Single-molecule imaging of DNA repair in single living cells.

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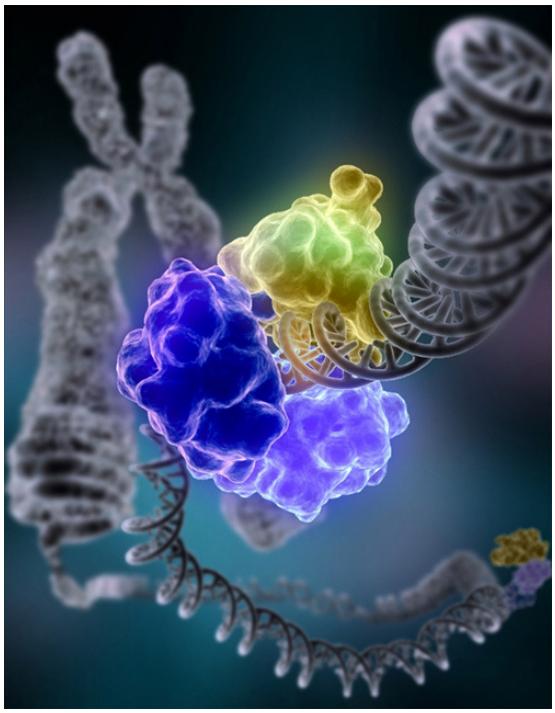
Every single day an individual cell must deal with ~10 000 lesions in order to prevent accumulation of harmful mutations, which might lead to cancer. Understanding the mechanism of DNA repair is therefore of central importance to our understanding of cancer and for the development of new therapeutics against it. Repair pathways are highly conserved, in both prokaryotes and eukaryotes, and studying the simpler pathways in bacteria provides key insight into the mechanism used by human cells to repair damaged DNA.

We apply an interdisciplinary approach to understand the mechanistic details of DNA repair pathways (Nucleotide Excision Repair, Mismatch Repair, Base Excision Repair) in living *Escherichia coli* (and human cells in near future). We use a combination of cutting-edge single-molecule methods to elucidate how repair enzymes participate in removal of damaged nucleotides. Firstly, live super-resolution microscopy combined with single-particle tracking is used to study the behaviour of individual proteins as they scan the genome and repair damaged DNA. To complement this, we use cell biology, genetics and TIRF microscopy to verify and extend the conclusions established using a super-resolution microscopy. Together, this will provide a comprehensive understanding of the bacterial repair pathway, and constitute a starting point to understanding the way mutations in human repair proteins contribute to the development of cancer.



Repair enzyme recognizing damage nucleotide