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4-29-2021

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### **Recommended Citation**

Takashima, Maya; Al-Bana, Huda; and Holcomb, Grace, "Role of the Pvr signaling Pathway in a Fly Model for Myotonic Dystrophy Type 1" (2021). *Research and Creativity Symposium*. 111.  
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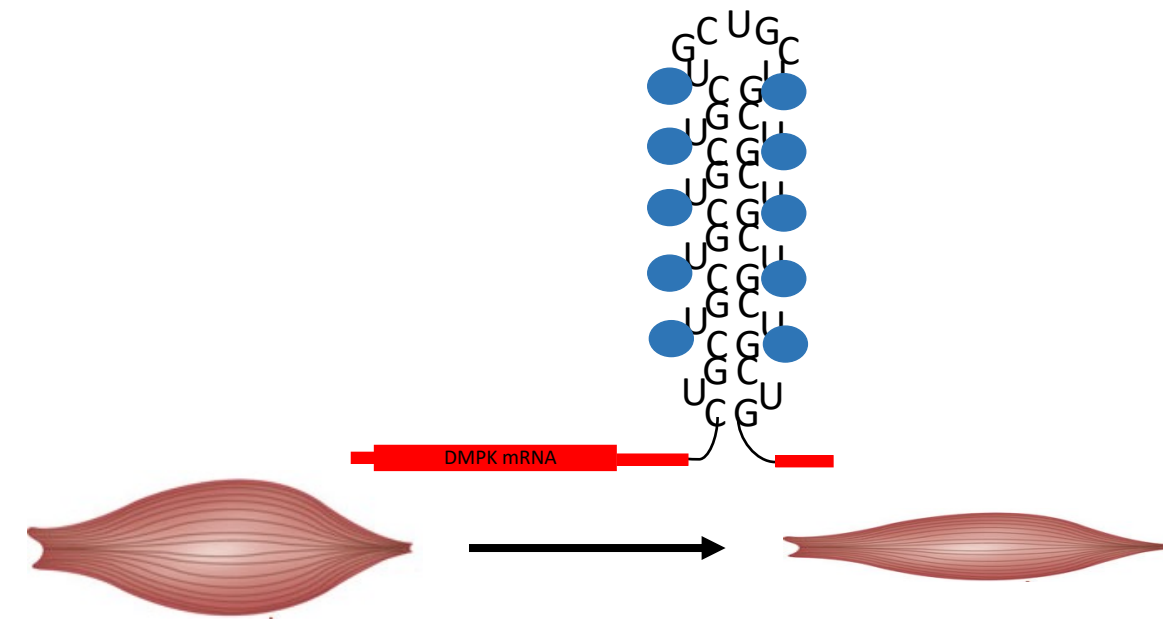
# Role of the Pvr signaling Pathway in a Fly Model for Myotonic Dystrophy Type 1

Maya Takashima, Huda Al-Bana, Grace Holcomb, Dr. Ginny Morriss

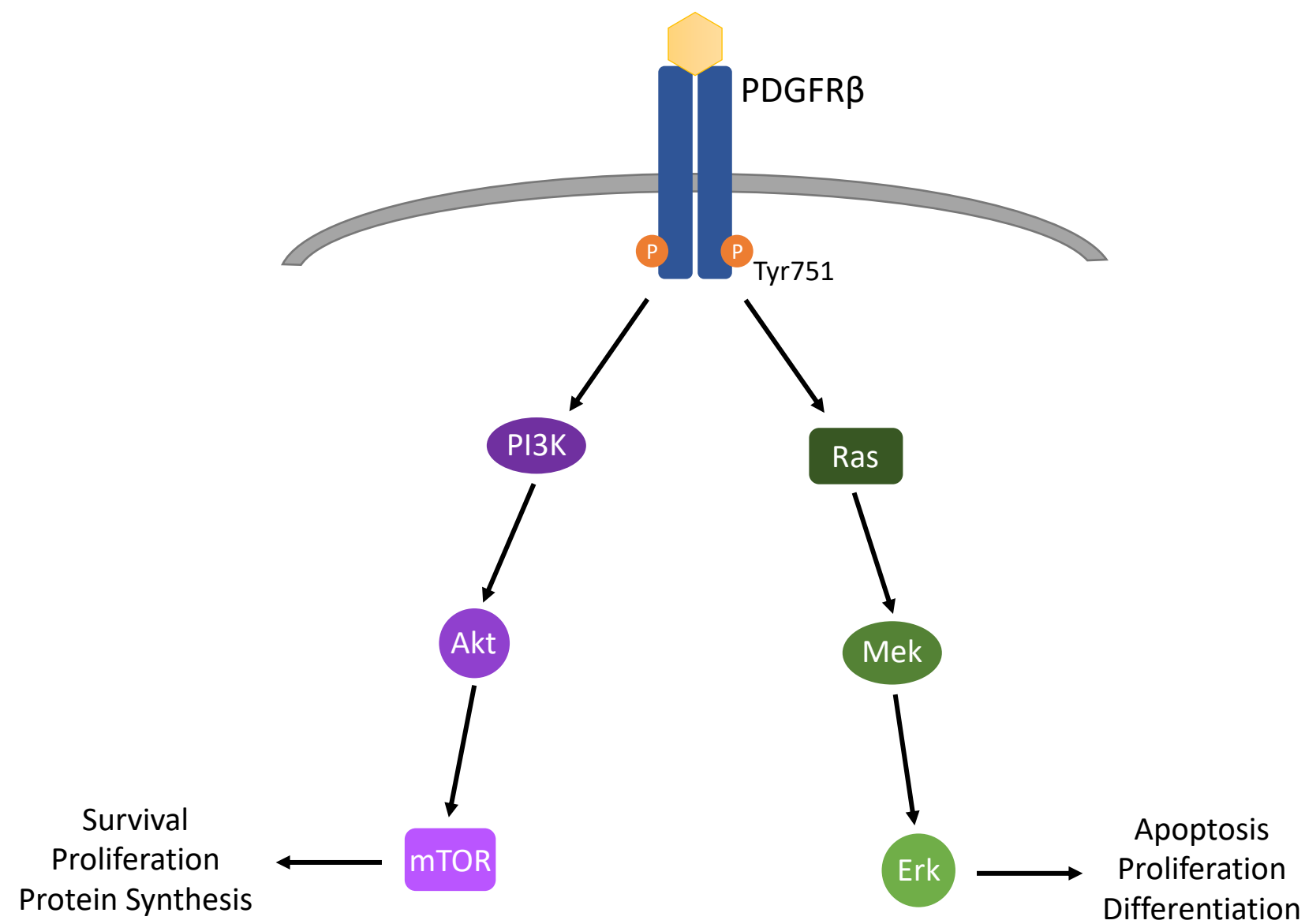
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## Introduction

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<sup>1</sup>. 50-3000 repeats are present in DM1 patients.



- The platelet-derived growth factor receptor  $\beta$  (PDGFR $\beta$ ) is involved in cell growth, survival, and skeletal muscle hypertrophy<sup>2</sup>.
- PDGFR $\beta$  deregulation has been shown to be implicated in Duchenne Muscular Dystrophy<sup>3</sup>.
- A previous study showed that PDGFR $\beta$  activation was significantly reduced in DM1<sup>4</sup>.
- 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 PDGFR $\beta$  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 PDGFR $\beta$  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.

**Pvr** PDGF- and VEGF-receptor related (CG8222, FBgn0032006) *D. melanogaster* Gene

Feature type: protein coding gene  
Sequence Location: 2L:8,220,980..8,239,878 [-]  
Gene model status: Current  
Cyto genetic Map: 28F4-28F5

64 Alleles 29 Stocks 13 Transcripts 13 Polypeptides 339 References

Gene Snapshot >

**BDSC:58429** (FBst0058429) *D. melanogaster* Stock Center 58429 Stock

Genotype: w<sup>1118</sup>; P[UAS-Pvr.D]8 Collection: Bloomington Drosophila Stock Center

58998 w[\*]; P[w[+mC]=UAS-Pvr.D]3 Add To Cart

Components and genes:  
w[\*]  
Associated Genes:  
w (allele - classic)  
P[UAS-Pvr.D]3  
Associated Genes:  
Pvr (coding), UAS (regulatory)  
Comments:  
Expresses Pvr under UAS control.  
Map:  
Chr. 3.

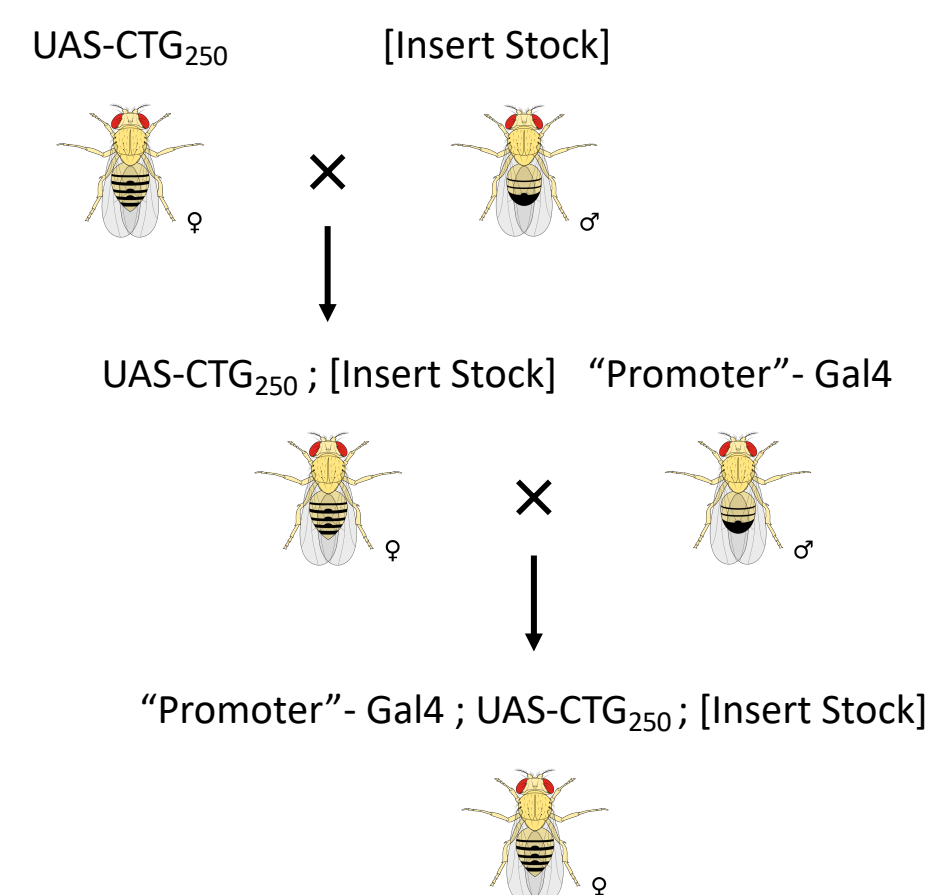
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Identifier for publication: RRID:BDSC\_58998

Mating schemes were planned by working backwards

- Determined desired genotype of progeny
- Used stock fly genotypes to produce desired progeny

Want:  
Promoter-Gal4 ; UAS-CTG<sub>250</sub> ; [insert stock]

Have:  
Promoter-Gal4  
UAS-CTG<sub>250</sub>/UAS-CTG<sub>250</sub>  
[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

I would like to thank Dr. Morriss for the opportunity to be a part of her lab and her guidance and encouragement throughout this project.

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