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Researchers develop whole genome sequencing approach for mutation discovery

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The Stowers Institute's Hawley Lab and Molecular Biology Facility have developed a "whole-genome sequencing approach" to mapping mutations in fruit flies. The novel methodology promises to reduce the time and effort required to identify mutations of biological interest. The work was published in the May issue of the journal *Genetics*.

The team mapped a fruit-fly mutation caused by the compound ethyl methanesulfonate (EMS) by determining the DNA sequence of the mutant fly's genome. The results provide insight into the mechanism of EMS mutageneseis and into gene conversion events involving balancer chromosomes — genetic tools used to prevent genetic recombination between homologous chromosomes during meiosis.

Model organisms like fruit flies are used in research for studying both normal biological processes and human disease. Fruit fly genes can be inserted, deleted or modified, and large numbers of flies can be randomly mutated to generate interesting phenotypes relevant to human disease. Finding the mutated gene responsible for an interesting phenotype is labor intensive and time consuming, and many mutations that cause medically relevant phenotypes are not discovered. The new approach lowers the barrier to finding mutations and greatly accelerates the discovery of genes important for human health.

"This approach will change the way fruit fly genetics is done," said Scott Hawley, Ph.D., Investigator and co-equal senior author on the publication. "Traditional mapping approaches to identify mutations are

inefficient procedures. Our whole-genome sequencing approach is fast and cost effective. Among other potential uses, it also carries the potential to pinpoint inheritable molecular characteristics that are controlled by several genes at once."

"The traditional mapping method could take months to years depending on the complexity of the phenotype," said Karen Staehling-Hampton, Ph.D., Managing Director of Molecular Biology and co-equal senior author on the paper. "This advance will allow us to map mutations of interest in just a few weeks. The next-generation sequencing technology used for this project is extremely exciting. It will allow researchers to sequence genomes for a few thousand dollars, a cost unheard of just a few years ago. It will also enable them to take their science in new directions and answer new questions that were not possible with traditional sequencing technology."

Source: Stowers Institute for Medical Research