

STELLINGEN BEHOREND BIJ HET PROEFSCHRIFT

Meiotic and mitotic functions of mammalian RAD18 in DNA double-strand break repair

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1. RAD18 functions as a DNA repair protein at a stalled replication machinery in S phase, and at sites of DNA double-strand breaks throughout the cell cycle (this thesis).
2. In the absence of detectable damage-induced accumulation of a fluorescent-tagged protein, it is not excluded that this protein is functioning at the damaged sites (this thesis).
3. The presence of an ubiquitin binding domain in a protein allows the ubiquitylation of that protein independent of an E3 ligase (Hoeller et al. 2007, *Molecular Cell* 26: 891–898, this thesis).
4. ATM kinase-mediated transcriptional silencing at persistent mitotic DSBs, and ATR kinase-mediated transcriptional silencing at persistent meiotic DSBs correlates with ubiquitylation of histone H2A (Shanbhag et al. 2010, *Cell* 141: 970–981, this thesis).
5. In mammalian meiotic homologous recombination, PCNA (proliferating cell nuclear antigen) regulates the choice between crossover and noncrossover pathways after its modification at lysine residue K164, most likely by SUMO (small ubiquitin-like modifier) (this thesis).
6. In addition to housing ribosome biogenesis, nucleoli may serve as a sensor of DNA damage and a storage site of proteins implicated in damage response pathways.
7. To elucidate the molecular mechanism of repair of the SPO11 induced DSBs in meiosis provides an impressive challenge to science, compared to studies on the relatively simple mechanisms repairing DSBs in mitotic cells.
8. Being scooped would get a more positive connotation if scientific journals would accept that confirmation of published data by an independent study can be published as an integral part of a research paper addressing a subsequent step.

9. Ubiquitin is ubiquitous, but ubiquitylation is a very special and well-controlled biochemical reaction which determines the fate of many proteins in a widely different manner, either providing proteins with a new function or leading to their demise.
10. "Imagination is more important than knowledge. Logic will get you from A to B. Imagination will take you everywhere" (Albert Einstein)
11. The extrovert and conformist aspects of the typical Dutch character are exemplified by the inescapable "fraktatie" at a birthday, and the indispensable "agenda" to make an appointment.