

# Review

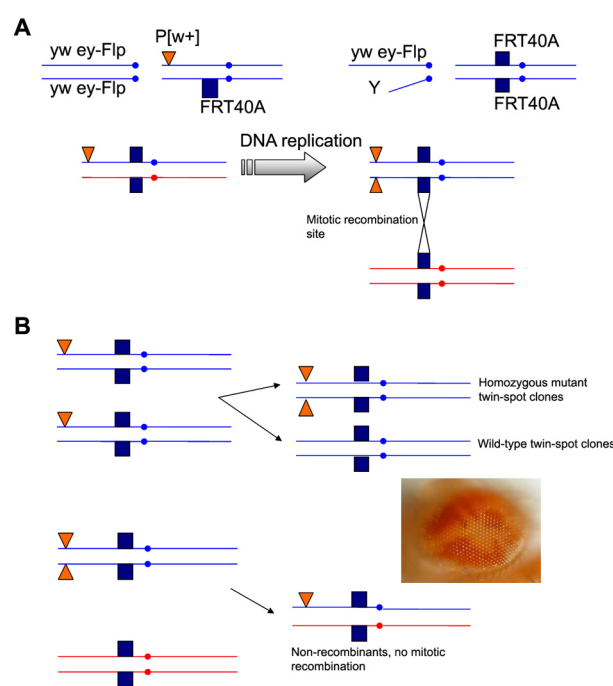
## Fostering a New Generation of Scientists: Integrating Research into Undergraduate Science Education

Kathy Ngo and Neda Asem

As the top public research university in the nation, the importance of undergraduate research at UCLA, has been emphasized now more than ever. UCLA, with \$773 million dollars reserved for scientific research, offers a variety of valuable opportunities for students through the Undergraduate Research Center for Sciences, Engineering and Mathematics and the Center for Academic and Research Excellence (URC-CARE). Furthermore, an increasing number of fellowships have become available to promote undergraduate research including the Undergraduate Research Fellows and Scholars Program, Beckman Research Scholarship, and Howard Hughes Undergraduate Research Program.

The need to integrate research in undergraduate education has been recently increasing, as it becomes a key component in mission statements of various funding agencies. Incoming students with very little or perhaps no science background have limited opportunities available to them to conduct “serious” research in the sciences, thus, making the Undergraduate Research Consortium of Functional Genomics (URCFG) unique. Initiated by Professor Utpal Banerjee, chairman and professor in the Department of Molecular, Cell, and Developmental Biology, the goal of this HHMI-funded program is to stimulate the excitement of scientific research to undergraduates as early as their first or second years. Thus far, 304 undergraduates have gone through the introductory research program, 116 students in the advanced research program, and more recently, six undergraduates have co-authored a scientific publication (Chen et al., 2005; Liao et al., 2006).

Undergraduate education in universities now emphasizes an investigative learning approach: stressing critical thinking abilities and novel ideas as this is the essence of graduate school. Nevertheless, students pursuing graduate studies have had little, if any, prior research experiences. Their views of how scientific research “should” be done and what actually goes on in the laboratory can be strikingly different. The goal of the URCFG program is to expose students to independent research as early as possible in their undergraduate career and “get their feet wet.” “We’re having them do graduate-level research and



**Figure 1.** Using mitotic recombination as a functional genomics tool. Through the course of 10 weeks, students recombine transposable P-elements, which disrupt a gene in *Drosophila* genome, and a Flipase Recognition Target (FRT) to generate mosaic clones. By looking at the phenotype of the mosaic clones, students conclude whether the gene plays an important role in *Drosophila* eye development. The P-element is represented in orange and FRT site is represented in blue. (A) Meiotic recombination of the P-element and the FRT site. After a meiotic recombination event occurs, mosaic analysis can be done, where the progeny inherits half of the DNA from each parent, red and blue strand. The purpose of this cross is to have meiotic recombination occur between the FRT site and P-element insertion. This will allow for mosaic analysis of the gene of interest in the next generation. (B) Mosaic analysis by eye-specific Flipase-induced mitotic recombination. After recombination occurs at the FRT site, the result is multiple genotypes in the *Drosophila* eye, with mutant twin-spot, wild-type twin spot, and non-recombinant, heterozygous cells. The phenotypes of cell genotypes are then analyzed via light and electron microscopy.



**Figure 2.** Dynamics of LS10H class, consisting of the didactic, laboratory and computer component. Lectures are given in parallel with the student's current experiments (top left). Students spend most of their time in the laboratory setting up crosses, dissecting and analyzing tissues via fluorescent microscopy (right panel). In computer sessions, Mendelian genetics are reinforced and students are taught how to do database searches (bottom left).

taking freshmen from high school," said John Olson, current HHMI-instructor of the LS10H course.

Each quarter, approximately twenty first- and second-year students from a diverse combination of majors are enrolled in the honors class, Life Sciences 10 Honors (LS10H). The students learn about fly pushing, *Drosophila* genetics, microscopy, and tissue dissection. Many of them have no research experience and a limited science background; subsequently their training begins with the basics. After the foundation has been laid, the students in LS10H become ecstatic about their work and the results they obtain. LS10H is a unique in that it is a discovery-based course and is extremely individualized. Past research projects have focused on Flipase (Flp)-mediated recombination that has been recently very useful for gene knockout experiments. In the past program, students generate lines in which genes are disrupted by P-element mutagenesis and recombined with the Flipase Recognition Target (FRT); this gives other scientists interested in elucidating the role of disrupted genes access to a very convenient starting point. Presently, students are tracing lineages of genes throughout the developmental stages of *Drosophila*. By determining when and where specific genes are turned on via enhancer-trap lines, it is possible to elucidate precursors of cell types. The information from these genomic screens will be publicly available to the scientific community. Thus, the work of the students in LS10H is meaningful and collectively can have a high impact on the research community.

Throughout the course, students integrate what is learned from lecture into a hands-on experiment to make a novel discovery. The lecture series given is in parallel with current experiments to help the students understand the underlying principles of their research. The rest of time remaining is spent in the laboratory, typically 12-20 hours, setting up crosses, dissecting and mounting tissues, and analyzing data via microscopy. In computer sessions, basic concepts in Mendelian genetics are reinforced; students learn to obtain information about their assigned lines in an international *Drosophila* genomics database, Flybase, such as insertion sites and gene functions.

The purpose of the LS10H class is to expose students to all aspects of graduate school, including the mechanics of scientific writing. Midterm examinations are replaced by a National Institutes of Health-style grant proposal on the current project in the class. Writing a successful grant proposal is essential as virtually all scientific research requires funding. In addition, communication to the scientific community, in the form of publications, summarizes findings. Instead of a final examination, students submit a written report of their data and results in the proper Cell-paper format. To assist them on writing the grant proposal and the final paper, students are taught how use the PubMed database for literature searches through library sessions. The demands and expectations of students in the program set by instructors of this course are extremely high: "I expect them to put the time into it. Students pretty much plan their own schedule,"



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commented Olson. Although a high level of independence is often required, many resources are made available to the students. First, they can seek help from instructors of the course, Utpal Banerjee and John Olson. Utpal Banerjee has been studying signal transduction using *D. melanogaster* as a model organism for twenty-seven years at UCLA. John Olson, a teaching faculty member with extensive teaching and research experience in yeast and *Drosophila* genetics, intracellular transport and cell trafficking mechanisms in various model organisms, is readily accessible to students for advice and guidance. The course teaching assistant, Nikki Villarasa, and advanced undergraduate students in the program are also available to students for assistance. The amount of resources available at the students' disposal is virtually unlimited and one of a kind.

With such challenges placed on their shoulders, it is, nevertheless, an immensely rewarding experience for the students. Having participated in the program, not only do students gain valuable research experiences, but they may become an undergraduate author in a scientific publication upon completion of the project. This is evident by the phenomenal number of 134 undergraduate authors in the previous publication in PLOS Biology (Chen et al., 2005) and a publication currently in preparation with 265 undergraduate authors (Call et al.). Furthermore, students leaving the program become very successful in their careers; they go on to the prestigious medical schools and graduate schools in the nation including John Hopkins University, Stanford University, and Duke University. Many advanced students in the program have received numerous prestigious research fellowships offered by the university. For example, one of the students in the program, Kevin Yackle, now a senior and fourth-year advanced student in the program who plans to pursue a M.D/Ph.D. joint degree program, has had many notable research accomplishments. Yackle has won many research awards and fellowships for his work such as the Howard Hughes Undergraduate Research Program Fellowship. Despite the difficulties and long-work hours, many students excel in the class. "I am amazed by the students. We set the challenges very high and the students do the work and come through," said Olson. Those who participate in the program are very driven and have a very high degree of self-motivation; this allows them meet the high standards set by the instructors.

Why promote undergraduate research, one may ask? Why is this so important, considering most students going through the program have just entered the university? "Undergraduates have a lot of potential, not fulfilled by the didactic training from classes," said Banerjee, "It is a shame not to tap into that potential." Research is a vital component of undergraduate science education; this is what one must realize. "There is lots of information out there with the genomic databases available now; there are many opportunities that are available," added Olson, "The sooner we get undergraduates involved, the sooner we can put the story together to understand more about



**Figure 3.** Kevin Yackle, fourth year undergraduate (center) under guidance of Utpal Banerjee, chairman and professor of the MCDB Department (right) and Jamie Marshall, previous undergraduate student at URCFG, now a graduate students working for Dr. Banerjee.

developmental processes, and bring scientific research to the next level." The purpose of the discovery-based education is to allow undergraduates to investigate an important but difficult problem collectively. Genomic screening fits into that category because it cannot be done individually. Using the idea of genomic screening as a starting point, the previous LS10H program focused on using mitotic recombination as a functional genomics tool to understand the role of genes in *Drosophila* eye development. Through the course of this program, 2382 lethal lines have been used and over 2000 lines have been analyzed and verified.

Collectively, these Flippase Recognition Target (FRT) recombinant lines generated by undergraduates are made available to the scientific community through the Kyoto Stock Center. Extending this principle, the program has shifted focus in solving another difficult problem: using mitotic recombination as a functional genomics tool for genome-wide cell lineage analysis of imaginal tissues. The cell lineage analysis approach will exploit the enhancer-trap lines as tools for identifying markers for certain genes turned on at different stages during development. Through this program, whether participating in the previous project or the current cell lineage project, undergraduates are making a novel discovery and they understand the underlying scientific principles. This is the defining characteristic of scientific research and the fundamental concept of discovery-based education.

Although this unique program would provide undergraduates with the necessary research experience earlier on in their education, the cost of maintaining the program is quite expensive, due to two principle problems: it is quite individualized and the source of outside funding is limited. To provide more opportunities to a larger pool of undergraduates, Utpal Banerjee has proposed

a solution: a minor in biomedical research, which has recently been approved by the College of Letters and Science. As part of the Biosciences Initiative to promote and enhance undergraduate education, the minor will serve two purposes: foster entering students to become leading scientists as well as building an undergraduate science community.

There are four major components of the Biomedical Research minor: (1) early training and recruitment, (2) independent research based on interest, (3) building an undergraduate research community, and (4) exploring the ethics and philosophy of scientific research. "In the LS10H class, students do a small part of a large genetic screen," said Ira Clark, coordinator of the Biomedical Research minor, "However; this is very expensive to run. The minor expands this idea to a larger population of students. We recruit students early with strong interest in research." This recruitment is in the form of an introductory research classes: LS10H, LS5HA, and Honors Collegium 70A. In contrast to

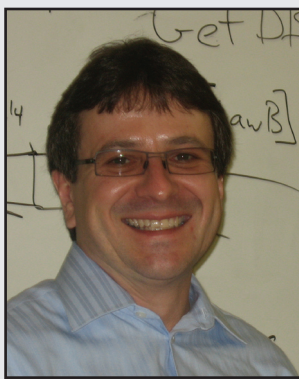
the discovery-based and laboratory-centered LS10H class, the LS5HA class is a didactic training class in which the goal is to reach a larger pool of students. The purpose of these classes, nevertheless, is the same: students do not have to be intimidated about science. "We hope they become more excited about research and excited about science," said Clark. Ira Clark, who has had extensive experience working with *Drosophila*, started doing research early in his high school education. Fascinated and excited about science, Clark became involved in undergraduate research during his first year in college as an undergraduate at Harvard University. Having been involved in research much earlier in his career, Clark wants to motivate students to start research early. The reality is, Clark said, "The problems presently facing undergraduate research include: late entry into labs, minimal research training prior to lab entry, poor information leads to poor lab choice, and the perspective of 'undergraduate research islands', in which one is not aware of other research

## FACULTY SYNOPSES



**Dr. Utpal Banerjee**

Dr. Utpal Banerjee received a Ph.D. in Physical Chemistry at Caltech. He completed his postdoctoral research studying the receptor tyrosine kinase, *Sevenless*, during *Drosophila* eye development under Seymour Benzer at Caltech, the founder of neurogenetics. Studying cell-to-cell signaling using *Drosophila* as a model organism at UCLA for 27 years, Dr. Banerjee is one of the only two HHMI professors at UCLA to be awarded the HHMI grant for enhancing undergraduate research. His lab discovered the interaction of *son-of-sevenless* in EGFR signaling cascade.



**Dr. John Olson**

Dr. John Olson is an HHMI instructor for the LS10H class. He obtained his Ph.D. in Microbiology and Immunology at Virginia Commonwealth University working for Guy Cabral, whose lab is interested in studying the effects of drug of abuse on the immune system. For his dissertation, John Olson studied the effects of human cannabinoid receptor CB1 in human nerve-type cells. John Olson did his postdoctoral research in studying protein transport and cell trafficking in the endocytic pathway of *Saccharomyces cerevisiae*.



**Dr. Ira Clark**

Dr. Ira Clark is currently the coordinator of the Biomedical Research minor. As an undergraduate at Harvard University, he worked with *Drosophila*, isolating overlapping lamda phage clones of the Dpp complex from *Drosophila pseudoobscura*, using Southern blots to identify strongly conserved regions. For his dissertation, he worked in the Jan Lab studying microtubules dynamics during oocyte formation in *Drosophila*.

projects beyond his or her specialized area.” The goal of the biomedical research minor is to break that mold. The minor will help students to be successful in the laboratory.

Upon completion of the introductory research courses, students are placed into labs with a faculty at the College or other professional schools, based on their research interests. The Faculty Advisory Committee, consisting of distinguished faculty member from various departments, is available to assist students in choosing their labs. In addition, the minor also aims to foster an undergraduate science community, where students working on different projects come together and discuss research with their peers. To fulfill this aspect, students participate in journal club seminars (LS 193H) and research presentations (LS 194H), as well as the annual undergraduate research symposium. The Journal club seminars will help students in their critical thinking skills, analyzing other research by presenting latest research papers in various topics. Lastly, students will put biomedical research in a ‘social context’ through a course on science policy and ethics (MCDB 60) and an upper division course in either the history or philosophy of science. By exposing students to all aspects of scientific research, the hope is to build a scientific community and provide undergraduate researchers with the necessary knowledge and awareness needed to become successful leading scientists of the future.

Those interested in pursuing a career in the sciences are strongly advised to start research as early as possible. There are many research opportunities available to students and students are encouraged to take advantage of these opportunities. “Stay focused on your goals and don’t give up,” said Olson, “If I were to choose another career, I would not have it any other way; it would still be in ‘science’.”

## REFERENCES

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Liao et al. (2006). An Efficient Genetic Screen in *Drosophila* to Identify Nuclear-Encoded Genes with Mitochondrial Function. Genetics 174: 525-33