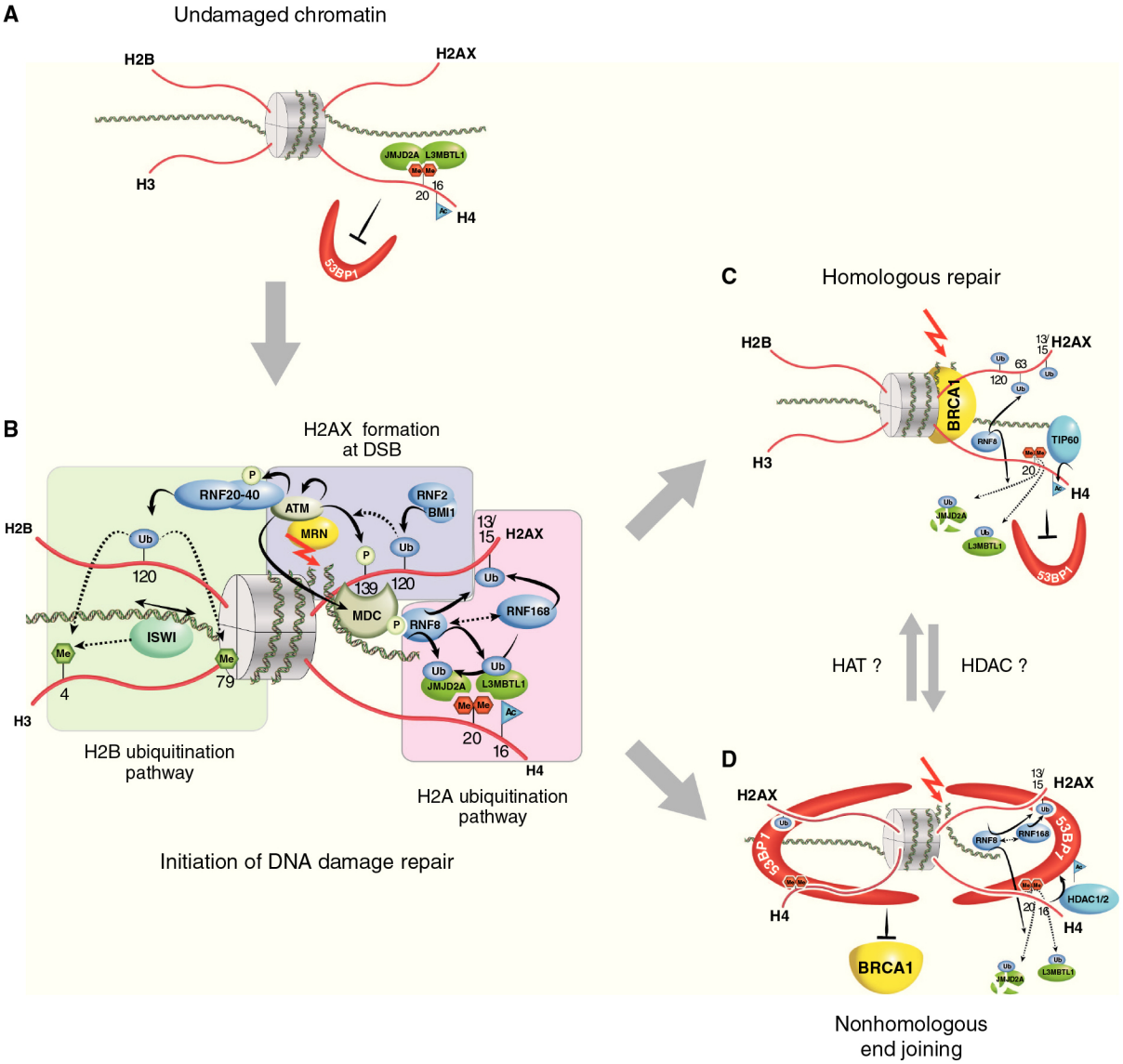

Figure 4. Role of histone PTMs in DNA damage repair. (*A*) Before DNA damage, L3MBTL1 and JMJD2A (possibly also JMJD2B) bind, via their Tudor domains, to H4K20me2 (red hexagons), hindering access by DNA repair proteins, such as 53BP1. (*B*) When double-strand DNA breaks occur (red arrow), the DNA damage–sensing proteins, such as MRN, act to initiate cascades of protein and histone tail PTMs (blue-shaded area). In particular, the phosphorylation of H2A at S139 represents the conversion of H2A into H2A.X. Subsequent chromatin-remodeling events occur as a consequence of H2B ubiquitination (green-shaded area), whereas further ubiquitination events on H2A.X alter local chromatin structure (pink-shaded area). This latter RNF8/RNF168-catalyzed H2A ubiquitination pathway also polyubiquitinates JMJD2A/B for degradation, whereas L3MBTL1 is removed by RNF8-mediated ubiquitination. This then allows DSBs in DNA to be repaired by homologous recombinant repair (HRR), where joining occurs between two similar or identical strands of DNA (*C*); or by nonhomologous end joining (NHEJ), in which the two DNA ends are joined directly, usually with no sequence homology, although, in some cases, regions of microhomology are used (*D*). (*C*) During HRR, TIP60 acetylates H4K16, RNF8 ubiquitinates H2AK63, and selectively allows for BRCA1 binding but not 53BP1. (*D*) If NHEJ is required, H4K16 is deacetylated (presumably by HDAC1,2) and H2AK15 is ubiquitinated. 53BP1 binds to both H4K20me2 and H2AK15ub, whereas BRCA1 is excluded. To illustrate 53BP1 oligmer formation, only histone H4 and H2AX tails are illustrated in this panel.