LaRP1 and LaRP1b binding mechanism to Poly-A Binding Protein by Single Crystal XRD

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Introduction

- La-related proteins, LaRP1 and LaRP1b, regulate protein biosynthesis and translation factors by interacting with TOP (5′-terminal oligopyrimidine tract) mRNAs. [8, 9, 15]
- Poly-A Binding Protein (PABP) is a multi domain protein involved in mRNA polyadenylation as well as translation regulation by mediating interactions between the mRNA and other proteins. [6]
- The project explores the binding mechanism of LaRP1 and LaRP1b through a conserved PAM2 (PABP-interacting motif 2) motif to the MLLE domain of PABP by Single Crystal X-Ray Diffraction. The expectation is that these LaRPs bind MLLE similarly to other known PAM2 carrying proteins.
- Understanding how LaRPs interact with mRNA may open new ways to treat some diseases, as they play a critical role in gene expression. [11]

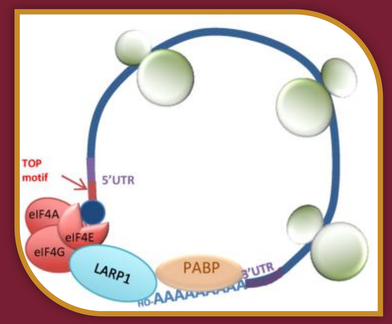

Figure 1: Proposed LaRP1 and PABP mRNA interaction [13]

Methods

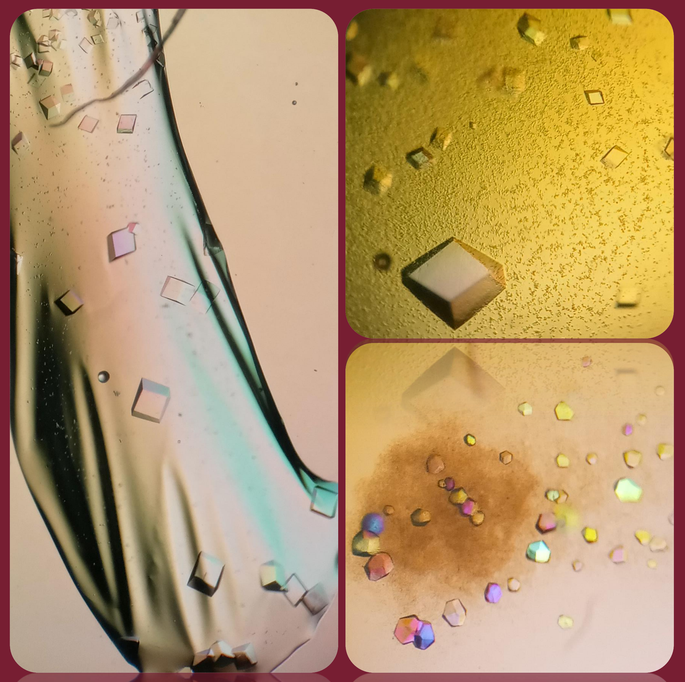

Figure 2: Single crystals containing peptides of the PAM2 sequences of both LaRP proteins, bound to the MLLE domain, grown by hanging-drop vapor diffusion.

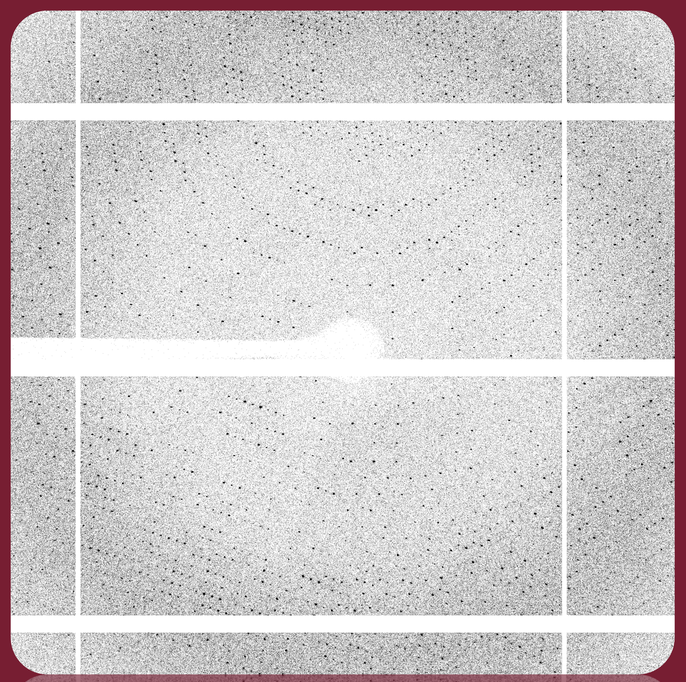

Figure 3: Diffraction pattern of protein crystal as visualized with HKL2000. Diffracted at Brookhaven National Laboratory.

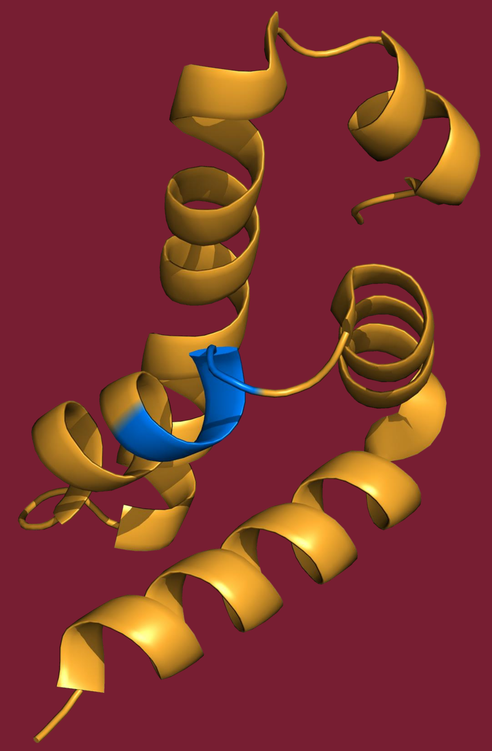

Figure 4: MLLE domain with signature amino acid sequence highlighted as seen with PyMOL.

Discussion

- The data gathered was used to index the crystals' unit cell orientation and dimensions using the software HKL2000.
- Further data refinement for structural determination was done by molecular replacement using the software Phenix.
- The refined data will reveal the physical binding conformation of the MLLE with the peptide and a 3-D model of the complex' structure will be rendered with the software PyMOL.

References