

8 REFERENCES

- Aboobaker A, Blaxter M (2003) Hox gene evolution in nematodes: novelty conserved. *Curr Opin Genet Dev* 13:593-8
- Akarsu AN, Stoilov I, Yilmaz E, Sayli BS, Sarfarazi M (1996) Genomic structure of HOXD13 gene: a nine polyalanine duplication causes synpolydactyly in two unrelated families. *Hum Mol Genet* 5:945-52
- Akasaka T, Kanno M, Balling R, Mieza MA, Taniguchi M, Koseki H (1996) A role for mel-18, a Polycomb group-related vertebrate gene, during the anterior-posterior specification of the axial skeleton. *Development* 122:1513-22
- Albrecht AN, Kornak U, Boddrich A, Suring K, Robinson PN, Stiege AC, Lurz R, Stricker S, Wanker EE, Mundlos S (2004) A molecular pathogenesis for transcription factor associated poly-alanine tract expansions. *Hum Mol Genet* 13:2351-9
- Albrecht AN, Schwabe GC, Stricker S, Boddrich A, Wanker EE, Mundlos S (2002) The synpolydactyly homolog (spd) mutation in the mouse -- a defect in patterning and growth of limb cartilage elements. *Mech Dev* 112:53-67
- Alkema MJ, van der Lugt NM, Bobeldijk RC, Berns A, van Lohuizen M (1995) Transformation of axial skeleton due to overexpression of bmi-1 in transgenic mice. *Nature* 374:724-7
- Aoki T, Okada N, Wakamatsu T, Tamura TA (2002) TBP-interacting protein 120B, which is induced in relation to myogenesis, binds to NOT3. *Biochem Biophys Res Commun* 296:1097-103
- Barna M, Hawe N, Niswander L, Pandolfi PP (2000) Plzf regulates limb and axial skeletal patterning. *Nat Genet* 25:166-72
- Barna M, Merghoub T, Costoya JA, Ruggero D, Branford M, Bergia A, Samori B, Pandolfi PP (2002) Plzf mediates transcriptional repression of HoxD gene expression through chromatin remodeling. *Dev Cell* 3:499-510
- Barrow JR, Thomas KR, Boussadia-Zahui O, Moore R, Kemler R, Capecchi MR, McMahon AP (2003) Ectodermal Wnt3/beta-catenin signaling is required for the establishment and maintenance of the apical ectodermal ridge. *Genes Dev* 17:394-409

- Becker D, Jiang Z, Knodler P, Deinard AS, Eid R, Kidd KK, Shashikant CS, Ruddle FH, Schughart K (1996) Conserved regulatory element involved in the early onset of Hoxb6 gene expression. *Dev Dyn* 205:73-81
- Berthelsen J, Zappavigna V, Ferretti E, Mavilio F, Blasi F (1998) The novel homeoprotein Prep1 modulates Pbx-Hox protein cooperativity. *Embo J* 17:1434-45
- Boles RG, Pober BR, Gibson LH, Willis CR, McGrath J, Roberts DJ, Yang-Feng TL (1995) Deletion of chromosome 2q24-q31 causes characteristic digital anomalies: case report and review. *Am J Med Genet* 55:155-60
- Boulet AM, Capecchi MR (2004) Multiple roles of Hoxa11 and Hoxd11 in the formation of the mammalian forelimb zeugopod. *Development* 131:299-309
- Boutell JM, Thomas P, Neal JW, Weston VJ, Duce J, Harper PS, Jones AL (1999) Aberrant interactions of transcriptional repressor proteins with the Huntington's disease gene product, huntingtin. *Hum Mol Genet* 8:1647-55
- Bradford MM (1976) A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem* 72:248-54
- Bugge M, Bruun-Petersen G, Brondum-Nielsen K, Friedrich U, Hansen J, Jensen G, Jensen PK, Kristoffersson U, Lundsteen C, Niebuhr E, Rasmussen KR, Rasmussen K, Tommerup N (2000) Disease associated balanced chromosome rearrangements: a resource for large scale genotype-phenotype delineation in man. *J Med Genet* 37:858-65
- Burke AC, Nelson CE, Morgan BA, Tabin C (1995) Hox genes and the evolution of vertebrate axial morphology. *Development* 121:333-46
- Calabrese O, Bigoni S, Gualandi F, Trabanelli C, Camera G, E. C (2000) A new mutation in HOXD13 homeodomain causes a novel human limb malformation by producing selective loss of function. *Europ J Hum Genet* 8 (suppl. 1):140
- Calin GA, Sevignani C, Dumitru CD, Hyslop T, Noch E, Yendamuri S, Shimizu M, Rattan S, Bullrich F, Negrini M, Croce CM (2004) Human microRNA genes are frequently located at fragile sites and genomic regions involved in cancers. *Proc Natl Acad Sci U S A* 101:2999-3004
- Capdevila J, Izpisua Belmonte JC (2001) Patterning mechanisms controlling vertebrate limb development. *Annu Rev Cell Dev Biol* 17:87-132

- Capdevila J, Tsukui T, Rodriguez Esteban C, Zappavigna V, Izpisua Belmonte JC (1999) Control of vertebrate limb outgrowth by the proximal factor Meis2 and distal antagonism of BMPs by Gremlin. *Mol Cell* 4:839-49
- Caronia G, Goodman FR, McKeown CM, Scambler PJ, Zappavigna V (2003) An I47L substitution in the HOXD13 homeodomain causes a novel human limb malformation by producing a selective loss of function. *Development* 130:1701-12
- Carpenter EM, Goddard JM, Davis AP, Nguyen TP, Capecchi MR (1997) Targeted disruption of Hoxd-10 affects mouse hindlimb development. *Development* 124:4505-14
- Carroll SB (1995) Homeotic genes and the evolution of arthropods and chordates. *Nature* 376:479-85
- Carson JP, Eichele G, Chiu W (2005) A method for automated detection of gene expression required for the establishment of a digital transcriptome-wide gene expression atlas. *J Microsc* 217:275-81
- Catala M (2000) [Control of the positioning of the vertebrate limb axes during development]. *Morphologie* 84:17-23
- Chang CP, Brocchieri L, Shen WF, Largman C, Cleary ML (1996) Pbx modulation of Hox homeodomain amino-terminal arms establishes different DNA-binding specificities across the Hox locus. *Mol Cell Biol* 16:1734-45
- Chang CP, Jacobs Y, Nakamura T, Jenkins NA, Copeland NG, Cleary ML (1997) Meis proteins are major *in vivo* DNA binding partners for wild-type but not chimeric Pbx proteins. *Mol Cell Biol* 17:5679-87
- Chang CP, Shen WF, Rozenfeld S, Lawrence HJ, Largman C, Cleary ML (1995) Pbx proteins display hexapeptide-dependent cooperative DNA binding with a subset of Hox proteins. *Genes Dev* 9:663-74
- Chen Y, Knezevic V, Ervin V, Hutson R, Ward Y, Mackem S (2004) Direct interaction with Hoxd proteins reverses Gli3-repressor function to promote digit formation downstream of Shh. *Development* 131:2339-47
- Chen Y, Zhao X (1998) Shaping limbs by apoptosis. *J Exp Zool* 282:691-702
- Clack JA (2002) An early tetrapod from 'Romer's Gap'. *Nature* 418:72-6
- Coates MI, Clack JA (1990) Polydactyly in the earliest known tetrapod limbs. *Nature* 347:66-69
- Cohn MJ, Tickle C (1999) Developmental basis of limblessness and axial patterning in snakes. *Nature* 399:474-9

- Davis AP, Capecchi MR (1994) Axial homeosis and appendicular skeleton defects in mice with a targeted disruption of hoxd-11. *Development* 120:2187-98
- Davis AP, Capecchi MR (1996) A mutational analysis of the 5' HoxD genes: dissection of genetic interactions during limb development in the mouse. *Development* 122:1175-85
- Davis AP, Witte DP, Hsieh-Li HM, Potter SS, Capecchi MR (1995) Absence of radius and ulna in mice lacking hoxa-11 and hoxd-11. *Nature* 375:791-5
- Dawid IB, Breen JJ, Toyama R (1998) LIM domains: multiple roles as adapters and functional modifiers in protein interactions. *Trends Genet* 14:156-62
- de Graaff W, Tomotsune D, Oosterveen T, Takihara Y, Koseki H, Deschamps J (2003) Randomly inserted and targeted Hox/reporter fusions transcriptionally silenced in Polycomb mutants. *Proc Natl Acad Sci U S A* 100:13362-7
- de la Cruz CC, Der-Avakian A, Spyropoulos DD, Tieu DD, Carpenter EM (1999) Targeted disruption of Hoxd9 and Hoxd10 alters locomotor behavior, vertebral identity, and peripheral nervous system development. *Dev Biol* 216:595-610
- Debeer P, Bacchelli C, Scambler PJ, De Smet L, Fryns JP, Goodman FR (2002) Severe digital abnormalities in a patient heterozygous for both a novel missense mutation in HOXD13 and a polyalanine tract expansion in HOXA13. *J Med Genet* 39:852-6
- Del Campo M, Jones MC, Veraksa AN, Curry CJ, Jones KL, Mascarello JT, Ali-Kahn-Catts Z, Drumheller T, McGinnis W (1999) Monodactylous limbs and abnormal genitalia are associated with hemizygosity for the human 2q31 region that includes the HOXD cluster. *Am J Hum Genet* 65:104-10
- Deschamps J (2004) Developmental biology. Hox genes in the limb: a play in two acts. *Science* 304:1610-1
- Deschamps J, van den Akker E, Forlani S, De Graaff W, Oosterveen T, Roelen B, Roelfsema J (1999) Initiation, establishment and maintenance of Hox gene expression patterns in the mouse. *Int J Dev Biol* 43:635-50
- Di Paola J, Goldman T, Qian Q, Patil SR, Schute BC (2004) Breakpoint of a balanced translocation (X:14) (q27.1;q32.3) in a girl with severe hemophilia B maps proximal to the factor IX gene. *J Thromb Haemost* 2:437-40
- Dlugaszewska B, Silahtaroglu A, Menzel C, Kubart S, Cohen M, Mundlos S, Tumer Z, Kjaer K, Friedrich U, Ropers HH, Tommerup N, Neitzel H, Kalscheuer VM (2005)

- Breakpoints around the HOXD cluster result in various limb malformations. *J Med Genet*
- Dolle P, Dierich A, LeMeur M, Schimmang T, Schuhbaur B, Chambon P, Duboule D (1993) Disruption of the Hoxd-13 gene induces localized heterochrony leading to mice with neotenic limbs. *Cell* 75:431-41
- Drossopoulou G, Lewis KE, Sanz-Ezquerro JJ, Nikbakht N, McMahon AP, Hofmann C, Tickle C (2000) A model for anteroposterior patterning of the vertebrate limb based on sequential long- and short-range Shh signalling and Bmp signalling. *Development* 127:1337-48
- Duboule D (1994) How to make a limb? *Science* 266:575-6
- Dudley AT, Ros MA, Tabin CJ (2002) A re-examination of proximodistal patterning during vertebrate limb development. *Nature* 418:539-44
- Eid R, Koseki H, Schughart K (1993) Analysis of LacZ reporter genes in transgenic embryos suggests the presence of several cis-acting regulatory elements in the murine Hoxb-6 gene. *Dev Dyn* 196:205-16
- Fan J, Otterlei M, Wong HK, Tomkinson AE, Wilson DM, 3rd (2004) XRCC1 co-localizes and physically interacts with PCNA. *Nucleic Acids Res* 32:2193-201
- Fantes J, Redeker B, Breen M, Boyle S, Brown J, Fletcher J, Jones S, Bickmore W, Fukushima Y, Mannens M (1995) Aniridia-associated cytogenetic rearrangements suggest that a position effect may cause the mutant phenotype. *Hum Mol Genet* 4:415-22
- Favier B, Le Meur M, Chambon P, Dolle P (1995) Axial skeleton homeosis and forelimb malformations in Hoxd-11 mutant mice. *Proc Natl Acad Sci U S A* 92:310-4
- Favier B, Rijli FM, Fromental-Ramain C, Fraulob V, Chambon P, Dolle P (1996) Functional cooperation between the non-paralogous genes Hoxa-10 and Hoxd-11 in the developing forelimb and axial skeleton. *Development* 122:449-60
- Ferretti E, Schulz H, Talarico D, Blasi F, Berthelsen J (1999) The PBX-regulating protein PREP1 is present in different PBX-complexed forms in mouse. *Mech Dev* 83:53-64
- Fognani C, Kilstrup-Nielsen C, Berthelsen J, Ferretti E, Zappavigna V, Blasi F (2002) Characterization of PREP2, a paralog of PREP1, which defines a novel sub-family of the MEINOX TALE homeodomain transcription factors. *Nucleic Acids Res* 30:2043-51

- Fromental-Ramain C, Warot X, Lakkaraju S, Favier B, Haack H, Birling C, Dierich A, Doll e P, Chambon P (1996) Specific and redundant functions of the paralogous Hoxa-9 and Hoxd-9 genes in forelimb and axial skeleton patterning. *Development* 122:461-72
- Gaunt SJ (2000) Evolutionary shifts of vertebrate structures and Hox expression up and down the axial series of segments: a consideration of possible mechanisms. *Int J Dev Biol* 44:109-17
- Gehring WJ, Affolter M, Burglin T (1994) Homeodomain proteins. *Annu Rev Biochem* 63:487-526
- Gerard M, Duboule D, Zakany J (1993) Structure and activity of regulatory elements involved in the activation of the Hoxd-11 gene during late gastrulation. *Embo J* 12:3539-50
- Glassner BJ, Weeda G, Allan JM, Broekhof JL, Carls NH, Donker I, Engelward BP, Hampson RJ, Hersmus R, Hickman MJ, Roth RB, Warren HB, Wu MM, Hoeijmakers JH, Samson LD (1999) DNA repair methyltransferase (Mgmt) knockout mice are sensitive to the lethal effects of chemotherapeutic alkylating agents. *Mutagenesis* 14:339-47
- Goodman F, Giovannucci-Uzielli ML, Hall C, Reardon W, Winter R, Scambler P (1998) Deletions in HOXD13 segregate with an identical, novel foot malformation in two unrelated families. *Am J Hum Genet* 63:992-1000
- Goodman FR (2002) Limb malformations and the human HOX genes. *Am J Med Genet* 112:256-65
- Goodman FR, Bacchelli C, Brady AF, Brueton LA, Fryns JP, Mortlock DP, Innis JW, Holmes LB, Donnenfeld AE, Feingold M, Beemer FA, Hennekam RC, Scambler PJ (2000) Novel HOXA13 mutations and the phenotypic spectrum of hand-foot-genital syndrome. *Am J Hum Genet* 67:197-202
- Goodman FR, Majewski F, Collins AL, Scambler PJ (2002) A 117-kb microdeletion removing HOXD9-HOXD13 and EVX2 causes synpolydactyly. *Am J Hum Genet* 70:547-55
- Goodman FR, Mundlos S, Muragaki Y, Donnai D, Giovannucci-Uzielli ML, Lapi E, Majewski F, McGaughran J, McKeown C, Reardon W, Upton J, Winter RM, Olsen BR, Scambler PJ (1997) Synpolydactyly phenotypes correlate with size of expansions in HOXD13 polyalanine tract. *Proc Natl Acad Sci U S A* 94:7458-63

- Gould A, Itasaki N, Krumlauf R (1998) Initiation of rhombomeric Hoxb4 expression requires induction by somites and a retinoid pathway. *Neuron* 21:39-51
- Gould A, Morrison A, Sproat G, White RA, Krumlauf R (1997) Positive cross-regulation and enhancer sharing: two mechanisms for specifying overlapping Hox expression patterns. *Genes Dev* 11:900-13
- Grafstrom RC, Pegg AE, Trump BF, Harris CC (1984) O6-alkylguanine-DNA alkyltransferase activity in normal human tissues and cells. *Cancer Res* 44:2855-7
- Griffin C, Kleinjan DA, Doe B, van Heyningen V (2002) New 3' elements control Pax6 expression in the developing pretectum, neural retina and olfactory region. *Mech Dev* 112:89-100
- Guha U, Gomes WA, Kobayashi T, Pestell RG, Kessler JA (2002) In vivo evidence that BMP signaling is necessary for apoptosis in the mouse limb. *Dev Biol* 249:108-20
- Herault Y, Beckers J, Gerard M, Duboule D (1999) Hox gene expression in limbs: colinearity by opposite regulatory controls. *Dev Biol* 208:157-65
- Herault Y, Fraudeau N, Zakany J, Duboule D (1997) Ulnaless (Ul), a regulatory mutation inducing both loss-of-function and gain-of-function of posterior Hoxd genes. *Development* 124:3493-500
- Hill A, Wagner A, Hill M (2003) Hox and paraHox genes from the anthozoan Parazoanthus parasiticus. *Mol Phylogenet Evol* 28:529-35
- Innis JW, Goodman FR, Bacchelli C, Williams TM, Mortlock DP, Sateesh P, Scambler PJ, McKinnon W, Guttmacher AE (2002) A HOXA13 allele with a missense mutation in the homeobox and a dinucleotide deletion in the promoter underlies Guttmacher syndrome. *Hum Mutat* 19:573-4
- Izpisua-Belmonte JC, Duboule D (1992) Homeobox genes and pattern formation in the vertebrate limb. *Dev Biol* 152:26-36
- Jiang G, Yang F, van Overveld PG, Vedanarayanan V, van der Maarel S, Ehrlich M (2003) Testing the position-effect variegation hypothesis for facioscapulohumeral muscular dystrophy by analysis of histone modification and gene expression in subtelomeric 4q. *Hum Mol Genet* 12:2909-21
- Johnson RL, Riddle RD, Laufer E, Tabin C (1994) Sonic hedgehog: a key mediator of anterior-posterior patterning of the limb and dorso-ventral patterning of axial embryonic structures. *Biochem Soc Trans* 22:569-74

- Johnson RL, Tabin CJ (1997) Molecular models for vertebrate limb development. *Cell* 90:979-90
- Kan SH, Johnson D, Giele H, Wilkie AO (2003) An acceptor splice site mutation in HOXD13 results in variable hand, but consistent foot malformations. *Am J Med Genet* 121A:69-74
- Kjaer KW, Hedeboe J, Bugge M, Hansen C, Friis-Henriksen K, Vestergaard MB, Tommerup N, Opitz JM (2002) HOXD13 polyalanine tract expansion in classical synpolydactyly type Vordingborg. *Am J Med Genet* 110:116-21
- Kleinjan DA, Seawright A, Schedl A, Quinlan RA, Danes S, van Heyningen V (2001) Aniridia-associated translocations, DNase hypersensitivity, sequence comparison and transgenic analysis redefine the functional domain of PAX6. *Hum Mol Genet* 10:2049-59
- Kleinjan DA, van Heyningen V (2004) Long-Range Control of Gene Expression: Emerging Mechanisms and Disruption in Disease. *Am J Hum Genet* 76
- Kleinjan DJ, van Heyningen V (1998) Position effect in human genetic disease. *Hum Mol Genet* 7:1611-8
- Kmita M, Duboule D (2003) Organizing axes in time and space; 25 years of colinear tinkering. *Science* 301:331-3
- Kmita M, Fraudeau N, Herault Y, Duboule D (2002a) Serial deletions and duplications suggest a mechanism for the collinearity of Hoxd genes in limbs. *Nature* 420:145-50
- Kmita M, Tarchini B, Duboule D, Herault Y (2002b) Evolutionary conserved sequences are required for the insulation of the vertebrate Hoxd complex in neural cells. *Development* 129:5521-8
- Knezevic V, De Santo R, Schughart K, Huffstadt U, Chiang C, Mahon KA, Mackem S (1997) Hoxd-12 differentially affects preaxial and postaxial chondrogenic branches in the limb and regulates Sonic hedgehog in a positive feedback loop. *Development* 124:4523-36
- Knittel T, Kessel M, Kim MH, Gruss P (1995) A conserved enhancer of the human and murine Hoxa-7 gene specifies the anterior boundary of expression during embryonal development. *Development* 121:1077-88
- Knoepfler PS, Calvo KR, Chen H, Antonarakis SE, Kamps MP (1997) Meis1 and pKnox1 bind DNA cooperatively with Pbx1 utilizing an interaction surface disrupted in oncoprotein E2a-Pbx1. *Proc Natl Acad Sci U S A* 94:14553-8

- Knoepfler PS, Kamps MP (1995) The pentapeptide motif of Hox proteins is required for cooperative DNA binding with Pbx1, physically contacts Pbx1, and enhances DNA binding by Pbx1. *Mol Cell Biol* 15:5811-9
- Knoepfler PS, Kamps MP (1997) The highest affinity DNA element bound by Pbx complexes in t(1;19) leukemic cells fails to mediate cooperative DNA-binding or cooperative transactivation by E2a-Pbx1 and class I Hox proteins - evidence for selective targetting of E2a-Pbx1 to a subset of Pbx-recognition elements. *Oncogene* 14:2521-31
- Knoepfler PS, Lu Q, Kamps MP (1996) Pbx-1 Hox heterodimers bind DNA on inseparable half-sites that permit intrinsic DNA binding specificity of the Hox partner at nucleotides 3' to a TAAT motif. *Nucleic Acids Res* 24:2288-94
- Knosp WM, Scott V, Bachinger HP, Stadler HS (2004) HOXA13 regulates the expression of bone morphogenetic proteins 2 and 7 to control distal limb morphogenesis. *Development* 131:4581-92
- Kondo T, Dolle P, Zakany J, Duboule D (1996) Function of posterior HoxD genes in the morphogenesis of the anal sphincter. *Development* 122:2651-9
- Kondo T, Duboule D (1999) Breaking colinearity in the mouse HoxD complex. *Cell* 97:407-17
- Kondo T, Zakany J, Duboule D (1998) Control of colinearity in AbdB genes of the mouse HoxD complex. *Mol Cell* 1:289-300
- Kornberg RD, Lorch Y (1992) Chromatin structure and transcription. *Annu Rev Cell Biol* 8:563-87
- Kraus P, Fraidenraich D, Loomis CA (2001) Some distal limb structures develop in mice lacking Sonic hedgehog signaling. *Mech Dev* 100:45-58
- Krokan H, Haugen A, Myrnes B, Guddal PH (1983) Repair of premutagenic DNA lesions in human fetal tissues: evidence for low levels of O6-methylguanine-DNA methyltransferase and uracil-DNA glycosylase activity in some tissues. *Carcinogenesis* 4:1559-64
- Kwan CT, Tsang SL, Krumlauf R, Sham MH (2001) Regulatory analysis of the mouse Hoxb3 gene: multiple elements work in concert to direct temporal and spatial patterns of expression. *Dev Biol* 232:176-90
- Lauderdale JD, Wilensky JS, Oliver ER, Walton DS, Glaser T (2000) 3' deletions cause aniridia by preventing PAX6 gene expression. *Proc Natl Acad Sci U S A* 97:13755-9

- Laufer E, Nelson CE, Johnson RL, Morgan BA, Tabin C (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
- Lawrence HJ, Fischbach NA, Largman C (2005) HOX genes: not just myeloid oncogenes any more. *Leukemia* 19:1328-30
- Lebedev O (1997) Fins made for walking. *Nature* 390:21-22
- Lehoczky JA, Williams ME, Innis JW (2004) Conserved expression domains for genes upstream and within the HoxA and HoxD clusters suggests a long-range enhancer existed before cluster duplication. *Evol Dev* 6:423-30
- Lewandoski M, Sun X, Martin GR (2000) Fgf8 signalling from the AER is essential for normal limb development. *Nat Genet* 26:460-3
- Loots GG, Locksley RM, Blanksespoor CM, Wang ZE, Miller W, Rubin EM, Frazer KA (2000) Identification of a coordinate regulator of interleukins 4, 13, and 5 by cross-species sequence comparisons. *Science* 288:136-40
- Lower KM, Kumar R, Woollatt E, Villard L, Gecz J, Sutherland GR, Callen DF (2004) Partial Androgen Insensitivity Syndrome and t(X;5): Are There Upstream Regulatory Elements of the Androgen Receptor Gene? *Horm Res* 62:208-214
- Lu Q, Kamps MP (1997) Heterodimerization of Hox proteins with Pbx1 and oncoprotein E2a-Pbx1 generates unique DNA-binding specificities at nucleotides predicted to contact the N-terminal arm of the Hox homeodomain--demonstration of Hox-dependent targeting of E2a-Pbx1 in vivo. *Oncogene* 14:75-83
- Lu Q, Knoepfler PS, Scheele J, Wright DD, Kamps MP (1995) Both Pbx1 and E2A-Pbx1 bind the DNA motif ATCAATCAA cooperatively with the products of multiple murine Hox genes, some of which are themselves oncogenes. *Mol Cell Biol* 15:3786-95
- Lux A, Beil C, Majety M, Barron S, Gallione CJ, Kuhn HM, Berg JN, Kioschis P, Marchuk DA, Hafner M (2005) Human retroviral gag- and gag-pol-like proteins interact with the transforming growth factor-beta receptor activin receptor-like kinase 1. *J Biol Chem* 280:8482-93
- Mackem S, Knezevic V (1999) Do 5'Hoxd genes play a role in initiating or maintaining A-P polarizing signals in the limb? *Cell Tissue Res* 296:27-31
- Maconochie M, Nonchev S, Morrison A, Krumlauf R (1996) Paralogous Hox genes: function and regulation. *Annu Rev Genet* 30:529-56

- Maconochie MK, Nonchev S, Studer M, Chan SK, Popperl H, Sham MH, Mann RS, Krumlauf R (1997) Cross-regulation in the mouse HoxB complex: the expression of Hoxb2 in rhombomere 4 is regulated by Hoxb1. *Genes Dev* 11:1885-95
- Manktelow E, Shigemoto K, Brierley I (2005) Characterization of the frameshift signal of Edr, a mammalian example of programmed -1 ribosomal frameshifting. *Nucleic Acids Res* 33:1553-63
- Mansfield JH, Harfe BD, Nissen R, Obenauer J, Srineel J, Chaudhuri A, Farzan-Kashani R, Zuker M, Pasquinelli AE, Ruvkun G, Sharp PA, Tabin CJ, McManus MT (2004) MicroRNA-responsive 'sensor' transgenes uncover Hox-like and other developmentally regulated patterns of vertebrate microRNA expression. *Nat Genet*
- Manzanares M, Bel-Vialar S, Ariza-McNaughton L, Ferretti E, Marshall H, Maconochie MM, Blasi F, Krumlauf R (2001) Independent regulation of initiation and maintenance phases of Hoxa3 expression in the vertebrate hindbrain involve auto- and cross-regulatory mechanisms. *Development* 128:3595-607
- Manzanares M, Cordes S, Ariza-McNaughton L, Sadl V, Maruthainar K, Barsh G, Krumlauf R (1999) Conserved and distinct roles of kreasler in regulation of the paralogous Hoxa3 and Hoxb3 genes. *Development* 126:759-69
- Manzanares M, Cordes S, Kwan CT, Sham MH, Barsh GS, Krumlauf R (1997) Segmental regulation of Hoxb-3 by kreasler. *Nature* 387:191-5
- Manzanares M, Nardelli J, Gilardi-Hebenstreit P, Marshall H, Giudicelli F, Martinez-Pastor MT, Krumlauf R, Charnay P (2002) Krox20 and kreasler co-operate in the transcriptional control of segmental expression of Hoxb3 in the developing hindbrain. *Embo J* 21:365-76
- Marlin S, Blanchard S, Slim R, Lacombe D, Denoyelle F, Alessandri JL, Calzolari E, Drouin-Garraud V, Ferraz FG, Fourmaintraux A, Philip N, Toublanc JE, Petit C (1999) Townes-Brocks syndrome: detection of a SALL1 mutation hot spot and evidence for a position effect in one patient. *Hum Mutat* 14:377-86
- Martinez P, Rast JP, Arenas-Mena C, Davidson EH (1999) Organization of an echinoderm Hox gene cluster. *Proc Natl Acad Sci U S A* 96:1469-74
- Masuda Y, Sasaki A, Shibuya H, Ueno N, Ikeda K, Watanabe K (2001) Dlxin-1, a novel protein that binds Dlx5 and regulates its transcriptional function. *J Biol Chem* 276:5331-8

- Matsuda T, Suzuki H, Oishi I, Kani S, Kuroda Y, Komori T, Sasaki A, Watanabe K, Minami Y (2003) The receptor tyrosine kinase Ror2 associates with the melanoma-associated antigen (MAGE) family protein Dlxin-1 and regulates its intracellular distribution. *J Biol Chem* 278:29057-64
- Mercader N, Leonardo E, Azpiazu N, Serrano A, Morata G, Martinez C, Torres M (1999) Conserved regulation of proximodistal limb axis development by Meis1/Hth. *Nature* 402:425-9
- Mercader N, Leonardo E, Piedra ME, Martinez AC, Ros MA, Torres M (2000) Opposing RA and FGF signals control proximodistal vertebrate limb development through regulation of Meis genes. *Development* 127:3961-70
- Morrison A, Ariza-McNaughton L, Gould A, Featherstone M, Krumlauf R (1997) HOXD4 and regulation of the group 4 paralog genes. *Development* 124:3135-46
- Morrison A, Moroni MC, Ariza-McNaughton L, Krumlauf R, Mavilio F (1996) In vitro and transgenic analysis of a human HOXD4 retinoid-responsive enhancer. *Development* 122:1895-907
- Mortlock DP, Innis JW (1997) Mutation of HOXA13 in hand-foot-genital syndrome. *Nat Genet* 15:179-80
- Muncke N, Wogatzky BS, Breuning M, Sistermans EA, Endris V, Ross M, Vetrie D, Catsman-Berrevoets CE, Rappold G (2004) Position effect on PLP1 may cause a subset of Pelizaeus-Merzbacher disease symptoms. *J Med Genet* 41:e121
- Muragaki Y, Mundlos S, Upton J, Olsen BR (1996) Altered growth and branching patterns in synpolydactyly caused by mutations in HOXD13. *Science* 272:548-51
- Nakamura M, Watanabe T, Yonekawa Y, Kleihues P, Ohgaki H (2001) Promoter methylation of the DNA repair gene MGMT in astrocytomas is frequently associated with G:C --> A:T mutations of the TP53 tumor suppressor gene. *Carcinogenesis* 22:1715-9
- Nakatsu Y, Hattori K, Hayakawa H, Shimizu K, Sekiguchi M (1993) Organization and expression of the human gene for O6-methylguanine-DNA methyltransferase. *Mutat Res* 293:119-32
- Nelson CE, Morgan BA, Burke AC, Laufer E, DiMambro E, Murtaugh LC, Gonzales E, Tessarollo L, Parada LF, Tabin C (1996) Analysis of Hox gene expression in the chick limb bud. *Development* 122:1449-66
- Niswander L, Jeffrey S, Martin GR, Tickle C (1994) A positive feedback loop coordinates growth and patterning in the vertebrate limb. *Nature* 371:609-12

- Niswander L, Martin GR (1992) Fgf-4 expression during gastrulation, myogenesis, limb and tooth development in the mouse. *Development* 114:755-68
- Niswander L, Tickle C, Vogel A, Booth I, Martin GR (1993) FGF-4 replaces the apical ectodermal ridge and directs outgrowth and patterning of the limb. *Cell* 75:579-87
- Nixon J, Oldridge M, Wilkie AO, Smith K (1997) Interstitial deletion of 2q associated with craniosynostosis, ocular coloboma, and limb abnormalities: cytogenetic and molecular investigation. *Am J Med Genet* 70:324-7
- Nourani A, Utley RT, Allard S, Cote J (2004) Recruitment of the NuA4 complex poises the PHO5 promoter for chromatin remodeling and activation. *Embo J* 23:2597-607
- Okabe H, Satoh S, Furukawa Y, Kato T, Hasegawa S, Nakajima Y, Yamaoka Y, Nakamura Y (2003) Involvement of PEG10 in human hepatocellular carcinogenesis through interaction with SIAH1. *Cancer Res* 63:3043-8
- Ono R, Kobayashi S, Wagatsuma H, Aisaka K, Kohda T, Kaneko-Ishino T, Ishino F (2001) A retrotransposon-derived gene, PEG10, is a novel imprinted gene located on human chromosome 7q21. *Genomics* 73:232-7
- Ono R, Shiura H, Aburatani H, Kohda T, Kaneko-Ishino T, Ishino F (2003) Identification of a large novel imprinted gene cluster on mouse proximal chromosome 6. *Genome Res* 13:1696-705
- Oosterveen T, Niederreither K, Dolle P, Chambon P, Meijlink F, Deschamps J (2003) Retinoids regulate the anterior expression boundaries of 5' Hoxb genes in posterior hindbrain. *Embo J* 22:262-9
- Oue N, Shigeishi H, Kuniyasu H, Yokozaki H, Kuraoka K, Ito R, Yasui W (2001) Promoter hypermethylation of MGMT is associated with protein loss in gastric carcinoma. *Int J Cancer* 93:805-9
- Packer AI, Crotty DA, Elwell VA, Wolgemuth DJ (1998) Expression of the murine Hoxa4 gene requires both autoregulation and a conserved retinoic acid response element. *Development* 125:1991-8
- Panman L, Zeller R (2003) Patterning the limb before and after SHH signalling. *J Anat* 202:3-12
- Pegg AE, Dolan ME, Scicchitano D, Morimoto K (1985) Studies of the repair of O6-alkylguanine and O4-alkylthymine in DNA by alkyltransferases from mammalian cells and bacteria. *Environ Health Perspect* 62:109-14

- Peichel CL, Prabhakaran B, Vogt TF (1997) The mouse Ulnaless mutation deregulates posterior HoxD gene expression and alters appendicular patterning. *Development* 124:3481-92
- Pellerin I, Schnabel C, Catron KM, Abate C (1994) Hox proteins have different affinities for a consensus DNA site that correlate with the positions of their genes on the hox cluster. *Mol Cell Biol* 14:4532-45
- Popperl H, Featherstone MS (1992) An autoregulatory element of the murine Hox-4.2 gene. *Embo J* 11:3673-80
- Rancourt DE, Tsuzuki T, Capecchi MR (1995) Genetic interaction between hoxb-5 and hoxb-6 is revealed by nonallelic noncomplementation. *Genes Dev* 9:108-22
- Reese JS, Allay E, Gerson SL (2001) Overexpression of human O6-alkylguanine DNA alkyltransferase (AGT) prevents MNU induced lymphomas in heterozygous p53 deficient mice. *Oncogene* 20:5258-63
- Roelen BA, de Graaff W, Forlani S, Deschamps J (2002) Hox cluster polarity in early transcriptional availability: a high order regulatory level of clustered Hox genes in the mouse. *Mech Dev* 119:81-90
- Rosso S, Bollati F, Bisbal M, Peretti D, Sumi T, Nakamura T, Quiroga S, Ferreira A, Caceres A (2004) LIMK1 regulates Golgi dynamics, traffic of Golgi-derived vesicles, and process extension in primary cultured neurons. *Mol Biol Cell* 15:3433-49
- Rowe DA, Fallon JF (1982) The proximodistal determination of skeletal parts in the developing chick leg. *J Embryol Exp Morphol* 68:1-7
- Sakumi K, Shiraishi A, Shimizu S, Tsuzuki T, Ishikawa T, Sekiguchi M (1997) Methylnitrosourea-induced tumorigenesis in MGMT gene knockout mice. *Cancer Res* 57:2415-8
- Sambrook J, Fritsch EF, Maniatis T (1989) Molecular Cloning : A Laboratory Manual. Cold Spring Harbor Laboratory Press
- Saunders JW, Jr. (1998) The proximo-distal sequence of origin of the parts of the chick wing and the role of the ectoderm. 1948. *J Exp Zool* 282:628-68
- Schumacher A, Magnusson T (1997) Murine Polycomb- and trithorax-group genes regulate homeotic pathways and beyond. *Trends Genet* 13:167-70
- Sham MH, Vesque C, Nonchev S, Marshall H, Frain M, Gupta RD, Whiting J, Wilkinson D, Charnay P, Krumlauf R (1993) The zinc finger gene Krox20 regulates HoxB2 (Hox2.8) during hindbrain segmentation. *Cell* 72:183-96

- Shanmugam K, Green NC, Rambaldi I, Saragovi HU, Featherstone MS (1999) PBX and MEIS as non-DNA-binding partners in trimeric complexes with HOX proteins. Mol Cell Biol 19:7577-88
- Sharp TV, Munoz F, Bourboulia D, Presneau N, Darai E, Wang HW, Cannon M, Butcher DN, Nicholson AG, Klein G, Imreh S, Boshoff C (2004) LIM domains-containing protein 1 (LIMD1), a tumor suppressor encoded at chromosome 3p21.3, binds pRB and represses E2F-driven transcription. Proc Natl Acad Sci U S A 101:16531-6
- Sharpe J, Nonchev S, Gould A, Whiting J, Krumlauf R (1998) Selectivity, sharing and competitive interactions in the regulation of Hoxb genes. Embo J 17:1788-98
- Shashikant CS, Bieberich CJ, Belting HG, Wang JC, Borbely MA, Ruddle FH (1995) Regulation of Hoxc-8 during mouse embryonic development: identification and characterization of critical elements involved in early neural tube expression. Development 121:4339-47
- Shen WF, Chang CP, Rozenfeld S, Sauvageau G, Humphries RK, Lu M, Lawrence HJ, Cleary ML, Largman C (1996) Hox homeodomain proteins exhibit selective complex stabilities with Pbx and DNA. Nucleic Acids Res 24:898-906
- Shen WF, Montgomery JC, Rozenfeld S, Moskow JJ, Lawrence HJ, Buchberg AM, Largman C (1997a) AbdB-like Hox proteins stabilize DNA binding by the Meis1 homeodomain proteins. Mol Cell Biol 17:6448-58
- Shen WF, Rozenfeld S, Lawrence HJ, Largman C (1997b) The Abd-B-like Hox homeodomain proteins can be subdivided by the ability to form complexes with Pbx1a on a novel DNA target. J Biol Chem 272:8198-206
- Shigemoto K, Brennan J, Walls E, Watson CJ, Stott D, Rigby PW, Reith AD (2001) Identification and characterisation of a developmentally regulated mammalian gene that utilises -1 programmed ribosomal frameshifting. Nucleic Acids Res 29:4079-88
- Shrimpton AE, Levinsohn EM, Yozawitz JM, Packard DS, Jr., Cady RB, Middleton FA, Persico AM, Hootnick DR (2004) A HOX gene mutation in a family with isolated congenital vertical talus and Charcot-Marie-Tooth disease. Am J Hum Genet 75:92-6
- Shubin N, Tabin C, Carroll S (1997) Fossils, genes and the evolution of animal limbs. Nature 388:639-48
- Siebert PD, Chenchik A, Kellogg DE, Lukyanov KA, Lukyanov SA (1995) An improved PCR method for walking in uncloned genomic DNA Nucleic Acids Res. Vol. 23, pp 1087-8

- Simon J (1995) Locking in stable states of gene expression: transcriptional control during Drosophila development. *Curr Opin Cell Biol* 7:376-85
- Slavotinek A, Schwarz C, Getty JF, Stecko O, Goodman F, Kingston H (1999) Two cases with interstitial deletions of chromosome 2 and sex reversal in one. *Am J Med Genet* 86:75-81
- Small KM, Potter SS (1993) Homeotic transformations and limb defects in Hox A11 mutant mice. *Genes Dev* 7:2318-28
- Smith-Sorensen B, Lind GE, Skotheim RI, Fossa SD, Fodstad O, Stenwig AE, Jakobsen KS, Lothe RA (2002) Frequent promoter hypermethylation of the O6-Methylguanine-DNA Methyltransferase (MGMT) gene in testicular cancer. *Oncogene* 21:8878-84
- Sordino P, Duboule D (1996) A molecular approach to the evolution of vertebrate paired appendages. *TREE* 11:114-119
- Sordino P, van der Hoeven F, Duboule D (1995) Hox gene expression in teleost fins and the origin of vertebrate digits. *Nature* 375:678-81
- Spitz F, Gonzalez F, Duboule D (2003) A global control region defines a chromosomal regulatory landscape containing the HoxD cluster. *Cell* 113:405-17
- Spitz F, Gonzalez F, Peichel C, Vogt TF, Duboule D, Zakany J (2001) Large scale transgenic and cluster deletion analysis of the HoxD complex separate an ancestral regulatory module from evolutionary innovations. *Genes Dev* 15:2209-14
- Spitz F, Montavon T, Monso-Hinard C, Morris M, Ventruto ML, Antonarakis S, Ventruto V, Duboule D (2002) A t(2;8) balanced translocation with breakpoints near the human HOXD complex causes mesomelic dysplasia and vertebral defects. *Genomics* 79:493-8
- Stanyon CA, Bernard O (1999) LIM-kinase1. *Int J Biochem Cell Biol* 31:389-94
- Steffan JS, Kazantsev A, Spasic-Boskovic O, Greenwald M, Zhu YZ, Gohler H, Wanker EE, Bates GP, Housman DE, Thompson LM (2000) The Huntington's disease protein interacts with p53 and CREB-binding protein and represses transcription. *Proc Natl Acad Sci U S A* 97:6763-8
- Steplewski A, Krynska B, Tretiakova A, Haas S, Khalili K, Amini S (1998) MyEF-3, a developmentally controlled brain-derived nuclear protein which specifically interacts with myelin basic protein proximal regulatory sequences. *Biochem Biophys Res Commun* 243:295-301

- Summerbell D (1974) A quantitative analysis of the effect of excision of the AER from the chick limb-bud. *J Embryol Exp Morphol* 32:651-60
- Summerbell D, Lewis JH, Wolpert L (1973) Positional information in chick limb morphogenesis. *Nature* 244:492-6
- Sun X, Mariani FV, Martin GR (2002) Functions of FGF signalling from the apical ectodermal ridge in limb development. *Nature* 418:501-8
- Suzuki M, Ueno N, Kuroiwa A (2003) Hox proteins functionally cooperate with the GC box-binding protein system through distinct domains. *J Biol Chem* 278:30148-56
- Tadin-Strapps M, Warburton D, Baumeister FA, Fischer SG, Yonan J, Gilliam TC, Christiano AM (2004) Cloning of the breakpoints of a de novo inversion of chromosome 8, inv(8)(p11.2q23.1) in a patient with Ambras syndrome. *Cytogenet Genome Res* 107:68-76
- Taniguchi T, Garcia-Higuera I, Andreassen PR, Gregory RC, Grompe M, D'Andrea AD (2002) S-phase-specific interaction of the Fanconi anemia protein, FANCD2, with BRCA1 and RAD51. *Blood* 100:2414-20
- te Welscher P, Fernandez-Teran M, Ros MA, Zeller R (2002a) Mutual genetic antagonism involving GLI3 and dHAND prepatterns the vertebrate limb bud mesenchyme prior to SHH signaling. *Genes Dev* 16:421-6
- te Welscher P, Zuniga A, Kuijper S, Drenth T, Goedemans HJ, Meijlink F, Zeller R (2002b) Progression of vertebrate limb development through SHH-mediated counteraction of GLI3. *Science* 298:827-30
- Thompson AA, Nguyen LT (2000) Amegakaryocytic thrombocytopenia and radio-ulnar synostosis are associated with HOXA11 mutation. *Nat Genet* 26:397-8
- Tickle C, Munsterberg A (2001) Vertebrate limb development--the early stages in chick and mouse. *Curr Opin Genet Dev* 11:476-81
- Tsou AP, Chuang YC, Su JY, Yang CW, Liao YL, Liu WK, Chiu JH, Chou CK (2003) Overexpression of a novel imprinted gene, PEG10, in human hepatocellular carcinoma and in regenerating mouse livers. *J Biomed Sci* 10:625-35
- Tsuzuki T, Sakumi K, Shiraishi A, Kawate H, Igarashi H, Iwakuma T, Tominaga Y, Zhang S, Shimizu S, Ishikawa T, et al. (1996) Targeted disruption of the DNA repair methyltransferase gene renders mice hypersensitive to alkylating agent. *Carcinogenesis* 17:1215-20

- van der Hoeven F, Zakany J, Duboule D (1996) Gene transpositions in the HoxD complex reveal a hierarchy of regulatory controls. *Cell* 85:1025-35
- Wagner GP, Amemiya C, Ruddle F (2003) Hox cluster duplications and the opportunity for evolutionary novelties. *Proc Natl Acad Sci U S A* 100:14603-6
- Wahba GM, Hostikka SL, Carpenter EM (2001) The paralogous Hox genes Hoxa10 and Hoxd10 interact to pattern the mouse hindlimb peripheral nervous system and skeleton. *Dev Biol* 231:87-102
- Whiting J, Marshall H, Cook M, Krumlauf R, Rigby PW, Stott D, Allemand RK (1991) Multiple spatially specific enhancers are required to reconstruct the pattern of Hox-2.6 gene expression. *Genes Dev* 5:2048-59
- Wiestler O, Kleihues P, Pegg AE (1984) O6-alkylguanine-DNA alkyltransferase activity in human brain and brain tumors. *Carcinogenesis* 5:121-4
- Wirth J, Nothwang HG, van der Maarel S, Menzel C, Borck G, Lopez-Pajares I, Brondum-Nielsen K, Tommerup N, Bugge M, Ropers HH, Haaf T (1999) Systematic characterisation of disease associated balanced chromosome rearrangements by FISH: cytogenetically and genetically anchored YACs identify microdeletions and candidate regions for mental retardation genes. *J Med Genet* 36:271-8
- Yang N, Mizuno K (1999) Nuclear export of LIM-kinase 1, mediated by two leucine-rich nuclear-export signals within the PDZ domain. *Biochem J* 338 (Pt 3):793-8
- Yau TO, Kwan CT, Jakt LM, Stallwood N, Cordes S, Sham MH (2002) Auto/cross-regulation of Hoxb3 expression in posterior hindbrain and spinal cord. *Dev Biol* 252:287-300
- Yekta S, Shih IH, Bartel DP (2004) MicroRNA-directed cleavage of HOXB8 mRNA. *Science* 304:594-6
- Yin X, Warner DR, Roberts EA, Pisano MM, Greene RM (2005) Identification of novel CBP interacting proteins in embryonic orofacial tissue. *Biochem Biophys Res Commun* 329:1010-7
- Yokouchi Y, Sakiyama J, Kameda T, Iba H, Suzuki A, Ueno N, Kuroiwa A (1996) BMP-2/-4 mediate programmed cell death in chicken limb buds. *Development* 122:3725-34
- Zakany J, Duboule D (1999) Hox genes in digit development and evolution. *Cell Tissue Res* 296:19-25
- Zakany J, Fromental-Ramain C, Warot X, Duboule D (1997) Regulation of number and size of digits by posterior Hox genes: a dose-dependent mechanism with potential evolutionary implications. *Proc Natl Acad Sci U S A* 94:13695-700

- Zakany J, Kmita M, Duboule D (2004) A dual role for Hox genes in limb anterior-posterior asymmetry. *Science* 304:1669-72
- Zeller R, Deschamps J (2002) Developmental biology: first come, first served. *Nature* 420:138-9
- Zhang F, Nagy Kovacs E, Featherstone MS (2000) Murine *hoxd4* expression in the CNS requires multiple elements including a retinoic acid response element. *Mech Dev* 96:79-89
- Zhou ZQ, Manguino D, Kewitt K, Intano GW, McMahan CA, Herbert DC, Hanes M, Reddick R, Ikeno Y, Walter CA (2001) Spontaneous hepatocellular carcinoma is reduced in transgenic mice overexpressing human O6- methylguanine-DNA methyltransferase. *Proc Natl Acad Sci U S A* 98:12566-71
- Zou H, Niswander L (1996) Requirement for BMP signaling in interdigital apoptosis and scale formation. *Science* 272:738-41
- Zuniga A, Haramis AP, McMahon AP, Zeller R (1999) Signal relay by BMP antagonism controls the SHH/FGF4 feedback loop in vertebrate limb buds. *Nature* 401:598-602