العنوان بالانجليزيه:

Integrity of immunoglobulin variable regions is supported by GANP during AID-induced somatic hypermutation in germinal center B cells

الملخص بالانجليزيه:

Immunoglobulin affinity maturation depends on somatic hypermutation (SHM) in immunoglobulin variable (IgV) regions initiated by activation-induced cytidine deaminase (AID). AID induces transition mutations by C→U deamination on both strands, causing C:G→T:A. Error-prone repairs of U by base excision and mismatch repairs (MMRs) create transversion mutations at C/G and mutations at A/T sites. In Neuberger's model, it remained to be clarified how transition/transversion repair is regulated. We investigated the role of AID-interacting GANP (germinal center-associated nuclear protein) in the IgV SHM profile. GANP enhances transition mutation of the non-transcribed strand G and reduces mutation at A, restricted to GYW of the AID hotspot motif. It reduces DNA polymerase η hotspot mutations associated with MMRs followed by uracil-DNA glycosylase. Mutation comparison between IgV complementary and framework regions (FWRs) by Bayesian statistical estimation demonstrates that GANP supports the preservation of IgV FWR genomic sequences. GANP works to maintain antibody structure by reducing drastic changes in the IgV FWR in affinity maturation.

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