

## Developmental Biology

Volume 247, Issue 2, 15 July 2002, Pages 351-366

Regular Article

*Fgf4* Positively Regulates *scleraxis* and Tenascin Expression in Chick Limb TendonsFrédérique Edom-Vovard<sup>1</sup> ... Delphine Duprez<sup>1,2</sup> [Show more](#)<https://doi.org/10.1006/dbio.2002.0707>[Get rights and content](#)Under an Elsevier [user license](#)[open archive](#)

## Abstract

In vertebrates, tendons connect muscles to skeletal elements. Surgical experiments in the chick have underlined developmental interactions between tendons and muscles. Initial formation of tendons occurs autonomously with respect to muscle. However, further tendon development requires the presence of muscle. The molecular signals involved in these interactions remain unknown. In the chick limb, *Fgf4* transcripts are located at the extremities of muscles, where the future tendons will attach. In this paper, we analyse the putative role of muscle-*Fgf4* on tendon development. We have used three general tendon markers, *scleraxis*, tenascin, and *Fgf8* to analyse the regulation of these tendon-associated molecules by *Fgf4* under different experimental conditions. In the absence of *Fgf4*, in muscleless and aneural limbs, the expression of the three tendon-associated molecules, *scleraxis*, tenascin, and *Fgf8*, is down-regulated. Exogenous implantation of *Fgf4* in normal, aneural, and muscleless limbs induces *scleraxis* and tenascin expression but not that of *Fgf8*. These results indicate that *Fgf4* expressed in muscle is required for the maintenance of *scleraxis* and tenascin but not *Fgf8* expression in tendons.




## Keywords





*Fgf4*; *Fgf8*; *scleraxis*; tenascin; tendons; limb bud; chick embryo[Recommended articles](#)[Citing articles \(107\)](#)

## References



## REFERENCES

- 1 S. Becker, G. Pasca, D. Strumpf, T. Volk  
**Reciprocal signaling between *Drosophila* epidermal muscle attachment cells and their corresponding muscles**  
*Development*, 124 (1997), pp. 2615-2622
- 2 M. Benjamin, J.R. Ralphs  
**The cell and developmental biology of tendons and ligaments**  
*Int. Rev. Cytol.*, 196 (2000), pp. 85-130  
[Article](#) [PDF \(5MB\)](#)
- 3 B. Brand, B. Christ, H.J. Jacob  
**An experimental analysis of the developmental capacities of distal part of avian leg buds**

- 4 D. Brown, D. Wagner, X. Li, J.A. Richardson, E.N. Olson  
**Dual role of the basic helix–loop–helix transcription factor *scleraxis* in mesoderm formation and chondrogenesis during mouse embryogenesis**  
Development, 126 (1999), pp. 4317-4329
- 5 M. Catala, C. Ziller, F. Lapointe, N.M. Le Douarin  
**The potentials of the caudal most part of the neural crest are restricted to melanocytes and glia**  
Mech. Dev., 95 (2000), pp. 77-87  
[Article](#)  [PDF \(2MB\)](#)
- 6 B.P. Chan, K.M. Chan, N. Maffulli, S. Webb, K.K.H. Lee  
**Effect of basic fibroblast growth factor. An in vitro study of tendon healing**  
Clin. Orthop., 342 (1997), pp. 239-247
- 7 B.P. Chan, S.C. Fu, L. Qin, K.M. Lee, C.G. Rolf, K.M. Chan  
**Effects of basic fibroblast growth factor (bFGF) on early stages of tendon healing. A rat patellar model**  
Acta Orthop. Scand., 71 (2000), pp. 513-518
- 8 A. Chevallier, M. Kieny, A. Mauger  
**Limb–somite relationship: Origin of the limb musculature**  
J. Embryol. Exp. Morphol., 41 (1977), pp. 245-258
- 9 M. Chiquet, D. Fambrough  
**Chick myotendinous antigen. I. A monoclonal antibody as a marker for tendon and muscle morphogenesis**  
J. Cell Biol., 98 (1984), pp. 1926-1936
- 10 B. Christ, H.J. Jacob, M. Jacob  
**Experimental analysis of the origin of the wing musculature in avian embryos**  
Anat. Embryol., 150 (1977), pp. 171-186
- 11 B. Christ, C.P. Ordahl  
**Early stages of chick somite development**  
Anat. Embryol., 191 (1995), pp. 381-396
- 12 K.L. Clase, P.J. Mitchell, P.J. Ward, C.M. Dorman, S.E. Johnson, K. Hannon  
**Fgf5 stimulates expansion of connective tissue fibroblasts and inhibits skeletal muscle development in the limb**  
Dev. Dyn., 219 (2000), pp. 368-380
- 13 J.S. Colvin, B. Feldman, J.H. Nadeau, M. Goldfarb, D.M. Ornitz  
**Genomic organization and embryonic expression of the mouse fibroblast growth factor 9 gene**  
Dev. Dyn., 216 (1999), pp. 72-88
- 14 P. Cserjesi, D. Brown, K.L. Ligon, G. Lyons, N.G. Copeland, D.J. Gilbert, N.A. Jenkins, E.N. Olson  
**Sclexis: A basic helix–loop–helix protein that prefigures skeletal formation during mouse embryogenesis**  
Development, 121 (1995), pp. 1099-1110
- 15 D. Duprez, F. Lapointe, F. Edom-Vovard, K. Kostakopoulou, L. Robson  
**Sonic Hedgehog (SHH) specifies muscle pattern at tissue and cellular level, in the chick limb bud**  
Mech. Dev., 82 (1999), pp. 151-163  
[Article](#)  [PDF \(3MB\)](#)
- 16 D. D'Souza, K. Patel  
**Involvement of long- and short-range signalling during early tendon development**  
Anat. Embryol., 200 (1999), pp. 367-375
- 17 F. Edom-Vovard, M.A. Bonnin, D. Duprez  
**Fgf8 transcripts are located in tendons during embryonic chick limb development**  
Mech. Dev., 108 (2001), pp. 203-206  
[Article](#)  [PDF \(338KB\)](#)
- 18 F. Edom-Vovard, M.A. Bonnin, D. Duprez  
**Misexpression of Fgf4 in the chick limb inhibits myogenesis by down-regulating Fkrl expression**

- 19 V. Hamburger, H. Hamilton  
**A series of normal stages in the development of the chick embryo**  
J. Morphol., 88 (1951), pp. 49-92
- 20 J.K. Han, G.R. Martin  
**Embryonic expression of Fgf-6 is restricted to the skeletal muscle lineage**  
Dev. Biol., 158 (1993), pp. 549-554  
[Article](#)  [PDF \(604KB\)](#)
- 21 O. Haub, M. Goldfarb  
**Expression of the fibroblast growth factor-5 gene in the mouse embryo**  
Development., 112 (1991), pp. 397-406
- 22 J.M. Hurlle, J.R. Hinchliffe, M.A. Ros, M.A. Critchlow, J.M. Genis-Galvez  
**The extracellular matrix architecture relating to myotendinous pattern formation in the distal part of the developing chick limb: An ultrastructural, histochemical and immunocytochemical analysis**  
Cell Differ. Dev., 27 (1989), pp. 103-120  
[Article](#)  [PDF \(3MB\)](#)
- 23 J. Joseph-Silverstein, S.A. Consigli, K.M. Lyser, C. Ver Pault  
**Basic fibroblast growth factor in the chick embryo: Immunolocalization to striated muscle cells and their precursors**  
J. Cell Biol., 108 (1989), pp. 2459-2466
- 24 G. Kardon  
**Muscle and tendon morphogenesis in the avian hind limb**  
Development, 125 (1998), pp. 4019-4032
- 25 M. Kieny, A. Chevallier  
**Autonomy of tendon development in the embryonic chick wing**  
J. Embryol. Exp. Morphol., 49 (1979), pp. 153-165
- 26 O. deLapeyriere, V. Ollendorff, J. Planche, M.O. Ott, S. Pizette, F. Coulier, D. Birnbaum  
**Expression of the Fgf6 gene is restricted to developing skeletal muscle in the mouse embryo**  
Development, 118 (1993), pp. 601-611
- 27 J.E. Mackie, R.P. Tucker  
**The tenascin-C knockout revisited**  
J. Cell Sci., 112 (1999), pp. 3847-3853
- 28 R. Martini, M. Schachner  
**Complex expression pattern of tenascin during innervation of the posterior limb buds on the developing chicken**  
J. Neurosci. Res., 28 (1991), pp. 261-279
- 29 I.J. Mason, F. Fuller-Pace, R. Smith, C. Dickson  
**FGF-7 (keratinocyte growth factor) expression during mouse development suggests roles in myogenesis, forebrain regionalisation and epithelial-mesenchymal interactions**  
Mech. Dev., 45 (1994), pp. 15-30  
[Article](#)  [PDF \(2MB\)](#)
- 30 R. Merino, Y. Ganan, D. Macias, A.N. Economides, K.T. Sampath, J.M. Hurlle  
**Morphogenesis of digits in the avian limb is controlled by FGFs, TGFbetas, and noggin through BMP signaling**  
Dev. Biol., 200 (1998), pp. 35-45  
[Article](#)  [PDF \(764KB\)](#)
- 31 E.N. Meyers, M. Lewandoski, G.R. Martin  
**An Fgf8 mutant allelic series generated by Cre- and Flp-mediated recombination**  
Nat. Genet., 18 (1998), pp. 136-141
- 32 G. Oliver, R. Wehr, N.A. Jenkins, N.G. Copeland, B.N.R. Cheyette, V. Hartenstein, S.L. Zipursky, P. Gruss  
**Homeobox genes and connective tissue patterning**

Development, 121 (1995), pp. 693-705

- 33 C.P. Ordahl, N.M. Le Douarin  
**Two myogenic lineages within the developing somite**  
Development, 114 (1992), pp. 339-353
- 34 K. Patel, R. Nittenberg, D. D'Souza, C. Irving, D. Burt, D.G. Wilkinson, C. Tickle  
**Expression and regulation of *Cek-8*, a cell to cell signalling receptor in developing chick limb buds**  
Development, 122 (1996), pp. 1147-1155
- 35 M.P. Pautou, I. Hedayat, M. Kieny  
**The pattern of muscle development in the chick leg**  
Arch. Anat. Microsc. Morphol. Exp., 71 (1982), pp. 193-206
- 36 L.G. Robson, T. Kara, A. Crawley, C. Tickle  
**Tissue and cellular patterning of the musculature in chick wings**  
Development, 120 (1994), pp. 1265-1276
- 37 P.M. Rong, M.A. Teillet, C. Ziller, N.M. Le Douarin  
**The neural tube/notochord complex is necessary for vertebral but not limb and body wall striated muscle**  
Development, 115 (1992), pp. 657-672
- 38 M.A. Ros, F.B. Rivero, J.R. Hinchliffe, J.M. Hurle  
**Immunohistological and ultrastructural study of the developing tendons of the avian foot**  
Anat. Embryol., 192 (1995), pp. 483-496
- 39 C. Schramm, M. Solursh  
**The formation of premuscle masses during chick wing bud development**  
Anat. Embryol., 182 (1990), pp. 235-247
- 40 R. Schweitzer, J.H. Chyung, L.C. Murtaugh, A.E. Brent, V. Rosen, E.N. Olson, A. Lassar, C.J. Tabin  
**Analysis of tendon cell fate using *scleraxis*, a specific marker for tendons and ligaments**  
Development, 128 (2001), pp. 3855-3866
- 41 G.B. Shellswell, L. Wolpert  
**The pattern of muscle and tendon development in the chick wing**  
D.A. Ede, J.R. Hinchliffe, M. Balls (Eds.), Vertebrate Limb and Somite Morphogenesis, Cambridge Univ. Press, Cambridge (1977)
- 42 L.E. Stein  
**Effects of serum, fibroblast growth factor, and platelet-derived growth factor on explants or rat tail tendon: A morphological study**  
Acta Anat. (Basel), 123 (1985), pp. 247-252
- 43 M.A. Teillet, N.M. Le Douarin  
**Consequences of neural tube and notochord excision on the development of the peripheral nervous system in the chick embryo**  
Dev. Biol., 98 (1983), pp. 192-211  
[Article](#)  [PDF \(34MB\)](#)
- 44 R.P. Tucker, R. Chiquet-Ehrismann, M.P. Chevron, D. Martin, R.J. Hall, J. Ronelle, B.P. Rubin  
**Teunerin2 is expressed in tissues that regulates limb and somite pattern formation and is induced in vitro and in situ by *Fgf8***  
Dev. Dyn., 220 (2001), pp. 27-39
- 45 T. Volk  
**Singling out *Drosophila* tendon cells: A dialogue between two distinct cell types**  
Trends Genet., 15 (1999), pp. 448-453  
[Article](#)  [PDF \(2MB\)](#)
- 46 B. Wehrle-Haller, M. Koch, S. Baumgartner, J. Spring, M. Chiquet  
**Nerve-dependent and independent tenascin expression in the developing chick limb bud**  
Development, 112 (1991), pp. 627-637
- 47 P.X. Xu, J. Cheng, J.A. Epstein, R.L. Maas  
**Mouse *Eya* genes are expressed during limb tendon development and encode a transcriptional activation function**  
Proc. Natl. Acad. Sci. USA, 94 (1997), pp. 11974-11979

48 T. Yamitzky, L. Min, T. Volk

**The *Drosophila* neuregulin homologs vein mediates inductive interactions between myotubes and their epidermal attachment cells**

Genes Dev., 11 (1997), pp. 2691-2700

<sup>1</sup> Present address: CNRS UMR7622, 9 quai Saint Bernard, Bat C, 6<sup>ème</sup> étage, case 24, 75252 Paris Cedex 05 France.

<sup>2</sup> To whom correspondence should be addressed. Fax: +33 (1) 48 73 43 77. E-mail: Duprez@ccr.jussieu.fr.

Copyright © 2002 Elsevier Science (USA). All rights reserved.

**ELSEVIER**

[About ScienceDirect](#) [Remote access](#) [Shopping cart](#) [Contact and support](#) [Terms and conditions](#) [Privacy policy](#)

Cookies are used by this site. For more information, visit the [cookies page](#).

Copyright © 2017 Elsevier B.V. or its licensors or contributors. ScienceDirect ® is a registered trademark of Elsevier B.V.

 **RELX** Group™