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A role of SUMOylation in proteostasis, centromere integrity and the DNA damage response

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Stellingen
Behorend bij het proefschrift getiteld

A Role for SUMOylation in Proteostasis, Centromere Integrity and the DNA Damage response

1. During recovery post-heat shock, most SUMOylated proteins are degraded. Chronic HSF1 inhibition interferes with the degradation of these SUMOylated proteins (this thesis).
2. The deSUMOylation activity of SENP6 is needed for the faithful assembly of most of the constitutive centromere-associated network subunits at the centromere (this thesis).
3. Despite being the focus of most of the previous studies, SUMO chain formation does not exclusively signal for degradation of SUMOylated target proteins (this thesis).
4. The SUMOylation of CSB alters molecular interactions that stabilize CSB at sites of DNA damage and therefore promote efficient transcription-coupled nucleotide excision repair (this thesis).
5. During cell stress, SUMO contributes to activation of pro-survival pathways (Enserink, 2015, Cell Division).
6. One unresolved key question is how SUMOylation achieves substrate specificity with its limited number of enzymes, compared to the large number of substrates (Pichler et al., 2017, BioMol Concepts).
7. Downstream consequences of SUMOylation are target-specific, but are usually caused by altered interactions of the modified protein with other macromolecules including proteins, DNA or RNA (Flotho and Melchior, 2013).
8. The striking dependency of proliferating cells compared to non-dividing cells on reversible SUMOylation provides one of the rationales for targeting the SUMO pathway in cancer therapy (Flotho and Melchior, 2013).
9. Being able to identify SUMO target proteins, SUMO sites and components of the SUMO machinery that are deregulated in specific human diseases, such as cancer and neurodegenerative disorders, is an important step in developing new therapies and potent drugs (Eifler, 2015).
10. The aim of science should not only be to pursue answers but also to seek for more questions.
11. While investigating a hypothesis, one should always put similar efforts in evaluating alternative explanations for a given result.
12. A collective change of behaviour concerning environmental issues is far more effective than waiting around for political action.