



**Fig. 1.** General scheme indicating how three serial fidelity steps during chromosomal replication can produce the low error rate of  $\sim 10^{-10}$  errors per base per round of replication. The steps are (a) discrimination by the polymerase against inserting an incorrect base (error rate  $\sim 10^{-5}$ ); (b) proofreading (editing) of misinserted bases (e.g. T-T) by the 3'→5' exonuclease associated with the polymerase (escape rate  $\sim 10^{-2}$ ); and (c) removal of remaining mismatches (e.g. T-C,) by postreplicative DNA mismatch repair (MMR) (escape rate  $\sim 10^{-3}$ ).

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