

Institute: Institute of Environmental Sciences

Topic: Interplay between the dosage compensation and the dominance phenomenon

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Background information:

Most mutations are recessive – their effects are not visible or very weak in heterozygotes, even if they lead to complete protein inactivation. However, the dominance of the wild-type alleles is not an inevitable and obvious feature of the diploid organisms as it seems to signal that the expression of the fully functional genes is twice too high. The most popular dominance theories assume that transcription activity does not change despite an inactivating mutation. However, the best strategy leading to dominance would be to detect internal disturbances caused by not fully functional alleles and adjust the expression of the corresponding genes to counteract them while keeping the basal expression level low. Numerous cases of transcriptional compensation have been described. However, the more systematic studies performed with yeast knock-outs and aneuploids did not find widespread compensatory expression changes for this species. Recent studies on mice, zebrafish, and *Caenorhabditis elegans* suggest that the wild-type allele upregulation may depend on the abnormal gene expression products. Fragments of transcripts degraded through the nonsense-mediated or non-stop decay pathways may trigger increased expression of the corresponding genes.

The main question to be addressed in the project:

Estimation of the contribution of the wild-type alleles' expression upregulation to their dominance over alleles harboring protein-truncating variants in yeast and humans.

Information on the methods/description of work:

Analysis of the population-level expression data.

Additional information (e.g. Special requirements from the student):

- MSc in biology, bioinformatics, or related fields
- ability to work with the command line
- knowledge of R or python would be advantageous.

Place/name of potential foreign collaborator:

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References (max.3):

- [1] D. Bourguet, "The evolution of dominance," *Heredity*, vol. 83, no. 1, Art. no. 1, Jul. 1999, doi: 10.1038/sj.hdy.6885600.
- [2] M. A. El-Brolosy and D. Y. R. Stainier, "Genetic compensation: A phenomenon in search of mechanisms," *PLoS Genet.*, vol. 13, no. 7, p. e1006780, Jul. 2017, doi: 10.1371/journal.pgen.1006780.
- [3] M. F. Basilicata and C. I. K. Valsecchi, "The good, the bad, and the ugly: Evolutionary and pathological aspects of gene dosage alterations," *PLOS Genet.*, vol. 17, no. 12, p. e1009906, Dec. 2021, doi: 10.1371/journal.pgen.1009906.