# Abstract

The genomic information of organisms is constantly challenged by genotoxic insults. Elaborate repair and signalling mechanisms have developed to maintain genome integrity. The most harmful type of damage is a DNA double strand break (DSB) that if inappropriately processed can promote genome instability, a hallmark of cancer. Hence, repair of DSBs needs to be coordinated with the DNA damage response that mediates apoptotic death of damaged cells. Multiple protein ubiquitylation events at the sites of DSBs regulate damage recognition, repair, and signalling processes. However, the spatiotemporal calibration of DNA repair and the apoptotic response remains poorly understood. This work identifies the E4 ubiquitin ligase UFD-2 as a mediator of DNA repair and apoptosis response. During the course of homologous recombination (HR) at DSBs, UFD-2 forms nucleolar foci, which also contain substrate processivity factors including the ubiquitin-selective segregase CDC-48, the deubiquitylation enzyme ATX-3, and the proteasome. UFD-2 foci are retained until recombination intermediates are removed by the Holliday junction processing enzymes GEN-1, MUS-81, or XPF-1. In the absence of UFD-2, the removal of RAD-51-marked DSB repair foci is delayed indicative of inefficient repair. Similarly to *ufd-2* deletion or E4 ubiquitin ligase inactivation, elevated RAD-51 levels lead to defects in DNA damage-induced apoptosis. UFD-2 foci formation also depends on the pro-apoptotic *Caenorhabditis elegans* (*C. elegans*) p53 tumour suppressor homolog CEP-1, suggesting an intricate coordination between DSB processing and the apoptotic response. In summary, this work establishes a central role for the E4 ubiquitin ligase UFD-2 in the coordination between the DNA repair process and the apoptotic response that allows faithful repair of DNA damage.