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Molecule of the month: Synaptic plasticity – Protein miRNA interactions

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Figure 1: Protein interactions with Atx2, Ago, and DDX. In this figure, line-colors and various interactions with other genes are red Down-regulation, green Up-regulation, beige Regulation, purple Co-expression, brown Physical Interaction, turquoise dotted Predicted Protein Interaction, and mauve dotted Predicted TFactor Regulation [4].

miRNAs (microRNAs) are small RNAs that are transcribed from intron and other non-coding RNAs. miRNAs are utilized by the cell's molecular biological machinery to help control transcription [1]. There are more than 500 known miRNAs involved in neuronal function including development, transport, and neuronal plasticity. [2] However, what of the neuronal proteins that interacts with these miRNAs? In this month's Editorial, we examine a few protein-protein interactions of proteins that interact with the miRNAs and demonstrate additional network pathways in which these proteins function in neurons.

The protein product Atx2 (Ataxin-2 protein) is implicated in the human neurodegenerative disease, *spinocerebellar ataxia*. In studies in the brains of the fruit fly, *Drosophila*, Atx2 was identified as a miRNA pathway component. Both miRNA and Atx2 components were involved in long-term plasticity of synapses in these studies. Interestingly, the control of translation occurs locally in proximity to the involved synapses. In addition, Atx2 interacts with the Me31B family DEAD box helicases - DHH1 – (also termed DDX helicases) that interact with Argonaute (Ago) and affect function of miRNAs [1, 3] (Figure 1).



Figure 2: Protein interactions with CREB, MECP2, and FMRP. In this figure, line-colors and various interactions with other

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genes are red Down-regulation, green Up-regulation, beige Regulation, purple Co-expression, brown Physical Interaction, turquoise dotted Predicted Protein Interaction, and mauve dotted Predicted TFactor Regulation [4].

The contributions of miRNAs to synaptic plasticity are extensive study. For example, CREB (cAMP responsive element binding protein), MECP2 (methyl CpG binding protein 2), and FMRP (fragile X mental retardation protein) interact with miRNAs in their role as mediators of synaptic plasticity within dendrites. The RISC machinery is utilized post-DICER action, producing the miRNAs *in situ* as above. Post-translation inhibition occurs for these proteins following bursts of synaptic activity mediated by the rapid increase of calcium levels. These activities occur in mouse forebrain and are involved in long-term memory in Drosophila **[5] (Figure 2)**.

The two figures illustrate various gene interactions, up to 100 **[4]**. It is left as a puzzle for the interested reader to identify the various genes and their functions in the figures **[6]**.

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