



Transcription-coupled DNA and RNA deamination plus reverse transcription as an explanation of somatic hypermutation. See publication number 20 for discussion and references of the respective roles of AID, MSH2-MSH6, Pol- η , RPA and transcription-coupled γ INF-ADAR1 mediated A-to-I pre-mRNA editing. The RNA Polymerase II complex copies the transcribed strand (TS) recruiting RPA, AID, MSH2-MSH6, Pol- η and ADAR1. AID deaminates C-to-U (looping orange arrow) in single-stranded regions on both DNA strands. ADAR1 deaminates emerging A nucleotides to inosine (looping green arrow) in the nascent pre-mRNA (A-to-I) in the context of both an imperfect dsRNA duplex and a WA motif. Thus AID deamination leads to C-G mutational targeting at WRCY sites (Phase I) and ADAR1 deamination subsequently leads to A-T mutational targeting at WA sites in DNA following error-prone reverse transcription by Pol- η to produce the cDNA copy of the TS (Phase II).