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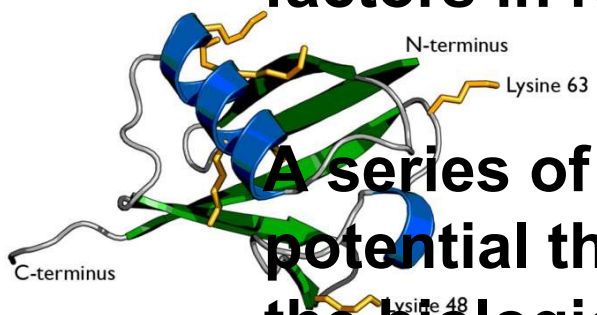
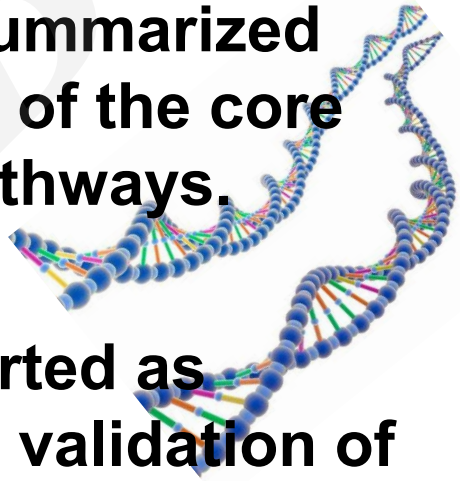
Role of deubiquitinating enzymes in DNA double-strand break repair

Key words: Deubiquitinating enzymes (DUBs), DNA-damage response (DDR), DNA repair, Non-homologous end joining (NHEJ), Homologous recombination (HR)

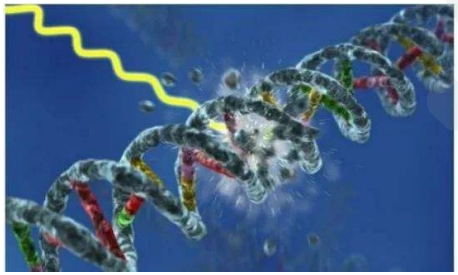
Research Summary

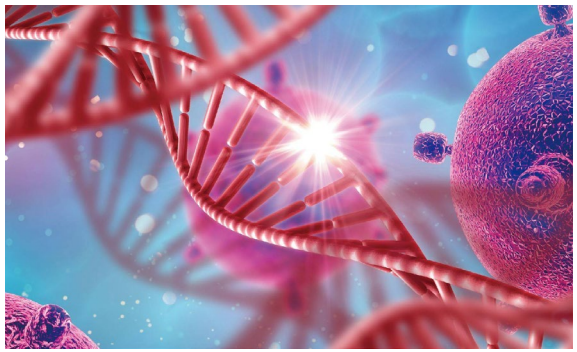
This review mainly focused on the role of deubiquitinating enzymes (DUBs) in repairing DNA double-strand breaks and summarized the deubiquitination modification of the core factors in NHEJ and HR repair pathways.





A series of DUBs have been reported as potential therapeutic targets, and validation of the biological substrate of these DUBs is solidifying.





Innovation points

- **Introduction** of the four types of DNA repair and six sub-families of deubiquitinating enzymes .

- **Summary** of the most updated research progress about deubiquitinating enzymes in DNA double-strand break repair.

- **Emphasis** of the newly identified interplay among DUB family members in therapeutics.

Table 1 DUBs involved in DNA damage

DUB	Substrates	Reference
USP1	CHK1	Nijman et al.,2005a; Guervilly et al.,2011
USP3	CHK1; RNF168	Cheng et al.,2018; Doil et al., 2009
USP4	CtIP and MRN complex	Liu et al.,2015; Wijnhoven et al.,2015
USP7	TIP60; MRN-MDC1 complex	Sun et al.,2005
USP11	BRCA1-PALB2-BRCA2 complex	Schoenfeld et al.,2004; Orthwein et al.,2015
USP13	RAP80-BRCA1 complex	Li et al.,2017
USP14	Ku70	Sharma et al.,2020
USP16	RNF8/RNF168	Shanbhag et al., 2010
USP20	Claspin	Yuan et al.,2014
USP28	Claspin; PIRH2 and CHK2	Wang et al.,2018; Zhang et al.,2006
USP38	HDAC1	Yang et al.,2019
USP39	CHK2	Wu et al.,2019a
USP47	IK	Ka et al.,2020
USP50	Ku70	Cai et al.,2018
USP51	H2AK13,15ub	Wang et al., 2016
BRCC36	BRCA1-RAP80 complex	Cooper et al., 2009; Dong et al., 2003; Shao et al., 2009; Sobhian et al., 2007; Wang and Elledge, 2007; Feng, 2010; Hu, 2011a
OTUB1	E2s	Juang et al., 2012; Wiener et al., 2012; Sato et al., 2012
OTUB2	RNF168, BRCA1-RAP80 complex	Altun et al.,2015
OTUD4	Unclear	Wu et al.,2019b
OTUD5	Ku80	Li et al.,2019
UCHL3	Rad51/Ku80	Luo et al.,2016
POH1	RNF8 and Rad51	Butler et al., 2012
BAP1	BRCA1, RAD51 and RPA	Ismail et al.,2014