

## **GANP regulates the choice of DNA repair pathway by DNA-PKcs interaction in AID-dependent IgV region diversification.**

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RNA export factor germinal center-associated nuclear protein (GANP) interacts with activation-induced cytidine deaminase (AID) and shepherds it from the cytoplasm to the nucleus and toward the IgV region loci in B cells. In this study, we demonstrate a role for GANP in the repair of AID-initiated DNA damage in chicken DT40 B cells to generate IgV region diversity by gene conversion and somatic hypermutation. GANP plays a positive role in IgV region diversification of DT40 B cells in a nonhomologous end joining-proficient state. DNA PKcs physically interacts with GANP, and this interaction is dissociated by dsDNA breaks induced by a topoisomerase II inhibitor, etoposide, or AID overexpression. GANP affects the choice of DNA repair mechanism in B cells toward homologous recombination rather than nonhomologous end joining repair. Thus, GANP presumably plays a critical role in protection of the rearranged IgV loci by favoring homologous recombination of the DNA breaks under accelerated AID recruitment.

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