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Sommario	The stability of our genome is constantly challenged by several genotoxic threats. DNA double-strand breaks (DSBs) are the most dangerous DNA lesions that, if not repaired, can lead to cancer initiation and progression and/or ageing. These detrimental consequences can only be avoided if cells promptly recognize the lesions and signal their presence, thus promoting either efficient repair and transient cell cycle arrest or cell death and cellular senescence. This is the role of the DNA damage response (DDR) proteins and the newly identified damage-induced non coding RNAs. We recently discovered that RNA polymerase II is recruited to DSBs and synthetizes damage-induced non-coding RNAs (dilncRNAs). DROSHA- and DICER-mediated processing of dilncRNAs generates small RNA species, named DNA damage response RNA (DDRNAs) (Francia, 2012), that localize to DSBs via pairing with dilncRNAs and promote DDR signaling (Michelini et al., in press). Similar small non-coding RNA species discovered in plants are involved in DNA repair by homologous recombination (HR) (Wei, 2012, Gao, 2014, Wang, 2016). In line with these results, I report that transcriptional inhibition impairs recruitment of the HR proteins BRCA1, BRCA2, and RAD51 to DSBs, while partially promoting DNA end resection. Moreover, I show DNA:RNA hybrids accumulation at DSBs in

	mammalian cells by both DRIP analyses and imaging techniques. Damage-induced DNA:RNA hybrids form upon the hybridization of RNA species, likely dilncRNAs, to the resected DSBs DNA ends generated during the S/G2 cell cycle phase. I also report that purified recombinant BRCA1 binds DNA:RNA hybrids in vitro; moreover, DNA:RNA hybrids in vivo contribute to BRCA1 recruitment to DSBs. Consistent with the need to tightly regulate DNA:RNA hybrid levels, I demonstrate that RNase H2, the major RNase H activity in mammalian nuclei, is recruited to DSBs through direct interaction with RAD51. In summary, I report for the first time that DNA:RNA hybrids accumulate at DSBs in mammalian cells in a cell-cycle- and DNA end resection-depended way. At DSBs, BRCA1 directly recognizes DNA:RNA hybrids and likely controls their turn-over by mediating the recruitment of RNase H2 via RAD51.
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