**Ernestina Schipani, M.D., Ph.D.**

William Wikoff Smith Professor of Orthopaedic Surgery

University of Pennylvania

Perelman Medical School

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**Ernestina.Schipani@Pennmedicine.upenn.edu**

**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, 60/60 (highest score), Liceo Classico Pitagora, Crotone, Italy

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

**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, Universityof 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*.*

**The hypoxia signaling pathway in development ans 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 AR084536 (Schipani, PI)** 06/03/25-04/31/30

NIH/NIAMS $295,000 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.

**R01 DK113039 (Jueppner, PI)** 09/15/18-06/30/29

NIH/NIDDK $12,249 (Schipani) 0.84 calendar months

Role: Sub-award PI

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.

**R01 AR075770 (Ma, PI)** 09/23/20-01/31/26

NIH/NIAMS 0.80 calendar months

Role: Sub-award 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.

**Major Previous Grants**

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

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| 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. |
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| 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 |
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| 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. |
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| 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 AR055655NIH/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 scince 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 AR074079NIH/NIAMS

 **PI**

 The goal of this study is to determine the role of TFAM in osteoblast biology.

2024 *Energy Metabolism in Skeletal Development and Disease, ASBMR Premeeting*

R13 AR081110 NIH/NIAMS

 **Co-PI**

 Major Goals: To discuss the recent advances on the role of energy metabolism in skeletal development and disease; including the role of hypoxia and mitochondria-mediated mechanisms, and its involvement in the response of bone to anabolic therapies and metabolic diseases such as diabetes.

**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 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, 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

2018-2022: 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

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 Leuwen, 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 Fellowhip 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**

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| American Journal of Endocrinology and Metabolism |
| Arthritis and Rheumatism |
| BloodBone |
| Calcified Tissue International |
| Cancer Research |
| Development |
| Developmental BiologyDevelopmental Cell |
| Cell MetabolismeLife |
| EMBO |
| FASEBEndocrinology |
| Genes and Development |
| Human Molecular GeneticsJBMR |
| Journal of Cell Biology |
| Journal of Clinical Endocrinology and Metabolism |
| Journal of Clinical InvestigationJCI Insights |
| Journal of Experimental Research  |
| Journal of Orthopedic Research |
| Journal of Biological Chemistry |
| Molecular Cancer Research |
| MCB |
| Molecular EndocrinologyNature |
| Nature MedicineNature 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**, Group Leader, INSERM, Paris, France

2008 Ellinoora Aro, MD-PhD/Surgeon, University of Turku, Finland

2008-2011 Richa Khatri, MD/General Surgeon, Coeur D Alene, ID

2009-2010 Wanida Ono, DDS-PhD/Associate Professor, Dental School, University of Texas, Houston, TX

2009-2010 Elisa Araldi, PhD/Assistant Professor, University of Parma, Parma, Italy

2010-2011 Erinn Rankin, PhD/Associate 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**, Plastic Surgeon, Shriners Children Hospital, Boston

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**Senior Associate Scientist, Univesrity of Michigan, 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**

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| --- | --- |
| 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 2107 201820192021202220232023 | 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) 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)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)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) Hypoxia and mitochondria in skeletal development an somitogenesis. IRM Seminar, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Seminar)How hypoxia and Mitochondria shape up the skeleton. PCMD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Short talk, Invited)How hypoxia and Mitochondria shape up the skeleton. IRM Annual Retreat, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA (Short Talk, invited)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, 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

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 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

2024 ASBMR Advisory Committee

**Visiting Professorships, Seminars, and Extramural Invited Presentations**

**National**

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| 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 chondrogenesisKeystone 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 chondrogenesisUC Davis, Sacramento, CA (Visiting Professor) |
| 2005 | Hypoxia and HIF-1alpha in chondrogenesisNYAS 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) |
| 20172018201820212021202220242024 | 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) Enhancing mitochondrial respiration causes severe intracellular hypoxia and death of hypoxic cells. February 14, National Cancer Institute, NIH, Bethesda, MD (Lecture)Suppressing mitochondrial respiration is critical for hypoxia tolerance in the fetal growth plate. July 13, University of Little Rock, Little Rock, AR (Lecture)Hypoxia and mitochondria in skeletal development. March 3rd, University of Colorado, Denver, CO (Mack Clayton Lecture)Hypoxia and mitochondria in skeletal development. March 25th, UCSF, San Francisco, CA (Lecture)How hypoxia and mitochondria shape up the skeleton. October 17th, Northeastern University, Boston, MA (Lecture)Mitochondria, HIFs and the Control of Bone Mass. Annual Scientific Retreat Lawrence Family Bone Disease Program of Texas, Houston, TX (Keynote Lecture)Oxygen on the brink: how hypoxia and mitochondria shape the skeleton. UCIrvine, Irvine, CA (Invited Lecture) |

International

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| 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 |
| 20172018 201820182018201920192021202120222022202320232024 | Impairment of mitochondrial respiration promotes survival of hypoxic cells. The Tumor Microenvironment: 15th International Workshop, April 26-29, Miami Beach, FL, USAChoke 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, USAGrowth 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, USAImpairment of mitochondrial respiration promotes survival of HIF-1alpha deficient chondrocytes in vivo. Therapeutic targeting of hypoxia-sensitive pathways,Keystone Symposia, April 10-14, Oxford, UKThe 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, MIMitochondria and HIFs in skeletal development. Gordon Research Conference on Cartilage, March 17-22, Galveston, TX, USASuppressing mitochondrial respiration is critical for hypoxia tolerance in the fetal growth plate. The Tumor Microenvironment: 16th International Workshop, June 13-15, Miami Beach, FL, USAHypoxia and Mitochondria in skeletal development. ECTS, May 6-8, Digital CongressChoke 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 20Meet-the-Professor, ASBMR, September 8-12, Austin, TX, USAHypoxia Signaling and Cell Metabolism in the Skeleton. 4th H. Fleisch Workshop, November 20-22, Brugge, BelgiumHow Hypoxia and Mitochondria Shape up the Skeleton. Keystone Hypoxia: From Basic Mechanisms to Emerging Therapies, May 28-31, Killarney, KY, Ireland.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 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.
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46. 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 address this issue, 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.***
47. 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.***
48. 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-2α (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.***
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**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 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)
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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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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.
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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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8. Mangiavini L and **Schipani E.** TUNEL assay for detection of cell death. **Methods Mol Biol 2014**; **1130:245-8**. (Invited)

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Other media

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.**