

Developmental Biology 13e, Chapter 21 Literature Cited

Abarca-Buis, R. F., M. Bustamante, R. Cuervo, D. Aguilar-Fernández-de-Lara and J. Chimal-Monroy. 2011. Smad8 is expressed in the anterior necrotic zone: evidence for a role of bone morphogenetic proteins/SMAD signaling in the activation of a molecular cascade that culminates in cell death. *Dev. Growth Differ.* 53: 780–792.

Abbasi, A. A. 2011. Evolution of vertebrate appendicular structures: Insight from genetic and palaeontological data. *Dev. Dyn.* 240: 1005–1016.

Adamska, M., B. T. MacDonald, Z. H. Sarmast, E. R. Oliver and M. H. Meisler. 2004. *En1* and *Wnt7a* interact with *Dkk1* during limb development in the mouse. *Dev. Biol.* 272: 134–144.

Agarwal, P. and 7 others. 2003. *Tbx5* is essential for forelimb bud initiation following patterning of the limb field in the mouse embryo. *Development* 130: 623–633.

Ahn, D. and R. K. Ho. 2008. Triphasic expression of posterior Hox genes during development of pectoral fins in zebrafish: Implications for the evolution of vertebrate paired appendages. *Dev. Biol.* 322: 220–233.

Ahn, K., Y. Mishina, M. C. Hanks, R. R. Behringer and E. B. Crenshaw. 2001. BMPR-IA signaling is required for the formation of the apical ectoderma ridge and dorso-ventral patterning of the limb. *Development* 128: 4449–4461.

Ahn, S. and A. L. Joyner. 2004. Dynamic changes in the response of cells to positive hedgehog signaling during mouse limb patterning. *Cell* 118: 505–616.

Akiyama, H., M. C. Chaboissier, J. F. Martin, A. Schedl and B. de Crombrugghe. 2002. The transcription factor *Sox9* has essential roles in successive steps of the chondrocyte differentiation pathway and is required for expression of *Sox5* and *Sox6*. *Genes Dev.* 16: 2813–2828.

Alberch, P. 1985. Developmental constraints: Why Saint Bernards often have an extra digit and poodles never do. *Am. Nat.* 126: 430–433.

Altabef, M. and C. Tickle. 2002. Initiation of dorso-ventral axis during chick limb development. *Mech. Dev.* 116: 19–27.

- Alvarado, D. M. and 9 others. 2011. Pitx1 haploinsufficiency causes clubfoot in humans and a clubfoot-like phenotype in mice. *Hum. Mol. Genet.* 20: 3943–3952.
- Ballock, R. T. and R. J. O'Keefe. 2003. The biology of the growth plate. *J. Bone Joint Surg. Am.* 85A: 715–726.
- Bellus, G. A., I McIntosh, E. A. Smith, A. S. Aylsworth, I. Kaitila, W. A. Horton, G. A. Greenhaw, J. T. Hecht and C. A. Francomano. 1995. A recurrent mutation in the tyrosine kinase domain of fibroblast growth factor receptor 3 causes hypochondroplasia. *Nat. Genet.* 10: 357–359.
- Bénazet, J. D., M. Bischofberger, E. Tiecke, A. Gonçalves, J. F. Martin, A. Zuniga, F. Naef and R. Zeller. 2009. A self-regulatory system of interlinked signaling feedback loops controls mouse limb patterning. *Science* 323: 1050–1053.
- Boulet, A. M., A. M. Moon, B. R. Arenkiel and M. R. Capecchi. 2004. The roles of Fgf4 and Fgf8 in limb bud initiation and outgrowth. *Dev. Biol.* 273: 361–372.
- Brunet, L. J., J. A. McMahon, A. P. McMahon and R. M. Harland. 1998. Noggin, cartilage, morphogenesis, and joint formation in the mammalian skeleton. *Science* 280: 1455–1457.
- Burke, A. C., C. E. Nelson, B. A. Morgan and C. Tabin. 1995. Hox genes and the evolution of vertebrate axial morphology. *Development* 121: 333–346.
- Capdevila, J. and R. L. Johnson. 1998. Endogenous and ectopic expression of *noggin* suggests a conserved mechanism for regulation of BMP function during limb and somite patterning. *Dev. Biol.* 197: 205–217.
- Carrington, J. L. and J. F. Fallon. 1988. Initial limb budding is independent of apical ectodermal ridge activity: Evidence from a limbless mutant. *Development* 104: 361–367.
- Chapman, D. L. and 9 others. 1996. Expression of the T-box family genes *Tbx1–Tbx5* during early mouse development. *Dev. Dyn.* 206: 379–390.
- Charite, J., W. de Graaff, S. Shen and J. Deschamps. 1994. Ectopic expression of Hoxb-8 causes duplication of the ZPA in the forelimb and homeotic transformation of axial structures. *Cell* 78: 589–601.

Chaturvedi, R. and 9 others. 2005. On multiscale approaches to three-dimensional modelling of morphogenesis. *J. R. Soc. Interface* 2: 237–253.

Chen, H. and 8 others. 1998. Limb and kidney defects in *Lmx1b* mutant mice suggest an involvement of *LMX1B* in human nail patella syndrome. *Nat. Genet.* 19: 51–55.

Cohn, M. J. and C. Tickle. 1999. Developmental basis of limblessness and axial patterning in snakes. *Nature* 399: 474–479.

Cooper, K. L., J. K. Hu, D. ten Berge, M. Fernandez-Teran, M. A. Ros and C. J. Tabin. 2011. Initiation of proximal-distal patterning in the vertebrate limb by signals and growth. *Science* 332: 1083–1086.

Cooper, K. L., S. Oh, Y. Sung, R. R. Dasari, M. W. Kirschner and C. J. Tabin. 2013. Multiple phases of chondrocyte enlargement underlie differences in skeletal proportions. *Nature* 495: 375–378.

Cooper, L. N. 2009. “Evolution and Development of Cetacean Appendages.” PhD Thesis, Kent State University.

Cooper, L. N., C. J. Cretekos and K. E. Seras. 2012. The evolution and development of mammalian flight. *Wiley Interdiscip. Rev. Dev Bio.* 1: 773–779.

Crawford, K. and D. L. Stocum. 1988a. Retinoic acid coordinately proximalizes regenerative pattern and blastema differential affinity in axolotl limbs. *Development* 102: 687–698.

Crawford, K. and D. L. Stocum. 1988b. Retinoic acid proximalizes level-specific properties responsible for intercalary regeneration in axolotl limbs. *Development* 104: 703–712.

Crossley, P. H., G. Monowada, C. A. MacArthur and G. R. Martin. 1996. Roles for Fgf8 in the induction, initiation, and maintenance of chick development of the tetrapod limb. *Cell* 84: 127–136.

Cunningham, T. J. and G. Duester. 2015. Mechanisms of retinoic acid signalling and its roles in organ and limb development. *Nat. Rev. Mol. Cell Biol.* 16: 110–123.

Cunningham, T. J., C. Chatzi, L. L. Sandell, P. A. Trainor, and G. Duester. 2011. *Rdh10* mutants deficient in limb field retinoic acid signaling exhibit normal limb patterning but display

interdigital webbing. *Dev. Dyn.* 240: 1142–1150.

Cunningham, T. J., X. Zhao, L. L. Sandell, S. M. Evans, P. A. Trainor, and G. Duester. 2013. Antagonism between retinoic acid and fibroblast growth factor signaling during limb development. *Cell Rep.* 3: 1503–1511.

Dahn, R. D. and J. F. Fallon. 2000. Interdigital regulation of digit identity and homeotic transformation by modulating BMP signaling. *Science* 289: 438–441.

Davis, A. P., D. P. Witte, H. M. Hsieh-Li, S. S. Potter and M. R. Capecchi. 1995. Absence of radius and ulna in mice lacking *hoxa-11* and *hoxd-11*. *Nature* 375: 791–795.

Davis, M. C., R. D. Dahn and N. H. Shubin. 2007. An autopodial-like pattern of Hox expression in the fins of a basal actinopterygian fish. *Nature* 447: 473–476.

Dealy, C. N., A. Roth, D. Ferrari, A. M. C. Brown and R. A. Kosher. 1993. *Wnt-5a* and *Wnt-7a* are expressed in the developing chick limb bud in a manner that suggests roles in pattern formation along the proximodistal and dorsoventral axes. *Mech. Dev.* 43: 175–186.

DeLaurier, A., R. Schweitzer and M. Logan. 2006. Pitx1 determines the morphology of muscle, tendon, and bones of the hindlimb. *Dev. Biol.* 299: 22–34.

Deng, C., A. Wynshaw-Boris, F. Zhou, A. Kuo and P. Leder. 1996. Fibroblast growth factor receptor-3 is a negative regulator of bone growth. *Cell* 84: 911–921.

Detwiler, S. R. 1918. Experiments on the development of the shoulder girdle and the anterior limb of *Ambystoma punctatum*. *J. Exp. Zool.* 25: 499–538.

Dreyer, S. D. and 7 others. 1998. Mutations in *LMX1B* cause abnormal skeletal patterning and renal dysplasia in nail patella syndrome. *Nat. Genet.* 19: 47–50.

Drossopoulou, G. and 6 others. 2000. A model for anteriorposterior patterning of the vertebrate limb based on sequential long-and short-range Shh signalling and BMP signalling. *Development* 127: 1337–1348.

Duboc, V. and M. P. Logan. 2011. Pitx1 is necessary for normal initiation of hindlimb outgrowth through regulation of Tbx4 expression and shapes hindlimb morphologies via targeted growth

control. *Development* 138: 5301–5309.

Fallon, J. F. and G. M. Crosby. 1977. Polarizing zone activity in limb buds of amniotes. In D. A. Ede et al. (eds.), *Vertebrate Limb and Somite Morphogenesis*. Cambridge University Press, Cambridge, 55–59.

Fernandez-Teran, M. and M. A. Ros. 2008. The apical ectodermal ridge: Morphological aspects and signaling pathways. *Int. J. Dev. Biol.* 52: 857–871.

Fondon, J. W. and H. R. Garner. 2004. Molecular origins of rapid and continuous morphological evolution. *Proc. Natl. Acad. Sci. USA* 101: 18058–18063.

Freitas, R., C. Gómez-Marín, J. M. Wilson, F. Casares, and J. L. Gómez-Skarmeta. 2012. *Hoxd13* contribution to the evolution of vertebrate appendages. *Dev. Cell* 23: 1219–1229.

Freitas, R., J. L. Gómez-Skarmeta, and P. N. Rodrigues. 2014. New frontiers in the evolution of fin development. *J. Exp. Zool. B. Mol. Dev. Evol.* 322: 540–552.

Fromental-Ramain, C., X. Warot, N. Messadecq, M. LeMeur, P. Dollé and P. Chambon. 1996. *Hoxa-13* and *Hoxd-13* play a crucial role in the patterning of the limb autopod. *Development* 122: 2997–3011.

Galli, A., D. and 8 others. 2010. Distinct roles of Hand2 in initiating polarity and posterior Shh expression during the onset of mouse limb bud development. *PLoS Genet.* 6: e1000901.

Gañan, Y., D. Macias, R. D. Basco, R. Merino and J. M. Hurle. 1998. Morphological diversity of the avian foot is related with the pattern of *msx* gene expression in the developing autopod. *Dev. Biol.* 196: 33–41.

Garrity, D. M., S. Childs, and M. C. Fishman. 2002. The *heart-strings* mutation in zebrafish causes heart/fin Tbx5 deficiency syndrome. *Development* 129: 4635–4645.

Gibson-Brown, J. J. and 6 others. 1996. Evidence of a role for T-box genes in the evolution of limb morphogenesis and the specification of forelimb/hindlimb identity. *Mech. Dev.* 56: 93–101.

Gingerich, P. D., S. M. Raza, M. Arif, M. Anwar and X. Zhou. 1994. New whale from the Eocene of Pakistan and the origin of cetacean swimming. *Nature* 368: 844–847.

Gish, D. T. 1985. *Evolution: The Challenge of the Fossil Record*. Creation-Life Publishers, San Diego, CA.

Glimm, T., R. Bhat and S. A. Newman. 2020. Multiscale modeling of vertebrate limb development. *Wiley Interdiscip. Rev. Syst. Biol. Med.* 12: e1485.

Grandel, H. and M. Brand. 2011. Zebrafish limb development is triggered by a retinoic acid signal during gastrulation. *Dev. Dyn.* 240: 1116–1126.

Gros, J. and C. J. Tabin. 2014. Vertebrate limb bud formation is initiated by localized epithelial-to-mesenchymal transition. *Science* 343: 1253–1256.

Gros, J., J. K. Hu, C. Vinegoni, P. F. Feruglio, R. Weissleder and C. J. Tabin. 2010. WNT5A/JNK and FGF/MAPK pathways regulate the cellular events shaping the vertebrate limb bud. *Curr. Biol.* 20: 1993–2002.

Grotewold, L. and U. Rüther. 2002. The Wnt antagonist Dickopf-1 is regulated by BMP signaling and c-Jun and modulates programmed cell death. *EMBO J.* 21: 966–975.

Gurnett, C. A., A. M. Bowcock, F. R. Dietz, J. A. Morcuende, J. C. Murray and M. B. Dobbs. 2007. Two novel point mutations in the long-range SHH enhancer in three families with triphalangeal thumb and preaxial polydactyly. *Am. J. Med. Genet. A* 143: 27–32.

Hamburger, V. 1938. Morphogenetic and axial self-differentiation of transplanted limb primordia of 2-day chick embryos. *J. Exp. Zool.* 77: 379–400.

Harfe, B. D., P. J. Scherz, S. Nissim, H. Tian, A. P. McMahon and C. J. Tabin. 2004. Evidence for an expansion-based temporal Shh gradient in specifying vertebrate digit identities. *Cell* 118: 517–528.

Harrison, R. 1969. Harrison stages and description of normal development of the spotted salamander, *Ambystoma punctatum* (Linn). In S. Wilens (ed.) *Organization and Development of the Embryo*. Yale University Press, New Haven, CT, 44–66.

Harrison, R. G. 1918. Experiments on the development of the forelimb of *Ambystoma*, a self-differentiating equipotential system. *J. Exp. Zool.* 25: 413–461.

Hartmann, C. and C. J. Tabin. 2001. Wnt-14 plays a pivotal role in inducing synovial joint formation in the developing appendicular skeleton. *Cell* 104: 341–351.

Hentschel, H. G., T. Glimm, J. A. Glazier, and S. A. Newman. 2004. Dynamical mechanisms for skeletal pattern formation in the vertebrate limb. *Proc. Biol. Sci.* 271: 1713–1722.

Hertwig, O. 1925. Haploidkernige Transplante als Organisatoran diploidkeniger Extremitaten bei Triton. *Anat. Anz.* 60: 112–118.

Hinchliffe, J. R. 1991. Developmental approaches to the problem of transformation of limb structure in evolution. In J. R. Hinchliffe (ed.), *Developmental Patterning of the Vertebrate Limb*. Plenum, New York, 313–323.

Honig, L. S. and D. Summerbell. 1985. Maps of strength of positional signaling activity in the developing chick wing bud. *J. Embryol. Exp. Morphol.* 87: 163–174.

Hornstein, E. and 8 others. 2005. The microRNA miR-196 acts upstream of Hoxb8 and Shh in limb development. *Nature* 438: 671–674.

Iten, L. E. 1982. Pattern specification and pattern regulation in the embryonic chick limb bud. *Am. Zool.* 22: 117–129.

Itou, J. and 6 others. 2012. Islet1 regulates establishment of the posterior hindlimb field upstream of the *Hand2-Shh* morphoregulatory gene network in mouse embryos. *Development* 139: 1620–1629.

Izpisúa-Belmonte, J.-C., C. Tickle, P. Dollé, L. Wolpert and D. Duboule. 1991. Expression of the homeobox *Hox-4* genes and the specification of position in chick wing development. *Nature* 350: 585–589.

Kahn, J. and 11 others. 2009. Muscle contraction is necessary to maintain joint progenitor cell fate. *Dev. Cell* 16: 734–743.

Kawakami, Y. and 12 others. 2011. Islet1-mediated activation of the beta-catenin pathway is necessary for hindlimb initiation in mice. *Development* 138: 4465–4473.

Kawakami, Y. and 9 others. 1996. BMP signaling during bone pattern determination in the developing limb. *Development* 122: 3557–3566.

Kawakami, Y. and 6 others. 2001. WNT signals control FGF-dependent limb initiation and AER induction in the chick embryo. *Cell* 104: 891–900.

Kieny, M. 1960. Rôle inducteur du mésoderme dans la différenciation précoce du bourgeon de membre chez l'embryon de poulet. *J. Embryol. Exp. Morphol.* 8: 457–467.

Knezevic, V. and 6 others. 1997. Hoxd-12 differentially affects preaxial and postaxial chondrogenic branches in the limb and regulates Sonic hedgehog in a positive feedback loop. *Development* 124: 4523–4536.

Kondo, S. and T. Miura. 2010. Reaction-diffusion model as a framework for understanding biological pattern formation. *Science* 329: 1616–1620.

Kosher, R. A., M. P. Savage, and S. C. Chan. 1979. In vitro studies on the morphogenesis and differentiation of the mesoderm subjacent to the apical ectodermal ridge of the embryonic chick limb-bud. *J. Embryol. Exp. Morph.* 50: 75–97.

Koyama, E. and 13 others. 2008. A distinct cohort of progenitor cells participates in synovial joint and articular cartilage formation during mouse limb skeletogenesis. *Dev. Biol.* 316: 62–73.

Krabbenhoft, K. M. and J. F. Fallon. 1989. The formation of leg or wing specific structures by leg bud cells grafted to the wing bud is influenced by proximity to the apical ridge. *Dev. Biol.* 131: 373–382.

Kronenberg, H. M. 2003. Developmental regulation of the growth plate. *Nature* 423: 332–336.

Kumar, S. and G. Duester. 2014. Retinoic acid controls body axis extension by directly repressing *Fgf8* transcription. *Development* 141: 2972–2977.

Lam, W., J. Oh and M. G. Davey. 2022. Turing patterning and upper limb development. *Journal of Hand Surgery (European Volume)* 47: 1085–1088.

Laufer, E., C. E. Nelson, R. L. Johnson, B. A. Morgan and C. Tabin. 1994. Sonic hedgehog and Fgf-4 act through a signaling cascade and feedback loop to integrate growth and patterning of the developing limb bud. *Cell* 79: 993–1003.

Laufer, E., R. Dahn, O. E. Orozco, C. Y. Yeo, J. Pisenti, D. Henrique, U. K. Abbott, J. F. Fallon and C. Tabin. 1997a. The *Radical fringe* expression boundary in the limb bud ectoderm regulates AER formation. *Nature* 386: 366–367.

Laufer, E., S. Pizette, H. Zou, O. E. Orozco and L. Niswander. 1997b. BMP expression in duck interdigital webbing: A reanalysis. *Science* 278: 305.

Lettice, L. A. and 8 others. 2003. A long-range Shh enhancer regulates expression in the developing limb and fin and is associated with preaxial polydactyly. *Human Mol. Genet.* 12: 1725–1735.

Lettice, L. A., A. E. Hill, P. S. Devenney and R. E. Hill. 2008. Point mutations in a distant sonic hedgehog *cis*-regulator generate a variable regulatory output responsible for preaxial polydactyly. *Human Mol. Genet.* 2008 17: 97–985.

Lewandoski, M., X. Sun and G. R. Martin. 2000. Fgf8 signalling from the AER is essential for normal limb development. *Nat. Genet.* 26: 460–463.

Litingtung, Y., R. D. Dahn, Y. Li, J. F. Fallon and C. Chiang. 2002. Shh and Gli3 are dispensable for limb skeleton formation but regulate digit number and identity. *Nature* 418: 979–983.

Liu, J. and 33 others. 2012. Genome and transcriptome sequencing of lung cancers reveal diverse mutational and splicing events. *Genome Res.* 22: 2315–2327.

Logan, M., H.-H. Simon and C. Tabin. 1998. Differential regulation of T-box and homeobox transcription factors suggests roles in controlling chick limb-type identity. *Development* 125: 2825–2835.

Loomis, C. A., R. A. Kimmel, C. X. Tong, J. Michaud and A. Joyner. 1998. Analysis of the genetic pathway leading to formation of ectopic apical ectodermal ridges in mouse *Engrailed-1* mutant limbs. *Development* 125: 1137–1148.

López-Martínez, A. and 7 others. 1995. Limb-patterning activity and restricted posterior localization of the amino-terminal product of sonic hedgehog cleavage. *Curr. Biol.* 5: 791–796.

Lopez-Rios, J. and 9 others. 2012. GLI3 constrains digit number by controlling both progenitor proliferation and BMP-dependent exit to chondrogenesis. *Dev. Cell.* 22: 837–848.

Lorda-Diez, C. I., J. A. Montero, M. J. Diaz-Mendoza, J. A. Garcia-Porrero and J. M. Hurle. 2011. Defining the earliest transcriptional steps of chondrogenic progenitor specification during

the formation of the digits in the embryonic limb. *PLOS ONE* 6: e24546.

Maas, S. A. and J. F. Fallon. 2005. Single base pair change in the long-range Sonic hedgehog limb-specific enhancer is a genetic basis for preaxial polydactyly. *Dev. Dyn.* 232: 345–348.

MacCabe, J. A., J. Errick and J. W. Saunders, Jr. 1974. Ectodermal control of dorso-ventral axis in leg bud of chick embryo. *Dev. Biol.* 39: 69–82.

Macias, D., Y. Gañon, T. K. Sampath, M. E. Piedra, M. A. Ros and J. M. Hurle. 1997. Role of BMP2 and OP-1 (BMP7) in programmed cell death and skeletogenesis during chick limb development. *Development* 124: 1109–1117.

Maden, M. 1985. Retinoids and the control of pattern in regenerating limbs. *Ciba Found. Symp.* 1113: 132–355.

Mahmood, R., J. Bresnick, A. Hornbruch, C. Mahony, N. Morton, K. Colquhoun, P. Martin, A. Lumsden, C. Dickson and I. Mason. 1995. A role for FGF-8 in the initiation and maintenance of vertebrate limb outgrowth. *Curr. Biol.* 5: 797–806.

Mao, J., E. McGlenn, P. Huang, C. J. Tabin and A. P. McMahon. 2009. Fgf-dependent Etv4/5 activity is required for posterior restriction of Sonic Hedgehog and promoting outgrowth of the vertebrate limb. *Dev. Cell* 16: 600–606.

Mariani, F. V., C. P. Ahn, and G. R. Martin. 2008. Genetic evidence that FGFs have an instructive role in limb proximal-distal patterning. *Nature* 453: 401405.

Marques, S. R., Y. Lee, K. D. Poss, and D. Yelon. 2008. Reiterative roles for FGF signaling in the establishment of size and proportion of the zebrafish heart. *Dev. Biol.* 321: 397–406.

Meinhardt, H. 2008. Models of biological pattern formation: From elementary steps to the organization of embryonic axes. *Curr. Top. Dev. Biol.* 81: 1–63.

Mercader, N., E. Leonardo, M. E. Piedra, C. Martínez-A, M. A. Ros and M. Torres. 2000. Opposing RA and FGF signals control proximodistal vertebrate limb development through regulation of *Meis* genes. *Development* 127: 3961–3970.

Merino, R., J. Rodriguez-Leon, D. Macias, Y. Gañan, A. N. Economides and J. M. Hurle. 1999. The BMP antagonist Gremlin regulates outgrowth, chondrogenesis and programmed cell death in the developing limb. *Development* 126: 5515–5522.

Merino, R., Y. Gañan, D. Macias, A. N. Economides, K. T. Sampath and J. M. Hurle. 1998. Morphogenesis of digits in the avian limb is controlled by FGFs, TGFbs, and noggin through BMP signaling. *Dev. Biol.* 200: 35–45.

Minguillon, C., J. Del Buono and M. P. Logan. 2005. Tbx5 and Tbx4 are not sufficient to determine limb-specific morphologies but have common roles in initiating limb outgrowth. *Dev. Cell* 8: 75–84.

Molven, A., C. V. E. Wright, R. Bremiller, E. M. De Robertis and C. B. Kimmel. 1990. Expression of a homeobox gene product in normal and mutant zebrafish embryos: Evolution of the tetrapod body plan. *Development* 109: 279–288.

Montavon, T. and 8 others. 2011. A regulatory archipelago controls Hox genes transcription in digits. *Cell* 147: 1132–1145.

Montavon, T., J. F. Le Garrec, M. Kerszberg and D. Duboule. 2008. Modeling Hox gene regulation in digits: Reverse collinearity and the molecular origin of thumbness. *Genes Dev.* 22: 346–359.

Mori, C., N. Nakamura, S. Kimura, H. Irie, T. Takigawa and K. Shiota. 1995. Programmed cell death in the interdigital tissue of the fetal mouse limb is apoptosis with DNA fragmentation. *Anat. Rec.* 242: 103–110.

Mortlock, D. P. and J. W. Innis. 1997. Mutation of HOXA13 in hand-foot-genital syndrome. *Nat. Genet.* 15: 179–181.

Mundy, C. and 7 others. 2011. Synovial joint formation requires local Ext1 expression and heparan sulfate production in developing mouse embryo limbs and spine. *Dev. Biol.* 351: 70–81.

Muneoka, K. and S. V. Bryant. 1982. Evidence that patterning mechanisms in developing and regenerating limbs are the same. *Nature* 298: 369–371.

Muragaki, Y., S. Mundlos, J. Upton and B. R. Olsen. 1996. Altered growth and branching patterns in synpolydactyly caused by mutations in *HOXD13*. *Science* 272: 548–551.

Murugan, N. J. and 9 others. 2022. Acute multidrug delivery via a wearable bioreactor facilitates long-term limb regeneration and functional recovery in adult *Xenopus laevis*. *Sci. Adv.* 8: eabj2164.

Naiche, L. A. and V. E. Papaioannou. 2003. Loss of Tbx4 blocks hindlimb development and affects vascularization and fusion of the allantois. *Development* 130: 2681–2693.

Newman, S. A. 1996. Sticky fingers: Hox genes and cell adhesion in vertebrate development of the tetrapod limb. *BioEssays* 18: 171–174.

Newman, S. A. and H. L. Frisch. 1979. Dynamics of skeletal pattern formation in developing chick limb. *Science* 205: 662–668.

Newman, S. A. and R. Bhat. 2007. Activator-inhibitor dynamics of vertebrate limb pattern formation. *Birth Def. Res. C Embryol. Today* 81: 305–319.

Niswander, L., S. Jeffrey, G. R. Martin and C. Tickle. 1994. A positive feedback loop coordinates growth and patterning in the vertebrate limb. *Nature* 371: 609–612.

Nohno, T. and 7 others. 1991. Involvement of the *Chox-4* chicken homeobox genes in determination of anteroposterior axial polarity during limb development. *Cell* 64: 1197–1205.

Noro, M. and 7 others. 2011. Role of paraxial mesoderm in limb/flank regionalization of the trunk lateral plate. *Dev. Dyn.* 240: 1639–1649.

Ohuchi, H. and 11 others. 1997. The mesenchymal factor Fgf10 initiates and maintains the outgrowth of the chick limb bud through interaction with Fgf8, and apical ectodermal factor. *Development* 124: 2235–2244.

Ohuchi, H. and S. Noji. 1999. Fibroblast-growth-factor-induced additional limbs in the study of initiation of limb formation, limb identity, myogenesis, and innervation. *Cell Tissue Res.* 296: 45–56.

Ohuchi, H. and 7 others. 1998. Correlation of wing-leg identity in ectopic FGF-induced chimeric limbs with the differential expression of chick *Tbx5* and *Tbx4*. *Development* 125: 51–60.

Oliver, G., C. V. E. Wright, J. Hardwicke and E. M. De Robertis. 1988. A gradient of homeodomain protein in developing forelimbs of *Xenopus* and mouse embryos. *Cell* 55: 1017–1024.

Ouimette, J. F., M. L. Jolin, A. L’Honore, A. Gifuni and J. Drouin 2010. Divergent transcriptional activities determine limb identity. *Nat. Commun.* 1: 35.

Parker, H. G. and 16 others. 2009. An expressed *Fgf4* retrogene is associated with breed-defining chondrodysplasia in domestic dogs. *Science* 325: 995–998.

Parr, B. A. and A. P. McMahon. 1995. Dorsalizing signal *wnt-7a* required for normal polarity of D-V and A-P axes of the mouse limb. *Nature* 374: 350–353.

Parr, B. A., M. J. Shea, G. Vassileva and A. P. McMahon. 1993. Mouse *Wnt* genes exhibit discrete domains of expression in early embryonic CNS and limb buds. *Development* 119: 247–261.

Pizette, S. and L. Niswander. 1999. BMPs negatively regulate structure and function of the limb apical ectodermal ridge. *Development* 126: 883–894.

Pizette, S., C. Abate-Shen and L. Niswander. 2001. BMP controls proximodistal outgrowth, via induction of the apical ectodermal ridge, and dorsoventral patterning in the vertebrate limb. *Development* 128: 4463–4474.

Pollak, R. D. and J. F. Fallon. 1976. Autoradiographic analysis of macromolecular synthesis in prospectively necrotic cells of the chick limb bud. II. Nucleic acids. *Exp. Cell Res.* 100: 15–22.

Probst, S. and 9 others. 2011. SHH propagates distal limb bud development by enhancing CYP26B1-mediated retinoic acid clearance via AER-FGF signalling. *Development* 138: 1913–1923.

Rallis, C., B. G. Bruneau, J. Del Buono, C. E. Seidman, J. G. Seidman, S. Nissim, C. J. Tabin and M. P. Logan. 2003. *Tbx5* is required for forelimb bud formation and continued outgrowth. *Development* 130: 2741–2751.

Raspopovic, J., L. Marcon, L. Russo, and J. Sharpe. 2014. Modeling digits. Digit patterning is controlled by a BMP-Sox9-Wnt Turing network modulated by morphogen gradients. *Science* 345: 566–570.

Riddle, R. D., M. Ensini, C. Nelson, T. Tsuchida, T. M. Jessell and C. Tabin. 1995. Induction of the LIM homeobox gene *Lmx1* by *WNT7a* establishes dorsoventral pattern in the vertebrate limb. *Cell* 83: 631–640.

Riddle, R. D., R. L. Johnson, E. Laufer and C. Tabin. 1993. Sonic hedgehog mediates the polarizing activity of the ZPA. *Cell* 75: 1401–1416.

Rodriguez-Esteban, C., J. W. R. Schwabe, J. De La Peña, B. Foys, B. Eshelman and J. C. Izpisúa-Belmonte. 1997. Radical fringe positions the apical ectodermal ridge at the dorsoventral boundary of the vertebrate limb. *Nature* 386: 360–366.

Rodriguez-Esteban, C., T. Tsukui, S. Yonei, J. Magallon, K. Tamura and J. C. Izpisúa-Belmonte. 1999. T-box genes *Tbx4* and *Tbx5* regulate limb outgrowth and identity. *Nature* 398: 814–818.

Ros, M. A. and 8 others. 2003. The chick *oligozeugodactyly (ozd)* mutant lacks Sonic hedgehog function in the limb. *Development* 130: 527–537.

Ros, M. A., G. E. Lyons, S. Mackem, and J. F. Fallon. 1994. Recombinant limbs as a model to study homeobox gene regulation during limb development. *Dev. Biol.* 166: 59–72.

Roselló-Díez, A., C. G. Arques, I. Delgado, G. Giovinazzo, and M. Torres. 2014. Diffusible signals and epigenetic timing cooperate in late proximo-distal limb patterning. *Development* 141: 1534–1543.

Roselló-Díez, A., M. A. Ros and M. Torres. 2011. Diffusible signals, not autonomous mechanisms, determine the main proximodistal limb subdivision. *Science* 332: 1086–1088.

Rosenquist, G. C. 1971. The origin and movement of the limb-bud epithelium and mesenchyme in the chick embryo as determined by radioautographic mapping. *J. Embryol. Exp. Morphol.* 25: 85–96.

Rowe, D. A., J. M. Cairnes and J. F. Fallon. 1982. Spatial and temporal patterns of cell death in limb bud mesoderm after apical ectodermal ridge removal. *Dev. Biol.* 93: 83–91.

Rubin, L. and J. W. Saunders, Jr. 1972. Ectodermal–mesodermal interactions in the growth of limbs in the chick embryo: Constancy and temporal limits of the ectodermal induction. *Dev. Biol.* 28: 94–112.

Sagai, T., M. Hosoya, Y. Mizushina, M. Tamura and T. Shiroishi. 2005. Elimination of a long-range *cis*-regulatory module causes complete loss of limb-specific Shh expression and truncation of the mouse limb. *Development* 132: 797–803.

Sandell, L. L. and 9 others. 2007. RDH10 is essential for synthesis of embryonic retinoic acid and is required for limb, craniofacial, and organ development. *Genes Dev.* 21: 1113–1124.

Sato, K., R. Seki, M. Noro, H. Yokoyama and K. Tamura. 2010. Morphogenetic change of the limb bud in the hand plate formation. *J. Exp. Zool.* 314B: 539–551.

Saunders, J. W., Jr. 1948. The proximal-distal sequence of origin of the parts of the chick wing and the role of the ectoderm. *J. Exp. Zool.* 108: 363–404.

Saunders, J. W., Jr. 1972. Developmental control of three-dimensional polarity in the avian limb. *Ann. NY Acad. Sci. USA* 193: 29–42.

Saunders, J. W., Jr. and C. Reuss. 1974. Inductive and axial properties of prospective wing-bud mesoderm in the chick embryo. *Dev. Biol.* 38: 41–50.

Saunders, J. W., Jr. and J. F. Fallon. 1966. Cell death in morphogenesis. In M. Locke (ed.), *Major Problems of Developmental Biology*. Academic Press, New York, 289–314.

Saunders, J. W., Jr. and M. T. Gasseling. 1968. Ectodermal-mesodermal interactions in the origin of limb symmetry. In R. Fleischmajer and R. E. Billingham (eds.), *Epithelial-Mesenchymal Interactions*. Williams & Wilkins, Baltimore, MD, 78–97.

Saunders, J. W., Jr., J. M. Cairns and M. T. Gasseling. 1957. The role of the apical ridge of ectoderm in the differentiation of the morphological structure and inductive specificity of limb parts of the chick. *J. Morphol.* 101: 57–88.

Saunders, J. W., Jr., M. T. Gasseling and L. C. Saunders. 1962. Cellular death in morphogenesis of the avian wing. *Dev. Biol.* 5: 147–178.

Scherz, P. J., B. D. Harfe, A. P. McMahon and C. J. Tabin. 2004. The limb Shh-Fgf feedback loop is terminated by the expansion of former ZPA cells. *Science* 305: 396–369.

Scherz, P. J., E. McGlenn, S. Nissim and C. J. Tabin. 2007. Extended exposure to Sonic hedgehog is required for patterning the posterior digits of the vertebrate limb. *Dev. Biol.* 308: 343–354.

Schneider, I. and N. H. Shubin. 2013. The origin of the tetrapod limb: From expeditions to enhancers. *Trends Genet.* 29: 419–426.

Sekine, K. and 10 others. 1999. Fgf10 is essential for limb and lung formation. *Nat. Genet.* 21: 138–141.

Sessions, S. K. and S. B. Ruth. 1990. Explanation for naturally occurring supernumerary limbs in amphibians. *J. Exp. Zool.* 254: 38–47.

Sessions, S. K., D. M. Gardiner and S. V. Bryant. 1989. Compatible limb patterning mechanisms in urodeles and anurans. *Dev. Biol.* 131: 294–301.

Sessions, S. K., R. A. Franssen and V. C. Horner. 1999. Morphological clues from multilegged frogs: Are retinoids to blame? *Science* 284: 800–802.

Sheth, R. and 8 others. 2012. Hox genes regulate digit patterning by controlling the wavelength of a Turing-type mechanism. *Science* 338: 1476–1480.

Shubin, N. H. 2008. *Your Inner Fish*. Pantheon, New York.

Shubin, N. H., E. B. Daeschler and F. A. Jenkins, Jr. 2006. The pectoral fin of *Tiktaalik roseae* and the origin of the tetrapod limb. *Nature* 440: 764–771.

Spitz, F., F. Gonzalez and D. Duboule. 2003. A global control region defines a chromosomal regulatory landscape containing the HoxD cluster. *Cell* 113: 405–417.

Stocum, D. L. and J. F. Fallon. 1982. Control of pattern formation in urodele limb ontogeny: A review and hypothesis. *J. Embryol. Exp. Morphol.* 69: 7–36.

Storm, E. E. and D. M. Kingsley. 1999. GDF5 coordinates bone and joint formation during digit development. *Dev. Biol.* 209: 11–27.

Summerbell, D. and J. H. Lewis. 1975. Time, place, and positional value in the chick limb bud. *J. Embryol. Exp. Morphol.* 33: 621–643.

Sun, M. and 16 others. 2008. Triphalangeal thumb-polysyndactyly syndrome and syndactyly type IV are caused by genomic duplications involving the long range, limb-specific SHH enhancer. *J. Med. Genet.* 45: 589–595.

Suzuki, T. and J. F. Fallon. 2021. The dynamic spatial and temporal relationships between the phalanx-forming region and the interdigits determine digit identity in the chick limb autopod. *Dev. Dyn.* 250(9):1318–1329.

Suzuki, T., S. M. Hasso and J. F. Fallon. 2008. Unique SMAD1/5/8 activity at the phalanx-forming region determines digit identity. *Proc. Natl. Acad. Sci. USA* 105: 4185–4190.

Szebenyi, G., M. P. Savage, B. B. Olwin and J. F. Fallon. 1995. Changes in the expression of fibroblast growth factor receptors mark distinct stages of chondrogenesis in vitro and during chick limb skeletal patterning. *Dev. Dyn.* 204: 446–456.

Tabin, C. J. and A. P. McMahon. 2008. Grasping limb patterning. *Science* 321: 350–352.

Tabin, C. J. and L. Wolpert. 2007. Rethinking the proximodistal axis of the vertebrate limb in the molecular era. *Genes Dev.* 21: 1433–1442.

Takeuchi, J. K. and 7 others. 2003. Tbx5 specifies the left/right ventricles and ventricular septum position during cardiogenesis. *Development* 130: 5953–5964.

Takeuchi, J. K. and 8 others. 1999. Tbx5 and Tbx4 genes determine the wing/leg identity of limb buds. *Nature* 398: 810–814.

Tanaka, M. 2013. Molecular and evolutionary basis of limb field specification and limb initiation. *Dev. Growth Differ.* 55: 149–163.

Tanaka, M., K. Tamura, S. Noji, T. Nohno and H. Ide. 1997. Induction of additional limb at the dorsal-ventral boundary of a chick embryo. *Dev. Biol.* 182: 191–203.

- Tarchini, B. and D. Duboule. 2006. Control of Hoxd genes' collinearity during early limb development. *Dev. Cell* 10: 93–103.
- Tarchini, B., D. Duboule and M. Kmita. 2006. Regulatory constraints in the evolution of the tetrapod limb anterior-posterior polarity. *Nature* 443: 985–988.
- Tavormina, P. L. and 9 others. 1995. Thanatophoric dysplasia (types I and II) caused by distinct mutations in fibroblast growth factor receptor 3. *Nat. Genet.* 9: 321–328.
- te Welscher, P., A. Zuniga, S. Kuijper, T. Drenth, H. J. Goedemans, F. Meijlink, and R. Zeller. 2002. Progression of vertebrate limb development through SHH-mediated counteraction of GLI3. *Science* 298: 827–830.
- ten Berge, D., S. A. Brugmann, J. A. Helms and R. Nusse. 2008. Wnt and FGF signals interact to coordinate growth with cell fate specification during limb development. *Development* 135: 3247–3257.
- Thewissen, J. G. M., L. N. Cooper, J. C. George and S. Bajpai. 2009. From land to water: The origin of whales, dolphins, and porpoises. *Evol. Educ. Outreach* 2: 272–288.
- Thewissen, J. G., L. N. Cooper, M. T. Clementz, S. Bajpai and B. N. Tiwari. 2007. Whales originated from aquatic artiodactyls in the Eocene epoch of India. *Nature* 450: 1190–1194.
- Thewissen, J. G., M. J. Cohn, L. S. Stevens, S. Bajpai, J. Heyning and W. E. Horton, Jr. 2006. Developmental basis for hind-limb loss in dolphins and origin of the cetacean bodyplan. *Proc. Natl. Acad. Sci. USA* 103: 8414–8418.
- Tickle, C., D. Summerbell and L. Wolpert. 1975. Positional signaling and specification of digits in chick limb morphogenesis. *Nature* 254: 199–202.
- Todt, W. L. and J. F. Fallon. 1987. Posterior apical ectodermal ridge removal in chick wing bud triggers a series of events resulting in defective anterior pattern. *Development* 101: 501–515.
- Tufan, A. C. and R. S. Tuan. 2001. Wnt regulation of limb mesenchymal chondrogenesis is accompanied by altered N-cadherin-related functions. *FASEB J.* 15: 1436–1438.

- Turing, A. M. 1952. The chemical basis of morphology. *Philos. Trans. R. Soc. London* 237B: 37–72.
- Vargas, A. O. and J. F. Fallon. 2005a. Birds have dinosaur wings: The molecular evidence. *J. Exp. Zool.* 304B: 86–90.
- Vargas, A. O. and J. F. Fallon. 2005b. The digits of the wing of birds are 1, 2, and 3: A review. *J. Exp. Zool.* 304B: 206–219.
- Verheyden, J. M. and X. Sun. 2008. An Fgf–Gremlin inhibitory feedback loop triggers termination of limb bud outgrowth. *Nature* 454: 638–641.
- Vogel, A., C. Rodriguez and J.-C. Izpisúa-Belmonte. 1996. Involvement of Fgf8 in initiation, outgrowth, and patterning of the vertebrate limb. *Development* 122: 1737–1750.
- Vogel, A., C. Rodriguez, W. Warnken and J.-C. Izpisúa-Belmonte. 1995. Dorsal cell fate specified by chick Lmx1 during vertebrate limb development. *Nature* 378: 716–720.
- Vokes, S. A., H. Ji, W. H. Wong and A. P. McMahon. 2008. A genome-scale analysis of the cis-regulatory circuitry underlying *sonic hedgehog*-mediated patterning of the mammalian limb. *Genes Dev.* 22: 2651–2663.
- Webster, M. K. and D. J. Donoghue. 1996. Constitutive activation of fibroblast growth factor receptor 3 by the transmembrane domain point mutation found in achondroplasia. *EMBO J.* 15: 520–527.
- Wellik, D. M. and M. R. Capecchi. 2003. *Hox10* and *Hox11* genes are required to globally pattern the mammalian skeleton. *Science* 301: 363–367.
- Wessells, N. K. 1977. *Tissue Interaction and Development*. Benjamin Cummings, Menlo Park, CA.
- Wolpert, L. 2010. Arms and the man: The problem of symmetric growth. *PLoS Biol.* 8: e1000477
- Woltering, J. M., D. Noordermeer, M. Leleu and D. Duboule. 2014. Conservation and divergence of regulatory strategies at Hox loci and the origin of tetrapod digits. *PLoS Biol.* 12:

e1001773.

Xu, X. L. and 6 others . 1998. Fibroblast growth factor receptor 2-mediated reciprocal regulatory loop between Fgf8 and Fgf10 is essential for limb induction. *Development* 125: 753–765.

Yang, L. and 9 others. 2006. Isl1Cre reveals a common Bmp pathway in heart and limb development. *Development* 133: 1575–1585.

Yang, Y. and 10 others. 1997. Relationship between dose, distance and time in Sonic Hedgehog-mediated regulation of anteroposterior polarity in the chick limb. *Development* 124: 4393–4404.

Yang, Y. and S. H. Kozin. 2009. Cell signaling regulation of vertebrate limb growth and patterning. *J. Bone Joint Surg. Am.* 91: 76–80.

Yang, Y. Z. and L. Niswander. 1995. Interaction between signaling molecules Wnt7a and Shh during vertebrate limb development: Dorsal signals regulate anteroposterior patterning. *Cell* 80: 939–947.

Yin, M. and M. Pacifici. 2001. Vascular regression is required for mesenchymal condensation and chondrogenesis in the developing limb. *Dev. Dyn.* 222: 522–533.

Yokouchi, Y., J. Sakiyama, T. Kameda, H. Iba, A. Suzuki, N. Ueno and A. Kuroiwa. 1996. BMP2/4 mediate programmed cell death in chicken limb buds. *Development* 122: 3725–3734.

Yokouchi, Y. and 6 others. 1995. Misexpression of *Hoxa13* induces cartilage homeotic transformation and changes in adhesiveness in chick limb buds. *Genes Dev.* 9: 2509–2522.

Yonei-Tamura, S., T. Endo, H. Yajima, H. Ohuichi, H. Ida and K. Tamura. 1999. FGF7 and Fgf10 directly induce the apical ectodermal ridge in chick embryos. *Dev. Biol.* 211: 133–143.

Zákány, J., M. Kmita and D. Duboule. 2004. A dual role for Hox genes in limb anterior-posterior asymmetry. *Science* 304: 1669–1672.

Zaleske, D. J. 1985. Development of the upper limb. *Hand Clin.* 1: 383–390.

Zhang, Y. T., M. S. Alber, and S. A. Newman. 2013. Mathematical modeling of vertebrate limb development. *Math. Biosci.* 243: 1–17.

Zhang, Z., J. M. Verheyden, J. A. Hassell and X. Sun. 2009. FGF-regulated Etv genes are essential for repressing Shh expression in mouse limb buds. *Dev. Cell* 16: 607–613.

Zhao, X., I. O. Sirbu, F. A. Mic, N. Molotkova, A. Molotkov, S. Kumar, and G. Duester. 2009. Retinoic acid promotes limb induction through effects on body axis extension but is unnecessary for limb patterning. *Curr. Biol.* 19: 1050–1057.

Zhu, J. and S. Mackem. 2011. Analysis of mutants with altered Shh activity and posterior digit loss supports a biphasic model for Shh function as a morphogen and mitogen. *Dev. Dyn.* 240: 1303–1310.

Zhu, J., R. Patel, A. Trofka, B. D. Harfe and S. Makem. 2022. Sonic hedgehog is not a limb morphogen but acts as a trigger to specify all digits in mice. *Dev. Cell* 57: 2048–2062.e4.

Zhu, J., Y. T. Zhang, M. S. Alber and S. A. Newman. 2010. Bare bones pattern formation: A core regulatory network in varying geometries reproduces major features of vertebrate limb development and evolution. *PLoS ONE* 5: e10892.

Zou, H. and L. Niswander. 1996. Requirement for BMP signaling in interdigital apoptosis and scale formation. *Science* 272: 738–741.

Zuniga, A. 2015. Next generation limb development and evolution: Old questions, new perspectives. *Development* 142: 3810–3820.

Zuniga, A. and R. Zeller. 2014. In Turing's hands: The making of digits. *Science* 345: 516–517.

Zuniga, A. and R. Zeller. 2020. Dynamic and self-regulatory interactions among gene regulatory networks control vertebrate limb bud morphogenesis. *Curr. Top. Dev. Biol.* 139: 61–88.

Zuniga, A., A. P. Haramis, A. P. McMahon and R. Zeller. 1999. Signal relay by BMP antagonism controls the Shh/Fgf4 feedback loop in vertebrate limb buds. *Nature* 401: 598–602.

Zuzarte-Luis, V. and J. M. Hurle. 2005. Programmed cell death in the embryonic vertebrate limb. *Semin. Cell Dev. Biol.* 16: 261–269.

Zwilling, E. 1955. Ectoderm-mesoderm relationship in the development of the chick embryo limb bud. *J. Exp. Zool.* 128: 423–441.