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Blocking Endogenous FGF-2 Activity Prevents Cranial Osteogenesis

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Abstract

Normal growth and morphogenesis of the cranial vault reflect a balance between cell proliferation in the sutures and osteogenesis at the margins of the cranial bones. In the clinical condition craniosynostosis, the sutures fuse prematurely as a result of precocious osteogenic differentiation and craniofacial malformation results. Mutations in several *fibroblast growth factor receptor* (*FGFR*) genes have now been identified as being responsible for the major craniosynostotic syndromes. We have used a grafting technique to manipulate the levels of endogenous FGF-2 ligand in embryonic chick cranial vaults and thereby perturb morphogenesis. Implantation of beads loaded with FGF-2 did not affect normal cranial development at physiological concentrations, although they elicited a morphogenetic response in the limb. Implantation of beads loaded with a neutralising antibody to FGF-2 generated a concentration-dependent response. When a single bead was implanted, the grafts grew to a massive size as a result of increased cell division in the tissue. With greater inactivation of FGF-2 protein (two to three beads implanted), all further bone differentiation and cell proliferation was blocked. These data further support the emerging idea that the intensity of FGF-mediated signalling determines the developmental fate of the skeletogenic cells in the cranial vault. High and low levels correlate with differentiation and proliferation, respectively. A balance between the two ensures normal cranial vault morphogenesis. This is consistent with the observation that several *FGFR* mutations causing craniosynostosis result in constitutive activation of the receptor.

Keywords

neural crest; osteogenesis; FGF-2; cranium; suture

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References

REFERENCES

1 D. Burke, D. Wilkes, T.L. Blundell, S. Malcolm
Fibroblast growth factor receptors: Lessons from the genes
Trends Biochem. Sci., 23 (1998), pp. 59-62
Article PDF (947KB)

2 M.B.L. Carlton, W.H. Colledge, M.J. Evans
Crouzon-like craniofacial dysmorphology in the mouse is caused by an insertational mutation at the Fgf3/Fgf4 l

Feedback

Crouzon-like craniofacial dysmorphology in the mouse is caused by an insertational mutation at the *Fgf3/Fgf4* locus
Dev. Dyn., 212 (1998), pp. 242-249

3 C.-T.J. Chan, P. Thorogood
Pleiotropic features of syndromic craniosynostosis correlate with differential expression of fibroblast growth factor receptors 1 and 2 during human craniofacial development
Pediatr. Res., 45 (1999), pp. 46-53

4 J.D. Coffin, R.Z. Florkiewicz, J. Neumann, T. Mort-Hopkins, G.W. Dorn II, P. Lightfoot, R. German, P.N. Howles, A. Kier, B.A. O'Toole, J. Sasse, A.M. Gonzalez, A. Baird, T. Doetschman
Abnormal bone growth and selective translational regulation in basic fibroblast growth factor (FGF-2) transgenic mice
Mol. Biol. Cell, 6 (1995), pp. 1861-1873

5 M.M. Cohen Jr.
Sutural biology and the correlates of craniosynostosis
Am. J. Med. Genet., 47 (1993), pp. 581-616

6 M.J. Cohn, J.-C. Izpisua-Belmonte, H. Abud, J.K. Heath, C. Tickle
Fibroblast growth factors induce additional limb development from the flank of chick embryos
Cell, 80 (1995), pp. 739-746
Article PDF (3MB)

7 G.F. Couly, P.M. Coltey, N.M. Le Douarin
The triple origin of skull in higher vertebrates: A study in quail–chick chimeras
Development., 117 (1993), pp. 402-429

8 A-L. Delezoide, C. Benoist-Lasselin, L. Legeai-Mallet, M. Le Merrer, A. Munnich, M. Vekemans, J. Bonaventure
Spatio-temporal expression of FGFR1, 2 and 3 genes during human embryo-fetal ossification
Mech. Dev., 77 (1998), pp. 19-30
Article PDF (5MB)

9 I. Flamme, K. Schulze-Osthoff, H.J. Jacob
Mitogenic activity of chicken chorioallantoic fluid is temporally correlated to vascular growth in the chorioallantoic membrane and related to fibroblast growth factors
Development, 111 (1991), pp. 683-690

10 R.J. Gorlin, M.M. Cohen, L.S. Levin
Syndromes of the Head and Neck, Oxford Univ. Press, New York (1990)
p. 1–977

11 P.J. Green, F.S. Walsh, P. Doherty
Promiscuity of fibroblast growth factor receptors
BioEssays, 18 (1996), pp. 639-646

12 J.A. Greenwald, B.J. Mehrara, J.A. Spector, S.M. Warren, P.J. Fagenholz, L.E. Smith, P.J. Bouletreau, F.E. Crisera, H. Ueno, M.T. Longaker
Regional differentiation of cranial suture-associated dura mater *in vivo* and *in vitro*: Implications for suture fusion and patency
J. Bone Miner. Res., 15 (2000), pp. 2413-2430

13 V. Hamburger
A Manual of Experimental Embryology, Univ. of Chicago Press, Chicago (1960)
p. 1–221

14 V. Hamburger, H.L. Hamilton
A series of normal stages in the development of the chick embryo
J. Morphol., 88 (1951), pp. 49-92

15 J. Hanken, P. Thorogood
Evolution of the skull: A problem in pattern formation
Trends Ecol. Evol., 8 (1993), pp. 9-15
Article PDF (1MB)

16 J.R. Hinchliffe, D.R. Johnson
The Development of the Vertebrate Limb, Oxford Univ. Press, Oxford (1980)
p. 1–286

17 S. Iseki, A.O. Wilkie, G.M. Morriss-Kay
Fgfr1 and Fgfr2 have distinct differentiation- and proliferation-related roles in the developing mouse skull vault
Development, 126 (1999), pp. 5611-5620

18 S. Iseki, A.O.M. Wilkie, J.K. Heath, T. Ishimaru, K. Eto, G.M. Morriss-Kay
***Fgfr2* and *osteopontin* domains in the developing skull vault are mutually exclusive and can be altered by locally applied FGF2**
Development, 124 (1997), pp. 3375-3384

19 H.-J. Kim, D.P.C. Rice, P.J. Kettunen, I. Thesleff
FGF-, BMP- and Shh-mediated signalling pathways in the regulation of cranial suture morphogenesis and calvarial bone development
Development, 125 (1998), pp. 1241-1251

20 M.W. Klymkowsky, J. Hanken
Whole-mount staining of Xenopus and other vertebrates
Methods Cell Biol., 36 (1991), pp. 419-441
Article PDF (2MB)

21 J.P. Levine, J.P. Bradley, D.A. Roth, J.G. McCarthy, M.T. Longaker
Studies in cranial suture biology: Regional dura mater determines overlying suture biology
Plast. Reconstr. Surg., 101 (1998), pp. 1441-1447

22 I.J. Mason
The ins and outs of fibroblast growth factors
Cell, 78 (1994), pp. 547-552
Article PDF (785KB)

23 B.J. Mehrara, D. Most, J. Chang, S. Bresnick, A. Turk, S.A. Schendel, G.K. Gittes, M.T. Longaker
Basic fibroblast growth factor and transforming growth factor beta-1 expression in the developing dura mater correlates with calvarial bone formation
Plast. Reconstr. Surg., 104 (1999), pp. 435-444

24 B.J. Mehrara, R.J. Mackool, J.G. McCarthy, G.K. Gittes, M.T. Longaker
Immunolocalisation of basic fibroblast growth factor and fibroblast growth factor receptor-1 and receptor-2 in rat cranial sutures
Plast. Reconstr. Surg., 102 (1998), pp. 1805-1817

25 A. Montero, Y. Okada, M. Tomita, M. Ito, H. Tsurukami, T. Nakamura, T. Doetschman, J.D. Coffin, M.M. Hurley
Disruption of the fibroblast growth factor-2 gene results in decreased bone mass and bone formation
J. Clin. Invest., 105 (2000), pp. 1085-1093

26 D. Most, J.P. Levine, J. Chang, J. Sung, J.G. McCarthy, S.A. Schendel, M.T. Longaker
Studies in cranial suture biology: Up-regulation of transforming growth factor-beta1 and basic fibroblast growth factor mRNA correlates with posterior frontal cranial suture fusion in the rat
Plast. Reconstr. Surg., 101 (1998), pp. 1431-1440

27 M. Muenke, U. Schell
Fibroblast growth factor receptor mutations in human skeletal disorders
Trends Genet., 11 (1995), pp. 308-313
Article PDF (2MB)

28 L.A. Opperman
Cranial sutures as intramembranous bone growth sites
Dev. Dyn., 219 (2000), pp. 472-485

29 L.A. Opperman, T.M. Sweeney, J. Redmon, J.A. Persing, R.C. Ogle
Tissue interactions with underlying dura mater inhibit osseous obliteration of developing cranial sutures
Dev. Dyn., 198 (1993), pp. 312-322

30 A. Orr-Urtreger, M.T. Bedford, T. Burakova, E. Arman, Y. Zimmer, A. Yayon, D. Givol, P. Lonai
Developmental localization of the splicing alternatives of fibroblast growth factor receptor-2 (FGFR2)
Dev. Biol., 158 (1993), pp. 475-486
Article PDF (2MB)

31 W. Reardon, R.M. Winter
The molecular pathology of syndromic craniosynostosis
Mol. Med. Today, 1 (1995), pp. 432-437
Article PDF (9MB)

32 D. Ribatti, C. Urbinati, B. Nico, M. Rusnati, L. Roncali, A. Presta
Endogenous basic fibroblast growth factor is implicated in the vascularization of the chick embryo chorioallantoic membrane
Dev. Biol., 170 (1995), pp. 39-49
Article PDF (847KB)

33 A. Rizzino, P. Kazakoff, E. Ruff, C. Kuszynski, J. Nebelsick
Regulatory effects of cell density on the binding of transforming growth factor beta, epidermal growth factor, platelet-derived growth factor, and fibroblast growth factor
Cancer Res., 48 (1988), pp. 4266-4271

34 S. Sarkar, A. Petiot, A.J. Copp, P. Ferretti, P. Thorogood
FGF-2 promotes skeletogenic differentiation of cranial neural crest cells
Development, 128 (2001), pp. 2143-2152

35 S.C. Wheatley, C.M. Isacke, P.H. Crossley
Restricted expression of the hyaluronan receptor, CD44, during postimplantation mouse embryogenesis suggests key roles in tissue formation and patterning
Development, 119 (1993), pp. 295-306

36 A. Wilkie
Craniosynostosis: Genes and mechanisms
Hum. Mol. Genet., 6 (1997), pp. 1647-1656

37 J.C. Yu, J.S. McClintock, F. Gannon, X.X. Gao, J-P. Mobasser, M. Sharawy
Regional differences of dura osteoinduction: Squamous dura induces osteogenesis, sutural dura induces chondrogenesis and osteogenesis
Plast. Reconstr. Surg., 100 (1997), pp. 23-31

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