Thesis Abstract

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Title of Thesis:

Molecular evolution of microRNAs in bilaterian animals revealed by large-scale genomic analysis

Summary of Thesis:

MicroRNAs (miRNAs) are small noncoding RNAs that regulate the expression of mRNAs. Although miRNAs may have strongly influenced the evolution of animals, the details of their evolution remain to be resolved. Therefore, I focused on clarifying miRNA evolution by analyzing the conservation of miRNAs in both model and non-model species.

First, I predicted the fundamental regulatory relationships between miRNAs and their target genes that have been conserved throughout the evolution of the bilaterian animals. For this purpose, I designed a bioinformatics procedure to extract the conserved miRNA/target-gene pairs. This allowed 31 evolutionarily conserved miRNA/target-gene pairs to be predicted. The downregulation of six pairs was observed with a reporter-gene assay in HeLa cells. I speculated that these pairs were present in the primitive gene regulatory network of the common bilaterian ancestor.

I also focused on the "living fossil" *Triops cancriformis*, the tadpole shrimp. Because this non-model species has an interesting evolutionary history and morphology, I hypothesized that as-yet-undiscovered miRNA regulation and evolution would be revealed by comparing the miRNAs of this organism with those of model species. Deep sequencing identified 180 miRNAs and six components of the RNAi machinery. The expression patterns of four of the conserved *T. cancriformis* miRNAs differed from those of *Drosophila melanogaster*. Most conserved *T. cancriformis* miRNAs shared sequence similarities with those of the arthropods. In contrast, the let-7 sequence and DICER domain were more similar to those of the vertebrates than to those of the arthropods, suggesting that the miRNA system in *T. cancriformis* evolved in a unique way in part.

In conclusion, even when miRNA target genes are conserved among the species, they may have different functions depending on their expression patterns. I discuss the evolution of miRNAs in bilaterian animals, with reference to the knowledge of the miRNA biology of model and non-model species.

Key words: microRNA, evolution, development, genome informatics, comparative analysis