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Maya Takashima

Huda Al-Bana

Grace Holcomb

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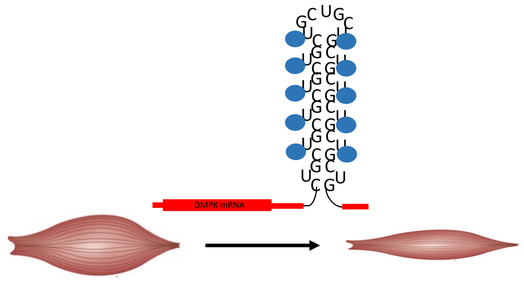
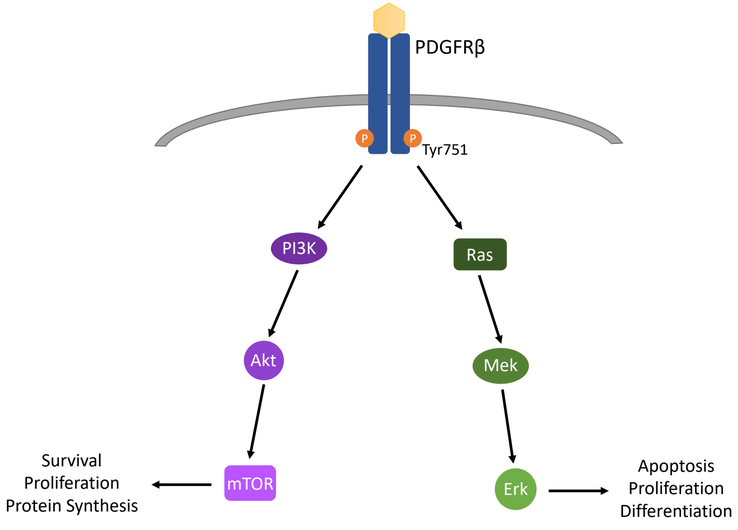
Maya Takashima, Huda Al-Bana, Grace Holcomb, Dr. Ginny Morriss
University of Mary Washington

Introduction

Myotonic Dystrophy Type 1 (DM1) is a multi-systemic genetic disorder that causes severe muscle weakening and wasting. This phenotype is the result of the expansion of CTG repeats at the 3' untranslated region in the DMPK gene[1]. 50-3000 repeats are present in DM1 patients.



- The platelet-derived growth factor receptor β (PDGFRβ) is involved in cell growth, survival, and skeletal muscle hypertrophy[2].
- PDGFRβ deregulation has been shown to be implicated in Duchenne Muscular Dystrophy[3].
- A previous study showed that PDGFRβ activation was significantly reduced DM1[4].
- With the involvement in cell growth, survival, and skeletal muscle hypertrophy, then the pathway's deregulation could contribute to the muscle wasting and weakening seen in DM1.
- The PDFGRβ signaling pathway signals through two downstream pathways: PI3K/Akt and Ras/Mek/Erk pathway. To activate these two pathways phosphorylation of Tyr751 is required.



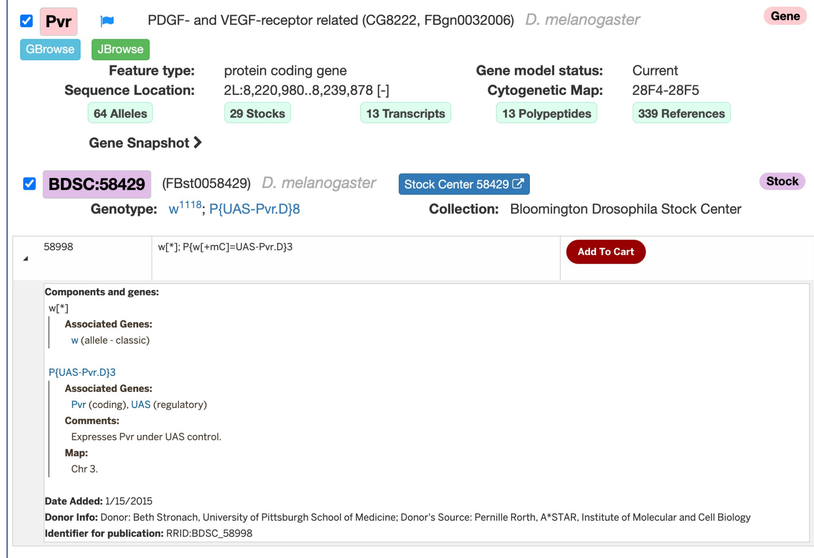
To look at the phenotypic changes that occur due to the CTG expansion, a Drosophila model was utilized. The Drosophila equivalent to the PDGFRβ pathway is the pvr pathway.

Objective

- To determine which downstream gene targets and *Drosophila* fly lines and stocks to utilize in mating schemes.
- To use a fly model to understand the role of the pvr signaling pathway in muscle wasting due to DM1 and determine which downstream pathway, PI3K/Akt and/or Ras/Mek/Erk is primarily affected.

Methods

Flybase is a database for *Drosophila* genes and genomes – it was utilized to determine the desired fly lines and stocks.
Flybase provides a link to Bloomington Stock Center, which offers more details on the stock and fly line, such as chromosomal location.

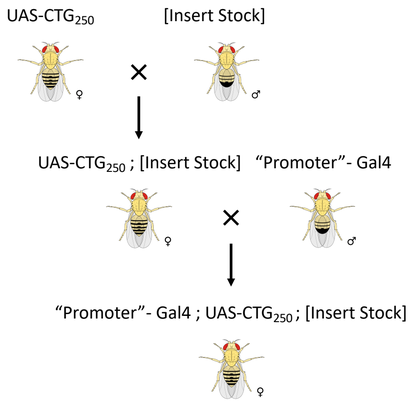


Mating schemes were planned by working backwards

1. Determined desired genotype of progeny
2. Used stock fly genotypes to produce desired progeny

Want:
Promoter-Gal4 ; UAS-CTG_{250} ; [insert stock]

Have:
Promoter-Gal4
UAS-CTG_{250}/UAS-CTG_{250}
[insert stock]



Methods (cont.)

Example of Cross:

$$\frac{UAS-CTG_{250}}{UAS-CTG_{250}};\frac{+}{+}\times\frac{+}{+};\frac{UAS-Pvr.D}{UAS-Pvr.D}$$

$$\downarrow$$

$$\frac{UAS-CTG_{250}}{+};\frac{UAS-Pvr.D}{+}\quad\frac{UAS-CTG_{250}}{+};\frac{UAS-Pvr.D}{+}$$

$$\frac{UAS-CTG_{250}}{+};\frac{UAS-Pvr.D}{+}\times\frac{+}{+};\frac{tub-Gal4}{TM3}$$

$$\downarrow$$

$$\frac{UAS-CTG_{250}}{+};\frac{tub-Gal4}{UAS-Pvr.D}\quad\frac{+}{+};\frac{tub-Gal4}{UAS-Pvr.D}$$

$$\frac{UAS-CTG_{250}}{+};\frac{UAS-Pvr.D}{tub-Gal4}\quad\frac{+}{+};\frac{UAS-Pvr.D}{tub-Gal4}$$

$$\frac{UAS-CTG_{250}}{+};\frac{tub-Gal4}{+}\quad\frac{+}{+};\frac{tub-Gal4}{+}$$

$$\frac{UAS-CTG_{250}}{+};\frac{TM3}{+}\quad\frac{+}{+};\frac{TM3}{+}$$

Future Directions

- To look at specific phenotypes that are characteristic of DM1, such as splicing and nuclear foci defects.
- To look at the molecular and physiological change due to modulation, flight tests will be conducted.
- Perform histological tests to look at the change in muscle architecture that is produced by the *in vivo* modulation.

Acknowledgements

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