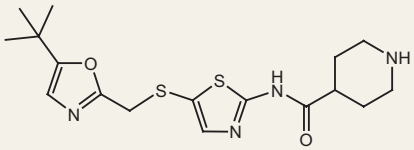
Monastrol (1305)
Selective inhibitor of mitotic kinesin Eg5



GW 843682X (2977)
Selective inhibitor of PLK1 and PLK3



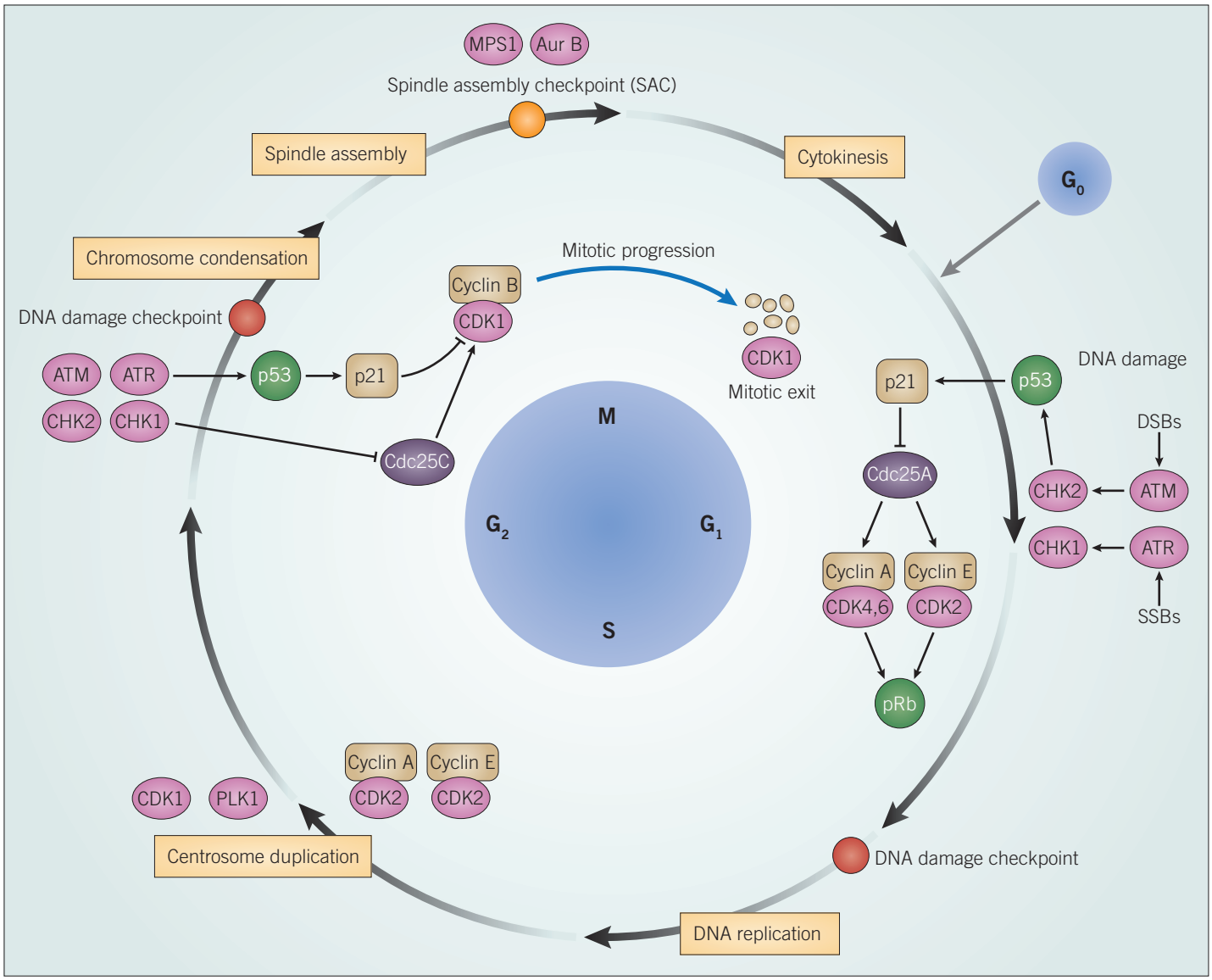
CCT 137690 (4291)
Potent pan-Aurora kinase inhibitor



SNS 032 (4075)
Potent cdk2, cdk7 and cdk9 inhibitor

Cell Cycle and DNA Damage Repair – continued

Figure 3 | Cell cycle progression and DNA repair



At specific points in the cell cycle, DNA damage is detected and repaired. The process is initiated by the DNA damage sensors, ATM and ATR kinase. Checkpoint kinases Chk1 and Chk2 initiate signaling cascades that activate DNA damage checkpoints in G_1 and G_2. The spindle assembly checkpoint (SAC) delays anaphase of mitosis until all chromosomes are properly aligned on the spindle, preventing aneuploidy. Kinases including aurora kinase B (Aur B), PLK1 and Mps1 are implicated at various control points in the cell cycle. (SSB = single strand break; DSB = double strand break).

Due to their role in chromosome segregation, aurora kinases and Plks are closely linked to mitotic progression. PLK1 promotes mitotic entry by inducing the degradation of Wee1 and the activation of Cyclin B/CDK1, and has additional roles in chromosome segregation and cytokinesis. PLK2 and PLK3 are involved in checkpoint-mediated cell cycle arrest and help ensure genetic stability. Aurora A has been linked to centrosome maturation and spindle assembly, and is overexpressed in many human cancers. Aurora B is involved in the spindle assembly checkpoint and cytokinesis, amongst other mitotic processes. Inhibitors of these enzymes therefore inhibit key mitotic processes, halting cell division.

Other mitotic spindle associated proteins that are being studied as potential therapeutic targets are Eg5 and Mps1. The mitotic kinesin Eg5 is a motor protein essential for bipolar spindle formation, and inhibition of Eg5 by compounds such as monastrol (Cat. No. 1305) results in mitotic arrest (Box 4). Mps1 (monopolar spindle 1) is a mitotic checkpoint kinase involved in the spindle assembly checkpoint, where it ensures correct chromosome segregation. Inhibition of Mps1 has been shown to decrease cancer cell viability *in vitro*, suggesting that Mps1 is another attractive therapeutic target associated with the mitotic spindle.

DNA Damage and p53

DNA damage is a common occurrence in all cells, and must be repaired in order for proliferation to occur successfully and accurately. Numerous kinases maintain cell cycle progression through regulatory checkpoints, which ensure that damaged DNA is not replicated. Cell cycle checkpoint kinases (Chks 1 and 2) and cdks act as control switches at various transition points in the cycle. Prolonged activation of Chks triggers senescence or apoptosis, through both p53-dependent and p53-independent mechanisms.

Several cellular DNA repair mechanisms exist to fix DNA damage and prevent its transmission to daughter cells. Genomic instability is a key characteristic of cancer cells which results from DNA damage, inefficient DNA repair, and failure to stop the cell cycle, often through inactivation of key checkpoint proteins such as ATM, ATR and p53. Inheritance of mutations in these key regulatory genes is often predictive of a higher cancer risk. If DNA damage is severe enough, however, the cell submits to mitotic catastrophe and dies. Certain cancer therapies, in particular chemotherapeutic agents, exploit this avenue (see table of chemotherapeutics, page 37).

ATM and ATR kinases are DNA damage sensor proteins that are activated in response to DNA damage and induce cell cycle arrest by coordinating the initiation, amplification and activation of the DNA damage checkpoint. In cancer cells with DNA damage, inhibiting these enzymes is therapeutically beneficial; the cell cycle continues in spite of significantly toxic DNA lesions, resulting in the death of the cell.

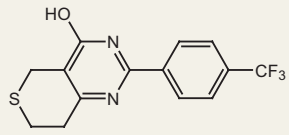
Key 'gatekeeper' proteins such as retinoblastoma protein (pRb) and p53 also prevent cell cycle progression in response to DNA damage, growth-inhibitory signals or oxidative stress. Like ATM and ATR, p53 is activated in response to cellular stresses including hypoxia and DNA damage. p53 is a key transcriptional regulator, and has been a thoroughly studied cancer target since its discovery over thirty years ago. p53 regulates a large number of genes involved in tumor suppression, including those with roles in cell cycle arrest, DNA repair and apoptosis. p53 is activated by several mechanisms, including phosphorylation by ATM, ATR, Chk1, casein kinase 2 and MAPKs. These modifications inhibit its association with MDM2, an E3 ubiquitin ligase that targets p53 for degradation by the ubiquitin-proteasome pathway. Phosphorylation prevents the turnover of p53, not only increasing its levels within the cell but also increasing its affinity for the p53 DNA binding site.

Inactivating mutations of p53 occur in a significant number of human cancers, making it a key target for gene and drug therapies. Nutlin-3 (Cat. No. 3984) is an MDM2 antagonist sold by Tocris under license. It potently inhibits the interaction between MDM2 and p53, inducing apoptosis in cancer cells. Other compounds may bind p53 directly to reactivate its wild-type functions (e.g. PRIMA-1^{MET}, Cat. No. 3710) or stabilize it via other mechanisms (Box 6).

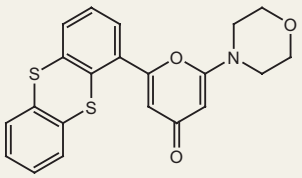
Many chemotherapeutic agents work by inducing toxic DNA lesions; these include the platinum cross-linking agents oxaliplatin (Cat. No. 2623) and carboplatin (Cat. No. 2626). Inhibiting DNA repair mechanisms of cancer cells can enhance the

Box 5: DNA Damage Checkpoint Inhibitors

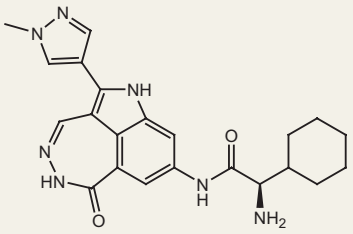
A full list of targets and related products are listed on pages 19-37



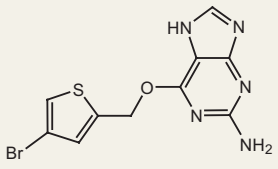
XAV 939 (3748)
Tankyrase inhibitor



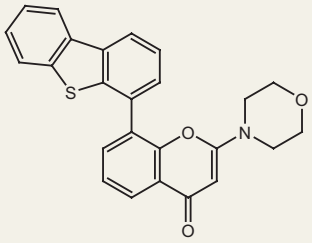
KU 55933 (3544)
Potent and selective ATM kinase inhibitor



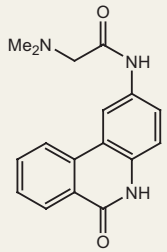
PF 477736 (4277)
Selective Chk1 inhibitor



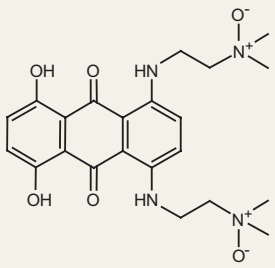
Lomeguatrib (4359)
MGMT inhibitor



NU 7441 (3712)
Potent and selective DNA-PK inhibitor



PJ 34 (3255)
Potent PARP inhibitor

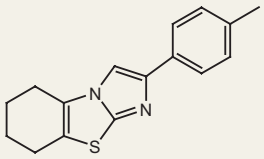


Banoxantrone (4219)
Prodrug topoisomerase II inhibitor

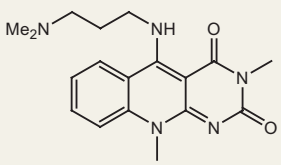
Cell Cycle and DNA Damage Repair – continued

Box 6: p53-related Products

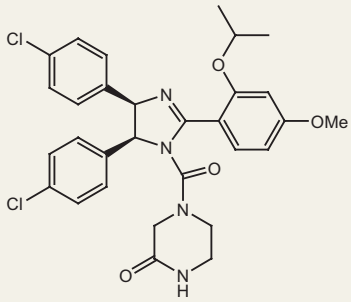
A full list of targets and related products are listed on pages 19-37



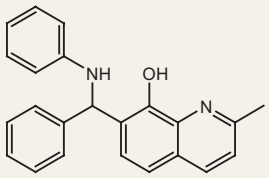
Cyclic Pifithrin-α (3843)
p53 inhibitor



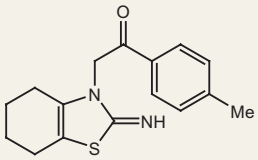
HLI 373 (3503)
Hdm2 inhibitor; activates p53-dependent transcription



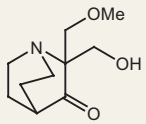
Nutlin-3 (3984)
MDM2 antagonist; inhibits MDM2-p53 interaction



NSC 66811 (2936)
MDM2 inhibitor. Disrupts MDM2-p53 interaction



Pifithrin-α (1267)
p53 inhibitor



PRIMA-1^{MET} (3710)
Restores mutant p53 activity

cytotoxic effects of DNA-damaging compounds administered in combination. For example, the ATM inhibitor KU 55933 (Cat. No. 3544) has been shown to enhance the cytotoxic effect of both ionizing radiation and etoposide (Cat. No. 1226). Alkylating and methylating agents such as temozolomide (Cat. No. 2706) bind to DNA and modify the O^6 of guanine residues, leading to DNA cross-linking. This alkylation is readily reversed by the activity of O^6-methylguanine-DNA methyltransferase (MGMT). Inhibition of MGMT through compounds such as lomeguatrib (Cat. No. 4359) can therefore enhance the antitumor activity of these alkylating agents (Box 5).

Other DNA repair proteins include poly(ADP-ribose) polymerase (PARP), which is linked to base-excision repair (BER), and DNA-dependent protein kinase (DNA-PK), which is involved in DNA double-strand break (DSB) repair. Cells that exhibit defective DNA-PK activity are more sensitive to ionizing radiation than normal cells. Topoisomerase inhibitors, such as etoposide (Cat. No. 1226) and camptothecin (Cat. No. 1100), trap topoisomerases in complex with the DNA, causing single and double strand breaks. PARP inhibitors also enhance the efficacy of radiation therapy and chemotherapy by preventing the repair of toxic DNA lesions; second and third generation PARP inhibitors include clinically relevant molecules.

Tumor cells can replicate in spite of incomplete DNA repair. In addition, most types of tumor cells seem to acquire the ability to proliferate endlessly, negating a barrier that normally limits the number of times a cell can divide. This replicative potential is linked to the loss of protective nucleotide sequences at the ends of chromosomes, known as telomeres. Telomeres are progressively shortened during each round of cell division, to the point where they lose their ability to protect the ends of DNA - this gradual reduction in length is known as 'telomere attrition.' Consequently, the chromosome ends fuse and cell death occurs. The inhibition of telomerase, which adds telomeres, could therefore provide a mechanism through which unlimited cell proliferation is curbed. BIBR 1532 (Cat. No. 2981) is one such telomerase inhibitor; it causes telomere shortening in rapidly proliferating cancer cells and induces growth arrest. By exploiting a cancer phenotype – rapid cell proliferation – inhibition of DNA repair pathways provides a key therapeutic avenue.

Cell Death and Drug Resistance

Cell Death and Drug Resistance

Resisting cell death is another key hallmark of cancer cells. Apoptosis – also known as programmed cell death – helps ensure cellular homeostasis and occurs in both normal physiological and pathological conditions. If DNA damage is severe enough, apoptosis is induced in order to eliminate the cell and its tumorigenic potential. Apoptosis is a complex process, and errors can occur in one of many pathways leading to it. In cancer, the ability to evade apoptosis is what helps enable the survival of malignant cells and contributes to their eventual neoplastic transformation.

Pro- and antiapoptotic proteins are involved in the complex network governing cell death. The Bcl-2 family contains both types of apoptotic proteins: for example, Bcl-2 is antiapoptotic, while Bax is proapoptotic. The Bcl-2-regulated apoptotic pathway is activated in response to cytotoxic stress, such as DNA damage and hypoxia, and involves more than 15 proteins that interact to regulate apoptosis. Mutations that activate prosurvival genes and/or disable proapoptotic genes are evident in many human cancers, providing evidence for the link between defective apoptosis and cancer development.

Cell death via apoptosis is executed by caspases in a tightly orchestrated system of proteolytic steps. Mutations or changes in the expression of caspases have been recently been noted in a variety of tumors and cell lines.

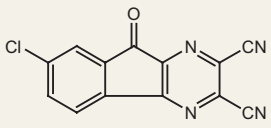
Pim1 kinase is also involved in apoptosis regulation. It is encoded by a proto-oncogene that is often overexpressed in cancer cells. This constitutively active serine/threonine kinase contributes to tumorigenesis by inhibiting apoptosis, in addition to promoting cell proliferation and genetic alteration.

Similar to apoptosis, the role of autophagy in cancer is complex. The mechanisms underlying its involvement in tumorigenesis are yet to be thoroughly elucidated. Autophagy functions to limit genomic instability and cell growth by degrading damaged cellular components, thus acting as a tumor suppressor. However, tumor cells also activate autophagy under stress or to meet an increase in metabolic demand, such as that which arises from rapid cell proliferation. By enabling the degradation of organelles and macromolecules, autophagy helps provide cells with nutrients under starvation conditions. This capacity to tolerate stress is important for tumor cell survival and as such, autophagy is a potential target for therapeutic modulation. Autophagy inhibitors such as chloroquine (Cat. No. 4109), when used in combination with chemotherapeutics, suppress tumor growth and spur cell death.

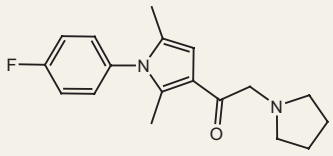
Proteins involved in the ubiquitin-proteasomal pathway may target key regulatory components. For example, USP7

Box 7: Apoptosis, Autophagy and Proteasome Key Products

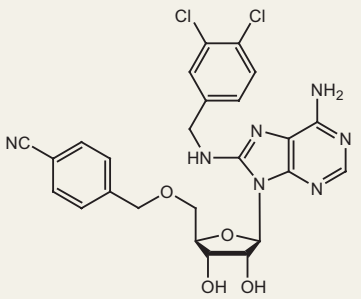
A full list of targets and related products are listed on pages 19-37



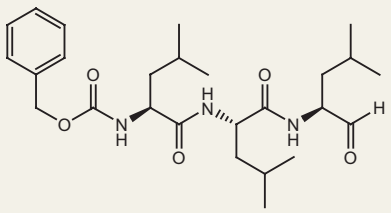
HBX 41108 (4285)
Selective USP7 inhibitor



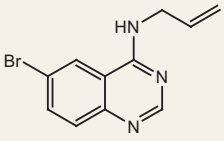
IU1 (4088)
USP14 inhibitor



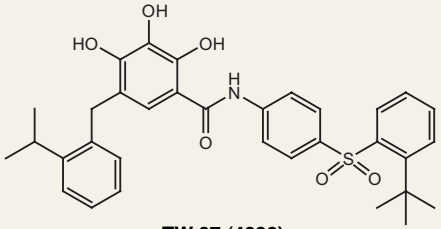
VER 155008 (3803)
Hsp70 inhibitor



MG 132 (1748)
Proteasome and calpain inhibitor. Inhibits NF-κB activation

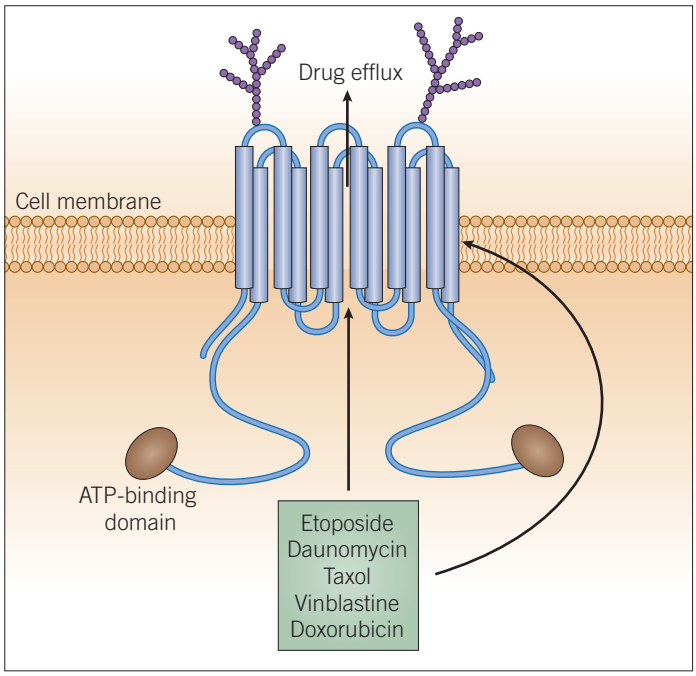


SMER 28 (4297)
Positive regulator of autophagy



TW 37 (4038)
Bcl-2 inhibitor; induces apoptosis

Figure 4 | Multidrug transporter



Multidrug transporters belong to the ABC (ATP Binding Cassette) superfamily of proteins that transport substances across membranes. Many are large multi transmembrane domain proteins such as this schematic representation of P-glycoprotein (from the gene, ABCB1 or MDR1). Numerous cytotoxic drugs are substrates for the P-glycoprotein transporter. Many of these substrates are hydrophobic and can be effluxed directly from the lipid bilayer of the cell membrane.

mediates p53 deubiquitination, which can be reversed by the Tocris licensed compound HBX 41108 (Cat. No. 4285) (Box 7). Disruption of proteasome activity has been proven clinically to have antitumor effects. Proteasome inhibitors such as MG 132 (Cat. No. 1748) induce cell cycle arrest by perturbing the degradation of cell cycle proteins. These compounds can stabilize propapoptotic proteins such as p53; reduce the levels of select antiapoptotic proteins such as Bcl-2; and may also repress propapoptotic NK-κB signaling.

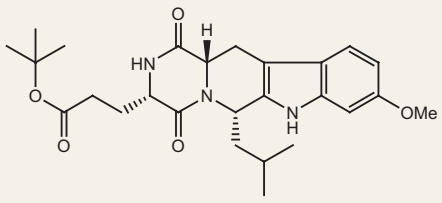
Multidrug Resistance

Another way in which cancer cells resist cell death is through the development of resistance to cancer therapeutics, termed 'multidrug resistance'. Increased expression of multidrug transporters leads to increased efflux of cytotoxic drugs.

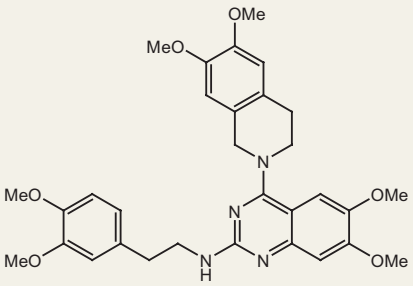
Multidrug transporters belong to the ATP-binding cassette (ABC) superfamily of proteins (Figure 4). P-glycoprotein (P-gp, ABCB1, MDR1) is a well-characterized human ABC transporter that was the first of its kind implicated in multidrug resistance. Substrates affected by this type of resistance include vinca alkaloids (vinblastine, Cat. No. 1256, and vincristine, Cat. No. 1257), anthracyclines (doxorubicin, Cat. No. 2252), and taxanes (such as taxol, Cat. No. 1097). Other transporters linked to the development of multidrug resistance include multidrug resistance-associated protein (MRP) and breast cancer resistance protein (BCRP). Ko 143 (Cat. No. 3241) is selective for BCRP over P-gp and MRP1 transporters, whilst CP 100356 (Cat. No. 4193) displays high affinity for P-gp and is selective against MRP1. PSC 833 (Cat. No. 4042) exhibits a different kind of activity – it modulates P-gp, reversing multidrug resistance to several cytotoxic drugs (Box 8).

Box 8: Multidrug Resistance Key Products

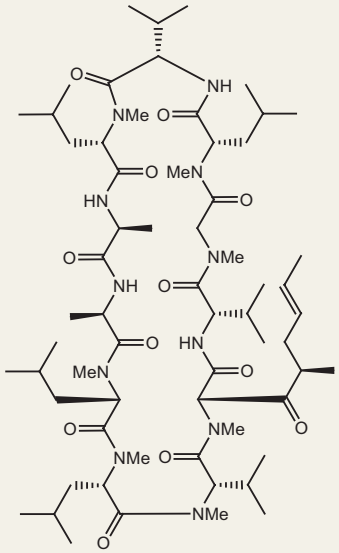
A full list of targets and related products are listed on pages 19-37



Ko 143 (3241)
Potent and selective BCRP inhibitor



CP 100356 (4193)
P-gp inhibitor



PSC 833 (4042)
Inhibitor of P-gp-mediated MDR

Angiogenesis

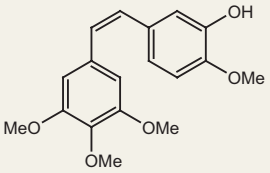
Products by Category	Page

Angiogenesis (also known as neovascularization) describes the generation of new blood vessels from pre-existing vasculature. It is a normal process in growth and development and is required for the formation of arteries, veins and capillaries. Proliferation of new blood vessels also has an essential role for the repair or regeneration of tissue during wound healing.

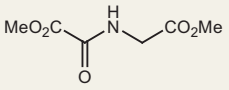
In order for tumor cells to survive, they must receive nutrients and oxygen from an increasingly hostile environment; as the tumor develops, cells near its center are gradually cut off from a regular blood supply and hypoxia is prevalent. Angiogenesis is one avenue by which tumor cells can continue to grow and develop; new blood vessels are grown to meet the metabolic demands of the tumor, to avoid the supply of oxygen and nutrients becoming rate-limiting. Hypoxic conditions stabilize the expression of hypoxia inducible factor-1 (HIF-1) and in turn, several angiogenic factors including VEGF, FGF and matrix metalloproteinases (MMPs) (Figure 5). Proteins such as thioredoxin and prolylhydroxylase that modulate the degradation of HIF-1 are of interest as potential therapeutic targets in cancer research.

Box 9: Angiogenesis Key Products

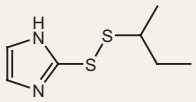
A full list of targets and related products are listed on pages 19-37



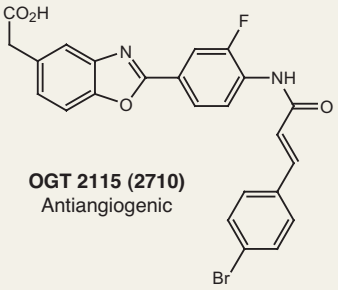
Combrestatin A4 (1495)
Antitumor, anti-angiogenic and antimetastatic agent



DMOG (4408)
Prolylhydroxylase inhibitor

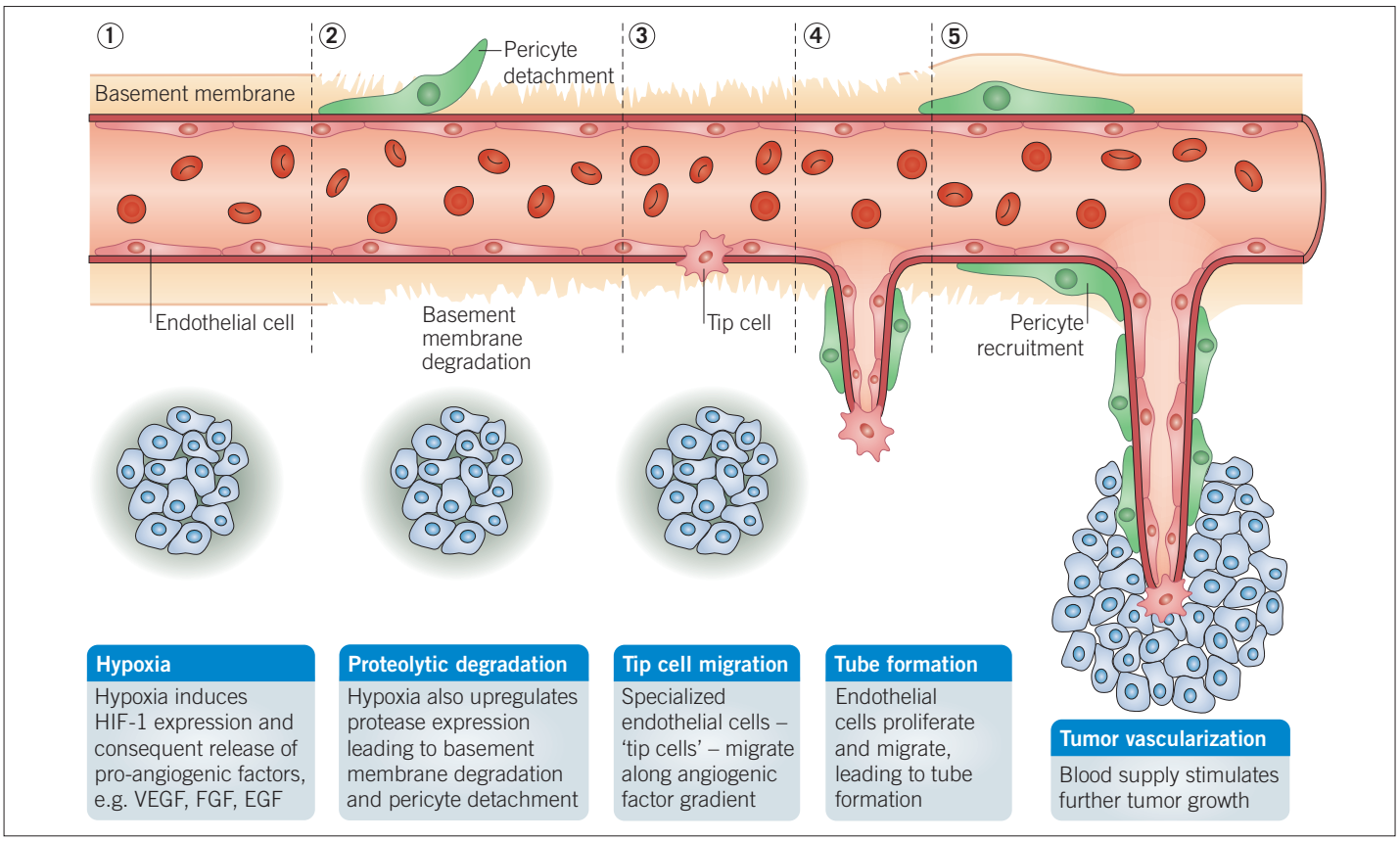


PX 12 (2954)
Competitive thioredoxin-1 inhibitor



OGT 2115 (2710)
Antiangiogenic

Figure 5 | Tumor vascularization



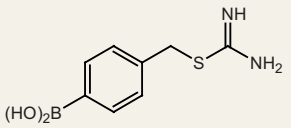
Invasion and Metastasis

Tumor metastasis is a multistep process involving the dissemination of tumor cells from the primary tumor to secondary tumors at a distant organ or tissue. One of the first steps in metastasis is the degradation of the basement membrane, a process in which MMPs have been implicated. MMPs are secreted by tumor cells themselves or by surrounding stromal cells stimulated by the nearby tumor. Numerous studies have linked altered MMP expression in different human cancers with poor disease prognosis. MMP-1, -2, -3, -7, -9, -13 and -14 all have elevated expression in primary tumors and/or metastases. Synthetic or natural inhibitors of MMPs result in inhibition of metastasis, while up-regulation of MMPs leads to enhanced cancer cell invasion. Other proteases, such as urokinase (uPA), are are also involved in extracellular matrix (ECM) degradation (Figure 6). This breakdown in matrix integrity establishes a route for the tumor cells to enter the bloodstream or lymphatic system where they can migrate to other areas of the body. Cancer cells can then begin to grow at a distant site by a process termed 'metastatic colonization.'

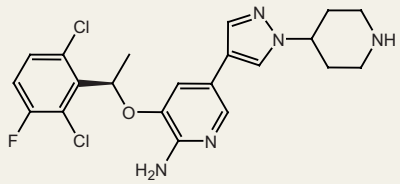
A process known as the epithelial-mesenchymal transition (EMT) enables cell mobility and facilitates the migration of epithelial cells that have gained mesenchymal characteristics. The MET receptor, also known as hepatocyte growth factor receptor (HGFR) is a proto-oncogenic receptor tyrosine kinase. The endogenous ligand for MET is hepatocyte growth factor/scatter factor (HGF), a disulfide-linked heterodimeric molecule produced predominantly by mesenchymal cells, hence MET receptor signaling is a key driver of invasive growth and the EMT. Aberrant activation of the HGF/MET pathway leads

Box 10: Invasion and Metastasis Key Products

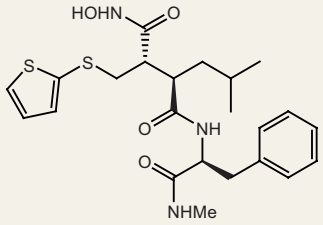
A full list of targets and related products are listed on pages 19-37



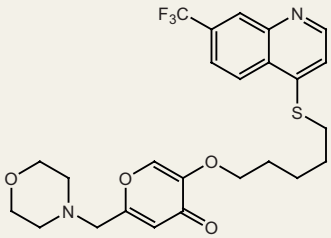
BC 11 (4372)
Selective urokinase (uPA) inhibitor



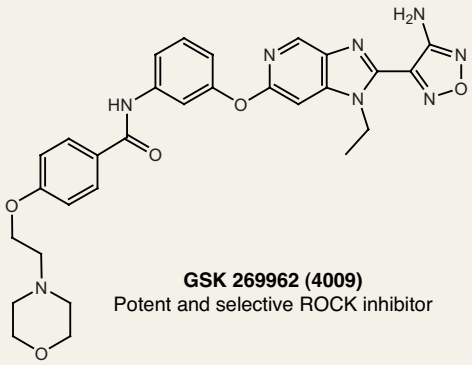
Crizotinib (4368)
Potent c-MET/ALK inhibitor



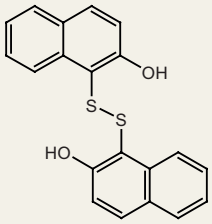
Batimastat (2961)
Potent, broad spectrum MMP inhibitor



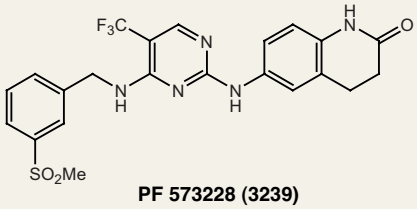
EHT 1864 (3872)
Potent inhibitor of Rac family GTPases



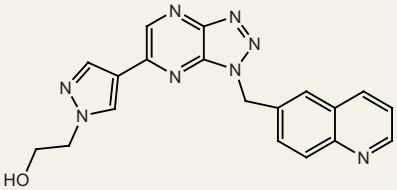
GSK 269962 (4009)
Potent and selective ROCK inhibitor



IPA 3 (3622)
Group I p21-activated kinase (PAK) inhibitor

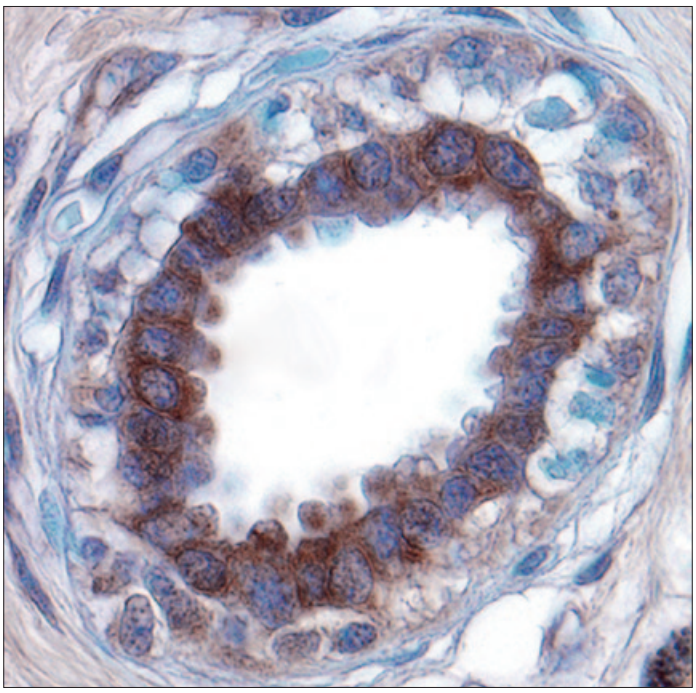


PF 573228 (3239)
Potent and selective FAK inhibitor



PF 04217903 (4239)
Highly selective c-Met inhibitor

Figure 6 | Extracellular matrix degradation



Urokinase-type Plasminogen Activator (uPA) expression detected in paraffin-embedded sections of human breast cancer tissue. uPA is a serine protease that is involved in ECM degradation, resulting in a loss of matrix integrity and a potential route through which tumor cells can to migrate to other tissues. Visualized here in brown using a Goat Anti-Human/Mouse uPA Affinity-purified Polyclonal Antibody (R&D Systems, Catalog #AF1310). Hematoxylin counterstain in blue.

to a variety of cancers. MET mutation is associated with a poor prognosis as it can trigger tumor growth, angiogenesis and metastasis.

Adhesive interactions play a critical role in metastatic tumor cell dissemination: for example, cadherins and integrins allow tumor cells to begin metastatic colonies at a second site. Focal adhesion kinase (FAK) also plays a part in cellular adhesion and functions at the site of cell attachment to the ECM. It is activated in response to integrin-ECM interactions, becoming a key focal point for numerous signaling components involved in cell growth and motility.

RhoA GTPase is one such signaling molecule modulated by FAK. Effectors of RhoA also include Rho-kinase (ROCK), which mediates its proliferative effects in tumor cells. The involvement of ROCK activity in proliferation has been elucidated by studies using ROCK-selective inhibitors, including Y 27632 (Cat. No. 1254) and GSK 269962 (Cat. No. 4009) (Box 10).

Rac is another member of the Rho family of GTPases, alongside RhoA and Cdc42. Inhibitors for multiple members of the Rac family have been synthesized (e.g. EHT 1864, Cat. No. 3872); others, such as NSC 23766 (Cat. No. 2161), interfere with Rac1 interactions – in this case, its activation by Rac-specific guanine nucleotide exchange factors (GEFs) (Box 10). Downstream of Rac1 and Cdc42 lie group I p21-activated kinases (PAKs 1-4). These molecules link Rho GTPases with cytoskeletal remodeling and cell motility, and have recently been shown to promote cell proliferation and regulate apoptosis. IPA 3 (Cat. No. 3622) promotes the inactive conformation of PAKs and inhibits PAK1-mediated signaling *in vivo*, exhibiting potential antitumor activity.

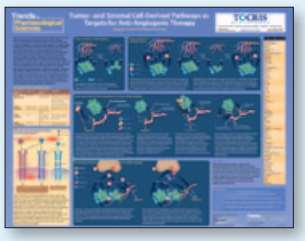
Metastasis is often closely linked to clinical prognosis. The mechanisms responsible for this process have consequently been of great interest in cancer research. In particular, the development of new pharmacological tools has helped elucidate the cellular changes and molecules involved in activating invasion and metastasis. Future research may also take into consideration the roles of immune cells and tumor metabolism in the dynamics of metastasis.

List of Acronyms

Acronym	Definition
ABC	ATP-binding cassette
AHR	Aryl hydrocarbon receptor
AMP	Adenosine monophosphate
AMPK	AMP-activated protein kinase
ATM	Ataxia telangiectasia mutated
ATP	Adenosine triphosphate
ATR	Ataxia telangiectasia and Rad3 related
BCRP	Breast cancer resistance protein
BER	Base-excision repair
Cdk	Cyclin-dependent kinase
Chk1	Checkpoint kinase 1
Chk2	Checkpoint kinase 2
c-MET	Hepatocyte growth factor receptor; also known as HGFR
DNA-PK	DNA-dependent protein kinase
DSB	Double strand break
ECM	Extracellular matrix
EGF	Epidermal growth factor
EMT	Epithelial-mesenchymal transition
ErbB	Epidermal growth factor receptor family; also known as EGFR
ERK	Extracellular signal-regulated kinase
FAK	Focal adhesion kinase
FGFR	Fibroblast growth factor
FLT3	Fms-like tyrosine kinase
FTase	Farnesylfarnesyltransferase
GEF	Guanine nucleotide exchange factor
GGTase 1	Geranylgeranyltransferase type 1
GPCR	G protein-coupled receptors
HDAC	Histone deacetylase
HGF	Hepatocyte growth factor
HIF-1	Hypoxia inducible factor-1
Hsp90	Heat shock protein 90
IGF1R	Insulin-like growth factor receptor

Acronym	Definition
JNK	c-Jun N-terminal kinase
MAPK	Mitogen-activated protein kinase
MDR	Multidrug resistance
MEK	also known as mitogen-activated protein kinase kinase, MAP2K
MGMT	O^6-methylguanine-DNA methyltransferase
MMP	Matrix metalloproteinase
Mps1	Monopolar spindle 1
MRP	Multidrug resistance-associated protein
mTOR	Mammalian target of rapamycin
NF-κB	Nuclear factor kappa B
PAK	p21-activated kinase
PARP	Poly(ADP-ribose) polymerase
PDGFR	Platelet-derived growth factor receptor
PDK	Phosphoinositide-dependent kinase-1
PI3K	Phosphoinositide 3-kinase
Plk	Polo-like kinase
PTEN	Phosphatase and tensin homolog
ROCK	Rho-kinase
RSK	Ribosomal S6 kinase
RTK	Receptor tyrosine kinase
S1P	Sphingosine-1-phosphate
S6K1	p70 ribosomal S6 kinase
SOS	Son of sevenless
SPHK1	Sphingosine kinase 1
SPHK2	Sphingosine kinase 2
SSB	Single strand break
STAT	Signal transducer and activator of transcription
TGF-β	Transforming growth factor β
uPA	Urokinase-type plasminogen activator
USP14	Ubiquitin carboxyl-terminase hydrolase 14
USP7	Ubiquitin-specific-processing protease 7; also known as ubiquitin carboxyl-terminal hydrolase 7
VEGFR	Vascular endothelial growth factor receptor

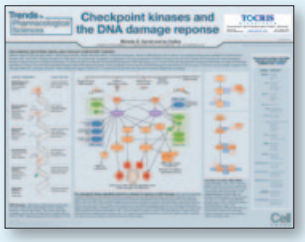
Related literature from Tocris that you may be interested in:



Tumor- and Stromal Cell-Derived Pathways as Targets for Anti-Angiogenic Therapy

N. Ferrara and Y. Crawford, Genentech

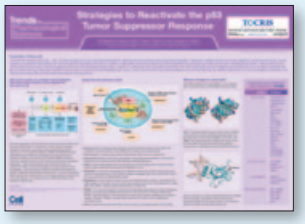
Angiogenesis is an integral process that occurs during tumorigenesis to supply nutrients to tumor cells. This poster summarizes antiangiogenic therapies targeting the VEGF pathway and the mechanisms of therapy resistance.



Checkpoint Kinases and the DNA Damage Response

M. Garrett and I. Collins, Institute of Cancer Research

Checkpoint kinases are a group of enzymes which regulate the progression of a cell through the cell cycle. This poster summarizes the response of the checkpoint kinase signaling network to DNA damage. It also highlights the different types of DNA damage that can occur and some of the treatment methods that are utilized in cancer therapy.



Strategies to Reactivate the p53 Tumor Suppressor Response

C. Brown *et al*, A*STAR

p53 is a key transcriptional regulator that is found to be frequently mutated and inactivated in tumors. This poster summarizes the main strategies that may be utilized to reactivate p53, including several small molecules and peptides which act to stabilize p53 and rescue wild-type activity.

MAPK Signaling

E. Zaganjor and M. Cobb, University of Texas Southwestern Medical Center

MAP kinase signaling is integral to the regulation of numerous cellular processes such as proliferation and differentiation, and as a result is an important focus of cancer research. This review discusses the regulation of the MAPK pathway and properties of MAPK cascades.

Stem Cell Growth and Differentiation

V. Christie and S. Przyborski, Durham University

Stem cells are unique in that they have the capacity to proliferate and differentiate into various defined cell types, including those found within the tumor mass in certain types of cancer. This review provides an overview of the small molecules used to control stem cell growth and differentiation.

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Cancer Research Products from Tocris

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Abl Kinase					
Inhibitors	3716	Adaphostin	$p210^{bcr/abl}$ kinase inhibitor	10 mg 50 mg	119 539
	4274	AP 24534	Potent multi-kinase and pan-BCR-ABL inhibitor	10 mg 50 mg	209 879
Akt (Protein Kinase B)					
Inhibitors	2558	10-DEBC	Selective Akt/PKB inhibitor	10 mg 50 mg	105 425
	3897	API-1	Selective Akt/PKB inhibitor. Antitumor	10 mg	255
	2151	API-2	Selective inhibitor of Akt/PKB signaling. Antitumor and antiviral	10 mg	235
	2926	FPA 124	Akt/PKB inhibitor	10 mg 50 mg	145 599
	4144	GSK 690693	Akt kinase inhibitor. Antitumor	10 mg 50 mg	235 999
	4168	PIT 1	Inhibits Akt signaling	10 mg 50 mg	129 575
	4398	SC 66	Allosteric Akt inhibitor	10 mg 50 mg	75 315
AMPK					
Activators	3336	A 769662	Potent AMPK activator	10 mg 50 mg	159 679
	2840	AICAR	AMPK activator	50 mg	95
	2864	Metformin	Activator of LKB1/AMPK; antidiabetic agent	100 mg	55
	4039	PT 1	AMPK activator	10 mg 50 mg	169 709
Inhibitors	3093	Dorsomorphin	Potent and selective AMPK inhibitor	10 mg 50 mg	159 679
Androgen Receptor					
Agonists	3812	CI-4AS-1	Steroidal androgen receptor agonist	10 mg 50 mg	169 795
	2822	Testosterone	Endogenous androgen receptor agonist	50 mg	55
Antagonists	3389	Bicalutamide	Non-steroidal androgen receptor antagonist	10 mg 50 mg	159 655
	4094	Flutamide	Non-steroidal androgen receptor antagonist	50 mg	35
	1759	Nilutamide	Androgen receptor antagonist. Orally active	100 mg	75
	3923	PF 998425	Non-steroidal androgen receptor antagonist	10 mg	169
Modulators	3813	TFM-4AS-1	Selective androgen receptor modulator (SARM)	10 mg 50 mg	169 795
Antiangiogenics					
Other	1495	Combretastatin A4	Inhibits tubulin polymerization. Antitumor, antiangiogenic and antimetastatic	10 mg 50 mg	159 655
	1461	Linomide	Immunomodulator with antiangiogenic properties	10 mg 50 mg	145 599
	2710	OGT 2115	Antiangiogenic. Heparanase inhibitor	1 mg 10 mg	59 119
	3750	TNP 470	Methionine aminopeptidase-2 inhibitor; antiangiogenic	5 mg	199

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Apoptosis and Autophagy Inducers					
Other	3868	CHM 1	Potent antitumor agent; inducer of apoptosis	10 mg 50 mg	129 575
	2841	Curcumin	Antitumor, anti-inflammatory and antioxidant	50 mg	49
	2137	2,3-DCPE	Selectively induces cancer cell apoptosis	10 mg 50 mg	75 315
	1770	Deguelin	Anticancer and antiviral agent; chemopreventive and proapoptotic	10 mg	159
	3590	Gambogic acid	Apoptosis inducer. Activates caspases and inhibits Bcl-2 family proteins	10 mg 50 mg	99 395
	4297	SMER 28	Positive regulator of autophagy	10 mg 50 mg	99 425
Aromatase					
Inhibitors	3388	Anastrozole	Potent aromatase (CYP19) inhibitor	10 mg 50 mg	159 655
	3759	Exemestane	Steroidal aromatase (CYP19) inhibitor	10 mg 50 mg	129 575
	4382	Letrozole	Potent, reversible non-steroidal aromatase inhibitor	10 mg 50 mg	55 199
	3278	YM 511	Potent aromatase (CYP19) inhibitor	10 mg 50 mg	129 575
Aryl Hydrocarbon Receptor					
Agonists	1803	ITE	Endogenous agonist of the aryl hydrocarbon receptor	10 mg	159
Antagonists	3859	6,2',4'-Trimethoxyflavone	Aryl hydrocarbon receptor antagonist	10 mg 50 mg	99 395
	3858	CH 223191	Potent aryl hydrocarbon receptor antagonist	10 mg 50 mg	129 575
ATM & ATR Kinase					
Inhibitors	2639	CGK 733	Selective inhibitor of ATR and ATM kinases	10 mg 50 mg	119 539
	3544	KU 55933	Potent and selective ATM kinase inhibitor	10 mg	169
	4176	KU 60019	Potent ATM kinase inhibitor	10 mg 50 mg	215 915
	3190	Mirin	MRN-ATM pathway inhibitor	10 mg 50 mg	119 539
Aurora Kinase					
Inhibitors	4291	CCT 137690	Potent pan-Aurora kinase inhibitor	10 mg 50 mg	195 825
	4066	TC-A 2317	Potent, selective Aurora kinase A inhibitor	10 mg 50 mg	189 819
	2458	ZM 447439	Inhibits Aurora kinase B	10 mg	209
Autotaxin					
Inhibitors	4196	HA 130	Selective autotaxin inhibitor	10 mg 50 mg	159 765
	3404	S 32826	Potent autotaxin inhibitor	10 mg	159
Bcl-2 Family					
Inhibitors	1541	HA14-1	Bcl-2 inhibitor. Induces apoptosis	10 mg 50 mg	119 509
	4038	TW 37	Bcl-2 inhibitor; induces apoptosis	10 mg 50 mg	199 849
Other	3367	AT 101	Downregulates Bcl-2 and Mcl-1; pro-apoptotic	10 mg 50 mg	129 575
	2160	Bax channel blocker	Inhibits Bax-mediated mitochondrial cytochrome c release	10 mg 50 mg	145 599
	1964	Gossypol	Pro-apoptotic; downregulates Bcl-2 and Bcl-XL	50 mg	75
	3816	Muristerone A	Stimulates Bcl-XL mRNA transcription; antiapoptotic	1 mg	169

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Broad Spectrum Protein Kinase Inhibitors					
Inhibitors	1683	K 252a	Protein kinase inhibitor	200 µg	215
	2002	Ro 31-8220 mesylate	Protein kinase inhibitor	10 mg	199
	1285	Staurosporine	Non-selective protein kinase inhibitor	100 µg	115
Calpain					
Inhibitors	2950	Acetyl-Calpastatin (184-210) (human)	Selective calpain inhibitor	1 mg	255
	3358	MG 101	Calpain inhibitor; activates p53-dependent apoptosis	5 mg	85
	1748	MG 132	Calpain and proteasome inhibitor. Inhibits NF-κB activation	5 mg	105
	1269	PD 150606	Cell permeable calpain inhibitor	10 mg 50 mg	129 575
Casein Kinase 1					
Inhibitors	2902	D 4476	Selective CK1 inhibitor. Also inhibits TGF-βRI	10 mg 50 mg	169 735
	3610	(*R*)-DRF053	Dual CK1/cdk inhibitor	10 mg 50 mg	199 849
	4281	PF 4800567	Selective casein kinase 1ε inhibitor	10 mg 50 mg	155 685
	3316	PF 670462	Potent and selective CK1ε and CK1δ inhibitor	10 mg 50 mg	169 709
Casein Kinase 2					
Inhibitors	3058	Ellagic acid	Selective inhibitor of CK2. Also inhibits glutathione S-transferase	50 mg	59
	2275	TBB	Selective cell-permeable CK2 inhibitor	10 mg 50 mg	75 285
	3675	TMCB	Dual-kinase inhibitor; inhibits CK2 and ERK8	10 mg 50 mg	105 425
Caspase					
Inhibitors	2172	AZ 10417808	Selective non-peptide caspase-3 inhibitor	10 mg 50 mg	169 735
	2166	Z-DEVD-FMK	Cell-permeable, irreversible caspase-3 inhibitor	1 mg	249
	2163	Z-VAD-FMK	Cell-permeable, irreversible caspase inhibitor	1 mg	199
Cdc25 Phosphatase					
Inhibitors	1867	NSC 663284	Potent, selective Cdc25 phosphatase inhibitor	10 mg	189
	1547	NSC 95397	Selective Cdc25 dual specificity phosphatase inhibitor	10 mg 50 mg	159 655
Cell Cycle Inhibitors					
Other	1417	Daidzein	Arrests cell cycle in G_1 phase	50 mg	85
	3715	Narciclasine	Antiproliferative agent; slows cell cycle progression	1 mg	135
Checkpoint Kinases					
Inhibitors	3034	NSC 109555	Selective Chk2 inhibitor	10 mg 50 mg	139 625
	2694	PD 407824	Selective inhibitor of Chk1 and Wee1	1 mg 10 mg	85 199
	4277	PF 477736	Selective Chk1 inhibitor	10 mg 50 mg	209 879
	2560	SB 218078	Inhibitor of checkpoint kinase 1 (Chk1)	1 mg 10 mg	99 235
	3038	TCS 2312	Potent Chk1 inhibitor	1 mg	159

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Chemokine Receptors					
Antagonists	3299	AMD 3100	Highly selective CXCR4 antagonist	10 mg	119
	4179	AMD 3465	Potent, selective CXCR4 antagonist	10 mg 50 mg	155 665
	2769	BX 513	Selective CCR1 antagonist	10 mg 50 mg	169 709
	3581	C 021	Potent CCR4 antagonist	10 mg 50 mg	159 765
	4320	FC 131	CXCR4 antagonist	1 mg	179
	2725	SB 225002	Potent and selective CXCR2 antagonist	10 mg 50 mg	159 655
	2724	SB 265610	Potent CXCR2 antagonist	1 mg 10 mg 50 mg	75 169 735
	3664	Teijin compound 1	Potent CCR2b antagonist	10 mg 50 mg	169 709
	2757	UCB 35625	Potent CCR1 and CCR3 antagonist	1 mg 10 mg	99 225
	3951	WZ 811	Potent CXCR4 antagonist	10 mg 50 mg	129 575
Cyclin-dependent Kinase					
Inhibitors	2072	Aminopurvalanol A	Cyclin-dependent kinase inhibitor	10 mg 50 mg	169 795
	2457	Arcyriaflavin A	Potent cdk4/cyclin D1 and CaM Kinase II inhibitor.	10 mg	169
	3968	AZD 5438	Potent cdk 1, 2 and 9 inhibitor	10 mg 50 mg	189 819
	3605	(*R*)-CR8	Dual cdk1/cdk5 inhibitor. Also inhibits CK1	10 mg 50 mg	199 849
	1398	Kenpaullone	Potent cyclin-dependent kinase inhibitor. Also inhibits GSK-3	10 mg	145
	2152	NSC 625987	Cdk4 inhibitor	10 mg 50 mg	139 625
	3135	NU 2058	Cdk1 and cdk2 inhibitor	10 mg 50 mg	129 575
	3301	NU 6140	Cdk2 inhibitor	10 mg 50 mg	169 709
	3140	PHA 767491	Dual cdc7/cdk9 inhibitor. Also inhibits MK-2	10 mg 50 mg	115 479
	1580	Purvalanol A	Cyclin-dependent kinase inhibitor	10 mg 50 mg	169 795
	1581	Purvalanol B	Cyclin-dependent kinase inhibitor	10 mg 50 mg	169 795
	4181	Ro 3306	Cdk 1 inhibitor	10 mg 50 mg	169 735
	2609	Ryuvidine	Cdk4 inhibitor	10 mg 50 mg	159 655
	4075	SNS 032	Potent cdk2, cdk7 and cdk9 inhibitor	10 mg 50 mg	189 819
	2907	SU 9516	Potent cdk2 inhibitor	10 mg 50 mg	115 479

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Cytokine and NF-κB Signaling					
Inhibitors	3713	Cryptotanshinone	STAT3 inhibitor. Also displays multiple other activities	10 mg 50 mg	109 455
	4079	Niclosamide	STAT3 inhibitor; also inhibits mTORC1 signaling	50 mg	75
	1947	PR 39 (porcine)	IκBα inhibitor	500 µg	255
	1778	Ro 106-9920	Inhibitor of NF-κB activation	10 mg 50 mg	119 539
	3035	SD 1008	JAK2/STAT3 signaling pathway inhibitor	10 mg 50 mg	129 575
	2476	SR 11302	Inhibitor of AP-1 transcription factor; antitumor agent	10 mg	169
	4426	Tanshinone IIA	Inhibits NF-κB and AP-1 DNA binding. Displays antioxidant properties	10 mg 50 mg	145 599
	2816	Withaferin A	Inhibits NF-κB activation	1 mg	105
Other	4316	Bropirimine	Immunomodulatory and antitumor compound	10 mg 50 mg	105 425
	4204	BTZO 1	MIF binder	10 mg 50 mg	105 425
DNA-dependent Protein Kinase					
Inhibitors	3271	Compound 401	Selective DNA-PK and mTOR inhibitor	10 mg 50 mg	159 655
	2088	DMNB	DNA-PK inhibitor	10 mg 50 mg	45 145
	2828	NU 7026	Selective DNA-PK inhibitor	10 mg 50 mg	139 625
	3712	NU 7441	Potent and selective DNA-PK inhibitor	10 mg 50 mg	159 765
Dynamin					
Inhibitors	1774	Dynamin inhibitory peptide	Dynamin inhibitor	1 mg	215
	1775	Dynamin inhibitory peptide, myristoylated	Cell-permeable dynamin inhibitor	1 mg	275
	1776	Dynamin inhibitory peptide, myristoylated (control)	Control peptide version of dynamin inhibitory peptide (Cat. No. 1774)	1 mg	275
	2897	Dynasore	Non-competitive dynamin inhibitor	10 mg 50 mg	109 455
	4222	Dynole 34-2	Dynamin I inhibitor	10 mg 50 mg	159 679
	3982	Mdivi 1	Dynamin inhibitor; attenuates mitochondrial division and apoptosis	10 mg 50 mg	75 315
	4224	MitMAB	Dynamin inhibitor	10 mg 50 mg	45 169
	4225	OctMAB	Dynamin inhibitor	10 mg 50 mg	45 169

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
EGFR					
Inhibitors	1276	AG 1478	Highly potent EGFR-kinase inhibitor	10 mg 50 mg	129 575
	0414	AG 490	EGFR-kinase inhibitor. Also JAK2, JAK3 inhibitor	10 mg 50 mg	99 395
	1555	AG 825	Selective ErbB2 inhibitor	10 mg 50 mg	105 425
	2417	BIBU 1361	Selective inhibitor of EGFR-kinase	1 mg 10 mg	85 199
	2416	BIBX 1382	Highly selective EGFR-kinase inhibitor	1 mg 10 mg	85 199
	3360	CGP 52411	EGFR inhibitor. Also inhibits Aβ42 fibril formation	10 mg 50 mg	119 539
	1110	Genistein	EGFR kinase inhibitor. Also estrogen and PPARγ ligand	10 mg 50 mg	45 145
	2239	GW 583340	Potent dual EGFR/ErbB2 inhibitor; orally active	10 mg 50 mg	159 765
	2646	HDS 029	Potent inhibitor of the ErbB receptor family	1 mg 10 mg	85 199
	3000	Iressa	Orally active, selective EGFR inhibitor	10 mg 50 mg	159 655
	3352	JNJ 28871063	Potent ErbB receptor family inhibitor	10 mg 50 mg	169 709
	1331	Lavendustin A	EGFR, $p60^{c\text{-}src}$ inhibitor	1 mg	145
	1037	PD 153035	EGFR-kinase inhibitor	10 mg 50 mg	119 509
	2615	PD 158780	Potent ErbB receptor family inhibitor	10 mg 50 mg	159 655
	3599	TAK 165	Potent and selective ErbB2 inhibitor	10 mg 50 mg	169 735
Estrogen and Related Receptors					
Agonists	1494	DPN	Highly potent ERβ agonist	10 mg 50 mg	99 451
	4276	ERB 041	Potent ERβ agonist	10 mg 50 mg	159 679
	3588	Estropipate	Estrogen receptor agonist and OATP1B1 inhibitor	50 mg	95
	3523	FERb 033	Potent and selective ERβ agonist	10 mg 50 mg	139 625
	1426	PPT	Subtype-selective ERα agonist	10 mg 50 mg	145 599
	2823	α-Estradiol	Endogenous estrogen receptor agonist	50 mg	59
	2824	β-Estradiol	Endogenous ER agonist	100 mg	59
Antagonists	1047	ICI 182,780	Estrogen receptor antagonist	1 mg 10 mg 50 mg	62 155 688
	2662	PHTPP	Selective ERβ antagonist	10 mg 50 mg	169 735
	0999	Tamoxifen	Estrogen receptor partial agonist/antagonist	100 mg	59
	3928	XCT 790	Selective ERRα antagonist/inverse agonist	10 mg 50 mg	139 625
	2183	ZK 164015	Potent estrogen receptor antagonist	10 mg 50 mg	145 599
Modulators	3999	Cyclofenil	Selective estrogen receptor modulator (SERM)	10 mg 50 mg	75 315
	2280	Raloxifene	Selective estrogen receptor modulator (SERM)	50 mg	75
Other	3705	Endoxifen	Potent antiestrogen; ERα ligand	10 mg 50 mg	169 735

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
FGFR					
Inhibitors	3724	PD 161570	Selective FGFR inhibitor	10 mg 50 mg	199 849
	3044	PD 173074	FGFR1 and -3 inhibitor	10 mg 50 mg	169 709
	3300	SU 5402	Potent FGFR and VEGFR inhibitor	1 mg	189
FLT3					
Inhibitors	4033	5'-Fluoroindirubinoxime	FLT3 inhibitor; displays antiproliferative activity	10 mg 50 mg	145 599
	2591	TCS 359	Potent FLT3 inhibitor	10 mg 50 mg	119 539
Focal Adhesion Kinase					
Inhibitors	3414	FAK Inhibitor 14	Selective FAK inhibitor	10 mg 50 mg	95 375
	4278	PF 431396	Dual FAK/PYK2 inhibitor	10 mg	209
	3239	PF 573228	Potent and selective FAK inhibitor	10 mg 50 mg	159 765
G-protein Signaling					
Inhibitors	2974	CCG 2046	Inhibitor of regulator of G-protein signaling 4 (RGS4)	10 mg 50 mg	119 539
	4028	CCG 63802	Inhibitor of regulator of G-protein signaling 4 (RGS4) protein	10 mg 50 mg	159 655
	3872	EHT 1864	Potent inhibitor of Rac family GTPases	10 mg 50 mg	169 795
	4266	ML 141	Selective inhibitor of Cdc42 Rho family GTPase	10 mg 50 mg	159 679
	2161	NSC 23766	Selective inhibitor of Rac1-GEF interaction; antioncogenic	10 mg 50 mg	119 539
	3324	QS 11	ARFGAP1 inhibitor; modulates Wnt/β-catenin signaling	10 mg 50 mg	159 655
	2221	Rac1 Inhibitor W56	Selective inhibitor of Rac1-GEF interaction	1 mg	179
	2222	Rac1 Inhibitor F56, control peptide	Control peptide version of Rac1 Inhibitor W56 (Cat. No. 2221)	1 mg	179
	2849	SecinH3	Sec7-specific GEF inhibitor (cytohesins)	10 mg 50 mg	189 819
Glycogen Synthase Kinase					
Inhibitors	4083	3F8	Potent and selective GSK-3β inhibitor	10 mg 50 mg	145 599
	3966	AR-A 014418	Selective GSK-3 inhibitor	10 mg 50 mg	139 625
	3194	BIO	Potent, selective GSK-3 inhibitor	10 mg 50 mg	129 575
	3874	BIO-acetoxime	Selective GSK-3α/β inhibitor	1 mg 10 mg	105 235
	1616	SB 216763	Potent, selective GSK-3 inhibitor	1 mg 10 mg 50 mg	65 139 625
	1617	SB 415286	Potent, selective GSK-3 inhibitor	10 mg 50 mg	159 655
	3869	TCS 2002	Potent GSK-3β inhibitor	10 mg 50 mg	159 765
	3835	TWS 119	GSK-3β inhibitor; induces neuronal differentiation in ESCs	10 mg	169

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Heat Shock Proteins					
Inhibitors	1515	17-AAG	Selective Hsp90 inhibitor	1 mg	135
	2610	17-DMAG	Water-soluble Hsp90 inhibitor	1 mg	189
	2435	CCT 018159	Hsp90 inhibitor	10 mg 50 mg	119 539
	3387	Gedunin	Hsp90 inhibitor; anticancer and antimalarial activity	10 mg	169
	1368	Geldanamycin	Selective Hsp90 inhibitor	1 mg	295
	3061	Macbecin I	Hsp90 inhibitor	1 mg	225
	1589	Radicicol	Hsp90 inhibitor	1 mg	109
	3803	VER 155008	Hsp70 inhibitor	10 mg 50 mg	169 709
Hedgehog Signaling					
Antagonists	3889	GANT 58	GLI1 antagonist; inhibits hedgehog (Hh) signaling	10 mg 50 mg	129 575
	3191	GANT 61	GLI antagonist; inhibits hedgehog (Hh) signaling	10 mg 50 mg	139 625
Inhibitors	1639	AY 9944	Inhibitor of hedgehog (Hh) signaling. Inhibits Δ7-dehydrocholesterol reductase	10 mg	139
	1623	Cyclopamine	Inhibitor of hedgehog (Hh) signaling	1 mg	159
	1974	SANT-1	Inhibitor of hedgehog (Hh) signaling; antagonizes smoothened activity	10 mg 50 mg	145 599
	3617	SANT-2	Inhibitor of hedgehog (Hh) signaling; antagonizes smoothened activity	10 mg 50 mg	159 655
	1638	U 18666A	Inhibitor of hedgehog (Hh) signaling. Also inhibits cholesterol synthesis	10 mg	159
HIF-1					
Inhibitors	4408	DMOG	Prolylhydroxylase inhibitor	10 mg 50 mg	55 215
	2954	PX 12	Competitive thioredoxin-1 inhibitor	10 mg 50 mg	105 425
Histone Deacetylase					
Inhibitors	2952	CI 994	Histone deacetylase inhibitor	10 mg 50 mg	115 479
	4001	KD 5170	Histone deacetylase inhibitor	10 mg	159
	2771	M 344	Histone deacetylase inhibitor	1 mg 10 mg 50 mg	55 119 509
	4077	MC 1568	Selectively inhibits HDAC class II (IIa)	10 mg 50 mg	159 655
	3747	NCH 51	Histone deacetylase inhibitor	10 mg 50 mg	139 625
	2521	NSC 3852	Histone deacetylase inhibitor	10 mg 50 mg	45 145
	4403	Pyroxamide	Histone deacetylase inhibitor	10 mg 50 mg	139 625
	2421	Scriptaid	Histone deacetylase inhibitor	10 mg 50 mg	109 455
	2682	Sodium 4-Phenylbutyrate	Histone deacetylase inhibitor	100 mg	75
	3850	Sodium butyrate	Histone deacetylase inhibitor	50 mg	45
	4270	TC-H 106	Class I histone deacetylase inhibitor	10 mg 50 mg	145 599
	1406	Trichostatin A	Histone deacetylase inhibitor	1 mg	159
	3402	Tubacin	HDAC 6 inhibitor; inhibits α-tubulin deacetylation.	1 mg	225
	2815	Valproic acid, sodium salt	Histone deacetylase inhibitor	100 mg	49

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
IκB Kinase					
Inhibitors	2539	IKK 16	Selective inhibitor of IKK	10 mg 50 mg	189 819
	2611	IMD 0354	Inhibitor of IKK-2	10 mg 50 mg	129 575
	4238	PF 184	Potent and selective IKK-2 inhibitor	10 mg	235
	3318	SC 514	IKK-2 inhibitor; attenuates NF-κB-induced gene expression	10 mg 50 mg	105 425
	2559	TPCA-1	Potent, selective inhibitor of IKK-2	10 mg	189
Insulin and Insulin-like Receptors					
Activators	1819	Demethylasterriquinone B1	Selective insulin RTK activator	5 mg	189
Agonists	3435	Insulin (human) recombinant expressed in yeast	Endogenous peptide agonist	10 mg	55
Inhibitors	2956	Picropodophyllotoxin	Selective IGF1R inhibitor	10 mg	169
	2768	PQ 401	IGF1R inhibitor	10 mg 50 mg	119 539
Integrin Receptors					
Antagonists	3900	TCS 2314	$\alpha_4\beta_1$ (VLA-4) antagonist	10 mg 50 mg	169 795
Inhibitors	4228	A 286982	Potent inhibitor of the LFA-1/ICAM-1 interaction	10 mg 50 mg	159 765
	3910	BIO 1211	Selective $\alpha_4\beta_1$ (VLA-4) inhibitor	1 mg	129
	3202	Echistatin, α1 isoform	$\alpha_V\beta_3$ and glycoprotein IIb/IIIa (integrin αIIbβ3) inhibitor	100 µg	275
	3498	RGDS peptide	Integrin binding sequence; inhibits integrin receptor function	10 mg	115
	4227	RWJ 50271	Inhibitor of LFA-1/ICAM mediated cell adhesion	10 mg 50 mg	159 679
JAK Kinase					
Inhibitors	1571	Cucurbitacin I	Selective inhibitor of STAT3/JAK2 signaling	1 mg	189
	2291	1,2,3,4,5,6-Hexabromocyclohexane	Inhibits JAK2 autophosphorylation	50 mg	95
	3395	Lestaurtinib	JAK2, FLT3 and TrkA inhibitor	1 mg	235
	4338	NSC 33994	JAK2 inhibitor	10 mg 50 mg	159 679
	4221	TCS 21311	Potent JAK3 inhibitor. Also inhibits GSK-3β and PKC	10 mg 50 mg	199 849
	3115	WHI-P 154	JAK3 kinase inhibitor. Also inhibits EGFR	10 mg 50 mg	129 575
	1367	ZM 39923	Potent, selective JAK3 inhibitor	10 mg 50 mg	145 599
	1366	ZM 449829	Potent, selective JAK3 inhibitor	10 mg 50 mg	119 539
Kinesin					
Inhibitors	3703	K 858	Selective ATP-uncompetitive mitotic kinesin Eg5 inhibitor	10 mg 50 mg	119 539
	1305	Monastrol	Selective inhibitor of mitotic kinesin Eg5	10 mg 50 mg	145 599
	2191	S-Trityl-L-cysteine	Potent, selective inhibitor of mitotic kinesin Eg5	50 mg	75
Ligases					
Inhibitors	3561	L189	DNA ligase I, III and IV inhibitor	10 mg 50 mg	129 575
	2978	PYR 41	Ubiquitin-activating enzyme (E1) inhibitor	10 mg 50 mg	169 795
	4375	SMER 3	Specific inhibitor of E3 ubiquitin ligase	10 mg 50 mg	145 599

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
MAPK					
Inhibitors	3314	BI 78D3	Selective, competitive JNK inhibitor	10 mg 50 mg	159 655
	3706	FR 180204	Selective ERK inhibitor	10 mg 50 mg	209 879
	1264	SB 202190	Potent, selective inhibitor of p38 MAPK	10 mg 50 mg	139 625
	1202	SB 203580	Selective inhibitor of p38 MAPK	1 mg 10 mg 50 mg	85 169 795
	1402	SB 203580	Selective inhibitor of p38 MAPK; water-soluble	10 mg	215
	1962	SB 239063	Potent, selective p38 MAPK inhibitor; orally active	10 mg	225
	3528	SCIO 469	Selective p38 MAPK inhibitor	10 mg 50 mg	189 819
	1496	SP 600125	Novel and selective JNK inhibitor	10 mg 50 mg	78 344
	3607	SU 3327	Selective JNK inhibitor	10 mg 50 mg	129 575
	3639	SX 011	p38 MAPK inhibitor	10 mg 50 mg	169 709
	4254	TAK 715	Potent p38 MAPK inhibitor; anti-inflammatory	10 mg 50 mg	159 765
	3222	TCS JNK 6o	Selective JNK inhibitor	10 mg 50 mg	169 735
	3916	VX 702	Orally active p38α and p38β inhibitor	10 mg	119
	3915	VX 745	Potent and selective p38α inhibitor	10 mg 50 mg	169 795
	4132	XMD 8-92	Selective ERK5/BMK1 inhibitor	10 mg 50 mg	189 819
	3101	XRP44X	Ras-Net pathway inhibitor	10 mg 50 mg	159 655
Matrix Metalloproteinase					
Inhibitors	2961	Batimastat	Potent, broad spectrum MMP inhibitor	1 mg 10 mg	99 235
	2632	CL 82198	Selective inhibitor of MMP-13	10 mg 50 mg	115 479
	3780	CP 471474	Broad spectrum MMP inhibitor	10 mg 50 mg	119 539
	4090	Doxycycline	Broad-spectrum MMP inhibitor; tetracycline derivative	50 mg	35
	2631	Marimastat	Broad spectrum MMP inhibitor	1 mg 10 mg	99 235
	2916	Ro 32-3555	Potent, collagenase-selective MMP inhibitor	10 mg	215
	4187	UK 356618	Potent and selective MMP-3 inhibitor	10 mg	235
	2900	UK 370106	Highly selective MMP-3 and MMP-12 inhibitor	10 mg	189
	4188	UK 383367	Potent and selective BMP-1 (PCP) inhibitor	1 mg 10 mg	99 235
	2633	WAY 170523	Potent and selective inhibitor of MMP-13	1 mg 10 mg	99 235

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
MEK					
Inhibitors	1777	Arctigenin	Potent MKK1 inhibitor. Also inhibits IκBα phosphorylation	10 mg 50 mg	75 315
	4192	PD 0325901	Selective inhibitor of MEK1/2	10 mg 50 mg	209 879
	4237	PD 184352	Selective MEK inhibitor	10 mg 50 mg	199 849
	2605	PD 198306	Selective inhibitor of MEK1/2	10 mg	225
	1213	PD 98059	MEK inhibitor	1 mg 10 mg 50 mg	55 119 509
	1969	SL 327	Selective inhibitor of MEK1 and MEK2; brain penetrant	1 mg 10 mg 50 mg	85 169 795
	1144	U0126	Potent, selective inhibitor of MEK1 and 2	5 mg 25 mg	169 735
Other	1868	U0124	Inactive analog of U0126 (Cat. No. 1144)	10 mg	145
MET					
Inhibitors	4368	Crizotinib	Potent c-MET/ALK inhibitor	10 mg 50 mg	195 825
	4239	PF 04217903	Highly selective c-Met inhibitor	10 mg 50 mg	209 879
	2693	PHA 665752	Potent and selective MET inhibitor	10 mg 50 mg	249 1055
	4101	SU 11274	Selective inhibitor of MET kinase activity	10 mg 50 mg	209 879
Methyltransferases					
Inhibitors	3842	5-Azacytidine	DNA methyltransferase inhibitor	50 mg	45
	4359	Lomeguatrib	MGMT inhibitor	10 mg 50 mg	189 819
	3295	RG 108	Non-nucleoside DNA methyltransferase inhibitor	10 mg 50 mg	115 479
	3861	UNC 0224	Potent G9a histone lysine methyltransferase (HMTase) inhibitor	10 mg 50 mg	169 795
	2293	Zebularine	DNA methyltransferase and cytidine deaminase inhibitor	10 mg	119
Microtubules					
Inhibitors	1364	Colchicine	Inhibitor of tubulin	1 g	95
	1643	D-64131	Inhibitor of tubulin polymerization. Antitumor *in vivo*	10 mg 50 mg	129 575
	1228	Nocodazole	Microtubule inhibitor	10 mg	75
	1697	Noscapine	Tubulin inhibitor; induces apoptosis	100 mg	75
Other	4138	ABT 751	Inhibitor of microtubule polymerization; antimitotic and antitumor	10 mg 50 mg	169 795
	3502	Epothilone B	Microtubule stabilization agent; promotes tubulin polymerization	100 µg	269
	2226	Flutax 1	Fluorescent taxol derivative	1 mg	179
	3728	Indibulin	Microtubule destabilizer	10 mg 50 mg	129 575
mTOR					
Inhibitors	3725	KU 0063794	Selective mTOR inhibitor	10 mg	209
	4257	PP 242	Dual mTORC1/mTORC2 inhibitor	10 mg 50 mg	189 819
	1292	Rapamycin	mTOR inhibitor; immunosuppressant	1 mg	215
	4247	Torin 1	Potent and selective mTOR inhibitor	10 mg 50 mg	209 879
	4248	Torin 2	Potent and selective mTOR inhibitor	10 mg 50 mg	189 819

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Multidrug Transporters					
Inhibitors	4193	CP 100356	P-gp inhibitor	10 mg 50 mg	189 819
	3241	Ko 143	Potent and selective BCRP inhibitor	1 mg 10 mg	79 215
	4107	Probenecid	MRP inhibitor	50 mg	25
	3722	Reversan	Selective MRP1 and P-gp inhibitor	10 mg 50 mg	169 709
Other	4042	PSC 833	Inhibitor of P-gp-mediated MDR	1 mg	189
	2944	XR 9051	Potent modulator of P-gp-mediated MDR	10 mg 50 mg	159 679
Other Kinases					
Inhibitors	3994	AZ 3146	Potent and selective monopolar spindle 1 (Mps1) kinase inhibitor	10 mg 50 mg	189 819
	2731	CGP 57380	Selective inhibitor of Mnk1	1 mg 10 mg 50 mg	75 169 709
	3622	IPA 3	Group I p21-activated kinase (PAK) inhibitor	10 mg 50 mg	95 375
	3604	(5*Z*)-7-Oxozeaenol	Potent and selective TAK1 MAPKKK inhibitor	1 mg	119
p53					
Inhibitors	3843	Cyclic Pifithrin-α	p53 inhibitor	10 mg 50 mg	129 575
	3503	HLI 373	Hdm2 inhibitor; activates p53-dependent transcription	10 mg 50 mg	129 575
	2936	NSC 66811	MDM2 inhibitor. Disrupts MDM2-p53 interaction	10 mg 50 mg	139 625
	3984	Nutlin-3	MDM2 antagonist; inhibits MDM2-p53 interaction	10 mg 50 mg	209 879
	1267	Pifithrin-α	p53 inhibitor. Also aryl hydrocarbon receptor agonist	10 mg 50 mg	119 539
	2443	RITA	p53-MDM2 interaction inhibitor; antitumor	1 mg 10 mg	75 169
	3929	SJ 172550	MDMX inhibitor. Disrupts MDMX-p53 interaction	10 mg 50 mg	139 625
Other	3023	CP 31398	p53-stabilizing agent	10 mg 50 mg	129 575
	3362	MIRA-1	Restores mutant p53 activity; proapoptotic	10 mg 50 mg	99 395
	2185	NSC 146109	Cell-permeable, genotype-selective antitumor agent; activates p53-dependent transcription	10 mg 50 mg	119 539
	2653	Pifithrin-μ	Inhibitor of p53-mitochondrial binding	10 mg 50 mg	75 315
	1862	PRIMA-1	Restores mutant p53 activity; induces apoptosis	10 mg 50 mg	105 425
	3710	PRIMA-1^{MET}	Restores mutant p53 activity	10 mg	119
	3214	RETRA	Antitumor agent; suppresses mutant p53-bearing cancer cells	10 mg 50 mg	129 575
	3365	Tenovin-1	Activates p53 transcriptional activity	10 mg 50 mg	75 315
	3356	WR 1065	p53 activator. Also ROS scavenger	10 mg 50 mg	75 285

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
PDGFR					
Inhibitors	1222	DMPQ	Potent, selective inhibitor of PDGFRβ	10 mg 50 mg	115 479
	3304	SU 16f	Potent and selective PDGFRβ inhibitor	10 mg 50 mg	169 709
	3335	SU 6668	PDGFR, VEGFR and FGFR inhibitor	10 mg 50 mg	159 679
PI 3-Kinase					
Inhibitors	3671	AS 252424	Selective inhibitor of PI 3-kinase γ	10 mg	189
	3578	AS 605240	Potent and selective PI 3-kinase γ (PI3Kγ) inhibitor	10 mg 50 mg	129 575
	3606	BAG 956	Dual PI 3-kinase and PDK1 inhibitor	10 mg 50 mg	199 849
	4026	GSK 1059615	Potent PI 3-kinase inhibitor	10 mg 50 mg	169 795
	1130	LY 294002	Selective PI 3-kinase inhibitor	2 mg 25 mg	109 455
	2418	LY 303511	Negative control of LY 294002 (Cat. No. 1130)	5 mg	109
	3977	3-Methyladenine	Class III PI 3-kinase inhibitor; also inhibits autophagy	50 mg	85
	2930	PI 103	Inhibitor of PI 3-kinase, mTOR and DNA-PK	1 mg 10 mg 50 mg	75 169 709
	2814	PI 828	PI 3-kinase inhibitor, more potent than LY 294002 (Cat. No. 1130)	1 mg 10 mg 50 mg	75 169 709
	3894	PP 121	Dual kinase inhibitor; inhibits PI 3K family kinases	10 mg 50 mg	139 625
	4264	TG 100713	PI3-kinase inhibitor	10 mg 50 mg	189 819
	1232	Wortmannin	Potent, irreversible inhibitor of PI 3-kinase. Also inhibitor of PLK1	1 mg 5 mg	75 285
Activators	1983	740 Y-P	Cell-permeable PI 3-kinase activator	1 mg	225
	4087	PS 48	PDK1 activator	10 mg 50 mg	99 395
Pim Kinase					
Inhibitors	3589	PIM-1 Inhibitor 2	Pim-1 kinase inhibitor	10 mg 50 mg	119 509
	2979	TCS PIM-1 1	Selective, ATP-competitive Pim-1 kinase inhibitor	10 mg 50 mg	129 575
	3714	TCS PIM-1 4a	Selective, ATP-competitive Pim kinase inhibitor	10 mg 50 mg	99 395
Polo-like Kinase					
Inhibitors	3116	Cyclapolin 9	Selective, ATP-competitive PLK1 inhibitor	10 mg 50 mg	115 479
	2977	GW 843682X	Selective inhibitor of PLK1 and PLK3	1 mg 10 mg 50 mg	75 169 735
	4292	SBE 13	Potent and selective PLK1 inhibitor	10 mg 50 mg	85 349

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Poly(ADP-ribose) Polymerase					
Inhibitors	3734	BYK 204165	Selective PARP-1 inhibitor	10 mg 50 mg	129 575
	3735	BYK 49187	PARP-1 and PARP-2 inhibitor	1 mg	85
	2496	DR 2313	Potent PARP inhibitor	1 mg 10 mg 50 mg	55 119 539
	4140	EB 47	Potent PARP-1 inhibitor	10 mg 50 mg	185 795
	2192	4-HQN	PARP inhibitor	50 mg	75
	4106	Nicotinamide	PARP-1 inhibitor	50 mg	25
	1401	NU 1025	Potent PARP inhibitor	10 mg 50 mg	119 539
	3255	PJ 34	Potent PARP inhibitor	10 mg 50 mg	139 625
	3736	UPF 1069	PARP-2 inhibitor	10 mg 50 mg	159 655
	3748	XAV 939	Tankyrase inhibitor; inhibits Wnt signaling	10 mg 50 mg	139 625
Proteasome					
Inhibitors	2564	AM 114	20S proteasome inhibitor	10 mg 50 mg	115 479
	4285	HBX 41108	Selective USP7 inhibitor	10 mg	175
	4088	IU1	USP14 inhibitor	10 mg 50 mg	129 575
	2267	Lactacystin	Cell-permeable, potent and selective proteasome inhibitor	200 µg	249
	4045	PSI	Proteasome inhibitor. Also prevents activation of NF-κB	5 mg	169
Protein Kinase D					
Inhibitors	3327	CID 755673	Selective protein kinase D inhibitor	10 mg	189
	3962	kb NB 142-70	Selective PKD inhibitor; analog of CID 755673 (Cat. No. 3327)	10 mg 50 mg	189 819
Raf Kinase					
Inhibitors	1381	GW 5074	Potent, selective c-Raf1 kinase inhibitor	10 mg 50 mg	145 599
	3185	L-779,450	Potent Raf kinase inhibitor	10 mg 50 mg	159 679
	2650	SB 590885	Potent B-Raf inhibitor	10 mg 50 mg	199 849
	1321	ZM 336372	Potent, selective c-Raf inhibitor	10 mg 50 mg	169 709

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Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Rho-kinases					
Inhibitors	0541	Fasudil	Inhibitor of cyclic nucleotide dependent- and Rho-kinases	10 mg 50 mg	119 509
	2485	Glycyl-H 1152	Selective Rho-kinase (ROCK) inhibitor. More selective analog of H 1152 dihydrochloride (Cat. No. 2414)	1 mg	209
	4009	GSK 269962	Potent and selective ROCK inhibitor	10 mg 50 mg	209 879
	3726	GSK 429286	Selective Rho-kinase (ROCK) inhibitor	1 mg 10 mg 50 mg	79 215 915
	2414	H 1152	Selective Rho-kinase (ROCK) inhibitor	1 mg	169
	2415	HA 1100	Cell-permeable, selective Rho-kinase inhibitor	10 mg	199
	4118	SB 772077B	Potent Rho-kinase inhibitor; vasodilator	10 mg 50 mg	215 915
	3667	SR 3677	Potent, selective Rho-kinase (ROCK) inhibitor	10 mg 50 mg	199 849
	1254	Y-27632	Selective p160ROCK inhibitor	1 mg 10 mg 50 mg	79 215 915
RSK					
Inhibitors	4037	BRD 7389	p90 ribosomal S6 kinase inhibitor	10 mg 50 mg	159 655
	4032	PF 4708671	S6K1 inhibitor	10 mg 50 mg	169 795
	2250	SL 0101-1	Selective p90 ribosomal S6 kinase (RSK) inhibitor	1 mg	249
Sir2-like Family Deacetylases					
Inhibitors	3233	AGK 2	Selective SIRT2 inhibitor	10 mg 50 mg	159 679
	2780	EX 527	Selective SIRT1 inhibitor	1 mg 10 mg 50 mg	65 159 655
	4127	Salermide	SIRT1 and SIRT2 inhibitor	10 mg 50 mg	95 375
	3521	Sirtinol	Selective sirtuin family deacetylase inhibitor	10 mg 50 mg	139 625
	1542	Splitomicin	Sir2p inhibitor	10 mg 50 mg	115 479
Sphingosine-1-phosphate					
Agonists	3601	CYM 5442	Selective $S1P_1$ receptor agonist	10 mg 50 mg	169 795
	4289	RP 001	Potent $S1P_1$ agonist	10 mg 50 mg	175 769
	2284	SEW 2871	Cell-permeable, selective $S1P_1$ receptor agonist	10 mg 50 mg	75 315
Antagonists	2392	JTE 013	$S1P_2$ receptor antagonist	10 mg	169
	4195	VPC 23019	$S1P_1$ and $S1P_3$ antagonist	10 mg	255
Inhibitors	3711	SK1-I	Sphingosine kinase 1 (SphK1) inhibitor; antiproliferative	10 mg	235
	2097	SKI II	Selective non-lipid inhibitor of sphingosine kinase	10 mg 50 mg	119 539

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Src Family Kinases					
Inhibitors	3914	A 419259	Inhibitor of Src family kinases	10 mg	235
	3963	AZM 475271	Src tyrosine kinase inhibitor	10 mg 50 mg	199 849
	4361	Bosutinib	Dual Src-Abl inhibitor; antiproliferative	10 mg	195
	2471	ER 27319	Selective Syk kinase inhibitor	10 mg 50 mg	115 479
	1629	Herbimycin A	Src family kinase inhibitor. Also Hsp90 inhibitor	100 µg	149
	2877	MNS	Selective inhibitor of Src and Syk	50 mg	75
	3063	1-Naphthyl PP1	Src family kinase inhibitor; also inhibits c-Abl	10 mg 50 mg	215 915
	3785	PD 166285	Potent Src inhibitor; also inhibits FGFR1, PDGFRβ and Wee1	1 mg 10 mg	85 199
	1923	pp60 c-src (521-533) (phosphorylated)	Inhibits tyrosine kinase activity of $pp60^{c\text{-}src}$ and $pp60^{v\text{-}src}$	1 mg	145
	1397	PP 1	Potent, selective Src inhibitor	10 mg	209
	1407	PP 2	Potent, selective Src inhibitor	10 mg	209
	3642	Src I1	Dual site Src kinase inhibitor	10 mg 50 mg	139 625
Telomerase					
Inhibitors	2981	BIBR 1532	Selective telomerase inhibitor	10 mg 50 mg	159 655
Other	2483	Costunolide	Inhibitor of human telomerase activity	1 mg 10 mg	59 145
	4253	TMPyP4 tosylate	Inhibitor of human telomerase	50 mg	75
TGF-β Receptors					
Inhibitors	2939	A 83-01	Selective inhibitor of TGF-βRI, ALK4 and ALK7	10 mg 50 mg	169 709
	2718	LY 364947	Selective inhibitor of TGF-βRI	1 mg 10 mg	75 169
	1614	SB 431542	Potent, selective inhibitor of TGF-βRI, ALK4 and ALK7	1 mg 10 mg	99 225
	3263	SB 505124	Selective inhibitor of TGF-βRI, ALK4 and ALK7	10 mg 50 mg	175 769
	3211	SB 525334	Selective inhibitor of TGF-βRI	10 mg 50 mg	159 765
	3269	SD 208	Potent ATP-competitive TGF-βRI inhibitor	10 mg 50 mg	139 625
	3742	SJN 2511	Selective inhibitor of TGF-βRI	10 mg 50 mg	139 625
Transferases					
Inhibitors	4200	C 646	Selective p300/CBP inhibitor	10 mg 50 mg	189 819
	2406	FTI 276	Farnesyltransferase (FTase) inhibitor; antitumor	1 mg	105
	2407	FTI 277	Prodrug form of FTI 276 (Cat. No. 2406)	1 mg	105
	2430	GGTI 298	Geranylgeranyltransferase I (GGTase I) inhibitor	1 mg	159
	4294	LB 42708	Selective farnesyltransferase (FTase) inhibitor	10 mg 50 mg	169 795
	3416	Tris DBA	*N*-myristoyltransferase-1 inhibitor; antiproliferative	10 mg 50 mg	95 375

Cancer Research Products – continued

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Translocation, Exocytosis & Endocytosis					
Inhibitors	4417	DBeQ	Selective and reversible p97 inhibitor	10 mg 50 mg	129 575
	3922	Eeyarestatin I	Potent inhibitor of ER-associated protein degradation and translocation	10 mg	169
	1850	Exo1	Inhibits Golgi-ER traffic; blocks exocytosis	10 mg 50 mg	99 395
	1987	Leptomycin B	Inhibits nuclear export of proteins; antitumor	5 µg	285
Other	1231	Brefeldin A	Disrupts protein translocation to Golgi	5 mg	119
	2334	D15	Endocytosis blocker	1 mg	159
Trk Receptors					
Agonists	3826	7,8-Dihydroxyflavone	TrkB agonist	10 mg 50 mg	129 575
Inhibitors	2617	AG 879	TrkA inhibitor	10 mg	145
	2238	GW 441756	Potent, selective TrkA inhibitor	10 mg 50 mg	159 765
Other	2837	BDNF (human)	Activates TrkB and p75 receptors	10 µg	279
	2087	NTR 368	$p75^{NTR}$ fragment; induces apoptosis	1 mg	159
	2272	Ro 08-2750	Inhibits NGF binding to $p75^{NTR}$ and TrkA	1 mg 10 mg 50 mg	65 159 655
Ubiquitin					
Inhibitors	3998	LDN 57444	Ubiquitin C-terminal hydrolase-L1 (UCH-L1) inhibitor	10 mg 50 mg	109 455
Other	2647	NSC 632839	Inhibitor of ubiquitin isopeptidase activity	10 mg 50 mg	105 425
Urokinase					
Inhibitors	0442	4-Chlorophenylguanidine	Urokinase (uPA) inhibitor	100 mg	159
	4372	BC 11	Selective urokinase (uPA) inhibitor	10 mg 50 mg	125 515
VEGFR					
Inhibitors	4350	Axitinib	Potent VEGFR-1, -2 and -3 inhibitor	10 mg	195
	3882	(*E*)-FeCP-oxindole	Selective VEGFR-2 inhibitor	10 mg	199
	3883	(*Z*)-FeCP-oxindole	Selective VEGFR-2 inhibitor	10 mg	199
	2542	Ki 8751	Potent, selective VEGFR-2 inhibitor	10 mg 50 mg	159 765
	1459	SU 4312	Potent inhibitor of VEGFR tyrosine kinase	10 mg	209
	3037	SU 5416	VEGFR inhibitor. Also inhibits KIT, RET, MET and FLT3	10 mg 50 mg	119 539
	3768	Sunitinib	Potent VEGFR, PDGFRβ and KIT inhibitor	10 mg 50 mg	169 795
	2475	ZM 323881	Potent, selective inhibitor of VEGFR-2	1 mg 10 mg	85 209
Other	2499	ZM 306416	Inhibitor of VEGF receptor tyrosine kinase	1 mg 10 mg	75 169

Category	Cat. No.	Product Name	Description	Unit Size	US Dollar
Wnt Signaling					
Other	4344	FH 535	Inhibitor of Wnt/β-catenin signaling	10 mg 50 mg	75 315
	4299	iCRT 14	Inhibits β-catenin-responsive transcription (CRT)	10 mg 50 mg	169 709
	3533	IWP 2	Inhibitor of Wnt processing and secretion; blocks β-catenin accumulation	10 mg 50 mg	139 625
	3532	*endo*-IWR 1	Axin stabilizer; promotes β-catenin phosphorylation	10 mg 50 mg	115 479
	3947	*exo*-IWR 1	Negative control for endo-IWR 1 (Cat. No. 3532)	10 mg 50 mg	115 479
	3534	PNU 74654	β-catenin binder; inhibits Wnt signaling	10 mg 50 mg	115 479

Prices are correct at the time of publication. For the latest information please visit www.tocris.com

Chemotherapeutics

Cat. No.	Product Name	Description	Unit Size	Dollar
4219	Banoxantrone	Prodrug topoisomerase II inhibitor	10 mg 50 mg	159 679
3681	Bendamustine	Cytostatic agent; exhibits DNA alkylating and purine analog properties	10 mg 50 mg	99 395
1100	Camptothecin	DNA topoisomerase inhibitor	25mg	59
2626	Carboplatin	DNA cross-linking antitumor agent	50 mg	85
2251	Cisplatin	Potent pro-apoptotic anticancer agent; activates caspase-3	50 mg	75
2688	CPT 11	DNA topoisomerase I inhibitor; antitumor	10 mg 50 mg	169 709
4091	Cyclophosphamide	Alkylating agent; chemotherapeutic	50 mg	45
2624	Decitabine	DNA methyltransferase inhibitor	10 mg 50 mg	115 479
3857	Dexrazoxane	Topoisomerase II inhibitor	10 mg 50 mg	105 425
4056	Docetaxel	Microtubule stabilizer	10 mg 50 mg	105 425
2252	Doxorubicin	Antitumor antibiotic agent. Inhibits DNA topoisomerase II	10 mg 50 mg	119 539
3260	Epirubicin	Inhibits DNA synthesis and function. Inhibits DNA topoisomerase II.	10 mg	159
1226	Etoposide	Topoisomerase II inhibitor	100 mg	109
3495	Fludarabine	Purine analog; inhibits DNA synthesis	10 mg 50 mg	105 425
3257	5-Fluorouracil	Inhibits RNA and DNA synthesis	50 mg	45
3259	Gemcitabine	DNA synthesis inhibitor	10 mg 50 mg	95 375
4103	6-Mercaptopurine	Purine analog; inhibits DNA and RNA synthesis	50 mg	35
1230	Methotrexate	Cytotoxic agent	100 mg	95
1807	2-Methoxyestradiol	Apoptotic and antiangiogenic agent	10 mg 50 mg	85 339
3258	Mitomycin C	DNA cross-linking antitumor agent	10 mg	119
4250	Mitoxantrone	Topoisomerase II inhibitor; immunosuppressive and antineoplastic agent	50 mg	95
2623	Oxaliplatin	DNA cross-linking antitumor agent	50 mg	105
2684	SN 38	DNA topoisomerase I inhibitor; antitumor	10 mg 50 mg	95 375
1621	Streptozocin	DNA alkylator; antitumor and induces diabetes	100 mg 500 mg	49 139
1097	Taxol	Promotes assembly and inhibits disassembly of microtubules	10 mg 50 mg	105 395
2706	Temozolomide	DNA-methylating antitumor agent	10 mg 50 mg	75 315
4061	6-Thioguanine	Anticancer and immunosuppressive agent	50 mg	25
1256	Vinblastine	Disrupts microtubules	10 mg 50 mg	95 375
1257	Vincristine	Disrupts microtubules	10 mg 50 mg	119 539
3401	Vinorelbine	Selective mitotic microtubule antagonist	10 mg 50 mg	119 509

Further Reading

Please refer to the list of recommended papers for more information.

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Barr *et al* (2004) Polo-like kinases and the orchestration of cell division. *Nat. Rev. Mol. Cell Biol.* **5** 429.

Castedo *et al* (2004) Cell death by mitotic catastrophe: a molecular definition. *Oncogene* **23** 2825.

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Lan and Cleveland (2010) A chemical tool box defines mitotic and interphase roles for Mps1 kinase. *J. Cell Biol.* **190** 21.

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Olsson et al (2011) Caspases and cancer. *Cell Death Differ.* 18(9):1441-9.

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R&D Systems, Inc.
614 McKinley Place NE
Minneapolis
MN 55413, USA
Phone: (800) 343-7475 (612) 379-2956
Fax: (612) 656-4400
info@RnDSystems.com

R&D Systems Europe, Ltd.
19 Barton Lane
Abingdon Science Park
Abingdon, OX14 3NB, UK
Phone: +44 (0) 1235 529449
Fax: +44 (0) 1235 533420
info@RnDSystems.co.uk

R&D Systems China Co., Ltd.
24A1 Hua Min Empire Plaza
726 West Yan An Road
Shanghai, PRC 200050
Phone: +86 (21) 52380373
Fax: +86 (21) 52371001
info@RnDSystemsChina.com.cn