BIOGRAPHICAL SKETCH

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NAME: Serrat, Maria Anne

eRA COMMONS USER NAME (credential, e.g., agency login): MASERRAT

POSITION TITLE: Associate Professor of Anatomy

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Miami University, Oxford, Ohio	B.A.	05/1999	Anthropology
Kent State University, Kent, Ohio	M.A.	05/2002	Anthropology
Kent State University, Kent, Ohio	Ph.D.	08/2007	Biomedical Sciences
Cornell University, Ithaca, New York	Postdoctoral	08/2009	Cartilage Imaging

A. Personal Statement

The objective of the proposed research is to determine how IGF binding protein (IGFBP) reduction in the perichondrium leads to growth acceleration in obesity. Perichondrium is the collagenous shell that surrounds skeletal growth plates, the regions of cartilage at the ends of bones where lengthening occurs. This hypothesis-driven, problem-solving project uses integrated *in vivo* and *in situ* approaches to evaluate the role of local IGFBPs in modulating IGF-I transport and linear growth velocity. The research uses live animal microscopy and protein assays with a mouse model that parallels human obesity. I have expertise in growth plate biology and extensive experience with the specialized methodologies described. My published work includes experience with transgenic mouse models, such as human growth hormone and Col2-GFP expressing animals. I have authored an invited authoritative review on the environment and skeletal growth for *Comprehensive Physiology*. My diverse background in biological anthropology and biomedical sciences is at an intersection that yields and demands independence and innovation. I designed a thesis project to examine effects of ambient housing temperature on limb length and bone blood flow in mice (described in a single-author paper in *Nature Protocols*), and developed an *in vitro* bone culture system to directly isolate temperature. I extended this work as a Postdoctoral Associate at Cornell University, where I used multiphoton imaging to quantify solute transport in growth plate cartilage *in vivo* and published a detailed protocol on the technique. As an Associate Professor, I have since established a functional live animal multiphoton imaging lab at Marshall University with students and research assistants. I have over six years experience mentoring undergraduate, graduate, and medical student projects. We have successfully obtained extramural student grants that have led to national conference presentations and publications. By keeping a tight focus on the project aims under my planned direction, we were able to generate enough pilot data to secure an R15 AREA grant to continue our temperature work. I am fully prepared to conduct this next phase of research. My plan is a consistent extension of prior projects and builds on the knowledge base, preliminary data, and collaborations that I have already established. I have a demonstrated record of peer-reviewed publications, consistently following competitive internal and extramural grants that I secured to fund my projects for over the past ten years. I received my first grant as an undergraduate in 1998 and have maintained consistent research support since a graduate student in 2004. Having obtained previous funding, I am experienced with grants administration and project leadership, and I understand the need for a clearly articulated research plan. The mentoring that I will receive during the COBRE project will help ensure continued funding success. Overall, my relevant experience and multidisciplinary background provide me with exceptionally strong and unique qualifications to direct this proposal as demonstrated by the related publications listed below.

1. **Serrat MA**, Lovejoy CO, King D. (2007). Age- and site-specific decline in insulin-like growth factor-I receptor expression is correlated with differential growth plate activity in the mouse hindlimb. *Anatomical Record*. 290(4): 375-381. PMID: 17331175.
2. **Serrat MA.** (2009). Measuring bone blood supply in mice using fluorescent microspheres. *Nature Protocols.* 4(12): 1749-1758. PMID: 19893510.
3. **Serrat MA**, Efaw ML*****, Williams RM. (2014). Hindlimb heating increases vascular access of large molecules to murine tibial growth plates measured by in vivo multiphoton imaging. *Journal of Applied Physiology*. 116(4):425-38. *Student Author. PMID: 24371019. PMCID: 3921350.
4. **Serrat MA**, Schlierf TJ*, Efaw ML*, Shuler FD, Godby J*, Stanko LM*, Tamski, HL*. (2015) Unilateral heat accelerates bone elongation and lengthens extremities of growing mice. *Journal of Orthopaedic Research*. 33(5): 692-8 *Student Authors. PMID: 25639189.

B. Positions and Honors

Positions and Employment

1998 Summer Intern, Cleveland Museum of Natural History, Ohio
1998-99 Research Assistant, Zoology, Miami University, Ohio
2000-02 Graduate Assistant, Anthropology, Kent State University, Ohio
2003-05 Teaching Fellow, Anthropology, Kent State University, Ohio
2002-07 Teaching Assistant, Gross Anatomy, Northeastern Ohio Universities College of Medicine
2007 Postdoctoral Teaching Fellow, Gross Anatomy, Northeastern Ohio Universities College of Medicine
2008-09 Postdoctoral Associate, Biomedical Sciences, Cornell University, Ithaca, New York
2009-15 Assistant Professor, Anatomy and Pathology, Marshall University, Huntington, West Virginia
2013- Clinical Assistant Professor, Orthopaedic Surgery, Marshall University School of Medicine
2014- Assistant Professor of Clinical and Translational Sciences, Marshall University School of Medicine
2015- Associate Professor, Anatomy and Pathology, Marshall University, Huntington, West Virginia

Professional Memberships

1999- Sigma Xi
2007- American Association of Anatomists
2009- American Physiological Society
2012- Orthopaedic Research Society
2013- American Society for Bone and Mineral Research

Other Professional Activities

2007-15 Manuscript reviewer: American Journal of Physiology (Regul Integr Comp Physiol.; Renal Physiol.); Anatomical Record; Animal Biology; Evolutionary Biology; Frontiers in Endocrinology; International Journal of Environmental Research and Public Health; Journal of Applied Physiology; Journal of Biomechanics; Journal of Human Evolution; Journal of Orthopaedic Research; Nutrients; PLoS ONE; Proceedings of the National Academy of Sciences; South African Journal of Science; Yearbook of Physical Anthropology
2011-13 Poster Judge: Marshall University School of Medicine Research Day; Scholander Competition, American Physiological Society at Experimental Biology; Appalachian Regional Cell Conference.
2011-12 Grant Reviewer: Cell Differentiation and Development Center, Marshall University; Graduate Women in Science National Fellowship Program; Marshall Health Translational Pilot Grant Program; Leakey Foundation
2013 Focus Group Participant: evaluation of Grant's Anatomy Dissector; Lippincott Williams and Wilkins
2013 Panelist: Research Skill and Publishing Strategies; Marshall University School of Medicine
2015 Symposium Chair and Organizer: American Association of Anatomists, Experimental Biology
2015 Abstract Reviewer: Orthopaedic Research Society 2016 Annual Meeting

Honors

2006 Excellence in Research, Graduate Student Senate, Kent State University
2006 Scholander Award, Runner-Up, American Physiological Society
2007 International Travel Award, Graduate Student Senate, Kent State University
2007 Juan Comas Prize, American Association of Physical Anthropologists

2009 Postdoctoral Poster Competition Finalist, American Association of Anatomists
2010 United States Bone and Joint Decade Young Investigator Initiative Participant
2011 Association of American Medical Colleges, Early Career Women Seminar Participant
2012 Excellence in Teaching Award, Marshall University School of Medicine Class of 2015
2014 Young Faculty Participation Award, American Association of Anatomists
2014 Academic Citizenship Excellence Award, Marshall University School of Medicine
2014 Creativity in Teaching Award, Marshall University School of Medicine Class of 2017
2015 Basmajian Award for Excellence in Teaching and Research, American Association of Anatomists
2015 Dean's Award for Excellence in Basic Science Research, Marshall University School of Medicine

C. Contribution to Science

1. My earliest publications addressed a fundamental question in skeletal biology: Mechanisms that control differential bone elongation in growth plates. Bones lengthen through a process of endochondral ossification, which involves proliferation and enlargement of chondrocytes in the growth plate. While growth plates are located at either end of each primary long bone, both ends do not contribute equally to limb lengthening. It is unclear how elongation rate is regulated in specific growth plates, and how this differential growth plate activity relates to limb length variation in mammals. These publications advanced the field by showing that pattern and rate of ossification in individual growth plates directly contribute to bone shape and length. This work collectively demonstrates that differential growth plate activity not only facilitates variability in skeletal proportions, but that it may do so through signaling of major systemic regulators such as insulin-like growth factor (IGF)-I. By providing evidence that the IGF-I receptor (IGF-IR) is expressed in high levels in only the most active growth plates, this line of research has revealed differential expression of the IGF-IR as a potential evolutionary mechanism for regulating limb length in a site-specific manner. These papers continue to be cited in orthopaedic and high-impact journals, such as the 2013 *Nature* paper listed below that cites my 2007 *Anatomical Record* study. I was co-investigator on my first publication in 2005, and have since been lead and corresponding author on all of my subsequent papers to date.

    a. Reno PL, DeGusta D, **Serrat MA**, Meindl RS, White TD, Eckhardt, RB, Kuperavage AJ, Galik K, Lovejoy CO. (2005). Plio-Pleistocene hominid limb proportions: Evolutionary reversals or estimation errors? *Current Anthropology*. 46: 575-588.
    b. **Serrat MA**, Reno PL, McCollum MA, Meindl RS, Lovejoy CO. (2007). Variation in mammalian proximal femoral development: comparative analysis of two distinct ossification patterns. *Journal of Anatomy.* 210(3): 249-258. PMID: 17331175. PMCID: 2100278.
    c. **Serrat MA**, Lovejoy CO, King D. (2007). Age- and site-specific decline in insulin-like growth factor-I receptor expression is correlated with differential growth plate activity in the mouse hindlimb. *Anatomical Record*. 290(4): 375-381. PMID: 17331175.
    d. Cooper KL, Oh S, Sung Y, Dasari RR, Kirschner MW, Tabin CJ. (2013). Multiple phases of chondrocyte enlargement underlie differences in skeletal proportions. Nature. 495(7441): 375-8. PMID: 23485973. PMCID: 3606657. **Cites Serrat et al., 2007**.

2. Building on the contributions described above, a substantial part of my research has since focused on the role of temperature in regulating limb length in mammals. My lab has shown that limbs of animals raised at warm ambient temperature are significantly and permanently longer than those of their siblings housed in the cold. These surprising observations have captivated scientists for over a century because most researchers assume that bone elongation is under tight genetic control. Results of my work show that not only can temperature modulate growth rate, but that the effect can be localized using mild, intermittent heat exposure to lengthen limbs on only one side of the body (a selected oral presentation at the 2013 Orthopaedic Research Society Annual Meeting). Our findings suggest that this phenotypic growth plasticity may at least partially result from enhanced vascular transport to the growth plate. Our ongoing work (presented at the American Society for Bone and Mineral Research 2015 Annual Meeting) is using heat to localize systemic drugs such as IGF-I to specific growth plates. This contribution is significant because it has the potential to profoundly impact treatment of a wide range of childhood growth disorders by providing a noninvasive method for lengthening limbs with localized warm temperature. I have received numerous national awards for this work (see Honors), am a recognized expert on the topic, and I have published an

invited authoritative review in *Comprehensive Physiology*. I have been the primary driving force in these projects, evinced by my role as lead and corresponding author on all of the publications.

a. **Serrat MA**, King D., Lovejoy CO. (2008). Temperature regulates limb length in homeotherms by directly modulating cartilage growth. *Proceedings of the National Academy of Sciences USA*. 105: 19347-52. **Rated 'Must Read' in Faculty of 1000 Biology.** PMID: 19047632. PMCID: 2614764.
b. **Serrat MA**, Williams RM, Farnum CE. (2009). Temperature alters solute transport in growth plate cartilage measured by *in vivo* multiphoton microscopy. *Journal of Applied Physiology*. 106: 2016-25. PMID: 19372302. PMCID: 2692772.
c. **Serrat MA.** (2014). Environmental temperature impact on bone and cartilage growth. *Comprehensive Physiology*. 4(2):621-55. **Invited Authoritative Review.** (includes new data). PMID: 24715562.
d. **Serrat MA**, Schlierf TJ*, Efaw ML*, Shuler FD, Godby J*, Stanko LM*, Tamski, HL*. (2015) Unilateral heat accelerates bone elongation and lengthens extremities of growing mice. *Journal of Orthopaedic Research*. 33(5): 692-8. *Student Authors. PMID: 25639189.

3. Some of my most exciting and novel contributions to date involve *in vivo* multiphoton imaging to assess molecular transport to cartilage plates of growing bones *in situ*, in a way not possible using other techniques. Delivery of systemic molecules into and through the dense matrix of avascular cartilage is a unique challenge of integrative physiology. The field of skeletal biology has made tremendous progress in elucidating the molecular intricacies of normal and abnormal bone growth, but we still have not been able to answer the fundamental question of how circulating factors actually reach growth plate cartilage, which is not penetrated by blood vessels. Major breakthroughs in cell biology have led to the development of drugs that can potentially combat incurable bone diseases, yet we still cannot figure out how to target the delivery of these agents to skeletal growth plates. Following my work using fluorescent microspheres to quantitatively assess temperature effects on bone blood flow, I began to use *in vivo* multiphoton microscopy to quantify heat-enhanced molecular transport into tibial growth plates of live mice. These papers demonstrated that the microvasculature surrounding the growth plate is exquisitely sensitive to temperature modulation, enhancing entry of large molecules that are otherwise size restricted at the vascular-cartilage interface. Our results not only show that growing bone has the capacity to adapt to the external environment, they highlight that temperature could be a novel strategy for enhancing molecular transport to specific sites in the skeleton. One of the most important aspects of this research program is the whole-animal, *in vivo* approach that can readily translate to clinical practice. This research has the potential to transform approaches that physicians take in treating a spectrum of bone elongation disorders by providing noninvasive methods for targeting therapeutics to impaired growth plates in the skeleton. As with the contributions above, I independently designed and implemented these projects and am lead and corresponding author on all of the resulting publications.

a. **Serrat MA.** (2009). Measuring bone blood supply in mice using fluorescent microspheres. *Nature Protocols.* 4(12): 1749-1758. PMID: 19893510.
b. **Serrat MA**, Williams RM, Farnum CE. (2009). Temperature alters solute transport in growth plate cartilage measured by *in vivo* multiphoton microscopy. *Journal of Applied Physiology*. 106: 2016-25. PMID: 19372302. PMCID: 2692772.
c. **Serrat MA**, Williams RM, Farnum CE. (2010). Exercise mitigates the stunting effect of cold temperature on limb elongation in mice by increasing solute delivery to the growth plate. *Journal of Applied Physiology*. 109: 1869-1879. PMID: 20930127. PMCID: 3006398.
d. **Serrat MA**, Efaw ML*****, Williams RM. (2014). Hindlimb heating increases vascular access of large molecules to murine tibial growth plates measured by in vivo multiphoton imaging. *Journal of Applied Physiology*. 116(4):425-38. *Student Author. PMID: 24371019. PMCID: PMC3921350.

Complete List of Published Work in My Bibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/1pilov-tJQmkH/bibliography/40205728/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

NIH/NIAMS
R15AR067451-01 Serrat (PI) 09/19/14-08/31/17
Heat enhanced molecular delivery to growth plates for targeted bone lengthening.
This multidisciplinary project uses *in vivo* multiphoton imaging and unilateral limb heating to study blood flow and molecular transport at cartilage-vascular interfaces of murine tibial growth plates. The hypothesis is that heat localizes delivery of systemic molecules into cartilage plates to promote bone lengthening.
Role: PI

Appalachian Clinical and Translational Science Institute Serrat (PI) 02/01/15-01/31/16
Dysregulated growth factor transport and accelerated bone elongation in childhood obesity.
This Marshall-funded pilot project uses *in vivo* multiphoton imaging and protein assays to collect pilot data for an NIH COBRE grant submission on molecular transport and linear growth acceleration in childhood obesity.
Role: PI

American Society for Bone and Mineral Research GAP Award Serrat (PI) 05/31/14-10/31/15
Heat enhanced molecular delivery to growth plates for targeted bone lengthening.
This multidisciplinary Grants in Aid project tests the hypothesis that heat localizes delivery of systemic molecules into cartilage plates to promote bone lengthening by using *in vivo* multiphoton imaging and western blotting to assess transport and activation of IGF-I in murine tibial growth plates.
Role: PI

Completed Research Support

NASA West Virginia Space Grant Consortium Serrat (PI) 08/01/14-07/31/15
Temperature effects on limb growth and IGF-I delivery to mouse bones
This project provides a research stipend to Miles Gray, a Marshall University Undergraduate, to test the hypothesis that localized heat treatment will increase the delivery of growth-essential nutrients to the limbs of developing mice, using fluorescent protein labeling and thin layer chromatography validation techniques.
Role: PI Mentor **Undergraduate Research Fellowship**

NASA West Virginia Space Grant Consortium Serrat (PI) 08/01/14-07/31/15
Unilateral heating to increase IGF-I uptake and bone length in mice
This project provides a research stipend to Holly Tamski, a Marshall University Graduate Student, to test the hypothesis that unilateral heating increases delivery of IGF-I to the growth plate to enhance extremity length.
Role: PI Mentor **Graduate Research Fellowship**

CCTS University of Kentucky Pilot Grant Program Serrat (PI) 08/15/13-02/14/15
Temperature enhanced bone elongation in growth plates.
This multidisciplinary project uses in vivo multiphoton imaging and unilateral limb heating to study blood flow and molecular transport at cartilage-vascular interfaces of murine tibial growth plates.
Role: PI

NASA West Virginia Space Grant Consortium Serrat (PI) 07/01/13-06/30/14
Unilateral heating: a novel model to induce differential extremity growth in mice
This project provides a research stipend to Jenna Vance, a Marshall University Undergraduate, to test the hypothesis that daily heat application will unilaterally increase limb length on the heat-treated side.
Role: PI (mentor) **Undergraduate Research Fellowship**

NSF Major Research Instrumentation MRI-R2 0959012 Norton (PI) 12/15/09-11/30/12
Acquisition of a Confocal/Multiphoton Microscope to Advance Cellular and Physiological Research at Marshall University. This project provides support for a combined confocal/multiphoton system for high-resolution microscopy and in vivo imaging at Marshall University's core imaging facility
Role: Major User and Oversight Committee Member