



Contribution ID: 38

Type: Oral Presentation

The characterization and crystallization of the TBR1 T-box domain in the presence and absence of the T-box Binding Element

Monday, 22 March 2021 16:40 (20 minutes)

TBR1 is a neuron-specific transcription factor involved in multiple aspects of cortical development, and has recently emerged as a master regulator of genes implicated in Autism Spectrum Disorder (ASD). It is thus possible that aberrant molecular interactions with TBR1 could underlie the altered neuro-molecular networks observed in Autism.

Currently there is no solved structure available of the TBR1 TBOX domain. In this study, we aim to obtain crystal structures of the TBR1 T-box domain in both the presence and absence of the T-box binding element, with the hope of elucidating its DNA-binding mechanism. The structure may be solved by molecular replacement using TBX21. This will shed more light on how TBR1 regulates ASD-related genes and could explain how aberrant molecular interactions influence neurodevelopmental disorders.

Preliminary structural characterization has been made by monitoring intrinsic tryptophan fluorescence and has revealed that the protein is properly folded. The DNA-binding function has been confirmed using an electrophoretic mobility shift assay. The DNA-binding properties were quantitatively assessed using fluorescence anisotropy and revealed a dissociation constant of 320 nM. Since the TBR1 T-box has been successfully characterized, it is ready for crystal trials.

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Session Classification: Molecular biophysics

Track Classification: Molecular biophysics