Genotoxic Stress Response: DNA Damage

The human genome is exposed to potentially deleterious genotoxic events during every cell division cycle. This endogenous source of DNA damage results from cellular metabolism or routine errors in DNA replication and recombination. In addition, cellular and organismal exposure to exogenous genotoxic agents such as ultraviolet light, oxidative stress, and chemical mutagens, leads to a variety of nucleotide modifications and DNA strand breaks. In order to combat these attacks on the genome, the cell has evolved a response system that induces cell cycle arrest to allow sufficient time to repair the incurred damage. The DNA damage response system also activates the appropriate DNA repair pathway or, in the case of irreparable damage, induces apoptosis.

In the last decade, the characterization of many proteins involved in sensing and responding to DNA damage has enhanced our understanding of these genotoxic stress responses. In addition, mutation in the genes that encode DNA damage response proteins can result in a number of genomic instability syndromes. Genomic instability syndromes are autosomal recessive disorders that result in a heightened predisposition to multiple types of cancer. Thus, the significance of the genotoxic stress response is indicated by disease in the absence of critical proteins that sense, relay, or transduce the signal.

From antibodies to ELISAs, R&D Systems manufactures and supports a range of products necessary for genotoxic stress response research.

Genotoxic Stress Response

ANALYTE	ANTIBODIES	ELISAs/ASSAYS
53BP1	H	
APE	H M R Ms	
ASC	H	
ATM	H M R	H
ATRIP	H M R	
Aurora A	H	
Aurora B	H	
BARD1	H M R	
BRCA1	H M R	
BRCA2	H	
Bub-1	H	
CARF	H	
CBP	H M R	
Chk1	H M R	H M R
Chk2	H M R	H M R
Claspin	H	
DNA-PKcs	H	
Endonuclease III		Ms
Endonuclease V		T4
H2AX	H M R	
MAD1L1	H	
MAD2L1	H R	
MCPH1	H	
MDM2	H M R	
MGMT	H M	
Mre11	H	
Nbs1	H M R	
NTH1	H	
OGG1		H
p21/CIP1/CDKN1A	H	H
p27/Kip1	H M R	H
p53	H M R	H M
p53R2	H	
p300	H	
Pin1	H M	
PLK3	H	
PLKK	X	
Rad1	H	
Rad17	H M R	H
SMC1	H M R	
UNG	H	
UVDE		Ms
XPA	H	
XPD	M	
XPE/DDB2	H	
XPV	H	

Key: H Human M Mouse Ms Multi-Species R Rat T4 Phage X *Xenopus*

Duoset® IC IP Kinase Assays

ANALYTE	SPECIES	CATALOG #
Chk1	H M R	DYC1630
Chk2	H M R	DYC1358

Inhibition of Immunoprecipitated Chk1 Kinase Activity

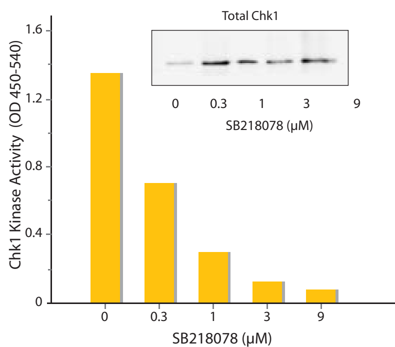

Figure 1. Chk1 kinase activity in HeLa cell lysates was assayed in the presence of increasing concentrations of Chk1-specific inhibitor SB218078 using R&D Systems Human/Mouse/Rat Active Chk1 DuoSet® IC IP Kinase Assay Kit (Catalog # DYC1630). Western blotting using R&D Systems goat anti-human/mouse/rat Chk1 affinity purified polyclonal antibody (Catalog # AF1630) was used to confirm equal amounts of Chk1 protein in the immunoprecipitates (inset).

Detection of Phosphorylated ATM

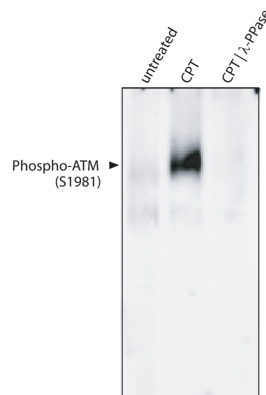

Figure 2. Western blot using R&D Systems rabbit anti-human phospho-ATM (S1981) affinity purified polyclonal antibody (Catalog # AF1655) to detect phosphorylation of ATM (Ataxia Telangiectasia Mutated). HeLa cells were untreated (left lane), treated with the Topoisomerase I inhibitor, camptothecin (CPT; middle lane), or treated with CPT and λ-phosphatase (right lane). This antibody also recognizes the comparable phosphorylated sites in mouse (S1987) and rat (S1952) ATM.

Quantification of Phosphorylated ATM

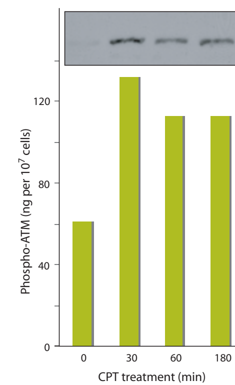

Figure 3. Quantification of phospho-ATM in human osteosarcoma U2-OS cells using R&D Systems Human phospho-ATM (S1981) DuoSet IC ELISA Kit (Catalog # DYC1655). Cells were left untreated or treated with camptothecin for the indicated time prior to cellular extract preparation. The same cellular extracts were immunoblotted (inset) with R&D Systems rabbit anti-human phospho-ATM (S1981) affinity purified polyclonal antibody (Catalog # AF1655). The DuoSet IC results correlate well with the Western blot data.