

Hello, my name is Andrew Jones, and I am a senior working in the lab of Dr. Elizabeth King. I would like to tell you about the project we conducted in partnership with the lab of Dr. Yves Chabu, titled "Identifying genetic background effects for cancer susceptibility."

cJun NH2 terminal kinase or JNK is a tumor suppressor and can be affected by its upstream regulator, Egr. When Egr is mutated, JNK loses control of its regulatory properties which can cause premature cell death. It can also produce oncogenes and lead to developmental deficiency. This deficiency can be expressed as diminishing eye pigmentation in mutant flies. The aim of this project was to cross mutated flies with a wildtype population and observe the heritability of this mutated expression.

We took flies from the Chabu lab carrying the Egr mutation along with several accompanying genes. The CYO gene leads to presentation of curly wings. GMR GAL 4 a driver of Egr. The TM3 Sb gene displays as stubby bristles in flies. These genes all work in conjunction to indicate whether the fly has the desired mutation. We crossed mutants with 7 lines of wild type founders from our own lab. The flies are from the Drosophila Synthetic Population Resource and feature natural gene variants from numerous locations. For crosses, the genotype that we observed had the Egr gene and its driver, GMR Gal4. It lacked the CYO gene meaning that the flies had straight wings.

These slides showcase the large variation displayed in crosses between founders and mutated flies. The top left image shows a fly without the TM3 Sb gene while the one to the right does have it. The next images show flies with straight and curly wings. Straight wings indicate the absence of the CYO gene. The bottom row shows various fly eyes. The first three are offspring of crosses while the last is an original mutated fly. This shows that there is a large range of sizes for eyes affected. It also signifies that crossed offspring did regain some level of pigmentation.

Imaging was done with a mounted camera. Flies were anesthetized and then set in a highly replicable position. All images were taken at the same magnification. I then used the image software ImageJ to trace eye shapes. A micrometer was used to determine the scale and find the area of the eye.

Here are some resulting plots. This left figure shows the eye area by parent founders. The far-right column labeled N/A is made up of original mutated flies which we found were significantly different from the crossed offspring. This told us that the offspring did experience the loss of function as a result of the Egr mutation, but to a lesser degree. The plot on the right shows the data delineated by sex. It demonstrates a large amount of variation between males and females for eye size. Analysis revealed that sex was a significant background effect.

Overall, we found that there was a significant difference in eye expression between crossed offspring and mutant parents. This indicates that the loss-of function effect is passed down from the parents. The

offspring did experience cell death, but it was not as severe as the parent generation. Sex was also found to be a background effect of significance.

This project is key because the use of natural variants via the DSPR founders allows us to take an unbiased approach to detecting novel effects. Major next steps are to map the JNK gene as well as observe other background effects from the CYO and TM3 Sb genes. Around 60% of fly DNA is conserved in humans, so discoveries in flies could have implications for our own species as well. A better understanding of tumor suppressors like JNK could potentially improve our ability to combat cancer.

Thank you for your time and if you have any questions, I would love to hear from you.