Research Statement

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September, 2004

Gene duplication is the most important source of genetic novelty. Its research is a major focus in molecular evolution. The recent availability of whole genome sequences and high-throughput functional data provide unprecedented opportunities to study the evolution of duplicate genes. I will continue my research in this exciting area. At the same time, by taking advantage of new genome technologies, I will carry out experimental evolution using yeast as a model organism. To achieve these goals, I will focus my research on the following areas:

1) *Duplicate gene preservation:* How duplicate genes are retained is an important issue. The significance of differential expression and protein interaction during this process has been proposed (Ohno, 1970; Force *et al.*, 1999; Hughes 1994; Gibson & Spring, 1998; Papp *et al*., 2003). Using microarray gene expression data in *S. cerevisiae*, I showed that a large proportion of duplicate genes diverge quickly in expression (Gu *et al.*, 2002). The underlying genetic mechanisms, however, are still unknown and I will explore them in the future. The relationship between protein interaction and duplicate gene preservation will also be investigated. The results from the latter study will shed light on evolution of protein interaction network in eukaryotic organisms.

2) *Functional compensation between duplicate genes:* Substantial functional redundancy exists between duplicate genes in yeast (Gu *et al.,* 2003). It is thus interesting to study the interplay between expression divergence and functional compensation between duplicate copies. How could duplicate genes with different expression profiles still compensate for each other's function? Some individual cases show that duplicate genes can adopt each other's expression pattern. How can this happen at the regulatory level? Is this a common mechanism? What is the relationship between this and the regulatory role of RNA? These questions outline one of my future research directions.

3) *Functional innovation of duplicate genes and expression evolution within and between species:* Functional redundancy between ancient duplicate genes suggests that some duplicate copies might for a long time retain the potential of developing novel functions. Individual cases from sequence analysis support this prediction (*e.g*. Ting *et al*., 2004). Another piece of evidence comes from gene expression evolution. In one of my recent studies, I found a significantly higher proportion of duplicate genes than singletons showing differential expression within and between species. The conclusion is also true for ancient duplicate genes (Gu *et al.*, 2004). The question of functional innovation among ancient duplicate genes (at both sequence and expression levels) will constitute an integrated part of my research plan. Furthermore, the role of duplicate genes in speciation will be studied.

As an evolutionary biologist, I have long been intrigued by the idea of directly observing dynamics of evolutionary changes. In addition to research on gene duplication, I will develop experimentally evolving systems using yeast as a model organism and interrogate the genetic changes underlying evolving phenotypes. The short generation time, abundant data and advanced techniques for genetic analysis make yeast suitable for this purpose. Two general topics will be investigated:

A) *Adaptive evolution:* By applying different strains to various living conditions (such as high temperature, different chemical compounds, *etc*.) and allowing them grow for enough generations, I will be able to answer questions such as: *Will the fitness of the descendent strains increase relative to the ancestral strains? What are the underlying genetic changes? Are these changes parallel in different evolving strains?* The combination of techniques from quantitative genetic analysis and tiling arrays (a microarray chip with whole yeast genome) will be used. Adaptation to chemical compounds will also provide insights into the evolution of drug resistance.

B) *Population genetics underlying laboratory evolution:* In a recent study, I found that the evolutionary rate was significantly accelerated in the laboratory strain of *S. cerevisiae*. The increase is larger for genes under stronger negative selection (Gu *et al*., submitted). The results suggest that relaxation of selection intensity is the dominant underlying reason, which is consistent with recurrent bottlenecks in the *S. cerevisiae* laboratory strain population. However, due to the mysterious origin of the laboratory strain of yeast (Mortimer & Johnston, 1986), it is currently difficult to show that the increase did occur in the laboratory. By manipulating population size and recombination, laboratory evolution will present evidences for/against different hypotheses. Relevant theoretical population genetics studies will be carried out.

Understanding evolution of duplicate genes is my ultimate intellectual goal. Seeing evolutionary process in the lab defines another aspect of my research interests. At some point, I hope to bridge these two areas. Finally, I appreciate the strength of collaboration, which I believe is the way science should be done.

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Teaching Interests

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September, 2004

What are my goals as a teacher?

Prepare students for their successful careers: I value my part in contributing to student's intellectual growth. Years after a student leaves my class, he/she may not remember the materials I teach, but if he/she can independently investigate a topic, critically evaluate the information and efficiently present the conclusion, I would consider my mission fulfilled.

Learn from teaching: Another much rewarding aspect of teaching is the opportunity to learn from the questions, observations, and challenges from one's students.

How I will teach?

- I support an individual-centered approach in teaching. I recognize that students learn in different ways with different paces. Every student should be encouraged to succeed. It is my responsibility to ensure that students who feel unprepared get the guidance they need to proceed with confidence.
- To be effective, a teacher must have a great understanding of the subject matter. It is also my obligation as a teacher to stay current in biology, engage in research and participate in conferences.
- I intend to give a diagnostic test in the first class to determine the prior knowledge students might already have. I might adjust the syllabus accordingly.
- In my lectures, I will try to explain concepts through real biological examples and encourage discussion.
- I will employ active, project-based learning whenever possible. By implementing team-structured projects in the classroom, I will also teach my students to collaborate – a vital skill in today's science.
- Students learn what we examine for. If we examine for facts - they will learn facts. Instead, I will examine them for problem-solving and self-education skills. The open-book take-home exams sometimes work the best to stimulate thinking. Essay questions are a great way to encourage students to learn to write well.

What can I teach?

My undergraduate and graduate training was very comprehensive. I have a solid knowledge of chemistry, statistics, computer sciences and biology. I am well qualified to teach such basic biology courses as *Genetics, Biochemistry*, and *Molecular Biology*. I am fluent in the evolutionary and population genetics theories as well as in the computational analysis of genetic sequences and functional data. Therefore, I am more suitable for teaching such classes as *Evolution, Molecular Evolution, Computational Biology, Population Genetics, Comparative Genomics, Evolutionary Genomics,* and *Bioinformatics*. These courses can be given at both introductory and advanced levels.