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Date of Birth June 19, 1962
Place of Birth Catanzaro, Calabria, Italy
Citizenship Italian and USA

Education and Training

10/1/75-07/1/79	High School Diploma, <u>60/60 (highest score)</u> , Liceo Classico Pitagora, Crotone, Italy
10/1979-10/1985	M.D., <u>Summa Cum Laude</u> , Medical School of Pisa and Sant'Anna School of Advanced Studies, Pisa, Italy
11/1985-07/1988	Specialty Degree in Endocrinology, <u>Summa Cum Laude</u> , Medical School of Pisa, University of Pisa, Pisa, Italy
11/1985-12/1989	Ph.D., <u>Summa Cum Laude</u> , 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

Other 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
11/2020-present	Member , Institute for Regenerative Medicine, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA

Licensure and Certifications

11/1985	Italian Medical License
12/1992	ECFMG

Research Interests

My laboratory focuses on skeletal development, leveraging insights from developmental biology to better understand skeletal diseases and identify potential new treatments.

Early in my career, I cloned the human PTH/PTHrP receptor and its gene, uncovering that gain-of-function mutations in this receptor are responsible for Jansen Metaphyseal Chondrodysplasia—a severe form of short-limbed dwarfism associated with hypercalcemia. Using mouse models carrying these mutations, I contributed to defining the PTH/PTHrP receptor's critical role in skeletal biology. Subsequently, I pioneered the concept that oxygen gradients regulate tissue morphogenesis during skeletal development. Beyond serving as a key metabolic substrate in enzymatic reactions such as mitochondrial respiration, oxygen also functions as a regulatory signal. My laboratory investigates how hypoxia and hypoxia-driven pathways influence skeletal development, aiming to uncover novel

mechanisms of cellular adaptation to low oxygen levels and identify therapeutic targets for cartilage and bone diseases.

To achieve these goals, we employ genetically modified mouse models and a wide array of in vivo, ex vivo, and in vitro approaches to analyze phenotypes and elucidate the underlying 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 and disease

HIF-1 and the reprogramming of metabolism in endochondral bone development

While studying the fetal growth plate, we became intrigued by its avascular nature, which led us to uncover the critical role of hypoxia-signaling pathways in skeletal development. Oxygen, beyond being a vital metabolic substrate, also functions as a key regulatory signal. We were among the first to propose that oxygen gradients are essential for tissue morphogenesis during skeletal development. Through our research, we discovered that the murine fetal growth plate exhibits a gradient of oxygenation, with a hypoxic core region. To further investigate, we developed the first conditional knockout model of hypoxia-inducible factor-1 alpha (HIF-1), providing definitive evidence that HIF-1 acts as a survival factor for hypoxic chondrocytes in the growth plate in vivo. The role of HIF-1 as a survival factor has since been confirmed in a variety of settings, including cancer models. We also established that HIF-1 is crucial for the timely differentiation of mesenchymal cells into chondrocytes and for joint development in vivo. Furthermore, we provided genetic evidence that vascular endothelial growth factor (VEGF)—a classical downstream target of HIF-1 and a known survival factor for chondrocytes—plays only a modest role in mediating HIF-1's survival function in cartilage. Instead, we showed that HIF-1-dependent metabolic reprogramming is a critical downstream mechanism supporting chondrocyte survival and differentiation. Notably, we demonstrated that HIF-1 reduces mitochondrial respiration and oxygen consumption in growth plate chondrocytes, a key adaptation ensuring their survival and proper differentiation under hypoxic conditions. Currently, we are investigating how the interplay between oxidative phosphorylation and HIF-1-mediated metabolic reprogramming governs skeletal development.

HIF1 and the reprogramming of metabolism in somitogenesis

In collaboration with Dr. Mark Lewandoski at NCI, we recently established that HIF-1 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. A manuscript reporting those findings is in preparation.

We are currently investigating whether the impairment of somitogenesis secondary to loss of HIF-1 is due to dysregulation of glycolysis and mitochondrial function in the presomitic mesoderm.

HIF-2 and the control of bone mass accrual and homeostasis

A gradient of oxygenation exists within the bone marrow, despite its high vascularization. This phenomenon underscores the complexity of the bone marrow microenvironment, where localized hypoxia plays critical roles in cellular function. In collaboration with Dr. Amato Giaccia at Stanford, we demonstrated that osteoblasts have the remarkable ability to produce and secrete erythropoietin (EPO), a hormone essential for erythropoiesis, when hypoxia-inducible factor-2 (HIF-2), another transcription factor central to the hypoxic response, is activated in those cells. Our findings suggest that transient pharmacological activation of the hypoxia signaling pathway in osteoblasts could serve as a therapeutic approach to enhance EPO production, especially in conditions characterized by EPO deficiency, such as chronic kidney disease. In addition to its role in EPO production, HIF-2 has distinct effects on skeletal development. Unlike HIF-1, HIF-2 plays a less critical role in growth plate development. Interestingly, however, our research uncovered that reducing or inhibiting HIF-2 in mesenchymal progenitors and their descendants during development leads to the formation of stronger bones with increased trabecular bone mass. This improvement is driven by the expansion of mesenchymal progenitor cells within the bone marrow, which subsequently differentiate into osteoblasts. By increasing the pool of these progenitors, we effectively enhanced bone-forming capacity. A particularly exciting breakthrough involved the testing a HIF-2 inhibitor, PT2399, which was originally developed to treat clear cell renal carcinoma. In mouse models of menopause (characterized by estrogen deficiency), this drug prevented bone loss and promoted bone formation by expanding the pool of early osteoblast precursors. These findings highlight a promising therapeutic avenue for addressing osteoporosis and other bone loss conditions by targeting HIF-2. Currently, our research employs unbiased methodologies, including transcriptomic analyses, to elucidate the molecular mechanisms underlying the expansion of mesenchymal progenitor cells when HIF-2 activity is pharmacologically suppressed. These studies aim to identify novel pathways that can be leveraged to optimize bone health therapeutics.

HIFs in the pathogenesis of fibroblastic tumors of the soft tissue and cartilage regeneration

Our laboratory has demonstrated that continuous activation of the hypoxia signaling pathway in mesenchymal progenitor cells of the limb bud may have detrimental effects on skeletal development. Specifically, this persistent activation leads to aggressive fibrosis in synovial joints, the development of fibroblastic tumors in soft tissue, and dwarfism by disrupting both the proliferation and hypertrophic differentiation of growth plate chondrocytes. These findings underscore the critical role of tightly regulated hypoxia signaling in maintaining skeletal health and normal development. Notably, we also discovered that activation of the hypoxia signaling pathway in mesenchymal progenitors results in the formation of ectopic cartilage in the soft tissues surrounding the growth plate and promotes matrix accumulation in the developing growth plate. These findings suggest that increased activity of the hypoxia signaling pathway may be sufficient to drive cartilage formation under certain conditions.

Taken together, if appropriately controlled, transient activation of hypoxia signaling could be harnessed to promote cartilage regeneration. By stimulating chondrogenesis while inhibiting hypertrophy, this strategy could enable cartilage repair in vitro and in vivo without inducing adverse outcomes, such as synovial fibrosis or fibroblastic tumor formation, provided the activation is carefully timed and transient. Our current research focuses on two main objectives: 1. Investigating the role of the hypoxia signaling pathway in the initiation and progression of fibroblastic tumors of the soft tissue; 2. Attempting to appropriately exploit the hypoxia signaling pathway for regenerating cartilage. These efforts aim to elucidate the dual role of hypoxia signaling in both pathology and regeneration, offering

insights into novel therapeutic strategies for conditions involving fibroblastic tumors and cartilage repair.

Grants

PRESENT and ACTIVE:

R01 HD112003 (Schipani, PI) 01/04/23-31/03/28
NIH/NICHD \$220,000 2.4 calendar months
Role: PI

Title: *Hypoxia and Mitochondria in Spine Development and Congenital Scoliosis*

The goal of this study is to advance our understanding of how hypoxia, hypoxia-driven pathways, and bioenergetic metabolism control somitogenesis.

R01 DK113039 (Jueppner, PI) 09/15/18-06/30/29
NIH/NIDDK \$12,249 (Schipani) 0.84 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 Metaphyseal Chondrodysplasia.

R01 AR075770 (Ma, PI) 09/23/20-01/31/26
NIH/NIAMS \$250,000 1.2 calendar months
Role: Co-Investigator

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.

PENDING:

R01 AR084536 (Schipani, PI) 04/01/25-04/31/30
NIH/NIAMS 3.0 calendar months
Role: PI

Title: *Mitochondrial Respiration and The Biology of Growth Plate Chondrocytes*

The goal of this study is to establish how oxidative phosphorylation controls chondrocyte hypertrophy in the murine developing growth plate.

Major Previous Grants

1993-2000 *PTH/PTHr Receptor Defects in Pseudohypoparathyroidism.*
R01-DK4718 NIH/NIDDK
Co-investigator

1996-2000 *Constitutively active PTH/PTHrP receptors in vivo.*
R01-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.*
R21 AR060689 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.*
RO1 AR058654 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.*
RO1 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*
RO1 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*
R21 AR067330 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.*
RO1 AR065403 NIH/NIAMS
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 science by increasing access to critical, specialized resources and expertise that are fundamental to the musculoskeletal research programs of center investigators.
- 2022 *2022 Bone and Teeth Gordon Research Conference and Seminar*
R13 AR080434 NIH/NIAMS
PI
Major Goals: The skeleton is an organ with numerous vital functions. The 2022 Bones and Teeth Gordon Research Conference and Seminar will discuss major new discoveries regarding the skeleton and its functions. Those new and exciting discoveries may lead to novel treatments of devastating diseases including osteoporosis, bone cancer, genetic disorders of the skeleton, and skeletal problems associated to diabetes.
- 2018-2023 *HIF-2alpha, a Novel Regulator of Osteoblastogenesis*
R01 AR073022 NIH/NIAMS
PI
The goal of this study is to determine the role of HIF2 in the regulation of bone mass and osteoblastogenesis.
- 2019-2024 *Mitochondria and TFAM in osteoblast biology*
R01 AR074079 NIH/NIAMS
PI
The goal of this study is to determine the role of TFAM in osteoblast biology.

Honors and Awards

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| 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 Research Conferences
2022	Chair of 2022 Bone and Teeth Gordon Research Conferences

Memberships in Professional Societies

1992-present	American Society for Bone and Mineral Research 2000-2018, 2022, 2023 – Abstract reviewer 1996, 1997, 2000, 2005, 2006, 2012,2013,2014,2019,2020,2023 – Moderator ASBMR meeting 2008 – Co-Chair State-of-the-Art Lecture A: Role of oxygen sensing pathways 2014 – Chair Skeletal Development abstract review category 2015 – Chair Skeletal Development abstract review category 2015 – Co-chair Symposium “Metabolism of Bone Cells” 2015 – Discussion Leader “Grant writing workshop” 2015-2017 – Member Education and Membership Committee 2015-2016 – Member Organizing Committee ASBMR 2016 2017-2019 – Council Member 2017 – Council Liaison Women Committee 2017 – Member Annual Meeting Program Advisory Committee 2018 – Council Liaison Development Committee 2018 – Member Nominating Committee 2018-2019 – Council Liaison Publications Committee 2019 – Co-chair Symposium “Cutting Edge Concepts: CRISPR beyond the mouse” 2019-2021 – Member Annual Meeting Advisory Committee 2021-2023 – Member Publications Committee 2022 – Member Award Committee 2024- Chair Premeeting Symposium on “Energy Metabolism in Skeletal Development and Disease” 2024-Member 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, 2 nd conference on Skeletal Biology and Medicine, The New York Academy of Sciences 2011 – Moderator of session, 4 th 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 University, Ad hoc reviewer
2015	NIA- ZAG1 ZIJ-8 (M2) (PO1), Ad hoc reviewer
2015	NIAMS-ZRG1-MOSS-U02, Ad hoc reviewer
2017	NIAMS-Special Emphasis Panel, Ad hoc reviewer
2017	UMHS-PUHSC Joint Institute, University of Michigan, Ad hoc reviewer
2018-2022:	NIH-SBDD Study Section, Ad hoc reviewer
2018	NIAMS Special Emphasis 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, Washington 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
2021	NIDDK Board of Scientific Counselors Review
2021	NIH Directors Early Independence Awards, Ad Hoc Reviewer
2023	NIAMS-Special Emphasis Panel, R13/U13, Ad hoc Reviewer
2023	NIH- Special Emphasis Panel "ZRG1 MSOS V (02) M", Chair
2023-2024	NIH-U19, Chair
2023	PhD Thesis Committee-University of KU Leuven, Belgium, External Reviewer
2023	PhD Thesis Committee-University of Monash, Melbourne, Australia, External Reviewer
2023	Pilot Grant Musculoskeletal Center-Washington University, St.Louis, External Reviewer
2024	GWIS National Fellowship Program, 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
2021-2023	Guest Editor-Bone Reports
2021-2023	Reviewing Editor-eLife
2021-2024	Associate Editor-JCI Insight
2024	Associate Editor-Endocrinology
2024-	Consulting 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, 2 nd year Medical Students, Harvard Medical School, Boston, MA
2004-2005	Lecturer – Molecular mechanisms of bone and joint formation, 2 nd 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 Orthopaedic 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, Shenzhen, China
2012-2020	Christophe Merceron, PhD/ Young Investigator Award-ASBMR Senior Medical Information Associate, Prime Vigilance, Ann Arbor, MI
2021-2022	Lorenzo Arboit, MD, PhD Student University of Strasbourg, Strasbourg, France
2017-2023	Mohammed Parvez-Khan, PhD/ Travel Award-ASBMR , Research Assistant Professor, University of Toledo, Toledo, OH
2021-2024	Elena Sabini. MD. PhD student University of Pisa, Pisa, Italy
2022-2024	Giulia Lanzolla, MD/ Travel Award-ASBMR , Assistant Professor, University of Cagliari, Italy

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 Pseudohypoparathyroidism, 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

2019	Developmental Biology, School of Medicine, University of Michigan, Ann Arbor, MI (Seminar)
2021	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)
2022	Hypoxia and mitochondria in skeletal development and somitogenesis. IRM Seminar, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Seminar)
2023	How hypoxia and Mitochondria shape up the skeleton. PCMD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Short talk, Invited)
2023	How hypoxia and Mitochondria shape up the skeleton. IRM Annual Retreat, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Short Talk, invited)
2023	How hypoxia and Mitochondria shape up the skeleton. IDOM 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, Department 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
2024-	Chair DCOAP Committee, Department of Orthopedic Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

National and International Committees

1994	Scientific Committee for the 4 th International Symposium on Endocrinology under 35
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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
2024	ASBMR Advisory 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 plate: 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.

- 2012 Louis V. Avioli Seminar Series, April 20, St. Louis, MO (Visiting Professor)
Fibrocytes and marrow fibrosis.
- 2012 Meet-the-Professors, ASBMR, October 12-15, Minneapolis, MN (Invited Seminar)
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)
- 2022 How hypoxia and mitochondria shape up the skeleton. October 17th, Northeastern
University, Boston, MA (Lecture)
- 2024 Mitochondria, HIFs and the Control of Bone Mass. Annual Scientific Retreat
Lawrence Family Bone Disease Program of Texas, Houston, TX (Keynote Lecture)
- 2024 Oxygen on the brink: how hypoxia and mitochondria shape the skeleton. UC Irvine,
Irvine, CA (Invited Lecture)

International

- 1991 Cloning of the human PTH/PTHrP receptor. Istituto di Endocrinologia, Università
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 Collège 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

- 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
- 2019 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 Research Conference on Cartilage, March 17-22, Galveston, TX, USA
- 2021 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
- 2022 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
- 2022 Meet-the-Professor, ASBMR, September 8-12, Austin, TX, USA
- 2023 Hypoxia Signaling and Cell Metabolism in the Skeleton. 4th H. Fleisch Workshop, November 20-22, Brugge, Belgium
- 2023 How Hypoxia and Mitochondria Shape up the Skeleton. Keystone Hypoxia: From Basic Mechanisms to Emerging Therapies, May 28-31, Killarney, KY, Ireland.
- 2024 How Hypoxia and Mitochondria Shape up the Skeleton. Gordon Research Conference on Collagen, July 9-24, New London, NH, USA.
- Mitochondria and the Control of Skeletal Development. Gordon Research Conference on Bone and Teeth, January 28-February 2, Galveston, TX, USA

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 opossum 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. BsmI 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, Bringham 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*), Bringham 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 III. 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, Stuhmann 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 1b 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 1b, 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.
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This study investigated the role of hypoxia and HIFs in regulating expression of collagen prolyl 4-hydroxylases (C-P4Hs) in chondrocytes in vitro. Briefly, C-P4Hs are key enzymes in collagen synthesis as the resulting 4-hydroxyprolines are necessary for the stability of all collagen molecules. C-P4H I is the main form in most cells, but C-P4H II is the major form in chondrocytes. We utilized primary epiphyseal growth plate chondrocytes isolated from newborn mice with conditionally inactivated HIF-1 or HIF-2 genes, and we showed that C-P4H I and II mRNA levels were increased in hypoxic chondrocytes, the induction being HIF-1 but not HIF-2 dependent. Furthermore, the increases in the C-P4H mRNA levels were associated with increased amounts of the C-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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98. **Schipani E**, Wu C, Rankin BE and Giaccia A. Role of osteoblasts in regulating bone marrow angiogenesis during bone development and homeostasis. **Front. Endocrinol** **2013** Jul 10;4:85.
99. **Schipani E**, Mangiavini L and Merceron C. ATF4 and HIF-1 in bone: an intriguing relationship. **JBMR** **2013**; 28:1866-9.
100. Mangiavini L, Araldi E, Khatri R, Wilson TLS, Gerard-O'Riley R, Rankin EB, Giaccia AJ and **Schipani E**. Loss of VHL in mesenchymal cells of the limb bud alters multiple steps of endochondral bone development. **Dev Biol** **2014**; 393(1):124-36. *This study investigated the role of VHL in mesenchymal progenitor cells of the limb bud and their descendants. Briefly,*

loss of VHL in limb bud mesenchyme did not alter the timely differentiation of mesenchymal cells into chondrocytes. However, it caused structural collapse of the cartilaginous growth plate as a result of impaired proliferation, delayed terminal differentiation, and ectopic death of chondrocytes. This phenotype was associated to delayed replacement of cartilage by bone. Our findings demonstrate that VHL regulates bone morphogenesis as its loss considerably alters size, shape and overall development of the skeletal elements.

101. Merceron C, Mangiavini L, Wilson TLS, Robling A, Giaccia AJ, Shapiro I, Risbud M and **Schipani E**. Loss of HIF-1 α in the notochord results in cell death and complete disappearance 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-1 α (HIF-1 α) is expressed in NP cells but its function in NP development and homeostasis is largely unknown. We thus conditionally deleted HIF-1 α 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-1 α 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-1 α 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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combination with a reduced amount of isoenzyme I. (* co-senior authors) **JBC** **2015**; 90:16964-16978.

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substantially decreased HO, and again lack of de novo soft-tissue HO. Genetic loss of Hif1 α in mesenchymal cells marked by Prx-cre prevented the formation of the mesenchymal condensations. Pharmacologic inhibition of Hif1 α had a similar effect on mesenchymal condensation development. Our findings indicate that Hif1 α represents a promising target to prevent and treat pathologic extraskelatal bone.

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112. Agarwal S, Loder SJ, Cholok D, Peterson J, Li J, Breuler C, Cameron Brownley R, Hsin Sung H, Chung M, Kamiya N, Li S, Zhao B, Kaartinen V, Davis TA, Qureshi AT, **Schipani E** (*I provided critical reagents and I critically reviewed the manuscript*), Mishina Y, Levi B. Scleraxis-Lineage Cells Contribute to Ectopic Bone Formation in Muscle and Tendon. **Stem Cells** **2017**; 35:705-10
113. Wang C, Xu CX, Alipppe Y, Qu C, Xiao J, **Schipani E** (*I provided critical reagents and I critically reviewed the manuscript*), Civitelli R, Abu-Amer Y and Mbalaviele G. Chronic inflammation triggered by NLRP3 inflammasome in myeloid cells promotes growth plate dysplasia by mesenchymal cells. **Sci.Rep.** **2017**; 7:4880.
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- manuscript*), Sabbagh Y, Xu L, Srour EF, Alvarez MB, Kacena MA, Salusky IB, Nemeth E, White KE. Erythropoietin stimulates murine and human fibroblast growth factor-23, revealing novel roles for bone and bone marrow. **Haematologica** 2017; 102(11):e427-e43
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 120. Yao Q, Parvez Khan M, Merceron C, LaGory E, Tata Z, Mangiavini L, Hu J, Vemulapalli K, Chandel NS, Giaccia AJ, **Schipani E**. Suppressing mitochondrial respiration is critical for hypoxia tolerance in the fetal growth plate. **Developmental Cell** 201;49: 748-763 (*Preview in the same issue of Dev Cell; featured in Science Signaling 2019;12*). **Oxygen (O₂) is both an indispensable metabolic substrate in various enzymatic reactions, including mitochondrial respiration, and a regulatory signal that controls the stability and activity of the transcription factor Hypoxia-Inducible Factor 1alpha (Hif1a), a key mediator of the cellular adaptation to low O₂ tension (hypoxia). Hypoxic cells require Hif1a to survive. Additionally, Hif1a is an inhibitor of mitochondrial respiration. Hence, we hypothesized that enhancing mitochondrial respiration is detrimental to the survival of hypoxic cells in vivo. We addressed this question in the fetal growth plate, which is an avascular and hypoxic structure formed by chondrocytes and a matrix enriched in collagens and proteoglycans. Our study demonstrates that mitochondrial respiration is dispensable for growth plate development during fetal life. More importantly, its impairment prevents both the extreme hypoxia as well as the pathological and massive cell death observed in fetal growth plates lacking Hif1a. These findings show that enhancing mitochondrial respiration is detrimental**

to the survival of growth plate chondrocytes by, at least in part, increasing intracellular hypoxia. We thus propose that partial suppression of mitochondrial respiration is crucial during normal embryonic development to protect the tissues that are physiologically hypoxic from lethal intracellular anoxia.

121. Merceron C, Ranganathan K, Castellini L, Wang E, Tata Z, Mangiavini L, Parvez Khan M, Levi B, Giaccia AJ, **Schipani E**. Hypoxia Inducible Factor-2alpha is a negative regulator of osteoblastogenesis and bone mass accrual. **Bone Research** 2019;7:7. *Osteoblasts, which are the cells forming bone, operate in a hypoxic environment. Hypoxia Inducible Factor-2alpha (HIF2) is one of the mediators of the cellular response to hypoxia. However, its role in the 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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130. Mendoza-Reinoso V, Schnepf PM, Baek DY, Rubin JR, **Schipani E** (*I contributed to the design of the study and I critically reviewed the manuscript*), Keller ET, McCauley LK, Roca H. Bone marrow macrophages induce inflammation by efferocytosis of apoptotic prostate cancer cells via HIF-1α stabilization. **Cells.** **2022** ;11(23):3712.
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132. Lanzolla G, Khan MP, Sabini E, Giaccia A, **Schipani E**. Erythropoietin and skeletal crosstalks in physiology and disease. **Current Opinion in Endocrine and Metabolic Research** **2023**; 29: 100436.
133. Sabini E, Arboit L, Khan MP, Lanzolla G, **Schipani E**. Oxidative phosphorylation in bone cells. **Bone Rep.** **2023**;18:101688. doi: 10.1016/j.bonr.2023.101688.
134. **Schipani E**, Carmeliet G. Cell metabolism ad bone cells. **Bone Rep.** **2023**;19:101719. doi: 10.1016/j.bonr.2023.101719
135. Warren A, Porter RM, Reyes-Castro O, Ali MM, Marques-Carvalho A, Kim HN, Gatrell LB, **Schipani E** (*I contributed to the design of the study and I critically reviewed the manuscript*), Nookaew I, O'Brien CA, Morello R, Almeida M. The NAD salvage pathway in mesenchymal cells is indispensable for skeletal development in mice. **Nat Commun.** **2023**;14(1):3616
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137. Sabini E, **Schipani E**. The hypoxia signature across skeletal progenitor cells. **J Bone Miner Res.** 2024;39(4):373-374
138. Lanzolla G, Merceron C, Khan MP, Sabini E, Giaccia A, **Schipani E**. Osteoblastic erythropoietin is not required for bone mass accrual. **JBMR Plus** 2024; 8(6). *Our study explores the role of erythropoietin (EPO), a hormone best known for its role in producing red blood cells, in bone health. While the kidneys produce most EPO, we now know that bone cells, specifically osteoblasts (which build bone), can also produce and release EPO when oxygen levels are low. However, the importance of this bone-derived EPO remains unclear. To investigate, we created a mouse model where EPO production was specifically turned off in bone-building cells and their precursors. In young adult mice, we found that the absence of osteoblast-derived EPO did not significantly impact bone growth or red blood cell production. Our findings suggest that EPO from osteoblasts may not play a major role in bone or blood health during early adulthood. However, we believe it could be more important under specific conditions, such as aging, bone healing, or disease. Future studies will help us better understand the potential functions of EPO produced by bone cells in these contexts.*
139. Khan MP, Sabini E, Beigel K, Lanzolla G, Laslow BM, Wang D, Merceron C, Giaccia A, Long F, Taylor DM, **Schipani E**. HIF1 safeguards cortical bone formation against impaired oxidative phosphorylation. **JCI Insight** 2024; 9(18):e182330. *Our study explores how cells produce energy and how this affects the development of strong, healthy bones. Bones, especially the outer shell of long bones called cortical bone, need energy to grow and maintain their structure. Cells use two main ways to make energy: oxidative phosphorylation (OxPhos), which relies on oxygen and mitochondria (the cell's power plants), and glycolysis, which can work without oxygen. We focused on a protein called TFAM, which helps mitochondria function properly. In mice that were missing TFAM in certain bone cells, the outer shell of their long bones became thinner and weaker, leading to fractures. These mice also had problems with energy production in a layer of bone-forming cells called the periosteum, which is crucial for bone growth and repair. Interestingly, we found that activating another protein, HIF1, could help compensate for the energy production problems caused by TFAM loss. HIF1 pushes cells to use glycolysis instead of OxPhos. By boosting HIF1, some of the bone defects were improved, showing that cells can switch energy strategies to some extent. The significance of our study is twofold: it highlights how important mitochondria and OxPhos are for building strong bones, and it suggests that tweaking how cells make energy could be a future treatment for conditions like osteoporosis or other bone fragility diseases.*
140. Lanzolla G, Sabini E, Beigel K, Khan MP, Sherry Liu X, Wang D, Laslow B, Taylor D, Bellido T, Giaccia A, **Schipani E**. Pharmacological inhibition of HIF2 protects against bone loss in an experimental model of estrogen deficiency. **PNAS** 2024;121. *In this study, we looked at how a lack of estrogen, such as during menopause or certain medical conditions,*

can lead to weaker bones and a higher risk of fractures. Our focus was on the spongy part of bones called trabecular bone, which is particularly affected. Bone health depends on a balance between making new bone and breaking down old bone, and estrogen deficiency disrupts this balance. We investigated how HIF-2 α (HIF2), which helps cells respond to low oxygen levels in the bone marrow, affects this process. We discovered that reducing or blocking HIF2 in bone-making cells during development leads to stronger bones with more trabecular bone mass. This happens because more bone-forming cells, called osteoblasts, are created. Excitingly, we tested a drug called PT2399 that blocks HIF2 and found it could prevent bone loss in mice with low estrogen levels, mimicking menopause. This drug increased the number of bone-forming cells by expanding the pool of early bone cell precursors. In short, our study highlights a new way to strengthen bones and prevent bone loss in conditions like menopause by targeting HIF2, offering potential for better treatments in the future.

Completed Publications in Scientific Journals: Not Peer-Reviewed

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 IKK α 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)
13. Merceron C. and **Schipani E.** Chondrocytes: a few grains of softness in a hard bone world. **BoneKey 2013** (Meeting Report of the Annual Meeting of the American Society for Bone and Mineral Research 2012. (Invited)
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

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