Genetics Notes Chapter 13: The Genetic Control of Development

13.1-The Genetic Approach to Development

- Early on the study of the development of embryos was done by transplantation of a part of tissue from one embryo to another embryo and then observing the results.
- Transplanted regions that caused morphological changes in the accepting embryo were called **organizers** and the molecules that induced these changes (although they were unknown) were deemed **morphogens**.
- Study of embryonic development stalled until more recently, where uses of drosophila, zebrafish, lab mice, and nematode worms have proven advantageous.

13.2-Genetics of Drosophila Development

- In this chapter we are concerned with **tool-kit genes**, those genes that determine specific cell types, tissues, organ building, and overall body plan.
- This subset of genes make up only a small number of the total genome.
- These genes were studied in drosophila by studying the developmental monstrosities that resulted from these gene mutations. Mutation either arose naturally in laboratory populations or were induced through mutagens like radioactivity.
- Some of the first toolkit genes studied were those relating to appendages and segmentation.
- A **homeotic gene** is one that controls the development of a structure in a plant or animal
- A homeotic mutation is often controlled by the mutation of one gene.
- The mutated development is often a likeness of another structure. For example a leg instead of an antennae. This is because most appendages are made up of essentially the same building blocks-**serially reiterated structures.**
- Homeotic mutations cause structural changes within these serially reiterated structure families.
- Mutations can cause complete loss of function (no development) or gain of function (they develop into a completely new structure).
- These genes now called Hox genes are traced back to 8 loci in drosophila.
- In the homozygous dominant they are lethal, but sublethal normally in the heterozygous.
- Hox genes are found in 2 different clusters on the drosophilias third chromosome, interestingly, they are organized from head to tail aligned like the body plan of the fly.
- The determination of Hox genes spatial control was determined through two technologies:
    - In-situ hybridization of mRNA transcripts
    - Immunolocalization of protein expression
- All hox genes have a highly conserved DNA sequence called a **homeobox** which encodes for a **homeoprotein domain.**
- It was discovered that this homeobox encodes a transcription binding factor which regulates the transcription of other genes.
- It was discovered that the homeobox is widely conserved in organisms throughout the animal kingdom and that all animals have hox genes that are similarly clustered and similarly spatially expressed as those in the flies.

13.3-Defining the Entire Toolkit

- It was realized that mutation of these hox genes had unknown effects on the embryo, including lethal effects.
- Genes with gene products provided from the female to the egg are **maternal-effect genes** and depend only on the maternal genotype.
- Some genes are only active after fertilization in the zygote.
- There are 5 classes of genes that determine the development of the fly
  - First class is all maternal-effect genes that control the anteposterior axis. Without these functioning genes the anterior region of the embryo is missing.
  - Zygotically active gap genes have mutations that lead to large gaps in segmentation.
  - Mutations in zygotically active pair rule genes are missing a segment or more of one of the paired segments. Can be even skipped or odd skipped.
  - Zygotically active segment-polarity genes have mutations in the patterning of segments.
  - The final class are the hox genes which alter the appearance of segments.
- It is examined that all tool-kit genes are expressed **spatially and over time** and most produce gene products that work as transcription factors or inducers in biochemical pathways.

13.4-Spatial Regulation of Gene Expression in Development

- To define a position in an embryo genes must contain positional information specifying its location on the antereoposterior axis (similar to longitude), location across the dorsal ventral axis (latitude), and position in the germ layers (altitude or depth).
- Early on the **Bicoid** protein is translated from mRNA and localized to one anterior pole in the drosophilia embryo.
- Bicoid slowly diffuses through the embryo forming a **protein gradient**.
- This concentrational gradient provides positional information about locations along the anteposterior axis this helps govern which genes are expressed as gene expression is linked to the levels of Bicoid proteins.
- This is true for gap genes that are activated through the cooperative binding of bicoid proteins directly to promoters.
- Each stripe in the pair rule genes are controlled by cis-regulatory enhancers and promoter, each have their own unique combination of proteins including activators and repressors that turn each gene on.
- The combined and sequential activity of maternal effect, gap, pair-rule, and segment-polarity proteins establish the basic segmented body plan of the embryo and larva.
- GO THROUGH EXPRESSION OF HOX PROTEINS

13.5 Posttranscriptional Regulation of Gene Expression in Development

- In drosophila many genes are identified that govern sex determination.
- The doublesex gene is necessary to the development of sexual identity. Mutants develop into intermediate intersex individuals. Although this is the same locus different gene products are produced in different sexes.
- The Tra protein splices the dsx protein into the dsxM RNA and the dsxF RNA.
- In an early nematode embryo one cell divides into 4 cells called **blastomeres.**
- Each blastomere will have its own lineage.
- Temporal expression is just as important as spatial expression.

- The lin 4 controls the transition from the first larval stage to the second.
- The let 7 stage encodes transition from late larval to adulthood.

13.6-The Many Roles of Toolkit Genes

- Toolkit genes oftentimes play multiple roles in different areas of embryonic development.
- One gene the Hedgehog gene in drosophilia is homologous to genes found in three different vertebrates responsible for vertebrate development (including in humans).
- The diverse roles that these genes can play also occur whithin the organism, (the hedgehog genes play a role in the development of limbs, feather buds, and nueral connections in chickens, for example) the differences are a result in the different signal transduction pathways that these genes participate in resulting from cooperative effects of other toolkit genes working at the same time.

13.7-Development and Diseases

- In people with certain types of polydactyly mutations of a Cis regulatory sequence of the sonic hedgehog (shh) gene resulted in extra digits often inherited in the dominant fashion.
- Mutations in the coding sequence of the shh gene or its signal transduction pathway cause *holoprosencephaly* which can lead to brain and head development issues in the heterozygous and can be lethal in the homozygous.
- Human cancers have been linked to mutations in toolkit and signal transduction pathway genes.