

## LECTURE 31

### Hox genes and birth of "Evo-Devo" (Drosophila body plan genes, part 3)

From CHAPTER 21, p. 1190-1196, 1199.

Figures covered: Fig. 21-41 to 21-46, 21-50

#### Quick overview of last lecture:

- **SEGMENTATION GENES: a hierarchy of genes in 3 classes** that act sequentially to refine positional information set up by egg polarity genes; their products define increasingly finer territories, define differences between body segments. The 3 classes:
  - **Gap genes:** encode transcriptional repressors (eg. Krüppel); expressed in multisegmt. domains of early syncytial embryo; expr'n activ'd by specific concs. of egg pol. TFs & refined by cross-repress'n via other gap TFs)
  - **Pair-rule genes:** encode TFs (activators & repressors, e.g. Eve), express'n regulated by complex enhancers that bind combinations of egg pol. & gap TFs at diff't AP-axial levels; expressed in 7 stripes (alternate segm'ts)
  - **Segment polarity genes:** encode TFs (e.g., Engrailed) and components of Wingless & Hedgehog signaling pathways; express'n regulated by pair-rule, gap, and egg pol. TFs; expressed in 14 narrow stripes (sub-region of every segment) at cellular blastoderm stage; **parasegment boundaries** defined by Wg-expressing cell row on 1 side, Hh- and En-expressing row on other
- Segmentation gene products, w/ exception of Engrailed, are only transiently expressed. Their positional information is preserved by products of **Homeotic selector genes** (today's lecture).

#### HOMEOTIC SELECTOR GENES (aka. homeotic genes, HOM-C genes) and patterning of AP-axis

- Homeotic mutations cause body part transformations (eg., antenna to leg in *Antp* mutants; haltere to wing in *Ultrabithorax* mutants)
- Homeotic selector genes:
  - activated after segment'n genes establish segment boundaries
  - region-specifically activated by egg polarity & segm'n gene products (provide permanent record of positional info. set up by these)
  - select body segment specific programs (e.g. ectopic *Antp* in head transforms antenna to leg, **Fig. 21-41**)
- Classical genetic studies: Ed Lewis & other geneticists spent many years mapping Dros. homeotic mutations (eg., *Bithorax*, **Fig. 21-42**) to two multigenic regions: *Antennapedia* & *bithorax* complexes (**Fig. 21-43**)
- **Fig. 21-43:** HOM-C genes lie in 2 separated complexes in *Drosophila* genome (by splitting of single ancestral complex present in more primitive invertebrates; single, larger complex intact in other insects):
  - ***Antennapedia* complex:** 5 genes that specify head & thoracic segment identities
  - ***Bithorax* complex:** 3 genes that specify abdominal segment identities
- **Fig. 21-45:** Relative gene order in HOM-complex correlates with relative expression domains along AP-axis

- Protein products of HOM-C genes contain **homeodomain (HD) DNA binding domain**: 60 aa domain also conserved in other devel. regulators, including Bicoid, Eve, & Engrailed, & many others not in complexes
- **Antp loss-of-function mutants** (no Antp in T2): 2<sup>nd</sup> legs to antennae (Antp drives leg development AND REPRESSES antennal fate, default state in absence of Antp!)
- **Posterior Predominance**: HOM-C genes are repressed by products of genes “posterior” to them in HOM-C (Example: Ubx represses *Antp*; haltere to wing transf'n in Ubx mutants due to posterior expansion of Antp expression)
- **Conclusion**: HOM-C genes specify unique features of body segm'ts; act like switches, drive one body region program while simultaneously repressing more anterior program
- After decay of segmentation gene products, HOM-C regulated by:
  - **Trithorax group genes**: maintain expression of activated HOM-C genes
  - **Polycomb group genes**: maintain repression of inactive HOM-C genes (**Fig. 21-44**: loss-of-function mutation of Polycomb group gene *esc* causes ectopic activation of HOM-C genes, extreme posterior predominance evident)
    - **Polycomb protein** binds multiple sites in *Drosophila* chromosomes, including ANT-C and BX-C, as part of multi-protein repression complex
  - **auto-activation** (in some cases)
- **Larval imaginal discs (Fig. 21-50)**: precursors get “Hox-code” specific for their origin in embryo ectoderm; grafting expt's show their fates are determined & stable for many cell generations; “remember” their origins unless Hox codes abnormal – causing transf'n
- AP-axis specification in vertebrates is regulated by HOM-C homologs called Hox genes
- **Fig. 21-45**: Several duplications of entire HOM-C during evolution, 4 Hox complexes in mammals; relative order still correlates w/ relative expression order along AP-axis.
- Identif'n & studies of HOM-C/Hox genes in multiple species led to birth of new discipline: **Evolutionary Developmental Biology (Evo-Devo)**: genetic changes altering embryonic development provide raw-material for evol'n. HOM-C genes were 1st/best paradigm for asking how morphological evolution might come about via changes in embryonic gene expression programs: melding of developmental biology, molecular genetic, genomic/bioinformatics approaches and evolutionary theory