GGSB Prelim Q1 – Hang Chen

Question 1:

Transcriptional adaptation:

- Concept: mutations in one gene -> Expression modulation in **other** genes -> phenotypic rescue

- Why it is important: to maintain fitness in the presence of harmful mutations / robustness under perturbations
- How it caught attention: different phenotypes between knockouts and knockdowns

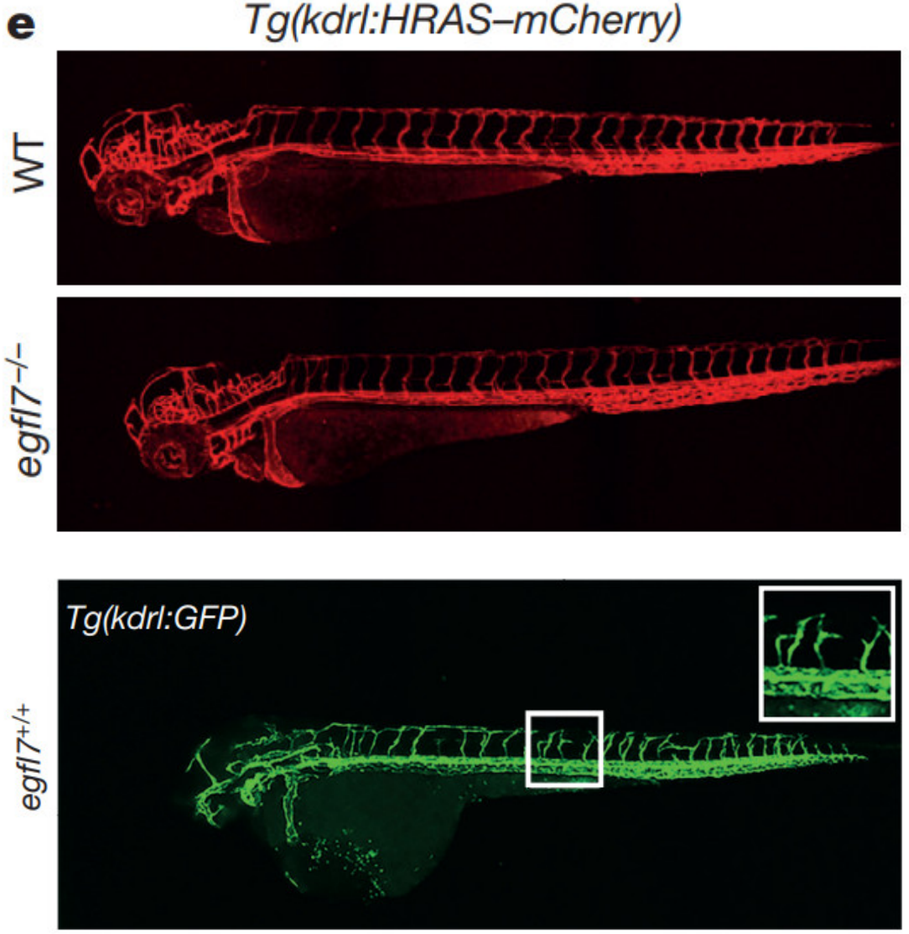
- Note: Knockouts are by early stop codon, not entire gene deletion
- Note: Morpholinos are synthetic antisense nucleotide analogs

Example of *Egfl7* and vasculogenesis

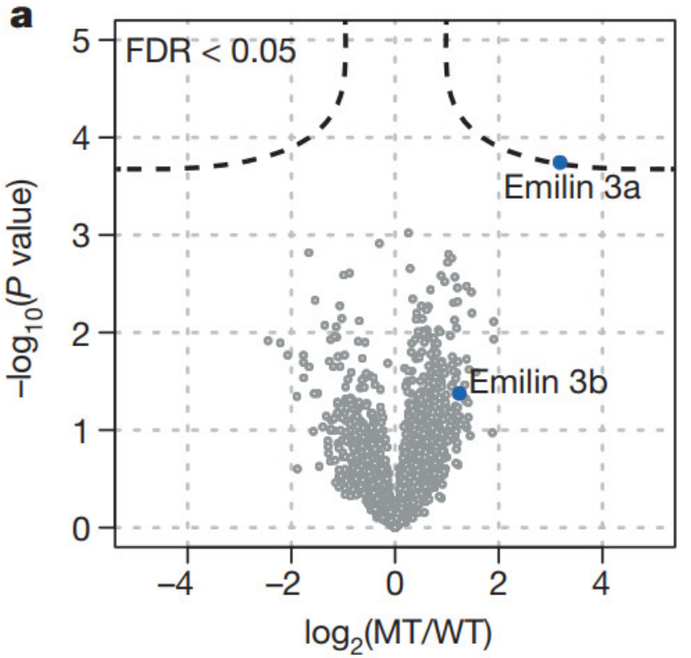
-MO

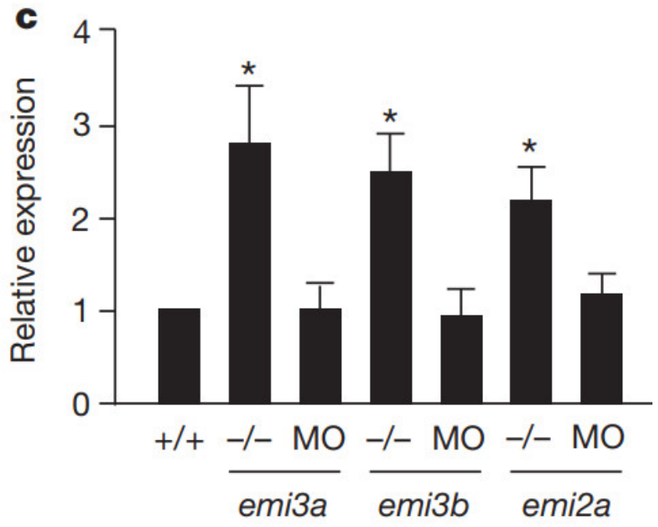
-MO

+MO



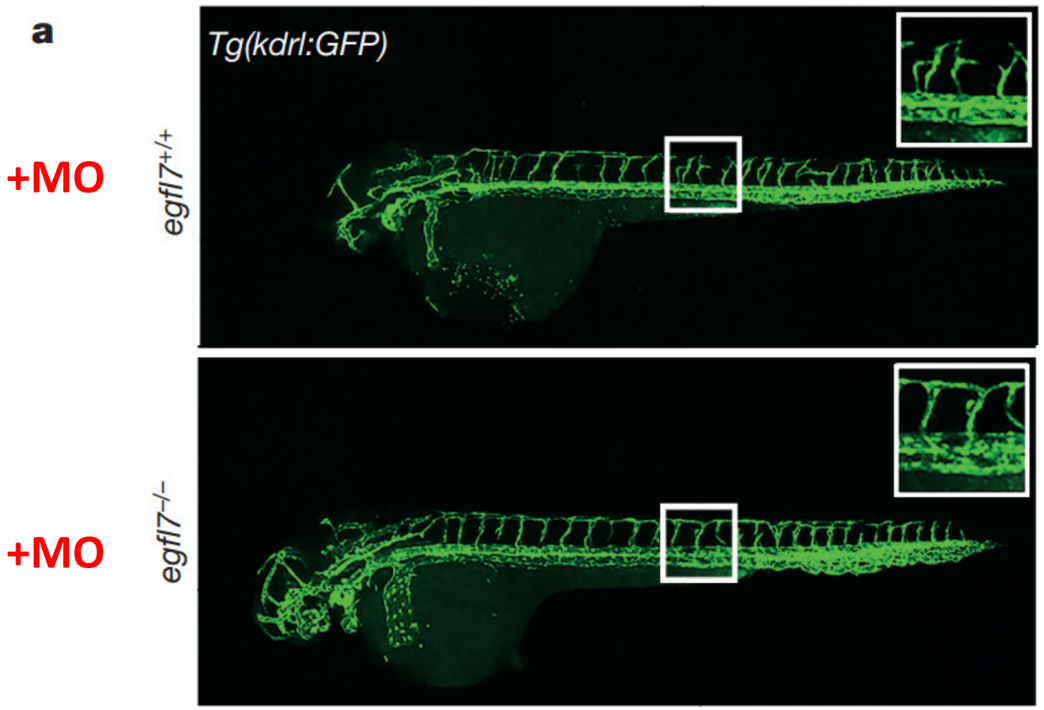
Rossi et al., 2015





(also extracellular matrix proteins)

Question 2:



Rossi et al., 2015

1	2	3
WT/WT	KO/KO	KO/KO
↓ +MO	↓	↓ **+MO**
Defective phenotype	Normal phenotype	Still normal phenotype (**not off-target or MO effects**)

(If the vasculogenesis deficiency was caused by MO, then group 1 and 3 should have the same phenotype)

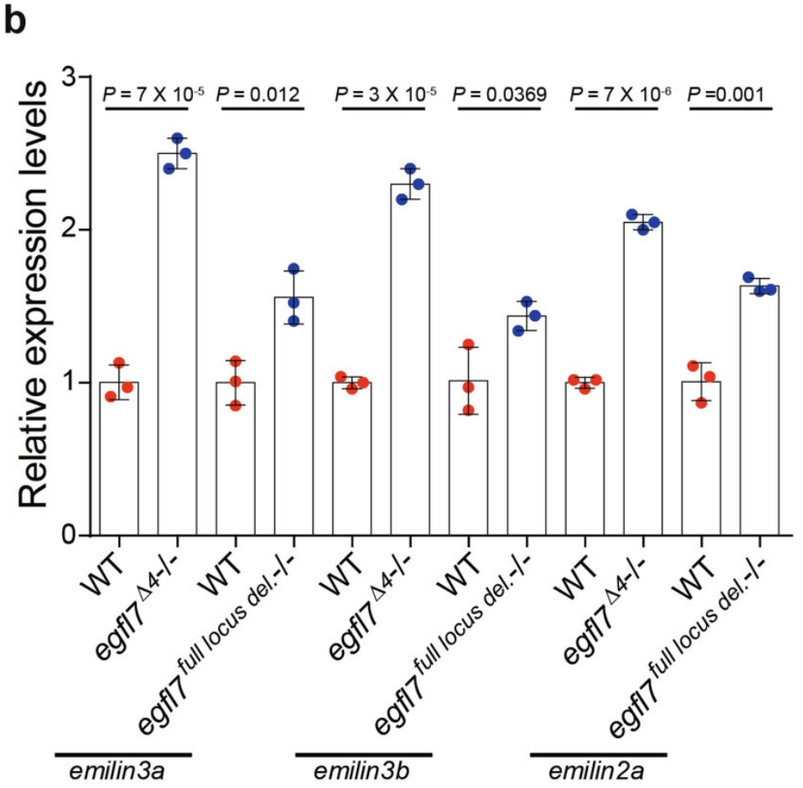
Mutation

Early stop and degradation

The products induce other gene transcription

The products inhibit other mRNA degradation

One possibility: increased transcription



EI-Brolosy et al., 2019

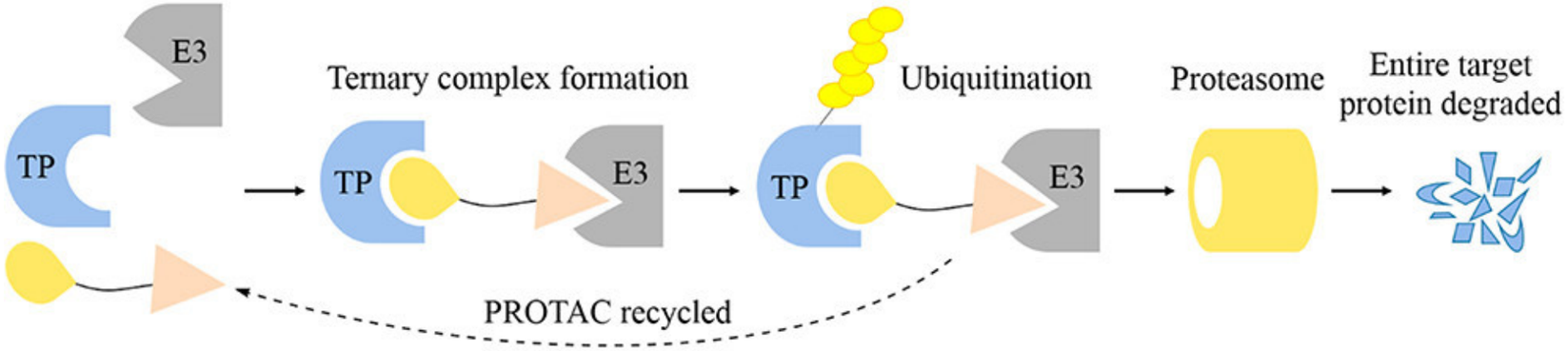
Question 3 and 4:

Another possibility: decreased degradation

Experiment design:

- *In silico* search for RBPs ->
- PROTAC for the RBPs in KO ->
- expect MO-like phenotype and no RNA increase for adapting genes

(Ctrl: PROTAC for irrelevant RBPs in KO, expect WT-like phenotype)



Gao et al., 2020

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