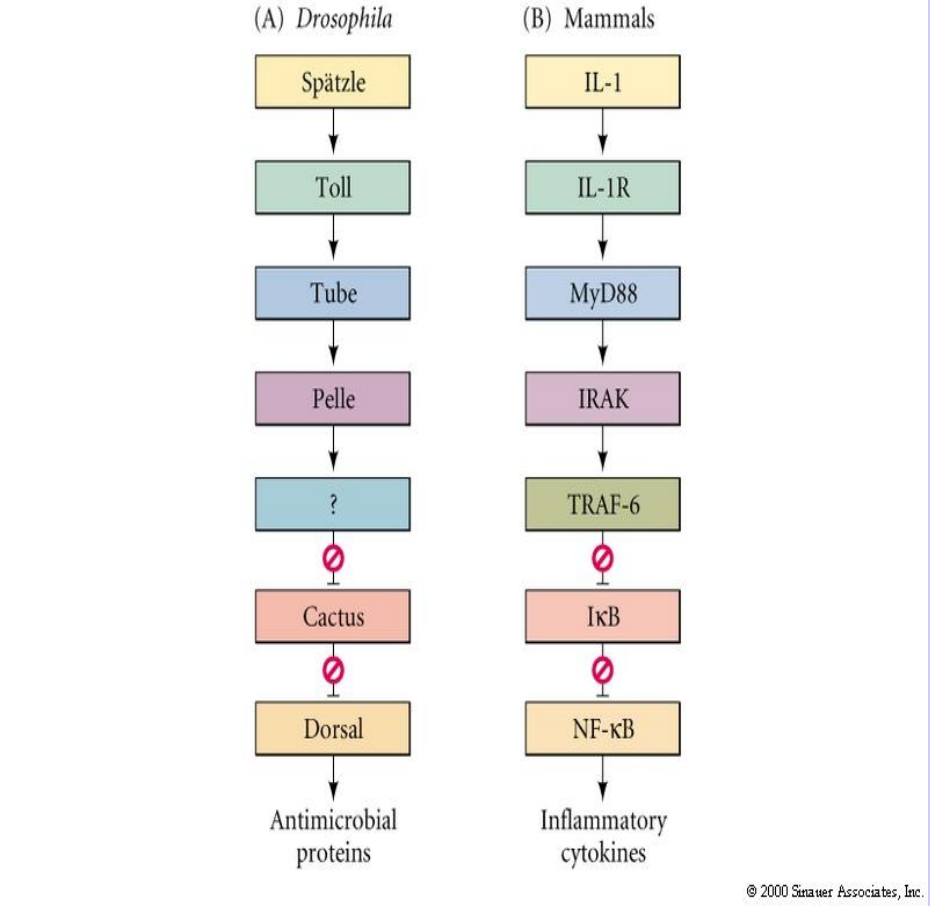
Pathways are Units

Homologous Pathways

- Genes can be homologous
- Whole signaling pathways can also be homologous
  - provide a toolkit
  - but what they do depends on what they are hooked up to
  - evolution “uses” these conserved pathways but selection of this larger unit can also be for different function

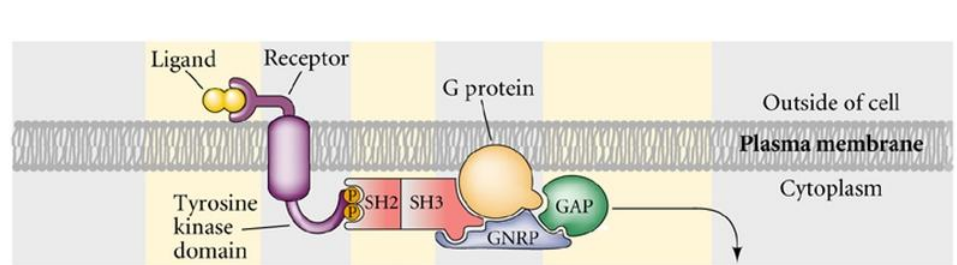
Example 1

- Dorsal - cactus
  - flies use to specify DV polarity and antimicrobial
- NF-κB - IκB
  - activation of inflammatory response
- External signal to transcription factor



Example II

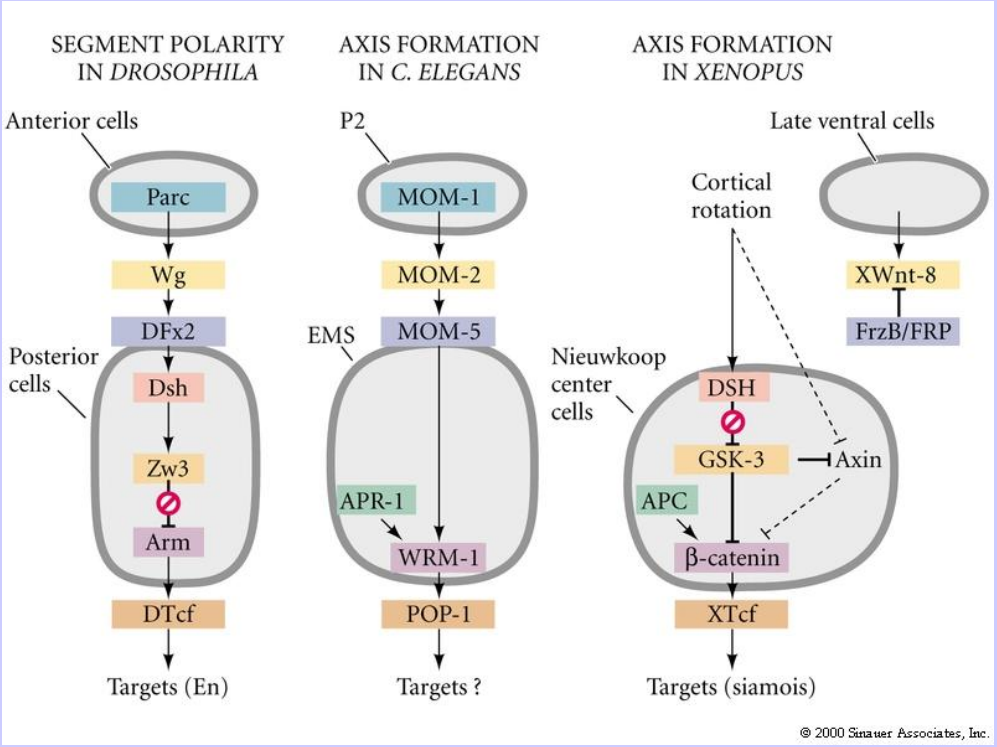
- RTK pathway
  - Boss binds to sevenless in fly photoreceptors
  - Lin-3 binds to Let-23 in nematode vulva
  - EGF binds to EGF-R in mammalian skin



Organism and tissue	Ligand	Recep-tor tyrosine kinase	SH2-SH3 protein	G-protein	GTPase activator and GDP/GTP exchange proteins	Effect
C. elegans vulva	LIN-3 protein	LET-23 protein	SEM-5	LET-60 protein	gap-1	Vulval cell differentiation and division
Mammalian skin	EGF	EGF receptor	GRB2	RAS protein	GAP/GNRP	Epidermal cell division
Drosophila eye	Bride of sevenless	Seven-less	Drk	Ras 1	*Gap1*/son of sevenless	Differentiation of photoreceptor seven in each ommatidium

Example III

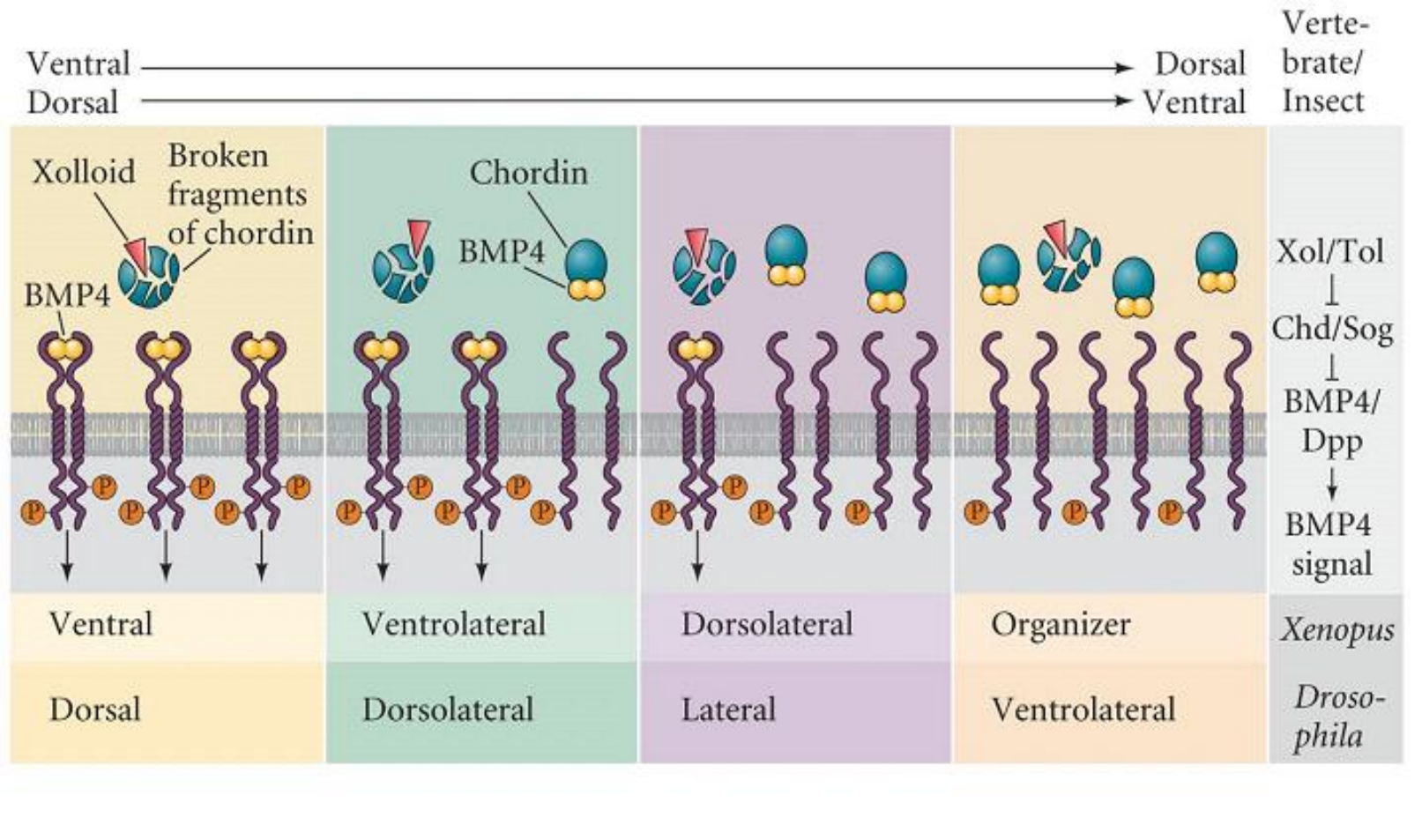
- Wnt
  - flies segment polarity
  - worm axis formation
  - frog axis formation
- Pathways are similar (colors indicate homologs) but not identical



Example IV. Graded Extracellular Protein Interactions in Neural Ectoderm

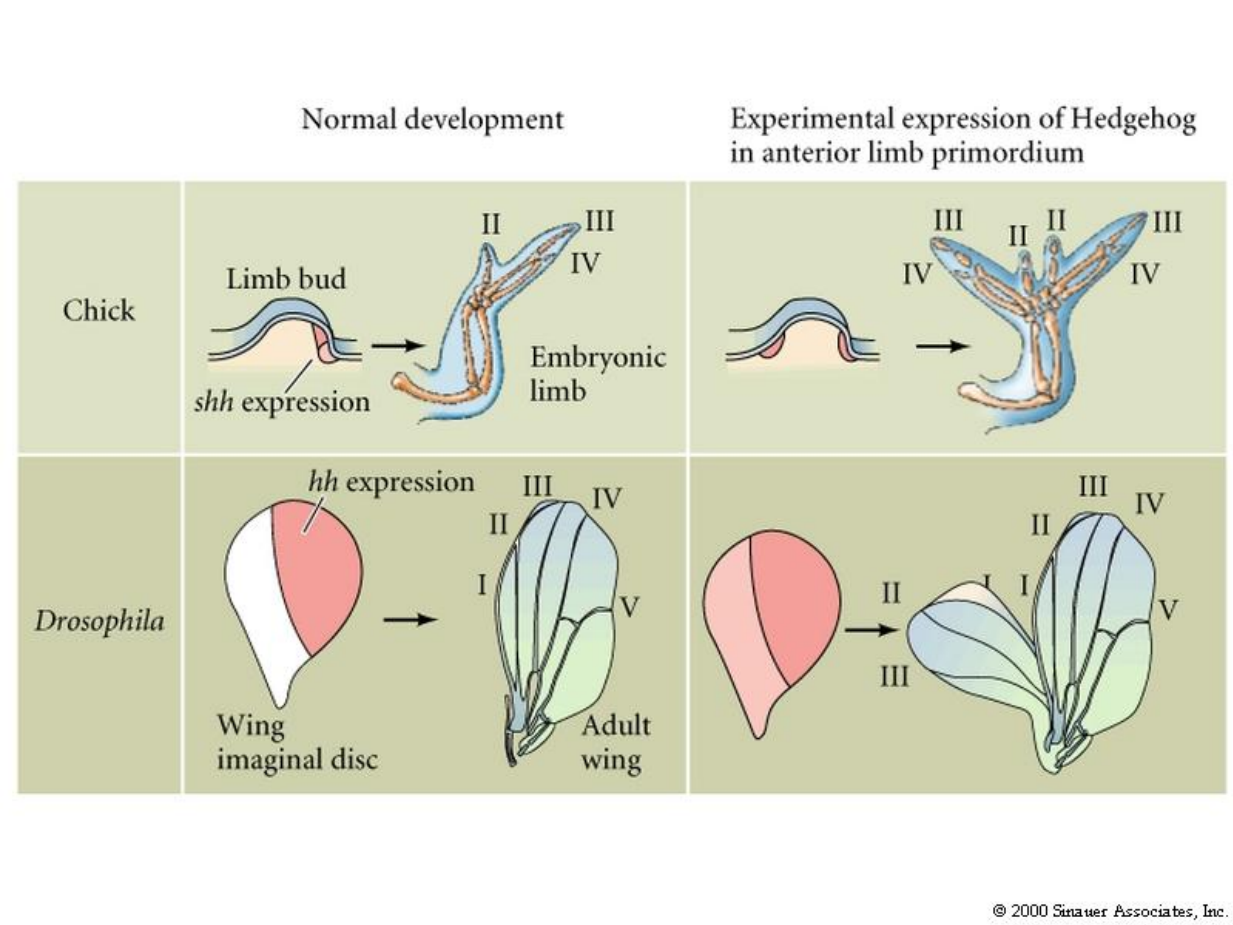
- Chordin/BMP4 (frogs)
- Short Gastrulation/Decapentaplegic (flies)
- Chordin (Sog) prevents BMP (Dpp) from entering its territory, allowing neural ectoderm to form
- Xolloid (Tolloid) degrades Chordin (Sog)

Neural Ectoderm Specification



Xolloid forms gradient of chordin that opposes BMP

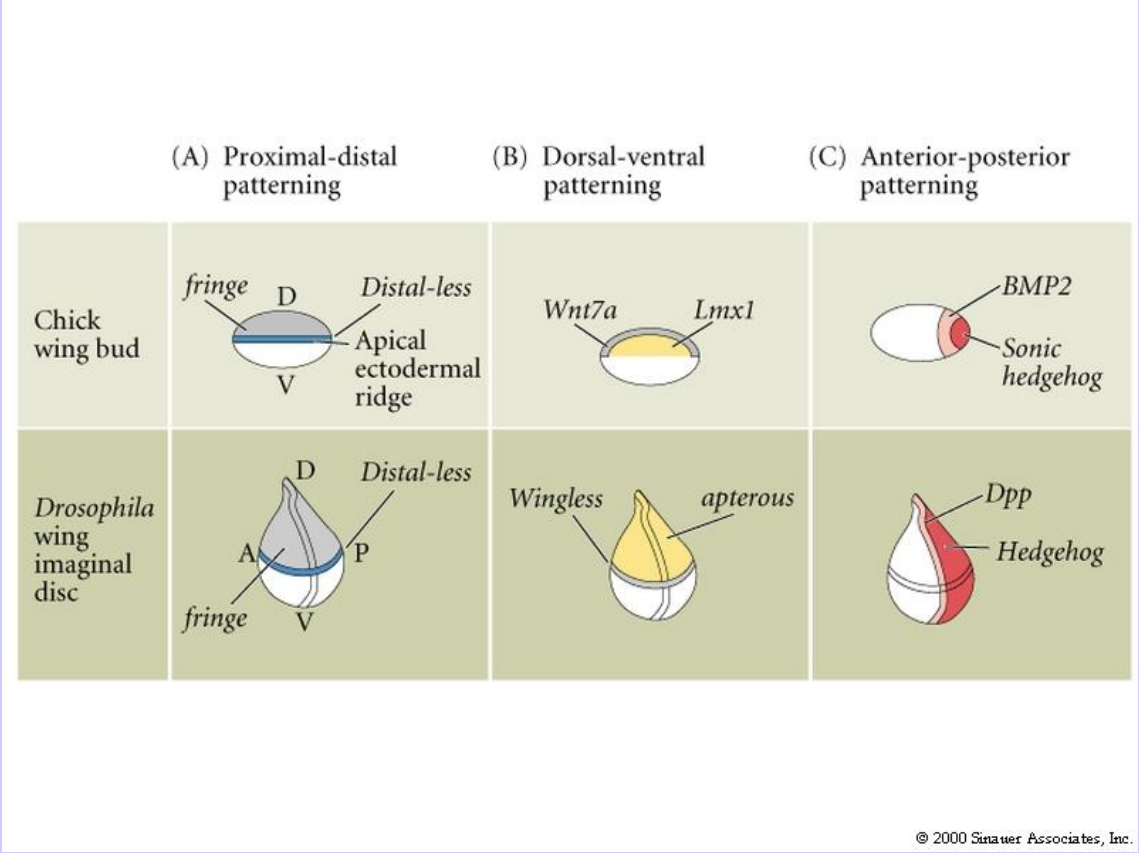
A-P Axis Homologies



Ectopic *Shh* mirror duplicates digits; Ectopic *Hh* mirror duplicates wing structures

Limb

- Other axes also use conserved molecules
- Upstream or downstream controlled with different molecules in insects and vertebrates



Modularity and Change

Why is Modularity Important?

- Development is complex and delicate with many contingencies
- How can organisms evolve without destroying themselves?
- Modularity
  - independent and hierarchical units which can be altered without changing the rest
- Examples
  - parasegments, imaginal discs, organ rudiments, fields, signaling pathways, lineages
- Control regions (enhancers) also modular
  - Coordination of sets of genes

What Processes Lead to Changes?

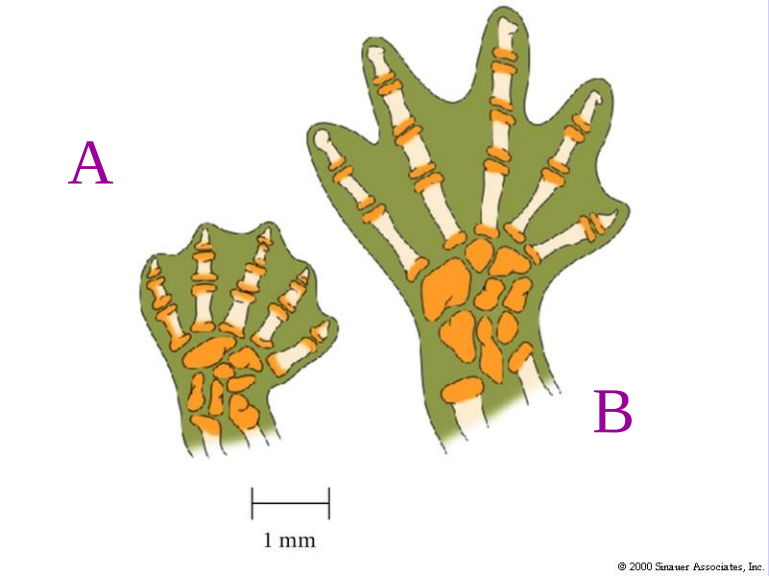
- A. Dissociation
  - independence of parts
    - heterochrony: shift in relative timing
    - allometry: differential growth of parts
- B. Duplication and Divergence
  - duplication makes for redundancy
    - frees one to evolve with little constraint
- C. Co-option
  - a given protein or structure can be used in a different and new way

A. Dissociation

- Modules can change in time or in space
  - *Heterochrony* (shift in relative timing of two processes)
    - sea urchins that skip larval stage by suppressing larval genes (premature *wnt5* expression does not lead to larva)
    - salamanders that change in production or response to larval hormones may partially arrest in a stage
      - can skip larval stage or stay in it fully or partially
      - *heterometry* is change in amount of protein or structure

Dissociation: Heterochrony in Salamander Limb

- Juvenile pattern in adult foot of species A allows tree climbing
- Species B less webbed adult foot but its juvenile like A adult



Dissociation: Allometry

- Allometry (space)
- Differential growth of modules can change body plan
  - e.g. from altering amounts or sensitivity to growth factors
  - Result: differential growth of whale head bones (modules) from embryo to adult produces big upper jaw with nose on tip

Allometry in Mammals