# 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

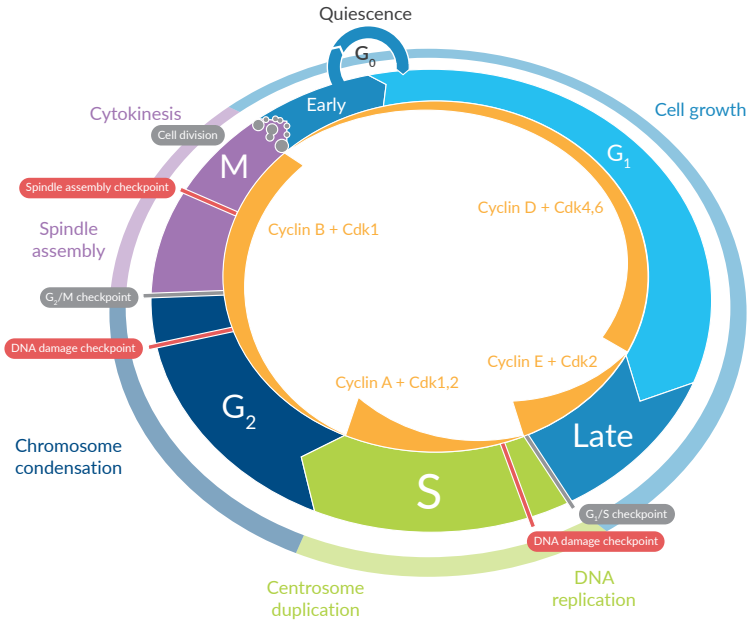
*Item No. 10009349*

- Easy-to-use kit for flow cytometric analysis of cell cycle progression
- Determine the percentage of cells in G0/G1, G2, 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 *in vitro* |
| 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 µM); also inhibits Cdk7/cyclin H, Cdk5/p35, and cell division cycle (cdc)/cyclin B ($IC_{50}$s = 0.49, 0.16, and 0.65 µM, 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

**www.caymanchem.com/kinases**

## 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 |

*See all PARP1 inhibitors at www.caymanchem.com*

## 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

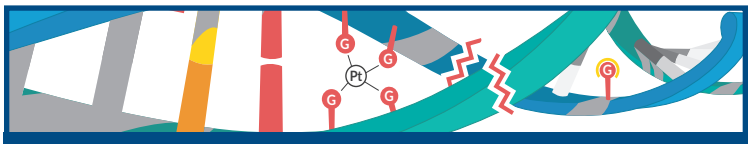
| Item No. | Product Name |
|---|---|
| 21266 | MK-1775 |
| 35391 | Wee1 Inhibitor |

*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 |




Browse all DNA Damage & Repair products 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 β-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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