MicroRNA Regulation of Human Protein-Protein Interaction Network

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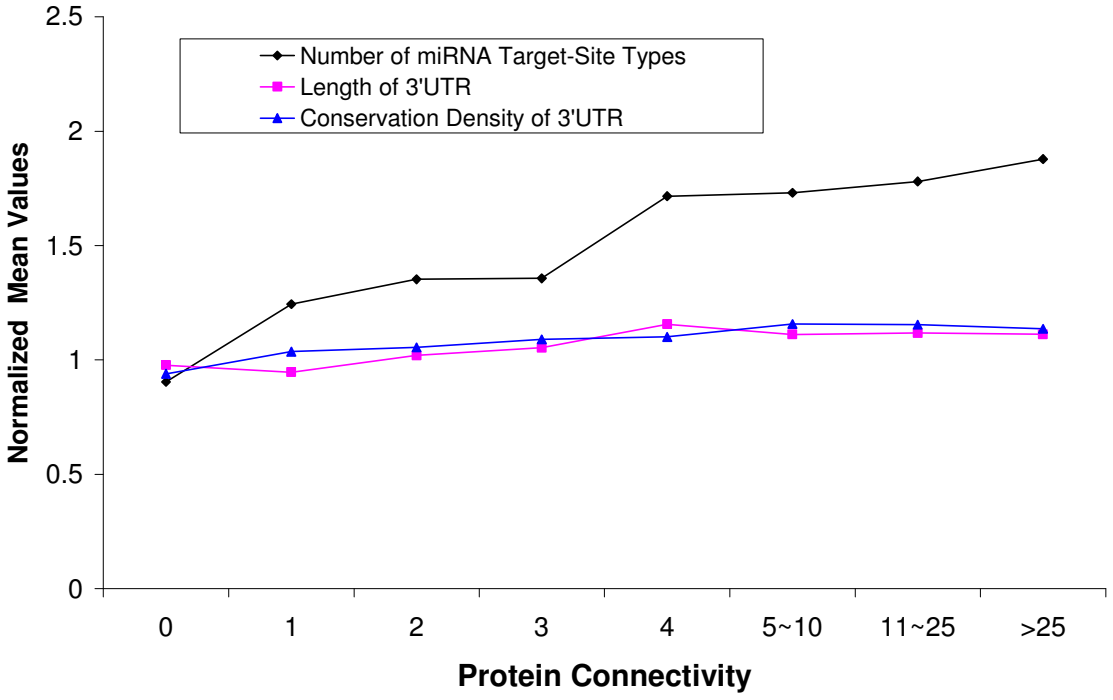
Supplementary Information
3'UTR analysis across PPIN

To rule out the possibility that the correlation between the number of miRNA target-site types and protein connectivity is a side effect of 3'UTR variations across the PPIN, we calculated the length and conservation of 3'UTR against protein connectivity (Fig. S1). As in Lewis *et al.* (2005), conservation was measured by the number of conserved 7mers per 1,000 nt. As can be seen in Fig.S1, the strikingly increasing tendency of miRNA target-site types with protein connectivity can not be explained as a side effect of the variation of 3'UTR length or conservation, since the variation of these two factors is very limited across the whole range of protein connectivity.

Fig. S1

Variations of the number of miRNA target-site types (black), the length of 3'UTR (pink), the conservation density of 3'UTR (blue) with protein connectivity. For comparison, the value of each point was normalized by the corresponding mean value in the whole dataset.



Analysis of miRNA tissue expression range and target gene abundance

As a complementary analysis, we also studied the relationship between miRNA tissue expression range and number of target genes. We used the miRNA expression data from Barad *et al.* (2004), which surveyed the expression of 150 human miRNAs in five tissues by oligonucleotide microarrays. According to Barad *et al.* (2004), we called a family of miRNA genes "expressed in a given tissue" if at least the signal of one miRNA member in the family is more than 500. We found a significant positive correlation between the tissue expression range of a miRNA and its target gene number (Spearman's rank correlation, $Rs = 0.34$, $P < 2\times10^{-3}$, $N = 83$). In addition, the same correlation was observed when we used the predicted miRNA tissue specificity inferred from "target-site depletion" (Farh *et al.* 2005) (data not shown). Thus, our results suggest that broadly expressed miRNA genes tend to regulate more target genes.