SUMMARY

DNA polymerases μ (polμ), lambda (polλ) and TdT are three enzymes of the polX family that share homology in sequence and functional domain organization. We showed previously that polμ participates in light chain but surprisingly not in heavy chain gene rearrangement, which suggested that another polymerase should be involved. We show here that Ig heavy chain junctions from polλ-deficient animals have CDR3s of reduced size with normal N additions, thus indicating that polλ is indeed recruited during heavy chain gene rearrangement at a step that likely precedes the action of TdT. In contrast to previous in vitro studies, this analysis does not reveal overlapping or compensatory activities for V(D)J recombination among polμ, polλ and TdT. In particular, polμ/polλ double-deficient mice display the strict addition of their individual phenotype, and TdT neither compete with the two others at the heavy chain rearrangement step nor contribute to light chain end processing.