PARP1, also known as poly(ADP-ribose) polymerase 1, is an enzyme involved in DNA repair and various cellular processes. Here are some key points about PARP1:

DNA repair: PARP1 is primarily known for its role in DNA repair, particularly in base excision repair (BER) and single-strand break repair (SSBR). It detects and binds to DNA damage, such as single-strand breaks, and catalyzes the addition of poly(ADP-ribose) (PAR) chains to itself and other target proteins, leading to the recruitment of repair factors.

PARylation: PARP1 transfers ADP-ribose units from NAD+ molecules to target proteins, a process known as PARylation. PARylation serves as a signal for DNA repair proteins to be recruited to the damaged site, facilitating the repair process.

Genome stability: PARP1 plays a crucial role in maintaining genome stability by repairing DNA damage and preventing the accumulation of DNA lesions. Inhibition or depletion of PARP1 can lead to an increase in DNA damage and genomic instability.

Regulation of gene expression: PARP1 is involved in the regulation of gene expression. It interacts with various transcription factors, chromatin remodeling complexes, and histone-modifying enzymes to modulate chromatin structure and gene transcription.

Role in cell death: PARP1 is involved in different forms of cell death, including apoptosis, necrosis, and parthanatos. Excessive activation of PARP1 can lead to energy depletion and cell death through the depletion of NAD+ and ATP, which is referred to as PARP-mediated cell death.

Therapeutic targeting: PARP1 has emerged as an important target in cancer therapy. Inhibitors of PARP1, known as PARP inhibitors, have been developed and are used in the treatment of certain cancers, particularly those with deficiencies in DNA repair pathways (e.g., BRCA1/2 mutant cancers). PARP inhibitors selectively target cancer cells that rely on PARP1-mediated DNA repair mechanisms and have shown effectiveness in sensitizing tumors to chemotherapy or as monotherapy.

PARP1 is a multifunctional enzyme involved in DNA repair, gene regulation, and cell death pathways. Ongoing research continues to uncover new insights into the diverse roles of PARP1 and its potential as a therapeutic target in various diseases, particularly cancer.

A study reports that the DOC domain of HECTD3 interacts with the DNA binding domain of PARP1, and HECTD3 mediated the K63-linked polyubiquitination of PARP1 and stabilized the latter expression. Moreover, the Cysteine (Cys) 823 (ubiquitin-binding site) mutation of HECTD3 significantly reduced PARP1 polyubiquitination and HECTD3 was involved in the recruitment of ubiquitin-related molecules to PARP1 ubiquitin-binding sites (Lysines 209 and 221, respectively). Lastly, activation of EGFR-mediated signalling pathways by HECTD3 regulates PARP1 polyubiquitination.

These results unveil the potential role of HECTD3 in glioblastoma and strongly preconise further investigation and consider HECTD3 as a promising therapeutic marker for glioblastoma treatment [1].

PARP-1 polymorphisms are involved in the development of glioma in Chinese individuals. Also serum cytokine levels can be considered among the potential risk factors for developing glioma [2].

1)

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2)
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