SF3B1 Association with Chromatin Determines Splicing Outcomes.

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Abstract:

Much remains unknown concerning the mechanism by which the splicing machinery pinpoints short exons within intronic sequences and how splicing factors are directed to their pre-mRNA targets. One probable explanation lies in differences in chromatin organization between exons and introns. Proteomic, co-immunoprecipitation, and sedimentation analyses described here indicate that SF3B1, an essential splicing component of the U2 snRNP complex, is strongly associated with nucleosomes. ChIP-seq and RNA-seq analyses reveal that SF3B1 specifically binds nucleosomes located at exonic positions. SF3B1 binding is enriched at nucleosomes positioned over short exons flanked by long introns that are also characterized by differential GC content between exons and introns. Disruption of SF3B1 binding to such nucleosomes affects splicing of these exons similarly to SF3B1 knockdown. Our findings suggest that the association of SF3B1 with nucleosomes is functionally important for splice-site recognition and that SF3B1 conveys splicing-relevant information embedded in chromatin structure.

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