

# PARP Enzymes and Assay Kits

The 17-member PARP (Poly ADP-Ribose Polymerase) family is involved in a variety of cell functions such as DNA repair, genome stability, chromatin remodeling, mitotic spindle assembly, and more. PARP1/2 inhibitors have significant clinical activity in several types of cancer. Considerable efforts are under way to develop inhibitors

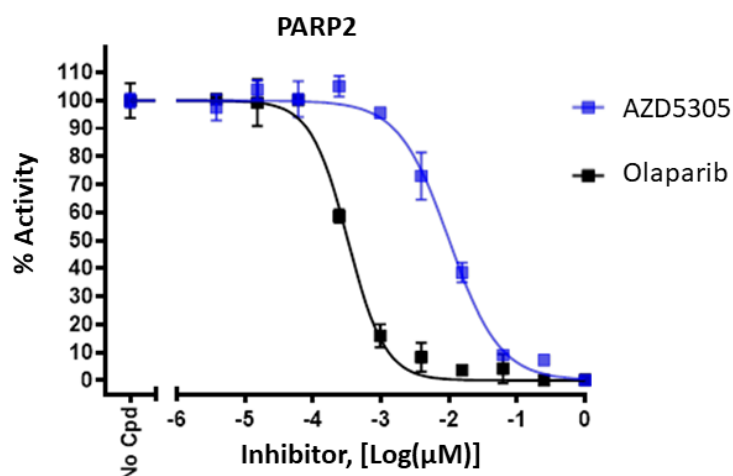
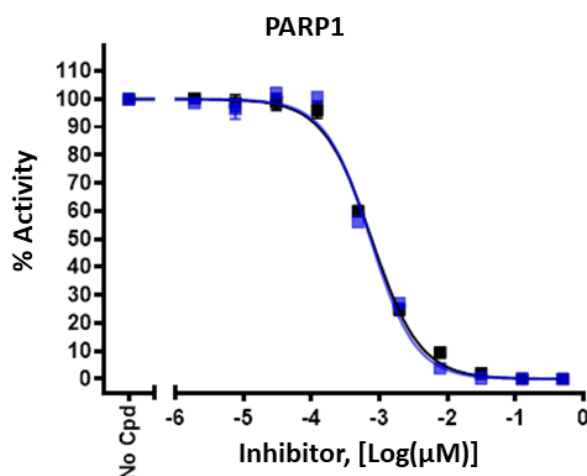
against other family members, notably PARP7. BPS Bioscience offers one of the most extensive product lines on the market, with over 20 robust validated assay kits to assess the activity of most family members. Custom enzymes as well as screening and profiling services are also available.



## PARP Assay Kits: ELISA

BPS Bioscience has developed assay kits for many PARP family members in addition to PARP1 and 2, including PARP3, 6, 7, 10, 11, 14, and 15, and PARP5A and PARP5B (known as TNKS1 and TNKS2, respectively), provided as

chemiluminescent and colorimetric assays. Many exist in both 96-well and 384-well formats. Of note, PARP8, PARP9 and PARP12 testing is available only through our services.



Data show a distinctive inhibition profile for PARP1 and PARP2 using Olaparib and AZD5305. The two inhibitors have a similar IC<sub>50</sub> for PARP1 inhibition (7 and 8 nM, left panel) whereas they have different IC<sub>50</sub> for PARP2

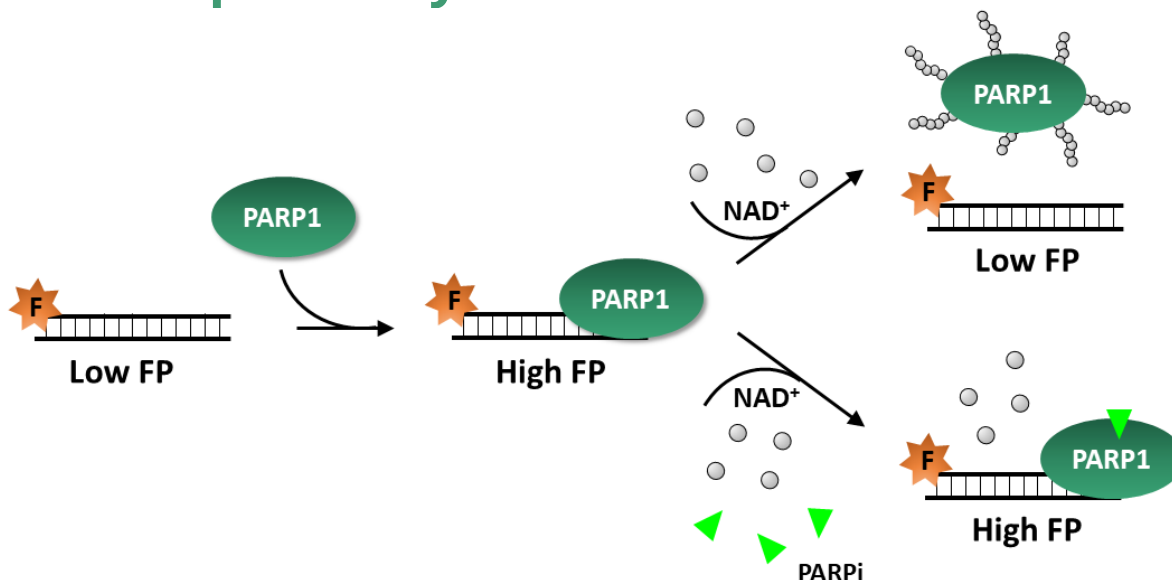
inhibition (0.3 nM for Olaparib and 100 nM for AZD5305, right panel), demonstrating the exquisite sensitivity of the assays. This will help scientists better prioritize their compounds for development.

	PARP1	PARP2	PARP3	PARP5A*	PARP5B*	PARP6	PARP7	PARP10	PARP11	PARP14	PARP15
PARPtrap™	80584 78317	78296 78317									
Chemiluminescent	80551 80569	80552	80553	80573 80579 80574 80575	80578 80572 80576 80577	80556	79729	80560	80561	80568	80567
Colorimetric	80580	80581		80582	80583						
AlphaLisa™		80702									

\* PARP5A and PARP5B are also known as TNKS1 and 2, respectively



## PARPtrap™ Assay Kits

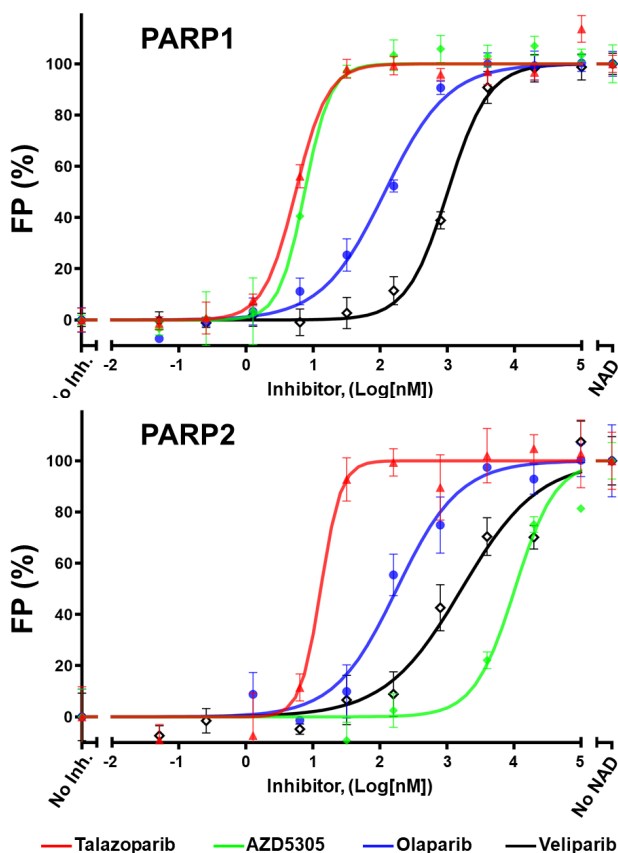


PARP1 and PARP2 bind to damaged DNA and auto-ribosylate in the presence of  $NAD^+$ . This causes their dissociation from the DNA due to the accumulated negative charge of the ribosyl polymer. Some inhibitors prevent auto-ribosylation, which results in PARP remaining on the DNA (trapping). Trapped PARP-DNA

complexes are highly cytotoxic to cancer cells, therefore such inhibitors may be desirable for cancer treatment.

Our unique PARPtrap™ assay uses principles of Fluorescence Polarization (FP). In the absence of ribosylation, PARP binds to the fluorescent DNA probe, forming a large complex and resulting in the emission of highly polarized light. Following auto-ribosylation, PARP dissociates from the DNA probe, which then rotates freely and emits little polarized light. Addition of a PARP inhibitor results in the trapping of PARP onto the fluorescent DNA probe and increases the FP signal in a dose dependent manner.

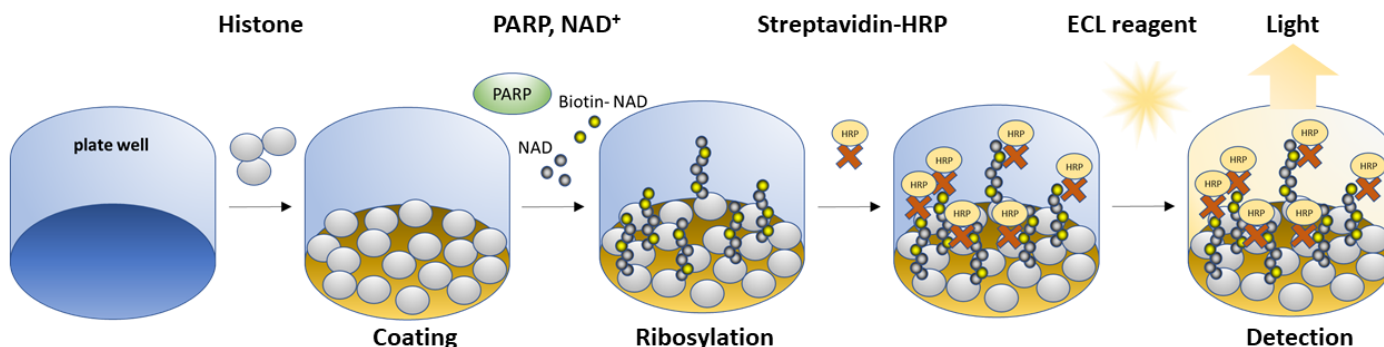
The Combo PARPtrap™ Assay Kit for PARP1 and PARP2 (#78317) is particularly useful to directly and specifically compare, in a single assay, the effect and potency of a compound on both PARP1 and 2.



### Advantages

- Homogeneous
- Fluorescence Polarization (FP) technology
- Sensitive and robust
- Supplied in 96-well and 384-well formats
- Highly specific optimized DNA substrates for PARP1 (PARPtrap™ Assay Kit for PARP1, #80584) or PARP2 (PARPtrap™ Assay Kit for PARP2, #78296)

## Services



Our screening services will accelerate your research and drug discovery program. Biochemical screens are a fast, reliable, and inexpensive way to identify PARP inhibitors. Our assays use a histone substrate and biotin-labeled NAD<sup>+</sup>. PARP activity is detected by adding Streptavidin-HRP and a chemiluminescent or colorimetric HRP substrate.

We pledge to provide you with high quality data in a timely manner. Our team of experts and our broad portfolio make it easy to:

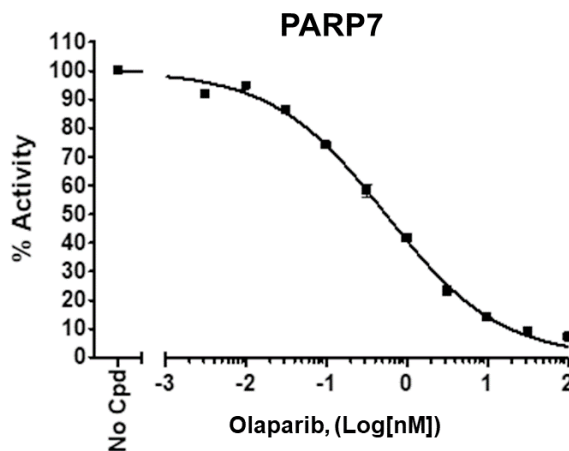
- Screen for inhibitors using existing PARP assays
- Assay development or assay optimization
- IC<sub>50</sub> determination or single point concentration

- Receive data within days of compound submission
- Perform follow-up studies using the same lots of enzymes manufactured at our San Diego Facility

## Application Example

**Published in:** Wang H. *et al.*, Discovery of Pamiparib (BGB-290), a potent and selective Poly (ADP-ribose) polymerase (PARP) inhibitor in clinical development. *J. Med. Chem.* 2020; **63**: 15541-15563. [PMID:33264017](#).

Pamiparib is a selective oral PARP1/2 inhibitor that has demonstrated PARP-DNA trapping as well as strong



anti-tumor activity and CNS penetration in pre-clinical models. In this study, pamiparib was titrated against individual PARP proteins using corresponding assay buffers and solutions for each chemiluminescent assay kit: PARP1/2/3, PARP5A and PARP5B. PARP6, PARP7, PARP8, PARP10, PARP11 and PARP12 were tested at BPS Bioscience.

PARP member	PARP1	PARP2	PARP3	PARP5A	PARP5B	PARP6	PARP7	PARP8	PARP10	PARP11	PARP12
Pamiparib IC <sub>50</sub> (nM)	1.30	0.92	68	230	140	>100,000	11,000	8,400	11,000	2,700	2,400

Pamiparib selectivity profile shows that it is equally potent at inhibiting PARP1 and PARP2, with an EC<sub>50</sub> of 1.3 nM and 0.93 nM. It is about 50 times less potent against PARP3, and displays very low affinity toward other PARP family members. Thus, pamiparib is a potent and selective

inhibitor of PARP1 and PARP2.

Human clinical pharmacology, pharmacokinetics, safety profiles and potential drug interaction are currently being investigated in several clinical trials.

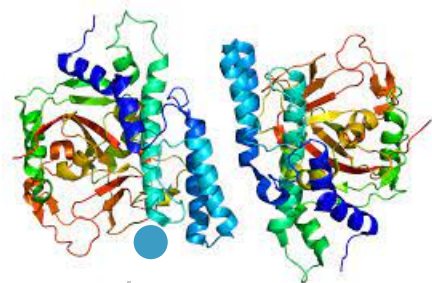


## PARP Enzymes

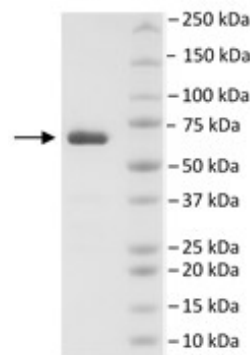
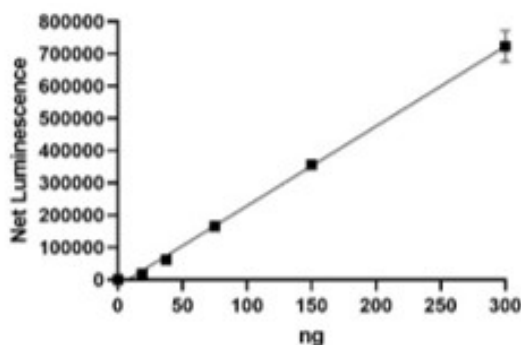
BPS Bioscience offers an extensive product line of recombinant PARP family member proteins. Purified, tagged recombinant PARP proteins are enzymatically

active and suitable for assay development and inhibitor screening or profiling (e.g.  $IC_{50}$  determination).

PARP member	1	2	3	5A	5B	6	7	9	10	11	12	14	15
Cat#	80501 80521	80502	80503	80504	80505 80515	80506	80527	80509	80522	80511	80513	80514	80517



Structure of the PARP1 protein, based on PyMOL rendering of PDB 1uk0. Emw-Own work without modification (CC BY-SA 3.0)



PARP14 activity titration (left) and protein purity visualized by Coomassie staining (right)



## Supporting Products

Assay kit components, such as substrates and buffers, can be purchased separately for convenience, including:

- Histone Mixture (5X), His-tag ([#52029](#))
- Opti-PARP Assay Mixture ([#79814](#))
- 10X PARP Assay Buffer ([#80602](#))

>30 PARP inhibitors are available to use as control or to optimize your assay. In addition, a sampling set of eight PARP inhibitors (PARPi) including PARPi with a broad

binding specificity like Olaparib, Niraparib, Rucaparib, Talazoparib, Veliparib, as well as more selective PARPi. AZD5305 is specific toward PARP1, XAV939 is specific toward PARP5A and PARP5B, and RBN-2397 is specific toward PARP7.

- Set of PARP Inhibitors, 8 x 50  $\mu$ l ([#78318](#))

These inhibitors have been used to optimize and validate some of our assay kits, with data visible on our website.



**Committed to Excellence:** ISO 9001:2015-certified Quality Management