Regulation of TCR by ubiquitylation of RNA polymerase II.

Transcription-coupled repair (TCR) is the mechanism through which mutations in actively transcribed genes are preferentially repaired. a | Elongating RNA polymerase II (pol II), which has a unique pattern of phosphorylation on its carboxy-terminal domain (CTD), encounters a damaged DNA segment. The stalled polymerase (b) then recruits the ubiquitin (Ub)-ligase Rsp5 (c), which in turn ubiquitylates the largest subunit of pol II in a CTD-phosphorylation-dependent manner. d | Ubiquitylation is followed by the proteasomal destruction of at least one subunit of polymerase, recruitment of the repair machinery and restoration of DNA integrity.
The ubiquitin (Ub)–proteasome system regulating transcription at numerous levels. a | Interactions of an activator with the general transcriptional machinery (green) functions to b | recruit ubiquitin ligase(s) to the site of transcription and ubiquitylates many factors, including the activator, RNA polymerase II (pol II) and histones. c | These ubiquitylation events in turn recruit the 26S proteasome, which d | simultaneously destroys the activator and promotes elongation of transcription by pol II. Importantly, this proposed mechanism limits uncontrolled transcription in two ways — by destroying the activator at each cycle of promoter 'firing' and by ensuring that interactions between pol II and the proteasome are made in an activator- and promoter-dependent manner.