Title: Putative Targets of the PP2A Serine/Threonine Phosphatase Complex In Regulating Dendritic Morphology

Authors: Andre Golshir (agolshir1@student.gsu.edu), Shatabdi Bhattacharjee (sbhattacharjee2@student.gsu.edu), Daniel N. Cox (dcox18@gsu.edu)
Faculty mentor: Daniel N. Cox, PhD
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Abstract

Proper dendritic development is essential for functional neuronal networks. Elucidating the molecular mechanisms that regulate dendritic diversification is therefore essential to understanding the formation and modulation of functional neural circuitry. PP2A is a serine/threonine phosphatase that is evolutionarily conserved from yeast to mammals. In *Drosophila*, the PP2A complex is composed of a catalytic subunit encoded by *microtubule star (mts),* a scaffolding subunit encoded by *PP2A-29B* and one of four alternate regulatory subunits encoded by *widerborst (wdb)*, *twins, PP2A-B'* and *CG4733*. Previous studies in the lab showed that specific RNAi-mediated knockdown of various PP2A subunits in CIV neurons severely impaired dendritic complexity. Knockdown of *mts, PP2A-29B,* and *wdb* led to a significant reduction in the total dendritic length and the number of branches compared to control. Knockdown of the other three PP2A regulatory subunits did not have an effect on CIV dendritic morphology, suggesting that *wdb* is the relevant regulatory subunit associated with this complex in this class of da neurons. In contrast, defects in *mts* and *PP2A-29B* in CI neurons leads to increased dendritic complexity via *de novo* filopodia formation. However, knockdown of only *CG4733* leads to a decrease in total dendritic length suggesting that this subunit is required for modulating the activity of the complex in CI. The present study is aimed at identifying substrates of this complex and understanding how these putative targets regulate dendritic morphology in dendritic arborization neurons of *D. melanogaster*. Phenotypic analyses suggest that the Fragile X mental retardation protein (FMRP) and the transcription factor FoxO may function as targets of the PP2A complex in CIV neurons while FoxO may be a target of this complex in CI neurons. We study these targets using a combination of genetic perturbations and immunohistochemistry to observe whether *mts* and various proteins interact to promote dendritic morphology.