# How is DNA damage efficiently recognized and repaired in chromatin?

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A fundamental problem in DNA excision repair is how a small number of damaged bases within the huge genome can be discriminated from normal bases present in vast excess. In mammalian nucleotide excision repair (NER) pathway, the xeroderma pigmentosum group C (XPC) protein complex recognizes "unpaired" normal bases and recruits the basal transcription/NER factor TFIIH. The XPD helicase in TFIIH then scans a DNA strand in a 5' to 3' direction, and blockage of this translocation verifies the presence and location of DNA damage, thereby inducing excision of the damage-containing oligonucleotide. Biochemical studies have revealed that, when XPC binds to a DNA mismatch site devoid of damage, the NER machinery driven by XPD can move along a DNA strand and find damage at a distal position. This "patrolling" system may ensure efficient and accurate detection of DNA damage for repair, and not only mismatches but also some spontaneous DNA damage, such as abasic sites, may serve as the XPC-anchoring sites. Furthermore, our results suggest that DNA topological stresses may enhance DNA damage recognition in NER. In this lecture, histone modifications as well as higher-order chromatin structures possibly associated with the NER process will be also discussed.

**References**

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