Ernestina Schipani, M.D., Ph.D.
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Date of Birth June 19, 1962

Place of Birth Catanzaro, Calabria, Italy

Citizenship Italian and USA

Education and Training

10/1979-10/1985	M.D., Summa Cum Laude, Medical School of Pisa and Sant'Anna School of Advanced Studies, Pisa, Italy
11/1985-07/1988	Specialty Degree in Endocrinology, Summa Cum Laude, Medical School of Pisa, University of Pisa, Pisa, Italy
11/1985-12/1989	Ph.D., Summa Cum Laude, Sant'Anna School of Advanced Studies, Pisa, Italy
09/1987-10/1987	Visiting Fellow, Department of Internal Medicine, Bone Division Jewish Hospital, Washington University, St. Louis, MO
02/1990-10/1993	Research Fellow, Department of Internal Medicine, Massachusetts General Hospital-Harvard Medical School, Boston, MA
11/1992-03/1993	Visiting Fellow, Department of Molecular Pathophysiology, National Institutes of Health, Bethesda, MD
07/1994-07/1996	Research Fellow, Department of Internal Medicine, Massachusetts General Hospital, Boston, MA

Academic, Administrative, and Clinical Appointments

Academic Appointments

10/1993-11/1993	**Instructor**, Division of Endocrinology, Department of Internal Medicine, Harvard Medical School, Boston, MA
12/1993-05/1994	**Assistant Professor of Medicine (with tenure)**, Division of Endocrinology, Department of Internal Medicine, University of Pisa Medical School of Pisa, Pisa, Italy
06/1994-06/1997	**Instructor**, Division of Endocrinology, Department of Internal Medicine, Massachusetts General Hospital -Harvard Medical School, Boston, MA
07/1997-05/2006	**Assistant Professor of Medicine**, Division of Endocrinology, Department of Internal Medicine, Massachusetts General Hospital - Harvard Medical School, Boston, MA
05/2006-06/2011	**Associate Professor of Medicine**, Division of Endocrinology, Department of Internal Medicine, Massachusetts General Hospital - Harvard Medical School, Boston, MA

07/2011-08/2013	**Professor of Medicine (with tenure)**, Division of Endocrinology, Department of Internal Medicine, Indiana University Medical School, Indianapolis, IN
07/2011-08/2013	**Professor of Anatomy and Cell Biology**, Department of Anatomy and Cell Biology, Indiana University Medical School, Indianapolis, IN
09/2013-10/2020	**Professor of Orthopaedic Surgery (with tenure)**, Department of Orthopaedic Surgery, University of Michigan Medical School, Ann Arbor, MI
09/2013-10/2020	**Professor of Medicine,** Division of Endocrinology, Department of Medicine, University of Michigan Medical School, Ann Arbor, MI
03/2015-10/2020	**Professor of Cell and Developmental Biology**, University of Michigan Medical School, Ann Arbor, MI
11/2020-present	**William Wikoff Professor of Orthopedic Surgery**, **Full Professor of Orthopedic Surgery (with tenure)**, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA

Clinical Appointments

05/1996-09/2008	**Assistant in Biology**, Department of Internal Medicine, Massachusetts General Hospital, Boston, MA
09/2008-06/2011	**Associate in Biology**, Department of Internal Medicine, Massachusetts General Hospital, Boston, MA
06/2011-06/2017	**Consultant**, Department of Internal Medicine, Massachusetts General Hospital, Boston, MA
08/2011-08/2013	**Full Member**, Melvin and Bren Cancer Center, Indiana University Medical School, Indianapolis, IN
03/2015-10/2020	**Member**, Center for Organogenesis, University of Michigan Medical School, Ann Arbor, MI

Licensure and Certifications

11/1985	Italian Medical License
12/1992	ECFMG

Research Interests

I have a long-standing interest in the study of cartilage and bone development. Over the years, I have used cartilage and bone tissues as models to establish essential principles in the broader fields of receptor and hypoxia biology.

The PTH/PTHrP receptor (PTHR1) in development and disease

I was a member of the team who cloned the cDNAs encoding the rat and opossum parathyroid hormone (PTH)/PTH related peptide (PTHrP) receptors (*also known as PTHR1s*), and I cloned the human homolog of this receptor and its gene. My study solved a long-lingering question in the field by proving that the PTH/PTHrP receptors expressed in bone and kidney are identical proteins. Next, I demonstrated that, at odds with what had been for a long time hypothesized, Pseudohypoparathyroidism type 1b, a rare endocrine disorder of calcium and phosphate homeostasis, was not caused by mutations in the PTH/PTHrP receptor gene. This finding prompted a wide genome search that eventually led to the identification of the Gsalpha gene as the one responsible for Pseudohypoparathyroidism type 1b.

More importantly, I discovered that gain-of-function mutations of the PTH/PTHrP receptor result in Jansen Metaphyseal Chondrodysplasia, a severe form of short-limbed dwarfism associated with

hypercalcemia. Jansen Metaphyseal Chondrodysplasia has been one of the first examples in the literature of a human disease being caused by a constitutively active G-protein coupled receptor. Taking advantage of the mutations I had identified in patients, I generated transgenic mice expressing a constitutively active PTH/PTHrP receptor (Jansen receptor) in chondrocytes and osteoblasts, respectively. Lessons from these transgenic mice have contributed to shaping up our current understanding of the role of the PTH/PTHrP receptor in cartilage and bone development and homeostasis, and hematopoiesis.
My laboratory is currently collaborating with my former mentor Dr. Harald Jueppner at MGH-Harvard Medical School to identify potential therapeutic avenues for the treatment of Jansen Metaphyseal Chondrodysplasia (*Awarded R01 DK113039, Dr. Schipani Co-Investigator, Dr. Jueppner PI).*

The Hypoxia Signaling Pathway in development, disease, and regeneration
Studying the fetal growth plate, I was intrigued by its avascularity; this simple observation prompted me to discover that the hypoxia-signaling pathway is essential in skeletal development. Oxygen is not only an indispensable metabolic substrate but also a regulatory signal. I pioneered the notion that gradients of oxygenation are crucial for tissue morphogenesis during skeletal development. My laboratory currently studies the role of the hypoxia signaling pathway in skeletal development and homeostasis with the overall goal of unveiling both novel aspects of the cellular adaptation to hypoxia and new avenues for the treatment of cartilage and bone diseases.

The hypoxia signaling pathway, mitochondria and the reprogramming of metabolism in skeletal development
I discovered that the murine fetal growth plate displays a gradient of oxygenation with an inner, hypoxic region. I generated the first conditional knockout model of hypoxia-inducible factor 1alpha (HIF1) reported in the literature, and I provided unequivocal evidence that HIF1, which is a transcription factor and a key mediator of the cellular adaptation to hypoxia, is a survival factor for growth plate chondrocytes. My laboratory also demonstrated that HIF1 is necessary for timely differentiation of mesenchymal cells into chondrocytes and for joint development in vivo. HIF1 promotes glycolysis and lactate production but impairs mitochondrial respiration. Along those lines, we showed that HIF1-dependent suppression of mitochondrial respiration and thereby oxygen consumption has a key role in endochondral bone development because it protects growth plate chondrocytes that are physiologically hypoxic from lethal intracellular anoxia.
My laboratory is currently investigating how the interplay between mitochondria and HIF1-dependent reprogramming of metabolism controls skeletal development *(R01 AR074079, Dr. Schipani PI).*

HIF2 and the control of bone mass accrual and homeostasis
Despite its high degree of vascularization, a gradient of oxygenation is also present in the bone marrow. In collaboration with Tom Clemens at University of Alabama and Amato Giaccia at Stanford, we provided evidence that activation of the hypoxia signaling pathway in cells of the osteoblast lineage increases the number and size of bone marrow blood vessels, augments trabecular bone mass mainly by inhibiting bone resorption, and enables osteoblasts to produce and secrete erythropoietin, and thus causes polycythemia. Erythropoietin is a classical downstream target of HIF2. Together with HIF1, HIF2 is another crucial mediator of the cellular adaptation to hypoxia.

Notably, my laboratory also recently demonstrated that loss of osteoblastic HIF2 increases bone mass accrual by promoting bone formation without significantly affecting bone resorption. **We are currently investigating whether pharmacological inhibition of HIF2 phenocopies the genetic experiment. HIF2 can be selectively inhibited by small molecules that are now in clinical trials in patients with renal carcinoma. Inhibiting HIF2 could thus represent a therapeutic approach for the treatment of the low bone mass observed in chronic diseases, osteoporosis or aging. Additionally, we are using unbiased approaches to establish how the loss of osteoblastic HIF2 promotes bone formation** (*R01 AR073022, Dr. Schipani PI*)**.**

The hypoxia signaling pathway, mitochondria and the reprogramming of metabolism in somitogenesis

My laboratory recently established that HIF1 is critical for spine development as its loss in the presomitic mesoderm impairs somitogenesis and causes spine and rib malformations that closely mimic those observed in patients with Jarcho-Levin Syndrome**,** a rare form of spondylothoracic dysplasia.

We are currently investigating whether the impairment of somitogenesis secondary to loss of HIF1 is due to dysregulation of glycolysis and mitochondrial function in the presomitic mesoderm in collaboration with Dr. Mark Lewandoski at NCI (*R01 in preparation*).

Role of the hypoxia signaling pathway in the pathogenesis of fibroblastic tumors of the soft tissue and cartilage regeneration

My laboratory showed that continuous activation of the hypoxia signaling pathway in mesenchymal progenitors of the limb bud is detrimental to the skeleton as it causes aggressive fibrosis of the synovial joints, fibroblastic tumors of the soft tissue, and dwarfism by impairing both proliferation and hypertrophy of growth plate chondrocytes. Notably, continuous activation of the hypoxia signaling pathway in mesenchymal progenitors also leads to the formation of ectopic cartilage in the soft tissue surrounding the growth plate. This latter finding suggests that increased activity of the hypoxia signaling pathway may be sufficient to generate cartilage. Thus, if appropriately exploited, transient activation of the hypoxia signaling pathway could help with the regeneration of cartilage in vitro and in vivo by both promoting chondrogenesis and inhibiting hypertrophy, possibly without causing synovial fibrosis or fibroblastic tumors when transiently turned on in vivo.

My laboratory is currently investigating the role of the hypoxia signaling pathway in the onset of fibroblastic tumors of the soft tissue *(Departmental funds).*

We are also exploiting the hypoxia signaling pathway for regenerating cartilage in vitro and in vivo (*R01 AR075770, Dr. Schipani PI*).

Grants

PRESENT and ACTIVE:

R01 AR073022 (Schipani, PI) 01/11/19-12/31/23
NIH/NIAMS $220,000 2.4 calendar months
Role: PI
Title: *HIF-2alpha, a Novel Regulator of Osteoblastogenesis*
The goal of this study is to determine the role of HIF2 in the regulation of bone mass and osteoblastogenesis.

R01 AR074079 (Schipani, PI) 07/15/19-11/30/24
NIH/NIAMS $274,000 3.6 calendar months
Role: PI
Title: *Mitochondria and TFAM in osteoblast biology*
The goal of this study is to establish the role of mitochondrial respiration in osteoblast biology.

R01 AR075770 (Schipani, PI) 09/23/20-01/31/26
NIH/NIAMS $250,000 1.2 calendar months
Role: PI
Title: *Regenerating Hyaline Cartilage Using Nanofibrous Hollow Microspheres and Synergizing TGF-beta and HIF*

The goal of this study is to establish a novel approach to promote chondrogenesis and prevent chondrocyte hypertrophy.

R01 DK113039 (Jueppner, PI) 09/15/18-06/30/23
NIH/NIDDK $12,249 (Schipani) 0.6 calendar months
Role: Co-Investigator
Title: *PTH Inverse Agonists as Therapy for Jansens' Disease*
The goal of this study is the identification of therapeutic avenues for the treatment of Jansen Metaphsyseal Chondrodysplasia.

Major Previous Grants

1993-2000 *PTH/PTHr Receptor Defects in Pseudohypoparathyroidism.*
RO1-DK4718 NIH/NIDDK
Co-investigator

1996-2000 *Constitutively active PTH/PTHrP receptors in vivo.*
RO1-DK5070 NIH/NIDDK
Co-investigator

1997-2005 *Parathyroid hormone and Osteoporosis: Therapy and Basic Mechanisms.*
P50-AR4485 NIH/NIAMS
PI Project V
The major goal: To use transgenic animals expressing a constitutively active PTH/PTHrP receptor in cells of the osteoblast lineage to define how activation of this receptor modulates bone remodeling.

1997-2005 *Parathyroid hormone and Osteoporosis: Therapy and Basic Mechanisms.*
P50-AR4485 NIH/NIAMS
PI Bone Analysis Core
The major goal: to serve each of the individual projects of the SCOR in performing routine histology, in situ hybridization, immunohistochemistry, and hormonal measurements.

1999-2011 *Developmental Regulation of Bone Morphogenesis.*
PO1- DK56246 NIH/NIDDK
PI High Resolution Histology Core
The major goal: to serve each of the individual projects in performing routine histology, in situ hybridization and immunohistochemistry.

2002-2006 *Carboxyl-terminal PTH Receptors in Bone Cells.*
RO1-AR4706 NIH/NIAMS
Co-investigator

2003-2011 *Hormonal Control of Calcium Metabolism.*
PO1-DK11794 NIH/NIDDK
Co-investigator Project V

2003-2011 *Hormonal Control of Calcium Metabolism.*
PO1-DK11794 NIH/NIDDK
Co-investigator, Tissue Phenotyping Core

2004-2006 *PTH1R regulation in bone biology using mouse models.*
RO1-DK0228 NIH/NIDDK
Co-investigator

2004-2005 *Modulation of bone remodeling by administration of OPG, Alendronate or Zoledronate.*
Amgen
PI
The major goal: to investigate how treatment with OPG, alendronate or zoledronate affects bone remodeling in a mouse model of high bone turnover secondary to expression of a constitutively active PTH/PTHrP receptor in cells of the osteoblast lineage.

2005-2010 *Specialized Center for Cell Based Therapy [SCCT].*
U54-HL081030-01
PI Bone Analysis Core
The major goal: to serve each of the individual projects in performing routine histology, in situ hybridization and immunohistochemistry

2008-2010 *Modulation of bone remodeling by concomitant administration of OPG and PTH.*
Amgen
PI
The major goal: to study how administration of OPG modulates the bone marrow fibrosis in mice expressing a constitutively active PTH/PTHrP receptor in cells of the osteoblast lineage.

2011-2013 *Identification of a novel bone marrow population.*
NIH/NIAMS
PI
The major goal: to study a novel bone marrow population recently identified in the bone marrow and its contribution to bone marrow fibrosis.

2003-2014 *Role of Hypoxia in Differentiation.*
NIH/NIAMS
PI
The major goal: to study the role of hypoxia signaling pathways in endochondral bone development.

2009-2014 *Notch and hypoxia in intervertebral disc development.*
NIH/NIAMS
Co-investigator
The major goal: to study the role of Notch and hypoxia signaling pathways in intervertebral disc development.

2013-2018 *Role of HIF-1 in intervertebral disc function*
R01 AR055655 NIH/NIAMS
Co-investigator
The major goal of this project is to investigate the role of HIF-1 in intervertebral disc development and function.

2015-2017 *Exploring the physiological role of osteoblastic Epo and osteoblastic EpoR*
NIH/NIAMS
PI

The major goal: to study the role of osteoblastic EPO and osteoblastic EPOR in bone and bone marrow development and homeostasis.

2016-2017 *Suppression of b-catenin hyperactivity by HIFs: Implications in colon cancer therapeutics.*
McCubed University of Michigan
Co-PI
The major goal: to provide critical mouse models for the execution of the study.

2016-2017 *Role of the Hypoxia Signaling Pathway in Spine Development.*
Pediatric Orthopaedic Society of North America
Co-investigator
The major goal: to study whether loss of HIF-1a in somites alters somitogenesis and results in spine deformities, and eventually scoliosis.

2013-2019 *HIF-1alpha, a survival and differentiation factor for cartilage.*
NIAMS/NIH
PI
The goal of this project is to study the role of mitochondrial metabolism downstream of HIF1 as a survival and differentiation factor for chondrocytes.

2016-2020 *P30 Michigan Integrative Musculoskeletal Health Core Center*
NIH/NIAMS
Histology Core Director
The Michigan Integrative Musculoskeletal Health Core Center (MiMHC) will enable vertically integrative, multi-scale musculoskeletal scince by increasing access to critical, specialized resources and expertise that are fundamental to the musculoskeletal research programs of center investigators.

Honors and Awards

1985	M.D., Summa Cum Laude, Sant'Anna School of Advanced Studies and Medical School of Pisa, Pisa, Italy
1989	Ph.D., Summa Cum Laude, Sant'Anna School of Advanced Studies, Pisa, Italy
1990-1993	Fellowship, Ministero della Ricerca Scientifica, Italy. Special grant for a scientific studies abroad; awarded by the Italian government
1993	Concorso for Assistant Professor Position at University of Pisa, prestigious national competition for university faculty positions, Italian government
1994-1996	National Osteoporosis Foundation Fellowship
1995	Travel Award of the International Conference on Calcium Regulating Hormones
1995	Young Investigator Award, American Society for Bone and Mineral Research
2019	Paula Stern Achievement Award-ASBMR Esteemed Award
2019	Fellow of the ASBMR
2020	Co-Chair of 2020 Bone and Teeth Gordon Conferences Elected Chair of 2022 Bone and Teeth of Gordon Conferences

Memberships in Professional Societies

1992-present:	American Society for Bone and Mineral Research 2000-2018 – Abstract reviewer 1996, 1997, 2000, 2005, 2006, 2012,2013,2014,2019,2020 – moderator ASBMR meeting 2008 – Co-Chair State-of-the-Art Lecture A: Role of oxygen sensing pathways 2014 – Category Chair of the Skeletal Development abstract review category 2015 – Category Chair of the Skeletal Development abstract review category 2015 – Co-chair Symposium "Metabolism of Bone Cells" 2015 – Discussion Leader "Grant writing workshop" 2015-2017 – Member of the Education and Membership Committee 2015-2016 – Member of the Organizing Committee ASBMR 2016 2017-2019 – Council Member 2017 – Council Liaison Women Committee 2017 – Annual Meeting Program Advisory Committee 2018 – Council Liaison Development Committee 2018 – Nominating Committee 2018-2019 – Council Liaison Publications Committee 2019 – Co-chair Symposium "Cutting Edge Concepts: CRISPR beyond the mouse" 2019-2021 – Annual Meeting Advisory Committee
1994-2011:	American Society for Endocrinology
1999	Moderator of one session Endocrine Society meeting
2002-2011:	American Society of Matrix Biology
2004-present:	Association of Osteobiology
2005-present:	ASCI
2005-2011:	The New York Academy of Sciences 2007 – Moderator of session, 2nd conference on Skeletal Biology and Medicine, The New York Academy of Sciences 2011 – Moderator of session, 4th conference on Skeletal Biology and Medicine, The New York Academy of Sciences
2007-2015	International Bone and Mineral Society

Editorial Positions, Boards, and Peer-Review Services

Grant Review Activities

1999-2000	Medical Research Council (MRC, Canada), Ad hoc reviewer
2006	VA Grants, Ad hoc reviewer
2006	Committee for Review of Research Proposals, Harvard Stem Cell Institute, Harvard Medical School, Ad hoc reviewer
2007	Pilot and feasibility grants, Yale Core Center for Musculoskeletal Disorders, Medical School, Yale University, Ad hoc reviewer
2007-2011	NIH SBSR Study Section, Regular Member
2008	Pilot and Feasibility grants, Center for Metabolic Bone Diseases, University of Alabama, Ad hoc reviewer
2008-2014	ASBMR Career Enhancement Award Committee
2009	NIH-NCI Cell Biology Special Emphasis, Ad hoc reviewer
2013	NIH-MTE Study Section, Ad hoc reviewer
2013	NIH-Special Emphasis Panel" Musculoskeletal Development, Injury and Regeneration", Chair

2014	NIH-Special Emphasis Panel "ZRG1 MOSS-U03", Chair
2014-2018	NIH-MTE Study Section, Regular Member
2014	NIH-NIAMS, Roundtable discussion on the role of disc degeneration in back pain
2015-present:	Fibrodysplasia Ossificans Progressiva (FOP) Foundation, Ad hoc Reviewer
2015	Pilot Projects, Yale Diabetes Center, Medical School, Yale Univesrity, Ad hoc reviewer
2015	NIA- ZAG1 ZIJ-8 (M2) (PO1), Ad hoc reviewer
2015	NIAMS-ZRG1-MOSS-U02, Ad hoc reviewer
2017	NIAMS-Special Emphasys Panel, Ad hoc reviewer
2017	UMHS-PUHSC Joint Institute, University of Michigan, Ad hoc reviewer
2018-present:	NIH-SBDD Study Section, Ad hoc reviewer
2018	NIAMS Special Emphasys Panels, Ad hoc reviewer
2018	Swiss National Science Foundation, Ad hoc reviewer
2018-present:	NIA PO1s Ad hoc reviewer
2019	Pilot and feasibility grants, Department of Medicine, Medical School, Wahington University, Ad hoc reviewer
2019	Pilot and Feasibility grants, Dental School, University of Michigan, Ad hoc reviewer
2019	Pilot and feasibility grants, Musculoskeletal Center, Medical School, University of Michigan, Ad hoc reviewer
2019	Pilot and feasibility grants, Center for Organogenesis, Medical School, University of Michigan, Ad hoc reviewer

Editorial Board

01/2001-01/2016	BoneKEy (Nature Publishing Group)
01/2002-12/2005	Endocrinology
07/2004-05/2015	Journal of Bone and Mineral Research
01/2007-01/2021	Bone
01/2016-12/2020	Endocrinology
10/2021-present	Journal of Bone and Mineral Research

Editor

2014-2015	Section Editor-Current Osteoporosis Reports
2015	Scientific Reports (Nature Publishing Group)
2019-2020	Guest Editor-Bone
2021-2022	Section Editor- Current Osteoporosis Reports
2021-2022	Guest Editor-Bone Reports
2021-present	Reviewing Editor-eLife
2021-present	Associate Editor-JCI Insight

Ad-hoc manuscript reviewer

American Journal of Endocrinology and Metabolism
Arthritis and Rheumatism
Blood
Bone
Calcified Tissue International
Cancer Research
Development
Developmental Biology
Developmental Cell

Cell Metabolism
eLife
EMBO
FASEB
Endocrinology
Genes and Development
Human Molecular Genetics
JBMR
Journal of Cell Biology
Journal of Clinical Endocrinology and Metabolism
Journal of Clinical Investigation
Journal of Experimental Research
Journal of Orthopedic Research
Journal of Biological Chemistry
Molecular Cancer Research
MCB
Molecular Endocrinology
Nature Medicine
Nature Communication
Osteoarthritis and Cartilage
PLoS Genetics
PLoSone
PNAS
Science
Science Signaling
Stem Cells
Science Translational Medicine
Stem Cell Reports

Teaching

Teaching of Students in Courses

2000-2008	Tutor – Course of Pathophysiology in the Renal/Musculoskeletal/Endocrine Block, 2nd year Medical Students, Harvard Medical School, Boston, MA
2004-2005	Lecturer – Molecular mechanisms of bone and joint formation, 2nd year Medical Students, Harvard Medical School, Boston, MA
2015	Lecturer – Molecular and Cellular Mechanisms of Cartilage and Bone Development, Clinical Residents-Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI
2015	Lecturer – Hypoxia signaling pathways in development, CDB 582/583 Course "Stem cells to regenerative biology", University of Michigan, Ann Arbor, MI
2016	Lecturer – Endocrine Regulation of Bone and Calcium/Phosphate homeostasis I, Clinical Residents-Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI
2016	Lecturer – Endocrine Regulation of Bone and Calcium/Phosphate homeostasis II, Clinical Residents-Department of Orthopedic Surgery, University of Michigan, Ann Arbor, MI
2016	Lecturer – Spine Development, Clinical Residents-Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI
2016-2017	Lecturer – Permanent Cartilage and Bone, Musculoskeletal Course-Medical School, University of Michigan, Ann Arbor, MI

2016-2017	Lecturer – Bone formation, Musculoskeletal Course-Medical School, University of Michigan, Ann Arbor, MI
2016-2019	Lecturer- Bone Formation, Musculoskeletal Course-Dental School, University of Michigan, Ann Arbor, MI
2016-present	Lecturer– Permanent Cartilage and Bone, Musculoskeletal Course-Dental School, University of Michigan, Ann Arbor, MI
2016-2017	Lecturer – Permanent Cartilage and Bone, Histology Course for graduate and undergraduate students, University of Michigan, Ann Arbor, MI
2016-2017	Lecturer-Histology Course for graduate and undergraduate students "Bone formation", University of Michigan, Ann Arbor, MI
2017	Lecturer- VitD and Rickets, Clinical Residents-Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI
2017-2019	Lecturer- Skeletal Development, Clinical Residents-Department of Orthopaedic Surgery, University of Michigan, Ann Arbor, MI
2017-2019	Lecturer- Permanent Cartilage and Adult Bone, IInd year Medical Students, University of Michigan, Ann Arbor, MI

Laboratory and Other Research Supervisory and Training Responsibilities

1998-present	Advisory role for 2-3 postdoctoral fellows
1998-2011	PI at the Histology Core, Endocrine Unit, MGH, Boston, MA
2004-2005	External advisor member of the PhD thesis defense committee-Tissue Engineering Department, Stony Brook University, NY
2011	Member of the PhD thesis defense committee, Harvard Dental School, MA
2014	Member of the PhD qualifying exam committee, Department of Physiology, Medical School, University of Michigan, Ann Arbor, MI
2016	Member of the PhD qualifying exam committee, Department of Physiology, Medical School, University of Michigan, Ann Arbor, MI
2016-present	PI at the Histology Core, Orthopaedic Research Laboratory, Medical School, University of Michigan, Ann Arbor, MI
2017	Mentor of a thesis with honors at College of Literature, Science and the Arts, University of Michigan, Ann Arbor, MI
2018	Member of a PhD thesis defense committee, Department of Orthopedic Surgery, Medical School, University of Michigan, Ann Arbor, MI
2018	Member of a PhD thesis defense committee, Department of Cell and Developmental Biology, University of Hong Kong, Hong Kong, China
2019	Member of a Master thesis defense committee, Department of Orthodontics, Dental School, University of Michigan, Ann Arbor, MI

Formally Supervised Trainees

2000	Anna Giovannetti, PhD/ Research Associate, University of Pisa, Pisa, Italy
2001-2002	Anja Maier, MD/ Private Practice Physician
1999-2002	Laura Calvi, MD**/ Young Investigator Award-ASBMR**, Haddad Investigator Award, K08 Award (NIH), Professor, Medical School, University of Rochester, NY
2003-2004	Riccardo Chiusaroli, PhD/ Head of Histology and Pathology, Rottapharm, Monza, Italy
2005-2008	Masanobu Ohishi, MD-PhD/ Assistant Professor with tenure, Medical School, University of Kiushu, Japan
2005-2006	Sylvain Provot, PhD**/Young Investigator Award-ASBMR**, Assistant Professor with tenure, INSERM, Paris, France
2008	Ellinoora Aro, MD-PhD/Resident General Surgery, University of Helsinki,

	Finland
2008-2011	Richa Khatri, MD/ Resident General Surgery, Western Michigan University, Kalamazoo, MI
2009-2010	Wanida Ono, DDS-PhD/Associate Professor, Dental School, University of Texas, Houston, TX
2009-2010	Elisa Araldi, PhD/ Assistant Professor, ETH Zurich, Zurich, Switzerland
2010-2011	Erinn Rankin, PhD/ Assistant Professor, Radiation Oncology, Stanford, CA
2011-2015	Laura Mangiavini, MD/Associate Professor, University of San Raffaele, Milano, Italy
2015-2017	Kavitha Ranganathan, MD/**Young Investigator Award-ASBMR**, Resident General Surgery, University of Michigan Medical School, Ann Arbor, MI
2015-2018	Angela Yao, PhD/**Young Investigator Award-ASBMR**, Assistant Professor, University of Science and Technology, Shenzen, China
2012-2020	Christophe Merceron, PhD/ **Young Investigator Award-ASBMR,** Research Investigator**,** Medical School, University of Michigan, Ann Arbor, MI

Local and Regional Presentations and Lectures

1993	The human PTH/PTH receptor from cloning to human diseases, Endocrine Division Lectures Massachusetts General Hospital, Boston, MA
1993	The PTH/PTHrP receptor in Pseudohypoparathyrioidism, Pediatric Department Lectures Massachusetts General Hospital, Boston, MA
1995	The PTH/PTHrP receptor in Jansen Metaphyseal Chondrodysplasia, Pediatric Endocrine Grand Rounds Massachusetts General Hospital, Boston, MA
2004	Jansen's PTH/PTHrP receptors in bone growth and remodeling, Endocrine Grand Rounds Massachusetts General Hospital, Boston, MA
2004	Jansen's PTH/PTHrP receptors in bone growth and remodeling, Endocrine Grand Rounds Brigham and Women's Hospital, Boston, MA
2004	Hypoxia, HIF-1 alpha and VHL in endochondral bone development, Grand Round-Harvard Dental School, Boston, MA
2005	Hypoxia and HIF-1 alpha in growth plate development, Orthopaedic Research Seminar Series 2004-2005 Children's Hospital, Boston, MA
2006	Constitutively active PTH/PTHrP receptors in bone stromal cells, 4th Symposium on Membrane Biology, Massachusetts General Hospital, Boston, MA
2012	Hypoxia Signaling Pathway in Development and in Differentiation, Tumor Microenvironment Seminar Series-Cancer Center-IU School of Medicine, Indianapolis, IN
2012	HIFs and VHL in cartilage, bone and hematopoiesis, Bone Seminar Series, IU School of Medicine, Indianapolis, IN
2013	Hypoxia signaling pathways in organogenesis. MSK Seminar Series, October 9, University of Michigan, Ann Arbor, MI (Seminar)
2013	Hypoxia signaling pathways in cartilage, bone and hematopoiesis: an update. Endocrine Seminar Series, November 1, University of Michigan, Ann Arbor, MI (Seminar).
2014	HIFs and VHL in cartilage and bone development. Orthopaedic Surgery Grand Rounds, February 11, University of Michigan, Ann Arbor, MI (Seminar)
2014	Hypoxia signaling pathways in development and differentiation. Seminar Series, December 9, Nephrology Division, University of Michigan, Ann Arbor, MI (Seminar)
2015	Hypoxia signaling pathways in development and differentiation. Seminar Series, January 15, Division of Hematology Oncology, University of Michigan, Ann Arbor, MI (Seminar)

2015	Hypoxia signaling pathways in development of the nucleus pulposus. April 27, The Frederick J. Fisher Pediatric Orthopaedic Lectureship, University of Michigan, Ann Arbor, MI (Invited Talk)
2016	Role of HIF-1a in spine development. April 25, The Frederick J. Fisher Pediatric Orthopaedic Lectureship, University of Michigan, Ann Arbor, MI (Invited Talk)
2016	HIFs and the osteogenesis-angiogenesis coupling. May 6, T32 Training Grant Seminar Series, Plastic Surgery University of Michigan, Ann Arbor, MI (Seminar)
2017	Impairment of mitochondrial respiration promotes survival of hypoxic chondrocytes. March 3rd, Endocrine Grand Round, Department of Medicine-Endocrinology, School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2017	Impairment of mitochondrial respiration promotes survival of hypoxic chondrocytes. "Brown Bag" Seminar Series, Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2107	Choke to start the engine: how impairment of mitochondrial function can improve survival of hypoxic cells *in vivo.* Department of Physiology School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2018	Enhancing mitochondrial respiration causes severe intracellular hypoxia and death of hypoxic cells. Brown Bag" Seminar Series, Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2019	Hypoxia, HIFs and mitochondria in skeletal development. Brown Bag" Seminar Series, Department of Cell and Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2021	Hypoxia and mitochondria in skeletal development an somitogenesis, IRM seminar, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Seminar)

Committee, Organizational, and Volunteer Services

Local

2004-2005	ECOR Subcommittee for Review of Research Proposals, Massachusetts General Hospital, Boston, MA
2000-2010	SRAC, Massachusetts General Hospital, Boston, MA
2014-2015	RO1 Boot Camp, UMICH, Ann Arbor, MI
2014-present:	RAC Committee, Department of Orthopedics, Medical School, University of Michigan, Ann Arbor, MI
2014-2015	LAUNCH Committee, Dental School, University of Michigan, Ann Arbor, MI
2015-present:	BioArtography Committee, Department of Cell and Developmental Biology, Medical School, University of Michigan, Ann Arbor, MI
2015-2016	Award Nominating Committee, Department of Cell and Developmental Biology, Medical School, University of Michigan, Ann Arbor, MI
2015-2016	Graduate Students Admissions Committee, Department of Cell and Developmental Biology, Medical School, University of Michigan, Ann Arbor, MI
2016-2017	LAUNCH Committee, Dental School, University of Michigan, Ann Arbor, MI
2017-2108	Search Committee for Faculty Positions, Dental School, University of Michigan, Ann Arbor, MI

2018	Committee for abstract selection, Annual Symposium, Departmemt of - Medicine;University of Michigan, Ann Arbor, MI
2019-2020	Search Committee for Faculty Positions, Department of Cell and Developmental Biology, Medical School, University of Michigan, Ann Arbor, MI
2019-2020	Search Committee for Faculty Positions, Dental School, University of Michigan, Ann Arbor, MI

National and International Committees

1994	Scientific Committee for the 4th International Symposium on Endocrinology under 35
2007-2011	Scientific Committee for IBMS Davos, Workshop: Bone Biology & Therapeutics, International Bone of Mineral Society
06/07-06/2011	Member IBMS Council, International Bone Mineral Society
2009-2011	Scientific Committee IBMS meeting 2011, International Bone of Mineral Society
2009-2010	Scientific Committee Parathyroids 2010
03/2011	Discussion Leader, Gordon Conference on Cartilage Biology and Pathology, March 6-11, 201, Ventura, CA
06/2012-06/2015	Member Nominating Committee, International Bone Mineral Society
04/2013	Discussion Leader, Gordon Conference on Cartilage Biology and Pathology, April 7-11, 2013, Les Diablerets, Switzerland
09/2014-present:	Board Member of the Osteobiology Association
03/2015	Discussion Leader, Gordon Conference on Cartilage Biology and Pathology, March 22-27, 2015, Galveston, TX
2015-2016	ASBMR Organizing Committee
2015-2017	ASBMR Education and Membership Committee
2016-2017	ASBMR Annual Meeting Program Advisory Committee
2017-2019	ASBMR Council
2017	ASBMR Council Liason Women Committee
2018	ASBMR Council Liason Development Committee
2018	ASBMR Nominating Committee
2019	ASBMR Council Liason Publications Committee
2019-2020	ASBMR Annual Meeting Advisory Committee
2021-2023	ASBMR Publication Committee

Visiting Professorships, Seminars, and Extramural Invited Presentations

National

1992	The human PTH/PTH receptor: from cloning to human diseases. Molecular Pathophysiology Branch, NIH, Bethesda, MD (Seminar)
1999	Constitutively active PTH/PTHrP receptors: in vitro studies. ASBMR, Workshop on structure function of the PTH/PTHrP receptor St. Louis, MO (Seminar)
1999	The PTH/PTHrP receptor in endochondral bone development. American Society of Nephrology, Miami, FL (Lecture)
2000	Jansen PTH/PTHrP receptor in bone development. Endocrine Grand Rounds, NIH, Bethesda, MD (Visiting Professor)
2000	The PTH/PTHrP receptor in endochondral bone development. American Society of Pediatric Nephrology, Boston, MA (Lecture)
2000	Jansen PTH/PTHrP receptor in bone development.

Molecular Medicine Seminar Series, April 17, University of Connecticut Health Center, CT (Visiting Professor)

2002 The role of HIF-1alpha and VHL in endochondral bone development.
American Society for Matrix Biology, November 6-9, Houston, TX (Lecture)

2002 Hypoxia and HIF-1alpha in endochondral bone development.
Endocrine Grand Rounds, Yale University, New Haven, CT (Visiting Professor)

2003 Molecular mechanisms of endochondral bone development.
HSS-Cornell University, New York, NY (Visiting Professor)

2003 Hypoxia and HIF-1alpha in endochondral bone development.
Amgen, Thousand Oaks, CA (Visiting Scientist)

2004 Hypoxia and HIF-1alpha in chondrogenesis
Keystone Symposium on "Biology of Hypoxia: The role of oxygen sensing in development, normal function and disease (D3)", March 25-30, Steamboat Spring Colorado (Lecturer) Meeting Review in Genes and Dev., 2004, 18:2183-2194.

2005 Hypoxia and HIF-1alpha in endochondral bone development.
Departmental Research Seminar Series, Department of Pathology, UAB, Birmingham, AL (Visiting Professor)

2005 Role of hypoxia and HIF-1alpha in chondrogenesis.
Orthopaedic Research Seminar Series, March 23, Washington University, St. Louis, MO (Visiting Professor)

2005 Hypoxia and HIF-1alpha in endochondral bone development.
Endocrine Grand Rounds, NIH, Bethesda, MD (Visiting Professor)

2005 Molecular mechanisms of endochondral bone development.
Cedars Sinai UCLA, Los Angeles, CA (Visiting Professor)

2005 Hypoxia and HIF-1alpha in chondrogenesis
UC Davis, Sacramento, CA (Visiting Professor)

2005 Hypoxia and HIF-1alpha in chondrogenesis
NYAS Conference Skeletal Development and Remodeling, May 18-21, New York, NY (Seminar)

2006 PTH and the PTH/PTHrP receptor in bone stromal cells.
UC Davis, Sacramento, CA (Visiting Professor)

2006 Molecular mechanisms of endochondral bone development: a transgenic approach.
UC Davis, Sacramento, CA (Visiting Professor)

2006 Hypoxia and HIF-1alpha in chondrogenesis.
Mesenchymal Stem Cell Biology: a Symposium, March 17, UCSF, San Francisco, CA (Seminar)

2006 Hypoxia and HIF-1alpha in chondrogenesis.
Workshop on Growth Plate, June 11-15, Portland, OR (Seminar)

2007 Growth plate development and hypoxia.
Meet the Professors, ASBMR, September 16-19, Honolulu (Seminar)

2007 Hypoxia and HIF-1alpha in chondrogenesis.
Orthopaedic Grand Rounds, Thomas Jefferson University, Philadelphia, PA (Visiting Professor)

2008 The fetal growth place: a developmental model of cellular adaptation to hypoxia.
Children Memorial Hospital, Northwestern University, June 20, Chicago, IL (Visiting Professor)

2008 The fetal growth plate: a developmental model of cellular adaptation to hypoxia.
Department of Biochemistry, NJMC, Newark, NJ (Visiting Professor)

2009 Analysis of bone marrow stroma: lessons from mutant.
Endocrine Grand Rounds, Yale University, New Haven, CT (Visiting Professor)

2009 Hypoxia and HIFs in chondrogenesis.
FASEB Meeting, April 18-22, New Orleans, LA (Lecture)

2009 Hypoxia-dependent collagen modifications in limb bud development.

NYAS Conference Skeletal Biology and Medicine, April 29-May 2, New York, NY (Seminar)

2010 Dual action of pVHL in limb bud mesenchyme.
Keystone Symposia-hypoxia: Molecular Mechanisms of Oxygen Sensing and Response Pathways, January 19-24, Keystone, CO (Invited Short Talk)

2010 Oxygen sensing in cartilage and bone development.
ASBMR, October 15-19, Toronto, Canada (Lecture)

2010 Oxygen sensing in cartilage and bone development.
Rolanette and Berdon Lawrence Bone Disease Program of Texas Seminar Series. December 3, Houston, TX (Visiting Professor)

2012 HIFs and VHL in cartilage, bone and hematopoiesis.
Louis V. Avioli Seminar Series, April 20, St. Louis, MO (Visiting Professor)

2012 Fibrocytes and marrow fibrosis.
Meet-the-Professors, ASBMR, October 12-15, Minneapolis, MN (Invited Seminar)

2012 HIFs and VHL in cartilage, bone and hematopoiesis.
October 12, Department of Medicine, UMI School of Medicine, Ann Arbor, MI (Visiting Professor)

2012 VHL in organogenesis.
4th International Research Conference on Multiple Hereditary Exostoses, The Children's Hospital of Philadelphia Research Institute, November 1-4, Philadelphia, PA (Seminar)

2012 HIFs and VHL in cartilage, bone and hematopoiesis.
November 15, Department of Chemical Engineering, USC, Columbia, SC (Visiting Professor)

2012 HIFs and VHL in cartilage, bone and hematopoiesis.
December 6, Institute for Reproductive Health and Regenerative Medicine, Department of Pathology, KUMC, Kansas City, KS (Visiting Professor)

2013 Hypoxia signaling pathways in cartilage, bone and hematopoiesis: an update.
Endocrine Seminar Series, November 1, University of Michigan, Ann Arbor, MI (Seminar)

2013 Hypoxia signaling pathways in cartilage and development and homeostasis.
December 6, Lerner Institute, Cleveland Clinic, Cleveland, OH (Seminar)

2015 HIFs and VHL in cartilage and bone development: a role for angiogenesis.
April 20, University of Delaware, Newark, DE (Seminar)

2017 Choke to start the engine: how impairment of mitochondrial function can improve survival of hypoxic cells *in vivo.* April 21, Medical School-Yale University, New Heaven, CT (Lecture)

2018 Enhancing mitochondrial respiration causes severe intracellular hypoxia and death of hypoxic cells. February 14, National Cancer Institute, NIH, Bethesda, MD (Lecture)

2018 Suppressing mitochondrial respiration is critical for hypoxia tolerance in the fetal growth plate. July 13, University of Little Rock, Little Rock, AR (Lecture)

2021 Hypoxia and mitochondria in skeletal development. March 3rd, University of Colorado, Denver, CO (Mack Clayton Lecture)

2021 Hypoxia and mitochondria in skeletal development. March 25th, UCSF, San Francisco, CA (Lecture)

International

1991 Cloning of the human PTH/PTHrP receptor. Istituto di Endocrinologia, Universita di Pisa, Italy

1994 The human PTH/PTH receptor: from cloning to human diseases. International

Symposium on "Endocrinology under 35" Rome, Italy

1997 The PTH/PTHrP receptor in Jansen Metaphyseal Chondrodysplasia. Deutsche Gesellschaft Für Endokrinologie, May 6-8, Lübeck, Germany

1998 Constitutively active PTH/PTHrP receptors: in vivo and in vitro studies. Séminar des Chaire de Communications Cellulaires (Pr. J-P. Changeux) et de Médecine Expérimentale (Pr. P. Corvol) du Collége de France, February 26-27, Paris, France

1999 The PTH/PTHrP receptor in endochondral bone development. Workshop on Osteobiology, June 3-6, Gallipoli, Italy

2000 Jansen PTH/PTHrP receptor in bone development. Workshop on Osteobiology, Wurzburg, Germany

2003 The PTH/PTHrP receptor in bone growth and remodeling. 30th European Symposium on Calcified Tissues (ECTS), May 8-12, Rome, Italy

2003 Hypoxia and HIF-1alpha in endochondral bone development. 1st Joint Meeting IBMS/JBMS, June 3-7, Osaka, Japan

2005 Hypoxia and HIF-1alpha in chondrogenesis. Gordon Conference on Cartilage, June 5-8, Il Ciocco, Italy

2005 Hypoxia and HIF-1alpha in chondrogenesis. Gordon Conference on Bone and Teeth, July 10-15, The University of New England, Maine, USA

2006 Hypoxia and HIF-1alpha in chondrogenesis. 20Th International Meeting of Biochemistry and Molecular Biology, June 19-23, Kyoto, Japan

2006 Hypoxia and HIF-1alpha in chondrogenesis. Research Symposium Developmental Biology in Orthopaedics, October 26-28, Toronto, Canada

2008 HIF-1alpha and chondrocytes: a tale of paradoxes. Shriners Hospital for Children-McGill University, May 28, Montreal, Canada

2009 PTH and bone marrow stroma. The 3rd meeting of Bone and Cartilage Frontier, Tokyo, Japan

2010 PTH and stem cells. Parathyroids 2010, February 11-13, Pisa, Italy

2011 HIFs and VHL in cartilage: a tale of paradoxes. Gordon Conference on Cartilage Biology and Pathology, March 6-11, Ventura, CA, USA

2011 Hypoxia signaling pathway in cartilage, bone and hematopoiesis. 3rd Joint Meeting IBMS/ECTS Athens, May 7-11, Greece

2012 Hypoxia signaling pathway in cartilage, bone and hematopoiesis
Hypoxia 2012, April 4-5, Nantes, France

2013 Hypoxia signaling pathway in organogenesis. Dealing with Hypoxia: Regulatory Aspects in Cells, Tissues and Organisms, June 8-12, Oulu, Finland

2013 HIF-1alpha is essential for the development of the nucleus pulposus.
Second International Research Meeting, "New Horizons in Intervertebral Disc Research," November 6-8, Philadelphia, PA, USA

2015 Fibrosis and HIF-1alpha-dependent tumors of the soft tissue upon loss of VHL in mesenchymal progenitors. The Tumor Microenvironment: 14th International Workshop, August 27-29, Vancouver, British Columbia, Canada

2016 HIFs and the osteogenesis-angiogenesis coupling. Advances in Mineral Metabolism: International Workshop, March 27-31, Snowmass, CO, USA

2016 Hypoxia signaling pathways in bone.
Meet-the-Professor, Advances in Mineral Metabolism: International Workshop, March 27-31, Snowmass, CO, USA

2016 HIFs and hypoxia in joint health and disease. Tackling Joint Disease by Understanding Crosstalk between Cartilage and Bone Research Symposium, April 28-30, Rosemont, IL, USA

2017 Impairment of mitochondrial respiration promotes survival of hypoxic cells. The Tumor Microenvironment: 15th International Workshop, April 26-29, Miami Beach, FL, USA

2018 Choke to start the engine: how the impairment of mitochondrial function enables survival of hypoxic chondrocytes in vivo. Gordon Conference on Bone and Teeth,

January 28-February 2, Galveston, TX, USA.

2018 Growth plate development and closure from embryos to adult. AAOS/ORS The physis: Fundamental knowledge to a fantastic future through research. February 7-9, Rosemont, IL, USA.

2018 Impairment of mitochondrial respiration promotes survival of HIF-1alpha deficient chondrocytes in vivo. Therapeutic targeting of hypoxia-sensitive pathways,Keystone Symposia, April 10-14, Oxford, UK.

2018 The hypoxia signaling pathway in skeletal development. First annual fibrodysplasia ossificans progressive (FOP) and traumatic heterotopic ossification (HO) symposium. September 21, University of Michigan, Ann Arbor, MI.

2019 Mitochondria and HIFs in skeletal development. Gordon Conference on Cartilage, March 17-22, Galveston, TX, USA.

2019 Suppressing mitochondrial respiration is critical for hypoxia tolerance in the fetal growth plate. The Tumor Microenvironment: 16th International Workshop, June 13-15, Miami Beach, FL, USA.

2021 Hypoxia and Mitochondria in skeletal development. ECTS, May 6-8, Digital Congress.

2021 Choke to start the engine: how the impairment of mitochondrial function enables survival of hypoxic chondrocytes. HYPOXYGEN Webinar "Effects of Hypoxia on the biology of tumors and normal cells", October 20.

Patents

Patent: 5,840,853 Date: Nov 24, 1998. Parathyroid Hormone receptor and DNA encoding the same receptor. I was member of the team who cloned the rat and opossum PTH/PTHrP receptor, and I then cloned the human homolog.

Bibliography

Completed Publications in Scientific Journals: Peer-Reviewed

1. Pacini F, Elisei R, Anelli S, Gasperini L, **Schipani E** (*I contributed to the analysis of the data*), Pinchera A. Circulating neuron-specific enolase in medullary thyroid cancer. **The International Journal of Biological Markers 1986**;1:85-88.

2. Vitti P, Chiovato L, Lopez G, Lombardi A, Santini F, Mammoli C, Bassi P, Gryczynska M, **Schipani E** *(I contributed to the analysis of the data)* Tosti-Balducci M, Fenzi GF, Pinchera A. Measurement of TSAb directly in serum using FRTL-5 cells. **J Endocrinol Invest 1988**; 11:313-317.

3. Marcocci C, Pacini F, Elisei R, **Schipani E** (*I contributed to the collection and analysis of the data*), Ceccarelli C, Miccoli P, Arganin M, Pinchera A. Clinical and biological behavior of bone metastases from differentiated thyroid carcinoma. **Surgery 1989**; 106:960-966.

4. Jüppner H, Abou-Samra AB, Uneno S, **Schipani E** *(I performed some of the key experiments and I contributed to the analysis of the data)*, Keutmann HT, Potts JT Jr, Segre

GV. Properties of amino-terminal parathyroid hormone-related peptide modified at position 11-13. **Peptides 1990**; 11:1139-1142.

5. Jüppner H, Abou-Samra AB, Freeman M, Kong XF, **Schipani E** *(I performed numerous of the critical experiments that led to the cloning of the opossun PTH/PTHrP receptor cDNA)*, Richards J, Kolakowski LF, Hock F, Potts JT Jr, Kronenberg HM, Segre GV. A G protein-linked receptor for parathyroid hormone and parathyroid hormone-related peptide**. Science 1991**; 254:1024-1026.

6. Abou-Samra AB, Jüppner H, Force T, Freeman M, Kong XF, **Schipani E** *(I performed some of the critical experiments that led to the cloning of the rat PTH/PTHrP receptor cDNA)*, Urena P, Richards J, Bonventre JV, Potts JT Jr, Kronenberg HM, Segre GV. Expression cloning of a common receptor for parathyroid hormone and parathyroid hormone-related peptide from rat osteoblast-like cells: A single receptor stimulates intracellular accumulation of both cAMP and inositol trisphosphates and increases intracellular free calcium. **Proc Natl Acad Sci USA 1992**; 89:2732-2736.

7. Hustmyer FG, **Schipani E** *(I contributed to the analysis of the data),* Peacock M. Bsml polymorphism at the parathyroid hormone receptor locus (PTHR) in three populations. **Hum Mol Genet 1993**; 2:1330.

8. **Schipani E**, Karga H, Karaplis AC, Potts JT Jr, Kronenberg HM, Segre GV, Abou-Samra AB, Jüppner H. Identical complementary deoxyribonucleic acids encode a human renal and bone parathyroid hormone (PTH)/PTH-related peptide receptor. **Endocrinology 1993**;132(5):2157-2165. ***This paper was the first report of the cloning of the human PTH/PTHrP receptor.***

9. Fukayama S, **Schipani E** *(I contributed to the design of the study, to the analysis of the data and to the writing of the manuscript),* Jüppner H, Lanske B, Kronenberg HM, Abou-Samra AB, Bringhurst FR. Role of protein kinase-A in homologous down-regulation of parathyroid hormone (PTH)/PTH-related peptide receptor messenger ribonucleic acid in human osteoblast-like SaOS-2 cells. **Endocrinology 1994**; 134:1851-1858.

10. Jüppner H, **Schipani E** *(I performed numerous critical experiments, and I contributed to the design of the study and to the analysis of the data)*, Bringhurst FR, McClure I, Keutmann HT, Potts JT Jr., Kronenberg HM, Abou-Samra AB, Segre GV, Gardella TJ. The extracellular, amino-terminal region of the Parathyroid Hormone (PTH)/PTH-related peptide receptor determines the binding affinity for carboxyl-terminal fragments of PTH(1-34). **Endocrinology 1994**; 134:879-884.

11. Kong XF, **Schipani E** *(I cloned and characterized the human gene encoding the PTH/PTHrP receptor)*, Lanske B, Joun H, Karperien M, Defize LHK, Jüppner H, Potts JT

Jr., Segre GV, Kronenberg HM, Abou-Samra A-B. The rat, mouse and human genes encoding the receptor for parathyroid hormone and parathyroid hormone-related peptide are highly homologous. **Biochem Biophys Res Commun 1994**;200:1290-1299.

12. Gelbert L, **Schipani E** *(I contributed to the analysis of the data and to the writing of the manuscript),* Jüppner H, Abou-Samra A-B, Segre GV, Naylor S, Drabkin H, White R, Heath H lll. Chromosomal localization of the parathyroid hormone/parathyroid hormone-related protein receptor gene to human chromosome 3p21.2-p24.2. **J Clin Endocrinol Metab 1994**; 79:1046-1048.

13. **Schipani E**, Hustmyer FG, Bergwitz C, Jüppner H. Polymorphism in exon M7 of the PTHR gene. **Hum Mol Gen 1994**; 3:1210.

14. **Schipani E**, Weinstein LS, Bergwitz C, Iida-Klein A, Kong XF, Stuhrmann M, Kruse K, Whyte MP, Murray T, Schmidtke J, van Dop C, Brickman AS, Crawford JD, Potts JT Jr., Kronenberg HM, Abou-Samra AB, Segre GV, Jüppner H. Pseudohypoparathyroidism type lb is not caused by mutations in the coding exons of the human parathyroid hormone (PTH)/PTH-related peptide receptor gene. **J Clin Endocrinol Metab 1995**; 80:1611-1621. ***The study demonstrated that, differently from what had been for long time hypothesized, Pseudohypoparathyroidism type Ib, a rare endocrine disorder of calcium and phosphate homeostasis, is not caused by mutations in the PTH/PTHrP receptor gene. This finding prompted Dr. Harald Jueppner and Dr. Schipani to start a wide genome search that eventually led to identification of the Gsalpha gene as the gene critically involved in the pathogenesis of Pseudohypoparathyroidism type 1b (see below).***

15. **Schipani E**, Kruse K, Jüppner H. A constitutively active mutant PTH/PTHrP receptor in Jansen type metaphyseal chondrodysplasia. **Science 1995**;268:98-100. ***This paper was the first report of mutant, constitutively active PTH/PTHrP receptor in Jansen's metaphyseal chondrodysplasia, a severe form of short-limbed dwarfism associated to hypercalcemia. This discovery defined the cause of a devastating human disease, and showed the PTH/PTHrP receptor is a crucial regulator of endochondral bone development. Jansen's metaphyseal chondrodysplasia has been one of the first examples in the literature of a human disease being caused by a constitutively active G-protein coupled receptor. The mutant PTH/PTHrP receptors identified in Jansen's metaphyseal chondrodysplasia have been valuable tools for in vitro structure-functions studies directed to investigate how this receptor couples to and activates G-proteins. More importantly, they have allowed the generation of transgenic mice that, in combination with knockout models, have defined the critical role of the PTH/PTHrP receptor in endochondral bone development.***

16. Orloff JJ, Kats Y, Urena P, **Schipani E** *(I contributed to the analysis of the data),* Vasavada R, Philbrick W, Behal A, Abou-Samra AB, Segre GV, Jüppner H. Further evidence for a novel receptor for amino-terminal parathyroid hormone-related protein on keratinocytes and squamous carcinoma cell lines. **Endocrinology 1995**; 136:3016-3023.

17. Gardella TJ, Luck MD, Jensen GS, **Schipani** *E (I performed some of the key experiments and contributed to the analysis of the data)*, Potts JT, Jueppner H. Inverse agonism of amino-terminally truncated parathyroid hormone (PTH) and PTH-related peptide (PTHrP) analogs revealed with constitutively active mutant PTH/PTHrP receptors. **Endocrinology 1996**; 137:3936-3941.

18. Jüppner H, **Schipani E**. Receptors for parathyroid hormone and parathyroid hormone-related peptide: from molecular cloning to definition of diseases. **Curr Opin Nephrol 1996**; 5:300-306.

19. **Schipani E**, Langman CB, Parfitt AM, Jensen GS, Kikuchi S, Kooh SW, Cole WG, Jueppner H. Constitutively activated receptors for parathyroid hormone and parathyroid hormone-related peptide in Jansen's metaphyseal chondrodysplasia. **N Engl J Med 1996**; 335:708-714.

20. Parfitt AM, **Schipani E** *(I contributed to the analysis of the data and to the writing of the manuscript)*, Rao DS, Kupin W, Han ZH, Jueppner H. Hypercalcemia due to constitutive activity of the Parathyroid Hormone (PTH)/PTH-related peptide receptor: Comparison with primary hyperparathyroidism. **J Clin Endocrinol Metab 1996**; 81:3584-3588.

21. **Schipani E**, Jensen GS, Pincus J, Nissenson RA, Gardella TJ, Jüppner H. Constitutive activation of the cyclic adenosine 3', 5'-monophosphate signaling pathway by parathyroid hormone (PTH)/PTH-related peptide receptors mutated at the two loci for Jansen's metaphyseal chondrodysplasia. **Mol Endocrinol 1997**; 11:851-858.

22. **Schipani E**, Lanske B, Hunzelman J, Luz A, Kovacs CS, Lee K, Pirro A, Kronenberg HM, Jüppner H. Targeted expression of constitutively active receptors for parathyroid hormone and parathyroid hormone-related peptide delays endochondral bone formation and rescues mice that lack parathyroid hormone-related peptide. **Proc Natl Acad Sci USA 1997**; 94:13689-13694. ***This study reported the generation and characterization of the first transgenic mouse model in which a constitutively active PTH/PTHrP receptor was expressed in vivo. This model significantly contributed to the understanding of the role of PTHrP and its receptor in endochondral bone development.***

23. Jüppner H, **Schipani E (***I contributed to the design of the experiments, and I performed some of them***)**, Bastepe M, Cole DEC, Lawson ML, Mannstadt M, Hendy GN, Plotkin H, Koshiyama H, Koh T, Crawford JD, Olsen BR, Vikkula M. The gene responsible for pseudohypoparathyroidism type Ib is paternally imprinted and maps in four unrelated kindreds to chromosome 20q13.3. **Proc Natl Acad Sci USA 1998**; 95:11798-803. ***The study was the first report of the genetic locus for Pseudohypoparathyroidism Ib a rare disorder of calcium and phosphate homeostasis. It was also the first demonstration that***

this disease is caused by a gene genetically imprinted. Future studies, which originated from this novel observation, demonstrated that deletions in the regulatory region of Gsalpha gene were the cause of Pseudohypoparathyroidism Ib.

24. **Schipani E**, Langman C, Hunzelman J, Le Merrer M, Loke KY, Dillon MJ, Silve C, Jüppner H. A novel Parathyroid Hormone (PTH)/PTH-related peptide receptor mutation in Jansen's metaphyseal chondrodysplasia. **J Clin Endocrinol Metab 1999**; 84:3052-3057.

25. Karp SJ, **Schipani E** *(I contributed to the design of the study and to the analysis of the data. I also performed some of the experiments described in the paper, and I generated and characterized one of the transgenic lines used in the study)*, St-Jacques B, Hunzelman J, Kronenberg H, McMahon AP. Indian Hedgehog coordinates endochondral bone development via Parathyroid Hormone related-Protein-dependent and -independent pathways. **Development 2000**; 27:543-548.

26. Calvi ML, Sims NA, Hunzelman JL, Knight MC, Giovannetti A, Saxton JM, Kronenberg HM, Baron H, **Schipani E**. Activated parathyroid hormone/parathyroid hormone-related protein receptor in osteoblastic cells differentially affects cortical and trabecular bone. **J Clin Invest 2001**; 107: 277-286 (***Commentary on the paper in the same issue). This paper reports the generation and characterization of a mouse transgenic line expressing a constitutively active PTH/PTHrP receptor in cells of the osteoblast lineage. The analysis of these transgenic mice has demonstrated that the PTH/PTHrP receptor is a crucial mediator of both bone forming and bone resorbing actions of PTH. Moreover, it has proven that the PTH/PTHrP receptor activity has different net effects in different bone compartments. These findings have underlined the complexity and heterogeneity of the osteoblast population and of their regulatory microenvironment.***

27. Calvi ML, **Schipani E**. The PTH/PTHrP receptor in Jansen's metaphyseal chondrodysplasia. **J Endocrinol Invest 2000**; 23:545-554. (Invited)

28. Long F, **Schipani E.** *(I contributed to the design of the study and to the analysis of the data. I also performed some of the critical experiments reported in the paper)***,** Asahara H, Kronenberg H, Montminy M. The CREB family of activators is required for endochondral bone development. **Development 2001**; 128:541-550.

29. Carter PH, Petroni B, Gensure R, **Schipani E** *(I contributed to the design of the study and performed some of the key experiments)*, Potts JT, Jr, Gardella TJ. Selective and non-selective inverse agonists for constitutively active Type-1 Parathyroid Hormone Receptors: Evidence for altered receptor conformations. **Endocrinology 2001**; 142:1534-1545.

30. Chung UI, **Schipani E** *(I contributed to the design of the experiments; I also generated and*

characterized one of the mouse transgenic lines used in the study), McMahon AP, Kronenberg H. Indian Hedgehog couples chondrogenesis to osteogenesis in endochondral bone development. **J Clin Invest 2001**; 107:295-304. (***Commentary on the paper in the same issue.)***

31. Oliveria LM, Seminara B, Beranova M, Hayes FJ, Valkenburgh SB, **Schipani E. (***I trained Dr. Oliveria in the use of TGGE (temperature gradient gel electrophoreses), which is a screening method to detect genomic mutations. I also contributed to the analysis of the data)*, Costa EMF, Latronico AC, Crowley WF, Vallejo M. The importance of autosomal genes in Kallmann syndrome: genotype-phenotype correlations and neuroendocrine characteristics. **J Clin Endocrinol Metab 2001**; 86:1532-1538.

32. Beranova M, Oliveria LM, Bedecarrats GY, **Schipani E (***I trained Dr. Beranova in the use of TGGE (temperature gradient gel electrophoreses), which is a screening method to detect genomic mutations. I also contributed to the analysis of the data)*, Vallejo M, Ammini AC, Quintos JB, Hall JE, Martin KA, Hayes FJ, Pitteloud N, Kaiser UB, Crowley WF, Seminara SB. Prevalence, phenotypic spectrum, and modes of inheritance of gonadotropin-releasing hormone receptor mutations in idiopathic hypogonadotropic hypogonadism. **J Clin Endocrinol Metab 2001**; 86:1580-1588.

33. Imanishi Y, Hosokawa Y, Yoshimoto K, **Schipani E** *(I performed some of the experiments)*, Mallya S, Papanikolau A, Kifor O, Tokura T, Sablosky M, Ledgard F, Gronowicz G, Wang TC, Schmidt EV, Hall C, Brown EM, Bronson R, Arnold A. Primary hyperparathyroidism caused by parathyroid-targeted overexpression of cyclin D1 in transgenic mice. **J Clin Invest 2001**; 107:1093-1102.

34. Gori F, **Schipani E** *(I contributed to the design of the experiments and to the analysis of the data)*, Demay MB. Fibromodulin is expressed by both chondrocytes and osteoblasts during fetal bone development**. J Cell Biochem 2001**; 82:46-57.

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P4H proteins and C-P4H activity in hypoxia. Taken together, our findings indicate that the hypoxia-inducibility of the C-P4H isoenzymes is likely to ensure sufficient C-P4H activity for collagen synthesis occurring in chondrocytes in a hypoxic environment. These findings demonstrated for the first time that HIF-1 and not HIF-2 is a critical regulator of collagen synthesis in chondrocytes.

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of the nucleus pulposus. **PlosOne 2014**; 9(10):e110768. ***The intervertebral disc (IVD) is one of the largest avascular organs in vertebrates. The nucleus pulposus (NP), a highly hydrated and proteoglycan-enriched tissue, forms the inner portion of the IVD. The NP is surrounded by a multi-lamellar fibrocartilaginous structure, the annulus fibrosus (AF). This structure is covered superior and inferior side by cartilaginous endplates (CEP). The NP is a unique tissue within the IVD as it results from the differentiation of notochordal cells, whereas, AF and CEP derive from the sclerotome. The hypoxia inducible factor-1α (HIF-1α) is expressed in NP cells but its function in NP development and homeostasis is largely unknown. We thus conditionally deleted HIF-1α in notochordal cells and investigated how loss of this transcription factor impacts NP formation and homeostasis at E15.5, birth, 1 and 4 months of age, respectively. Histological analysis, cell lineage studies, and TUNEL assay were performed. Morphologic changes of the mutant NP cells were identified as early as E15.5, followed, postnatally, by the progressive disappearance and replacement of the NP with a novel tissue that resembles fibrocartilage. Notably, lineage studies and TUNEL assay unequivocally proved that NP cells did not transdifferentiate into chondrocyte-like cells but they rather underwent massive cell death, and were completely replaced by a cell population belonging to a lineage distinct from the notochordal one. Finally, to evaluate the functional consequences of HIF-1α deletion in the NP, biomechanical testing of mutant IVD was performed. Loss of the NP in mutant mice significantly reduced the IVD biomechanical properties by decreasing its ability to absorb mechanical stress. These findings are similar to the changes usually observed during human IVD degeneration. Our study thus demonstrates that HIF-1α is essential for NP development and homeostasis, and it raises the intriguing possibility that this transcription factor could be involved in IVD degeneration in humans.***

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185:3090-101. ***Loss of Vhl in mesenchymal progenitors of the limb bud caused severe fibrosis of the synovial joints and formation of aggressive masses with histologic features of mesenchymal tumors. Hif-1α and its downstream target connective tissue growth factor were necessary for the development of these tumors, which conversely still developed in the absence of Epas1, but at lower frequency. Human tumors of the soft tissue are a very complex and heterogeneous group of neoplasias. Our novel findings in genetically altered mice suggest that activation of the HIF signaling pathway could be an important pathogenetic event in the development and progression of at least a subset of these tumors.***

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Signaling. **J Bone Miner Res. 2016**; 31:1652-65.

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control osteoblast biology is still poorly understood. In this study, we used mouse genetic and demonstrated that HIF2 is an inhibitor of osteoblastogenesis and bone mass accrual. Moreover, we provided evidence that HIF2 may impair osteoblast differentiation at least in part by upregulating the transcription factor Sox9. HIF2 can be selectively inhibited by small molecules that are currently in clinical trials in patients with renal carcinoma. Inhibiting HIF2 could thus represent a therapeutical approach for the treatment of the low bone mass observed in chronic diseases, osteoporosis or aging.

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126. Tata Z, Merceron C, **Schipani E**. Fetal Growth Plate Cartilage: Histological and Immunohistochemical Techniques. **Methods Mol Biol 2021**; 2254:53-84.

127. Silagi ES, **Schipani E**, Shapiro IM, Risbud MV. The role of HIF proteins in maintaining the metabolic health of the interevertebral disc. **Nat Rev Rheumatol 2021**;17:426-439.

<u>Completed Publications in Scientific Journals: Not Peer-Reviewed</u>

1. **Schipani E**, Bergwitz C, Kronenberg HM, Segre GV, Jüppner H. The human PTH/PTHrP receptor. In: DeBellis A, Schipani E, eds. **Future Trends in Endocrinology, Frontiers in Endocrinology Series 1995**; 14:15-20.

2. **Schipani E**. Natriuretic peptides, cGMP, and growth plate development. BoneKEy commentary, **IBMS online 2001**. (Invited)

3. **Schipani E**. A genetic dissection of IKKα functions. BoneKEy commentary**, IBMS online 2002**. (Invited)

4. **Schipani E**. A novel PTH/PTHrP receptor (PPRc) mutation: the ongoing tale of PPRc and the growth plate becomes more complex. BoneKEy commentary, **IBMS online 2002**. (Invited)

5. **Schipani E**. Puzzles of Cartilage Biology. In "Meeting Report from the 24th Annual Meeting of the American Society for Bone and Mineral Research." BoneKEy commentary, **IBMS online 2002**. (Invited)

6. **Schipani E**. Otoconin 22 and Calcitonin: A novel modality of regulating calcium storages in lower vertebrates? **Endocrinology 2003,** News and Views; 144:3285-3286. (Invited)

7. **Schipani E**. Growth plate development: new pieces added to the puzzle. In: "Meeting Report from the 26th Annual Meeting of the American Society for Bone and Mineral Research." BoneKEy commentary, **IBMS online 2004**. (Invited)

8. **Schipani E**. Mutations of preproparathyroid hormone gene in primary hyperparathyroidism. **Clinical Cases in Mineral and Bone Metabolism 2004**; 1:107-108. (Invited)

9. **Schipani E**. On the road to the "big" chondrocytes. In: "Meeting Report from the 27th Annual Meeting of the American Society for Bone and Mineral Research." BoneKEy commentary, **IBMS online 2005**. (Invited)

10. **Schipani E**. Chondrocytes: old friends and new acquaintances. In: "Meeting Report from the 28th Annual Meeting of the American Society for Bone and Mineral Research." BoneKEy commentary, **IBMS online 2006**. (Invited)

11. **Schipani E**. Chondrocytes: a few pearls in an ocean of bones. In "Meeting Report from the 29th Annual Meeting of the American Society for Bone and Mineral Research." BoneKEy commentary, **IBMS online 2007.** (Invited)

12. **Schipani E,** Clemens TL: Hypoxia and the Hypoxia-Inducible Factors in the Skeleton. **BoneKey 2008**; 5:275-284. (Invited)

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14. Merceron C. and **Schipani E**. Intervertebral Disc: a rising star in the skeleton galaxy. **BoneKey 2013** Meeting Report of the Annual Meeting of the American Society for Bone and Mineral Research 2012. (Invited)

15. **Schipani E** and Kobayashi T. Editorial for "Special Issue on the Growth Plate". **Bone 2020**; 144:115796

Books

1. Bilezikian JP, Yoshimoto K, Pollak MR, **Schipani E**, Jüppner H, Brown EM, Arnold A, Thakker RV. Genetic Disorders of Parathyroid Hormone Action. **In "Genetics in Endocrinology," Lippincott, 2002**.

2. Carter PH, **Schipani E**. The PTH/PTHrP receptor in human diseases. **In "Hormone Resistance and Hypersensitivity States." Eds GP Chrousos, JM Olefsky, E Samols, Lippincott Williams and Wilkins, 2002**, p269-288. (Invited)

3. Jüppner H, **Schipani E**, Silve C. Jansen's metaphyseal chondrodysplasia and Blomstrand's lethal chondrodysplasia: two genetic disorders caused by PTH/PTHrP receptor mutations. In "**Principles of Bone Biology", Eds JP Bilezikian, LG Raisz, GA Rodan. 2nd edition, Academic Press, 2002**, p1117-1135.

4. **Schipani E**. Jansen's metaphyseal chondrodysplasia. **In "NORD Guide to Rare Disorders", Ed Ed Gruson, Lippincott, 2003**, pp 206-207.

5. Provot S, **Schipani E**, Wu J, Kronenberg H. Development of the Skeleton. In "**Osteoporosis", Eds R Marcus, D Feldman, DA Nelson, CJ Rosen. 3rd edition, Academic Press, 2007**, p241-269. (Invited)

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7. Mangiavini L, O'Riley R and **Schipani E.** Use of Knockout and Transgenic Mouse Models in Disc Research. In **"Intervertebral Disc" Eds M.Risbud and I.Shapiro, 2013,** p 341-352. (Invited)

8. Mangiavini L and **Schipani E.** TUNEL assay for detection of cell death. **Methods Mol Biol 2014**; **1130:245-8**. (Invited)

9. Mangiavini L, Merceron C and **Schipani E**. Analysis of mouse growth plate development. **Current Protocols in Mouse Biology 2016; 6: 67-130**. (Invited)

10. Tata Z, Merceron C, **Schipani E**. Fetal Growth Plate Cartilage: Histological and Immunohistochemical Techniques. **Methods Mol Biol. 2021**;2245:53-84. (Invited)

<u>Other media</u>

1. McMahon G, **Schipani E**, Strewler G. Tutorial case and tutor guide, "An appetite for success." **Disorders of the Musculoskeletal, Endocrine and Reproductive Systems. Human Systems. Harvard Medical School, 2004.**