Figure Legend

The upper part of the figure provides a simplified overview of class switch recombination (CSR) at the immunoglobulin heavy chain (IgH) locus. The germline locus comprises multiple variable (V), diversity (D) and junctional (J) exons. Each antibody isotype has a unique constant (C) region exon that is preceded by a repetitive sequence called the switch (S) region and a promoter that generates non-coding transcripts. Random recombination between V, D and J exons via VDJ recombination results in a functional heavy chain of the IgM isotype with clonal diversification of the antibody repertoire. B cell activation upon antigen encounter leads to expression of the activation induced deaminase (AID) which generates mutations in ssDNA in a co-transcriptional manner mostly in the VDJ and switch regions (indicated by the mutation spectra). Mutations in switch regions are processed to DNA breaks that serve as substrates for the non-homologous deletional recombination between the donor (Sμ) and an acceptor (Sα, in this example) switch regions leading to CSR and expression of a new antibody isotype, IgA. The repetitive switch regions range from 2-12 kb and switch sequences have high G clustering and high overall G-richness on the non-template strand (a representative stretch of switch region sequence is depicted). Upon transcription, these G-rich regions can form secondary structures like R loops, G-quadruplexes (G4) and G-loops, as shown in the lower panel.