

# THE CURRENT STATUS OF NUCLEOTIDE EXCISION REPAIR IN THE YEAST *SACCHAROMYCES CEREVISIAE*

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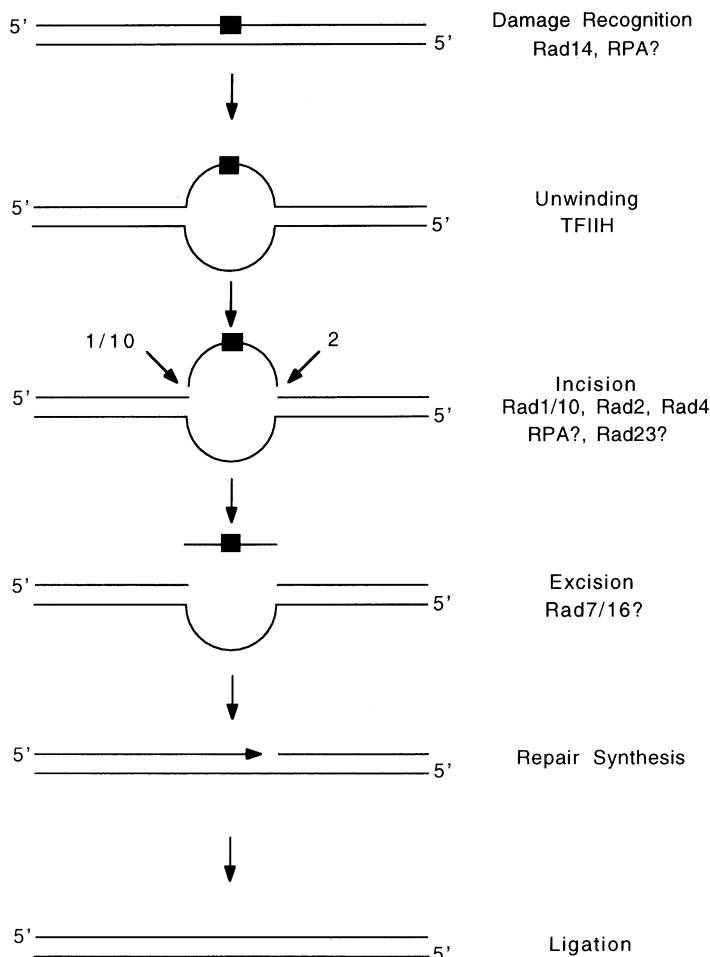
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## 1. ABSTRACT

The removal of UV radiation-induced pyrimidine dimers and (6–4) photoproducts as well as other bulky base adducts from the DNA of higher eukaryotes relies on the concerted action of about 30 proteins which excise base damage and restore the DNA to its native state. This process is known as nucleotide excision repair (NER), and the proteins involved are highly conserved throughout the *eukaryotae*. There are indications that the initial steps of NER are effected by a large preformed multi-protein complex comprising the RNA polymerase II transcription factor IIH (TFIIH) and other NER proteins known to be required for damage recognition and DNA incision. Humans with inactivating mutations in the genes encoding NER proteins suffer from the cancer-prone syndrome xeroderma pigmentosum (XP). In yeast, a mode of NER which is apparently coupled to transcription requires the activity of Rad26 protein, while transcription-independent NER requires the activity of the Rad7 and Rad16 proteins. Defects in transcription-dependent NER are associated with the human hereditary disorder Cockayne syndrome (CS).

## 2. PROTEINS REQUIRED FOR THE EARLY STEPS IN NUCLEOTIDE EXCISION REPAIR IN YEAST

NER can be conveniently considered in six sequential steps: base damage recognition, localized unwinding of the DNA flanking such lesions, bimodal incision, excision of damage-



**Figure 1.** Transcription-independent nucleotide excision repair (NER) in yeast. As described in the text the NER reaction can be thought of as occurring in six steps. The yeast proteins believed to be required for each of the early steps are indicated. Since the exact roles of the Rad7 and Rad16 proteins are unknown their assignment to the excision step is tentative based largely on their requirement for repair synthesis, but dispensability for DNA incision *in vitro* (Wang *et al.*, 1997; Reed *et al.*, 1998).

containing oligonucleotides, repair synthesis, and finally ligation of the repaired regions (Friedberg *et al.*, 1995; Figure 1). In the yeast *Saccharomyces cerevisiae* many of the genes involved in NER are known as *RAD* genes due to the sensitivity to ultraviolet (UV) radiation they confer when mutated. Genes involved in the early steps of NER fall into three groups: 1) Those essential for NER but not cell viability in the absence of DNA damage (*RAD1*, *RAD2*, *RAD4*, *RAD10*, *RAD14*); 2) those essential for NER and cell viability in the absence of DNA damage (*RAD3*, *TFB1*, *TFB2*, *TFB3*, *TFB4*, *SSL1*, *SSL2*); and 3) those not essential for NER or cell viability in the absence of DNA damage (*RAD7*, *RAD16*, *RAD23*).

## 2.1. Damage Recognition and Incision

Mutants in *RAD* genes from group 1 have been shown to be defective for the incision step of NER, an early event in the process, indicating their involvement either in the incision reaction itself or in events leading to incision such as damage recognition. Early