

BIOGRAPHICAL SKETCH

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NAME Linda J. Sandell, Ph.D.		POSITION TITLE Professor and Director of Research	
eRA COMMONS USER NAME sandelll			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Denver University, Denver, CO	B.A.	1969	Zoology
Denver University, Denver, CO	M.S.	1971	Biological Sciences
Northwestern University, Chicago, IL (Dr. A. Veis)	Ph.D.	1980	Biochemistry
University of Chicago, Chicago, IL (Dr. A. Dorfman)	Post-doc	1982	Molecular Biology

A. Positions and Honors

1982-1987 Assistant Professor, Departments of Biochemistry and Orthopedic Surgery and Division of Cell Biology, Rush Medical College, Rush Presbyterian-St. Luke's Medical Center, Chicago, IL

1987-1997 Faculty, Cell and Molecular Biology Training Program, University of Washington, Seattle, WA

1987-present Visiting Professor, Rush Presbyterian-St. Luke's Medical Center, Chicago, IL

1987-1993 Associate Professor, Department of Orthopaedics, University of Washington, Seattle, WA

1988-1993 Adjunct Associate Professor, Department of Biochemistry, University of Washington, Seattle, WA

1990-1994 Associate Career Scientist, Department of Veterans Affairs, Seattle, WA

1994-2001 Research Career Scientist, Department of Veterans Affairs, Seattle, WA

1993-1997 Adjunct Professor, Department of Biochemistry, University of Washington, Seattle, WA

1993-1997 Professor, Department of Orthopaedics, University of Washington, Seattle, WA

1997-present Professor, Department of Cell Biology and Physiology, Washington University School of Medicine, St. Louis, MO

1997-present Professor and Director of Research, Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, MO

1998-present Member, Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO

2008- present Mildred B. Simon Professor, Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, MO

Awards and Other Professional Activities

Kappa Delta Award for Basic Research in the Musculoskeletal System, ORS, AAOS, 1992

Chair, Collagen Gordon Conference, 1995

Chair, Bioengineering and Orthopaedic Sciences Gordon Conference, 1998

Advisory Council, National Arthritis and Musculoskeletal and Skin Diseases, NIH, 1998-2002

President, Orthopaedic Research Society, 1999-2000; Board of Directors, 1995-2001

President-elect, 2009-2011, Osteoarthritis Research Society International; Secretary General 2007-2009, Board of Directors 2001-2007,

ISTO Technologies, (Scientific Advisory Board), 2001-2006

President, Histochemical Society, 2007-2008.

Co-Chair and Founder, Gordon Conference, Biology and Pathology of Cartilage, 2003, Chair, 2005

President, American Society for Matrix Biology, 2005-2006.

Chair, OREF Basic Science Grant Review Committee, 2008-2011.

Editorships

Deputy Editor, Journal of Orthopaedic Research

Associate Editor, Journal of Histochemistry and Cytochemistry

Editorial Board, Journal of Biological Chemistry

Editorial Board, Osteoarthritis and Cartilage

Associate Editor, Connective Tissue Research

B. Selected peer-reviewed publications (last four years)

- Imamura, T., Imamura, C., Iwamoto, Y., and Sandell, L. J. Transcriptional co-activator CBP/p300 increase chondrocyte Cd-rap gene expression by multiple mechanisms including sequestration of the repressor CCAAT/enhancer-binding protein. **J Biol Chem.**, 280:16625-16634. **2005.**
- El-Zawawy, H., Silva, M, Sandell, L. J. and Wright, R. Ligamentous versus physeal failure in murine medial collateral ligament biomechanical testing., **J Biomechan.** 38(4): 703-6. **2005.**
- Pietka, T.A., Sandell, L.J., Charni, N., Ryan, R., Mistry, J and Garnero, P. Development of a New Enzyme Immunoassay (EIA) for Serum Type IIA Collagen N-propeptide (PIIANP) and Evaluation in Patients with Rheumatoid Arthritis. **Ann Rheum. Dis.** 64:1906. **2005.**
- McAlinden, A., Havlioglu, N., Liang, L., Davies, SD and Sandell, L. J. Alternative splicing of type II procollagen exon 2 is regulated by the combination of a weak 5' splice site and an adjacent intronic stem-loop cis element. **J. Biol. Chem.** 280:32700-32711. **2005.**
- Posey, K.L., Davies, S., Bales E.S., Haynes, R., Sandell, L. J. and Hetch J.T. In vivo human Cartilage Oligometric Matrix Protein (COMP) promoter activity. **Matrix Biol.** 24(8):539-49. **2005,**
- Okazaki, K., Davies, SR, Imamura, T., and Sandell, L. J. A Promoter Element Of The Cd-Rap Gene Is Required For Repression Of Gene Expression In Non-Cartilage Tissues In Vitro And In Vivo" **J. Cell. Biochem.** 97(4): 857-68. **2006.**
- Galatz, L.M., Sandell, J.L., Rothermilch, S.Y., Das, R., Mastny, A., Havlioglu, N., Silva, M.J. and Thomopoulos, S. Characteristics of the rat supraspinatus tendon during tendon-to-bone healing after acute injury. **J Orthopaedic Res** 24(3): 541-50. **2006.**
- El-Zawawy, H., Gill, C. Wright, R., and Sandell, L. J. Smoking Delays Chondrogenesis in a mouse model of closed tibial fracture healing., **J Orthopaedic Res** 24:2150-2158. **2006.**
- Wright, R., Allen, T., El-Zawawy., Brodt, M., Silva, M., Gill, C., Sandell, L.J., Medial collateral ligament healing in macrophage metalloelastase (MMP-12)-deficient mice. **J Orthopaedic Res** 24(11): 2106-13. **2006.**
- Fukui, N., Ikeda, Y., Ohnuki, T., Hikita, A., Tanaka, S., Yamane, S., Suzuki,R., Sandell, L.J., and Ochi, T., Pro-inflammatory cytokine tumor necrosis factor- α induces bone morphogenetic protein-2 in chondrocytes via mRNA stabilization and transcriptional up-regulation. **J Biol Chem.** 281:27229-27241. **2006.**
- Gill, C., Sandell, J. L., Hossam, E., Wright, R., Effect of Cigarette smoking on early medial collateral ligament healing in a mouse model., **J Orthopaedic Res.** 24 (12):2141-9. **2006.**
- Davies, S., Chang, L., Patra, D., Xing, X., Stokes, D., Posey, K., Hecht, J., Stormo, G., and Sandell, L.J. Computational Identification of Regulatory Motifs in Cartilage Expressed Genes. **Genome Res.** 17: 1438-1447. **2007.**
- McAlinden, A., Liang, L., Mukudai,Y., Imamura,T., and Sandell, L. J. Nuclear protein TIA-1 regulates alternative splicing by interaction with genomic DNA and precursor mRNA. **J Biol Chem.** 282: 24444-24454. **2007.**
- Patra, D., Xing, X., Davies, S., Bryan, J., and Sandell, L. J. Lack of Endochondral Ossification in Site-1 Protease Knockout Mouse. **J. Cell Biology** 179: 687-700. **2007.**
- Sharif, M, Kirwan, J., Charni, N., Sandell, L. J., Whittles, C., and Garnero,P., A 5-yr Longitudinal Study of Type IIA Collagen Synthesis and Total Type II Collagen Degradation in Patients with Knee Osteoarthritis-Association with Disease Progression. **Rheumatology** 46:938-943. **2007.**
- Jones, K., Sponseller, P., Erkula, G., Sakai, L., Ramirez, F., Dietz, H., Kost-Byerly, S., Bridwell,K., Sandell, L. J. Symposium on the Musculoskeletal Aspects of Marfan Syndrome: Meeting Report and State of the Science. **J Orthop Res** 25(3): 413-22. **2007.**
- Galatz,L., Rothermich,S., VanderPloeg, K., Petersen, B., Sandell, L. J. and Thomopoulos, S., Development of the supraspinatus tendon-to-bone insertion: localized expression of extracellular matrix and growth factor genes. **J Orthop Res,** 25 (12): 1621-8. **2007.**
- Fukui, N., Ikeda, Y., Ohnuki, T., Tanaka, Hikita, A., Mitomi, H., Mori, T., Juji, T., Katsuragawa, Y., Yamamoto, S., Sawabe, M., Yamane, S., S., Suzuki,R., Sandell, L.J., and Ochi, T., Regional Differences in Chondrocyte Metabolism in Osteoarthritis, **Arthr Rheum** 58 (1): 154-163. **2008.**
- Bay-Jensen, A.C., Andersen, T., Tabassi, N., Kristensen, P., Kjaersgaard-Andersen, P., Sandell, L.J., Garnero, P., Delaisse, J., Biochemical markers of type II collagen breakdown and synthesis are positioned at specific sites in human osteoarthritic knee cartilage. **Osteoarthritis and Cartilage** May 16 (5): 615 -623. **2008.**

- Imamura, T., Imamura, C., McAlinden, A., Davies, S., Iwamoto, Y., Sandell, L.J. A novel tumor necrosis factor- α responsive CCAAT/enhancer-binding protein site regulates cartilage *Cd-Rap* expression. ***Arthr Rheum*** Apr 58(5): 1366-1376. **2008**.
- Khan, I., Gilbert, S., Caterson, B., Sandell, L. J., Archer, C., Oxidative stress induces expression of osteoarthritis markers procollagen IIA and 3b3(-) in adult bovine articular cartilage. ***Osteoarthritis and Cartilage*** 16(6): 698-707; **2008**
- Sandell, L.J., Xiaoyun, X., Franz, C., Davies, S., Chang, L., and Patra, D., Exuberant expression of chemokine genes by adult human articular chondrocytes in response to IL-1 β . ***Osteoarthritis and Cartilage***, 16(12);1560-1571, **2008**.
- Rich, J., Rosova, I., Nolta, J., Myckatyn, T., Sandell, L.J., McAlinden, A., Upregulation of runx2 and osterix during in vitro chondrogenesis of human adipose-derived stromal cells. ***Biochem and Biophys Res Comm***, 372(1); 230-5; **2008**
- Borrelli, J., Silva, M., Zaegel, M., Franz, C. and Sandell, L.J. A single high energy impact load causes post-traumatic osteoarthritis in young rabbits. ***J Orthop Res***, 27(3);347-352, **2009**.
- Wang, Z., Bryan, J., Franz, C., Haviloglu, N., Sandell, L.J., Type IIB procollagen NH₂-Propeptide Induces Cell Death Through Interaction with Integrins $\alpha\beta 3$ and $\alpha\beta 5$. (**submitted**).
- Schmid, G.J., Kobayashi, K., Sandell, L.J. and Ornitz, D.M. Fibroblast growth factor expression during skeletal fracture healing in mice. ***Dev. Dyn.*** 238 (2) 766-74. **2009**.
- Roberts, S., Menage, J., Sandell, L.J., Evans, H., Richardson, J., Immunohistochemical Study of Collagen types I & II and Procollagen IIA in Human Cartilage Repair Tissue Following Autologous Chondrocyte Implantation. ***The Knee***, **2009**.

Reviews and Book Chapters (selected recent)

- Fukui, N and Sandell, L.J. Anabolic Aspects of Cartilage Repair in ***Topics in Bone Biology, Vol. 4. Bone and Osteoarthritis***, Bronner, F. and Farach-Carson, M.C., eds, Springer-Verlag, 97-108, **2007**.
- Sandell, L.J., Hering, T., and Heinegard, D. Cell Biology, Biochemistry and Molecular and Cell Biology of Articular Cartilage in Osteoarthritis in ***Osteoarthritis***, 4th Edition, Moskowitz, R, ed. (4): 73-106. **2007**.
- Sandell, L. J. Modern Molecular Analysis of a Traditional Disease: Progression in Osteoarthritis. ***Arthr Rheum***, 56 (8): 2474-7. **2007**.
- Sandell, L. J. Anabolic Factors in Degenerative Joint Disease. ***Curr Drug Targets.***, 8(2): 359-65. **2007**.
- Goldring, M. and Sandell, L. J. Transcriptional Control of Chondrocyte Gene Expression. In ***Osteoarthritis, Inflammation and Degradation: A Continuum***. *Buckwalter, J., Lotz, M. and Stoltz, J.-F IOS Press, Biomedical and Health Research*, 70:118-142. **2007**.
- Galatz, L., Rothermich, S., Vanderploeg, K., Petersen, B., Sandell, L. J. and Thomopoulos, S., Development of the supraspinatus tendon-to-bone insertion: localized expression of extracellular matrix and growth factor genes. ***J Orthop Res***, 25 (12): 1621-8. **2007**.
- Sandell, L. J. Multiple Hereditary Exostosis, EXT Genes, and Skeletal Development. ***J Bone Joint Surg***, 91: 58-62. **2009**.

Books

- Sandell, L.J. and Grodzinsky, A. (eds.). ***Clinical Applications of Tissue Engineering in Musculoskeletal Diseases***, American Academy of Orthopaedic Surgeons Press, Rosemont, IL, **2004**.
- Sandell, L. J. Metabolism of chondrocytes in osteoarthritis: why all this activity? *J Musculoskelet Neuronal Interact*, 8 (4): 307. **2009**.

C. CURRENT RESEARCH SUPPORT

R01 AR36994 Sandell (PI)
NIH/NIAMS

9/01/2005– 08/31/2010

“Regulation of Gene Expression in Cartilage”

The specific aims of this study are to 1) investigate the role of negative transcription factors during chondrogenesis, specifically AP-2, δ ef-1 and C/EBP 2) investigate the regulation of the type ii procollagen pre-mRNA alternative splicing switch that occurs during chondrogenesis. 3) determine the function of developmentally-expressed type IIA procollagen protein isoform in vivo. 4) investigate the mechanism of IL-1 β and TNF- α induction of BMP-2 in adult chondrocytes.

R01 AR 050847 Sandell (PI)

9/01/2007 – 8/31/2012

NIH/NIAMS

“Cis Regulatory Motifs in Adult Articular Chondrocytes”

This grant investigates the molecular basis for the severe chondrodysplasia caused by the lack of the enzyme Site-1-protease in cartilage and the lack of endochondral bone formation.

R01 AR 05554 Sandell (PI)

4/1/2009-3/31/2014

NIH/NIAMS

“Function and Regulation of CD-RAP”

The specific aims of this study are to: 1) determine the mechanism of the CD-RAP 183-bp regulatory domain that confers tissue specificity; 2) determine the role of additional negative/positive regulatory elements; 3) screen for and analyze co-regulators; 4) computational identification and functional validation of novel regulatory motifs.

R01 AR 053224 Cheverud (PI); Sandell (Co-investigator) 7/01/2006 – 6/30/2011

NIH

“ Genetic Variation in Murine Long Bone Growth and Development”

The goal of this project is to determine the genes that cause bone growth.

05-015 Silva (PI); Sandell (Co-investigator)

7/01/2008 – 6/30/2009

Orthopaedic Research and Education Foundation

“In Vivo Cartilage Changes after Mechanic Insult”

5P30CA9184208 Sandell (PI)

7/1/08 to 6/30/2009

NIH/NCI

Research Development Award in Developmental Therapeutics

“Novel Treatment for Breast Cancer with Chondrostatin”

1 U13 AR057296 Sandell (PI)

4/1/09-3/31/2013

NIH/NIAMS

Biomarkers for Osteoarthritis

The goal of this project is to support the continuation of the very successful set of meetings of the OA Biomarkers Network.

1 P30 AR057235 Sandell (PI)

4/1/09-3/31/2014

NIH

Core Center for Musculoskeletal Diseases

The goal of this project is to develop a Core Center in Musculoskeletal Disease at Washington University to bring together a substantial group of investigators from our large University complex to form an identifiable unit in the research community: Research in Musculoskeletal Diseases.

2 R01 DK065789-06A1 Long (PI); Sandell (Co-Investigator) 12/01/08 – 11/30/13

NIH/NIDDK

Indian Hedgehog Signaling in Osteoblast Differentiation

The main goal of this project is to understand the mechanism by which Ihh regulates the osteoblast lineage.