GANP regulates recruitment of AID to immunoglobulin variable regions by modulating transcription and nucleosome occupancy.

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Somatic hypermutation in B cells is initiated by activation induced cytidine deaminase-catalyzed C→U deamination at immunoglobulin variable regions. Here we investigate the role of the germinal centre-associated nuclear protein (GANP) in enhancing the access of activation-induced cytidine deaminase (AID) to immunoglobulin variable regions. We show that the nuclear export factor GANP is involved in chromatin modification at rearranged immunoglobulin variable loci, and its activity requires a histone acetyltransferase domain. GANP interacts with the transcription stalling protein Spt5 and facilitates RNA Pol-II recruitment to immunoglobulin variable regions. Germinal centre B cells from ganp-transgenic mice showed a higher AID occupancy at the immunoglobulin variable region, whereas B cells from conditional ganp-knockout mice exhibit a lower AID accessibility. These findings suggest that GANP-mediated chromatin modification promotes transcription complex recruitment and positioning at immunoglobulin variable loci to favour AID targeting.

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