







22 Sox9 21 Hapln1

33 Mcam 32 Heyl

- 1. Sox2: expressed in early neural plate and total neural tube in embryogenesis (major marker of neuro-epithelial progenitor cells)(1, 2)
- 2. *Olig3*: expressed specifically in the dorsal neural tube at E9.25 (*3*), establishes the neural crest–lateral neural plate boundary in zebrafish (*4*)
- 3. *Pax6*: expressed in the neuroepithelium and neural tube, required for ventral neural tube specification (5-7)
- 4. *Foxb1*: expressed in the dorsal domain of the neural tube, also mentioned as a roof plate (where pre-EMT neural crest cells reside) (8)
- 5. *Gbx2*: expressed in the neural tube and plate border during neural crest specification (2)
- 6. *Msx1*, and 7. *Msx2*: expressed in the neural crest (premigratory and migratory neural crest, as well as in the neural crest-derived mesenchyme of the pharyngeal arches) (9), essential for the development of the cranial and cardiac neural crest streams (10)
- 8. *Wnt1*, and 9. *Wnt3a*: classic markers of the dorsal neural tube (11, 12)
- 10. Zic1: expressed in the neural plate border and dorsal neural tube progenitors (13, 14)
- 11. Zic4: expressed in the dorsal neural tube (15)
- 12. *Atoh1 (Math1)*: expressed by a population of neuronal progenitors in the dorsal domain of the central nervous system, found ventrally to the roof plate, not associated with neural crest (16, 17)
- 13. *Zic3*: expressed by the neural plate and neural crest in *Xenopus (18)*, transiently expressed in the dorsal neural tube in mouse embryos (*19*)
- 14. *Bmper*: expressed in the avian premigratory neural crest, responsible for mediating the EMT and migration (20)
- 15. *Mafb*: expressed by the cells of the dorsal neural tube/roof plate/pre-EMT domain (21)
- 16. *Lmx1a*: expressed by the cells of the dorsal neural tube/roof plate/pre-EMT domain (22) and lateral neural plate (23)
- 17. *Gdf*7: expressed by the dorsal neural tube/roof plate/pre-EMT neural crest, involved in sensory neurogenesis and gliogenesis (24)
- 18. *Hnf1b*: linked to the neural crest development, expressed by the roof plate (or dorsal neural tube/pre-EMT neural crest) at E9.5 (25, 26)
- 19. Dlx5: expressed in the neural plate border and branchial arches (13, 27)
- 20. *Pak3*: unbiasedly predicted to label the delaminating neural crest
- 21. *Hapln1*: unbiasedly predicted to label the delaminating neural crest
- 22. *Sox9*: expressed in premigratory and migratory neural crest, required for EMT and delamination of the neural crest cells and their survival (*13, 28*)
- 23. Sox10: expressed in migratory neural crest (13, 29), pan-neural crest marker
- 24. Ets1: expressed in premigratory and migratory neural crest (13), pan-neural crest marker
- 25. Tfap2b: expressed in premigratory neural crest (13), pan-neural crest marker
- 26. *Erbb3*: expressed by the migrating neural crest in mouse embryo (*30*)
- 27. *Tfap2a*: expressed in the neural plate border (13)
- 28. Foxd3: expressed by migratory neural crest cells (8, 28, 31), pan-neural crest marker
- 29. Snail: expressed by the neural plate border and migrating neural crest (32)
- 30. *Ret*: expressed by neural crest-derived cells (*33*)
- 31. *Ngfr*: expressed by the migrating neural crest in mice and human and mouse stem cells with neural crest properties (*34-38*)
- 32. *Heyl*: expressed by the neural crest-derived progenitors of a subtype of DRG (dorsal root ganglia) neurons (39)

- 33. *Mcam*: expressed in migrating avian trunk NC (40) and unbiasedly predicted to outline autonomic neurons and some mesenchymal cells
- 34. *Hsd11b2*: unbiasedly predicted to outline autonomic neurons and some mesenchymal cells
- 35. Smtnl2: unbiasedly predicted to define the developing progenitors of sensory neurons
- 36. *Nkain4*: gene coding for Na+/K+ transporting ATPase interacting 4, unbiasedly predicted to outline the emerging Schwann cell lineage
- 37. Sfrp5: unbiasedly predicted to outline developing progenitors of sensory neurons
- 38. *Prrx1*: expressed by developing neural crest-derived mesenchyme (41)
- 39. *Meox1*: expressed in neural crest-derived mesenchyme (42)
- 40. *Twist1*: expressed during EMT *in vitro*, and also during mesenchyme specification in drosophila (*43, 44*), unbiasedly predicted to outline the neural crest-derived mesenchyme in mouse
- 41. Foxc1: unbiasedly predicted to define the developing neural crest-derived mesenchyme
- 42. Car11: unbiasedly predicted to outline the progenitors of sensory neurons
- 43. *Neurog2*: expressed by neural crest cells and the progenitors of sensory neurons of the DRGs (45, 46)
- 44. Neurog1: expressed in sensory neurons of the DRGs at E9-E9.25 (46)
- 45. *Neurod1*: expressed by the developing neurons in the central and peripheral nervous system upon maturation (47)
- 46. Neurod4: expressed by the sensory neurons of the peripheral and cranial ganglia (48)
- 47. Phox2b: classical marker of autonomic neurons (49-51)
- 48. Ascl1: classical marker of autonomic neurons (52, 53)

References

- 1. V. Graham, J. Khudyakov, P. Ellis, L. Pevny, SOX2 functions to maintain neural progenitor identity. *Neuron* **39**, 749-765 (2003).
- 2. M. L. Martik, M. E. Bronner, Regulatory Logic Underlying Diversification of the Neural Crest. *Trends Genet* **33**, 715-727 (2017).
- 3. H. Takebayashi *et al.*, Non-overlapping expression of Olig3 and Olig2 in the embryonic neural tube. *Mech Dev* **113**, 169-174 (2002).
- 4. A. Filippi *et al.*, The basic helix-loop-helix olig3 establishes the neural plate boundary of the trunk and is necessary for development of the dorsal spinal cord. *Proc Natl Acad Sci U S A* **102**, 4377-4382 (2005).
- Y. Arai *et al.*, Role of Fabp7, a downstream gene of Pax6, in the maintenance of neuroepithelial cells during early embryonic development of the rat cortex. *J Neurosci* 25, 9752-9761 (2005).
- 6. N. Bertrand, F. Medevielle, F. Pituello, FGF signalling controls the timing of Pax6 activation in the neural tube. *Development* **127**, 4837-4843 (2000).
- 7. M. Schwarz *et al.*, Pax2/5 and Pax6 subdivide the early neural tube into three domains. *Mech Dev* **82**, 29-39 (1999).
- 8. P. A. Labosky, K. H. Kaestner, The winged helix transcription factor Hfh2 is expressed in neural crest and spinal cord during mouse development. *Mech Dev* **76**, 185-190 (1998).
- 9. A. J. Bendall, C. Abate-Shen, Roles for Msx and Dlx homeoproteins in vertebrate development. *Gene* **247**, 17-31 (2000).

- 10. M. Ishii *et al.*, Combined deficiencies of Msx1 and Msx2 cause impaired patterning and survival of the cranial neural crest. *Development* **132**, 4937-4950 (2005).
- 11. W. Hsu, A. J. Mirando, H. M. Yu, Manipulating gene activity in Wnt1-expressing precursors of neural epithelial and neural crest cells. *Dev Dyn* **239**, 338-345 (2010).
- 12. W. Yanfeng, J. P. Saint-Jeannet, P. S. Klein, Wnt-frizzled signaling in the induction and differentiation of the neural crest. *Bioessays* **25**, 317-325 (2003).
- 13. M. E. Bronner, M. Simoes-Costa, The Neural Crest Migrating into the Twenty-First Century. *Curr Top Dev Biol* **116**, 115-134 (2016).
- 14. J. Aruga, T. Tohmonda, S. Homma, K. Mikoshiba, Zic1 promotes the expansion of dorsal neural progenitors in spinal cord by inhibiting neuronal differentiation. *Dev Biol* **244**, 329-341 (2002).
- C. Gaston-Massuet, D. J. Henderson, N. D. Greene, A. J. Copp, Zic4, a zinc-finger transcription factor, is expressed in the developing mouse nervous system. *Dev Dyn* 233, 1110-1115 (2005).
- H. C. Lai, T. J. Klisch, R. Roberts, H. Y. Zoghbi, J. E. Johnson, In vivo neuronal subtype-specific targets of Atoh1 (Math1) in dorsal spinal cord. *J Neurosci* 31, 10859-10871 (2011).
- 17. C. Akazawa, M. Ishibashi, C. Shimizu, S. Nakanishi, R. Kageyama, A mammalian helix-loop-helix factor structurally related to the product of Drosophila proneural gene atonal is a positive transcriptional regulator expressed in the developing nervous system. *J Biol Chem* **270**, 8730-8738 (1995).
- K. Nakata, T. Nagai, J. Aruga, K. Mikoshiba, Xenopus Zic3, a primary regulator both in neural and neural crest development. *Proc Natl Acad Sci U S A* 94, 11980-11985 (1997).
- 19. T. Inoue, M. Ota, K. Mikoshiba, J. Aruga, Zic2 and Zic3 synergistically control neurulation and segmentation of paraxial mesoderm in mouse embryo. *Dev Biol* **306**, 669-684 (2007).
- 20. E. Coles, J. Christiansen, A. Economou, M. Bronner-Fraser, D. G. Wilkinson, A vertebrate crossveinless 2 homologue modulates BMP activity and neural crest cell migration. *Development* **131**, 5309-5317 (2004).
- 21. K. F. Liem, Jr., G. Tremml, T. M. Jessell, A role for the roof plate and its resident TGFbeta-related proteins in neuronal patterning in the dorsal spinal cord. *Cell* **91**, 127-138 (1997).
- 22. V. V. Chizhikov, K. J. Millen, Control of roof plate formation by Lmx1a in the developing spinal cord. *Development* **131**, 2693-2705 (2004).
- 23. K. J. Millen, J. H. Millonig, M. E. Hatten, Roof plate and dorsal spinal cord dl1 interneuron development in the dreher mutant mouse. *Dev Biol* **270**, 382-392 (2004).
- 24. L. Lo, E. L. Dormand, D. J. Anderson, Late-emigrating neural crest cells in the roof plate are restricted to a sensory fate by GDF7. *Proc Natl Acad Sci U S A* **102**, 7192-7197 (2005).
- 25. E. Barbacci *et al.*, Variant hepatocyte nuclear factor 1 is required for visceral endoderm specification. *Development* **126**, 4795-4805 (1999).
- 26. C. Coffinier, D. Thepot, C. Babinet, M. Yaniv, J. Barra, Essential role for the homeoprotein vHNF1/HNF1beta in visceral endoderm differentiation. *Development* **126**, 4785-4794 (1999).
- 27. M. J. Depew *et al.*, Dlx5 regulates regional development of the branchial arches and sensory capsules. *Development* **126**, 3831-3846 (1999).
- 28. M. Cheung *et al.*, The transcriptional control of trunk neural crest induction, survival, and delamination. *Dev Cell* **8**, 179-192 (2005).

- 29. E. M. Southard-Smith, L. Kos, W. J. Pavan, Sox10 mutation disrupts neural crest development in Dom Hirschsprung mouse model. *Nat Genet* **18**, 60-64 (1998).
- 30. S. Britsch *et al.*, The ErbB2 and ErbB3 receptors and their ligand, neuregulin-1, are essential for development of the sympathetic nervous system. *Genes Dev* **12**, 1825-1836 (1998).
- 31. M. Dottori, M. K. Gross, P. Labosky, M. Goulding, The winged-helix transcription factor Foxd3 suppresses interneuron differentiation and promotes neural crest cell fate. *Development* **128**, 4127-4138 (2001).
- 32. M. Simoes-Costa, M. E. Bronner, Establishing neural crest identity: a gene regulatory recipe. *Development* **142**, 242-257 (2015).
- 33. I. Mason, The RET receptor tyrosine kinase: activation, signalling and significance in neural development and disease. *Pharm Acta Helv* **74**, 261-264 (2000).
- 34. X. Jiang *et al.*, Isolation and characterization of neural crest stem cells derived from in vitro-differentiated human embryonic stem cells. *Stem Cells Dev* **18**, 1059-1070 (2009).
- 35. S. Thomas *et al.*, Human neural crest cells display molecular and phenotypic hallmarks of stem cells. *Hum Mol Genet* **17**, 3411-3425 (2008).
- 36. Y. M. Wilson, K. L. Richards, M. L. Ford-Perriss, J. J. Panthier, M. Murphy, Neural crest cell lineage segregation in the mouse neural tube. *Development* **131**, 6153-6162 (2004).
- 37. T. Mujtaba, M. Mayer-Proschel, M. S. Rao, A common neural progenitor for the CNS and PNS. *Dev Biol* **200**, 1-15 (1998).
- 38. D. L. Stemple, D. J. Anderson, Isolation of a stem cell for neurons and glia from the mammalian neural crest. *Cell* **71**, 973-985 (1992).
- 39. A. Mukhopadhyay, J. Jarrett, T. Chlon, J. A. Kessler, HeyL regulates the number of TrkC neurons in dorsal root ganglia. *Dev Biol* **334**, 142-151 (2009).
- 40. S. Alais *et al.*, HEMCAM/CD146 downregulates cell surface expression of beta1 integrins. *J Cell Sci* **114**, 1847-1859 (2001).
- 41. M. Logan *et al.*, Expression of Cre Recombinase in the developing mouse limb bud driven by a Prxl enhancer. *Genesis* **33**, 77-80 (2002).
- 42. A. F. Candia *et al.*, Mox-1 and Mox-2 define a novel homeobox gene subfamily and are differentially expressed during early mesodermal patterning in mouse embryos. *Development* **116**, 1123-1136 (1992).
- 43. M. Y. Feng, K. Wang, Q. T. Shi, X. W. Yu, J. S. Geng, Gene expression profiling in TWIST-depleted gastric cancer cells. *Anat Rec (Hoboken)* **292**, 262-270 (2009).
- 44. I. Castanon, M. K. Baylies, A Twist in fate: evolutionary comparison of Twist structure and function. *Gene* **287**, 11-22 (2002).
- 45. M. Zirlinger, L. Lo, J. McMahon, A. P. McMahon, D. J. Anderson, Transient expression of the bHLH factor neurogenin-2 marks a subpopulation of neural crest cells biased for a sensory but not a neuronal fate. *Proc Natl Acad Sci U S A* **99**, 8084-8089 (2002).
- 46. Q. Ma, C. Fode, F. Guillemot, D. J. Anderson, Neurogenin1 and neurogenin2 control two distinct waves of neurogenesis in developing dorsal root ganglia. *Genes Dev* **13**, 1717-1728 (1999).
- 47. J. E. Lee *et al.*, Conversion of Xenopus ectoderm into neurons by NeuroD, a basic helix-loop-helix protein. *Science* **268**, 836-844 (1995).
- 48. K. Takebayashi *et al.*, Conversion of ectoderm into a neural fate by ATH-3, a vertebrate basic helix-loop-helix gene homologous to Drosophila proneural gene atonal. *EMBO J* **16**, 384-395 (1997).

- 49. E. Coppola, F. d'Autreaux, F. M. Rijli, J. F. Brunet, Ongoing roles of Phox2 homeodomain transcription factors during neuronal differentiation. *Development* 137, 4211-4220 (2010).
- 50. A. Pattyn, X. Morin, H. Cremer, C. Goridis, J. F. Brunet, The homeobox gene Phox2b is essential for the development of autonomic neural crest derivatives. *Nature* **399**, 366-370 (1999).
- 51. L. Lo, M. C. Tiveron, D. J. Anderson, MASH1 activates expression of the paired homeodomain transcription factor Phox2a, and couples pan-neuronal and subtype-specific components of autonomic neuronal identity. *Development* **125**, 609-620 (1998).
- 52. L. Sommer, N. Shah, M. Rao, D. J. Anderson, The cellular function of MASH1 in autonomic neurogenesis. *Neuron* **15**, 1245-1258 (1995).
- 53. F. Guillemot *et al.*, Mammalian achaete-scute homolog 1 is required for the early development of olfactory and autonomic neurons. *Cell* **75**, 463-476 (1993).