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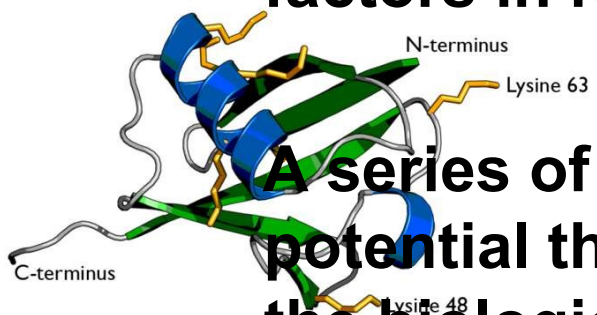
# Role of deubiquitinating enzymes in DNA double-strand break repair

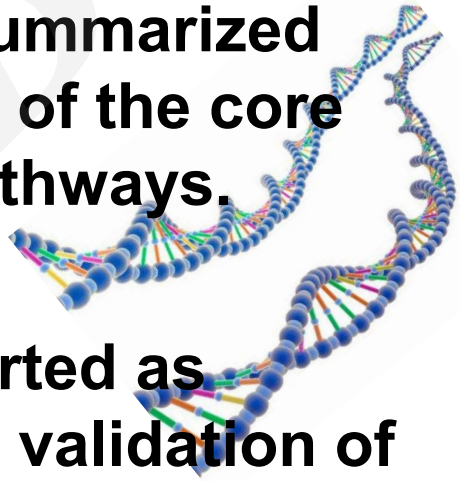
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**Key words: Deubiquitinating enzymes (DUBs), DNA-damage response (DDR), DNA repair, Non-homologous end joining (NHEJ), Homologous recombination (HR)**

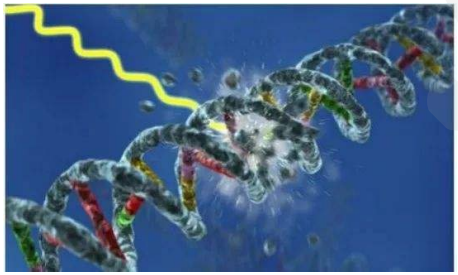
# *Research Summary*

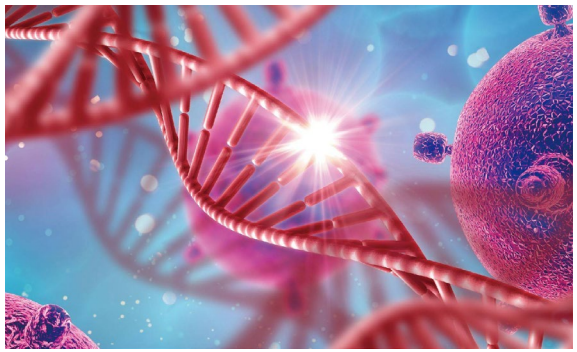
**This review mainly focused on the role of deubiquitinating enzymes (DUBs) in repairing DNA double-strand breaks and summarized the deubiquitination modification of the core factors in NHEJ and HR repair pathways.**



**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 |