COVID Severity-Related Genes' Effects on Respiration in Drosophila

Fope Ayangbayi, Alison Belonzi, Rosie Didonato, Bryce Showell

Introduction

COVID-19, cause by the virus SARS-CoV-2, is a contagious disease that attacks the respiratory system. Symptoms can range from severe to very mild, with the most severe complication involving respiratory failure. A genome wide association study identified two loci, one of which contains six genes. Both loci are strongly associated with respiratory failure. Since there is no known connection between these mutations and respiration, the effects of these gene mutations can be studied using Drosophila. Two of these genes have Drosophila homologues—as often is the case with human genes—which makes Drosophila a useful model organism for studying human diseases. For our study, we will be using knockouts for 3 of the homologues to observe if the genes affect respiratory rates.

Question

Do specific genes make an individual more susceptible to severe COVID-19 symptoms.

Hypothesis

We hypothesize that these mutated genes reduce respiration rates making individuals with these genetic mutations more susceptible to severe COVID-19 symptoms.

Methods and Materials

The respirometers were created cutting the tip off of a 1 ml pipette and inserting a 50 µl capillary micropipette tube. Internally, each respirometer had one layer of cotton, one layer of 0.01g soda lime, another layer of cotton, and space for the flies. When in use, the respirometers were sealed with clay. In order to create an airtight chamber for the experiment, two rectangular plastic containers were placed together to create a chamber. Petroleum jelly was used to create an airtight seal between the containers. Cardboard was cut to size and placed inside the chamber to be used as a tube holder. Dye solution along with 300 ml water was added to each chamber.

Results

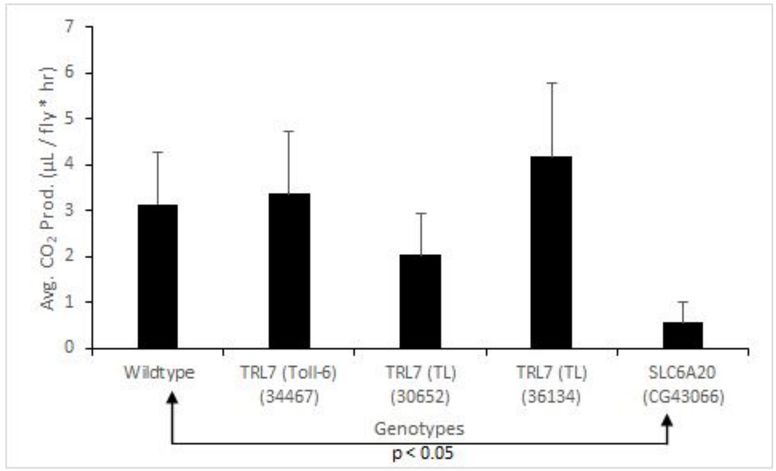


Figure 1: Average amount of CO2 produced per fly per hour for wild type Oregon R compared to mutants (n=7, Oregon R, n=4 Toll-6, n=4 TL, n=3 TL, n=2 SLC6A20). A two-tailed t-test was done to compare the WT to SLC6A20 ($p < 0.05$). Error bars represent s.e.m.

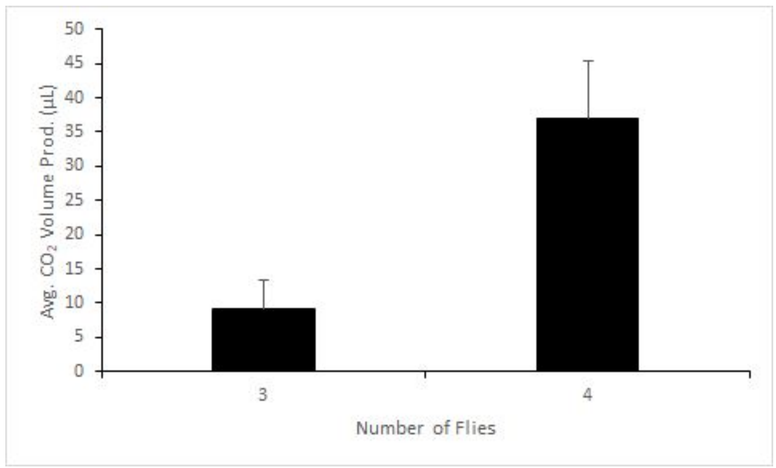


Figure 2: Average volume of CO_2 production in a vial by amount of flies in a vial. A two-tailed t-test was done to compare the average volumes for 3 and 4 flies ($p < 0.05$)

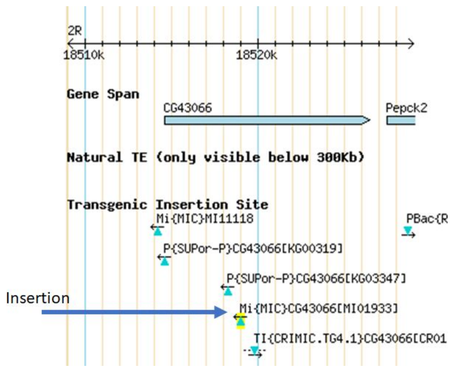
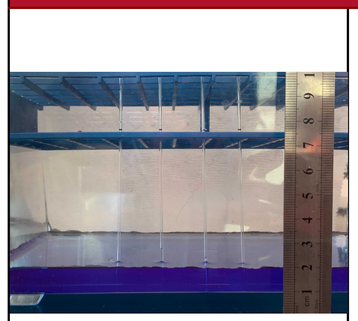


Figure 3: Transposable element for gene CG43066 (Sequence location for transposon: 2R:18,518,985 - 18,518,985).

Thurmond J, et al and the FlyBase Consortium. (2019) FlyBase 2.0: the next generation. Nucleic Acids Res. 47(D1) D759–D765

Methods and Materials (cont.)



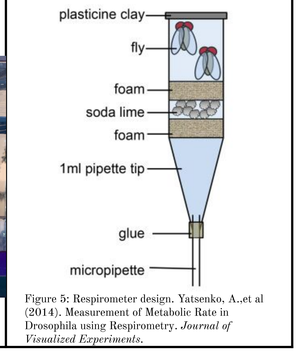


Figure 5: Respirometer design. Yatsenko, A.,et al (2014). Measurement of Metabolic Rate in Drosophila using Respirometry. *Journal of Visualized Experiments.*

Conclusions

- Our results show that there is a significant difference between the wild type Oregon-R and CG43066—the homologue for SLC6A20. However, for the sample of CG43066, n=2.
- Given the low sample size tested further research should be done to ensure more flies are tested in order to achieve a more stable average. If a new average were obtained, it could be further analyzed statistically to determine if any significant differences remain.
- SLC6A20 encodes a proline transporter, so the role of proline oxidation in the electron transport chain (ETC) could potentially explain the lower levels of respiration found in drosophila.
- This would help to better understand why, for some patients, COVID-19 is severe compared to those who may be asymptomatic or have mild symptoms. More studies would also need to be done to confirm if the results in Drosophila are the same as in humans.

Acknowledgements

We would like to thank Dr. Lee and Dr. Fried of the biology department at Rutgers- Camden for their help and guidance throughout this project, as well as the biology department at Rutgers-Camden for funding.

RUTGERS