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Novel Activities of *Mafb* Underlie Its Dual Role in Hindbrain Segmentation and Regional Specification

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Abstract

The bZip transcription factor *Mafb* is expressed in two segments of the developing vertebrate hindbrain: the rhombomeres 5 and 6. Loss of *Mafb* expression in the mouse mutant *kreisler* leads to elimination of r5 and to alterations of r6 regional identity. Here, we further investigated the role of *Mafb* in hindbrain patterning using gain-of-function experiments in the chick embryo. Our work has revealed novel functions for *Mafb*, including a positive autoregulatory activity, the capacity to repress *Hoxb1* expression, and the capacity to synergise with or antagonise Krox20 activity. These different activities appear to be spatially restricted in the hindbrain, presumably due to interactions with other factors. Reinvestigation of the *kreisler* mutation indicated that it also results in an ectopic activation of *Mafb* in rhombomere 3, accounting for the previously described molecular alterations of this rhombomere in the mutant. Together, these data allow us to refine our view of the dual function of *Mafb* in both segmentation and specification of anteroposterior identity in the hindbrain.

Keywords






hindbrain; rhombomere; segmentation; *Mafb*; Hox; Eph; *kreisler*; Krox20



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References

REFERENCES

- 1 J.C. Adams
Heavy metal intensification of DAB-based HRP reaction product
J. Histochem. Cytochem., 29 (1981), p. 775
- 2 L. Bally-Cuif, M. Wassef
Ectopic induction and reorganization of Wnt-1 expression in quail/chick chimeras
Development, 120 (1994), pp. 3379-3394
- 3 J.R. Barrow, H.S. Stadler, M.R. Capecchi
Roles of Hoxa1 and Hoxa2 in patterning the early hindbrain of the mouse
Development, 127 (2000), pp. 933-944

- 4 N. Becker, P. Gilardi-Hebenstreit, T. Seitanidou, D. Wilkinson, P. Chamay
Characterisation of the Sek-1 receptor tyrosine kinase
FEBS Lett., 368 (1995), pp. 353-357
[Article](#)  [PDF \(546KB\)](#)
- 5 E. Bell, R.J. Wingate, A. Lumsden
Homeotic transformation of rhombomere identity after localized Hoxb1 misexpression
Science, 284 (1999), pp. 2168-2171
- 6 V. Blank, N.C. Andrews
The Maf transcription factors: Regulators of differentiation
Trends Biochem. Sci., 22 (1997), pp. 437-441
[Article](#)  [PDF \(1MB\)](#)
- 7 F. Chatonnet, E.D. del Toro, O. Voiculescu, P. Chamay, J. Champagnat
Different respiratory control systems are affected in homozygous and heterozygous kreisler mutant mice
Eur. J. Neurosci., 15 (2002), pp. 684-692
- 8 O. Chisaka, T.S. Musci, M.R. Capecchi
Developmental defects of the ear, cranial nerves and hindbrain resulting from targeted disruption of the mouse homeobox gene Hox-1.6
Nature, 355 (1992), pp. 516-520
- 9 J.D. Clarke, A. Lumsden
Segmental repetition of neuronal phenotype sets in the chick embryo hindbrain
Development, 118 (1993), pp. 151-162
- 10 S.P. Cordes, G.S. Barsh
The mouse segmentation gene kr encodes a novel basic domain-leucine zipper transcription factor
Cell, 79 (1994), pp. 1025-1034
[Article](#)  [PDF \(5MB\)](#)
- 11 M. Davenne, M.K. Maconochie, R. Neun, A. Pattyn, P. Chambon, R. Krumlauf, F.M. Rijli
Hoxa2 and Hoxb2 control dorsoventral patterns of neuronal development in the rostral hindbrain
Neuron, 22 (1999), pp. 677-691
[Article](#)  [PDF \(676KB\)](#)
- 12 M.S. Deol
The abnormalities of the inner ear in kreisler mice
J. Embryol. Exp. Morphol., 12 (1964), pp. 475-490
- 13 V. Dupe, A. Lumsden
Hindbrain patterning involves graded responses to retinoic acid signalling
Development, 128 (2001), pp. 2199-2208
- 14 A. Eichmann, A. Grapin-Botton, L. Kelly, T. Graf, N.M. Le Douarin, M. Sieweke
The expression pattern of the mafB/kr gene in birds and mice reveals that the kreisler phenotype does not represent a null mutant
Mech. Dev., 65 (1997), pp. 111-122
[Article](#)  [PDF \(12MB\)](#)
- 15 S. Fraser, R. Keynes, A. Lumsden
Segmentation in the chick embryo hindbrain is defined by cell lineage restrictions
Nature, 344 (1990), pp. 431-435
- 16 M.A. Frohman, G.R. Martin, S.P. Cordes, L.P. Halamek, G.S. Barsh
Altered rhombomere-specific gene expression and hyoid bone differentiation in the mouse segmentation mutant, kreisler (kr)
Development, 117 (1993), pp. 925-936
- 17 A. Gavalas, M. Davenne, A. Lumsden, P. Chambon, F.M. Rijli
Role of Hoxa-2 in axon pathfinding and rostral hindbrain patterning
Development, 124 (1997), pp. 3693-3702

- 18 F. Giudicelli, E. Tallebourg, P. Chamay, P. Gilardi-Hebenstreit
Krox-20 patterns the hindbrain through both cell-autonomous and non cell-autonomous mechanisms
Genes Dev., 15 (2001), pp. 567-580
- 19 A. Graham, A. Lumsden
Patterning the cranial neural crest
Biochem. Soc. Symp., 62 (1996), pp. 77-83
- 20 G.A. Grammatopoulos, E. Bell, L. Toole, A. Lumsden, A.S. Tucker
Homeotic transformation of branchial arch identity after Hoxa2 overexpression
Development, 127 (2000), pp. 5355-5365
- 21 A. Grapin-Botton, M.A. Bonnin, L.A. McNaughton, R. Krumlauf, N.M. Le Douarin
Plasticity of transposed rhombomeres: Hox gene induction is correlated with phenotypic modifications
Development, 121 (1995), pp. 2707-2721
- 22 A. Grapin-Botton, M.A. Bonnin, M. Sieweke, N.M. Le Douarin
Defined concentrations of a posteriorizing signal are critical for Mafb/Kreisler segmental expression in the hindbrain
Development, 125 (1998), pp. 1173-1181
- 23 S. Guthrie, I. Muchamore, A. Kuroiwa, H. Marshall, R. Krumlauf, A. Lumsden
Neuroectodermal autonomy of Hox-2.9 expression revealed by rhombomere transpositions
Nature, 356 (1992), pp. 157-159
- 24 S. Guthrie
Patterning the hindbrain
Curr. Opin. Neurobiol., 6 (1996), pp. 41-48
[Article](#)  [PDF \(836KB\)](#)
- 25 V. Hamburger, H.L. Hamilton
A series of normal stages in the development of the chick embryo
J. Morphol., 88 (1951), pp. 49-92
- 26 S. Hirano, H. Tanaka, K. Ohta, M. Norita, K. Hoshino, R. Meguro, M. Kase
Normal ontogenic observations on the expression of Eph receptor tyrosine kinase, Cdk8, in chick embryos
Anat Embryol., 197 (1998), pp. 187-197
- 27 C. Irving, I. Mason
Signalling by FGF8 from the isthmus patterns anterior hindbrain and establishes the anterior limit of Hox gene expression
Development, 127 (2000), pp. 177-186
- 28 K. Kataoka, K.T. Fujiwara, M. Noda, M. Nishizawa
Mafb, a new Maf family transcription activator that can associate with Maf and Fos but not with Jun
Mol. Cell. Biol., 14 (1994), pp. 7581-7591
- 29 K. Kataoka, M. Nishizawa, S. Kawai
Structure-function analysis of the maf oncogene product, a member of the b-Zip protein family
J. Virol., 67 (1993), pp. 2133-2141
- 30 R. Keynes, G. Cook, J. Davies, A. Lumsden, W. Norris, C. Stern
Segmentation and the development of the vertebrate nervous system
J. Physiol., 84 (1990), pp. 27-32
- 31 R. Kos, M.V. Reedy, R.L. Johnson, C.A. Erickson
The winged-helix transcription factor FoxD3 is important for establishing the neural crest lineage and repressing melanogenesis in avian embryos
Development, 128 (2001), pp. 1467-1479
- 32 T. Lufkin, A. Dierich, M. LeMeur, M. Mark, P. Chambon
Disruption of the Hox-1.6 homeobox gene results in defects in a region corresponding to its rostral domain of expression
Cell, 66 (1991), pp. 1105-1119
[Article](#)  [PDF \(14MB\)](#)


- 33 A. Lumsden
The cellular basis of segmentation in the developing hindbrain
Trends Neurosci., 13 (1990), pp. 329-335
[Article](#)  [PDF \(1MB\)](#)

34 A. Lumsden, S. Guthrie
Alternating patterns of cell surface properties and neural crest cell migration during segmentation of the chick hindbrain
Dev. Suppl. (1991), pp. 9-15

35 A. Lumsden, R. Krumlauf
Patterning the vertebrate neuraxis
Science, 274 (1996), pp. 1109-1115

36 M. Manzanares, S. Cordes, C.T. Kwan, M.H. Sham, G.S. Barsh, R. Krumlauf
Segmental regulation of Hoxb-3 by kreisler
Nature, 387 (1997), pp. 191-195

37 M. Manzanares, S. Cordes, L. Ariza-McNaughton, V. Sadl, K. Maruthainar, G. Barsh, R. Krumlauf
Conserved and distinct roles of kreisler in regulation of the paralogous Hoxa3 and Hoxb3 genes
Development, 126 (1999), pp. 759-769

38 M. Manzanares, P.A. Trainor, S. Nonchev, L. Ariza-McNaughton, J. Brodie, A. Gould, H. Marshall, A. Morrison, C.T. Kwan, M.H. Sham, D.G. Wilkinson, R. Krumlauf
The role of kreisler in segmentation during hindbrain development
Dev. Biol., 211 (1999), pp. 220-237
[Article](#)  [PDF \(2MB\)](#)

39 M. Manzanares, J. Nardelli, P. Gilardi-Hebenstreit, H. Marshall, F. Giudicelli, M.T. Martinez-Pastor, R. Krumlauf, P. Chamay
Krox20 and kreisler co-operate in the transcriptional control of segmental expression of Hoxb3 in the developing hindbrain
Embo J., 21 (2002), pp. 365-376

40 I.J. McKay, I. Muchamore, R. Krumlauf, M. Maden, A. Lumsden, J. Lewis
The kreisler mouse: A hindbrain segmentation mutant that lacks two rhombomeres
Development, 120 (1994), pp. 2199-2211

41 C.B. Moens, Y.L. Yan, B. Appel, A.G. Force, C.B. Kimmel
valentino: A zebrafish gene required for normal hindbrain segmentation
Development, 122 (1996), pp. 3981-3990

42 C.B. Moens, S.P. Cordes, M.W. Giorgianni, G.S. Barsh, C.B. Kimmel
Equivalence in the genetic control of hindbrain segmentation in fish and mouse
Development, 125 (1998), pp. 381-391





43 P. Murphy, R.E. Hill
Expression of the mouse labial-like homeobox-containing genes, Hox 2.9 and Hox 1.6, during segmentation of the hindbrain
Development, 111 (1991), pp. 61-74

44 K. Niederreither, J. Vermot, B. Schuhbaur, P. Chambon, P. Dollé
Retinoic acid synthesis and hindbrain patterning in the mouse embryo
Development, 127 (2000), pp. 75-85

45 O. Pourquie
Vertebrate somitogenesis
Annu. Rev. Cell Dev. Biol., 17 (2001), pp. 311-350

46 V. Prince, A. Lumsden
Hoxa-2 expression in normal and transposed rhombomeres: Independent regulation in the neural tube and neural crest
Development, 120 (1994), pp. 911-923

47 V.E. Prince, C.B. Moens, C.B. Kimmel, R.K. Ho
Zebrafish hox genes: Expression in the hindbrain region of wild-type and mutants of the segmentation gene, valentino
Development, 125 (1998), pp. 393-406

- 48 F.G. Sajjadi, E.B. Pasquale
Five novel avian Eph-related tyrosine kinases are differentially expressed
Oncogene, 8 (1993), pp. 1807-1813
- 49 S. Schneider-Maunoury, P. Topilko, T. Seitandou, G. Levi, M. Cohen-Tannoudji, S. Poumin, C. Babinet, P. Charnay
Disruption of Krox-20 results in alteration of rhombomeres 3 and 5 in the developing hindbrain
Cell, 75 (1993), pp. 1199-1214
[Article](#)  [PDF \(24MB\)](#)
- 50 S. Schneider-Maunoury, T. Seitandou, P. Charnay, A. Lumsden
Segmental and neuronal architecture of the hindbrain of Krox-20 mouse mutants
Development, 124 (1997), pp. 1215-1226
- 51 S. Schneider-Maunoury, P. Gilardi-Hebenstreit, P. Charnay
How to build a vertebrate hindbrain. Lessons from genetics
C. R. Acad. Sci. III, 321 (1998), pp. 819-834
[Article](#)  [PDF \(2MB\)](#)
- 52 M.H. Sieweke, H. Tekotte, J. Frampton, T. Graf
Mafk is an interaction partner and repressor of Ets-1 that inhibits erythroid differentiation
Cell, 85 (1996), pp. 49-60
[Article](#)  [PDF \(254KB\)](#)
- 53 M. Studer, A. Gavalas, H. Marshall, L. Ariza-McNaughton, F.M. Rijli, P. Chambon, R. Krumlauf
Genetic interactions between Hoxa1 and Hoxb1 reveal new roles in regulation of early hindbrain patterning
Development, 125 (1998), pp. 1025-1036
- 54 M. Studer, A. Lumsden, L. Ariza-McNaughton, A. Bradley, R. Krumlauf
Altered segmental identity and abnormal migration of motor neurons in mice lacking Hoxb-1
Nature, 384 (1996), pp. 630-634
- 55 O.H. Sundin, G. Eichele
A homeo domain protein reveals the metameric nature of the developing chick hindbrain
Genes Dev., 4 (1990), pp. 1267-1276
- 56 P.J. Swiatek, T. Gridley
Perinatal lethality and defects in hindbrain development in mice homozygous for a targeted mutation of the zinc finger gene Krox20
Genes Dev., 7 (1993), pp. 2071-2084
- 57 T. Theil, L. Ariza-McNaughton, M. Manzanares, J. Brodie, R. Krumlauf, D.G. Wilkinson
Requirement for downregulation of kreisler during late patterning of the hindbrain
Development, 129 (2002), pp. 1477-1485
- 58 T. Theil, M. Frain, P. Gilardi-Hebenstreit, A. Flenniken, P. Charnay, D.G. Wilkinson
Segmental expression of the EphA4 (Sek-1) receptor tyrosine kinase in the hindbrain is under direct transcriptional control of Krox-20
Development, 125 (1998), pp. 443-452
- 59 P.A. Trainor, R. Krumlauf
Hox genes, neural crest cells and branchial arch patterning
Curr. Opin. Cell Biol., 13 (2001), pp. 698-705
[Article](#)  [PDF \(2MB\)](#)
- 60 O. Voiculescu, E. Taillebourg, C. Pujades, C. Kress, S. Buart, P. Charnay, S. Schneider-Maunoury
Hindbrain patterning: Krox20 couples segmentation and specification of regional identity
Development, 128 (2001), pp. 4967-4978
- 61 K.M. Wassarman, M. Lewandoski, K. Campbell, A.L. Joyner, J.L. Rubenstein, S. Martinez, G.R. Martin
Specification of the anterior hindbrain and establishment of a normal mid/hindbrain organizer is dependent on Gbx2 gene function
Development, 124 (1997), pp. 2923-2934
- 62 D.G. Wilkinson, M.A. Nieto

Detection of messenger RNA by in situ hybridization to tissue sections and whole mounts

Methods Enzymol., 225 (1993), pp. 361-373

[Article](#)  [PDF \(2MB\)](#)

63 D.G. Wilkinson

Genetic control of segmentation in the vertebrate hindbrain

Perspect. Dev. Neurobiol., 3 (1995), pp. 29-38

64 Q. Xu, G. Mellitzer, V. Robinson, D.G. Wilkinson

In vivo cell sorting in complementary segmental domains mediated by Eph receptors and ephrins

Nature, 399 (1999), pp. 267-271

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