

CURRICULUM VITAE

Takao Sakai, MD, PhD

Current Appointment

2013-Present Senior Research Group Leader (Senior Lecturer)
Department of Molecular and Clinical Pharmacology, Institute of Translational Medicine,
University of Liverpool, Sherrington Building, Ashton Street, Liverpool, UK
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Previous Appointments

2006-2013 Assistant Faculty Staff (joint appointment)
Department of Anatomical Pathology and Laboratory Medicine, Cleveland Clinic,
Cleveland, OH, USA

2005-2013 Assistant Professor
Department of Molecular Medicine, Cleveland Clinic Lerner College of Medicine of Case
Western Reserve University (CCLCM), Cleveland, OH, USA

2004-2013 Assistant Faculty Staff
Department of Biomedical Engineering (first appointment), and Orthopaedic and
Rheumatologic Research Center (second appointment), Lerner Research Institute,
Cleveland Clinic, Cleveland, OH, USA

2002-2004 Group Leader
Department of Molecular Medicine, Max-Planck Institute, Martinsried, Germany

1999-2001 Staff Pathologist
Department of Experimental Pathology, Lund University, Lund, Sweden

1996-1999 Research Associate
Departments of Medicine and Biomolecular Chemistry, University of Wisconsin-
Madison, Madison, WI, USA

1991-1996 Research Associate
Division of Hemopoiesis, Institute of Hematology, Jichi Medical School, Japan

1991 Research Associate
Department of Pathology, Mie University School of Medicine, Japan

Educational Qualifications

1991 PhD in Pathology, Jichi Medical University, Tochigi, Japan

1987 MD in Medicine, Faculty of Medicine, Toyama Medical and Pharmaceutical University,
Toyama, Japan

Certification and Licensure

1992 Certified Pathologist of the Japanese Society of Pathology (Certificate #1654)

1987 Japanese National Medical Board, M.D., National License (#310249)

Other Experience and Professional Service

[Editorial Board]

2018-Present Editorial Board, *Cells*

2014-Present Editorial Board, *Frontiers in Physiology*

2013-Present Editorial Board, *World Journal of Hepatology*

2010-Present Editorial Board, *The Journal of Biological Chemistry*

[Committee Service]

2014-Present Member, Biological Service Unit (BSU) committee, University of Liverpool, Liverpool

2011-2013 Member, Institutional Biosafety Committee, Cleveland Clinic, Cleveland, OH, USA

2007-2013 Member, Biological Resources Unit (BRU) Committee, Cleveland Clinic, Cleveland, OH,
USA

Honors and awards

- 2018 Invited speaker, The 107th Annual Meeting of the Japanese Society of Pathology, Sapporo, Japan
- 2017 'Meister Lecture', The 49th Japanese Society of Matrix Biology and Medicine, Tsu, Mie, Japan
- 2016 Presidential Award, The 25th Conference of the Asian Pacific Association for the Study of Liver (APASL), Tokyo, Japan
- 2015 Invited speaker, 18th International Symposium on Cells of the Hepatic Sinusoid (ISCHS), Asilomar, California, USA
- 2013 Session Chair, "Fibronectin, Integrins & Related Molecules" Gordon Conference
- 2012 Invited speaker, The 101st Annual Meeting of the Japanese Society of Pathology, Tokyo, Japan
- 2010 Invited speaker, International Summit on Fibrosis in Intestinal Inflammation, Cleveland, OH, USA
- 2007 Invited speaker, San Francisco Bay Area Seminar, San Francisco, CA, USA
- 2006 Invited speaker, The 35th Annual Midwest Connective Tissue Workshop, Chicago, IL, USA
- 2004 Research grant award, Frontier Food Foundation, Japan
- 2003 Invited speaker, "Epithelial Differentiation & Keratinization" Gordon Conference
- 2003 Invited speaker, 11th International Symposium on Basement Membrane, Chiba, Japan
- 2001 Research grant award, Active Scientific Program (ASP), Sweden
- 2001 Invited speaker, "Fibronectin, Integrins & Related Molecules" Gordon Conference
- 2001 Travel award, Cell Science Research Foundation, Japan
- 2000 Travel award, Swedish Cancer Research Foundation, Sweden
- 2000 Research grant award, The Scandinavia Japan Sasakawa Foundation, Japan
- 1999 Pathology Research Award, The 45th Annual Meeting of the Japanese Society of Pathology, Tokyo, Japan
- 1998 Fellowship award, The Foundation of Tage Blucher for Medical Research, Sweden
- 1998 Travel award, 4th CGGH International Symposium, Japan
- 1996-1998 Marion Merrell Dow Fellowship, Kansas City, MO, USA
- 1996 Fellowship award, Cell Science Research Foundation, Japan

Research Support

Medical Research Council (MRC), UK: Total Costs: £622,125.01 (01/12/2019 – 30/11/2022)

PI: Takao SAKAI

Title: *Molecular dissection of extracellular matrix-related adverse reactions caused by fluoroquinolone antibiotics* (Award Pending)

Fancl Inc.: Total Costs: £16,000.00 (21/05/2019 – 31/08/2020)

PI: Takao SAKAI

Title: *Molecular dissection of facial wrinkles: Contribution of tendon/ligament cells*

Nippi Inc.: JXR12881 Total Costs: £43,700.00 (01/09/2017 – 31/12/2021)

PI: Takao SAKAI

Title: *Biological function of collagen peptides*

Knowledge Exchange & Impact Voucher Total Costs: £10,000.00 (01/11/2018 – 31/07/2019)

PI: Takao SAKAI

Title: *Molecular dissection of hydroxyproline-containing peptides in tendon progenitor cells*

Sysmex Inc.: JXR12177 Total Costs: £97,904.00 (01/12/2015 – 31/10/2019)

PI: Takao SAKAI

Title: *Development of mechanistic extracellular matrix-derived biomarkers to predict the progression of liver fibrosis to cirrhosis*

Knowledge Exchange & Impact Voucher Total Costs: £10,000.00 (01/11/2015 – 30/06/2016)

PI: Takao SAKAI

Title: *Development of a novel non-invasive imaging strategy in living mice during the development of liver fibrosis*

University of Liverpool: JXG10658

Total Costs: £82,644.00 (01/09/2013 – 31/08/2017)

PI: Takao SAKAI

Title: *Mechanisms of dysregulated extracellular matrix fibril network formation in liver fibrosis and cirrhosis*

Cell Seed Inc.: #017037560501

Total Costs: \$60,000.00 (01/04/2010 – 31/03/2013)

PI: Takao Sakai

Title: *A novel cell-based scaffold to improve outcomes in tendon injuries*

The goal of this project is to develop in vivo mouse translational model for adult tendon injury using tendon cell-sheets.

NIH, USA: R01 DK074538

Total Costs: \$1,512,797.00 (01/06/2007 – 31/05/2013)

PI: Takao Sakai

Title: *Fibronectin deposition and TGF-beta activation in liver fibrosis*

The overall goal of this study is to determine the role of fibronectin and to elucidate mechanisms of TGF- β activation and the requirement of TGF- β for extracellular matrix induction following liver injury.

Selected Relevant Publications (from 75 Publications)

Peer-Reviewed Publications

- Hughes JH, Liu K, Plagge A, Wilson PJ, Sutherland H, Hughes AT, Milan AM, [Sakai T](#), Lakshminarayanan RR, Gallagher JA, Bou-Gharios G. A novel conditional alkaptonuria mouse model recapitulating the human condition reveals that targeting liver is a prerequisite for effective therapy. *Human Mol Gen* 2019. In Press.
- Kumra H, Sabatier L, Hassan A, [Sakai T](#), Mosher DF, Brinckmann J, Reinhardt DP. Roles of fibronectin isoforms in neonatal vascular development and matrix integrity. *PLoS Biol* 2018;Jul 23;16(7):e2004812. Doi: 10.1371/journal.pbio.2004812.
- Sakabe T, Sakai K, Maeda T, Sunaga A, Furuta N, Schweitzer R, Sasaki T, [Sakai T](#). Transcription factor scleraxis vitally contributes to progenitor lineage direction in wound healing of adult tendon in mice. *J Biol Chem* 2018;293:5766-5780.
(Selected as a cover image for April 20, 2018 issue of *J Biol Chem*)
- Chou CL, Rivera AL, Williams V, Welter JF, Mansour JM, Drazba JA, [Sakai T](#), Baskaran H. Micrometer scale guidance of mesenchymal stem cells to form structurally oriented large-scale tissue engineered cartilage. *Acta Biomater* 2017;60:210-219.
- Nielsen S, Quaranta V, Linford A, Emeagi P, Rainer C, Santos A, Ireland L, [Sakai T](#), Sakai K, Kim YS, Engle D, Campbell F, Palmer D, Ko JH, Tuveson D, Hirsch E, Mielgo A, Schmid M. Macrophage-secreted granulins supports pancreatic cancer metastasis by inducing liver fibrosis. *Nat Cell Biol* 2016;18:549-560.
- Iwasaki A, Sakai K, Moriya K, Sasaki T, Keene DR, Akhtar R, Miyazono T, Yasumura S, Watanabe M, Morishita S, [Sakai T](#). Molecular mechanism responsible for fibronectin-controlled alterations in matrix stiffness in advanced chronic liver fibrogenesis. *J Biol Chem* 2016;291:72-88.
- Sasaki T, Stoop R, [Sakai T](#), Hess A, Deutzmann R, Schlotzer-Schrehardt U, Chu ML, Mark K. Loss of fibulin-4 in abnormal collagen fibril assembly in bone, caused by impaired lysyl oxidase processing and collagen cross-linking. *Matrix Biol* 2016;50:53-66
- Cvoro A, Devito L, Milton FA, Noli L, Zhang A, Filippi C, Sakai K, Suh JH, Sieglaff DH, Dhawan A, [Sakai T](#), Ilic D, Webb P. A thyroid hormone receptor/KLF9 axis in human hepatocytes and pluripotent stem cells. *Stem Cells* 2015;33:416-428.
- Sakai K, Jawaid S, Sasaki T, Bou-Gharios G, [Sakai T](#). Transforming growth factor β -independent role of connective tissue growth factor in the development of liver fibrosis. *Am J Pathol* 2014;184:2611-2617.
- Crish J, Conti MA, [Sakai T](#), Adelstein RS, Egelhoff TT. Keratin 5-Cre-driven excision of nonmuscle myosin IIA in early embryo trophectoderm leads to placenta defects and embryonic lethality. *Dev Biol* 2013;382:136-148.
- Moriya K, Sakai K, Yan, MH, [Sakai T](#). Fibronectin is essential for survival but is dispensable for proliferation of hepatocytes in acute liver injury in mice. *Hepatology* 2012;56:311-321.
(Selected as a cover image for July, 2012 issue of HEPATOLOGY)
- Hayashi H, Sakai K, Baba H, [Sakai T](#). Thrombospondin-1 is a novel negative regulator of liver regeneration after partial hepatectomy through TGF- β 1 activation in mice. *Hepatology* 2012;55:1562-1573.

- Kumagai K, Sakai K, Kusayama Y, Akamatsu Y, Sakamaki K, Morita S, Sasaki T, Saito T, Sakai T. The extent of degeneration of cruciate ligament is associated with chondrogenic differentiation in patients with osteoarthritis of the knee. ***Osteoarthritis Cartilage*** 2012;20:1258-1267.
- Moriya K, Bae E, Honda K, Sakai K, Sakaguchi T, Tsujimoto I, Kamisoyama H, Keene DR, Sasaki T, Sakai T. A fibronectin-independent mechanism of collagen fibrillogenesis in adult liver remodeling. ***Gastroenterology*** 2011;140:1653-1663.
- Maeda T, Sakabe T, Sunaga A, Sakai K, Rivera AL, Keene DR, Sasaki T, Stavnezer E, Iannotti J, Schweitzer R, Ilic D, Baskaran H, Sakai T. Conversion of mechanical force into TGF- β -mediated biochemical signals. ***Curr Biol*** 2011;21:933-941.
- Tsujimoto I, Moriya K, Sakai K, Dickneite G, Sakai T. Critical role of factor XIII in the initial stages of carbon tetrachloride-induced adult liver remodeling. ***Am J Pathol*** 2011;179:3011-3019.
- Lorenz K, Grashoff C, Torka R, Sakai T, Langbein L, Bloch W, Aumailley M, Fässler R. Integrin-linked kinase is required for epidermal and hair follicle morphogenesis. ***J Cell Biol*** 2007;177:501-513.
- Honda K, Sakaguchi T, Sakai K, Schmedt C, Ramirez A, Jorcano JL, Tarakhovskiy A, Kamisoyama H, Sakai T. Epidermal hyperplasia and papillomatosis in mice with a keratinocyte-restrictive deletion of csk. ***Carcinogenesis*** 2007;28:2074-2081.
- Sakai T, Nyberg P, Cho KH, Caparon MG, Fässler R, Björck L. Interactions with fibronectin attenuate the virulence of *Streptococcus pyogenes*. ***EMBO J*** 2004;23:2166-2174.
- Sakai T, Li S, Docheva D, Grashoff C, Sakai K, Kostka G, Braun A, Pfeifer A, Yurchenco PD, Fässler R. Integrin-linked kinase (ILK) is required for polarizing the epiblast, cell adhesion and controlling actin accumulation. ***Genes Dev*** 2003;17:926-940.
- Yi M, Sakai T, Fässler R, Ruoslahti E. Antiangiogenic proteins require plasma fibronectin or vitronectin for *in vivo* activity. ***Proc Natl Acad Sci USA*** 2003;100:11435-11438.
- Sakai T, Johnson KJ, Murozono M, Sakai K, Magnuson MA, Wieloch T, Cronberg T, Isshiki A, Erickson HP, Fässler R. Plasma fibronectin supports neuronal survival and reduces brain injury following transient focal cerebral ischemia but is not essential for skin wound healing and hemostasis. ***Nat Med*** 2001;7:324-330.
- Sakai T, Jove R, Fässler R, Mosher DF. Role of the cytoplasmic tyrosines of β 1A integrins in transformation by v-src. ***Proc Natl Acad Sci USA*** 2001;98:3808-3813.
- Sakai T, Zhang Q, Fässler R, Mosher DF. Modulation of β 1A integrin functions by tyrosine residues in β 1 cytoplasmic domain. ***J Cell Biol*** 1988;141:527-538.

Reviews and Book Chapters

- Saneyasu T, Akhtar R, Sakai T. Modulation of matrix stiffness in liver fibrosis. ***BioMed Res Int*** 2016. DOI: 10.1155/2016/2646212. Epub Oct 9, 2016.
- Saneyasu T, Yoshioka S, Sakai T. Mechanisms of collagen network organization in response to tissue/organ damage. In: Extracellular Matrix. Travascio F, Ed. pp235-260. InTech. 2016. <http://dx.doi.org/10.5772/63163>.
- Hayashi H, Sakai T. Biological significance of local TGF- β activation in liver diseases. ***Front Physiol*** DOI: 10.3389/fphys.2012.00012.
- Sakabe T, Sakai T. Musculoskeletal diseases – Tendon. ***Br Med Bull*** 2011;99:211-225.
- Hayashi H, Sakai T. Animal models for the study of liver fibrosis: New insights from knockout mouse models. ***Am J Physiol Gastrointest Liver Physiol*** 2011;300:G729-G738, 2011.