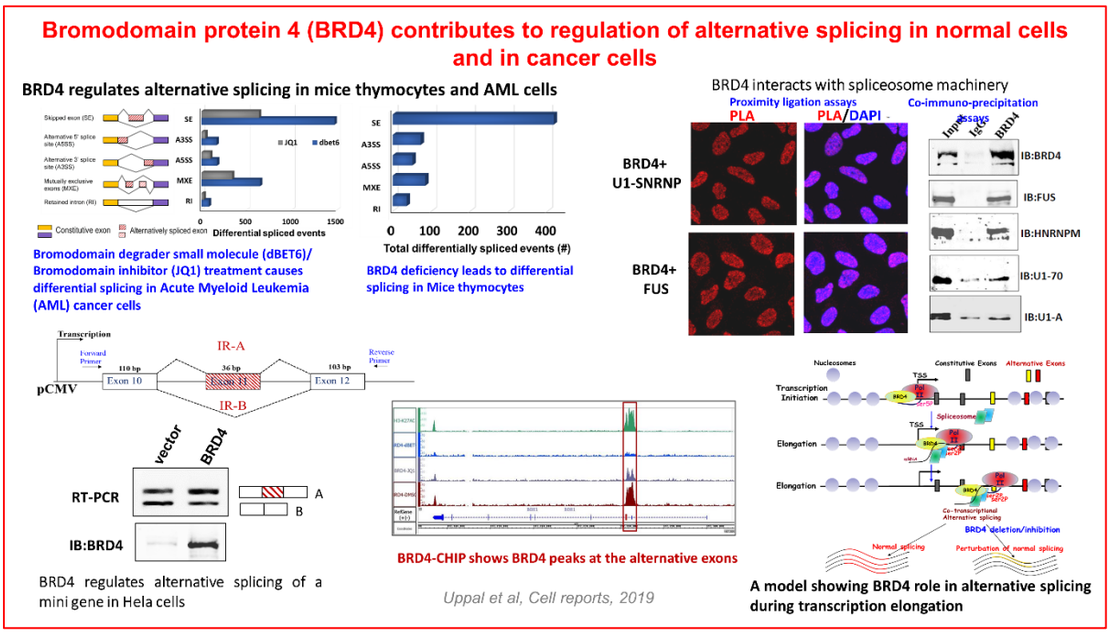
Bromodomain protein 4 (BRD4) contributes to regulation of alternative splicing in normal cells and in cancer cells

Protein diversity in a mammalian cell is generated from various mechanisms, alternative splicing of mRNA is one of them. BRD4 is an epigenetic regulator and a transcription factor, belongs to the BET (Bromodomain and extra terminal domain) family. BRD4 protein has been implicated in inducing oncogenic phenotypes in many cancers. BRD4 is of particular interest in cancer therapeutics as it is a potential druggable target for cancer treatment. Number of BET inhibitors, which act by blocking Bromodomain binding to chromatin, are being tested for their anti-cancer properties in FDA approved Phase I/II clinical trials. We have found that BRD4 deficiency alters patterns of transcript splicing both in normal thymocytes and in cancer cells by interacting with components of the spliceosome complex.

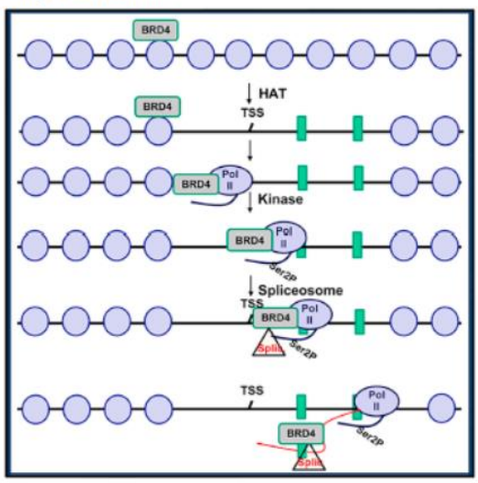


Article

Cell Reports

The Bromodomain Protein 4 Contributes to the Regulation of Alternative Splicing

Graphical Abstract



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In Brief

The bromodomain protein 4 (BRD4) is an important regulator of both normal development and tumorigenesis, regulating chromatin organization and transcription. Uppal et al. report that BRD4 also regulates alternative splicing: distinct patterns of alternative splicing are associated with depletion of BRD4 in T cell acute lymphoblastic leukemia (T-ALL) cancer cells and during thymocyte differentiation *in vivo*.

Highlights

- BRD4, which regulates chromatin and Pol CTD phosphorylation, also regulates RNA splicing
- BRD4 directly interacts with the splicing machinery
- Thymocyte subsets have distinct patterns of alternative splicing
- Depletion of BRD4 in T-ALL cells and thymocytes alters patterns of RNA splicing

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