# Stanford



# Eric Sibley, M.D., Ph.D.

Professor of Pediatrics (Gastroenterology)
Pediatrics - Gastroenterology

# **CLINICAL OFFICES**

• Pediatric Gastroenterology

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# Bio

#### CLINICAL FOCUS

- · Gastroenterology/Nutrition/Hepatology, Pediatric
- · Pediatric Gastroenterology

## ACADEMIC APPOINTMENTS

- · Professor, Pediatrics Gastroenterology
- Member, Maternal & Child Health Research Institute (MCHRI)

# ADMINISTRATIVE APPOINTMENTS

- Associate Chair for Academic Affairs, Department of Pediatrics, (2016- present)
- Co-Director, Stanford Gastroenterology NIH T32 Training Program, (2011- present)
- Assistant Dean for Academic Advising, Stanford University School of Medicine, (2012- present)
- Director, Junior Faculty Mentoring Program, North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition, (2016-present)
- Associate Director (Research), Stanford Pediatric Gastroenterology Training Program, (2004-present)
- Mentor and Steering Committee, Stanford Pediatric Mentoring Program, (2007- present)
- Senator, School of Medicine Faculty Senate, (2009- present)
- Chair/Vice-Chair, Growth, Development and Aging Section, American Gastroenterology Association, (2007-2011)
- Editor-In-Chief, Journal of Pediatric Gastroenterology and Nutrition, (2006-2010)
- Member, Clinical and Integrative Gastrointestinal Pathobiology Study Section, NIH, (2004-2007)
- Admissions Committee, Stanford University School of Medicine, (1998-2001)

#### HONORS AND AWARDS

- Distinguished Service Award, North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (2017)
- Member, American Clinical and Climatological Association (2010-present)
- Council, elected, American Gastroenterology Association (2007-2011)

- Council, elected, Society for Pediatric Research (2005-2008)
- Named Investigator Award, Stanford Digestive Disease Center (2002-2003)
- Young Faculty Investigator Award, North American Society for Pediatric Gastroenterology and Nutrition (1998)

#### PROFESSIONAL EDUCATION

- Residency: Harbor-UCLA Medical Center Pediatric Residency (1993) CA
- Internship: Harbor-UCLA Medical Center Pediatric Residency (1991) CA
- Fellowship: Stanford University School of Medicine Registrar (1996) CA
- Undergraduate Education, Harvard College, A.B., Biochemical Sciences (1982)
- Medical Education: Johns Hopkins University School of Medicine (1990) MD
- Graduate Education, The Johns Hopkins University, Ph.D., Biological Chemistry (1990)

#### LINKS

• Sibley Lab home page: http://med.stanford.edu/labs/eric\_sibley/

# Research & Scholarship

#### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Transcriptional Regulation of Intestine-Specific Gene Expression during Gut Development and Maturation.

The mammalian gastrointestinal tract matures from a primitive tube into morphologically and functionally distinct regions during development. The mature small intestine functions in the digestion and absorption of ingested nutrients. Expression of several nutrient hydrolases is spatially restricted to distinct segments along the cephalo-caudal axis of the small intestine and is temporally regulated during postnatal maturation. Intestinal lactase, the hydrolase responsible for the digestion of lactose in milk, is expressed at highest levels in the jejunal segment of the small intestine shortly after birth and then declines dramatically just prior to weaning in most mammals.

Our research is directed towards defining the mechanisms regulating the spatial and temporal restriction of lactase gene expression during intestinal development. The normal maturational decline in lactase enzymatic activity is correlated with a decline in lactase messenger RNA levels and is transcriptionally regulated. We are currently identifying maturation-specific lactase gene cis elements and characterizing the nuclear proteins interacting with those elements in cell culture and transgenic animals. We seek to define the interactions of the lactase gene elements and nuclear factors involved in mediating transcriptional control. The overall goal is to relate these lactase control mechanisms to the broader pathways specifying acquisition of a small intestinal phenotype. We are also investigating gene transfer methods to deliver specific genes to the intestine.

# **Teaching**

## STANFORD ADVISEES

#### **Academic Advising Dean**

Natasha Abadilla, Alexander Ball, Ellie Beam, Brian Boursiquot, Jamie Brett, Thomas Cervantes, Diana Chang, Ian Connolly, Dylan Griswold, Lichy Han, Luqman Hodgkinson, Julie Koenig, Yu-Jin Lee, Alexander Li, Grant Lin, George Liu, Max Liu, Paras Minhas, Nuriel Moghavem, Ragini Phansalkar, Jennia Rajaei, Benjie Smith, Yong Tang, Madina Tugizova, Aditya Ullal, Daivik Vyas

# **Publications**

# **PUBLICATIONS**

Impaired PGE2-stimulated Cl- and HCO3- secretion contributes to cystic fibrosis airway disease. PloS one

Sellers, Z. M., Illek, B., Figueira, M. F., Hari, G., Joo, N. S., Sibley, E., Souza-Menezes, J., Morales, M. M., Fischer, H., Wine, J. J. 2017; 12 (12): e0189894

PGE(2)-STIMULATED CL- SECRETION AND MUCOCILIARY CLEARANCE IN CYSTIC FIBROSIS AIRWAY

Sellers, Z., Illek, B., Figueira, M., Hari, G., Joo, N., Sibley, E., Fischer, H., Wine, J. J. WILEY-BLACKWELL.2015: 236

• Intestinal Pdx1 mediates nutrient metabolism gene networks and maternal expression is essential for perinatal growth in mice BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS

Chen, C., Leavitt, T., Sibley, E. 2012; 424 (3): 549-553

The human lactase persistence-associated SNP -13910\*T enables in vivo functional persistence of lactase promoter-reporter transgene expression HUMAN

Fang, L., Ahn, J. K., Wodziak, D., Sibley, E. 2012; 131 (7): 1153-1159

 PDX1 regulation of FABP1 and novel target genes in human intestinal epithelial Caco-2 cells BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS

Chen, C., Fang, R., Chou, L., Lowe, A. W., Sibley, E. 2012; 423 (1): 183-187

 Expression profiling identifies novel gene targets and functions for Pdx1 in the duodenum of mature mice AMERICAN JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY

Chen, C., Sibley, E. 2012; 302 (4): G407-G419

• Theodore E. Woodward Award: lactase persistence SNPs in African populations regulate promoter activity in intestinal cell culture. Transactions of the American Clinical and Climatological Association

Sibley, E., Ahn, J. K. 2011: 122: 155-165

• The Western Transition JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION

Sibley, E. 2011; 52 (1): 2

Congenital Disorders of Digestion and Absorption DIARRHEA: DIAGNOSTIC AND THERAPEUTIC ADVANCES

Mogul, D., Sibley, E., Guandalini, S., Vaziri, H. 2011: 159-75

• -13915\*G DNA polymorphism associated with lactase persistence in Africa interacts with Oct-1 HUMAN GENETICS

Olds, L. C., Ahn, J. K., Sibley, E. 2011: 129 (1): 111-113

 Increased HLA-DR Expression on Tissue Eosinophils in Eosinophilic Esophagitis JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION Patel, A. J., Fuentebella, J., Gernez, Y., Nguyen, T., Bass, D., Berquist, W., Cox, K., Sibley, E., Kerner, J., Nadeau, K. 2010; 51 (3): 290-294

• Three-dimensional optical method for integrated visualization of mouse islet microstructure and vascular network with subcellular-level resolution JOURNAL OF BIOMEDICAL OPTICS

Fu, Y., Lu, C., Lin, C., Juang, J., Enikolopov, G., Sibley, E., Chiang, A., Tang, S. 2010; 15 (4)

• Eotaxin and FGF enhance signaling through an extracellular signal-related kinase (ERK)-dependent pathway in the pathogenesis of Eosinophilic esophagitis. Allergy, asthma, and clinical immunology: official journal of the Canadian Society of Allergy and Clinical Immunology

Huang, J. J., Joh, J. W., Fuentebella, J., Patel, A., Nguyen, T., Seki, S., Hoyte, L., Reshamwala, N., Nguyen, C., Quiros, A., Bass, D., Sibley, E., Berquist, et al 2010; 6 (1): 25-?

■ Ciao and Shalom JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION

Sibley, E.

2010; 50 (1): 2

Pdx1 inactivation restricted to the intestinal epithelium in mice alters duodenal gene expression in enterocytes and enteroendocrine cells AMERICAN
JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY

Chen, C., Fang, R., Davis, C., Maravelias, C., Sibley, E.

2009; 297 (6): G1126-G1137

• Microtome-Free 3-Dimensional Confocal Imaging Method for Visualization of Mouse Intestine With Subcellular-Level Resolution GASTROENTEROLOGY

Fu, Y., Lin, C., Enikolopov, G., Sibley, E., Chiang, A., Tang, S.

2009; 137 (2): 453-465

• Expression profiling analysis of the effects of intestine-specific Pdx1 inactivation in mouse proximal small intestine

Chen, C., Sibley, E.

FEDERATION AMER SOC EXP BIOL.2009

Transient cytochalasin-D treatment induces apically administered rAAV2 across tight junctions for transduction of enterocytes JOURNAL OF GENERAL VIROLOGY

Fu, Y., Sibley, E., Tang, S.

2008; 89: 3004-3008

 Application of doxorubicin-induced rAAV2-p53 gene delivery in combined chemotherapy and gene therapy for hepatocellular carcinoma CANCER BIOLOGY & THERAPY

Chen, C., Lo, C., Lin, B., Sibley, E., Tang, S.

2008; 7 (2): 303-U3

• Genetic modification of somatic gut mucosa: An adeno-associated virus approach JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION

Tang, S., Sibley, E.

2006; 43 (2): 158-159

Spatio-temporal patterns of intestine-specific transcription factor expression during postnatal mouse gut development GENE EXPRESSION PATTERNS

Fang, R. X., Olds, L. C., Sibley, E.

2006; 6 (4): 426-432

• Lactase gene promoter fragments mediate differential spatial and temporal expression patterns in transgenic mice DNA AND CELL BIOLOGY

Wang, Z., Maravelias, C., Sibley, E.

2006; 25 (4): 215-222

 Proteasome modulating agents induce rAAV2-mediated transgene expression in human intestinal epithelial cells BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS

Tang, S. C., Sambanis, A., Sibley, E.

2005; 331 (4): 1392-1400

 Transcriptional regulation of the lactase-phlorizin hydrolase promoter by PDX-1 AMERICAN JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY

Wang, Z., Fang, R. X., Olds, L. C., Sibley, E.

2004; 287 (3): G555-G561

PCR-RFLP genotyping assay for a lactase persistence polymorphism upstream of the lactase-phlorizin hydrolase gene GENETIC TESTING

Chao, C. K., Sibley, E.

2004; 8 (2): 190-193

• Carbohydrate intolerance CURRENT OPINION IN GASTROENTEROLOGY

Sibley, E.

2004; 20 (2): 162-167

Genetic variation and lactose intolerance: detection methods and clinical implications. American journal of pharmacogenomics

Sibley, E.

2004; 4 (4): 239-245

• Lactase persistence DNA variant enhances lactase promoter activity in vitro: functional role as a cis regulatory element HUMAN MOLECULAR GENETICS Olds, L. C., Sibley, E.

2003; 12 (18): 2333-2340

• Regulation of intestine-specific spatiotemporal expression by the rat lactase promoter JOURNAL OF BIOLOGICAL CHEMISTRY

Lee, S. Y., Wang, Z., Lin, C. K., Contag, C. H., Olds, L. C., Cooper, A. D., Sibley, E.

2002; 277 (15): 13099-13105

• Subarachnoid hemorrhage and isolated atresia of the aortic arch JOURNAL OF EMERGENCY MEDICINE

Sibley, E., Doroshow, R. W., Milliken, J. C., Anand, S. K.

2002; 22 (2): 179-183

Lactase gene transcription is activated in response to hypoxia in intestinal epithelial cells MOLECULAR GENETICS AND METABOLISM

Lee, S. Y., Madan, A., Furuta, G. T., Colgan, S. P., Sibley, E.

2002; 75 (1): 65-69

 Thyroid hormone and the D-type cyclins interact in regulating enterocyte gene transcription 41st Annual Meeting of the Society-for-Surgery-of-the-Alimentary-Tract

Meng, S. F., Badrinarain, J., Sibley, E., Fang, R. X., Hodin, R.

SPRINGER.2001: 49-55

 GATA family transcription factors activate lactase gene promoter in intestinal Caco-2 cells AMERICAN JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY

Fang, R. X., Olds, L. C., Santiago, N. A., Sibley, E.

2001; 280 (1): G58-G67

• The homeodomain protein Cdx2 regulates lactase gene promoter activity during enterocyte differentiation GASTROENTEROLOGY

Fang, R. X., Santiago, N. A., Olds, L. C., Sibley, E.

2000; 118 (1): 115-127

• EVOLVING ASYMMETRIC HYPERTROPHIC PYLORIC-STENOSIS ASSOCIATED WITH HISTOLOGIC EVIDENCE OF EOSINOPHILIC GASTROENTERITIS PEDIATRIC RADIOLOGY

Blankenberg, F. G., Parker, B. R., Sibley, E., Kerner, J. A.

1995; 25 (4): 310-311

• SUBSTRATE PHOSPHORYLATION CATALYZED BY THE INSULIN-RECEPTOR TYROSINE KINASE - KINETIC CORRELATION TO AUTOPHOSPHORYLATION OF SPECIFIC SITES IN THE BETA-SUBUNIT JOURNAL OF BIOLOGICAL CHEMISTRY

FLORESRIVEROS, J. R., Sibley, E., Kastelic, T., Lane, M. D.

1989; 264 (36): 21557-21572

• CHARACTERIZATION OF THE MOUSE INSULIN-RECEPTOR GENE PROMOTER PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA

Sibley, E., Kastelic, T., Kelly, T. J., Lane, M. D.

1989; 86 (24): 9732-9736

• DIFFERENTIATION-INDUCED GENE-EXPRESSION IN 3T3-L1 PREADIPOCYTES - CHARACTERIZATION OF A DIFFERENTIALLY EXPRESSED GENE ENCODING STEAROYL-COA DESATURASE JOURNAL OF BIOLOGICAL CHEMISTRY

Ntambi, J. M., BUHROW, S. A., Kaestner, K. H., Christy, R. J., Sibley, E., Kelly, T. J., Lane, M. D.

1988; 263 (33): 17291-17300

• EXPRESSION OF THE DIFFERENTIATION-INDUCED GENE FOR FATTY ACID-BINDING PROTEIN IS ACTIVATED BY GLUCOCORTICOID AND CAMP PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA

Cook, J. S., Lucas, J. J., Sibley, E., BOLANOWSKI, M. A., Christy, R. J., Kelly, T. J., Lane, M. D.

1988; 85 (9): 2949-2953

• HIGH-LEVEL EXPRESSION OF A CLONED HLA HEAVY-CHAIN GENE INTRODUCED INTO MOUSE CELLS ON A BOVINE PAPILLOMAVIRUS VECTOR MOLECULAR AND CELLULAR BIOLOGY

DiMaio, D., Corbin, V., Sibley, E., Maniatis, T.

1984; 4 (2): 340-350