

## HD15 – LIMB

**RECOMMENDED READING:** Larsen's Human Embryology, 3rd Edition pages 315-328, 335-342  
Gilbert, Developmental Biology 8<sup>th</sup> Ed., Chapter 16, pp. 505-527

### GLOSSARY:

**apical ectodermal ridge (AER):** most distal rim of epithelium of the limb bud. It is a major signaling center in regulating patterning of the limb. Source of fibroblast growth factor (FGF) signal to underlying limb mesenchyme. Required for proper proximodistal (PD) outgrowth of the limb

**Induction:** the change in a cell or tissue's fate due to a signal from another tissue or cell.

**Limb field:** Area on body wall committed to form limb mesenchyme even before limb bud appears. Marked by expression of TBX4 or TBX5 transcription factors (which continue to be expressed in growing limb).

**Morphogen:** A secreted molecule that regulates induction. A concentration gradient of the molecule is frequently established.

**Progress Zone (PZ):** mesoderm below AER. Progressively more distal elements arise from this region over time. Long-standing PZ model says cells are plastic with indeterminate proximodistal identity until they exit the PZ. This model is inconsistent with more recent data. Newer progressive specification model says progenitor PD identity is established early, and that each PD element progenitor population is expanded sequentially.

**Sonic hedgehog (SHH):** a member of the hedgehog family of secreted signaling proteins. SHH is made by the ZPA (below) and regulates anterior/posterior patterning.

**Zone of Polarizing Activity (ZPA):** mesenchyme, just below the AER, on the posterior boundary of the limb bud. Major signaling center for the regulation of anterior/posterior patterning. Produces SHH.

**Dorsal limb ectoderm:** produces Wnt7a signal that promotes dorsal identity in underlying limb mesenchyme.

**LMX1B:** transcriptional factor that specifies dorsal limb mesenchymal identity

**Engrailed-1 (EN-1):** transcription factor expressed by ventral limb ectoderm that prevents expression of Wnt7a, and thereby promotes ventral limb mesenchyme identity

**HOX genes:** sets of transcription factors arrayed in four genomic clusters. Expressed in progressive fashion under the control of ZPA and AER signaling centers, these genes regulate differential morphology (identity) of limb elements.

**Reciprocal signaling:** In addition to regulating limb growth and patterning, the major signaling centers produce signals that maintain and regulate the activity of one another. The major positive signals are ZPA to AER; AER to ZPA; AER to PZ; PZ to AER; Dorsal ectoderm to ZPA. This crosstalk between signaling centers allows growth and patterning to occur in proper spatiotemporal fashion.

## **SOME LIMB MALFORMATION TERMINOLOGY**

Meromelia	Absence of part of a limb
Amelia	Absence of an entire limb
Phocomelia	Short, poorly formed limb
Ectrodactyly	Absence of fingers or toes
Polydactyly	Extra digits
Syndactyly	Fusion of digits
Adactyly	Absence of digits
Brachydactyly	Disproportionally short digits