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EGFR Polymorphisms in *Drosophila melanogaster*

By Stacie Chue, Neha Mehta, Samantha Poon, and Heather Trazino

**Introduction**

*Genome-wide association studies (GWAS)*- observational study that examines genetic variation in different *Drosophila* individuals to identify overarching associations between genetic variants and phenotypic traits.

In normal *D. melanogaster*, juvenile hormone along with Ecdysone plays an important role in development and prevents the larva from entering metamorphosis too soon.

Ecdysone trigger every molt: larva-to-larva as well as pupa-to-adult

- *EGFR*: gene that encodes for the epidermal growth factor receptor
- Transmembrane tyrosine kinase receptor that plays a significant role in regulating growth, cell fate determination and survival, and early embryonic planning
- EGFR signaling, along with MAPK complex, has been closely related to tumor and cancer formation
- Promotes the growth and development of lymphoblasts and other blood cell types

**Materials and Methods**

- Larva collected during committed wandering 3rd instar phase
- Ethanol was used for control specimen and as solvent for methoprene
- Larva were heat-shocked at 70°C using a thermal cycler for 10 minutes and crystal cells counted
- Same genotypes were treated with 25 microliters methoprene
- Crystals cells recounted
- *Genome Wide Association Study (GWAS)* conducted to find correlations

**Hypothesis**

- *Drosophila* larvae of varying genotypes exhibit different amounts of crystal cells with and without treatment
- Difference in crystal cell count, the phenotypic trait we are observing across genotypes, can be attributed to genetic variation
- Through observing genetic variation in crystal cell formation, with and without treatment, we hypothesize that specific genes, and the polymorphisms associated with these genes, influence hormone sensitivity

**Results**

**Mean Change in Crystal Cells +266 n=14 (had at least 2 non reference alleles)**

- *Drosophila* genotypes that have the non-reference allele exhibit greater crystal cell count than *Drosophila* with the reference allele
- Average crystal cell count with reference allele: ~38
- Average crystal cell count with non-reference allele: +266
- Indicates that EGFR gene increases crystal cell hormone sensitivity

**Discussion**

- *EGFR* Polymorphisms associated with *EGFR*
  - All polymorphisms are located within fourth intron, in a 30 base-pair proximity
  - *EGFR* normal associated polymorphisms appear to be correlated with increased crystal cell hormone sensitivity
  - *H3K27AC*- acetylation modification on *H3* that is associated with greater activation of transcription; often referred to as an “active enhancer mark”
  - *H3K4ME2*- methylation modification on *H3* is closely linked to facilitating tissue specificity, as well as Hox gene activation
  - Change in chromatin structure may cause binding of varying transcription factors to activate transcription of *EGFR* gene
  - May lead to different amino acid and protein formation

**Further Research**

- Broaden sample size to include more of the DGRP genotypes available for *Drosophila*
- Preemptively treat larvae for infection, which may have increased crystal cell count number
- Overexpress or knock-out *EGFR* gene to drive or prevent expression of gene
- Greater *EGFR* signaling will increase the number of crystal cells after methoprene treatment
- Measure *EGFR* RNA levels in untreated and methoprene treated larvae
- RNA will be higher in larvae that have undergone methoprene treatment

**Bibliography**

3. *Genome Browser*: image of intron, shows EGFR as a whole and the genes that are nearby.
4. Fly Treated with Ethanol (31908)
5. Fly Treated with Methoprene (31908)
6. *Materials and Methods*
7. *Results*
8. *Discussion*
9. *Images*