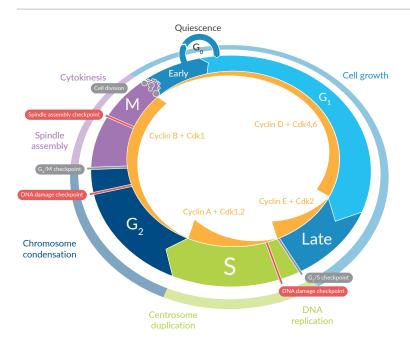
# Cell Cycle & DNA Damage

The cell cycle is a tightly regulated process of cell growth, DNA replication, and cell division. Progression through the phases of the cell cycle is controlled by cyclins in association with cyclin-dependent kinases (CDKs). Throughout this process, cells encounter several checkpoints designed to detect and correct issues such as DNA damage or improper spindle formation before allowing continuation of the cell cycle. Dysregulation of the cell cycle and checkpoint mechanisms can lead to aberrant proliferation and genomic instability and is often observed in cancer cells.





### CELL CYCLE ASSAY KITS

# Cell Cycle Phase Determination Kit *Item No.* 10009349

- Easy-to-use kit for flow cytometric analysis of cell cycle progression
- Determine the percentage of cells in G<sub>0</sub>/G<sub>1</sub>, G<sub>2</sub>, or S phase

### Senescence-Associated β-Galactosidase Staining Kit Item No. 602010

 Enables visual detection of senescent cells using a chromogenic substrate

### **CDK Inhibitors**

Cyclin-dependent kinases (CDKs) regulate progression through each stage of the cell cycle and are often dysregulated in cancer cells. Distinct CDKs and specific cyclin partners regulate different cell cycle phases. Cdk4/cyclin D and Cdk6/cyclin D drive progression through  $G_1$ , Cdk2/cyclin E regulates entry into S phase, Cdk1/cyclin A and Cdk2/cyclin A control progression through S phase, and Cdk1/cyclin B drives cells into mitosis.

Item No.	Product Name	Activity
21765	Butyrolactone I	An ATP-competitive inhibitor of Cdk1 ( $IC_{50}$ = 20 µg/ml in PC-14 cells); induces dose-dependent $G_2$ /M arrest, inhibits DNA synthesis, and decreases Cdk1 protein expression <i>in vitro</i>
18859	Cdk1/2 Inhibitor III	A cell-permeable inhibitor of Cdk1/cyclin B and Cdk2/cyclin A ( $IC_{50}$ s = 0.6 and 0.5 nM, respectively)
17666	LEE011	Targets Cdk4/cyclin D1 and Cdk6/cyclin D3 at nanomolar concentrations; prevents CDK-mediated $G_1/S$ phase transition, arresting the cell cycle in the $G_1$ phase, suppressing DNA synthesis, and inhibiting cancer cell growth
21560	LY2835219	Orally bioavailable dual inhibitor of Cdk4 and Cdk6 ( $IC_{50}$ s = 2 and 10 nM, respectively); induces $G_1$ arrest
13317	NU 6102	Inhibits Cdk1 and Cdk2 ( $IC_{50}$ s = 9.5 and 5.4 nM, respectively); delays cell entry into mitosis
21474	PHA-848125	An ATP-competitive inhibitor of Cdk2/cyclin A (IC $_{50}$ = 45 nM); at least 3-fold less potent at Cdk1, -3, -4, -5, and -7
16273	PD 0332991 (hydrochloride)	An orally active, selective inhibitor of Cdk4 (IC $_{50}$ = 11 nM) and Cdk6 (IC $_{50}$ = 16 nM); induces G $_{1}$ arrest
15149	Ro 3306	A cell-permeable, reversible inhibitor of Cdk1; selective for Cdk1/cyclin B1 ( $K_i = 35$ nM) over Cdk1/cyclin A ( $K_i = 110$ nM); induces reversible cell cycle arrest at the $G_2$ /M phase border
10009569	(R)-Roscovitine	An inhibitor of Cdk2/cyclin E (IC $_{50}$ = 0.1 $\mu$ M); also inhibits Cdk7/cyclin H, Cdk5/p35, and cell division cycle (cdc)/cyclin B (IC $_{50}$ s = 0.49, 0.16, and 0.65 $\mu$ M, respectively)

See all CDK inhibitors at www.caymanchem.com

# **DNA Damaging Agents**

At various points throughout the cell cycle, DNA damage can be caused by endogenous stressors, including reactive oxygen species, as well as compounds including topoisomerase inhibitors, DNA alkylating or crosslinking agents, and nucleoside analogs, triggering activation of DNA damage checkpoints. Many such agents have been used in chemotherapy regimens, as activation of the intra-S-phase DNA damage checkpoint and subsequent inhibition of DNA synthesis can lead to apoptosis or senescence.

### **DNA Topoisomerase Inhibitors**

Inhibition of DNA topoisomerases can lead to single- or double-strand breaks, depending on cell cycle phase and which topoisomerase is inhibited.

Item No.	Product Name
11694	Camptothecin
15007	Doxorubicin (hydrochloride)
12092	Etoposide
14180	Irinotecan (hydrochloride hydrate)
14129	Topotecan (hydrochloride)

See all DNA topoisomerase inhibitors at www.caymanchem.com

#### **DNA Alkylating Agents**

Alkylating agents react with and add alkyl groups to DNA bases, leading to DNA strand breaks, inhibition of cell division, and eventual cell death.

Item No.	Product Name
23693	Bendamustine (hydrochloride)
19527	4-hydroperoxy Cyclophosphamide
16665	Melphalan
11435	Mitomycin C
14163	Temozolomide

See all DNA alkylating agents at www.caymanchem.com

### **DNA Crosslinking Agents**

Platinum-based DNA crosslinkers can form inter- and intra-strand DNA crosslinks, as well as DNA-protein crosslinks, that interfere with DNA and RNA synthesis.

Item No.	Product Name
13112	Carboplatin
13119	Cisplatin
29001	Nedaplatin
13106	Oxaliplatin

See all platinum-based DNA crosslinking agents at www.caymanchem.com

#### Nucleoside Analogs

These anticancer agents can be incorporated into DNA during replication, leading to stalled replication forks and chain termination. Several nucleoside analogs also inhibit key cellular enzymes.

Item No.	Product Name
16069	Cytarabine
14154	Floxuridine
14128	Fludarabine
14416	5-Fluorouracil
11690	Gemcitabine
21366	Trifluorothymidine

See all nucleoside analogs at www.caymanchem.com

## Tools to Measure DNA Damage

# **DNA/RNA Oxidative Damage** (High Sensitivity) ELISA Kit

Item No. 589320

Measure the major oxidative damage markers 8-hydroxy-2'-deoxyguanosine, 8-hydroxyguanosine, and 8-hydroxyguanine in a variety of sample types.

## **DNA/RNA Oxidative Damage** (Clone 7E6.9) ELISA Kit

Item No. 501130

Measure the DNA oxidative damage marker 8-hydroxy-2'-deoxyguanosine and the RNA damage marker 8-hydroxyguanosine with equal selectivity and sensitivity.



Read our News article to compare these assay kits side-by-side and choose the best one for your experiments at www.caymanchem.com/DNA-RNA-Damage

# **DNA Damage Checkpoints & Repair**

Detection of DNA damage can activate cell cycle checkpoints in  $G_1$  phase, S phase, and at the  $G_2/M$  transition to arrest the cell cycle and allow for DNA repair. Ataxia-telangiectasia and Rad3-related protein/kinase (ATR) is activated in response to DNA replication stress and single-strand breaks, whereas Ataxia-telangiectasia mutated kinase (ATM) is primarily activated by double-strand breaks. ATR and ATM activate the checkpoint kinases Chk1 and Chk2, respectively, which regulate downstream effectors to control activation of CDK/cyclin complexes and cell cycle progression. Inhibiting the ATR/ATM-Chk1/Chk2 pathways, the additional checkpoint kinase Wee1, or DNA repair enzymes can force cells with damaged DNA to progress into mitosis, leading to mitotic catastrophe and cell death or senescence.

#### **ATM Inhibitors**

Item No.	Product Name
25648	AZD 0156
16336	Ku-55933
17502	Ku-60019

See all ATM inhibitors at www.caymanchem.com

#### **ATR Inhibitors**

Item No.	Product Name
17589	AZ 20
21035	AZD 6738
17587	VE-821

See all ATR inhibitors at www.caymanchem.com

# KINASE RESOURCE CENTER

- · Browse more than 1,300 kinase inhibitors
- · Find tools and resources for inhibitor selection



#### **PARP1** Inhibitors

Poly(ADP-ribose) polymerase 1 (PARP1) binds to various types of DNA lesions, where its activation facilitates chromatin reorganization around the DNA lesion and subsequent DNA repair. PARP1 inhibitors have been used to target the DNA damage response in several types of BRCA-mutated cancers.

Item No.	Product Name
11505	ABT-888 (hydrochloride)
19782	BMN 673
20842	MK-4827 (tosylate)
10621	Olaparib
33182	Pamiparib
15643	Rucaparib

#### Chk1 Inhibitors

Item No.	Product Name
34300	GDC-0575
20351	LY2603618
21490	LY2606368
17859	PF-477736
18131	SCH 900776
18130	UCN-01

#### Chk2 Inhibitors

Item No.	Product Name
19178	CCT241533 (hydrochloride)
21184	Chk2 Inhibitor
19811	NSC 109555

#### Wee1 Inhibitors

Item No.	Product Name
21266	MK-1775
35391	Wee1 Inhibitor

See all checkpoint kinase inhibitors at www.caymanchem.com

### **DNA Ligase Inhibitors**

DNA ligases seal nicks in the phosphodiester backbone during DNA replication and damage repair. DNA ligase inhibitors can sensitize cancer cells to the cytotoxic effects of DNA damaging agents.

Item No.	Product Name
18374	L189
22941	L67
18015	SCR7



See all PARP1 inhibitors at www.caymanchem.com

# Spindle Assembly Checkpoint

The spindle assembly checkpoint (SAC) is activated in the presence of unattached or improperly attached kinetochores during mitosis to inhibit the anaphase-promoting complex/cyclosome (APC/C) and prevent progression to anaphase. The mitotic checkpoint complex that is recruited to the kinetochores includes Mad2, BubR1, Bub3, and the APC/C coactivator Cdc20. The kinases Bub1, Mps1, Aurora B, and Plk1 are involved in regulation of the SAC.

### Mitotic Checkpoint Complex Modulators

Item No.	Product Name
17080	Apcin
22297	M2I-1
17550	N-4-Tosyl-L-arginine methyl ester (hydrochloride)
25835	proTAME

#### Mps1 Inhibitors

Item No.	Product Name
19991	AZ 3146
21660	BAY 12-17389
19175	Mps1-IN-1
25554	Mps1/TTK Inhibitor
31613	NMS-P715
10004412	Reversine

See all Mps1 inhibitors at www.caymanchem.com

#### Plk1 Inhibitors

Item No.	Product Name
17385	BI-2536
18193	BI-6727
18099	GSK461364
15553	ON-01910 (sodium salt)
21669	Ro 3280

See all Plk1 inhibitors at www.caymanchem.com

#### **Aurora B Inhibitors**

	Item No.	Product Name
	13647	AZD 1152 (hydrochloride)
	11602	AZD 1152-HQPA
	24199	Hesperadin
	13601	ZM 447439

See all Aurora inhibitors at www.caymanchem.com

# Modulators of Microtubule Dynamics

Microtubule inhibitors bind  $\beta$ -tubulin and affect microtubule dynamics and mitotic spindle assembly, activating the spindle assembly checkpoint. Taxanes stabilize pre-existing microtubules, while vinca alkaloids prevent microtubule polymerization.

#### **Taxanes**

Item No.	Product Name
22262	Cabazitaxel
11637	Docetaxel (hydrate)
10461	Paclitaxel
20741	7-epi Paclitaxel

#### Vinca Alkaloids

Item No.	Product Name
11762	Vinblastine (sulfate)
11764	Vincristine (sulfate)
21262	Vinorelbine (tartrate)

See all modulators of microtubule dynamics at www.caymanchem.com

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