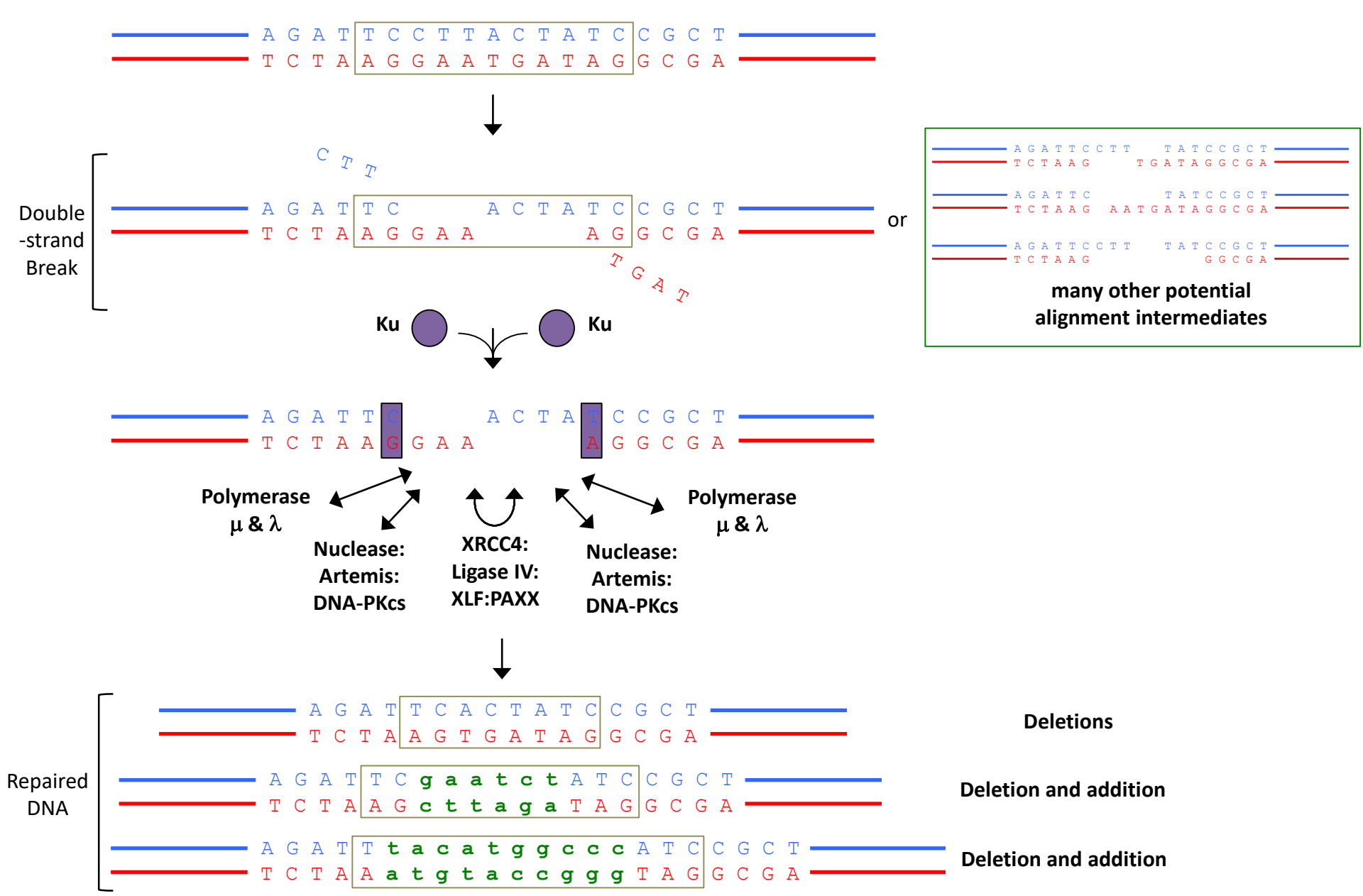
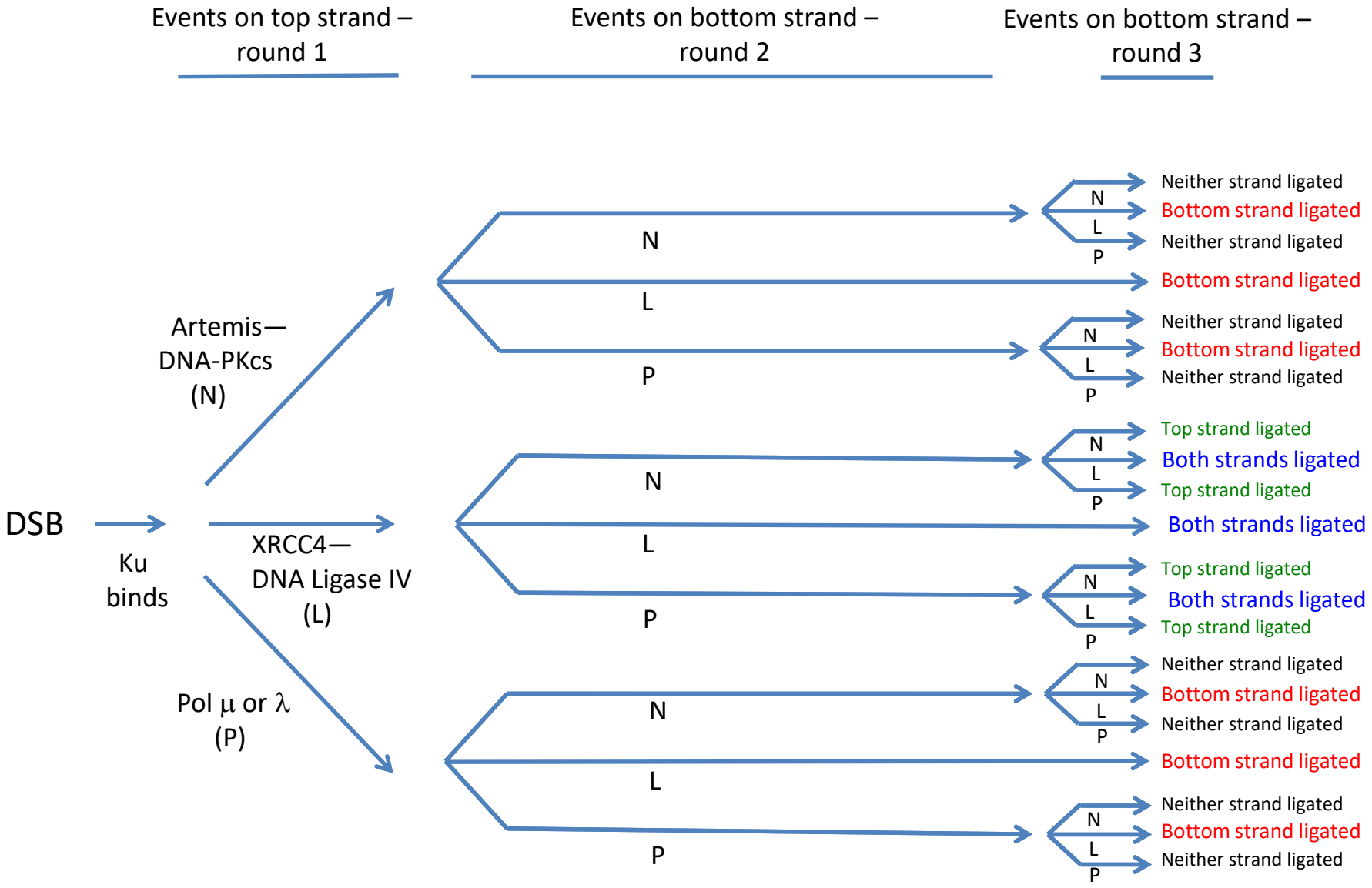
Supplemental Figure 1. Overview of nonhomologous end joining.
Schematic of DNA double-stranded breaks (DSBs) and its repair by nonhomologous end joining (NHEJ) (*top*). The Ku70–Ku80 heterodimer binds to DSBs and improves their subsequent binding by the NHEJ polymerase, nuclease and ligase complexes. These enzymes can act on DSBs in any order to resect and add nucleotides. Multiple rounds of resection and addition are possible, and nuclease and polymerase activities at each of the two DNA ends appear to be independent. Microhomology between the two DNA ends —present (dashed boxes), or newly created when the polymerases add nucleotides in a template-independent manner — is often used to guide end joining. The process is error-prone and can result in diverse DNA sequences at the repair junction (*bottom*). However, NHEJ is also capable of joining two DNA ends without nucleotide loss from either DNA end and without any addition. Nucleotide additions are depicted in green lowercase.

Supplementary Figure 2. The same DSB can be repaired in many different ways, depending on the order in which NHEJ proteins act.
This figure conveys the iterative nature of NHEJ and also illustrates that many different product junctions can form from the same starting DSB. After Ku binding to either DNA end or both ends of a double-strand break (DSB), the nuclease (N), polymerases (P), or the ligase complex (L) can bind in any order. In the simplest case, the ligase complex ligates the top strand, and then ligates the bottom strand, resulting in a fully repaired DSB site. This might occur at a DSB with two blunt DNA ends or two DNA ends with compatible overhangs. More typically, the nuclease or polymerases bind and modify either or both DNA ends. All of these pathways can eventually lead to a repaired DSB site, but yielding different amounts of nucleotide loss or addition. Therefore, all of the products shown on the right side are different from one other.

Suppl. Fig. 1


Double
-strand
Break
Ku
Ku
Polymerase
μ & λ
Nuclease:
Artemis:
DNA-PKcs
XRCC4:
Ligase IV:
XLF:PAXX
Nuclease:
Artemis:
DNA-PKcs
Polymerase
μ & λ
or
many other potential
alignment intermediates
Repaired
DNA
Deletions
Deletion and addition
Deletion and addition

Suppl. Fig. 2


Events on top strand – round 1
Events on bottom strand – round 2
Events on bottom strand – round 3
DSB
Ku binds
Artemis—DNA-PKcs (N)
XRCC4—DNA Ligase IV (L)
Pol μ or λ (P)
N
L
P
Neither strand ligated
Bottom strand ligated
Top strand ligated
Both strands ligated