

CURRICULUM VITAE

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Education: B.S., The University of Michigan; 1975
Ph.D., The University of Rochester School of Medicine; 1980

Career:

1974-1976: Undergraduate and postgraduate research; The University of Michigan, Department of Microbiology, Ann Arbor, MI

1976-1980: Doctoral thesis research training; The University of Rochester School of Medicine, Department of Microbiology, Rochester, NY

1980-1982: Postdoctoral fellow under the auspices of the American Muscular Dystrophy Association; The University of Connecticut, Genetics and Cell Biology, Storrs, CT

1982-1984: Research and development scientist; International Biotechnologies, Inc., New Haven, CT

1984-1985: Manager of Enzymology, Process Development and Microbiology; International Biotechnologies, Inc., New Haven, CT

1985-1986: Instructor, Department of Medicine, Endocrine Division, The University of Connecticut School of Medicine, Farmington, CT

1986-1992: Assistant professor, Department of Medicine, Endocrine Division, The University of Connecticut School of Medicine, Farmington, CT

1992-1995: Assistant Professor, Department of Surgery, Section of Plastic Surgery, Yale University School of Medicine, New Haven, CT

1995-1999: Associate Professor, Department of Surgery, Section of Plastic Surgery, Yale University School of Medicine, New Haven, CT

1999-present: re-appointed Associate Professor, Department of Surgery, Section of Plastic Surgery, Yale University School of Medicine, New Haven, CT

Professional Honors or Recognition:

NIH predoctoral trainee; 1976-80

American Cancer Society; 1978-79
Postdoctoral fellow, Muscular Dystrophy Assoc.; 1980-82
Norwich-Eaton Young Investigator Research Award; 1987
Young Investigator Award, Third International Conference on the Chemistry and Biology
Calcified Tissues; 1988
National Osteoporosis Foundation Research Grant; 1989
Dean's Award, Yale University; 1994
Ad Hoc Member VA Endocrine Study Section
Ad Hoc Member General Medicine B Study Section, NIH 2000
Ad Hoc Member "Bone Health and Military Readiness-2001"
Member of the editorial board, *Endocrinology* (2001-2004)

Grants:

NIH: RO1 DK47421, 1994-1997 AIGF receptor and binding protein patterns in bone cells.≡ PI:
Thomas L. McCarthy, 55% effort

NASA: NAGW-4550, 1995-1998 AMolecular mechanisms regulating IGF-I synthesis in bone.≡ PI:
Thomas L. McCarthy, 20% effort.

NIH: RO1 AR39201, 1994-2002 AControl of TGF- β and TGF- β receptor expression in bone.≡ PI:
Michael Centrella, (co-investigator: Thomas L. McCarthy, 20% effort) .

Arthritis Foundation, 1999-2002: AControl of Nuclear Transcription Factor CBFa1 Expression and
Activity in Bone Cells.≡ co-PIs: Michael Centrella, Thomas L. McCarthy. (Thomas L. McCarthy, 20% effort)

NIH 1RO1 DK56310, 2000-2004 ASex steroid regulation of IGF-I expression in bone.≡ PI: Thomas
L. McCarthy, 55% effort

Professional Service:

Ad Hoc Member VA Endocrine Study Section
Ad Hoc Member General Medicine B Study Section, NIH 2000
Ad Hoc Member "Bone Health and Military Readiness-2001"
Member of the editorial board, *Endocrinology* (2001-2004)

Bibliography

Peer-Reviewed Original Research:

1. McCarthy, T. L. System L amino acid uptake regulation as a function of population density, viral transformation, and growth state in the mouse embryo fibroblast cell lines 3T3 and SV3T3. Ph.D. thesis, the University of Rochester School of Medicine, Rochester, NY 14642 (1980).
2. McCarthy, T. L., B. Mroczkowski, E. Siegel, S. M. Heywood. Characterization of translational control RNA isolated from embryonic chick muscle. *Biochemistry* (1982) 22:935-941.

3. Mroczkowski, B., T. L. McCarthy, D. J. Zezza, P. W. Bragg, S. M. Heywood. Small RNA's involved in gene expression of muscle specific proteins. *Experimental Biology and Medicine* 1984) 9:277-283 (.)
4. Centrella, M., T. L. McCarthy, E. Canalis. Transforming growth factor beta is a bifunctional regulator of replication and collagen synthesis in osteoblast-enriched cell cultures from fetal rat calvariae. *J. Biol. Chem.* (1987) 262:2869-2874.
5. Canalis, E., T. McCarthy, M. Centrella. A bone-derived growth factor isolated from rat calvariae is β_2 microglobulin. *Endocrinology* (1987) 121:1198-1200.
6. Centrella, M., T. L. McCarthy, E. Canalis. Mitogenesis in fetal rat bone cells simultaneously exposed to transforming growth factor β and other growth regulators. *FASEB J.* (1987) 1:312-317.
7. Canalis, E., T. McCarthy, M. Centrella. Isolation and characterization of insulin-like growth factor I (somatomedin C) from cultures of fetal rat calvariae. *Endocrinology* (1988) 122:22-27.
8. Canalis, E., T. McCarthy, M. Centrella. Growth factors and the regulation of bone remodeling. *J. Clin. Invest.* (1988) 81: 277-281.
9. Centrella, M., T. L. McCarthy, E. Canalis. The skeletal tissue and transforming growth factor β . *FASEB J.* (1988) 2:3066-3073.
10. Canalis, E., M. Centrella, T. L. McCarthy. Effects of basic fibroblast growth factor on bone formation in vitro. *J. Clin. Invest.* (1988) 81:1572-1577.
11. Centrella, M., T. L. McCarthy, E. Canalis. Parathyroid hormone modulates transforming growth factor β activity and binding in osteoblastic cells. *Proc. Natl. Acad. Sci. USA* (1988) 85:5889-5893.
12. McCarthy, T. L., M. Centrella, E. Canalis. Further biochemical and molecular characterization of primary rat parietal bone cell cultures. *J. Bone Min. Res.* (1988) 3:401-408.
13. Centrella, M., T. L. McCarthy, E. Canalis. Tumor necrosis factor α inhibits collagen synthesis and alkaline phosphatase activity independently of its effect on DNA synthesis in osteoblast-enriched bone cell cultures. *Endocrinology* (1988) 123:1442-1448.
14. Canalis, E. T. McCarthy, M. Centrella. Isolation of growth factors from adult bovine bone matrix. *Calcif. Tissue Int.* (1988) 43:346-351.
15. Canalis, E., M. Centrella, T. L. McCarthy. Insulin-like growth factor I mediates selective effects of parathyroid hormone in bone cultures. *J. Clin. Invest.* (1989) 83:60-65.
16. McCarthy, T. L., M. Centrella, E. Canalis. Regulatory effects of insulin-like growth factor I and II on bone collagen synthesis in rat calvarial cultures. *Endocrinology* (1989) 124:301-309.

17. McCarthy, T. L., M. Centrella, E. Canalis. Parathyroid hormone enhances the transcript and polypeptide levels of insulin-like growth factor I in osteoblast-enriched cultures from fetal rat bone. *Endocrinology* (1989) 124:1247-1253.
18. Centrella, M., T. L. McCarthy, E. Canalis. Platelet-derived growth factor enhances deoxyribonucleic acid and collagen synthesis in osteoblast-enriched cultures from fetal rat parietal bone. *Endocrinology* (1989) 125:13-19.
19. Centrella, M., E. Canalis, T. L. McCarthy, J. J. Orloff, A. F. Stewart, K. L. Insogna. Parathyroid hormone-related protein modulates the effects of transforming growth factor β on deoxyribonucleic acid and collagen synthesis in fetal rat bone cells. *Endocrinology* (1989) 125:199-208.
20. McCarthy, T. L., M. Centrella, E. Canalis. Effects of fibroblast growth factors on deoxyribonucleic acid and collagen synthesis in rat parietal bone cells. *Endocrinology* (1989) 125:2118-2126.
21. Canalis, E., T. L. McCarthy, M. Centrella. Effects of platelet-derived growth factor on bone formation in vitro. *J. Cell. Phys.* (1989) 140:530-537.
22. Centrella, M., T. L. McCarthy, E. Canalis. β_2 microglobulin enhances insulin-like growth factor I binding and synthesis in bone cell cultures. *J. Biol. Chem.* (1989) 264:18268-18271.
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24. McCarthy, T. L., M. Centrella, E. Canalis. Cortisol inhibits the synthesis of insulin-like growth factor I in bone cell cultures. *Endocrinology* (1990) 126:1569-1575.
25. Canalis, E., T. L. McCarthy, M. Centrella. Differential effects of continuous and transient treatment with parathyroid hormone related peptide (PTHrp) on bone collagen synthesis. *Endocrinology* (1990) 126:1806-1812.
26. McCarthy, T. L., M. Centrella, E. Canalis. Cyclic AMP induces insulin-like growth factor I synthesis in osteoblast-enriched cultures. *J. Biol. Chem.* (1990) 265:15353-15356.
27. ten Dijke, P., K. K. Iwata, C. Goddard, C. Piehler, E. Canalis, T. L. McCarthy, M. Centrella. Recombinant transforming growth factor type β_3 : Biological activities and receptor binding properties in isolated bone cells. *Mol. Cell. Biology* (1990) 10:4473-4479.
28. Centrella, M., T. L. McCarthy, E. Canalis. Activin-A binding and biochemical effects in osteoblast-enriched cultures from fetal rat parietal bone. *Mol. Cell. Biology* (1991) 11:250-258.
29. Centrella, M., T.L. McCarthy, W.F. Kusmik, E. Canalis. Relative binding and biochemical effects of heterodimeric and homodimeric isoforms of platelet-derived growth factor in osteoblast-enriched cultures from fetal rat bone. *J. Cell. Phys.* (1991) 147:420-426.

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31. Canalis, E., T.L. McCarthy, M. Centrella. Effects of desamino (1-3) insulin-like growth factor I on bone cell function in rat calvarial cultures. *Endocrinology* (1991) 129:534-541.
32. Centrella, M., T.L. McCarthy, E. Canalis. Glucocorticoid regulation of transforming growth factor β 1 (TGF- β 1) activity and binding in osteoblast-enriched cultures from fetal rat bone. *Mol. Cell. Biol.* (1991) 11:4490-4496.
33. Canalis, E., M. Centrella, T.L. McCarthy. Regulation of insulin-like growth factor (IGF) II production in bone cultures. *Endocrinology* (1991) 129:2457-2462.
34. Centrella, M., T.L. McCarthy, E. Canalis. Transforming growth factor-beta (TGF- β) and bone remodeling. *The Journal of Bone and Joint Surgery* (1991) 73-A:1418-1428.
35. McCarthy, T.L., M. Centrella, E. Canalis. Constitutive synthesis of insulin-like growth factor II by primary osteoblast-enriched cultures from fetal rat calvariae. *Endocrinology* (1992) 130:1303-1308.
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64. Umayahara Y., J. Billiard, C. Ji, M. Centrella, T.L. McCarthy, P. Rotwein. CCAAT/enhancer binding protein δ is a critical regulator of insulin-like growth factor-I gene transcription in osteoblasts. *J. Biol. Chem.* (1999) 274:10609-10617.
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66. Ji, C., Y. Chen, T.L. McCarthy, M. Centrella. Cloning the promoter for transforming growth factor- β type III receptor: basal and conditional expression in fetal rat osteoblasts. *J. Biol. Chem.* (1999) 274:30487-30493.
67. McCarthy, T.L., C. Ji, Y. Chen, K. Kim, M. Centrella. Time- and dose-related interactions between glucocorticoid and cAMP on C/EBP-dependent IGF-I expression by osteoblasts. *Endocrinology* (2000) 141:127-137.

68. McCarthy, T.L., C. Ji, Y. Chen, K. Kim, M. Imagawa, Y. Ito, M. Centrella. Runt domain factor (Runx)-dependent effects on C/EBP δ expression and activity in osteoblasts. *J. Biol. Chem.* (2000) 275:21746-21753.
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Editorials, Reviews, Chapters, Books:

1. McCarthy, T. L., B. Mroczkowski, S. M. Heywood. The role of small cytoplasmic RNA's in muscle differentiation. *Limb Development and Regeneration*; Alan R. Liss, Inc., New York, NY. (1982).
2. Centrella, M., T. L. McCarthy, E. Canalis. Effects of transforming growth factors on bone cells; in: Connect. Tissue Res. (1989) 20:267-275; M. J. Glimcher, editor; Gordon and Breach Science Publishers S.A., publisher.
3. McCarthy, T. L., M. Centrella, E. Canalis. Insulin-like growth factor (IGF) and bone; in: Connect. Tissue Res. (1989) 20:277-282; M. J. Glimcher, editor; Gordon and Breach Science Publishers S.A., publisher.
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6. Canalis, E., T. L. McCarthy, M. Centrella. The role of growth factors in skeletal remodeling; in: Endocrinology and Metabolism Clinics of North America (1989) 18:903-918; R.D.Tiegs, editor; W.B. Saunders Company, Philadelphia.
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10. Centrella, M., T. L. McCarthy, E. Canalis. Growth factors and cytokines; in Bone, Volume 4, Bone Metabolism and Mineralization; (1991) pages 47-72; B. K. Hall, editor; CRC Press, Inc., Boca Raton, FL.
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12. Canalis, E., S. Varghese, T.L. McCarthy, and M. Centrella. Role of platelet derived growth factor in bone cell function. *Growth Regulation* (1992) 2:1-5.
13. Canalis, E., M. Centrella, T.L. McCarthy. The role of insulin-like growth factors in bone remodeling; in: Calcium Regulating Hormones and Bone Metabolism, (1992) pages 258-265; D.V. Cohn, C. Gennari and A.H. Tashjian, editors; Elsevier Science Publishers.
14. Centrella, M., H.M. Spinelli, J.A. Persing, and T.L. McCarthy. Invited discussion: The complexity of insulin-like growth factors in bone growth and remodeling. *Ann. Plastic Surg.* (1993) 31:434-438.
15. McCarthy, T.L., M. Centrella. Regulation of IGF activity in bone. Current Directions Insulin-like Growth Factor Research; (1993) pages 407-414; D. LeRoith and M. K. Raizada, editors; Plenum Press, New York.
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17. Centrella, M., J. M. Wozney, M. C. Horowitz, T. L. McCarthy. Cross-talk among bone cells by way of local growth factors; in: Biological Mechanisms of Tooth Eruption, Resorption, and Replacement by Implants, (1994) pages 35-43; Z. Davidovitch, editor. EBSCO Media (Birmingham, AL).
18. Centrella, M., V. Rosen, M. C. Horowitz, J. M. Wozney, T. L. McCarthy Transforming Growth Factor- β gene family members, their receptors, and bone cell function. *Endocrine Rev. Monographs* 4. Hormonal Regulation of Bone Mineral Metabolism, (1995) pages 211-226; D. D. Bikle, A. Negro-Vilar, editors. Endocrine Society Press (Bethesda, MD).
19. Centrella, M., S. Casinghino, C. Gundberg, T. L. McCarthy, J. Wozney, V. Rosen Changes in bone morphogenetic protein (BMP) sensitivity relative to differentiation in fetal rat bone cell cultures. *Ann. NY Acad. Sci.* (1996) 785:224-226.
20. Centrella, M., C.-H. Ji, D. Chang, S. Casinghino, T.L. McCarthy Regulators of TGF- β type I receptor promoter activity. 3rd Internet World Congress of Biomedical Sciences. (1996) <http://www.3iwc.riken.go.jp> (Bone Cell Biology Symposium).
21. Centrella M., T.L. McCarthy New evidence for links among nuclear factors, bone formation and disease, and TGF- β . *Endocrine News* (1997) 22:13-14.

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23. Centrella M. and T.L. McCarthy. Effects of Transforming Growth Factor- β and mechanical strain on osteoblast cell counts: and in vitro model for distraction osteogenesis. *Plastic and Reconstruct. Surgery* (2000) 105:137-139.

24. Centrella, M., T.L. McCarthy Invited discussion on: Effects of transforming growth factor- β and mechanical strain on osteoblast cell counts: an in vitro model for distraction osteogenesis, by Gosain et. al., *Plastic Reconstruct. Surg.* (2000) 105:137-139.

25. McCarthy, T.L., C. Ji, M. Centrella. Links among growth factors, hormones, and nuclear factors with essential roles in bone formation *Critical Rev Oral Biol. Med.* (2000) 11(4):409-22.

26. Centrella, M., T. L. McCarthy Targeted disruption of G-type natriuretic peptide: a focused assault on cartilagenous bone. *Trends Endocrinol. Metab.* (2001) 12:235-236.

27. McCarthy, T. L., M. Centrella Local IGF-I and bone formation. *Growth Horm. IGF Res.* (2001) 4:213-219.

Papers “in press”:

None

Papers “in revision”:

1. Ji, C., W. Chang, M. Centrella, T.L. McCarthy, Activation domains of CCAAT enhancer binding protein δ : regions required for native activity and prostaglandin E_2 -dependent transactivation of IGF-I gene expression in rat osteoblasts. *Molecular Endocrinology*

Paper “submitted”:

1. Knoll, B. I., T.L. McCarthy, M. Centrella, J. Shin. Strain-dependent control of TGF- β function in bone cells: biochemical events that may be associated with distraction osteogenesis.
2. Moro, L., M. Fornaro, T.L. McCarthy, M. Centrella, L. Languino. A novel autocrine mechanism activated by $\beta 1$ integrins that supports cell adhesion via IGF-II and type 1 IGF receptor.

Papers “in preparation”:

1. Parra, M., W. Chang, M. Centrella, T.L. McCarthy, Estrogen suppression of cAMP-induced IGF-I expression: defining physical and functional interactions between estrogen receptor α and CCAAT enhancer binding protein δ .
2. Chang, W., M. Parra, T.L. McCarthy, M. Centrella. Identification of an upstream suppresser element in the TGF- β receptor type III gene promoter and nuclear factors associated with this effect.
3. Dahwan, P., X. Peng, M. Centrella, T.L. McCarthy, S. Christakos Evidence for functional cooperation

between CCAAT/enhancer-binding protein beta and the VDR/RXR complex in the regulation of 25-hydroxyvitamin D3 24-hydroxylase transcription.

ANNOTATED Selected Bibliography:

1. Canalis, E., M. Centrella, T. L. McCarthy. Insulin-like growth factor I mediates selective effects of parathyroid hormone in bone cultures. *J. Clin. Invest.* (1989) 83:60-65.

2. McCarthy, T. L., M. Centrella, E. Canalis. Parathyroid hormone enhances the transcript and polypeptide levels of insulin-like growth factor I in osteoblast-enriched cultures from fetal rat bone. *Endocrinology* (1989) 124:1247-1253.

The above two references are the first observations that demonstrate PTH stimulation of IGF-I in bone (or any system), and that this ability to elevate IGF-I levels is responsible for the anabolic effects of PTH on bone. Recent studies by others using IGF-I knockout mice have corroborated these findings.

3. McCarthy, T. L., M. Centrella, E. Canalis. Cortisol inhibits the synthesis of insulin-like growth factor I in bone cell cultures. *Endocrinology* (1990) 126:1569-1575.

The above reference is the first observation (for any tissue) that pharmacological doses of glucocorticoid inhibit IGF-I synthesis in bone.

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