

Figure 6. Spatial regulation and IGCR1-mediated control of IgH recombination in early B-lymphopoiesis. (A) Reversible IgH contraction. The IgH locus is in an extended configuration in uncommitted progenitors, which allows D_H - J_H recombination to take place in the proximal domain. In pro-B cells, all 200 V_H genes participate in V_H - DJ_H rearrangements because of contraction of the IgH locus by looping. The V_H genes of the incompletely rearranged IgH allele are no longer available for V_H - DJ_H recombination because of decontraction in pre-B cells. (B) Control of IgH recombination by the IGCR1 insulator. See Chapter 4.6 for detailed description how the IGCR1 region controls the order of V(D)J recombination at the IgH locus. CTCF-binding regions (CBEs) are symbolized by red arrowheads. A brick wall indicates that the IGCR1 insulator restrains loop formation and recombination to the proximal IgH domain in uncommitted lymphoid progenitors. In pro-B cells, the IGCR1 element is neutralized by a so-far unknown mechanism, and locus contraction promotes V_H - DJ_H rearrangements. 3'RR, 3' regulatory region; E_μ , intronic enhancer.

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