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Constitutive Expression of Preproendothelin in the Cardiac Neural Crest Selectively Promotes Expansion of the Adventitia of the Great Vessels *in Vivo*Victoria L.T. Ballard ... Takashi Mikawa¹ [Show more](#)<https://doi.org/10.1006/dbio.2002.0818>[Get rights and content](#)Under an Elsevier [user license](#)[open archive](#)

Abstract

Cardiac neural crest cells are essential for normal development of the great vessels and the heart, giving rise to a range of cell types, including both neuronal and non-neuronal adventitial cells and smooth muscle. Endothelin (ET) signaling plays an important role in the development of cardiac neural crest cell lineages, yet the underlying mechanisms that act to control their migration, differentiation, and proliferation remain largely unclear. We examined the expression patterns of the receptor, ET_A, and the ET-specific converting enzyme, ECE-1, in the pharyngeal arches and great vessels of the developing chick embryo. *In situ* hybridization analysis revealed that, while ET_A is expressed in the pharyngeal arch mesenchyme, populated by cardiac neural crest cells, ECE-1 expression is localized to the outermost ectodermal cells of the arches and then to the innermost endothelial cells of the great vessels. This dynamic pattern of expression suggests that only a subpopulation of neural crest cells in these regions is responsive to ET signaling at particular developmental time points. To test this, retroviral gene delivery was used to constitutively express preproET-1, a precursor of mature ET-1 ligand, in the cardiac neural crest. This resulted in a selective expansion of the outermost, adventitial cell population in the great vessels. In contrast, neither differentiation nor proliferation of neural crest-derived smooth muscle cells was significantly affected. These results suggest that constitutive expression of exogenous preproET-1 in the cardiac neural crest results in expansion restricted to an adventitial cell population of the developing great vessels.

Keywords

cardiac neural crest; arch artery; great vessels; endothelin; retrovirus; chicken embryo; heart development

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References

REFERENCES

- 1 G.F. Albers, K.A. Peifley, A. Johns, J.F. Kleha, J.A. Winkles
Constitutive endothelin-1 overexpression promotes smooth muscle cell proliferation via an external autocrine loop
J. Biol. Chem., 269 (1994), pp. 10112-10118
- 2 H. Arai, S. Hori, I. Aramori, H. Ohkubo, S. Nakanishi



Cloning and expression of a cDNA encoding an endothelin receptor






Nature, 348 (1990), pp. 730-732

- 3 M. Bergwerff, M.E. Verberne, M.C. DeRuiter, R.E. Poelmann, A.C. Gittenberger-de Groot
Neural crest cell contribution to the developing circulatory system: Implications for vascular morphology?
Circ. Res., 82 (1998), pp. 221-231
- 4 D.E. Bockman, M.E. Redmond, K. Waldo, H. Davis, M.L. Kirby
Effect of neural crest ablation on development of the heart and arch arteries in the chick
Am. J. Anat., 180 (1987), pp. 332-341
- 5 G. Cheng, A. Wessels, R.G. Gourdie, R.P. Thompson
Spatiotemporal and tissue specific distribution of apoptosis in the developing chick heart
Dev. Dyn., 223 (2002), pp. 119-133
- 6 D.E. Clouthier, K. Hosoda, J.A. Richardson, S.C. Williams, H. Yanagisawa, T. Kuwaki, M. Kumada, R.E. Hammer, M. Yanagisawa
Cranial and cardiac neural crest defects in endothelin-A receptor-deficient mice
Development, 125 (1998), pp. 813-824
- 7 D.E. Clouthier, S.C. Williams, H. Yanagisawa, M. Wieduwilt, J.A. Richardson, M. Yanagisawa
Signaling pathways crucial for craniofacial development revealed by endothelin-A receptor-deficient mice
Dev. Biol., 217 (2000), pp. 10-24
[Article](#)  [PDF \(892KB\)](#)
- 8 D.H. Damon
VSM growth is stimulated in sympathetic neuron/VSM cocultures: Role of TGF-beta2 and endothelin
Am. J. Physiol. Heart Circ. Physiol., 278 (2000), pp. H404-H411
- 9 M. Das, E.C. Dempsey, J.T. Reeves, K.R. Stenmark
Selective expansion of fibroblast subpopulations from pulmonary artery adventitia in response to hypoxia
Am. J. Physiol. Lung Cell. Mol. Physiol., 282 (2002), pp. L976-L986
- 10 N. Emoto, M. Yanagisawa
Endothelin-converting enzyme-2 is a membrane-bound, phosphoramidon-sensitive metalloprotease with acidic pH optimum
J. Biol. Chem., 270 (1995), pp. 15262-15268
- 11 M.C. Gonzalez, S.M. Arribas, F. Molero, M.S. Fernandez-Alfonso
Effect of removal of adventitia on vascular smooth muscle contraction and relaxation
Am. J. Physiol. Heart Circ. Physiol., 280 (2001), pp. H2876-H2881
- 12 V. Hamburger, H.L. Hamilton
A series of normal stages in the development of the chick embryo
J. Morphol., 88 (1951), pp. 49-92
- 13 D. Henrique, J. Adam, A. Myat, A. Chitnis, J. Lewis, D. Ish-Horowicz
Expression of a Delta homologue in prospective neurons in the chick
Nature, 375 (1995), pp. 787-790
- 14 A. Inoue, M. Yanagisawa, S. Kimura, Y. Kasuya, T. Miyauchi, K. Goto, T. Masaki
The human endothelin family: Three structurally and pharmacologically distinct iso peptides predicted by three separate genes
Proc. Natl. Acad. Sci. USA, 86 (1989), pp. 2863-2867
- 15 M. Kalra, V.M. Miller
Early remodeling of saphenous vein grafts: Proliferation, migration and apoptosis of adventitial and medial cells occur simultaneously with changes in graft diameter and blood flow
J. Vasc. Res., 37 (2000), pp. 576-584
- 16 N. Kanzawa, C.P. Poma, K. Takebayashi-Suzuki, K.G. Diaz, J. Layliev, T. Mikawa
Competency of embryonic cardiomyocytes to undergo Purkinje fiber differentiation is regulated by endothelin receptor expression
Development, 129 (2002), pp. 3185-3194
- 17 H. Kempf, C. Linares, P. Convol, J.M. Gasc
Pharmacological inactivation of the endothelin type A receptor in the early chick embryo: A model of misarrangement of the

Pharmacological inactivation of the endothelin type A receptor in the early chick embryo: A model of mispatterning of the branchial arch derivatives

Development, 125 (1998), pp. 4931-4941

- 18 M.L. Kirby, T.F. Gale, D.E. Stewart
Neural crest cells contribute to normal aorticopulmonary septation
Science, 220 (1983), pp. 1059-1061
- 19 M.L. Kirby
Contribution of neural crest to heart and vessel morphology
R.P. Harvey, N. Rosenthal (Eds.), "Heart Development", Academic Press, San Diego (1999), pp. 179-193
[Article](#)  [PDF \(7MB\)](#)
- 20 Y. Kurihara, H. Kurihara, H. Oda, K. Maemura, R. Nagai, T. Ishikawa, Y. Yazaki
Aortic arch malformations and ventricular septal defect in mice deficient in endothelin-1
J. Clin. Invest., 96 (1995), pp. 293-300
- 21 Y. Kurihara, H. Kurihara, H. Suzuki, T. Kodama, K. Maemura, R. Nagai, H. Oda, T. Kuwaki, W.H. Cao, N. Kamada
Elevated blood pressure and craniofacial abnormalities in mice deficient in endothelin-1
Nature, 368 (1994), pp. 703-710
- 22 R. Lahav, C. Ziller, E. Dupin, N.M. Le Douarin
Endothelin 3 promotes neural crest cell proliferation and mediates a vast increase in melanocyte number in culture
Proc. Natl. Acad. Sci. USA, 93 (1996), pp. 3892-3897
- 23 N.M. Le Douarin
"The Neural Crest.", Cambridge University Press, Cambridge (1982)
- 24 C.S. Le Lièvre, N.M. Le Douarin
Mesenchymal derivatives of the neural crest: Analysis of chimaeric quail and chick embryos
J. Embryol. Exp. Morphol., 34 (1975), pp. 125-154
- 25 J. Li, K.C. Liu, F. Jin, M.M. Lu, J.A. Epstein
Transgenic rescue of congenital heart disease and spina bifida in Splotch mice
Development, 126 (1999), pp. 2495-24503
- 26 M.I. Lin, I. Das, G.M. Schwartz, P. Tsoulfas, T. Mikawa, B.L. Hempstead
Trk C receptor signaling regulates cardiac myocyte proliferation during early heart development *in vivo*
Dev. Biol., 226 (2000), pp. 180-191
[Article](#)  [PDF \(1MB\)](#)
- 27 C.W. Lo, M.F. Cohen, G.Y. Huang, B.O. Lazatin, N. Patel, R. Sullivan, C. Pauken, S.M. Park
Cx43 gap junction gene expression and gap junctional communication in mouse neural crest cells
Dev. Genet., 20 (1997), pp. 119-132
- 28 F.J. Manasek
Myocardial cell death in the embryonic chick ventricle
J. Embryol. Exp. Morphol., 21 (1969), pp. 271-284
- 29 J. Männer, J.M. Perez-Pomares, D. Macias, R. Munoz-Chapuli
The origin, formation and developmental significance of the epicardium: A review
Cells Tissues Organs, 169 (2001), pp. 89-103
- 30 T. Mikawa
Retroviral targeting of FGF and FGFR in cardiomyocytes and coronary vascular cells during heart development
Ann. N. Y. Acad. Sci., 752 (1995), pp. 506-516
- 31 T. Mima, H. Ueno, D.A. Fischman, L.T. Williams, T. Mikawa
Fibroblast growth factor receptor is required for *in vivo* cardiac myocyte proliferation at early embryonic stages of heart development
Proc. Natl. Acad. Sci. USA, 92 (1995), pp. 467-471
- 32 S. Miyagawa, M.L. Kirby
Pathogenesis of persistent truncus arteriosus induced by nimustine hydrochloride in chick embryos

- 33 S. Miyagawa-Tomita, K. Waldo, H. Tomita, M.L. Kirby
Temporospatial study of the migration and distribution of cardiac neural crest in quail-chick chimeras
Am. J. Anat., 192 (1991), pp. 79-88
- 34 V. Nataf, A. Grapin-Botton, D. Champeval, A. Amemiya, M. Yanagisawa, N.M. Le Douarin
The expression patterns of endothelin-A receptor and endothelin 1 in the avian embryo
Mech. Dev., 75 (1998), pp. 145-149
[Article](#)  [PDF \(2MB\)](#)
- 35 D.M. Noden
An analysis of migratory behavior of avian cephalic neural crest cells
Dev. Biol., 42 (1975), pp. 106-130
[Article](#)  [PDF \(19MB\)](#)
- 36 K. Opdecamp, L. Kos, H. Amheiter, W.J. Pavan
Endothelin signalling in the development of neural crest-derived melanocytes
Biochem. Cell. Biol., 76 (1998), pp. 1093-1099
- 37 T. Pexieder
Cell death in the morphogenesis and teratogenesis of the heart
Adv. Anat. Embryol. Cell. Biol., 51 (1975), pp. 3-99
- 38 R.E. Poelmann, T. Mikawa, A.C. Gittenberger-de Groot
Neural crest cells in outflow tract septation of the embryonic chicken heart: Differentiation and apoptosis
Dev. Dyn., 212 (1998), pp. 373-384
- 39 T. Sakurai, M. Yanagisawa, Y. Takuwa, H. Miyazaki, S. Kimura, K. Goto, T. Masaki
Cloning of a cDNA encoding a non-isopeptide-selective subtype of the endothelin receptor
Nature, 348 (1990), pp. 732-735
- 40 K.R. Stenmark, R.P. Mecham
Cellular and molecular mechanisms of pulmonary vascular remodeling
Annu. Rev. Physiol., 59 (1997), pp. 89-144
- 41 N. Suzuki, H. Matsumoto, C. Kitada, T. Masaki, M. Fujino
A sensitive sandwich-enzyme immunoassay for human endothelin
J. Immunol. Methods, 118 (1989), pp. 245-250
[Article](#)  [PDF \(384KB\)](#)
- 42 K. Takebayashi-Suzuki, L.B. Pauliks, Y. Eltsefon, T. Mikawa
Purkinje fibers of the avian heart express a myogenic transcription factor program distinct from cardiac and skeletal muscle
Dev. Biol., 234 (2001), pp. 390-401
[Article](#)  [PDF \(958KB\)](#)
- 43 K. Takebayashi-Suzuki, M. Yanagisawa, R.G. Gourdie, N. Kanzawa, T. Mikawa
In vivo induction of cardiac Purkinje fiber differentiation by coexpression of preproendothelin-1 and endothelin converting enzyme-1
Development, 127 (2000), pp. 3523-3532
- 44 G.C. Tucker, M. Delarue, S. Zada, J.C. Boucaut, J.P. Thiery
Expression of the HNK-1/NC-1 epitope in early vertebrate neurogenesis
Cell Tissue Res., 251 (1988), pp. 457-465
- 45 K. Waldo, S. Miyagawa-Tomita, D. Kumiski, M.L. Kirby
Cardiac neural crest cells provide new insight into septation of the cardiac outflow tract: aortic sac to ventricular septal closure
Dev. Biol., 196 (1998), pp. 129-144
[Article](#)  [PDF \(4MB\)](#)
- 46 K.L. Waldo, D. Kumiski, M.L. Kirby
Cardiac neural crest is essential for the persistence rather than the formation of an arch artery
Dev. Dyn., 205 (1996), pp. 281-292

- 47 M. Watanabe, A. Choudhry, M. Berlan, A. Singal, E. Siwik, S. Mohr, S.A. Fisher
Developmental remodeling and shortening of the cardiac outflow tract involves myocyte programmed cell death
Development, 125 (1998), pp. 3809-3820
- 48 H. Weber, M.L. Webb, R. Serafino, D.S. Taylor, S. Moreland, J. Norman, C.J. Molloy
Endothelin-1 and angiotensin-II stimulate delayed mitogenesis in cultured rat aortic smooth muscle cells: evidence for common signaling mechanisms
Mol. Endocrinol., 8 (1994), pp. 148-158
- 49 J.J. Wu, J.X. Chen, T.P. Rothman, M.D. Gershon
Inhibition of in vitro enteric neuronal development by endothelin-3: Mediation by endothelin B receptors
Development, 126 (1999), pp. 1161-1173
- 50 D. Xu, N. Emoto, A. Giaid, C. Slaughter, S. Kaw, D. deWit, M. Yanagisawa
ECE-1: A membrane-bound metalloprotease that catalyzes the proteolytic activation of big endothelin-1
Cell, 78 (1994), pp. 473-485
[Article](#)  [PDF \(5MB\)](#)
- 51 H. Yanagisawa, R.E. Hammer, J.A. Richardson, S.C. Williams, D.E. Clouthier, M. Yanagisawa
Role of Endothelin-1/Endothelin-A receptor-mediated signaling pathway in the aortic arch patterning in mice
J. Clin. Invest., 102 (1998), pp. 22-33
- 52 H. Yanagisawa, M. Yanagisawa, R.P. Kapur, J.A. Richardson, S.C. Williams, D.E. Clouthier, D. de Wit, N. Emoto, R.E. Hammer
Dual genetic pathways of endothelin-mediated intercellular signaling revealed by targeted disruption of endothelin converting enzyme-1 gene
Development, 125 (1998), pp. 825-836
- 53 M. Yanagisawa
The endothelin system. A new target for therapeutic intervention
Circulation, 89 (1994), pp. 1320-1322
- 54 M. Yanagisawa, H. Kurihara, S. Kimura, K. Goto, T. Masaki
A novel peptide vasoconstrictor, endothelin, is produced by vascular endothelium and modulates smooth muscle Ca²⁺ channels
J. Hypertens. Suppl., 6 (1988), pp. S188-S191

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