Molecule of the month: miRNA and Huntington's disease (HD)

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Huntington's disease (HD) has been intensely studied for many years. As we enter the miRNA age in molecular biology novel approaches are taking place in the study of HD. HD is a neurodegenerative disease and often involves depression prior to symptom onset. Symptoms include mental disorders as well as psychopathological, motor, and cognitive dysfunction. In HD, there is gliosis and loss of neurons in the brain's *caudate* nucleus, *striatum*, and frontal lobes. Dysfunction and loss of neurons involves CAG nucleotide repeats in the Huntingtin gene amino-end **[1].**

gene), the central gene at issue in Huntington's disease. Because of its central importance in the onslaught of this disease, it is important to portray these interactions. The genes shown interacting with the HTT gene are immediate interactions.

Figure 2: Network of input protein, Huntington – HTT with additional output neighbors. The study of miRNAs is a new field and much needs to be learned. 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 [5]. This figure is a continuation of the genes shown in Figure 1 and shows additional levels of interactions among the genes; i.e. many of these are downstream from the first level shown in Figure 1.
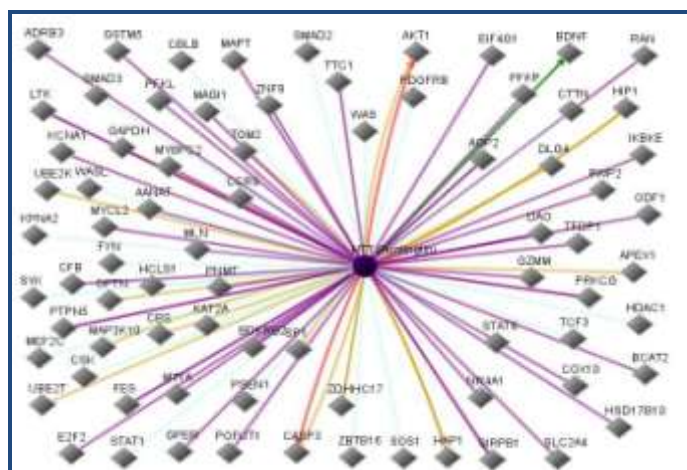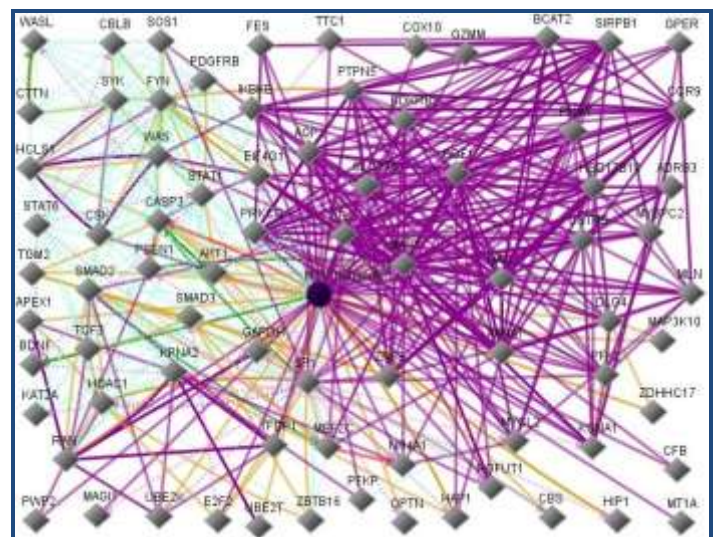

Figure 1: Network of input protein, Huntingtin - HTT - with immediate input neighbors. In this figure, line-colors and various interactions with other genes are red Down-regulation, green Up-regulation, beige Regulation, purple Co-expression, brown Physical Interaction, turquoise dotted Predicted Protein Interaction, and mauve dotted Predicted TFactor Regulation **[5].** This figure shows gene interactions of the HTT (Huntingtin

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miRNAs can attack or interact with multiple pathways. As an example of the study of miRNAs in HD, it has been shown that the miRNA, miR-22, is associated with protective mechanisms against Huntington's disease (HD). Moreover, miR-22 is anti-apoptotic. This miRNA may be anti-neurodegenerative since it shows decreased levels of expression in HD and Alzheimer's disease brain (AD). miR-22 possibly interacts with histone deacetylase 4 (HDAC4), REST corepresor 1 (Rcor1) and regulator of G-protein signaling 2 (Rgs2), three genes implicated in the pathogenesis of HD. Increased expression of miR-22 reduced degeneration of cortical and striatal cultured cells that had been exposed to Htt171-82Q, a fragment of mutated huntingtin. The use of miR-22 also reduced apoptosis of neurons exposed to tumor protein p53-inducible nuclear protein 1 (Tp53inp1) and mitogen-activated protein kinase 14/p38 (MAPK14/p38). In addition, miR-22 targeted Rgs2, HDAC4, and Rcor1 mRNAs **[2]**.

Figures 1, 2, 3, and **4** illustrate the gene expression and protein networks involving the Huntingtin, Rgs2, HDAC4, and Rcor1 proteins.) It is anticipated that in time, point and counterpoint network models for gene expression and protein interactions will become available as miRNA-miRNA interactions, protein-protein interactions, and miRNA-mRNA interactions become merged in highly sophisticated accessible databases. That would indeed be a new day in the progress of Molecular Biology and Medicine and perhaps help in the cure for the as yet incurable disease, HD **[3, 4]**. It is left as a puzzle for the interested reader to identify the various genes and their functions in the figures **[5, 6, 7]**.
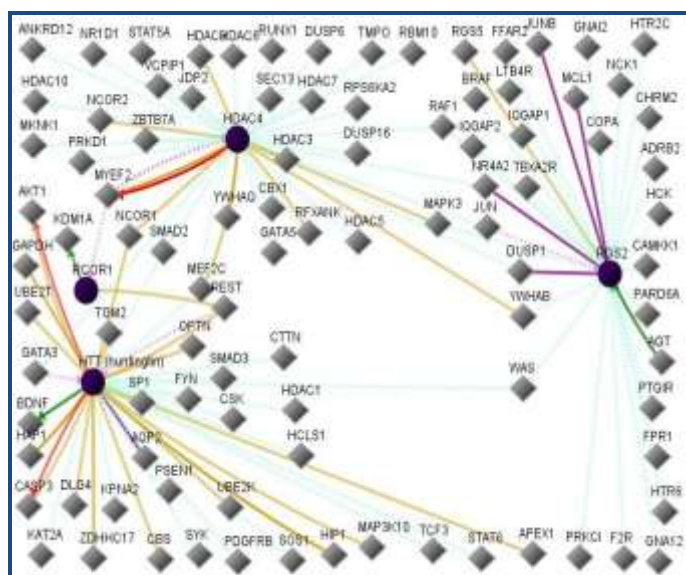

Figure 3: Network of input proteins Huntington – HTT, histone deacetylase 4 - HDAC4, REST corepressor 1 - Rcor1, regulator of G-protein signaling 2 - Rgs2 with immediate input neighbors. The study of miRNAs is a new field and much needs to be learned. In this figure, line-colors and various interactions 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 [5] As mentioned in the text, miR-22 targets HDAC4, RGS2, RCOR1. These genes as well as HTT are shown in this figure. The gene networks shown are immediate interactions.
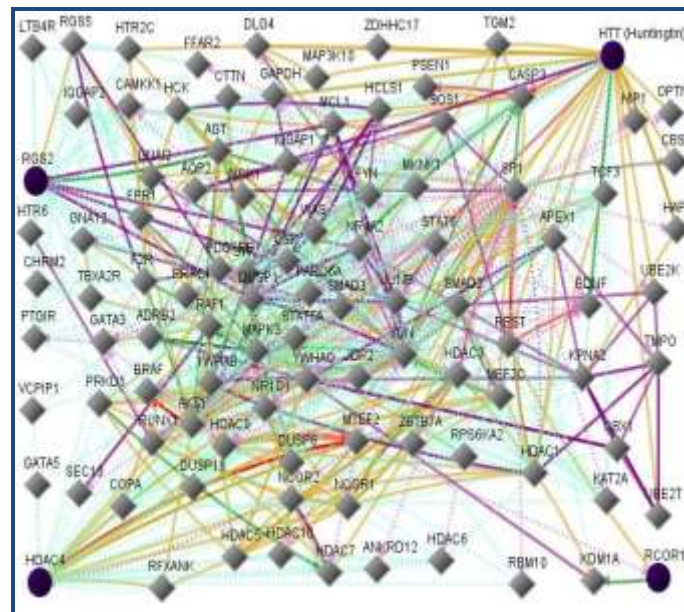

Figure 4: Network of input proteins Huntington – HTT, histone deacetylase 4 - HDAC4, REST corepressor 1 - Rcor1, regulator of G-protein signaling 2 - Rgs2 and additional output neighbors. The study of miRNAs is a new field and much needs to be learned. In this figure, line-colors and various interactions 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 **[5]**. This figure is a continuation of the genes shown in Figure 3 and shows additional levels of interactions among the genes; i.e. many of these are downstream from the first level shown in Figure 3.

Acknowledgment:
There are no financial conflicts.

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