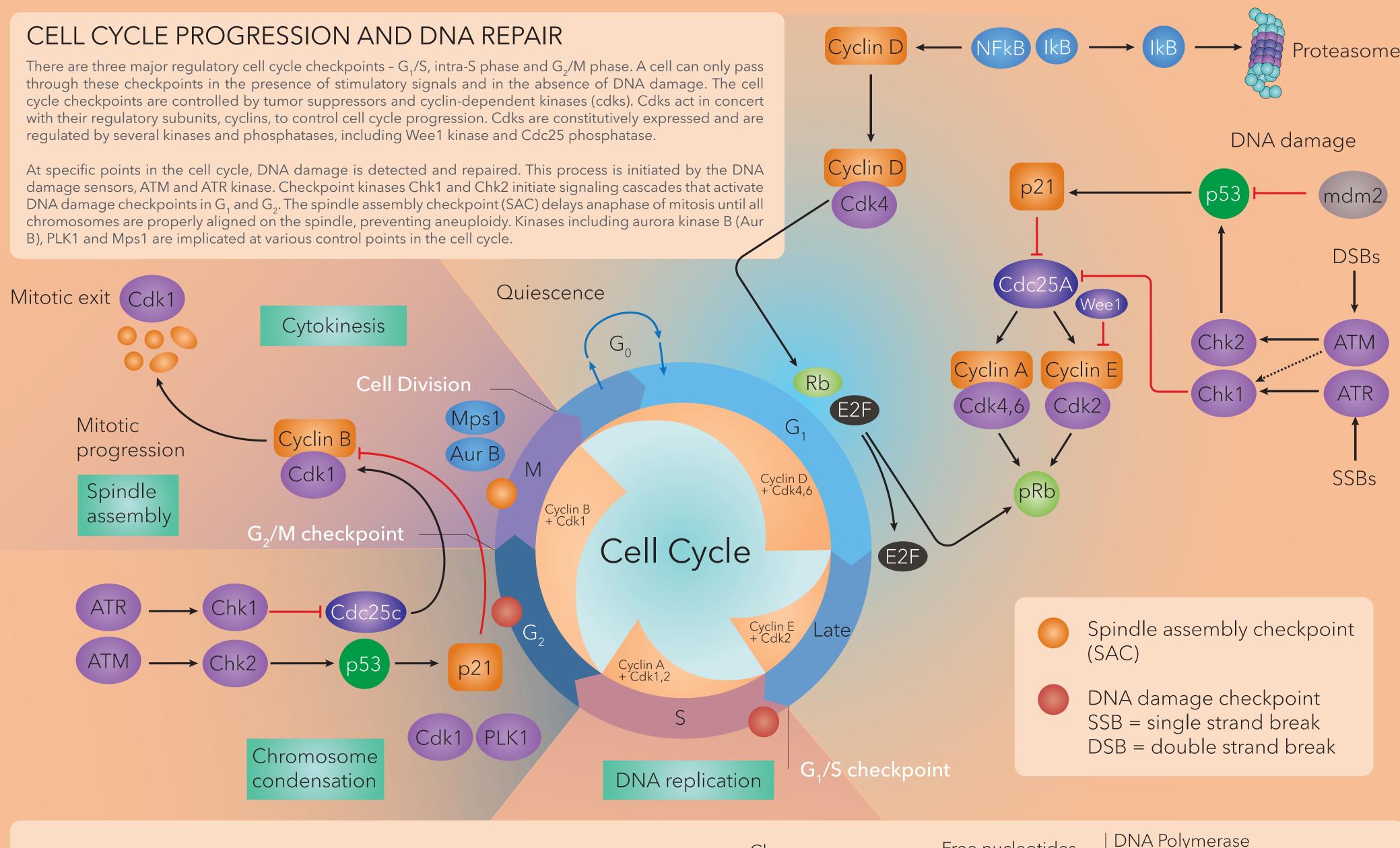
CELL CYCLE AND DNA DAMAGE REPAIR

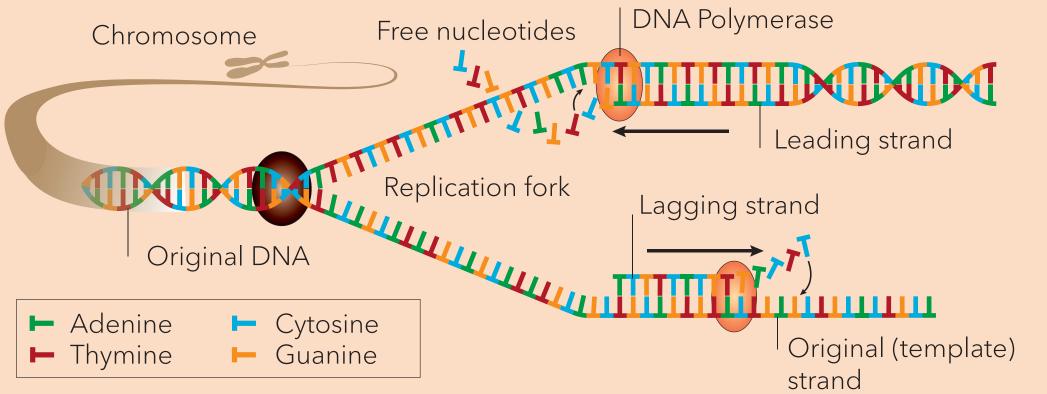
bietechne® Tocris

In normal cells, each stage of the cell cycle is tightly regulated. In cancer cells, many genes and proteins that influence the progression of the cell cycle are mutated or overexpressed - they become oncogenes. The proteins/ molecules involved in the regulation of the cell cycle, in particular those with a role in DNA replication and DNA damage, are important cancer therapeutic targets.



DNA REPLICATION

DNA replication occurs in five stages during S-phase; initiation, unwinding, primer synthesis, elongation and termination. Helicase enzymes "unwind" the DNA double helix, and telomerases reduce the resulting torsional strain, the single stands are now exposed and the replication fork is initiated. The leading strand of DNA is synthesized by Pol ϵ and the lagging strand is synthesized by Pol δ . PCNA is a cofactor for both DNA polymerase δ and ϵ , where it acts as a DNA clamp, which is important in both DNA synthesis and repair. At the end of the termination phase, DNA ligases form a phosphodiester bond, which joins the DNA strands together, forming new doubled stranded DNA.



ATM & ATR Kinase	AZ 20, AZ 5704, KU 55933, Mirin, VE 821		
Aurora Kinases	Hesperadin, TC-A 2317, VX 680, ZM 447439		
Calpains	Acetyl-Calpastatin (184-210) (human), Calpeptin, E 64, MG 132, PD 150606		
Casein Kinase 1	D 4476, IC 261, PF 4800567, PF 5006739, PF 670462		
Casein Kinase 2	TBB, TBCA, TMCB, TTP 22		
Cdc25 Phosphatase	NSC 663284, NSC 95397		
Cell Cycle Inhibitors	10058-F4, Methotrexate, Narciclasine, Pyridostatin pentahydrochloride		
Checkpoint Kinases	CCT 241533, LY 2603618, NSC 109555, PD 407824, PF 477736, SB 218078, TCS 2312		
Cyclin-dependent Kinase	BSJ-03-123, BSJ-04-132, CDK8/19i, FMF-04-159-2, Kenpaullone, NVP 2, PD 0332991, Purvalanol A, Purvalanol B, Ro 3306, Senexin A, THAL SNS 032		
DNA-dependent Protein Kinase	NU 7026, NU 7441		

PRODUCTS AVAILABLE FROM TOCRIS				
ATM & ATR Kinase	AZ 20, AZ 5704, KU 55933, Mirin, VE 821	DNA, RNA and Protein Synthesis	4E1RCat, L189, Mithramycin A, NSC 617145	
Aurora Kinases	Hesperadin, TC-A 2317, VX 680, ZM 447439	Hsp70	VER 155008	
Calpains	Acetyl-Calpastatin (184-210) (human), Calpeptin, E 64, MG 132, PD 150606	Hsp90	17-AAG	
6 : 1/2: 4	·	IRE1	APY 29	
Casein Kinase 1	D 4476, IC 261, PF 4800567, PF 5006739, PF 670462	Kinesin	Dimethylenastron, K 858, Monastrol, SB 743921, S-Trityl-L-cysteine	
Casein Kinase 2	TBB, TBCA, TMCB, TTP 22		Docetaxel, Dolastatin 10, Flutax 1, Taxol, Vinblastine,	
Cdc25 Phosphatase	NSC 663284, NSC 95397	Microtubules	Vincristine Vincristine	
Cell Cycle Inhibitors	10058-F4, Methotrexate, Narciclasine, Pyridostatin pentahydrochloride	Monopolar Spindle 1 Kinase	AZ 3146	
		p53	Nutlin-3, PRIMA-1MET, RITA	
	CCT 241533, LY 2603618, NSC 109555, PD 407824, PF 477736, SB 218078, TCS 2312	Polo-like Kinase	GW 843682X, TC-S 7005	
Cyclin-dependent Kinase	BSJ-03-123, BSJ-04-132, CDK8/19i, FMF-04-159-2, Kenpaullone, NVP 2, PD 0332991, Purvalanol A, Purvalanol B, Ro 3306, Senexin A, THAL SNS 032	Poly (ADP-ribose) Polymerase	Nicotinamide, PJ 34, WIKI 4, XAV 939	
DNA-dependent Protein Kinase	NU 7026, NU 7441	Telomerase	BRACO 19 trihydrochloride, BIBR 1532, RHPS methosulfate, TMPyP4 tosylate	

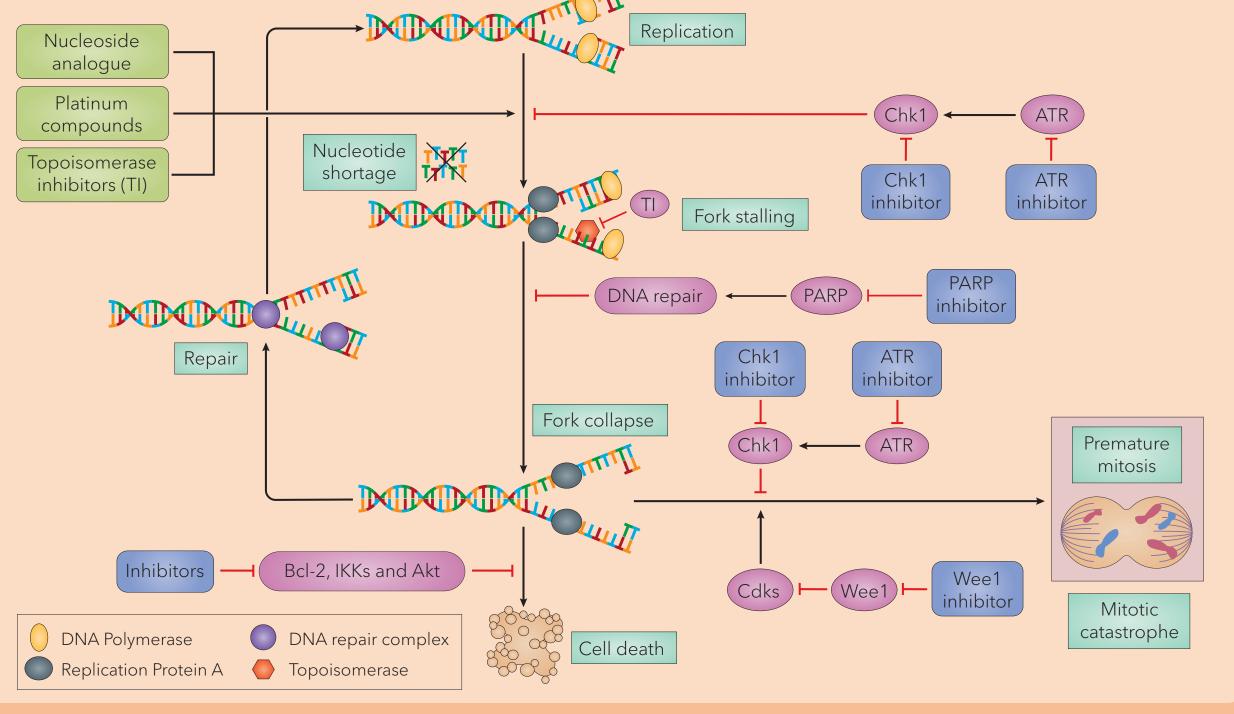
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TARGETING CANCER CELLS

Enhancing replicative stress by targeting critical DNA replication checkpoints and replication machinery, as well as depleting nucleotides, encourages fork stalling and fork collapse, which leads to mitotic catastrophe and death in cancer cells.



To request a copy of the Tocris Cancer Product Guide, or to view the PDF, please visit | tocris.com

Adapted from Edition 3 of the Tocris Cancer Product Guide











