PRODUCT FLYER

ALEXIS® BIOCHEMICALS

The PARP Family & ADP Ribosylation

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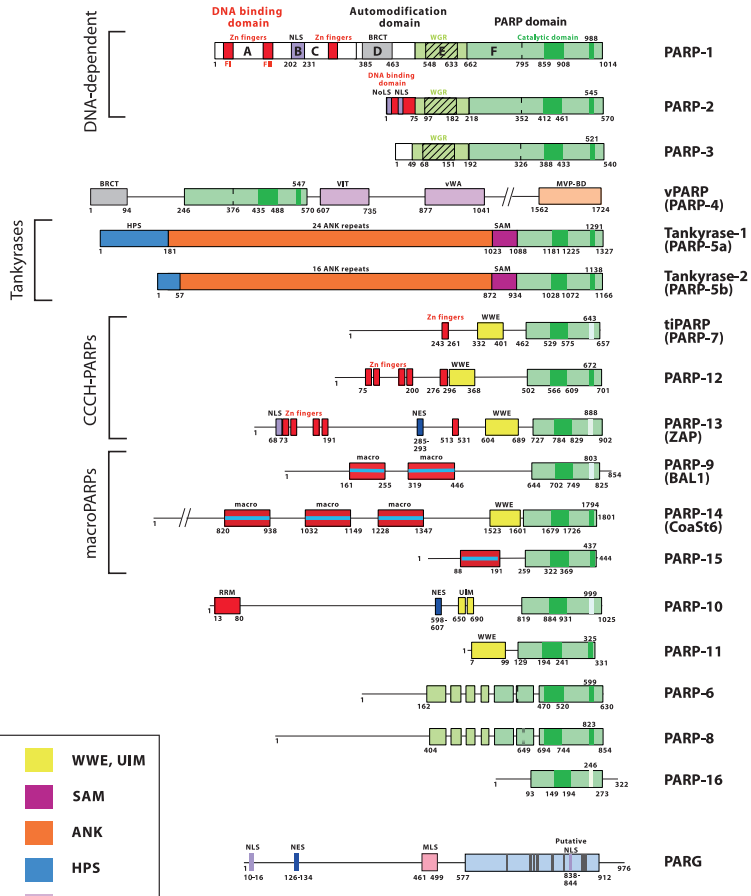
highlight

The PARP Family



Picture courtesy of J.C. Amé, V. Schreiber & G. de Murcia (CNRS, Strasbourg)

NEW PARP Isoform Specific Inhibitors see Page 6

Latest Insight

Third Zinc-binding Domain of PARP-1

PARP-1 contains three major segments that represent the biochemical activities of the enzyme: the DNA-binding domain (DBD), the automodification domain, and the catalytic domain. Recently, M.F. Langelier, et al. identified a third zinc finger domain in the DBD of human PARP-1. This domain mediates interdomain contacts important for DNA-dependent enzyme activation.

LIT: A third zinc-binding domain of human poly(ADP-ribose) polymerase-1 coordinates DNA-dependent enzyme activation: M.F. Langelier, et al.; J. Biol. Chem. **283**, 4105 (2008)

The PARP Family

Introduction

Poly(ADP-ribosyl)ation is a post-translational modification process which plays a critical role in diverse cellular functions such as DNA damage detection and repair, transcriptional regulation, intracellular trafficking, chromatin modification, mitotic apparatus formation, and cell death. The process is mediated by members of the family of poly(ADP-ribose) polymerases (PARPs), which transfer ADP-ribose (ADPr) units from nicotinamide dinucleotide (NAD) to certain residues in PARPs and onto target proteins. PARPs also mediate the polymerization of ADP-riboses via glycosidic bonds, creating long and branched ADP-ribose polymers, which are subsequently degraded by polyADP-ribose glycohydrolase (PARG). ADP-ribose polymers are thought to modify protein functions. In humans, the PARP family members are encoded by 17 different genes, while PARP-1 is the founding member [1-3].

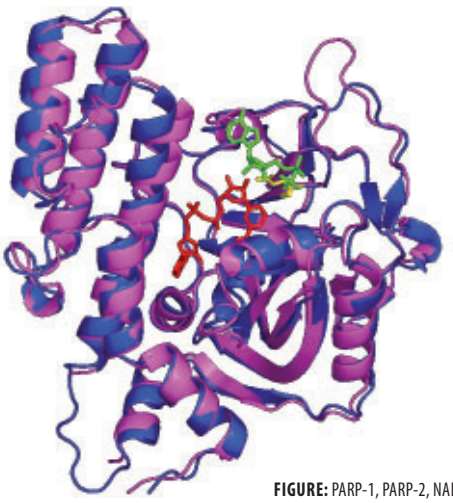


FIGURE: PARP-1, PARP-2, NAD and CarbaNAD in complex.
Picture courtesy of J.C. Amé & V. Schreiber (CNRS, Strasbourg)

DNA Repair (Cell Survival)

PARP-1 has been implicated in multiple DNA repair pathways including single-strand break repair (SSBR), double strand break (DSB) repair and base excision repair (BER). The molecular mechanism of BER may involve a local chromatin relaxation mediated either by covalent modification of histones with poly(ADP-ribose) or by non-covalent interaction of histones with poly(ADP-ribose) that automodifies the enzyme. This might regulate the accessibility to other DNA repair proteins. In addition PARP-1 or poly(ADP-ribose) (PAR) may directly recruit repair proteins like XRCC1 (X-ray repair cross-complementing 1) to the site of DNA damage [4-7]. PARP-2 is the only other known member of the PARP family to be activated by DNA strand breaks [8]. Although its DNA-binding domain is different from that of PARP-1, PARP-2 has been shown to interact with the SSBR/BER repair factors XRCC1, DNA polymerase β and DNA ligase III [9]. PARP-2 seems to be involved in later steps of the repair processes [10]. Beside its role in DNA repair, PARP-2 has been shown to be involved in diverse processes such as spermatogenesis, adipogenesis and T cell development [11].

BRCA1 and BRCA2 are tumor suppressor proteins important for DSB repair by homologous recombination. For a review see [12]. It has been demonstrated that BRCA1 or BRCA2 deficient cells have lost their ability to repair single-strand breaks by homologous recombination (HR) after PARP-1 depletion or inhibition, which can result in cell cycle arrest and apoptosis [13, 14]. This specific killing of tumor cells led to PARP inhibitors entering clinical trials and the screen for genes mediating such lethal sensitivity [15, 16]. Interestingly, two recent studies showed that antitumor chemotherapy with platinum analogs and PARP inhibitors can induce counter-mutation restoring HR capabilities of BRCA2 deficient cells [17, 18].

DNA-independent Activation

Recent findings revealed that PARP-1 can be activated by a DNA independent mode [19, 20]. This alternative mechanism is mediated by phosphorylated ERK2, showing that PARP-1 plays a role in the ERK signalling cascade mediating growth and differentiation. Activated PARP-1 increased ERK2-catalyzed Elk1 phosphorylation, histone acetylation, and the expression of the Elk1-targeted gene c-Fos [19].

Apoptosis / Necrosis (Cell Death)

Whereas activation of PARP-1 by mild genotoxic stimuli may facilitate DNA repair and cell survival, massive DNA damage may trigger hyperactivation of PARP-1 and cell death [21]. Excessive PARP-1 activity and PAR synthesis have been shown to induce cell death by causing NAD^+/ATP depletion [22-23] as well as triggering the release and nuclear translocation of apoptosis inducing factor [24, 25]. AIF induced cell death in response to the alkylating agent N-methyl-N'-nitro-N'-nitrosoguanidine (MNNG) requires calpains and Bax next to PARP-1 [26]. Recent results indicate a direct toxicity of PAR itself causing cellular death independent of energetic or transcriptional changes [27, 28]. PARP-1 activation is thought to be a key mediator of neuronal death during excitotoxicity, ischemia, and oxidative stress, as well as being of importance for other neuronal diseases [29-30].

PARP and Transcription

PARP-1 may regulate transcription by at least two different mechanisms. It can act as a modulator of the chromatin structure, but also functions as a component of enhancer/promoter regulatory complexes. PARP-1 can interact with the enhancers and promoters of genes by a) direct sequence-specific binding to enhancers, b) recruitment via DNA binding transcription factors (e.g. NF-κB), and c) direct binding to DNA structures.

LIT: [1] Poly(ADP-ribose): novel functions for an old molecule: V. Schreiber, et al.; Nat. Rev. Mol. Cell Biol. **7,** 517 (2006) ▪ [2] cDNA sequence, protein structure, and chromosomal location of the human gene for poly(ADP-ribose) polymerase: B. W. Cherney, et al.; PNAS **84,** 8370 (1987) ▪ [3] Human nuclear NAD+ ADP-ribosyltransferase: localization of the gene on chromosome 1q41-q42 and expression of an active human enzyme in Escherichia coli: H. Herzog, et al.; PNAS **86,** 3514 (1989) ▪ [4] XRCC1 is specifically associated with poly(ADP-ribose) polymerase and negatively regulates its activity following DNA damage: M. Masson, et al.; Mol. Cell Biol. **18,** 3563 (1998) ▪ [5] Poly(ADP-ribose) binds to specific domains in DNA damage checkpoint proteins: J. M. Pleschke, et al.; J. Biol. Chem. **275,** 40974 (2000) ▪ [6] A requirement for PARP-1 for the assembly or stability of XRCC1 nuclear foci at sites of oxidative DNA damage: S. F. El-Khamisy, et al.; Nucleic Acids Res. **31,** 5526 (2003) ▪ [7] The role of poly(ADP-ribose) in the DNA damage signaling network: M. Malanga & F. R. Althaus; Biochem. Cell Biol. **83,** 354 (2005) ▪ [8] PARP-2, a novel mammalian DNA damage-dependent poly(ADP-ribose) polymerase: J. C. Ame, et al.; J. Biol. Chem. **274,** 17860 (1999) ▪ [9] Poly(ADP-ribose) polymerase-2 (PARP-2) is required for efficient base excision DNA repair in association with PARP-1 and XRCC1: V. Schreiber, et al.; J. Biol. Chem. **277,** 23028 (2002) ▪ [10] Feedback-regulated poly(ADP-ribosyl)ation by PARP-1 is required for rapid response to DNA damage in living cells: O. Mortusewicz, et al.; Nucleic Acids Res. **35,** 7665 (2007) ▪ [11] Toward specific functions of poly(ADP-ribose) polymerase-2: J. Yelamos, et al.; Trends Mol. Med. **14,** 169 (2008) ▪ [12] Role of BRCA1 and BRCA2 as regulators of DNA repair, transcription, and cell cycle in response to DNA damage: K. Yoshida & Y. Miki; Cancer Sci. **95,** 866 (2004) ▪ [13] Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase: H. E. Bryant, et al.; Nature **434,** 913 (2005) ▪ [14] Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy: H. Farmer, et al.; Nature **434,** 917 (2005) ▪ [15] Clinical poly(ADP-ribose) polymerase inhibitors for the treatment of cancer: C. Lewis & J. A. Low; Curr. Opin. Investig. Drugs **8,** 1051 (2007) ▪ [16] A synthetic lethal siRNA screen identifying genes mediating sensitivity to a PARP inhibitor: N. C. Turner, et al.; EMBO J., **Epub ahead of print**, (2008) ▪ [17] Secondary mutations as a mechanism of cisplatin resistance in BRCA2-mutated cancers: W. Sakai, et al.; Nature **451,** 1116 (2008) ▪ [18] Resistance to therapy caused by intragenic deletion in BRCA2: S. L. Edwards, et al.; Nature **451,** 1111 (2008) ▪ [19] DNA-independent PARP-1 activation by phosphorylated ERK2 increases Elk1 activity: a link to histone acetylation: M. Cohen-Armon, et al.; Mol. Cell **25,** 297 (2007) ▪ [20] PARP-1 activation in the ERK signaling pathway: M. Cohen-Armon; TIPS **28,** 556 (2007) ▪ [21] Poly(ADP-ribose) makes a date with death: J. T. Heeres & P. J. Hergenrother; Curr. Opin. Chem. Biol. **11,** 644 (2007) ▪ [22] Poly(ADP-ribose) polymerase is a mediator of necrotic cell death by ATP depletion: H. C. Ha & S. H. Snyder; PNAS **96,** 13978 (1999) ▪ [23] Alkylating DNA damage stimulates a regulated form of necrotic cell death: W. X. Zong, et al.; Genes Dev. **18,** 1272 (2004) ▪ [24] Mediation of poly(ADP-ribose) polymerase-1-dependent cell death by apoptosis-inducing factor: S. W. Yu, et al.; Science **297,** 259 (2002) ▪ [25] Apoptosis-inducing factor mediates poly(ADP-ribose) (PAR) polymer-induced cell death: S. W. Yu, et al.; PNAS **103,** 18314 (2006) ▪ [26] Sequential activation of poly(ADP-ribose) polymerase 1, calpains, and Bax is essential in apoptosis-inducing factor-mediated programmed necrosis: R. S. Moubarak, et al.; Mol. Cell Biol. **27,** 4844 (2007) ▪ [27] Poly(ADP-ribose) (PAR) polymer is a death signal: S. A. Andrabi, et al.; PNAS **103,** 18308 (2006) ▪ [28] Neither energy collapse nor transcription underlie in vitro neurotoxicity of poly(ADP-ribose) polymerase hyper-activation: S. Fossati, et al.; Neurochem. Int. **50,** 203 (2007) ▪ [29] The role of poly(ADP-ribose) polymerase-1 in CNS disease: T. M. Kauppinen & R. A. Swanson; Neuroscience **145,** 1267 (2007) ▪ [30] Multiple roles for poly(ADP-ribose)polymerase-1 in neurological disease: T. M. Kauppinen; Neurochem. Int. **50,** 954 (2007)

PARP Proteins

Standard PARP Proteins

PARP-1 (human) (rec.) (high purity)

[Poly(ADP-ribose) Polymerase-1 (human) (rec.)]
ALX-201-063-C020 20 µg
Produced in Sf9 cells.

LIT: Overproduction and large-scale purification of the human poly(ADP- ribose) polymerase using a baculovirus expression system: H. Giner, et al.; Gene **114,** 279 (1992) ▪ Poly(ADP-ribose) reactivates stalled DNA topoisomerase I and Induces DNA strand break resealing: M. Malanga & F.R. Althaus; J. Biol. Chem. **279,** 5244 (2004)

PARP-2 (mouse) (rec.) (high purity)

[Poly(ADP-ribose) Polymerase-2 (mouse) (rec.)]
ALX-201-064-C020 20 µg
Produced in Sf9 cells.

LIT: PARP-2, A novel mammalian DNA damage-dependent poly(ADP-ribose) polymerase: J.C. Ame, et al.; J. Biol. Chem. **274,** 17860 (1999) ▪ A bidirectional promoter connects the poly(ADP-ribose) polymerase 2 (PARP-2) gene to the gene for RNase P RNA. structure and expression of the mouse PARP-2 gene: J.C. Ame, et al.; J. Biol. Chem. **276,** 11092 (2001) ▪ Poly(ADP-ribose) reactivates stalled DNA topoisomerase I and Induces DNA strand break resealing: M. Malanga & F.R. Althaus; J. Biol. Chem. **279,** 5244 (2004)

PARP-3 (human) (rec.) (high purity)

[Poly(ADP-ribose) Polymerase-3 (human) (rec.)]
ALX-201-170-C020 20 µg
Produced in Sf9 cells.

LIT: PARP-3 localizes preferentially to the daughter centriole and interferes with the G1/S cell cycle progression: A. Augustin, et al.; J. Cell Sci. **116,** 1551 (2003) ▪ Tankyrase-1 polymerization of poly(ADP-ribose) is required for spindle structure and function: P. Chang et al.; Nature Cell Biology **7,** 1133 (2005)

PARP Family Proteins & Related Products

Product	Source	Purity	Prod. No.	Size
PARP-1 (human) (rec.) (His)	Produced in Sf21 cells	≥98%	ALX-201-250-C010	10 µg
PARP-1 (Cat. Dom.) (human) (rec.) (His)	Produced in Sf21 cells	>90 %	ALX-201-232-C020	20 µg
PARP-1 (BRCT Domain) (human) (rec.) (His)	Produced in E. coli	≥98%	ALX-201-255-C020	20 µg
PARP-1 (E988K mutant) (human) (rec.)	Produced in Sf21 cells	≥95 %	ALX-201-254-C010	10 µg
PARP-1b (human) (rec.) (active) (His)	Produced in Sf21 cells	≥95%	ALX-201-253-C020	20 µg
PARP-1 (bovine)	Isolated from calf thymus	~90%	ALX-202-042-C010	10 µg
PARP-1 (bovine)	Isolated from calf thymus	~98%	ALX-202-046-C010	10 µg
PARP-1 (bovine) (automod.) Standard	Isolated from calf thymus		ALX-202-044-R100	100 µl
PARP-2 (mouse) (rec.) (His)	Produced in Sf21 cells	≥98%	ALX-201-251-C010	10 µg
PARP-3 (human) (rec.) (His)	Produced in Sf21 cells	≥98%	ALX-201-252-C010	10 µg
Poly(ADP-ribose) [PAR] Standard	Automodified PARP-1	≥95%	ALX-202-043-C001	1 µg
PARG (bovine)	Isolated from calf thymus		ALX-202-045-UC01	0.1 U

VPARP (PARP-4)

Vault poly(ADP-ribose) polymerase (VPARP; PARP-4) was originally identified as a minor protein component of the vault ribonucleoprotein particle [1]. Vaults have been implicated in multidrug resistance of human tumors and are thought to be involved in macromolecular assembly and/or transport [2]. In addition to the association of VPARP with the cytoplasmic vault particle, subpopulations of VPARP localize to the nucleus and the mitotic spindle, indicating that VPARP may have other cellular functions. Recently, VPARP has been shown to associate with telomerase activity and interact with exogenously expressed telomerase-associated protein 1 (TEP1) in mammalian cells [3].

LIT: [1] The 193-kD vault protein, VPARP, is a novel poly(ADP-ribose) polymerase: V.A. Kickhoefer, et al.; J. Cell Biol. **146,** 917 (1999) ▪ [2] Cellular functions of vaults and their involvement in multidrug resistance: E. Steiner, et al.; Curr. Drug Targets **7,** 923 (2006) ▪ [3] Vault poly(ADP-ribose) polymerase is associated with mammalian telomerase and is dispensable for telomerase function and vault structure in vivo: Y. Liu, et al.; Mol. Cell. Biol. **24,** 5314 (2004)

NEW VPARP (human) (rec.) (His)

[Minor Vault p193 Protein (human) (rec.) (His); PARP-4 (human) (rec.) (His)]
ALX-201-286-C010 10 µg
Produced in *E. coli*.

LIT: In silico characterization of the family of PARP-like poly(ADP-ribosyl)transferases (pARTs): H. Otto, et al.; BMC Genomics **6,** 139 (2005)

XRCC1

Human XRCC1 (X-ray repair cross-complementing 1) is involved in base excision repair (BER) and single strand break repair (SSBR) and thought to act as a scaffolding protein for other repair factors. It has been shown to physically interact with several enzymes known to be involved in the repair of SSBs, including DNA ligase IIIα, DNA polymerase β, APE1, polynucleotide kinase/phosphatase, poly(ADP-ribose) polymerases 1 and 2 (PARP-1 and 2) and 8-oxoguanine DNA glycosylase (OGG1) [1-6].

LIT: [1] XRCC1 polypeptide interacts with DNA polymerase beta and possibly poly (ADP-ribose) polymerase, and DNA ligase III is a novel molecular ‚nick-sensor' in vitro: K. W. Caldecott, et al.; Nucleic Acids Res. **24,** 4387 (1996) ▪ [2] Reconstitution of DNA base excision-repair with purified human proteins: interaction between DNA polymerase beta and the XRCC1 protein: Y. Kubota, et al.; EMBO J. **15,** 6662 (1996) ▪ [3] Role of XRCC1 in the coordination and stimulation of oxidative DNA damage repair initiated by the DNA glycosylase hOGG1: S. Marsin, et al.; J. Biol. Chem. **278,** 44068 (2003) ▪ [4] XRCC1 stimulates human polynucleotide kinase activity at damaged DNA termini and accelerates DNA single-strand break repair: C. J. Whitehouse, et al.; Cell **104,** 107 (2001) ▪ [5] Poly(ADP-ribose) polymerase-2 (PARP-2) is required for efficient base excision DNA repair in association with PARP-1 and XRCC1: V. Schreiber, et al.; J. Biol. Chem. **277,** 23028 (2002) ▪ [6] Spatial and temporal cellular responses to single-strand breaks in human cells: S. Okano, et al.; Mol. Cell. Biol. **23,** 3974 (2003)

Product	Source / Host	Specificity	Application	Prod. No.	Size
PAb to XRCC1 (human)	From rabbit	Human	ELISA, ICC, IP, WB	ALX-210-304-R050	50 µl
PAb to XRCC1 (human)	From rabbit	Human	ICC, IP, WB	ALX-210-539-R100	100 µl
PAb to XRCC1 (human) (exon 17)	From rabbit	Human	ICC, IHC, IP, WB	BET-A300-065A	0.1 mg
PAb to XRCC1 (human) (phosphorylated) (pSer^{461})	From rabbit	Human	WB	BET-A300-147A	0.1 mg
PAb to XRCC1 (human) (phosphorylated) (pSer^{475})	From rabbit	Human	WB	BET-A300-227A	0.1 mg
PAb to XRCC1 (human) (phosphorylated) (pSer^{485}/pThr^{488})	From rabbit	Human	WB	BET-A300-231A	0.1 mg
PAb to XRCC1 (human) (phosphorylated) (pSer^{518}/pThr^{519}/pThr^{523})	From rabbit	Human	WB	BET-A300-059A	0.1 mg
PAb to XRCC1 (phosphorylated) (pSer^{461})	From rabbit	Human, mouse	IHC (PS)	BET-IHC-00116	0.1 ml
PAb to XRCC1 (phosphorylated) (pSer^{485}/pThr^{488})	From rabbit	Human, mouse	IHC (PS)	BET-IHC-00117	0.1 ml
PAb to XRCC1 (phosphorylated) (pSer^{518}/pThr^{519}/pThr^{523})	From rabbit	Human, mouse	IHC (PS)	BET-IHC-00115	0.1 ml

Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

PARP Antibodies

Standard Antibodies

MAb to Poly(ADP-ribose) (10H)

ALX-804-220-R100 100 µl

CLONE: 10H. **ISOTYPE:** Mouse IgG3. **IMMUNOGEN:** Purified poly(ADP-ribose). **SPECIFICITY:** Recognizes poly(ADP-ribose) synthesized by a broad range of PARPs (poly(ADP-ribose) polymerases) like human, mouse, rat or *Drosophila* PARP enzyme. **APPLICATION:** FC, IHC (PS), ICC, WB.

LIT: Monoclonal antibodies to poly(adenosine diphosphate ribose) recognize different structures: H. Kawamitsu, et al.; Biochemistry **23,** 3771 (1984) (Original Reference) ▪ For a comprehensive bibliography please visit our website.

FOR MORE INFORMATION SEE BACKCOVER

PAb to Poly(ADP-ribose) (96-10-04)

ALX-210-890-R100 100 µl

From rabbit. **IMMUNOGEN:** Poly(ADP-ribose) with methylated BSA. **SPECIFICITY:** Recognizes poly(ADP-ribose) of 6-100 bases in size, synthesized *in vitro* or *in vivo*. Shows some cross-reactivity with BSA. **APPLICATION:** ELISA, ICC, WB.

LIT: Failure to degrade poly(ADP-ribose) causes increased sensitivity to cytotoxicity and early embryonic lethality: D.W. Koh, et al.; PNAS **101,** 17699 (2004) ▪ Ataxia telangiectasia mutated (ATM) signaling network is modulated by a novel poly(ADP-ribose)-dependent pathway in the early response to DNA-damaging agents: J.F. Haince, et al.; J. Biol. Chem. **282,** 16441 (2007) ▪ For a comprehensive bibliography please visit our website.

MAb to PARP-1 (C2-10)

ALX-804-210-R050 50 µl

CLONE: C2-10. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Purified calf thymus PARP-1 (poly(ADP-ribose) polymerase-1). **SPECIFICITY:** Recognizes an epitope in the C-terminal part of the DNA binding domain of human, mouse, rat, hamster and primate PARP-1. Detects bands ~116kDa (intact PARP-1) and ~85kDa (apoptosis-induced cleavage fragment) by Western blot. **APPLICATION:** ELISA, ICC, IP, WB.

LIT: Structural and functional analysis of poly(ADP ribose) polymerase: an immunological study: D. Lamarre, et al.; Biochim. Biophys. Acta **950,** 147 (1988) ▪ Cleavage of poly(ADP-ribose) polymerase by a proteinase with properties like ICE: Y.A. Lazebnik, et al.; Nature **371,** 346 (1994) ▪ Nuclear poly(ADP-ribose) polymerase-1 rapidly triggers mitochondrial dysfunction: G. Cipriani, et al.; J. Biol. Chem. **280,** 17227 (2005) ▪ For a comprehensive bibliography please visit our website.

MAb to PARP-2 (4G8)

ALX-804-639-L001 1 ml

CLONE: 4G8. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant mouse PARP-2 (poly(ADP-ribose) polymerase-2). **SPECIFICITY:** Recognizes an epitope in domain E of human and mouse PARP-2. Detects a band of ~62kDa by Western blot. **APPLICATION:** ELISA, WB.

LIT: Anti-Poly-ADP-Ribose Polymerase-2 (PARP-2) Mouse MAb 4G8: Y. Monreal, et al.; Hybridoma **25,** 102 (2006)

MAb to VPARP (human) (p193-4)

ALX-801-023-C125 125 µg
ALX-801-023-C250 250 µg

CLONE: p193-4. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** VPARP (minor vault p193 protein; PARP-4). **SPECIFICITY:** Recognizes epitope aa 491-494 of human VPARP. **APPLICATION:** IHC (FS, PS), ICC, IP, WB.

LIT: The Mr 193,000 vault protein is up-regulated in multidrug-resistant cancer cell lines: A.B. Schroeijers, et al.; Cancer Res. **60,** 1104 (2000) ▪ The formation of vault-tubes: a dynamic interaction between vaults and vault PARP: A. Van Zon, et al.; J. Cell Sci. **116,** 4391 (2003) ▪ For a comprehensive bibliography please visit our website.

MAb to Tankyrase-1 (human) (19A449)

ALX-804-234-C100 100 µg

CLONE: 19A449. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant human tankyrase-1 (PARP-5a). **SPECIFICITY:** Recognizes human tankyrase-1. Detects a band of ~120kDa by Western blot. **APPLICATION:** WB.

LIT: Tankyrase, a poly(ADP-ribose) polymerase at human telomeres: S. Smith, et al.; Science **282,** 1484 (1998) ▪ Mammalian telomeres end in a large duplex loop: J.D. Griffith, et al.; Cell **97,** 503 (1999) ▪ Tankyrase is a golgi-associated mitogen-activated protein kinase substrate that interacts with IRAP in GLUT4 vesicles: N.W. Chi & H.F. Lodish; J. Biol. Chem. **275,** 38437 (2000) ▪ For a comprehensive bibliography please visit our website.

PARP Family Antibodies & Related Products

Product	Source / Host / Isotype	Specificity	Application	Prod. No.	Size
MAb to Poly(ADP-ribose) [PAR] (10H)	Mouse IgG3	Human, mouse, rat	FC, ICC, IHC (PS), WB	ALX-804-220-R100	100 µl
PAb to Poly(ADP-ribose) [PAR]	Ab: 96-10-04 / From rabbit	Human, mouse, rat	ELISA, ICC, WB	ALX-210-890-R100	100 µl
MAb to PARP-1 (C2-10)	Mouse IgG1	Human, mouse, rat, primate	ELISA, ICC, IP, WB	ALX-804-210-R050	50 µl
MAb to PARP-1 (F1-23)	Mouse IgG1	Human, bovine	ELISA, ICC, IP, WB, FUNC	ALX-804-211-R050	50 µl
PAb to PARP-1	From rabbit	Human, mouse, bovine, chicken	ELISA, ICC, IHC (FS, PS)	ALX-210-302-R100	100 µl
PAb to PARP-1	From rabbit	Human, mouse, rat, monkey, bovine	ICC, IP, WB, FUNC	ALX-210-221-R100	100 µl
PAb to PARP-1 (human)	From goat (serum)	Human, mouse	WB	ALX-210-897-R100	100 µl
PAb to PARP-1 (human)	From rabbit (supernatant)	Human, mouse (weak)	ICC, IHC, IP, WB	ALX-210-895-R100	100 µl
PAb to PARP-1 (mouse)	From rabbit (supernatant)	Mouse, human (weak)	ICC, IHC, IP, WB	ALX-210-619-R100	100 µl
PAb to PARP-1 (BRCT Domain)	From rabbit	Human, mouse	IP, WB	ALX-210-540-R100	100 µl
PAb to PARP-1 (197-214)	From rabbit	Human, bovine, chicken	ELISA, ICC, IP, WB	ALX-210-219-R100	100 µl
PAb to PARP-1 (215-228)	From rabbit	Human, bovine, chicken	ELISA, ICC, WB	ALX-210-220-R100	100 µl
PAb to PARP-1 (509-524)	From rabbit	Human, mouse, rat, bovine	ELISA, IP, WB, FUNC	ALX-210-222-R100	100 µl
MAb to PARP-2 (4G8)	Mouse IgG1	Human, mouse	ELISA, WB	ALX-804-639-L001	1 ml
PAb to PARP-2	Ab: Yuc / From rabbit	Human, mouse, monkey	ELISA, ICC, IP, WB	ALX-210-303-R100	100 µl
PAb to PARP-2	Ab: Yuc / From rabbit, purified	Human, mouse, monkey	ICC	ALX-210-896-R100	100 µl
PAb to PARP-2 (mouse)	From rabbit (supernatant)	Mouse, human (weak)	ICC, IHC, IP, WB	ALX-210-899-R100	100 µl
MAb to PARP-3 (LA6B10)	Mouse IgM	Human, mouse	ICC	ALX-804-466-R100	100 µl
PAb to PARP-3	From rabbit	Human, mouse, monkey	ICC, IP, WB	ALX-210-541-R100	100 µl
MAb to VPARP/PARP-4 (p193-4)	Mouse IgG1	Human	ICC, IHC (FS, PS), IP, WB	ALX-801-023-C125	125 µg
MAb to VPARP/PARP-4 (p193-6)	Mouse IgG2b	Human	ICC, IHC (FS), WB	ALX-801-024-C125	125 µg
MAb to VPARP/PARP-4 (p193-10)	Mouse IgG2a	Human	IHC, WB	ALX-801-025-C125	125 µg
MAb to Tankyrase-1 [PARP-5a] (19A449)	Mouse IgG	Human, mouse	WB	ALX-804-234-C100	100 µg
MAb to PARP-10 (human) (5H11)	Rat IgG1	Human	ICC, IP, WB	ALX-804-626-L001	1 ml
PAb to PARP-10 (300-350) (human)	From rabbit	Human	IP, WB	BET-A300-665A	0.1 mg
PAb to PARP-16 (human)	From rabbit	Human	WB	ASB-ARP33751-P050	50 µg
PAb to PARN (mouse)	From rabbit	Mouse	WB	ASB-ARP37393-T100	100 µg

NEW

PAb to PARP-3

ALX-210-541-R100 100 µl

From rabbit. **IMMUNOGEN:** Recombinant human PARP-3 (poly(ADP-ribose) polymerase-3). **SPECIFICITY:** Recognizes human, mouse and monkey PARP-3. **APPLICATION:** ICC, IP, WB.

LIT: PARP-3 localizes preferentially to the daughter centriole and interferes with the G1/S cell cycle progression: A. Augustin, et al.; J. Cell Sci. **116,** 1551 (2003)

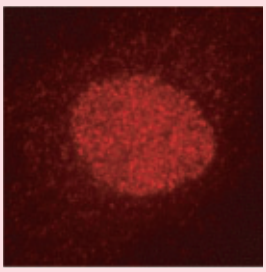


FIGURE: Immunodetection of PARP-3 in mouse embryonic fibroblasts fixed with 2% Formaldehyde-0.1% Triton. Dilution: 1/200.

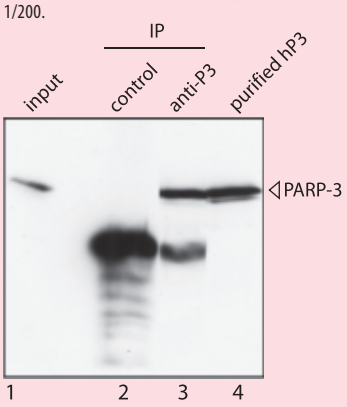


FIGURE: Immunoprecipitation. Cell lysates prepared from COS-1 cells were immunoprecipitated with the anti-PARP-3 antibody (lane 3) or with a control antibody (lane 2). Lane 1: input 1:15. Lane 4: purified recombinant human poly(ADP-ribose) polymerase-3.

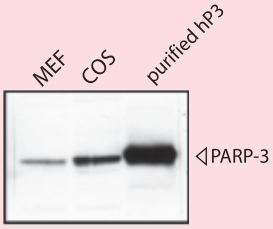


FIGURE: Western blot analysis. Mouse embryonic fibroblasts (MEF), simian COS-1 cells (COS), purified recombinant human poly(ADP-ribose) polymerase-3.

Latest Insight

Review on PARP-2

The catalytic activity of PARP-1 and PARP-2 has been shown to be induced by DNA-strand breaks, indicating that both enzymes play a role in the cellular response to DNA damage. J. Yelamos, et al. reviewed recent data that suggest unique functions for PARP-2 in specific biological processes such as adipogenesis, genome surveillance, spermatogenesis and T cell development.

LIT: Toward specific functions of poly(ADP-ribose) polymerase-2: J. Yelamos, et al.; Trends Mol. Med. **14,** 169 (2008) (Review)

PARP-3

Human PARP-3 (hPARP-3) (540aa, with an approx. mass of 67kDa) is a core component of the centrosome and preferentially localized to the daughter centriole throughout the cell cycle. The N-terminal domain (54aa) of hPARP-3 is responsible for its centrosomal localization.

An attractive hypothesis is that the presence of both PARP-1 and PARP-3 at the centrosome may link the DNA damage surveillance network to the mitotic fidelity checkpoint.

LIT: PARP-3 localizes preferentially to the daughter centriole and interferes with the G1/S cell cycle progression: A. Augustin, et al.; J. Cell Sci. **116,** 1551 (2003)

MAb to PARP-3 (LA6B10)

ALX-804-466-R100 100 µl

CLONE: LA6B10. **ISOTYPE:** Mouse IgM. **IMMUNOGEN:** Synthetic peptide corresponding to N-terminal aa 8-22 ($M^{8}APKPKPWVQTEGPE^{22}$) of human PARP-3 (poly(ADP-ribose) polymerase-3). **SPECIFICITY:** Recognizes human and mouse PARP-3. **APPLICATION:** ICC.

LIT: PARP-3 localizes preferentially to the daughter centriole and interferes with the G1/S cell cycle progression: A. Augustin, et al.; J. Cell Sci. **116,** 1551 (2003) ▪ Tankyrase-1 polymerization of poly(ADP-ribose) is required for spindle structure and function: P. Chang, et al.; Nat. Cell Biol. **7,** 1133 (2005)

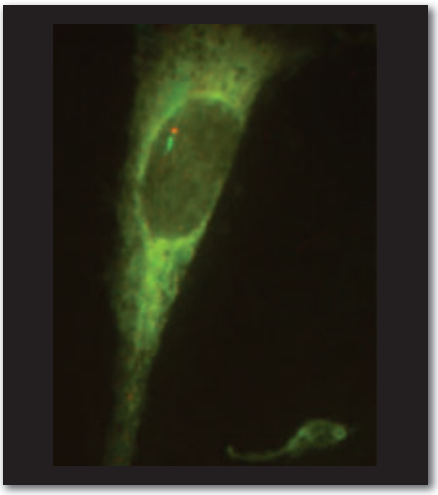


FIGURE: PARP-3 (red) preferentially localizes to the daughter centriole. The mother centriole (green) is immunostained with anti-acetylated α-tubulin in 3T3 cells. *Picture courtesy of C. Spenlehauer & G. de Murcia (CNRS, Strasbourg).*

PARP-10

M. Yu, et al. [1] identified and characterized a novel 150kDa protein, designated PARP-10. PARP-10 can associate with the oncoprotein c-Myc and possesses PARP activity, capable of poly (ADP-ribosyl)ating itself and core histones but neither Myc nor Max. PARP-10 shuttles between the nuclear and cytoplasmic compartments that is controlled at least in part by a leucine-rich nuclear export sequence. Functionally PARP-10 inhibits transformation of primary cells (rat embryo fibroblasts). PARP-10 might play a role in the control of cell proliferation. To regulate its target genes, c-Myc recruits several different cofactors. K. Lesniewicz, et al. [2] suggest that PARP-10 may function as an additional cofactor that is recruited by c-Myc. H.Y. Chou, et al. [3] suggested that cell cycle-dependent phosphorylation of PARP-10 by CDK2 plays crucial functions in cell proliferation.

LIT: [1] PARP-10, a novel Myc-interacting protein with poly(ADP-ribose) polymerase activity, inhibits transformation: M. Yu, et al.; Oncogene **24,** 1982 (2005) ▪ [2] Overlap of the gene encoding the novel poly(ADP-ribose) polymerase Parp10 with the plectin 1 gene and common use of exon sequences: K. Lesniewicz, et al.; Genomics **86,** 38 (2005) ▪ [3] CDK-dependent activation of poly(ADP-ribose) polymerase member 10 (PARP10): H.Y. Chou, et al.; J. Biol. Chem. **281,** 15201 (2006)

MAb to PARP-10 (human) (5H11)

ALX-804-626-L001 1 ml

CLONE: 5H11. **ISOTYPE:** Rat IgG1. **IMMUNOGEN:** Recombinant human PARP-10 (poly(ADP-ribose) polymerase-10) (aa 1-907). **SPECIFICITY:** Recognizes human PARP-10. **APPLICATION:** ICC, IP, WB.

LIT: PARP-10, a novel Myc-interacting protein with poly(ADP-ribose) polymerase activity, inhibits transformation: M. Yu, et al.; Oncogene **24,** 1982 (2005)

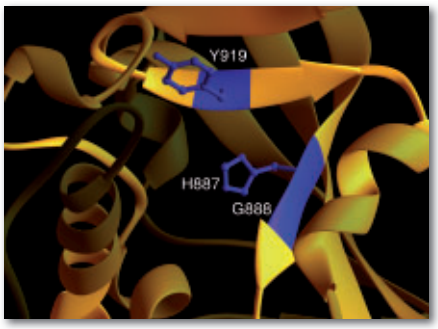


FIGURE: Catalytic domain of PARP-10: *Picture courtesy of B. Lüscher (University Aachen)*

c-Myc

The proto-oncogene c-Myc is implicated in various physiological processes, like cell growth, proliferation, loss of differentiation and cell death. It also has been implicated in the loss of dysfunction of insulin-producing beta cells in diabetes. Recent studies in mice suggest that c-Myc has unexpected functions during both self-renewal and the differentiation of stem and early progenitor cells. In an effort to identify novel c-Myc-interacting proteins, M. Yu, et al. (Oncogene **24,** 1982 (2005)) recently discovered that PARP-10 can associate with the oncoprotein c-Myc.

MAb to c-Myc (human) (4H3)

ALX-804-627-L001 1 ml

CLONE: 4H3. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Recombinant human c-Myc (aa 1-262). **SPECIFICITY:** Recognizes human and zebrafish c-Myc. **APPLICATION:** ICC, IP, WB.

MAb to c-Myc (human) (6A10)

ALX-804-632-L001 1 ml

CLONE: 6A10. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Human c-Myc (aa 1-262). **SPECIFICITY:** Recognizes human c-Myc. **APPLICATION:** ICC, IP, WB.

The Widest Panel of PARP Inhibitors

PARP Inhibitors

ABT-888

NEW

ALX-270-444-M001 1 mg
ALX-270-444-M005 5 mg

Potent inhibitor of PARP-1 and PARP-2 (potency ≤5nM *in vitro*). Suitable for *in vivo* studies. Has excellent bioavailability and good blood-brain permeation. Increases tumor growth delay resulting from radiation and DNA-damaging agents.

LIT: Inhibition of poly(ADP-ribose) polymerase enhances cell death and improves tumor growth delay in irradiated lung cancer models: J.M. Albert, et al.; Clin. Cancer Res. **13,** 3033 (2007) ▪ ABT-888, an orally active poly(ADP-ribose) polymerase inhibitor that potentiates DNA-damaging agents in preclinical tumor models: C.K. Donawho, et al.; Clin. Cancer Res. **13,** 2728 (2007)

5-AIQ . HCl

[5-Aminoisoquinolinone . HCl]
ALX-270-285-M001 1 mg
ALX-270-285-M005 5 mg

Water-soluble, potent inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1).

LIT: Effects of 5-aminoisoquinolinone, a water-soluble, potent inhibitor of the activity of poly (ADP-ribose) polymerase on the organ injury and dysfunction caused by haemorrhagic shock: M.C. McDonald, et al.; Br. J. Pharmacol. **130,** 843 (2000) ▪ **For a comprehensive bibliography please visit our website.**

3-Methyl-5-AIQ . HCl

ALX-270-450-M001 1 mg
ALX-270-450-M005 5 mg

Water-soluble, potent inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1) (IC_{50}=0.23µM) *in vitro*. Exhibits outstanding therapeutic benefits in models of myocardial infarction, ischaemia-reperfusion of the liver and kidney, heart transplantation and acute lung inflammation.

LIT: Synthesis and PARP-1 inhibitory activity of 3-substituted analogues of the potent water-soluble PARP inihbitor 5-aminoisoquinolin-1-one (5-AIQ): E. C. Y. Woon, et al.; Bioorg. Med. Chem. (submitted), (2006)

3-Aminobenzamide

ALX-270-044-G001 1 g
ALX-270-044-G005 5 g

Inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1). Has minimal effect on bacterial toxin-mediated ADP-ribosylation. Apoptosis inhibitor.

LIT: Cell death protection by 3-aminobenzamide and other poly(ADP-ribose)polymerase inhibitors: different effects on human natural killer and lymphokine activated killer cell activities: D. Monti, et al.; BBRC **199,** 525 (1994) ▪ **For a comprehensive bibliography please visit our website.**

4-Amino-1,8-naphthalimide

ALX-270-250-M010 10 mg

Potent inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1) (IC_{50}=0.18µM). About 1000-fold more potent than 3-aminobenzamide (Prod. No. ALX-270-044).

LIT: Specific inhibitors of poly(ADP-ribose) synthetase and mono(ADP-ribosyl)transferase: M. Banasik, et al.; J. Biol. Chem. **267,** 1569 (1992) ▪ 4-Amino-1,8-naphthalimide: a novel inhibitor of poly(ADP-ribose) polymerase and radiation sensitizer: A. Schlicker, et al.; Int. J. Radiat. Biol. **75,** 91 (1999) ▪ **For a comprehensive bibliography please visit our website.**

Benzamide

ALX-270-174-G005 5 g

Inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1). Neuroprotectant.

LIT: Cytotoxicity of a new IMP dehydrogenase inhibitor, benzamide riboside, to human myelogenous leukemia K562 cells: H.N. Jayaram, et al.; BBRC **186,** 1600 (1992) ▪ Nitric oxide activation of poly(ADP-ribose) synthetase in neurotoxicity: J. Zhang, et al.; Science **263,** 687 (1994)

DPQ

[3,4-Dihydro-5-[4-(1-piperidinyl)butoxy]-1(2H)-isoquinolinone]
ALX-270-221-M001 1 mg
ALX-270-221-M005 5 mg

Very potent poly(ADP-ribose) polymerase-1 (PARP-1) inhibitor.

LIT: Dihydroisoquinolines: the design and synthesis of a new series of potent inhibitors of poly(ADP-ribose) polymerase: M.J. Suto, et al.; Anticancer Drug Des. **6,** 107 (1991) ▪ Comet assay as a novel approach for studying DNA damage in focal cerebral ischemia: differential effects of NMDA receptor antagonists and poly(ADP-ribose) polymerase inhibitors: L. Giovannelli, et al.; J. Cereb. Blood Flow Metab. **22,** 697 (2002) ▪ **For a comprehensive bibliography please visit our website.**

NEW 3-(4-Chlorophenyl)quinoxaline-5-carboxamide

ALX-270-486-M005 5 mg

Potent quinoxaline-based PARP inhibitor with a 5–fold selectivity towards PARP-2 (IC_{50}=7nm) over PARP-1 (IC_{50}=33nM). Brain-permeant. Exhibits good pharmacokinetics.

LIT: Discovery of quinazolinone and quinoxaline derivatives as potent and selective poly(ADP-ribose) polymerase-1/2 inhibitors: A. Iwashita, et al.; FEBS Lett. **579,** 1389 (2005) ▪ Discovery of potent and selective PARP-1 and PARP-2 inhibitors: SBDD analysis via a combination of X-ray structural study and homology modeling: J. Ishida, et al.; Bioorg. Med. Chem. **14,** 1378 (2006)

DR2313

ALX-270-452-M001 1 mg
ALX-270-452-M005 5 mg
ALX-270-452-M025 25 mg

Potent, water soluble competitive PARP inhibitor (IC_{50}=0.20µM and 0.24µM for PARP-1 and PARP-2 respectively).

LIT: A newly synthesized poly(ADP-ribose) polymerase inhibitor, DR2313 [2-methyl-3,5,7,8-tetrahydrothiopyrano[4,3-d]-pyrimidine-4-one]: pharmacological profiles, neuroprotective effects, and therapeutic time window in cerebral ischemia in rats: H. Nakajima, et al.; Pharmacol. Exp. Ther. **312,** 472 (2005)

EB-47 . 2HCl . $2H_2O$

ALX-270-383-M001 1 mg
ALX-270-383-M005 5 mg

Very potent and water soluble PARP-1 inhibitor (IC_{50}=45nM, 100% inhibition at 200nM). Shows cytoprotective effects against oxidative damage in cells and *in vivo* models of reperfusion injury and inflammation.

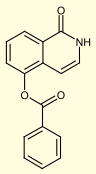
LIT: The discovery and synthesis of novel adenosine substituted 2,3-dihydro-1H-isoindol-1-ones: potent inhibitors of poly(ADP-ribose) polymerase-1 (PARP-1): P.G. Jagtap, et al.; Bioorg. Med. Chem. Lett. **14,** 81 (2004)

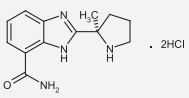
Latest Insight

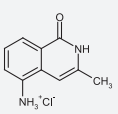
PARP-2 Specific Inhibitor

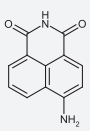
PARP-1 and PARP-2 are poly(ADP-ribose) polymerases, which are involved in the maintenance of genomic integrity under conditions of genotoxic stimuli. The presence of two PARP enzymes that are both activated by DNA breaks, raises questions about their individual roles under pathological conditions. R. Pellicciari, et al. recently identified a new potent and selective PARP-2 inhibitor 5-benzoyloxyisoquinolin-1(2*H*)-one, with 60-fold selectivity for PARP-2 over PARP-1. This new inhibitor can be used for further characterization of PARP-2 in pathophysiological conditions.

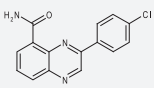
LIT: On the Way to Selective PARP-2 Inhibitors. Design, Synthesis, and Preliminary Evaluation of a Series of Isoquinolinone Derivatives: R. Pellicciari, et al.; ChemMedChem, **Epub ahead of print,** (2008)

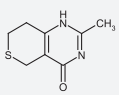


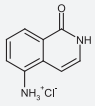

ABT-888

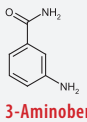

3-Methyl-5-AIQ . HCl

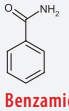

4-Amino-1,8-naphthalimide

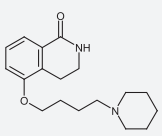

3-(4-Chlorophenyl) quinoxaline-5-carboxamide

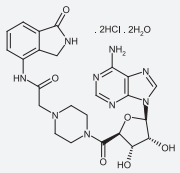

DR2313


5-AIQ . HCl


3-Aminobenzamide


Benzamide


DPQ


EB-47 . 2HCl . $2H_2O$

4-Hydroxyquinazoline

ALX-270-279-G001 1 g

Inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1).

LIT: Regulation of kinase cascades and transcription factors by a poly(ADP-ribose) polymerase-1 inhibitor, 4-hydroxyquinazoline, in lipopolysaccharide-induced inflammation in mice: B. Veres, et al.; J. Pharmacol. Exp. Ther. **310,** 247 (2004) ▪ Critical role of PI3-kinase/Akt activation in the PARP inhibitor induced heart function recovery during ischemia-reperfusion: K. Kovacs, et al.; Biochem. Pharmacol. **71,** 441 (2006)

5-Iodo-6-amino-1,2-benzopyrone

ALX-270-278-M001 1 mg
ALX-270-278-M005 5 mg

Inhibitor of poly(ADP-ribose) polymerase-1 (PARP-1).

LIT: Reversion of malignant phenotype by 5-iodo-6-amino-1,2-benzopyrone a non-covalently binding ligand of poly(ADP-ribose) polymerase: P.I. Bauer, et al.; Biochimie **77,** 374 (1995) ▪ Cancer cell selectivity of 5-iodo-6-aminobenzopyrone (INH2BP) and methyl-3,5-diiodo-4(4'-methoxyphenoxy) benzoate (DIME): E. Kirsten & E. Kun; Int. J. Mol. Med. **5,** 279 (2000) ▪ Role of poly(ADP-ribose) synthetase activation in the development of experimental allergic encephalomyelitis: G.S. Scott, et al.; J. Neuroimmunol. **117,** 78 (2001) ▪ Inhibition of poly (ADP-ribose) synthetase by gene disruption or inhibition with 5-iodo-6-amino-1,2-benzopyrone protects mice from multiple-low-dose-streptozotocin-induced diabetes: J.G. Mabley, et al.; Br. J. Pharmacol. **133,** 909 (2001) ▪ **For a comprehensive bibliography please visit our website.**

1,5-Isoquinolinediol

ALX-480-039-M005 5 mg
ALX-480-039-M025 25 mg

Potent inhibitor of inducible nitric oxide synthase (iNOS; NOS II) in mouse macropaghes. Potently blocks poly(ADP-ribose) polymerase-1 (PARP-1). Neuroprotectant.

LIT: Specific inhibitors of poly(ADP-ribose) synthetase and mono(ADP-ribosyl)transferase: M. Banasik, et al.; J. Biol. Chem. **267,** 1569 (1992) ▪ Nitric oxide activation of poly(ADP-ribose) synthetase in neurotoxicity: J. Zhang, et al.; Science **263,** 687 (1994) ▪ All trans retinoic acid induces apoptosis in acute promyelocytic NB4 cells when combined with isoquinolinediol, a poly(ADP-ribose) polymerase inhibitor: D.M. Berry, et al.; Leuk. Res. **24,** 307 (2000) ▪ **For a comprehensive bibliography please visit our website.**

Minocycline . HCl

ALX-380-109-M050 50 mg

Semisynthetic. Tetracycline derivative with antimicrobial activity. Inhibitor of angiogenesis, apoptosis and poly(ADP-ribose) polymerase-1 (PARP-1). Anti-inflammatory and neuroprotective.

LIT: Minocycline up-regulates Bcl-2 and protects against cell death in mitochondria: J. Wang, et al.; J. Biol. Chem. **279,** 19948 (2004) ▪ Minocycline inhibits poly(ADP-ribose) polymerase-1 at nanomolar concentrations: C.C. Alano, et al.; PNAS **103,** 9685 (2006) ▪ Multiple neuroprotective mechanisms of minocycline in autoimmune CNS inflammation: K. Maier, et al.; Neurobiol. Dis. **25,** 514 (2007) ▪ **For a comprehensive bibliography please visit our website.**

Nicotinamide

ALX-460-008-G010 10 g

NU1025

[8-Hydroxy-2-methylquinazoline-4-one]

ALX-270-370-M001 1 mg
ALX-270-370-M005 5 mg
ALX-270-370-M025 25 mg

A potent poly(ADP-ribose) polymerase 1 (PARP-1) inhibitor (IC_{50}=400nM) that potentiates the cytotoxicity of various DNA-active agents, including the DNA-methylating compound MTIC, the DNA strand break-inducing drug temozolomide (Prod. No. ALX-420-044), topotecan (Prod. No. ALX-350-133), bleomycin (Prod. No. ALX-630-107), and ionizing radiation.

LIT: Potentiation of anti-cancer agent cytotoxicity by the potent poly(ADP-ribose) polymerase inhibitors NU1025 and NU1064: K.J. Bowman, et al.; Br. J. Cancer **78,** 1269 (1998) ▪ Potentiation of temozolomide and topotecan growth inhibition and cytotoxicity by novel poly(adenosine diphosphoribose) polymerase inhibitors in a panel of human tumor cell lines: C.A. Delaney, et al.; Clin. Cancer Res. **6,** 2860 (2000) ▪ **For a comprehensive bibliography please visit our website.**

6(5*H*)-Phenanthridinone

ALX-270-251-M010 10 mg

Poly(ADP-ribose)polymerase (PARP) inhibitor.

LIT: Specific inhibitors of poly(ADP-ribose) synthetase and mono(ADP-ribosyl)transferase: M. Banasik, et al.; J. Biol. Chem. **267,** 1569 (1992) ▪ Effect of 6(5H)-phenanthridinone, a poly (ADP-ribose)polymerase inhibitor, and ionizing radiation on the growth of cultured lymphoma cells: D. Weltin, et al.; Int. J. Radiat. Biol. **72,** 685 (1997) ▪ **For a comprehensive bibliography please visit our website.**

TIQ-A

[Thieno[2,3-c]isoquinolin-5-one]

ALX-270-365-M001 1 mg
ALX-270-365-M005 5 mg

Potent poly(ADP-ribose) polymerase-1 (PARP-1) inhibitor (IC_{50}=450nM). Neuroprotectant.

LIT: Novel isoquinolinone-derived inhibitors of poly(ADP-ribose) polymerase-1: pharmacological characterization and neuroprotective effects in an in vitro model of cerebral ischemia: A. Chiarugi, et al.; J. Pharmacol. Exp. Ther. **305,** 943 (2003) ▪ Towards new neuroprotective agents: design and synthesis of 4H-thieno[2,3-c] isoquinolin-5-one derivatives as potent PARP-1 inhibitors: R. Pellicciari, et al.; Farmaco **58,** 851 (2003)

PARG Inhibitor

ADP-HPD . ammonium salt . dihydrate

ALX-480-094-C060 60 µg

Potent, noncompetitive, and specific inhibitor of poly(ADP-ribose) glycohydrolase (PARG) (IC_{50}=120nM) versus ADP-ribose (IC_{50}=120µM). Does not affect the activities of either PARP-1 or NAD:arginine mono(ADP-ribosyl)-transferase A even at 1mM concentration.

LIT: Specific inhibition of poly(ADP-ribose) glycohydrolase by adenosine diphosphate (hydroxymethyl)pyrrolidinediol: J.T. Slama, et al.; J. Med. Chem. **38,** 389 (1995) ▪ Mechanism of inhibition of poly(ADP-ribose) glycohydrolase by adenosine diphosphate (hydroxymethyl) pyrrolidinediol: J.T. Slama, et al.; J. Med. Chem. **38,** 4332 (1995) ▪ A cellular defense pathway regulating transcription through poly(ADP-ribosyl)ation in response to DNA damage: S. Vispe, et al.; PNAS **97,** 9886 (2000)

Latest Insight

New Target for PARP Inhibition

Pigment epithelium-derived factor (PEDF) acts as a strong endogenous inhibitor of angiogenesis and reactive oxygen species generation in cell culture, and plays a protective role in the development and progression of angiogenic diseases. Recently, H. Chen, et al. showed that PARP inhibition with the specific inhibitor PJ-34 upregulates hyperglycemia-induced PEDF expression in HUVECs in a dose-dependent manner. This resulted in delayed activation of p38 MAP kinase and a concomitant decrease in apoptosis. Their results demonstrated that PEDF might represent a target for PARP inhibition.

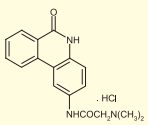
LIT: Upregulation of PEDF expression by PARP inhibition contributes to the decrease in hyperglycemia-induced apoptosis in HUVECs: H. Chen, et al.; BBRC **369,** 718 (2008)

PJ-34

ALX-270-289-M001 1 mg
ALX-270-289-M005 5 mg
ALX-270-289-M025 25 mg

Potent, water-soluble poly(ADP-ribose) polymerase (PARP) inhibitor (EC_{50}=20nM). Inhibits peroxynitrite (Prod. No. ALX-400-036)-induced cell necrosis (EC_{50}=20nM). Has significant, dose-dependent, anti-inflammatory effects in a variety of local inflammation models and provides cardioprotection by decreasing myocardial infarct size.

LIT: Protective effects of PJ34, a novel, potent inhibitor of poly(ADP-ribose) polymerase (PARP) in in vitro and in vivo models of stroke: G.E. Abdelkarim, et al.; Int. J. Mol. Med. **7,** 255 (2001) ▪ Activation of poly(ADP-ribose) polymerase contributes to the endothelial dysfunction associated with hypertension and aging: P. Pacher, et al.; Int. J. Mol. Med. **9,** 659 (2002) ▪ **For a comprehensive bibliography please visit our website.**



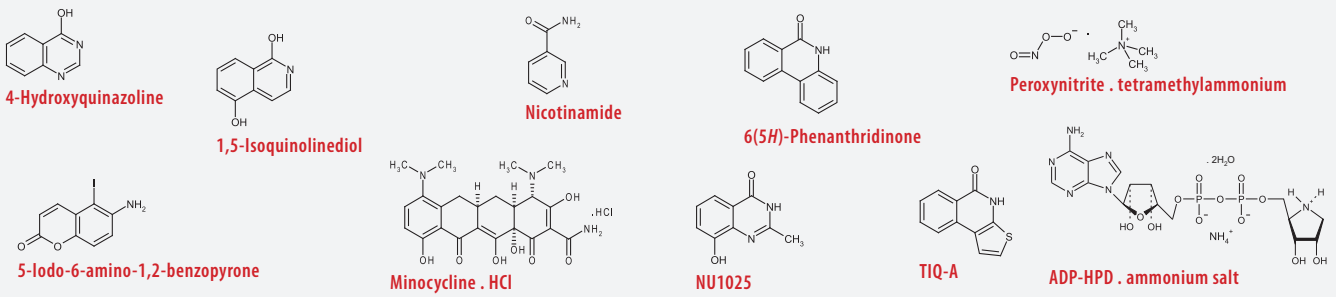
PARP Activator

Peroxynitrite . tetramethylammonium

ALX-400-036-L001 1 ml
ALX-400-036-5001 5 x 1 ml

This formulation of peroxynitrite has a low nitrite content (~1%), no hydrogen peroxide.

LIT: DNA damage induced by peroxynitrite: subsequent biological effects: C. Szabo & H. Ohshima; Nitric Oxide **1,** 373 (1997) ▪ Peroxynitrite: a biologically significant oxidant: M.P. Murphy, et al.; Gen. Pharmacol. **31,** 179 (1998)



Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

Sirtuins

Sirtuins (SIRTs 1-7), or class III histone deacetylases (HDACs), are NAD^+-dependent enzymes that target a wide range of cellular proteins in the nucleus, cytoplasm, and mitochondrium for post-translational modification by deacetylation (SIRT1, -2, -3 and -5) and/or ADP ribosylation (SIRT2, -3, -4 and -6). Sirtuins are involved in important biological processes ranging from apoptosis, cancer prevention, DNA damage repair, and regulation of energy expenditure to stress resistance.

SIRT1 has been shown to deacetylate several transcription factors, including the tumor suppressor protein p53, members of the FOXO family, HES-1 and HEY-2, PPAR-γ, MyoD, CTIP2, p300, PGC-1α, and NF-κB and has been linked to the regulation of aging. The functional interplay of SIRT1 and PARP-1 in response to DNA damage results in AIF (apoptosis inducing factor)-mediated cell death. These findings establish a functional link between the two NAD^+-dependent enzyme systems and provide a physiological interpretation for the mechanism of death in cells lacking SIRT1.

SIRT2 was shown to deacetylate α-tubulin and co-localizing with the cytoplasmic tubulin network, being involved in development. It also showed neuroprotective functions, controls insulin/IGF-1 levels in the cytoskeleton of Alzheimer disease and deacetylates p53 in the cytoplasm. The role of sirtuins in controlling basic cellular functions generated efforts in the development of small-molecule regulators that modulate their cellular function. Compounds that target sirtuins may be useful in the treatment of many diseases.

Standard Inhibitor

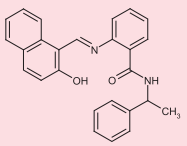
Sirtinol

[2-[(2-Hydroxynaphthalen-1-yl-methylene)amino]-N-(1-phenethyl)benzamide]

ALX-270-308-M001 1 mg
ALX-270-308-M005 5 mg

Specific cell permeable inhibitor of the sirtuin family of NAD-dependent deacetylases (ySir2: IC_{50}=48μM; hSIRT1: IC_{50}=131μM; hSIRT2: IC_{50}=58μM) with no effect on human HDAC1. Reported to inhibit Sir2p transcriptional silencing activity *in vivo* (IC_{50}=25μM) and NAD-dependent histone deacetylase activity of purified recombinant yeast Sir2p (IC_{50}=70μM) and hSIRT2 (IC_{50}=40μM) *in vitro*.

LIT: Identification of a class of small molecule inhibitors of the sirtuin family of NAD-dependent deacetylases by phenotypic screening: C.M. Grozinger, et al.; J. Biol. Chem. **276,** 38837 (2001) ▪ Human telomeric position effect is determined by chromosomal context and telomeric chromatin integrity: C.E. Koering, et al.; EMBO Rep. **3,** 1055 (2002) ▪ Design, synthesis, and biological evaluation of sirtinol analogues as class III histone/protein deacetylase (Sirtuin) inhibitors: A. Mai, et al.; J. Med. Chem. **48,** 7789 (2005) ▪ Sirt1 inhibitor, Sirtinol, induces senescence-like growth arrest with attenuated Ras-MAPK signaling in human cancer cells: H. Ota, et al.; Oncogene **25,** 176 (2006)



Antibodies

PAb to SIRT1 (25-75) (human)

BET-A300-687A 0.02 mg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 25-75 of human SIRT1 (NAD-dependent deacetylase sirtuin-1). **SPECIFICITY:** Recognizes human SIRT1. **APPLICATION:** IP, WB. BP: BET-BP300-687.

PAb to SIRT1 (700-747) (human)

BET-A300-688A 0.02 mg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 700-747 of C-terminal human SIRT1 (NAD-dependent deacetylase sirtuin-1). **SPECIFICITY:** Recognizes human SIRT1. **APPLICATION:** IP, WB. BP: BET-BP300-688.

PAb to SIRT2 (1-50) (human)

BET-A300-702A 0.1 mg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1-50 of human SIRT2 (NAD-dependent deacetylase sirtuin-2). **SPECIFICITY:** Recognizes human SIRT2. **APPLICATION:** IP, WB. BP: BET-BP300-702.

PAb to SIRT2 (350-389) (human)

BET-A300-703A 0.1 mg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 350-389 of C-terminal human SIRT2 (NAD-dependent deacetylase sirtuin-2). **SPECIFICITY:** Recognizes human SIRT2. **APPLICATION:** IP. BP: BET-BP300-703.

Inhibitors

NEW AGK2

ALX-270-484-M001 1 mg
ALX-270-484-M005 5 mg

Potent, selective and cell permeable inhibitor of sirtuin 2 (SIRT2) (IC_{50}=3.5μM). Rescues α-synuclein-mediated toxicity. Modifies inclusion morphology in a cellular model of Parkinson's disease. Protects against dopaminergic cell death. Leads to an increase in acetylated tubulin.

LIT: Sirtuin 2 inhibitors rescue alpha-synuclein-mediated toxicity in models of Parkinson's disease: T.F. Outeiro, et al.; Science **317,** 516 (2007)

Aristoforin

ALX-350-129-M001 1 mg

Stable and water-soluble derivative of hyperforin (Prod. No. ALX-350-097) inducing apoptosis. Antitumor agent. Inhibits sirtuins.

LIT: Aristoforin, a novel stable derivative of hyperforin, is a potent anticancer agent: M. Gartner, et al.; Chembiochem. **6,** 171 (2005) ▪ Phloroglucinol Derivatives Guttiferone G, Aristoforin, and Hyperforin: Inhibitors of Human Sirtuins SIRT1 and SIRT2: C. Gey, et al.; Angew. Chem. Int. Ed. Engl. **46,** 5219 (2007)

NEW B2

[CPNQ; 5-[4-(4-Chlorobenzoyl)-1-piperazinyl]-8-nitroquinoline]

ALX-270-485-MC05 0.5 mg

Cell permeable inhibitor of sirtuin 2 (SIRT2) (IC_{50}=35μM). Promotes inclusion formation in cellular models of both Huntington's disease and Parkinson's disease. Prevents huntingtin-mediated proteasome dysfunction and reduces α-synuclein-mediated toxicity.

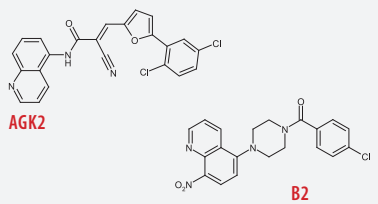
LIT: Pharmacological promotion of inclusion formation: a therapeutic approach for Huntington's and Parkinson's diseases: R.A. Bodner, et al.; PNAS **103,** 4246 (2006)

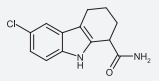
6-Chloro-2,3,4,9-tetrahydro-1*H*-carbazole-1-carboxamide

ALX-270-437-M001 1 mg

Potent cell permeable and metabolically stable specific inhibitor of hSIRT1 (IC_{50}=98nM *in vivo* / IC_{50}=38nM *in vitro*; compared to hSIRT2: IC_{50}=19μM and hSIRT3: IC_{50}=48μM) with no effect on human histone deacetylases (HDACs) class I and class II, nor NAD glycohydrolase (IC_{50}>100μg). Inhibits the deacetylation of p53 (IC_{50}=1μM).

LIT: Discovery of indoles as potent and selective inhibitors of the deacetylase SIRT1: A.D. Napper, et al.; J. Med. Chem. **48,** 8045 (2005)





Selected Latest Review Articles

The Sir 2 family of protein deacetylases: J.M. Denu; Curr. Opin. Chem. Biol. **9,** 431 (2005) ▪ Sirtuins (histone deacetylases III) in the cellular response to DNA damage – facts and hypotheses: M. Kruszewski & I. Szumiel; DNA Repair (Amst) **4,** 1306 (2005) ▪ Neuronal protection by sirtuins in Alzheimer's disease: T.S. Anekonda & P.H. Reddy; J. Neurochem. **96,** 305 (2006) ▪ Sirt1: a metabolic master switch that modulates lifespan: I.B. Leibiger & P.O. Berggren; Nat. Med. **12,** 34 (2006) ▪ The molecular biology of mammalian SIRT proteins: SIRT2 in cell cycle regulation: T. Inoue, et al.; Cell Cycle **6,** 1011 (2007) ▪ Sirtuin functions in health and disease: H. Yamamoto, et al.; Mol. Endocrinol. **21,** 1745 (2007) ▪ Sirtuins, nuclear hormone receptor acetylation and transcriptional regulation: J.R. Whittle, et al.; Trends Endocrinol. Metab. **18,** 356 (2007) ▪ Conserved metabolic regulatory functions of sirtuins: B. Schwer & E. Verdin; Cell Metab. **7,** 104 (2008)

NAD+ Metabolism

ADP-Ribosylation

Nuclear ADP-ribosylation reactions are critical for many physiological and pathophysiological outcomes, such as cellular differentiation and proliferation, genome integrity, carcinogenesis, cell survival and cell death, inflammation, and neuronal functions.

An interesting feature is the potential cross talk of mono- and poly-ADP-ribosylation reactions and other NAD+-dependent reactions, either directly through trans-ADP-ribosylation or indirectly through modulation of the NAD+ levels.

Cross talk of SIRT1 and poly-ADP-ribosylation reactions may provide balance between cell survival and cell death, longevity, and senescence. Moreover, SIRTs and mono- or poly-ADP-ribosylation pathways may provide a unified network for multicellular eukaryotes to deal with nutritional supply and environmental stress.

Various studies suggested different molecular mechanisms for how mono- and poly-ADP-ribosylation reactions are integrated in diverse physiological processes. Mono- and poly-ADP-ribosylation reactions may act on the level of signalling, modulation of chromatin structure, and epigenetic histone code.

Selected Review Article

Nuclear ADP-ribosylation reactions in mammalian cells: where are we today and where are we going?: P.O. Hassa, et al.; Microbiol. Mol. Biol. Rev. **70,** 789 (2006)

NAD: New Insights on a Key Signalling Player!

The pyridine nucleotides NAD and phosphorylated NAD (NADP) are major redox carriers in all organisms. Recent years have shown an increase of signalling and gene regulatory processes where NAD+ or NADP are metabolised. NAD+ serves as substrate for protein modification including protein deacetylation, and mono- and poly-ADP-ribosylation, while both NAD+ and NADP represent precursors of intracellular calcium-mobilizing molecules. It is beyond doubt that NADP-mediated signal transduction does not only regulate metabolic pathways, but holds a key position in the control of fundamental cellular processes. NAD+ kinases phosphorylate NAD+ to NADP and have potential roles in stress signalling and ROS generation. Components such as nicotinamide mononucleotide adenylyltransferase-1 (NMNAT1), which is involved in the NAD+-salvage pathway, and PARG might also contribute locally to the fine-tuning and the persistence, respectively, of PAR signalling at DNA-damage sites

Selected Review Articles

The new life of a centenarian: signalling functions of NAD(P): F. Berger, et al.; TIBS **29,** 111 (2004) ▪ A vital link between energy and signal transduction: M. Ziegler; FEBS J. **272,** 4561 (2005) ▪ NAD+ and NADH in cellular functions and cell death: W. Ying; Front. Biosci. **11,** 3129 (2006)

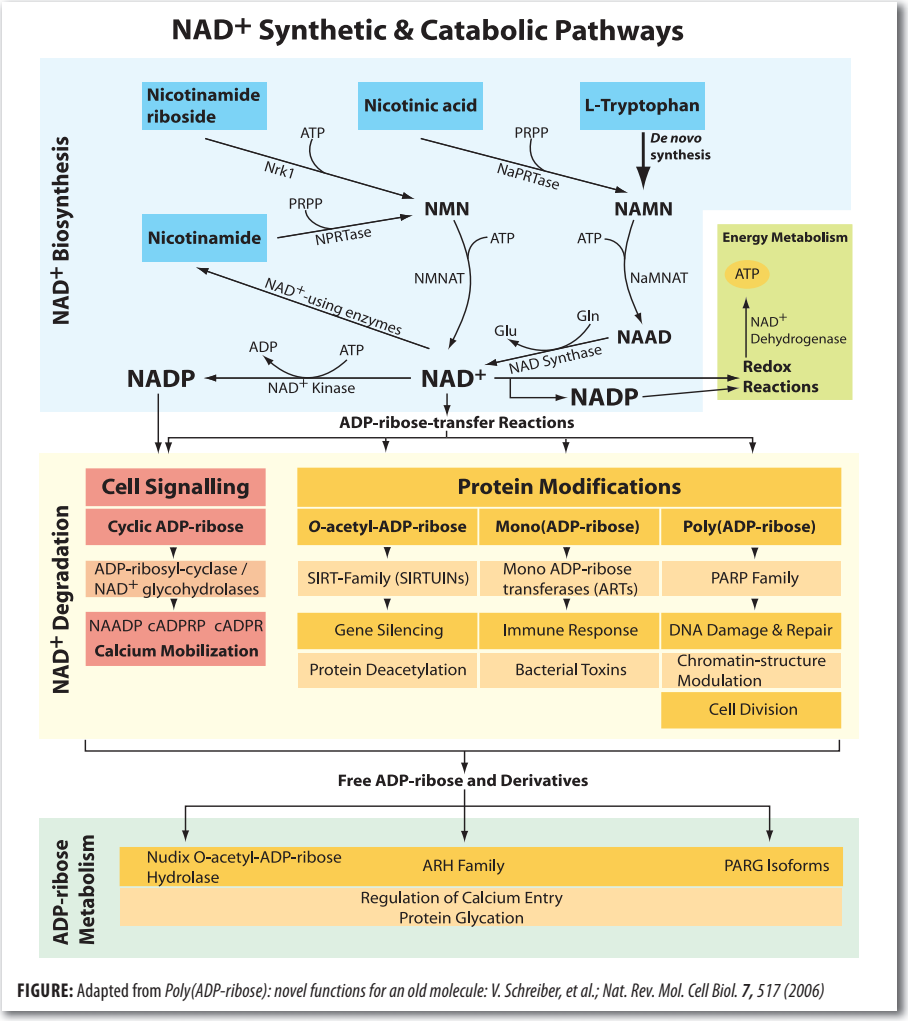


FIGURE: Adapted from *Poly(ADP-ribose): novel functions for an old molecule: V. Schreiber, et al.; Nat. Rev. Mol. Cell Biol. 7, 517 (2006)*

Highly Pure & Fully Active NAD Kinases

NAD Kinase (full length) (active) (human) (rec.) (His)

ALX-201-235-C050 50 µg

Produced in *E. coli*. Human NADK is fused at the N-terminus to a His-tag. **QUANTITY:** Sufficient for the preparation of >10µmol of NADP from NAD and ATP in 1ml of a 10mM solution. Free of any nucleotide converting side-activities.

LIT: Structural and functional characterization of human NAD kinase: F. Lerner, et al.; BBRC **288,** 69 (2001)

NAD Kinase (NT truncated) (active) (human) (rec.) (His)

ALX-201-236-C050 50 µg

Produced in *E. coli*. Human NADK (aa 64-446) is fused at the N-terminus to a His-tag. **QUANTITY:** Sufficient for the preparation of >10µmol of NADP from NAD and ATP in 1ml of a 10mM solution. Free of any nucleotide converting side-activities.

LIT: Structural and functional characterization of human NAD kinase: F. Lerner, et al.; BBRC **288,** 69 (2001)

NMNAT1 (human) (rec.) (His)

ALX-201-237-C100 100 µg

Produced in *E. coli*. Full length human NMNAT1 is fused at the N-terminus to a His-tag. **APPLICATION:** Well suited for the synthesis of NAD due to high specific activity (10-20U/mg) and high substrate selectivity compared to NMNAT3 (human) (recombinant) (Prod. No. ALX-201-238).

LIT: Molecular cloning, chromosomal localization, tissue mRNA levels, bacterial expression, and enzymatic properties of human NMN adenylyltransferase: M. Emanuelli, et al.; J. Biol. Chem. **276,** 406 (2001) ▪ **For a comprehensive bibliography please visit our website.**

NMNAT3 (human) (rec.) (His)

ALX-201-238-C100 100 µg

Produced in *E. coli*. Full length human NMNAT3 is fused at the N-terminus to a His-tag. **APPLICATION:** Well suited for the synthesis of NAD analogs due to lower substrate selectivity compared to NMNAT1 (human) (recombinant) (Prod. No. ALX-201-237).

LIT: Structural characterization of a human cytosolic NMN/NaMN adenylyltransferase and implication in human NAD biosynthesis: X. Zhang, et al.; J. Biol. Chem. **278,** 13503 (2003) ▪ Subcellular compartmentation and differential catalytic properties of the three human nicotinamide mononucleotide adenylyltransferase isoforms: F. Berger, et al.; J. Biol. Chem. **280,** 36334 (2005)

NAD+ Metabolism continued

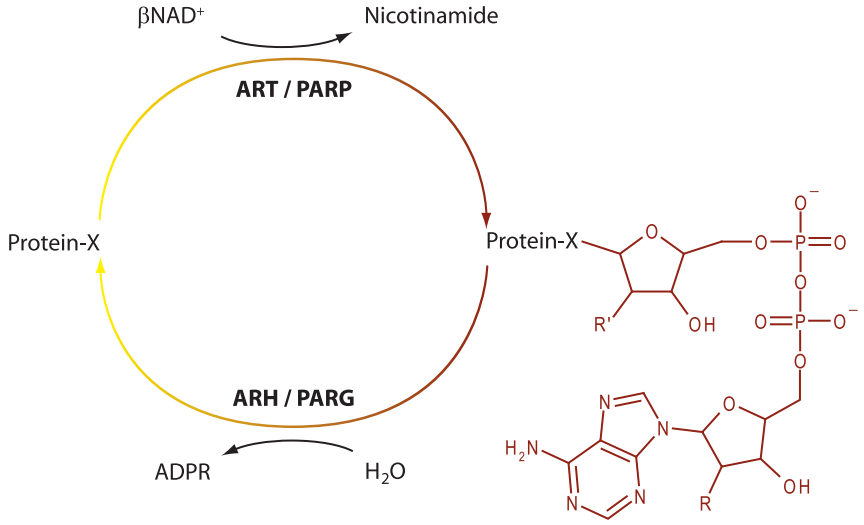


FIGURE: Posttranslational modification of proteins by reversible ADP-ribosylation. Adapted from: *The structure of human ADP-ribosylhydrolase 3 (ARH3) provides insights into the reversibility of protein ADP-ribosylation: C. Mueller-Dieckmann, et al.; PNAS **103,** 15026 (2006)*

NAD-dependent ADP-ribosylation

NAD-dependent ADP-ribosylation is a reversible posttranslational modification involved in many cellular processes including DNA-repair, transcription, telomere function and apoptosis. Mono- and poly-ADP-ribosyltransferases (mARTs and pARTs/PARPs) catalyze the transfer of the ADP-ribose moiety from NAD+ onto specific amino acid side chains in target proteins under the release of nicotinamide. This modification may lead to either activation or inactivation of the target protein. In contrast, protein-ADP-ribosylhydrolases (ARHs and PARGs) hydrolyze the α-glycosidic bond between ADP-ribose and the side chain, thereby restoring normal protein function (Figure) [1, 2].

Mono-ADP-ribosyltransferases (ARTs; mARTs)

Enzyme-modulated mono(ADP-ribosyl)ation was originally identified as the mechanism of action of several bacterial toxins [1]. The cholera, diphteria and pertussis toxins are mono-ADP-ribosyltransferases (ARTs; mARTs; EC 2.4.2.31), known to cause various pathologies after their translocation into mammalian host cells. These toxins interfere with protein synthesis, signal transduction, or cytoskeletal functions by ADP-ribosylating key target proteins such as elongation factor 2, G proteins, or actin.

Mammalian ARTs constitute a family of structurally related proteins expressed on the cell surface or secreted in the extracellular compartment. Five paralogs (ART1-5) have been cloned. Only four of them are expressed in human due to a defective ART2 gene, and six in the mouse as the result of ART2 gene duplication (ART2.1, ART2.2) [3]. ARTs are expressed in different tissues and are involved in many physiological processes, such as myogenesis and innate as well as adaptive immunity [4].

The ART substrate NAD gets released from damaged cells during inflammation. Upon exposure of T cells to NAD, ART2 catalyzes ADP-ribosylation of the purinergic receptor P2X7 and other functionally important cell surface proteins. ADP-ribosylation activates P2X7, triggering calcium flux, exposure of phosphatidylserine, and formation of large membrane pores, ultimately resulting in apoptosis [5-7]. In the extracellular environment, the signalling function of NAD is controlled by NAD-degrading ectoenzymes such as CD38 [8].

ADP-ribosylhydrolases (ARHs)

Three different ADP-ribosylhydrolases (ARH1-3) have been identified in human so far. ARH1 specifically hydrolyzes ADP-ribosylarginine, whereas ARH3 degrades poly-ADP-ribose but does not cleave ADP-ribosyl-asparagine, -diphthamide, or –cysteine bonds. In addition, ARH3 catalyzes the production of ADP-ribose from O-acetyl-ADP-ribose. The exact function of ARH2 has not been determined so far [9, 10].

LIT: [1] ADP-ribosylation: K. Ueda & O. Hayaishi; Annu. Rev. Biochem. **54,** 73 (1985) ▪ **[2]** The structure of human ADP-ribosylhydrolase 3 (ARH3) provides insights into the reversibility of protein ADP-ribosylation: C. Mueller-Dieckmann, et al.; PNAS **103,** 15026 (2006) ▪ **[3]** The family of toxin-related ecto-ADP-ribosyltransferases in humans and the mouse: G. Glowacki, et al.; Protein Sci. **11,** 1657 (2002) ▪ **[4]** Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte, et al.; Cell Immunol. **236,** 66 (2005) ▪ **[5]** NAD-induced T cell death: ADP-ribosylation of cell surface proteins by ART2 activates the cytolytic P2X7 purinoceptor: M. Seman, et al.; Immunity **19,** 571 (2003) ▪ **[6]** Triggering of T-cell apoptosis by toxin-related ecto-ADP-ribosyltransferase ART2: F. Scheuplein, et al.; Ann. N. Y. Acad. Sci. **1010,** 296 (2003) ▪ **[7]** P2X7 receptor-dependent and -independent T cell death is induced by nicotinamide adenine dinucleotide: H. Kawamura, et al.; J. Immunol. **174,** 1971 (2005) ▪ **[8]** CD38 controls ADP-ribosyltransferase-2-catalyzed ADP-ribosylation of T cell surface proteins: C. Krebs, et al.; J. Immunol. **174,** 3298 (2005) ▪ **[9]** Identification and characterization of a mammalian 39-kDa poly(ADP-ribose) glycohydrolase: S. Oka, et al.; J. Biol. Chem. **281,** 705 (2006) ▪ **[10]** The 39-kDa poly(ADP-ribose) glycohydrolase ARH3 hydrolyzes O-acetyl-ADP-ribose, a product of the Sir2 family of acetyl-histone deacetylases: T. Ono, et al.; PNAS **103,** 16687 (2006)

ART Proteins

NEW ART2.1 (rat) (rec.) (His)
[ecto-ADP-ribosyltransferase 1 (rat) (rec.) (His); ART2a (rat) (rec.) (His); RT6.1 (rat) (rec.) (His)]
ALX-201-287-C010 10 µg
Produced in *E. coli.*

LIT: Structure of the ecto-ADP-ribosyl transferase ART2.2 from rat: C. Mueller-Dieckmann, et al.; J. Mol. Biol. **322,** 687 (2002) ▪ Substrate binding and catalysis of ecto-ADP-ribosyltransferase 2.2 from rat: H. Ritter, et al.; Biochemistry **42,** 10155 (2003)

NEW ART2.2 (rat) (rec.) (His)
[ecto-ADP-ribosyltransferase 2 (rat) (rec.) (His); ART2b (rat) (rec.) (His); RT6.2 (rat) (rec.) (His)]
ALX-201-288-C010 10 µg
Produced in *E. coli.*

LIT: Expression, purification, crystallization and preliminary X-ray analysis of rat ecto-ADP-ribosyltransferase 2 (ART2.2): C. Mueller-Dieckmann, et al.; Acta Crystallogr. D. Biol. Crystallogr. **58,** 1211 (2002) ▪ Structure of the ecto-ADP-ribosyl transferase ART2.2 from rat: C. Mueller-Dieckmann, et al.; J. Mol. Biol. **322,** 687 (2002) ▪ Substrate binding and catalysis of ecto-ADP-ribosyltransferase 2.2 from rat: H. Ritter, et al.; Biochemistry **42,** 10155 (2003)

NEW ART2.2 (mouse) (rec.) (His)
[ecto-ADP-ribosyltransferase 2.2 (mouse) (rec.) (His); ART2b (mouse) (rec.) (His)]
ALX-201-289-C010 10 µg
Produced in *E. coli.*

LIT: Regulation of glutamate dehydrogenase by reversible ADP-ribosylation in mitochondria: A. Herrero-Yraola, et al.; EMBO J. **20,** 2404 (2001) ▪ Single domain antibodies from llama effectively and specifically block T cell ecto-ADP-ribosyltransferase ART2.2 in vivo: F. Koch-Nolte, et al.; FASEB J. **21,** 3490 (2007)

Related Products

Pertussis Toxin
[Islet-Activating Protein; PTX; Holotoxin]
ALX-630-003-C050 50 µg
Isolated from *Bordetella pertussis.* Major protein toxin produced by virulent strains of *Bordetella pertussis.* The purified protein consists of five dissimilar subunits: S-1 (MW 28kDa), S-2 (MW 23kDa), S-3 (MW 22kDa), S-4 (MW 11.7kDa) and S-5 (MW 9.3kDa), in a molar ratio of 1:1:1:2:1. S-1 (A protomer) is responsible for the enzymatic activity of the toxin. Together, S-2, S-3, S-4 and S-5 comprise the B oligomer, responsible for binding the toxin to the cell surface.

LIT: Subunit structure of islet-activating protein, pertussis toxin, in conformity with the A-B model: M. Tamura, et al.; Biochemistry **21,** 5516 (1982) ▪ Induction of a novel morphological response in Chinese hamster ovary cells by pertussis toxin: E.L. Hewlett, et al.; Infect. Immun. **40,** 1198 (1983) ▪ Structure-activity analysis of the activation of pertussis toxin: H.R. Kaslow, et al.; Biochemistry **26,** 123 (1987) ▪ Pertussis toxin and target eukaryotic cells: binding, entry, and activation: H. R. Kaslow & D. L. Burns; FASEB J. **6,** 2684 (1992) ▪ A proposed mechanism of ADP-ribosylation catalyzed by the pertussis toxin S1 subunit: C. Locht & R. Antoine; Biochimie **77,** 333 (1995)

NEW SpvB (*salmonella enterica*) (rec.) (His)
ALX-201-294-C010 10 µg
Produced in *E. coli.*

LIT: The spvB gene-product of the Salmonella enterica virulence plasmid is a mono(ADP-ribosyl)transferase: H. Otto, et al.; Mol. Microbiol. **37,** 1106 (2000) ▪ A steric antagonism of actin polymerization by a salmonella virulence protein: S.M. Margarit, et al.; Structure **14,** 1219 (2006)

ART Antibodies

MAb to ART1 (human) (GUGU1-A3)
ALX-802-020-L001 1 ml

CLONE: GUGU1-A3. **ISOTYPE:** Rat IgG2b. **IMMUNOGEN:** Vector containing the cDNA of human ART1 (ecto-ADP-ribosyltransferase 1; CD296). **SPECIFICITY:** Recognizes human ART1. **APPLICATION:** FC, ICC.

LIT: Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte, et al.; Cell. Immunol. **236,** 66 (2005)

PAb to ART1 (human)
ALX-215-037-R100 100 µl

From rabbit. **IMMUNOGEN:** Vector containing the cDNA of human ART1 (ecto-ADP-ribosyltransferase 1; CD296). **SPECIFICITY:** Recognizes human ART1. **APPLICATION:** FC, ICC.

LIT: See ALX-802-020

MAb to ART1 (mouse) (NOGU1-A111)
ALX-802-028-L001 1 ml

CLONE: NOGU1-A111. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of mouse ART1 (ecto-ADP-ribosyltransferase 1; CD296). **SPECIFICITY:** Recognizes mouse ART1. **APPLICATION:** FC, ICC.

PAb to ART1 (mouse)
ALX-215-038-R100 100 µl

From rabbit. **IMMUNOGEN:** Vector containing the cDNA of mouse ART1 (ecto-ADP-ribosyltransferase 1; CD296). **SPECIFICITY:** Recognizes mouse ART1. **APPLICATION:** FC, ICC.

LIT: See ALX-802-020

MAb to ART2.1 (mouse) (GUGU2-B54)
ALX-802-021-L001 1 ml

CLONE: GUGU2-B54. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of mouse ART2.1 (ecto-ADP-ribosyltransferase 2.1; ART2a). **SPECIFICITY:** Recognizes mouse ART2.1. **APPLICATION:** FC, ICC.

LIT: See ALX-802-020

MAb to ART2.2 (mouse) (NIKA-102)
ALX-802-022-L001 1 ml

CLONE: NIKA-102. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of mouse ART2.2 (ecto-ADP-ribosyltransferase 2.2; ART2b). **SPECIFICITY:** Recognizes mouse ART2.2. **APPLICATION:** FC, ICC.

LIT: A new monoclonal antibody detects a developmentally regulated mouse ecto-ADP-ribosyltransferase on T cells: subset distribution, inbred strain variation, and modulation upon T cell activation: F. Koch-Nolte, et al.; J. Immunol. **163,** 6014 (1999)

NEW rAb (Single Domain, VHH) to ART2.2 (mouse) (s+16a)
ALX-815-002-C050 50 µg

CLONE: s+16a. **ISOTYPE:** Llama IgG. **IMMUNOGEN:** Recombinant mouse ART2.2 (ecto-ADP-ribosyltransferase 2.2; ART2b). **SPECIFICITY:** Recognizes mouse ART2.2. **APPLICATION:** FUNC (blocking: effectively and specifically blocks ART2.2 *in vitro* and *in vivo*).

LIT: Single domain antibodies from llama effectively and specifically block T cell ecto-ADP-ribosyltransferase ART2.2 in vivo: F. Koch-Nolte, et al.; FASEB J. **21,** 3490 (2007)

PAb to ART2.2 (mouse)
ALX-215-039-R100 100 µl

From rabbit. **IMMUNOGEN:** Vector containing the cDNA of mouse ART2.2 (ecto-ADP-ribosyltransferase 2.2; ART2b). **SPECIFICITY:** Recognizes mouse ART2.2. **APPLICATION:** FC, ICC. FUNC (blocking).

LIT: Rapid induction of naive T cell apoptosis by ecto-nicotinamide adenine dinucleotide: requirement for mono(ADP-ribosyl)transferase 2 and a downstream effector: S. Adriouch, et al.; J. Immunol. **167,** 196 (2001) ▪ NAD-induced T cell death: ADP-ribosylation of cell surface proteins by ART2 activates the cytolytic P2X7 purinoceptor: M. Seman, et al.; Immunity **19,** 571 (2003) ▪ Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte, et al.; Cell. Immunol. **236,** 66 (2005)

MAb to ART3 (human) (GUGU3-A51)
ALX-802-023-L001 1 ml

CLONE: GUGU3-A51. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of human ART3 (ecto-ADP-ribosyltransferase 3). **SPECIFICITY:** Recognizes human ART3. **APPLICATION:** FC, ICC.

LIT: Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte, et al.; Cell. Immunol. **236,** 66 (2005) ▪ Expression of toxin-related human mono-ADP-ribosyltransferase 3 in human testes: M. Friedrich, et al.; Asian J. Androl. **8,** 281 (2006)

MAb to ART3 (mouse) (GUGU3-A34)
ALX-802-024-L001 1 ml

CLONE: GUGU3-A34. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of mouse ART3 (ecto-ADP-ribosyltransferase 3). **SPECIFICITY:** Recognizes mouse ART3. **APPLICATION:** FC, ICC.

LIT: Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte, et al.; Cell. Immunol. **236,** 66 (2005) ▪ Expression of toxin-related human mono-ADP-ribosyltransferase 3 in human testes: M. Friedrich, et al.; Asian J. Androl. **8,** 281 (2006)

MAb to ART4 (human) (NONI-B4)
ALX-802-025-L001 1 ml

CLONE: NONI-B4. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of human ART4 (ecto-ADP-ribosyltransferase 4; CD297). **SPECIFICITY:** Recognizes human ART4. **APPLICATION:** FC, ICC.

LIT: A panel of monoclonal antibodies recognizing GPI-anchored ADP-ribosyltransferase ART4, the carrier of the Dombrock blood group antigens: I. Parusel, et al.; Cell Immunol. **236,** 59 (2005) ▪ Use of genetic immunization to raise antibodies recognizing toxin-related cell surface ADP-ribosyltransferases in native conformation: F. Koch-Nolte; Cell. Immunol. **236,** 66 (2005)

PAb to ART4 (human)
ALX-215-042-R100 100 µl

From rabbit. **IMMUNOGEN:** Vector containing the cDNA of human ART4 (ecto-ADP-ribosyltransferase 4; CD297). **SPECIFICITY:** Recognizes human ART4. **APPLICATION:** FC, ICC.

LIT: See ALX-802-020

MAb to ART4 (mouse) (GUGU4-A53)
ALX-802-026-L001 1 ml

CLONE: GUGU4-A53. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Vector containing the cDNA of mouse ART4 (ecto-ADP-ribosyltransferase 4; CD297). **SPECIFICITY:** Recognizes mouse ART4. **APPLICATION:** FC, ICC.

LIT: See ALX-802-020

ARH Proteins

NEW ARH1 (human) (rec.) (His)
[ADP-ribosylarginine Hydrolase (human) (rec.) (His); ADPRH (human) (rec.) (His)]
ALX-201-290-C010 10 µg
Produced in *E. coli*.

LIT: The structure of human ADP-ribosylhydrolase 3 (ARH3) provides insights into the reversibility of protein ADP-ribosylation: C. Mueller-Dieckmann, et al.; PNAS **103,** 15026 (2006)

NEW ARH1 (mouse) (rec.) (His)
[ADP-ribosylarginine Hydrolase (mouse) (rec.) (His); Adprh (mouse) (rec.) (His)]
ALX-201-291-C010 10 µg
Produced in *E. coli*.

NEW ARH3 (human) (rec.) (His)
[ADP-ribosylhydrolase 3 (human) (rec.) (His); ADPRHL2 (human) (rec.) (His)]
ALX-201-292-C010 10 µg
Produced in *E. coli*.

LIT: The structure of human ADP-ribosylhydrolase 3 (ARH3) provides insights into the reversibility of protein ADP-ribosylation: C. Mueller-Dieckmann, et al.; PNAS **103,** 15026 (2006)

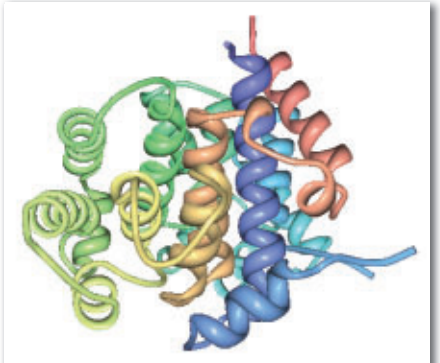


FIGURE: Crystal structure of human ARH3.

NEW ARH3 (mouse) (rec.) (His)
[ADP-ribosylhydrolase 3 (mouse) (rec.) (His); Adprhl2 (mouse) (rec.) (His)]
ALX-201-293-C010 10 µg
Produced in *E. coli*.

LIT: Functional localization of two poly(ADP-ribose)-degrading enzymes to the mitochondrial matrix: M. Niere, et al.; Mol. Cell Biol. **28,** 814 (2008) ▪ Structure of mouse ADP-ribosylhydrolase 3 (mARH3): C. Mueller-Dieckmann, et al.; Acta Crystallogr. Sect. F Struct. Biol. Cryst. Commun. **64,** 156 (2008)

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[ε-NAD⁺]
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Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

Clone 10H– The Standard DNA Damage Detection Marker

MAb to Poly(ADP-ribose) [PAR] (10H)

ALX-804-220-R100 100 µl

CLONE: 10H. **ISOTYPE:** Mouse IgG3. **IMMUNOGEN:** Purified poly(ADP-ribose). **SPECIFICITY:** Recognizes poly(ADP-ribose) synthesized by a broad range of PARPs (poly(ADP-ribose) polymerases) like human, mouse, rat or *Drosophila* PARP enzyme. **APPLICATION:** FC, ICC, IHC (PS), WB.

LIT: Monoclonal antibodies to poly(adenosine diphosphate ribose) recognize different structures: H. Kawamitsu, et al.; Biochemistry **23,** 3771 (1984) (Original Reference) ▪ Detection of poly(ADP-ribose) polymerase and its reaction product poly(ADP-ribose) by immunocytochemistry: J.H. Küpper, et al.; Histochem. J. **28,** 391 (1996) ▪ Multiparametric staining to identify apoptotic human cells: C. Negri, et al.; Exp. Cell Res. **234,** 174 (1997) ▪ Poly(ADP-ribose) immunostaining to detect apoptosis induced by a neurotoxic fragment of prion protein: A. Bürkle, et al.; Histochem. J. **31,** 711 (1999) ▪ Reactive oxygen species participate in mdr1b mRNA and P-glycoprotein overexpression in primary rat hepatocyte cultures: C. Ziemann, et al.; Carcinogenesis **20,** 407 (1999) ▪ Detection of poly(ADP-ribose) synthesis in Drosophila testes upon gamma-irradiation: S. Lankenau, et al.; Chromosoma **108,** 44 (1999) ▪ Quantitative nonisotopic immuno-dot-blot method for the assessment of cellular poly(ADP-ribosyl)ation capacity: R. Pfeiffer, et al.; Anal. Biochem. **275,** 118 (1999) ▪ Poly(ADP-ribosyl)ation, genomic instability, and longevity: A. Bürkle; Ann. N. Y. Acad. Sci. **908,** 126 (2000) ▪ Flow-cytometric assessment of cellular poly(ADP-ribosyl)ation capacity in peripheral blood lymphocytes: A. Kunzmann, et al.; Immun. Ageing **3,** 8 (2006) ▪ **For a comprehensive bibliography please visit our website.**

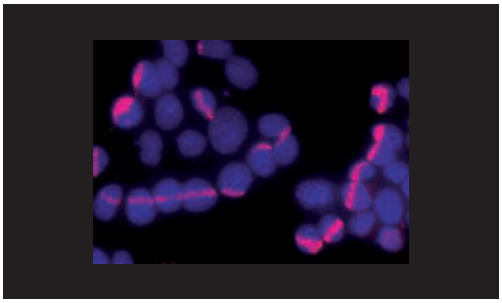


FIGURE: HeLa irradiated cells with a microbeam laser.
Picture courtesy of C. Spenlehauer & G. de Murcia (CNRS, Strasbourg)

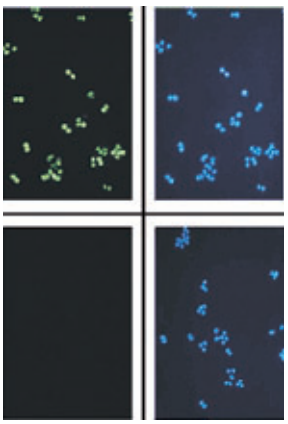


FIGURE: Detection of DNA damage.

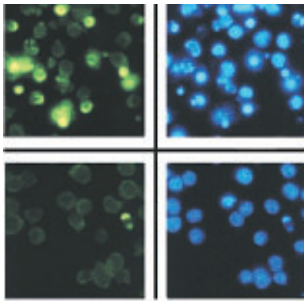


FIGURE: Detection of apoptotic cells by immunofluorescence.

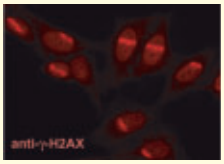
DNA Damage Marker

PAb to Histone γ-H2AX (human) (phosphorylated) (pSer^{139})

ALX-210-390-R050 50 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to Ser^{139}-phosphorylated human γ-histone H2AX (K^{134}ATQApSQEY^{142}). **SPECIFICITY:** Recognizes Ser^{139}-phosphorylated human H2AX. Does not cross-react with non-phosphorylated human H2AX. **APPLICATION:** ICC, WB.

LIT: Local DNA damage by proton microbeam irradiation induces poly(ADP-ribose) synthesis in mammalian cells: L. Tartier, et al.; Mutagenesis **18,** 411 (2003)



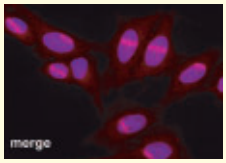


FIGURE: Detection of DNA damage in HeLa cells induced locally with anti-γ-H2AX PAb (Prod. No. ALX-210-390). Right) merged image of anti-γ-H2AX PAb and HOE 33258 (Prod. No. ALX-620-051) staining.
Pictures courtesy of C. Spenlehauer & G. de Murcia (CNRS, Strasbourg).

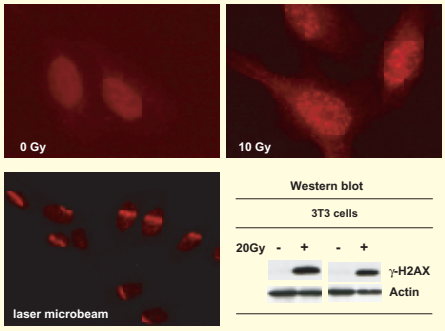


FIGURE: Detection of DNA damage induced globally (X-ray irradiation with 10 Gray) or locally (laser microbeam irradiation) with anti-γ-H2AX PAb (Prod. No. ALX-210-390).
Picture courtesy of C. Spenlehauer & G. de Murcia (CNRS, Strasbourg).

15-May-08