

TREVIGEN®

A Leader in the Fields of Apoptosis and DNA Damage and Repair

PRODUCT FOCUS

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(Please contact us so we can notify you of product release)

Poly(ADP-ribose) polymerase (PARP) is a nuclear protein of 116 kDa present at approximately 1×10^6 copies in somatic cells. Following activation by DNA strand breaks, poly(ADP-ribose) polymerase (PARP) hydrolyzes NAD and catalyzes the formation of poly(ADP-ribose) onto itself and other nuclear proteins with the release of nicotinamide.

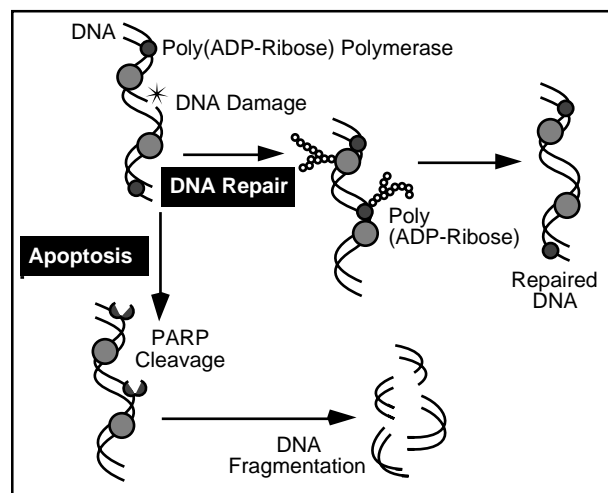
In response to low to moderate levels of DNA damage, PARP is activated and NAD levels in the cell decrease. Experiments with PARP inhibitors suggest that PARP activity may be necessary to rescue cells after low to moderate levels of DNA damage. In contrast, when cells experience massive levels of DNA damage and DNA strand breaks, activation of PARP can lead to depletion of NAD and ATP, resulting in a marked decrease in energy-dependent processes and in DNA repair. In this situation, activation of PARP by massive DNA damage may actually be a suicide response and leads to cell death before the cell can repair the DNA damage. This suicide response may be advantageous to the organism, since these cells, if allowed to survive, may exhibit high mutation rates.

PARP is a target for degradation by proteases induced during the process of apoptosis, resulting in the formation of two PARP fragments of 85 kDa and 25 kDa. The formation of these fragments is an early indication of the cell's commitment to programmed cell death.

Poly(ADP-ribose) polymerase, or PARP, is a nuclear protein whose role in several major cellular functions is only now being realized. Poly(ADP-ribosyl)ation is involved with chro-

matin decondensation, DNA replication, DNA repair, gene expression, malignant transformation, cellular differentiation and apoptosis. Studies of mice have shown that PARP activation may be involved with cerebral ischemia, traumatic brain injury, myocardial ischemia, type I diabetes, inflammatory bowel disease, collagen-induced arthritis, and multiple organ failure due to shock. Recently, a study showed that PARP activation is the principal determinant of MPTP-induced dopaminergic cell death, a model system for Parkinson's disease. Trevigen is committed to providing research products for studies involving PARP to promote the continuation of advances in this exciting field.

Trevigen offers a variety of PARP related products, including antibodies, purified recombinant PARP enzymes, a PARP Activity Assay Kit, a PARP Inhibition Assay Kit, and biotinylated NAD substrate.



PARP Related Products

<u>Catalog</u>	<u>Description</u>	<u>Price</u>
4667-50-K	PARP Assay Kit, 50 Samples	\$325
4669-96-K	PARP Inhibition Assay Kit, 96 Samples	\$350
4667-50-01	Human PARP Enzyme, 100 Units	\$175
4667-250-01	Human PARP Enzyme, 500 Units	\$595
4668-100-01	Human PARP Enzyme (HSA), 100 Units	\$265
4668-500-01	Human PARP Enzyme (HSA), 500 Units	\$895
4335-MC-100	Anti-PAR Monoclonal Antibody, 100 μ l	\$195
4336-BPC-100	Anti-PAR Polyclonal Antibody, 100 μ l	\$250
4338-MC-50	Anti-PARP Monoclonal Antibody, 50 μ g	\$155
4670-500-01	Biotinylated NAD, 500 μ l	\$125
4670-500-05	Biotinylated NAD, 5 x 500 μ l	\$565
4670-500-10	Biotinylated NAD, 10 x 500 μ l	\$1000

(Enquiry Bulk Quantities)

Why Trevigen?

Trevigen is recognized as a well established leader in the fields of apoptosis and DNA damage and repair. We have been assisting researchers for years with quality products and technical service unmatched by our competition. All of our products are tested in-house and in the field to make sure that our customers are receiving only the highest quality substrates and reagents. Our technical service department is always available to help you in using our products correctly, and with years of experience, we have compiled a vast database of knowledge for all kinds of situations and experiments. So who better to ask? This combination has proved vital to researchers just entering the field, and to those who have been disappointed time and again with results from other companies. After reviewing our PARP product line, contact us with any questions you have and you will realize that Trevigen has set the mark for the competition.

PARP Product Line

Poly(ADP-ribose) Polymerase (PARP) Activity Assay Kit

Catalog# 4667-50-K 50 Samples

This PARP assay kit allows the investigator to determine PARP activity by measuring the incorporation of radiolabeled NAD. Quantitative values are determined from acid-insoluble counts and scintillation counting. This test allows for a variety of applications.

- 1) **Direct measure of PARP Inhibition.** The assay provides purified PARP and activated DNA that may be used as a standard assay in quantitative analysis of PARP inhibition by exogenous agents.
- 2) **Indirect quantitative measure of DNA of damage** in cell extracts. PARP activity in cell extracts, without the addition of exogenous nicked DNA, reflects the degree of DNA damage present in cell or tissue extracts.
- 3) **Apoptosis.** Cleavage of PARP during apoptosis yields a 25 kDa and 89 kDa fragment during apoptosis. The assay may be used to determine the loss of PARP activity due to cleavage during apoptosis, as well as measure the induction of endogenous PARP early in apoptosis from DNA fragmentation, and later, the loss in activity due to proteolytic cleavage.

Human Poly (ADP-ribose) Polymerase (PARP) Protein

Catalog# 4667-50-01 (100 Units)
4667-250-01 (500 Units)

Trevigen now offers two grades of poly(ADP-ribose) polymerase. The standard enzyme is purified to approximately 50% purity, and is useful as a positive control for both Western blot analysis of ribosylated proteins and the PARP Activity Assay (cat.# 4667-50-K).

Catalog# 4668-100-01 (100 Units)
4668-500-01 (500 Units)

Trevigen also offers a new high specific activity (HSA) enzyme which is purified to greater than 95%. HSA PARP is useful for more detailed studies or for drug discovery applications.

Poly(ADP-ribose) Polymerase (PARP) Inhibition Assay Kit

Catalog# 4669-96-K 96 Samples

Experiments with PARP inhibitors suggest that PARP activity may be necessary to rescue cells after low to moderate levels of DNA damage. Trevigen's PARP Inhibition Assay is a 96 well microplate based assay utilizing our unique biotinylated NAD substrate to measure the inhibition of purified recombinant human PARP following the addition of an experimental compound. The kit provides a rapid assay in a non-isotopic colorimetric format.

Biotinylated NAD

Catalog# 4670-500-01 500 µl
4670-500-05 5 x 500 µl
4670-500-10 10 x 500 µl

Trevigen's biotinylated NAD (6-biotin-17-nicotinamide-adenine-dinucleotide) provides a convenient non-isotopic alternative to radiolabeled NAD for studies requiring this substrate. PARP hydrolyzes NAD and catalyzes the formation of poly(ADP-ribose) onto itself and other nuclear proteins, with the release of nicotinamide. Biotinylated NAD allows an indirect measure of PARP activity when biotin incorporation is detected using a conjugated-streptavidin detection system.

References:

1. Hauschildt, S., P. Scheipers, W.G. Bessler, and A. Mulsch. 1992. Induction of nitric oxide synthase in L929 cells by tumour-necrosis factor alpha is prevented by inhibitors of poly (ADP-ribose) polymerase. *Biochem. J.* **288**: 255-260.
2. Zhang, J., V.D. Dawson, T.M. Dawson, and S.H. Snyder. 1994. Nitric oxide activation of poly (ADP-ribose) synthetase in neurotoxicity. *Science* **263**: 687-689.
3. Kaufmann, S.H., S. Desnoyers, Y. Ottaviano, N.E. Davidson, and G.G. Poirier. 1993. Specific proteolytic cleavage of poly (ADP-ribose) polymerase: an early marker of chemotherapy-induced apoptosis. *Cancer Res* **53**: 3976-3986

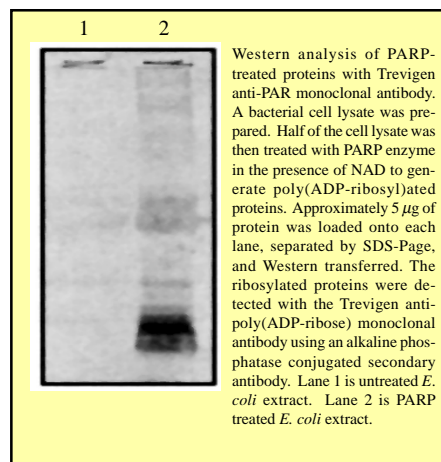
Enquiry Bulk Quantities

PARP Related Antibodies

Anti-PAR Polymer Monoclonal Antibody

Catalog# 4335-MC-100

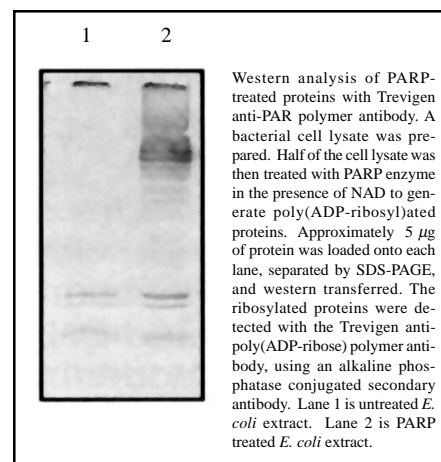
Trevigen makes available a monoclonal antibody specific for the poly (ADP-ribose) polymer (anti-PAR polymer). The poly (ADP-ribose) polymers are generated on the glutamic acid residues of nuclear proteins during the DNA repair process. The antibody is specific for poly(ADP-ribose) polymers (10 to 50 Units long) and does not recognize structurally related RNA, DNA, ADP-Ribose monomers, NAD or other nucleic acid monomers.



Anti-PAR Polymer Polyclonal Antibody

Catalog# 4336-BPC-100

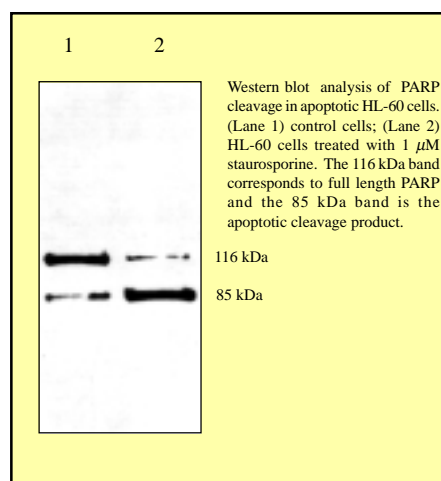
Poly(ADP-ribose) polymerase (PARP) converts NAD into nicotinamide and polymers of ADP-ribose at glutamic acid residues of nuclear proteins. The majority of polymer chains are linked to PARP itself through automodification. Poly(ADP-ribose)lation of subsets of nuclear proteins plays an important role in cell DNA repair, proliferation, replication, recombination, and apoptosis. The anti-PAR polymer rabbit polyclonal antibody was raised against Trevigen's pADPr (cat# 4336-100-01). It can be used to detect ribosylated proteins through immunodetection. pADPr and bacterially expressed human PARP-treated protein (cat# 4500-50-P) may be used as positive controls.



Anti-PARP Monoclonal Antibody (Clone C2-10)

Catalog# 4338-MC-50

The anti-poly(ADP-ribose) polymerase (PARP) mouse monoclonal antibody may be used for the analysis of PARP protein levels and the cleavage of PARP in apoptotic cells. It recognizes both the full length protein (116 kDa) as well as an 85 kDa cleavage fragment associated with apoptosis. The recognized epitope is within the C-terminal part of the DNA binding domain of PARP. The antibody cross reacts with PARP from human, monkey, hamster, rat, and mouse, but not from chicken.



References:

1. Satoh, M.S. and T. Lindahl. 1994. Role of poly (ADP-ribose) formation in DNA repair. *Nature* **356**:356-358.
2. Cherney, B. et al. 1991. Expression and mutagenesis of human poly (ADP-ribose) polymerase as a ubiquitin fusion protein from *Escherichia coli*. *Biochemistry* **30**:10420-10427.
3. Lamarre, D. et al. 1988. Structural and functional analysis of poly (ADP-ribose) polymerase: an immunological study. *Biochim Biophys Acta* **950**:147-160.