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## The Eye of the Fly: HHMI Professor and 138 Undergraduates Identify Essential Genes that Function in Eye Formation

A Howard Hughes Medical Institute (HHMI) professor and 138 of his undergraduates have co-authored a paper that provides the first genome-wide estimate of vital genes that are also essential for eye development of the common fruit fly, *Drosophila melanogaster*. The undergraduates are students in a unique biology class taught by HHMI professor Utpal Banerjee at the University of California, Los Angeles.

Banerjee and his students identified 501 essential genes responsible for processes such as repair, cell death, and cell replication in the fruit fly's developing eye. They report the results of their research and the impact of their research-based learning project in the February 2005 issue of *PLoS* (Public Library of Science) *Biology*.

"It won't be easy to find a paper with 138 undergraduate authors," said Banerjee, one of 20 HHMI professors who received \$1 million grants in 2002 to improve undergraduate biology education. "In fact, this could easily be the first paper ever published with that many undergraduate authors that has serious science in it."

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HHMI professors are recognized research scientists on the faculty of research universities who want to bring the excitement of scientific discovery into the undergraduate classroom. A new competition for HHMI professorships just opened, with 100 research universities invited to nominate scientist-educators and up to 20 new professors to be named in 2006.

The course, created and taught by Banerjee and his group of “teaching postdocs,” Jiong Chen, Allison Milchanowski, and Gerald Call at UCLA, melds education and professional research in functional genomics. The class is modeled on the process of scientific research, a search for new knowledge and exploration of previously uncharted territory. It includes lectures on background material, a computer lab to teach students to analyze the genetic effects of crosses or mating, and a wet lab in which the student researchers actually cross-breed flies.

As a mid-term exam, each student writes an NIH-style grant proposal for original research. The final is a scientific paper that summarizes the research findings.

Innovative undergraduate courses such as this, bringing education and research closer together, are the kind of transformation of the undergraduate science curriculum that HHMI was seeking when it established its professors program.

Banerjee gave the students a research problem that confronts geneticists who want to understand how a mutation affects an organ system, in this case, the eye, which is Banerjee's research focus. “The only way a geneticist can ask that question is to mutate that gene and see what happens to the eye,” Banerjee explained. “The problem is, if you mutate that gene, the fly is dead as an embryo. What has to be done, he said, is to “make the eye mutant without making the rest of the fly mutant.”

The work began with flies that are heterozygous for a lethal mutation. In other words, they have only one genetic copy of the mutant gene. The goal was to create flies that have the mutation in their eye cells but not throughout the organism and so, survive.

Achieving that goal required what Gerald Call, a postdoctoral fellow who works with Banerjee, called a “genetic trick” called mitotic recombination, in which chromosomes switch segments during cell division. This runs completely contrary to what the students learned in high school biology, said Banerjee. Recombination normally occurs when organisms make sperm and eggs but does not occur when an organism's other cells divide, the process of mitosis. What makes mitotic recombination possible in Banerjee's flies is the presence of flippase, an enzyme genetically engineered into the flies that is expressed only in the eye.

Through a series of five crosses or matings of successive generations of flies, the students created flies with homozygous lethal mutations in the eye, independently marked by eye color.

The use of flippase for mitotic recombination is a standard technique, used by *Drosophila* geneticists to study the impact of mutations. The real achievement of the class, Banerjee said, was using the method to make

homozygous mutations in the eye of all the lethal mutations available and creating a database describing the phenotypes or expressions of the mutations. The venture also created stocks that other researchers can use to determine the function of these genes in other tissues.

“None of us knew what was going to happen,” said Joy Wu, a senior now applying to graduate programs in neuroscience. “It put us all on the same playing field.” Added third-year student Albert Cespedes, “This course offered me a chance to do real research, an opportunity I never expected to have as an undergraduate.”

Wu and Cespedes said the course has changed their career plans. “It's pretty much shaped my future by reinforcing my interest in genetics and development,” said Wu. Cespedes, who plans to go to medical school, now is considering doing research too. “It never even dawned on me that research was an option until I took this course,” he said.

Banerjee said the course embodies what happens to practicing scientists as they work, making connections between ideas and results. “It's totally amazing how little of that is imparted in some undergraduate classrooms,” he observed.