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Universiteit Leiden



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Title: DNA damage responses in mammalian cells : focus on signaling and repair

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Propositions
Accompanying the thesis:

DNA DAMAGE RESPONSES IN MAMMALIAN CELLS
FOCUS ON SIGNALING AND REPAIR

1. The cohesin loading factor NIPBL promotes homologous recombination upon DNA damage. [This thesis]
2. Recruitment of TLS polymerases to sites of UV damage in non-replicating cells is more likely to reflect an inability to repair rather than actual DNA synthesis. [This thesis]
3. The chromatin remodeling protein ALC1 stimulates the removal of CPD lesions indicating that the local chromatin environment can have a negative impact on NER. [This thesis]
4. ATR and related DNA damage sensing kinases all phosphorylate H2AX when activated by DNA damage but curiously not after transcription stalling. This means that either ATR is not activated or it functions in a non-canonical manner. [This thesis; Derheimer FA et al., Proc Natl Acad Sci U S A. 2007 Jul 31;104(31):12778-83]
5. Exo1 can extend ssDNA gaps created by NER in G0/G1 cells. [Sertic S et al., Proc Natl Acad Sci U S A. 2011 Aug 16;108(33):13647-52]
6. The fact that so many different ubiquitin ligases have been shown to cause RNA polymerase II ubiquitination after DNA damage prompts caution on the validity and interpretation of the data. [Starita LM et al., J Biol Chem. 2005 Jul 1;280(26):24498-505; Anindya R et al., Mol Cell. 2007 Nov 9;28(3):386-97; Harreman M et al., Proc Natl Acad Sci U S A. 2009 Dec 8;106(49):20705-10]
7. Deficiencies in DNA repair, origin licensing, ATR pathway signaling or centrosomal proteins can lead to microcephaly and dwarfism. This is strong support for a key role of efficient cell cycle progression in normal development. [Klingseisen A et al., Genes dev. 2011 Oct 1;25(19):2011-24]
8. The association of CSB with PCNA and pol δ questions whether RNA polymerase II degradation is required for TC-NER. [Anindya R et al., Mol Cell. 2007 Nov 9;28(3):386-97; Anindya R et al., Mol Cell. 2010 Jun 11;38(5):637-48]
9. A statement like 'the neutral comet assay was used to measure DSB' suggests unfamiliarity with the principles of comet assay.
10. Lack of prior knowledge promotes the formation of novel ideas or concepts; the real challenge is to get knowledgeable people to embrace them.