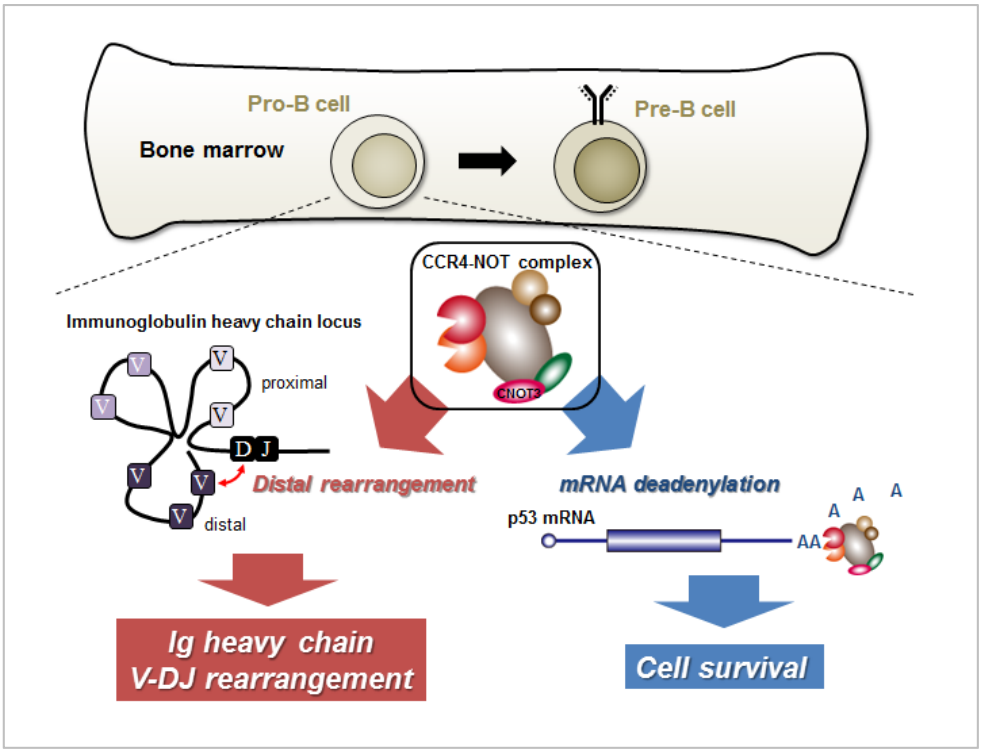
CNOT3 contributes to early B cell development by controlling Igh rearrangement and p53 mRNA stability

KEYWORDS: B cell development, CCR4-NOT complex, CNOT3, mRNA deadenylation, p53, Immunoglobulin gene recombination

ABSTRACT

The CCR4–NOT deadenylase complex plays crucial roles in mRNA decay and translational repression induced by poly(A) tail shortening. Although the in vitro activities of each component of this complex have been well characterized, its in vivo role in immune cells remains unclear. Inoue and Kurosaki group shows that mice lacking the CNOT3 subunit of this complex, specifically in B cells, have a developmental block at the pro- to pre–B cell transition. CNOT3 regulated generation of germline transcripts in the VH region of the immunoglobulin heavy chain (Igh) locus, compaction of the locus, and subsequent Igh gene rearrangement and destabilized tumor suppressor p53 mRNA. The developmental defect in the absence of CNOT3 could be partially rescued by ablation of p53 or introduction of a pre-rearranged Igh transgene. Thus, their data suggest that the CCR4–NOT complex regulates B cell differentiation by controlling Igh rearrangement and destabilizing p53 mRNA.



ARTICLE

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