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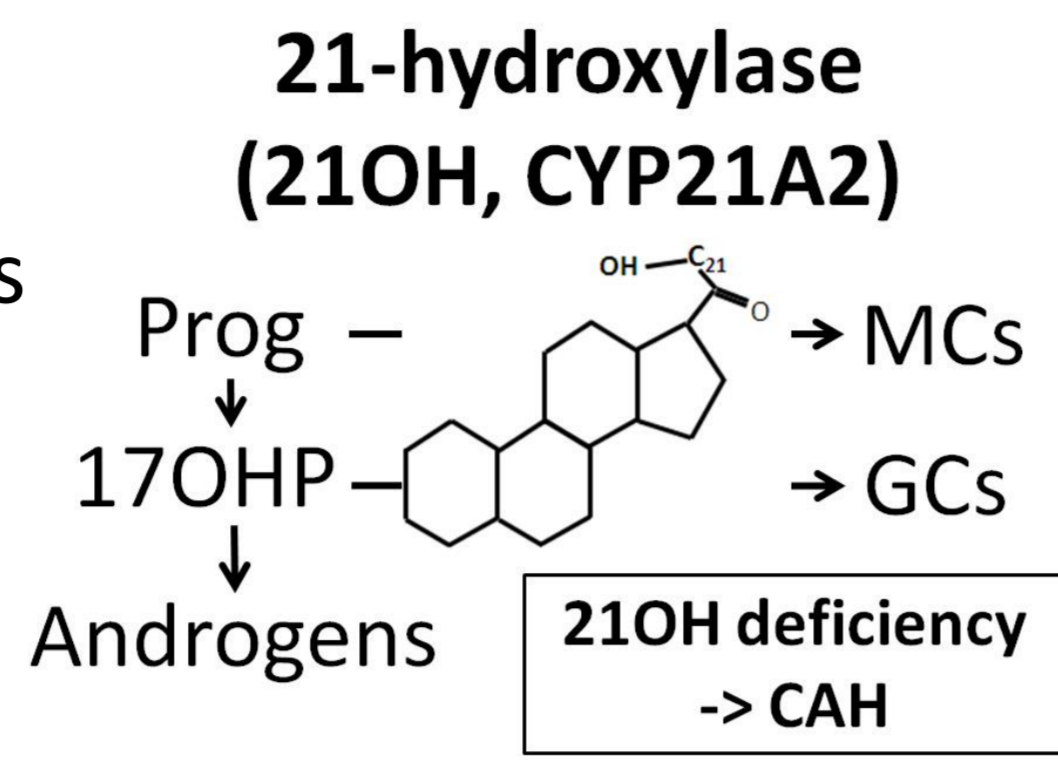
A novel animal model to explore the whole-organism response to 21-hydroxylase deficiency

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Introduction

Challenges in studying CAH (Congenital Adrenal Hyperplasia):

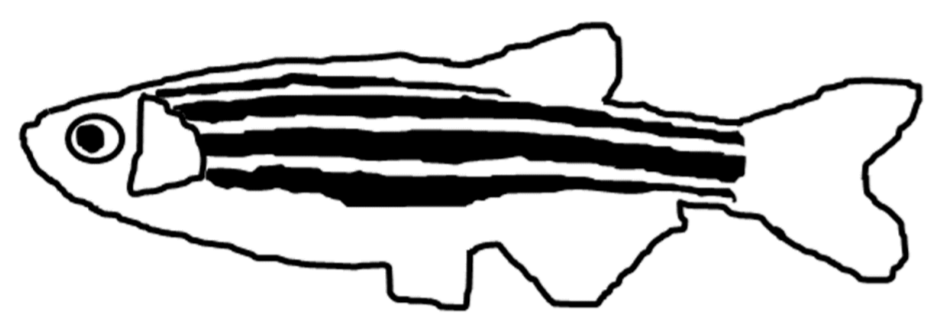
- Comorbidities in CAH patients on long-term treatment not fully understood
- *In vitro* studies on CAH mutations do not always correlate with patient phenotypes
- 21OH deficiency (21OHD) difficult to study in mice -> mutants are not viable
- Incomplete understanding of systemic consequences of 21OHD



Need for novel *in vivo* models for 21OH deficiency

Aim:

To establish a novel *in vivo* model for 21OHD using zebrafish



cyp21a2 mutants

Conclusions:

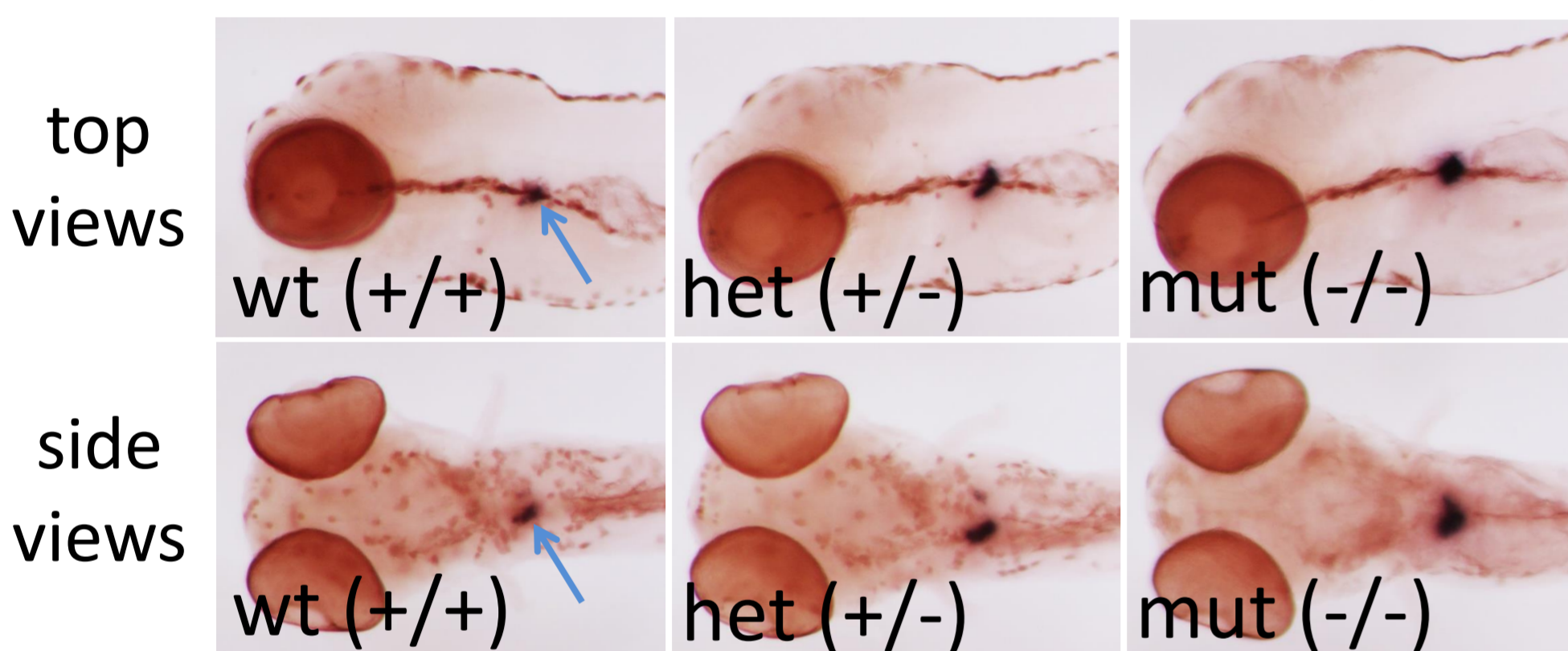
Zebrafish *cyp21a2* mutants are a promising model to study 21OHD

1. 21-hydroxylase is conserved in zebrafish
2. Zebrafish *cyp21a2* mutants have impaired GC signalling
3. Zebrafish *cyp21a2* mutants have dysregulated HPA axis

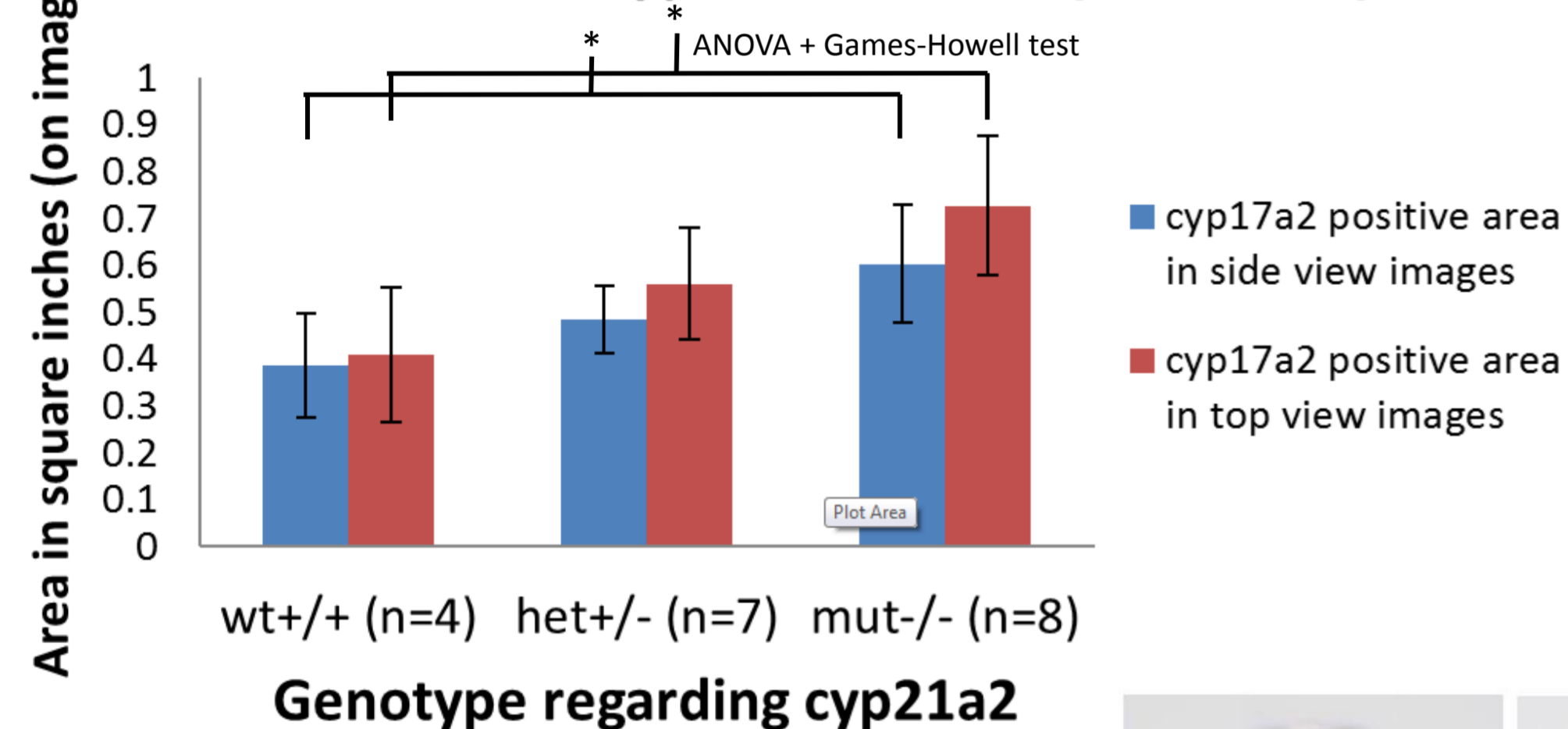
Results

5 days zebrafish *cyp21a2* mutants have enlarged interrenals (adrenals)

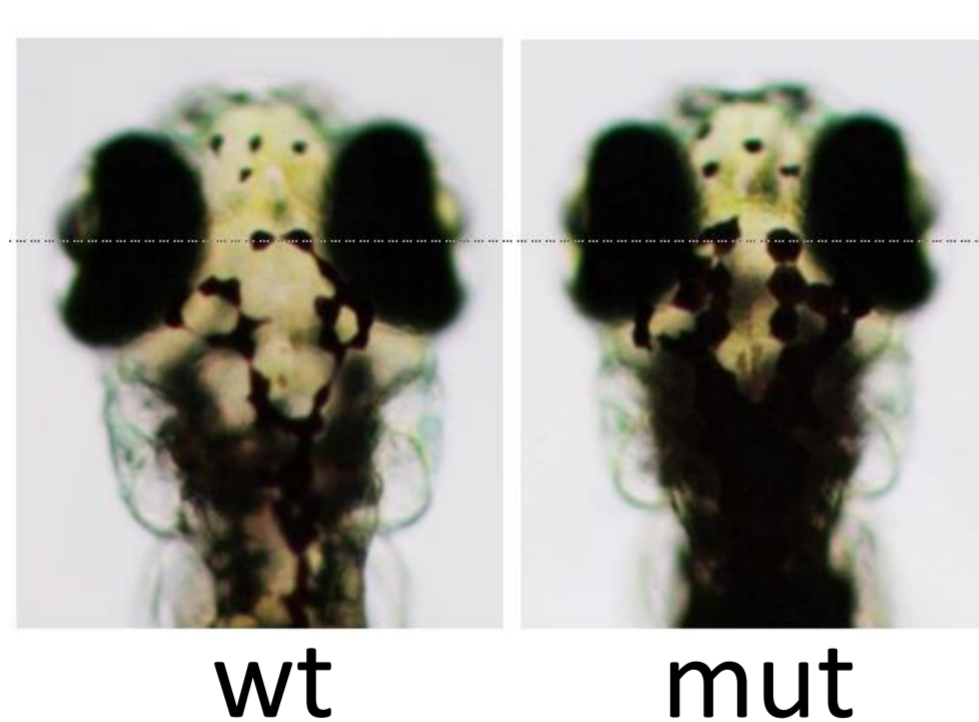
ISH against *cyp17a2* (interrenal, blue arrow) in *cyp21a2* mutants and siblings



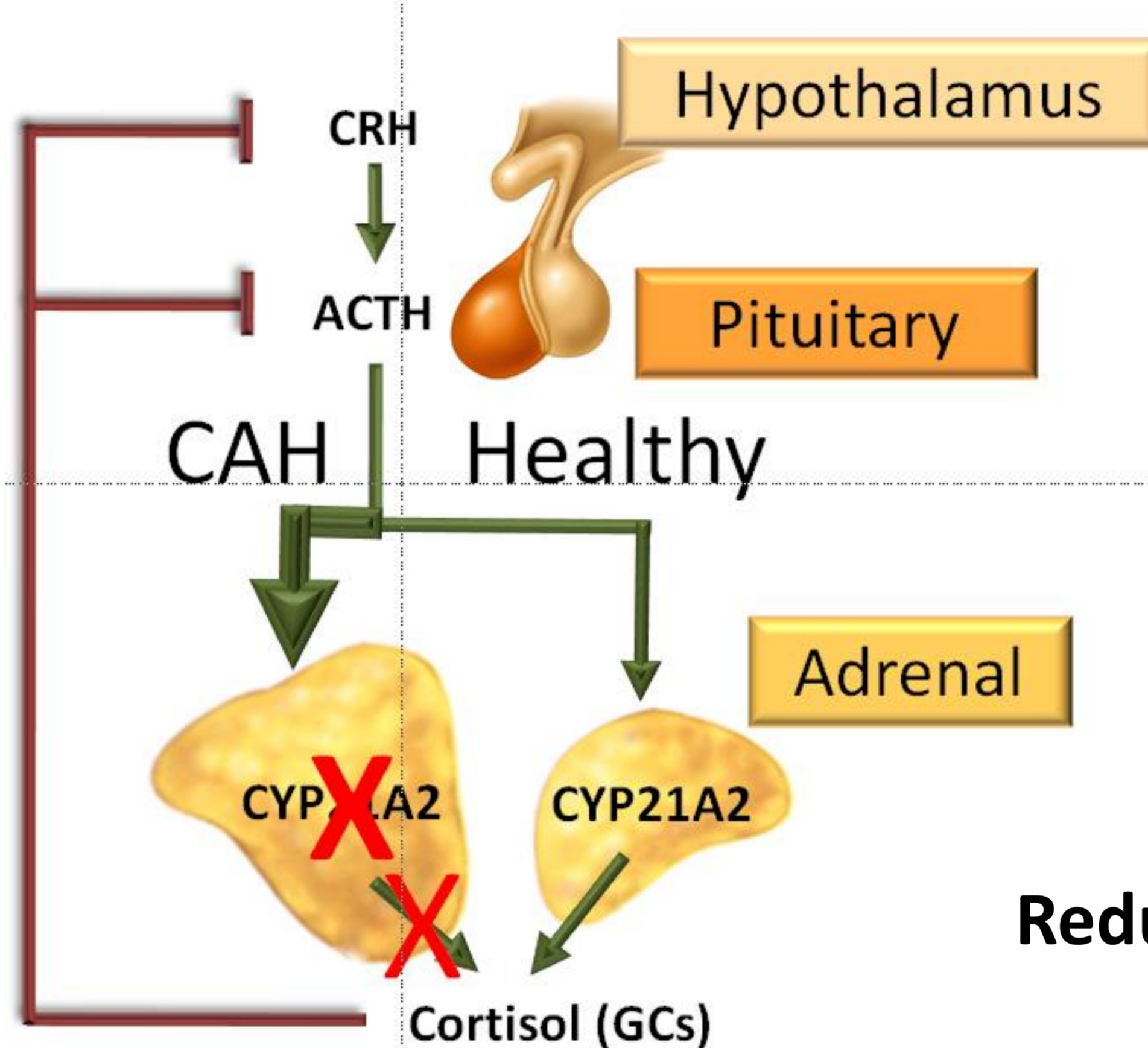
Size of interrenal gland in 5 days larvae stained for *cyp17a2* mRNA (area ± sd)



Cyp21a2 mutants display pigmentation phenotype (VBA, GC deficiency)

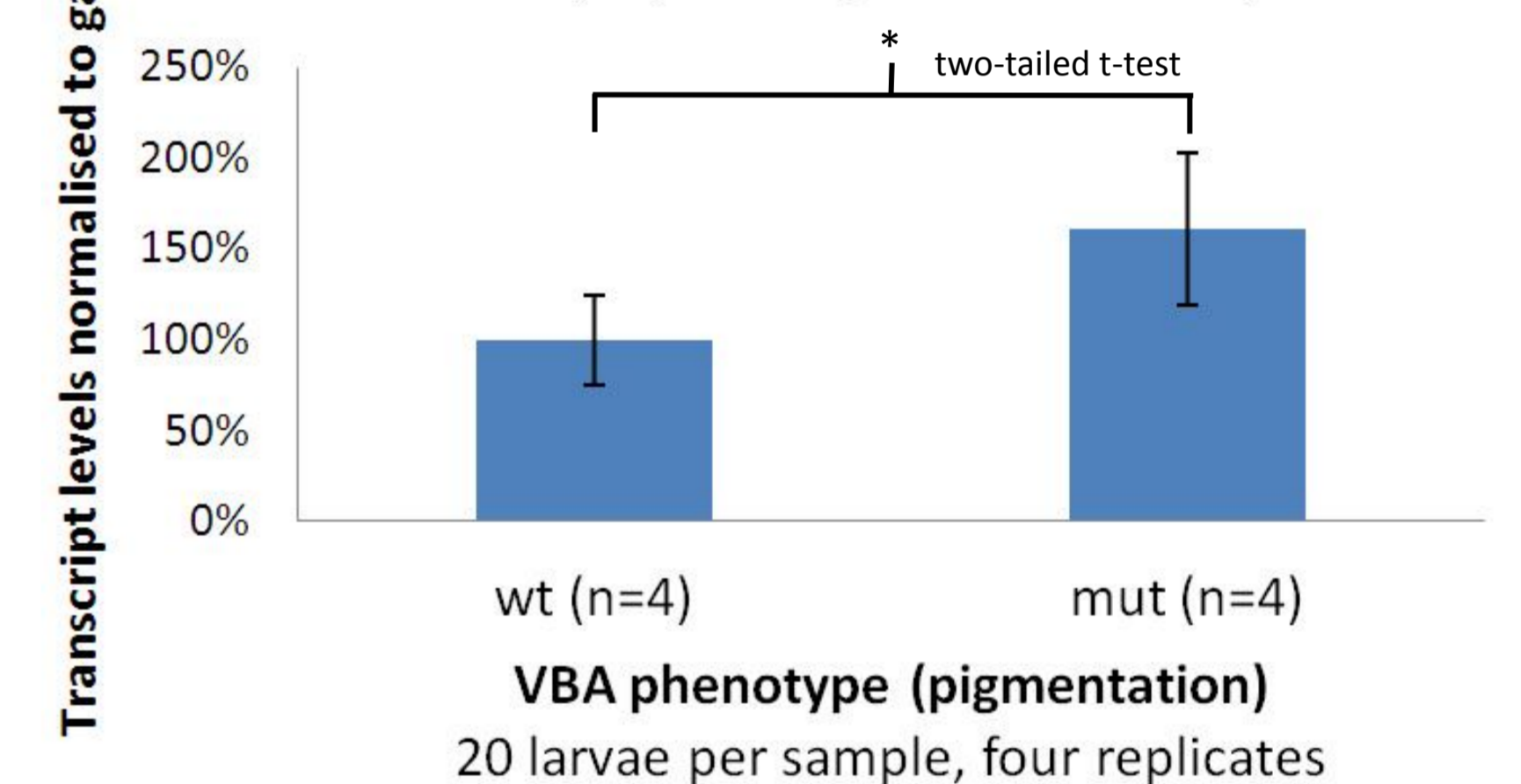


HPA axis



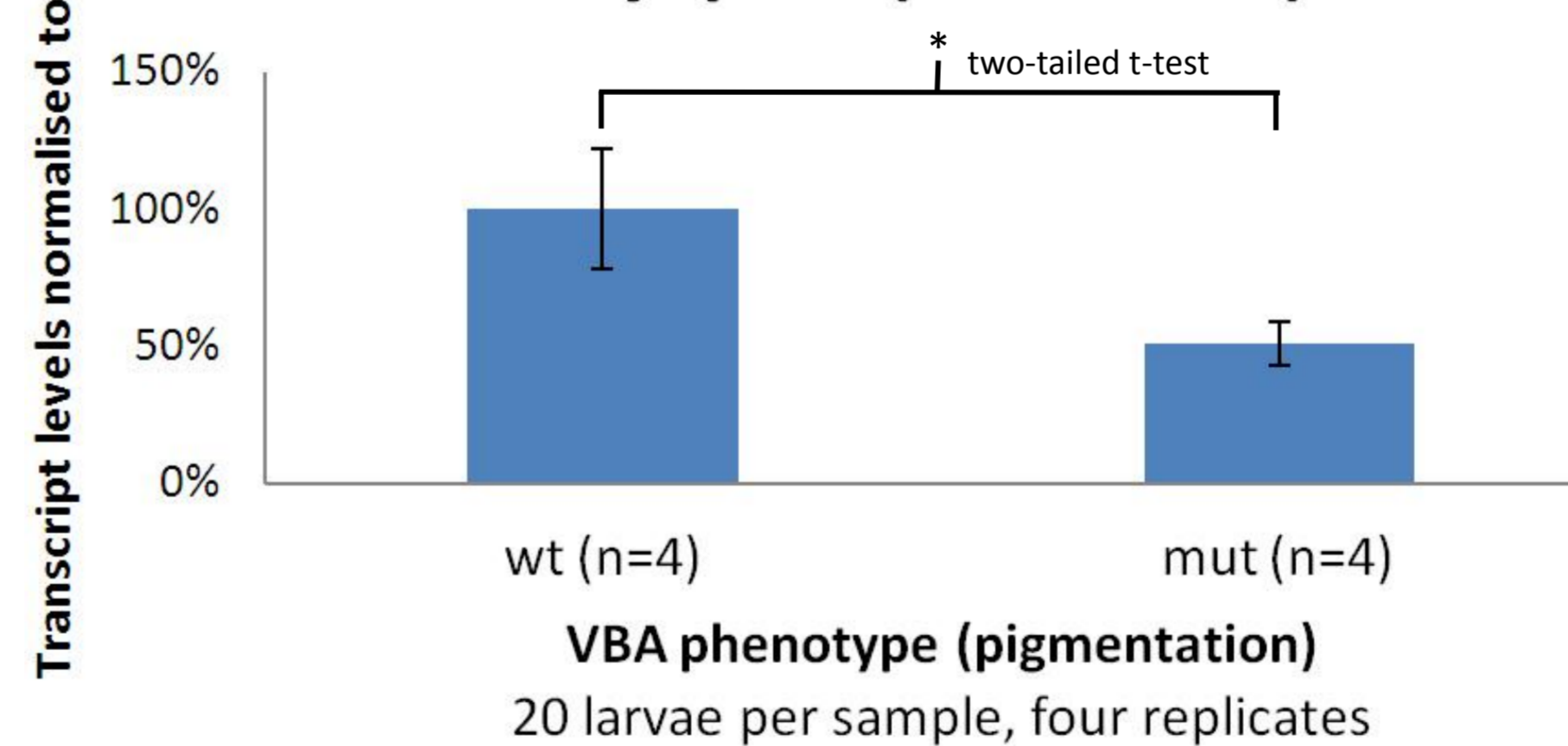
Increased expression of ACTH precursor *pomca* in *cyp21a2* mutants

pomca transcript levels in 5 days larvae by qPCR (mean ± sd)

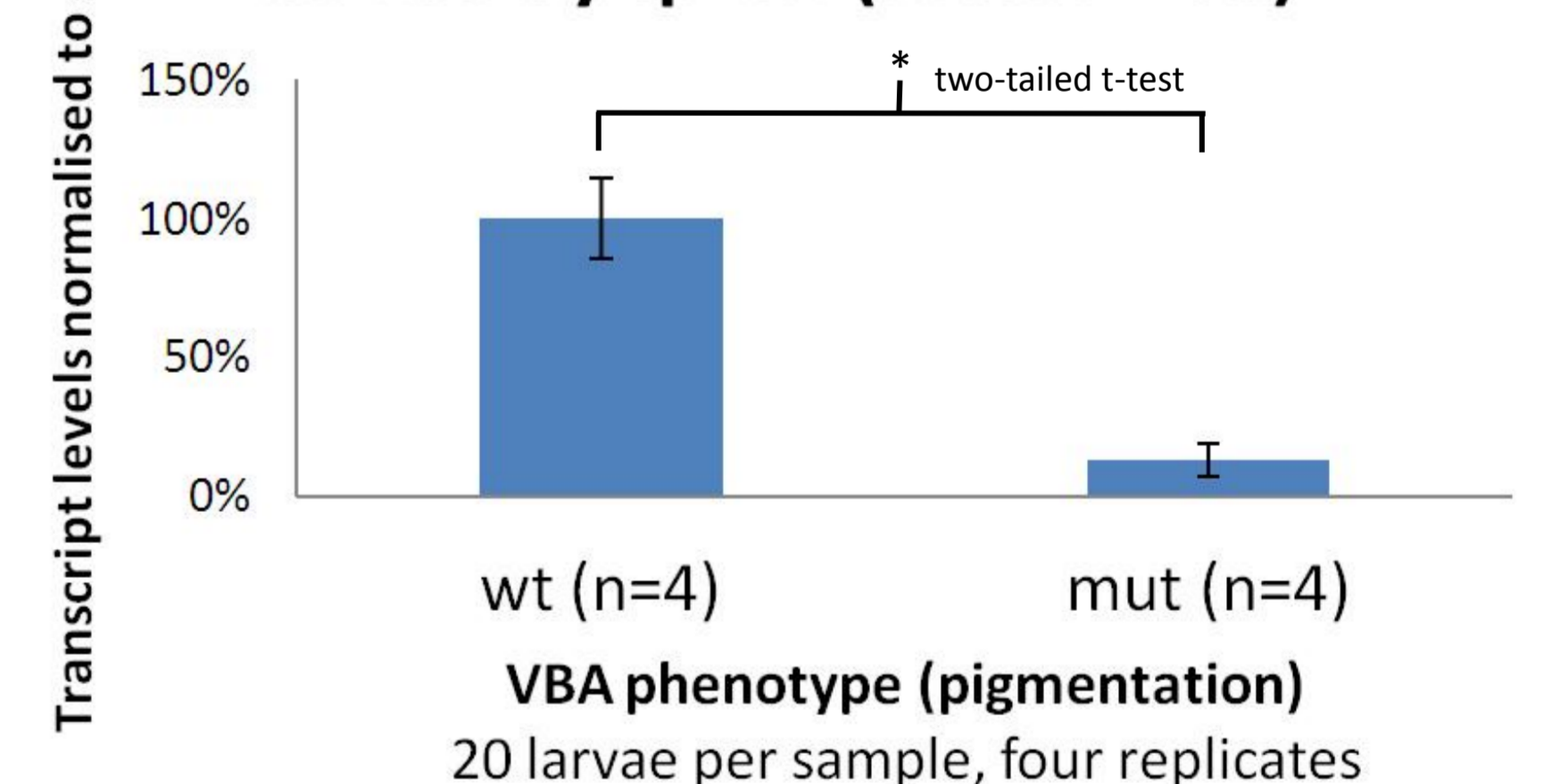


Reduced expression of GR targets *fkbp5* and *pck1* in *cyp21a2* mutants

pck1 transcript levels in 5 days larvae by qPCR (mean ± sd)

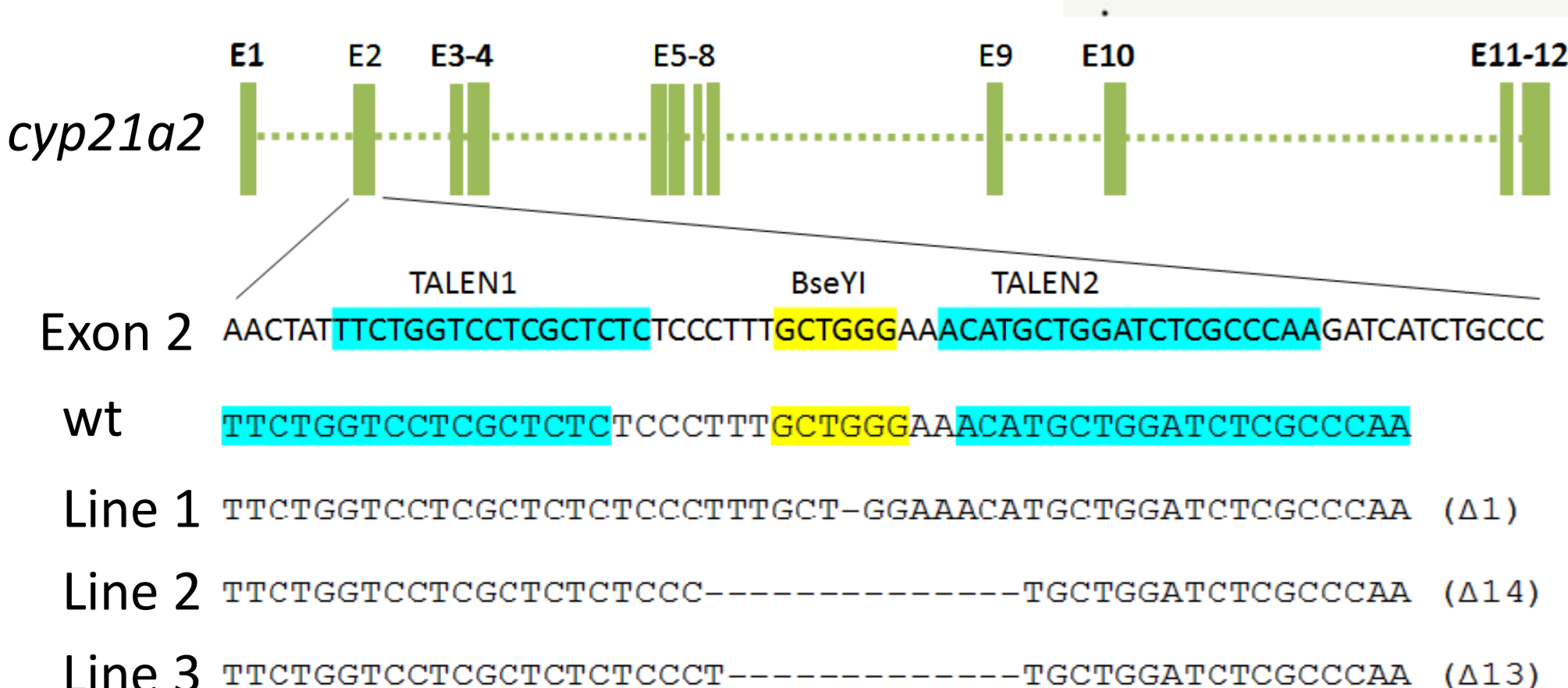
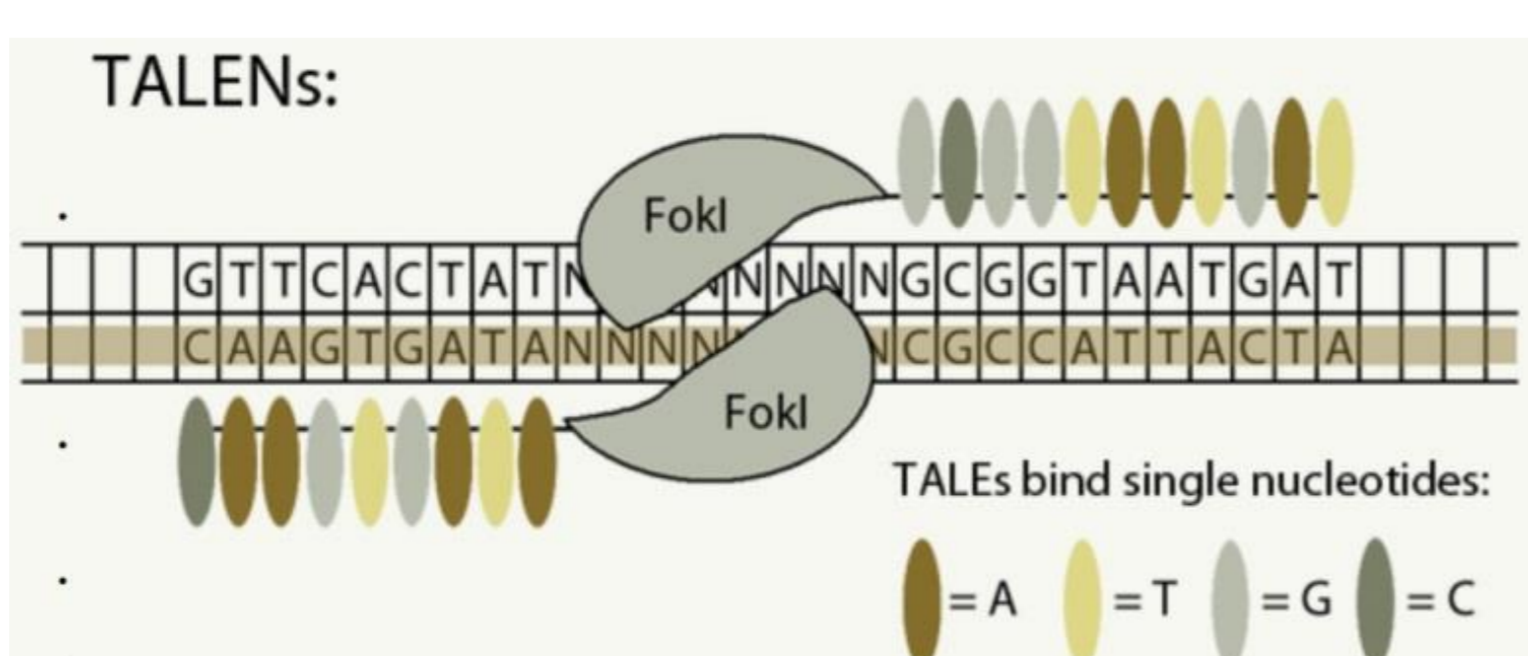


fkbp5 transcript levels in 5 days larvae by qPCR (mean ± sd)

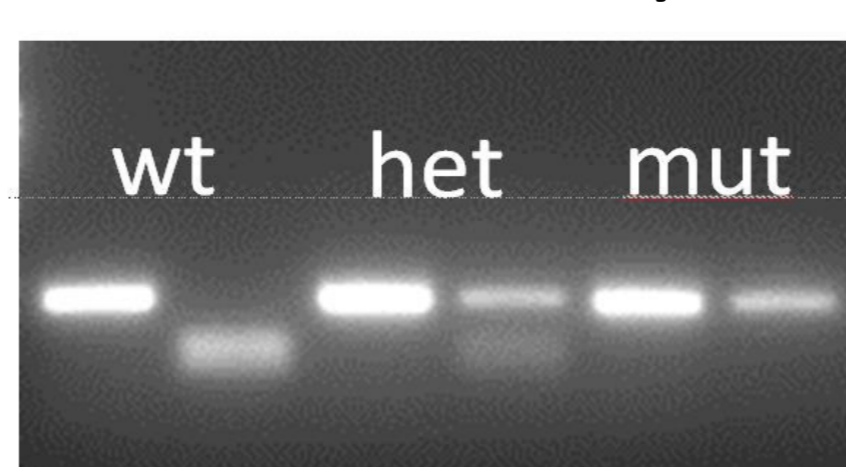


Material and Methods

Three *cyp21a2* mutant lines were generated by TALEN mediated mutagenesis



Genotyping by BseYI-assay



Acknowledgments



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