

UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
GRADUATE FACULTY APPLICATION

1. Name: Melda Onal
2. UAMS Graduate Program Sponsor: Cell Biology/Physiology Major field: Bone research
3. Present UAMS academic title or administrative position: Assistant Professor at the Physiology and Biophysics Department
- Date appointed this rank/position: 8/24/2017 Employed by: Physiology and Biophysics Department UAMS

4. Comments of Department Chair/Head or Program Director including: evidence of scholarly development, effectiveness as a teacher, quality of publications and reallocation of duties if this application is approved.

Dr. Onal is a new Assistant Professor on the Tenure Track. After completing her PhD here at UAMS in the IBS program in the laboratory of Charles O'Brien, she did postdoctoral training at the University of Wisconsin in the genetics of bone regulation. She is now very well prepared to apply this training to the investigation of transcriptional regulation of genes involved in bone remodeling. She can combine genetic mapping combined with the bone analytical technology available on campus to provide outstanding opportunities for graduate students. Her publications are of very high quality, and I expect that students will be eager to work with her.

Dr. Onal's time and effort is essentially 100% research in the first year, and the educational effort, including mentoring graduate students, will increase with time. If a student decides to enter her lab immediately, we can add some educational effort in the current year without any difficulty. There will be no need to reallocate duties as a result of her status as a member of the graduate faculty.

Department Chair/Head or Program Director 9/22/17 Date Graduate Council Representative

I have read the comments of my Department Chair/Head or Program Director and I do, do not (circle one) wish to supply additional information in support of my application.

Applicant's Signature 9/22/2017 Date

Approvals

B. Boyer
Chair, Graduate Faculty Committee 11/15/17 Date

E. C. Pote
Chair, Graduate Council 11/15/17 Date

[Signature]
Dean of the Graduate School 11/15/17 Date

INSTRUCTIONS FOR COMPLETION OF THE COMPUTERIZED FORM FOR APPLICATION TO THE UAMS GRADUATE FACULTY

1. Please read the form carefully and answer all questions. The form begins on the next page.
2. The form has been designed with fields for your responses, and these are indicated in blue and gray shading. Use the "tab" key to move between fields. The form will automatically expand to accommodate your entries. IF YOU NEED HELP IN ANY OF THE FIELDS, PRESS THE F1 KEY AND A HELP WINDOW WILL OPEN.
3. When you have completed the form, save it as a document on your own disk for future reference.
4. Print the document, and then obtain the appropriate signatures before submitting the form to the Graduate Office.

5. **List your planned involvement in graduate education (courses, theses, dissertations):**

I would like get rotation students and graduate students to mentor in my laboratory, in order to train them in the laboratory setting and to be their mentor for their theses and dissertation.

I would also like to participate in graduate-level classroom teaching, and would be happy to be in dissertation committees of graduate students.

I was already asked by the graduate student association (GSA) to be part of and help with this years research symposium, and I told them I would be very happy to help them.

6. **Briefly summarize your experience in graduate-level classroom teaching:**

Although I have experience in private tutoring and research training, I do not have any experience in graduate-level classroom teaching.

7. **Briefly summarize your experience in research and student research mentoring:**

I have directly mentored several graduate, medical and undergraduate students for extended periods of time including summer internships and long term laboratory employment. Specifically:

* summer internship - medical student Josh Campbell in the O'Brien Laboratory in UAMS

* long-term laboratory/research student employment - undergraduate students Allison Danielson and Jon Markert in the Pike Laboratory in UW

* summer internship - masters student Amrita Maheswari in the Pike Laboratory in UW

All of the students above were trained by me, conducted research under my mentorship, and became coauthors in my publications.

I have also worked closely with two graduate students Hillary St John and Sohel Shamsuzzaman, help train them in bone research, experimental design, manuscript writing etc. as well as helping and overseeing the writing of their thesis.

8. **Attach Curriculum Vita** showing educational background (including institutions attended, degrees awarded and dates), honors or awards received, scholarly or professional organization affiliations, teaching experience (give school, dates and advanced and graduate subjects taught), including student theses and/or dissertations supervised. Cite publications and research in progress.

CURRICULUM VITAE

Melda Onal

CITIZENSHIP and VISA STATUS: Permanent resident/Greencard holder

EDUCATION

2006	B.S.	Bilkent University, Ankara Turkey (Molecular Biology and Genetics)
2012	Ph.D.	University of Arkansas for Medical Sciences, Little Rock, Arkansas (Interdisciplinary Biomedical Sciences)
2017	Postdoctoral Fellow	University of Wisconsin, Madison, Wisconsin (Biochemistry Department)

PROFESSIONAL EXPERIENCE

2006-2012	Ph.D. student at University of Arkansas for Medical Sciences in the laboratory of Charles A. O'Brien, Department of Endocrinology
2012-2017	Postdoctoral Fellow at University of Wisconsin in the laboratory of J. Wesley Pike, Biochemistry Department
2017 -2017	Scientist at University of Wisconsin in the laboratory of J. Wesley Pike, Biochemistry Department
2017-present	Assistant Professor at Physiology and Biophysics Department of University of Arkansas for Medical Sciences (College of Medicine)

HONORS AND AWARDS

ASBMR President's Award	2010
UAMS Travel Award	2010
UAMS Graduate School Achievement Award	2010
ASBMR Young Investigator Travel Award	2011
UAMS Travel Award	2011

UAMS Graduate School Outstanding Achievement Award	2011
ASBMR Young Investigator Travel Grant	2012
ASBMR Young Investigator Travel Grant	2014
University of Wisconsin Biochemistry Travel Award	2014
ASBMR Young Investigator Award	2015
University of Wisconsin Biochemistry Travel Award	2015
Honorable Mention as a finalist for the Journal of Endocrinology	
Outstanding Trainee Manuscript Award	2016
ASBMR Young Investigator Travel Grant	2017

ADVISORY POSITIONS

2013-2017 Supervisor to undergraduate/graduate students

MAJOR RESEARCH INTERESTS

1. Genetic determinants of skeletal phenotypes
2. Role of Autophagy for skeletal aging
3. Transcriptional Regulation of Fibroblast Growth Factor 23 (FGF23) and its role for chronic kidney disease (CKD-MBD)
4. Calcium homeostasis and bone

SOCIETY MEMBERSHIP

American Society for Bone and Mineral Research

PUBLICATIONS

1. Xiong, J., **Onal, M.**, Jilka, R.L., Weinstein, R.S., Manolagas, S.C., and C.A. O'Brien. **Matrix-embedded cells control osteoclast formation.** *Nature Medicine*, 17:1235-41, 2011. PMID: PMC3192296
2. **Onal, M.**, Galli, C., Fu, Q., Xiong, J., Weinstein, R.S., Manolagas, S.C., and C.A. O'Brien. **The RANKL distal control region is required for the increase in RANKL expression, but not the bone loss, associated with hyperparathyroidism or lactation in adult mice.** *Molecular Endocrinology*, 26: 341-8, 2012. PMID: 22207718
3. **Onal, M.**, Xiong, J., Chen, X., Thostenson, J.D., Almeida, M., Manolagas, S.C., and C.A. O'Brien. **Receptor Activator of Nuclear Factor κ B Ligand (RANKL) Protein Expression by B Lymphocytes Contributes to Ovariectomy-induced Bone Loss.** *J Biol Chem*. 287(35):29851-60, 2012. PMID: 22782898
4. Almeida, M., Iyer, S., Martin-Millan, M., Bartell, S.M., Han, L., Ambrogini, E., **Onal, M.**, Xiong, J., Weinstein, R.S., Jilka, R.L., O'Brien, C.A., Manolagas, S.C. **The osteoblast progenitor ER α stimulates Wnt signaling and bone accrual.** *J Clin Invest*. 2013 Jan 2;123(1):394-404. PMID: 23221342

5. **Onal M**, Piemontese M, Xiong J, Wang Y, Han L, Ye S, Komatsu M, Selig M, Weinstein RS, Zhao H, Jilka RL, Almeida M, Manolagas SC, O'Brien CA. **Suppression of autophagy in osteocytes mimics skeletal aging.** *J Biol Chem.* 2013 Jun 14;288(24):17432-40. PMID: 23645674
6. Piemontese M, **Onal M**, Xiong J, Wang Y, Almeida M, Thostenson JD, Weinstein RS, Manolagas SC, O'Brien CA. **Suppression of autophagy in osteocytes does not modify the adverse effects of glucocorticoids on cortical bone.** *Bone* 2015 Jun;75:18-26. doi: 10.1016/j.bone.2015.02.005. PMID: 25700544
7. **Onal M**, Bishop KA, St John HC, Danielson AL, Riley EM, Piemontese M, Xiong J, Goellner JJ, O'Brien CA, Pike JW. **A DNA Segment Spanning the Mouse Tnfrsf11 Transcription Unit and Its Upstream Regulatory Domain Rescues the Pleiotropic Biologic Phenotype of the RANKL Null Mouse.** *J Bone Miner Res.* 2015 May;30(5):855-68. doi: 10.1002/jbmr.2417. PMID: 25431114
8. **Onal M**, St John HC, Danielson AL, Pike JW. **Deletion of the Distal Tnfrsf11 RL-D2 Enhancer that Contributes to PTH-Mediated RANKL Expression in Osteoblast Lineage Cells Results in a High Bone Mass Phenotype in Mice.** *J Bone Miner Res.* 2016 Feb;31(2):416-29. doi: 10.1002/jbmr.2698. PMID: 26332516
9. Meyer MB., Benkusky NA., **Onal M**, Pike JW. **Selective regulation of *Mmp13* by 1,25(OH)₂D₃, PTH, and Osterix through distal enhancers.** *J Steroid Biochem Mol Biol.* 2016 Nov;164:258-264. doi: 10.1016/j.jsbmb.2015.09.001. PMID: 26348136
10. Xiong J , Piemontese M , **Onal M** , Campbell J , Goellner JJ , Dusevich V , Bonewald L , Manolagas SC , and O'Brien CA. **Osteocytes, not osteoblasts or lining cells, are the main source of the RANKL required for osteoclast formation in remodeling bone.** *PLoS One.* 2015 Sep 22;10(9):e0138189. doi: 10.1371/journal.pone.0138189. PMID: 26393791
11. **Onal M**, St John HC, Danielson AL, Markert JW, Riley EM, Pike JW. **Unique Distal Enhancers Linked to the Mouse Tnfrsf11 Gene Direct Tissue-Specific and Inflammation-induced Expression of RANKL.** *Endocrinology.* 2016 Feb;157(2):482-96. doi: 10.1210/en.2015-1788. PMID: 26646205
12. Pike JW, Meyer MB, Benkusky NA, Lee SM, St John H, Carlson A, **Onal M**, Shamsuzzaman S. **Genomic Determinants of Vitamin D-Regulated Gene Expression.** *Vitam Horm.* 2016;100:21-44. doi: 10.1016/bs.vh.2015.10.011. PMID: 26827947
13. Piemontese M, **Onal M**, Xiong J, Han L, Thostenson JD, Almeida M, O'Brien CA. **Low bone mass and changes in the osteocyte network in mice lacking autophagy in the osteoblast lineage.** *Sci Rep.* 2016 Apr 11;6:24262. doi: 10.1038/srep24262. PMID: 27064143

14. Shamsuzzaman S, **Onal M**, St John HC, Jeffery JJ, Pike JW. **Absence of the Vitamin D Receptor Inhibits Atherosclerotic Plaque Calcification in Female Hypercholesterolemic Mice.** *J Cell Biochem.* 2017 May;118(5):1050-1064. doi: 10.1002/jcb.25679. Epub 2017 Jan 5. PMID: 27567005
15. Shamsuzzaman S, **Onal M**, John HCS, Pike JW. **Deletion of a Distal RANKL Gene Enhancer Delays Progression of Atherosclerotic Plaque Calcification in Hypercholesterolemic Mice.** *J Cell Biochem.* 2017 Apr 17. doi: 10.1002/jcb.26074. PMID: 28419519
16. Pike JW, Meyer MB, Lee SM, **Onal M**, Benkusky NA. **The vitamin D receptor: contemporary genomic approaches reveal new basic and translational insights.** *J Clin Invest.* 2017 Apr 3;127(4):1146-1154. doi: 10.1172/JCI88887. Epub 2017 Feb 27. PMID: 28240603
17. Meyer MB, Benkusky NA, Kaufmann M, Lee SM, **Onal M**, Jones G, Pike JW. **A Kidney-specific genetic control module in mice governs endocrine regulation of the cytochrome P450 gene *Cyp27b1* essential for vitamin D3 activation.** *J Biol Chem.* 2017 Aug 14. pii: jbc.M117.806901. doi: 10.1074/jbc.M117.806901. [Epub ahead of print] PMID: 28808057
18. **Onal M**, Carlson A. H., Meyer M.B., Benkusky N.A., Lee S. M., St John HC, Pike, J.W. **A novel distal enhancer of the mouse *Fgf23* gene mediates inflammatory regulation of FGF23 expression, and FGF23 induction in oxalate-induced CKD Model.** Submitted to *JBMRPlus*

POSTERS AND PRESENTATIONS

- 2009- **RANKL Expression in Osteocalcin-Expressing Cells, Not Necessarily Osteoblasts, is Essential for Osteoclast Formation In Vivo**
J. Xiong, **M. Onal**, P.E. Cazer, X. Chen, R.S. Weinstein, R.L. Jilka, S.C. Manolagas and C.A. O'Brien
- 2010-**The RANKL Distal Control Region is Required for Cancellous Bone Loss due to Dietary Calcium Deficiency but not Lactation**
Melda Onal, Carlo Galli, Priscilla Cazer, Jinhu Xiong, Xinrong Chen, Robert Weinstein, Stavros Manolagas, Charles O'Brien
- 2010- **Hypertrophic Chondrocytes and Osteocytes are Essential Sources of RANKL for Bone Growth and for Bone Remodeling, Respectively**
Jinhu Xiong, **Melda Onal**, Priscilla E. Cazer, Xinrong Chen, Stavros C. Manolagas, Robert L. Jilka, Robert S. Weinstein, and Charles A. O'Brien

2010-LPS Stimulates RANKL Expression in Bone Marrow Stromal Cells but Suppresses RANKL Expression in T Cells

Xinrong Chen, Priscilla Cazer, Jinhu Xiong, **Melda Onal**, Stavros C. Manolagas, Charles A. O'Brien

2011-Osteocyte Autophagy Declines with Age in Mice and Suppression of Autophagy Decreases Bone Mass

Haibo Zhao, Jinhu Xiong, **Melda Onal**, Priscilla E. Cazer, Robert S. Weinstein, Stavros C. Manolagas, and Charles A. O'Brien

2011-Increased RANKL Production by Osteocytes is a Major Mechanism Underlying the Bone Loss Induced by Unloading

Jinhu Xiong, **Melda Onal**, Priscilla E. Cazer, Stavros C. Manolagas, and Charles A. O'Brien

2011-RANKL Production by B Lymphocytes Contributes to the Bone Loss Induced by Inflammation and Ovariectomy

Melda Onal, Jinhu Xiong, Priscilla Cazer, Stavros Manolagas, Charles O'Brien

2012-Suppression of Autophagy in Osteoblasts and Osteocytes Increases Oxidative Stress and Recapitulates the Effects of Aging on the Murine Skeleton

Melda Onal, Jinhu Xiong, Shiqiao Ye, Li Han, Maria Jose Almeida, Priscilla Cazer, Stavros Manolagas, Charles O'Brien

2012- RANKL Produced by Osteocytes Contributes to the Bone Loss Induced by Hyperparathyroidism

Jinhu Xiong, **Melda Onal**, Stavros Manolagas, Charles O'Brien

2013- Suppression of autophagy in Osx1-Cre-expressing cells causes low bone mass and spontaneous fractures in mice.

Marilina Piemontese, **Melda Onal**, Yiying Wang, Jinhu Xiong, Priscilla Baltz, Rajamani Selvam, Stuart Berryhill, Li Han, Stavros Manolagas, Charles O'Brien.

2013- Osteocytes, but not osteoblasts, provide the RANKL required for bone remodeling in adult mice: novel insights from Sost-Cre;RANKL^{f/f} mice.

Jinhu Xiong, Rajamani Selvam, Yiying Wang, Marilina Piemontese, **Melda Onal**, Priscilla Baltz, Stavros Manolagas, Charles O'Brien

2013- Glucocorticoids Stimulate Osteocyte Autophagy in Mice but Suppression of Autophagy in Osteocytes does not Accentuate their Negative Impact on the Skeleton.

Marilina Piemontese, **Melda Onal**, Jinhu Xiong, Yiying Wang, Rajamani Selva1, Stuart Berryhill, Li Han, Erin Hogan, Robert Weinstein, Stavros Manolagas, Charles O'Brien

2014 - Unique Distal Enhancers Linked to the Mouse Tnfsf11 Gene Direct Tissue-Specific Expression and Inflammation induced Regulation of RANKL Expression.

Melda Onal, Hillary St John, Allison Danielson, Charles O'Brien, J. Wesley Pike

2015- A Complex Set of Distal Enhancers Linked to the Mouse *Tnfrsf11* Gene Direct Tissue- specific and Hormone-regulated Expression of RANKL.

Melda Onal, Hillary St John, Allison Danielson, Jon Markert, J. Wesley Pike

2015-Deletion of a Distal Enhancer of the RANKL Gene Delays the Progression of Atherosclerotic Plaque Calcification in Hypercholesterolemic Mice.

Sohel Shamsuzzaman, **Melda Onal**, Hillary St. John , J. Wesley Pike.

2017-*Transcriptional Regulation of the Fgf23 gene by 1,25-dihydroxyvitamin D3 is not mediated through enhancer elements located within the immediate vicinity of the Fgf23 gene locus.*

Carlson A. H., Meyer M.B., **Onal M.**, Benkusky N.A., Pike J.W.

2017- *A Novel Distal Enhancer of the Mouse Fgf23 Gene Mediates the Inflammation- and CKD-induced Expression of FGF23.* **Onal M.**,

Carlson A. H., Meyer M. B., Benkusky N. A., Lee S. M., St. John H. C., Pike, J. W.

