High fidelity DNA replication and repair: new structures and mechanisms using cryogenic electron microscopy

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Stellingen
behorend bij het proefschrijft getiteld

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1. Although it is the proteins that catalyse the different reactions which ensure high fidelity DNA replication, it is the DNA itself that governs and determines their activity (this thesis).

2. Different signals on DNA modulate the ATP hydrolysis cycle of MutS, allowing the initiation and termination of the mismatch repair reaction (this thesis).

3. The two activities of MutS, DNA binding/mismatch recognition and ATPase, are intimately linked such that the ligand at one active site dictates events at the other site (Hingorani DNA repair 2015).

4. The MutL protein acts as a 'traffic cop' on DNA that blocks access to the DNA polymerases at 3' resected end while stimulating the action of the UvrD helicase (this thesis).

5. The ability of MutL to assume radically different structures and its susceptibility to regulation by DNA strongly suggest that it is a switch important for coordination of events in DNA mismatch repair (Ban *et al. Cell* 1999*)*.

6. Cryo-EM's high-resolution revolution will soon be followed by a high-throughput revolution (Drulyte *et al.* Thermo Fisher 2022).

7. The rapid mix and plunge freezing capabilities of the Puffalot can be used to trap intermediate states in proteins that adopt multiple conformations (this thesis).

8. Blotting and plunging into cryogens usually takes seconds, during which time the sample can come into contact with the AWI hundreds to thousands of times (Klebl *et al.* Structure 2020).

9. Holding onto scientific ideas is only worth when results are there to support them.

10. Applied science can only develop and go further if basic research has laid the basis for it.