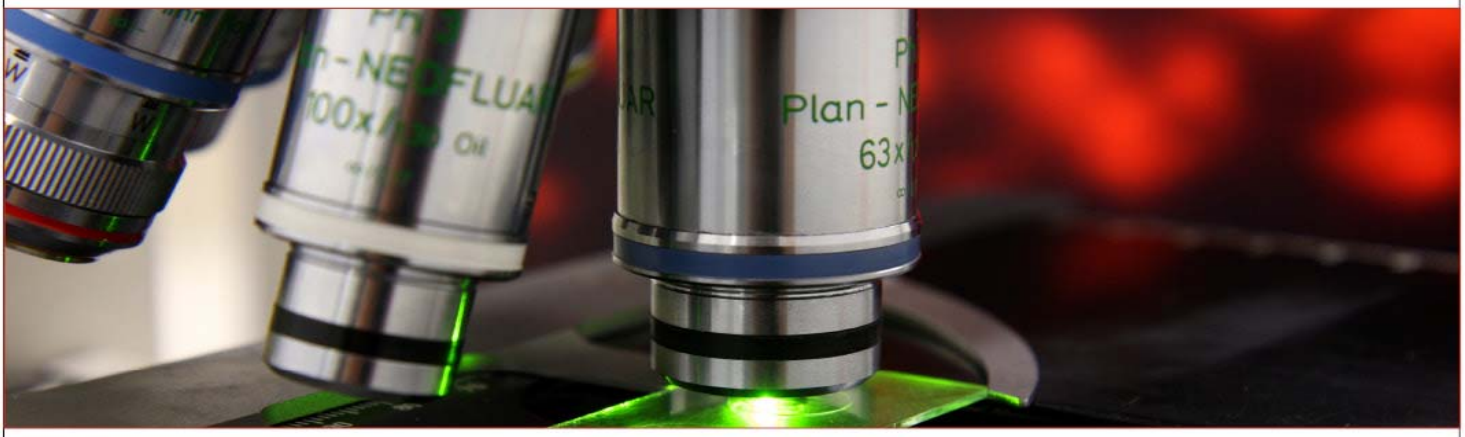
SÉMINAIRES ET CONFÉRENCES



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« Understanding how weak protein-protein interactions modulate DNA mismatch repair»

DNA mismatch repair (MMR) safeguards genome integrity by correcting replication errors. The coordinated actions of two proteins (MutS and MutL) initiate the mismatch repair response and defects in the genes encoding these proteins have been linked to sporadic and hereditary cancers. The processivity clamp, typically known to tether the replicative polymerase to DNA during DNA synthesis, also has key roles in several steps of MMR including initiation, mismatch excision, and strand re-synthesis. We have shown that MutL interacts with both MutS and the processivity clamp. Both interactions are essential for mismatch repair activity in vivo, but they are short-lived and, therefore, have been difficult to study at a molecular level. In this talk, I will discuss the approaches that we have used to stabilize these transient protein complexes. Our work unveils how recognition of a mismatch by MutS leads to nicking of the newly synthesized strand by MutL and provides new avenues to stabilize transient protein-protein interactions for structural characterization.

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