

# Novel technology makes studying gene function easier, faster and more efficient

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Studying the role genes play on basic biology and disease is now easier, faster and more efficient, say researchers at Baylor College of Medicine. They have developed a drug-based genetic platform that enables scientists to track genetic manipulations in the laboratory fruit fly without having to screen thousands of individual flies.

The researchers describe in *Cell Reports* the fundamentals of this new technology as well as examples of its applications. A companion paper in *STAR Protocols* shows how to set up, conduct and analyze the experimental procedures involved in this technology. Genetic tools and resources, including a plasmid library, to assist researchers in the implementation of this new methodology into their experimental systems, are freely available.

"The laboratory fruit fly is a widely used [animal model](#) in which to study the function of genes and mutations on [biological processes](#), both in health and disease," said first author Dr. Nick Matinyan, who was a graduate student in Dr. Koen J.T. Venken's lab at Baylor while he was working on this project. He currently is a postdoctoral fellow at Johns Hopkins University School of Medicine.

To study a particular gene's function, researchers first introduce it into thousands of fruit flies and then screen the flies individually to determine which ones incorporated the gene successfully. To distinguish the flies carrying the gene of interest from those that do not, a sort of 'tag' is added to the gene. Traditionally, this tag is a physical characteristic readily observed in flies. The tag can be certain [eye color](#), red, for instance, so researchers know that flies with red eyes are the ones carrying the gene of study. Body color, wing or [body shape](#), are other [physical traits](#) that typically are used to tag genetic features of interest.

"This process has worked well for many years, but a major downside is that visually screening thousands of flies individually under a microscope looking for a particular physical trait can become quite tedious and time consuming," said Venken assistant professor in the Verna and Marrs Mclean Department of Biochemistry and Molecular Biology at Baylor and co-corresponding author of the work.

"In the current work, we developed a system of drug-based markers for the selection or counter-selection of genes of study that has markedly improved the screening process," said Dr. Herman A. Dierick, associate professor of molecular and human genetics and neuroscience at Baylor and co-corresponding author of the work.

## **Simple selection vs. laborious screening**

The idea behind this novel technology is that, instead of tagging the genes of interest with a physical trait, they are tagged with another gene that confers the flies either resistance or sensitivity to specific drugs. Instead of manually screening for physical features, researchers can now use the drug to select or counter-select in a group of flies for those that are carrying the gene of interest.

An experiment to select for flies carrying the gene of interest using a drug-resistance tag would involve, first, introducing the gene of study and the associated resistance tag into the flies and then exposing all the flies to the drug, which has been added to their food. The flies that incorporated the gene of study also are resistant to the drug and will survive the exposure.

"This simpler, efficient strategy saves significant amount of time, freeing the researchers to be more productive," Matinyan said.

Other type of experiments may benefit from a counterselection strategy using drug-sensitivity tags.

"I think counter-selection would be very useful for scientists who study one gene and want to make many modifications to that same gene to investigate how that changes its function," said Venken, assistant professor of pharmacology and chemical biology, a member of the Dan L Duncan Comprehensive Cancer Center and a McNair Scholar. "In this

case, it's worthwhile to have a combination of drug-sensitivity and drug-resistance tags, which in combination can help select and counter-select for the genes of interest. Researchers can make many combinations of [genes](#) and select them, and then counter-select them in a subsequent step quickly and at very little cost."

"Time wise, I would estimate that this novel technology is at least 10 times faster than the traditional approach," Dierick said.

"We hope that this work provides a framework to accelerate the transition from lab bench to bed side," Matinyan said. "That by developing tools to make basic research easier, simpler, faster, we can shorten the time that it takes to go from understanding the fundamentals to implementing them as translational outcomes."

The main paper described here has a companion publication that is a technical step-by step guide for how to take these tags and drugs and implement them into particular projects.

"The protocol includes the nitty-gritty details for how to apply this in a researcher's lab, with the equipment they have available," said Matinyan. "For those interested in using this in another animal model, this companion paper provides a starting point."

**More information:** Multiplexed drug-based selection and counterselection genetic manipulations in *Drosophila*, *Cell Reports* (2021). [DOI: 10.1016/j.celrep.2021.109700](https://doi.org/10.1016/j.celrep.2021.109700)

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