Characterization of the Binding Affinity and Specificity of MBNL Proteins for RNA

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Myotonic dystrophy (dystrophia myotonica, DM) is a multisystem inherited disease that is characterized by progressive muscle wasting and weakness, cardiac conduction defects and other neuromuscular problems. A toxic RNA gain-of-function model suggests that a repeat expansion of poly(CUG) or poly(CCUG) RNA is responsible for the disease by sequestering RNA binding proteins from their normal function, such as pre-mRNA splicing. The MBNL proteins have been characterized as factors that are strongly recruited into ribonuclear foci comprised of the toxic RNA in muscle tissues from patients and have been demonstrated to regulate the alternative-splicing of four pre-mRNA that are misregulated in DM. Here, we employ in vitro binding assays with purified recombinant protein to probe the interaction of MBNL proteins with RNA. Our work aims to determine the RNA binding specificity of MBNL1, the binding site of MBNL1 protein and the binding specificity of MBNL2 and MBNL3.

Development of an Efficient Route to 2-Pyridyl MIDA Boronate and its Derivatives

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Pyridine represents an important motif in biologically active small molecules. However, introducing the 2-pyridyl moiety via the Suzuki reaction presents a number of challenges associated with the general instability of 2-pyridyl boranes. Recently 2-pyridyl MIDA boronate was discovered to be a stable surrogate for 2-pyridyl boronic acid, enabling efficient cross-couplings of this building block to aryl chlorides. Herein, we report a scalable and efficient route to 2-pyridyl MIDA boronate and its derivatives.