GGSB PRELIM QUESTION # 1

Phenotypic differences between gene knockouts (e.g., via mutations) and gene knockdowns (e.g., via RNAi or morpholinos) are often attributed to off-target effects of the RNA-interference reagents. However, genetic compensation (e.g., via transcriptional adaptation) offers an alternative explanation.

1. Explain the concept of transcriptional adaptation.

2. How can the phenomenon of transcriptional adaptation be distinguished from off-target RNAi or morpholino effects?

read again about egfl7MO injections paper

3. Propose alternative models by which transcriptional adaptation can be achieved. How would you distinguish between them?

Dosage compensation already reported

4. Propose an experiment to further test your model.

References

1. Genetic compensation: A phenomenon in search of mechanisms. El-Brolosy MA, Stainier DYR. PLoS Genet. 2017 Jul 13;13(7):e1006780. doi: 10.1371/journal.pgen.1006780. eCollection 2017 Jul. Review.PMID:28704371

2. Genetic compensation induced by deleterious mutations but not gene knockdowns. Rossi A, Kontarakis Z, Gerri C, Nolte H, Hölper S, Krüger M, Stainier DY. Nature. 2015 Aug 13;524(7564):230-3. doi: 10.1038/nature14580. Epub 2015 Jul 13. PMID:26168398

3. Genetic compensation triggered by mutant mRNA degradation. El-Brolosy MA, Kontarakis Z, Rossi A, Kuenne C, Günther S, Fukuda N, Kikhi K, Boezio GLM, Takacs CM, Lai SL, Fukuda R, Gerri C, Giraldez AJ, Stainier DYR. Nature. 2019 Apr;568(7751):193-197. doi: 10.1038/s41586-019-1064-z. Epub 2019 Apr 3. PMID:30944477