Generational research on drosophila sheds light on genetic mechanism of evolution

1 November 2010, by Janet Wilson

UCI doctoral student Molly Burke used fruit flies to determine that evolution results from small alterations in multiple parent genes rather than quickly spreading mutations of single genes

Molly Burke doesn't study fruit flies because she loves tiny, winged crawlers that feast on rotting bananas. No, like generations of geneticists before her, the UC Irvine doctoral student uses the flies because "they're easy to handle, they're cheap, and they share a surprising number of genes with higher organisms."

In fact, humans and fruit flies share 70 percent of the same genes, making us closer cousins than we might think. Now, with data from 600 generations of fruit flies, Burke and two UCI professors have addressed a question that has long bugged scientists.

For years, evolutionary biologists have dickered over whether sexual beings - including fruit flies and humans - evolve in the same way as asexual yeast and bacteria. The researchers say they've proved the answer is an emphatic no. It would seem to be esoterica only a scientist could appreciate. But ecology & evolutionary biology professor Michael Rose says the conclusion, reported recently in the journal *Nature*, could fundamentally alter the quest for new pharmaceuticals and other products.

It's the latest chapter in a rich record of evolutionary research based on the humble Drosophila melanogaster, Greek for "dark-bellied dew lover." "Few laboratory creatures have had such a spectacularly successful and productive history as drosophila," wrote Robert Kohler in his 1994 book, Lords of the Fly.

Embryologist Thomas Hunt Morgan and his students began using the red-eyed drosophila in 1908, breeding them by the hundreds in Morgan's famous Columbia University Fly Room. They doused them in acid, heated and iced them, and peered at them through magnifying glasses and - later - microscopes, seeking evidence of genetic change.

"It was actually his wife who made some of the big findings, not Morgan," notes ecology & evolutionary biology professor Tony Long, who co-authored the UCI study with Burke and Rose. "But he got the credit for it. This was 1920; there was no way a smart female geneticist was going to be credited with discovering the classic mutant."

The story goes that Lilian Sampson Morgan was the one who found a key white-eyed fly among the red-eyed horde. She and the rest of her husband's team went on to make groundbreaking conclusions about hereditary traits and sex chromosomes. He got a Nobel Prize; she got to raise their four kids.

Among the Morgans' successors were a trio of biologist-mathematicians who founded population genetics, giving evolutionary processes a quantitative basis. One, a provocative Englishman named J.B.S. Haldane, focused on identifying single genes that he believed could mutate and spread quickly across whole populations 0- as happens with asexual life forms. But Ronald Fisher and Sewall Wright disagreed, maintaining that small alterations in multiple parent genes added up

to changes in later generations, from life span to eye color.

Wright, a shy Midwesterner, never publicly criticized Haldane, but he did outlive him. In 1980, he published a paper reiterating his views, and he discussed them with eager, younger scientists. One was Rose, two floors up from Wright's office at the University of Wisconsin Madison. Rose says Wright helped set him on the path he has followed for 30 years: breeding fruit flies in search of answers to burning scientific questions, including whether a single gene or many cause evolution in sexual creatures.

Rose's UCI lab has bred an astounding 600 generations of flies since 1991 - the equivalent of 12,000 years of human existence. Rose has been able to manipulate their life span, developing both long-lived "Methuselah" flies and "live fast, die young" flies that mature and reproduce much more rapidly. All along, he says, he wanted proof that Wright was right. Powerful new computers and a new generation of researchers finally provided it.

Beginning in 2009, Burke ground up Rose's fly populations - both the "live fast" and control-group varieties - into genetic soups. After computers untangled their long streams of DNA, she pored over all of the flies' 14,000 sets of genes, looking for any variations linked to faster development. Burke found not one instance of a single gene spreading quickly. But she isolated more than 500 genes associated with sped-up development.

The experiment, Rose says, "is a total vindication of Wright and Fisher and a major defeat for Haldane and a lot of conventional geneticists who have sided with him."

Not so fast, says noted evolutionary biologist Richard Lenski of Michigan State University: "There are cases where a single gene affects something. But here's an example of rigorous research that really reveals just how complex some of these genetic traits can be."

Rose points out that if human disease is controlled by many genes, it would explain the difficulty in creating completely safe drugs. Side effects, for instance, are probably caused by medications targeted at a single gene, without taking into account other responsible genes.

On the research side, things have evolved as well: A female scientist is getting credit this time around. Burke was lead author on the Nature piece and was cited along with Rose and Long in a New York Times article on their work.

Provided by UC Irvine