BIOGRAPHICAL SKETCH

NAME: KIEL, DOUGLAS P.

eRA COMMONS USER NAME (DPKIEL):

POSITION TITLE: Professor of Medicine, Harvard Medical School and Director Musculoskeletal Research Center, Institute for Aging Research, Hebrew SeniorLife

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Duke University, Durham, NC	BS	05/1975	Science Education
University of North Carolina School of Medicine, Chapel Hill, N.C.	MD	05/1981	Medicine
Boston University School of Medicine, Boston, MA	MPH	06/1986	Epidemiology and Biostatistics

A. PERSONAL STATEMENT

As the Principal Investigator of the Framingham Osteoporosis Study for the past 25 years, I have had extensive experience in human translational research in epidemiology and genomics. Over the years I have led several major large cohort collaborations involving genome wide association studies and follow up of these genetic variants. These efforts provide a rich source of data for analyses by REC and PESC applicants. At the Institute for Aging Research at Hebrew SeniorLife, we have a group of genetic epidemiologic, biostatistical and bioinformatic colleagues who can serve as mentors. Furthermore, I have been an active leader and mentor for our geriatric fellowship and on a national level. Finally, I have previously served as a leader of the PESC in more remote cycles of this grant, which will be valuable to the success of our proposed PESC.

1. Zheng HF,* Forgetta V,* Hsu YH,* Estrada K,* Rosello-Diez A,* Leo PJ,* Dahia CL,* Park-Min KH,* Tobias JH,* Kooperberg C,* Kleinman A, Styrkarsdottir U, Liu CT, ….Spector TS, Cupples LA, Ohlsson C, Greenwood C, Jackson RD,† Rowe DW,† Loomis CA,† Evans DM,† Ackert-Bicknell CL,† Joyner AL,† Duncan EL,† Kiel DP,† Rivadeneira F,† Richards JB.† Whole-genome sequencing and imputation identifies *EN1* as a determinant of bone density and fracture. Nature. 2015 Sep 14. doi: 10.1038/nature14878. [Epub ahead of print] PMID: 26367794.
2. Estrada K, Styrkarsdottir U, Evangelou E, Hsu …., Richards JB, Brown MA, Stefansson K,Uitterlinden AG, Ralston SH, Ioannidis JP, Kiel DP, Rivadeneira F. Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture. Nat Genet. 2012;44(5):491-501. PMID: 22504420 PMCID: PMC3338864 NIHMS: 364577
3. Huang J, Hsu Y-H, Mo C, Abreu E, Kiel D P, Bonewald L.F., Brotto M, and Karasik D. METTL21C is a potential pleiotropic gene for osteoporosis and sarcopenia acting through the modulation of the NFκB signaling pathway *J Bone Mineral Res.* 2014 Jul;29(7):1531-40. doi: 10.1002/jbmr.2200.PMID:24677265 PMCID: PMC4074268
4. Kiel DP, Hannan MT, Barton BA, Bouxsein ML, Sisson E, Lang T, Allaire B, Dewkett D, Carroll D, Magaziner J, Shane E, Leary ET, Zimmerman S, Rubin C. Low magnitude mechanical stimulation to improve bone density in Persons of Advanced Age: A Randomized, Placebo-Controlled Trial J Bone Miner Res. 2015 July; 30 (7): pp 1319–1328 DOI: 10.1002/jbmr.2448 Jan 8. PMID: 25581217 [PubMed – in process]

B. POSITIONS AND HONORS

Positions and Employment

1986 - 1992 Associate Physician, Division of General Internal Medicine, Rhode Island Hospital, Brown University School of Medicine, Providence , RI

1992 - Director Musculoskeletal Research Center, Institute for Aging Research, Hebrew SeniorLife,

	Boston, MA
1992 - 1999	Assistant Professor of Medicine, Harvard Medical School Division on Aging, and Staff Physician , Beth Israel Deaconess Medical Center (BIDMC), Boston, MA
1992 - 2000	Assoc Director Medical Research, Hebrew Rehabilitation Center for Aged (HRCA), Boston, MA
1999 -	Director of Medical Research, Interdisciplinary Program on Aging, BIDMC/Harvard Medical School/Hebrew SeniorLife, Boston, MA
1999 - 2010	Adjunct Associate Professor of Medicine, (Non-voting Faculty), Brown University School of Medicine, Providence, RI
2010 -	Adjunct Professor of Medicine (Non-voting Faculty), Brown University School of Public Health, Department of Epidemiology, Providence, RI
2010 -	Professor of Medicine, Harvard Medical School, Boston, MA
2013 -	Associate Member , Broad Institute of MIT and Harvard University , Cambridge, MA

Other Experience and Professional Memberships

1994 -	Reviewer Epidemiology and Disease Control-2, Orthopedics, and Geriatrics & Rehabilitation Medicine Study Sections, NIAMS Career Awards, NIAMS SCOR Review, NIAMS K23 Review, HOP-T-02 Special Emphasis Panel, NIH
1998 -	Editorial Board, Clinical Densitometry
2000 -	Scientific Advisory Board/Education Committee, National Osteoporosis Foundation
2000 - 2003	Chair, Research Committee, American Geriatrics Society
2006 -	Technical Advisory Panel, Joint Commission Osteoporosis Initiative
2008 - 2011	Founding Member, NIA Clinical Trials Advisory Panel
2014 - 2015	Senior Associate Editor, Journal of Bone and Mineral Research
2015 - 2016	President, American Society for Bone and Mineral Research

Honors

2004	Nomination for Excellence in Mentoring Award, Harvard Medical School
2005	Outstanding Excellence in Geriatric Research All Categories, American Geriatrics Society
2007	Nomination for Excellence in Mentoring, Harvard Medical School
2008	Elected to Council, American Society for Bone and Mineral Research
2010	A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School
2013	Fellow, American Geriatrics Society
2013	Fellow, Gerontological Society of America

C. Contribution to Science

1. My early career focused on the epidemiology of osteoporosis and related fractures. I started the Framingham Osteoporosis Study, an ancillary study of the Framingham Heart Study, in 1991. Multiple lifestyle contributors to osteoporosis and fracture were examined in this study over the subsequent 25 years after we completed multiple assessments of bone mineral density, hand radiography, quantitative computed tomography, and fracture ascertainment, including estrogen use, thiazide diuretics, visual acuity, smoking, alcohol consumption, fruits and vegetable consumption, caffeine use, height loss, and silicon intake. All of these studies added to the growing attention that osteoporosis received in clinical practice. The study also shaped the use of bone densitometry by demonstrating that repeated screening within short intervals may not be useful. I served as the lead or senior author on most of the publications that have come out of this study.

    a. Kiel DP, Felson DT, Anderson JJ, Wilson PW, Moskowitz MA. Hip fracture and the use of estrogens in postmenopausal women: the Framingham study: N Engl J Med. 1987; 317(19):1169-1174. PMID: 3657888 PMCID: N/A
    b. Kiel DP, Zhang Y, Hannan MT, Anderson JJ, Baron JA, Felson DT. The effect of smoking at different life stages on bone mineral density in elderly men and women. Osteoporosis Int 1996;6(3):240-8. PMID: 8783299 PMCID: N/A
    c. Kiel DP, Hannan MT, Broe KE, Felson DT, Cupples LA. Can metacarpal cortical area predict the occurrence of hip fracture in women and men over 3 decades of follow up? Results from the

Framingham Osteoporosis Study. J Bone Miner Res. 2001;16(12):2260-6. PMID: 11760840 PMCID: N/A

d. Hannan MT, Broe KE, Cupples LA, Dufour AB, Rockwell M, Kiel DP. Height loss predicts subsequent hip fracture in men and women of the Framingham Study. J Bone Miner Res. 2012;27:146-152. PMCID: PMC3647683

2. Another area of my research focuses on the relation between bone mineralization and the development of vascular calcification. I developed a radiographic index to grade the severity of aortic calcification using either radiographs or images from dual energy x-ray absorptiometry (DXA). Based on work that I have done, one of the manufacturers of DXA equipment received FDA approval to include the grading of vascular calcification to their software. This research focus has also enabled several junior faculty who I have mentored to extend my work as part of their own research. I have also worked with a pharmaceutical company as part of their FDA filing, to review serial radiographs for aortic calcification as part of a randomized controlled trial of denosumab to treat osteoporosis.

    a. Kauppila LI, Polak J, Cupples LA, Hannan MT, Kiel DP, Wilson PWF. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis 1997;132(2):245-50. PMID: 9242971 PMCID: N/A
    b. Kiel DP, Kauppila LI, Cupples LA, Hannan MT, O'Donnell CJ, Wilson PW. Bone loss and the progression of abdominal aortic calcification over a 25 year period: The Framingham Heart Study. Calcif Tissue Int. 2001;68(5):271-6. Erratum in: Calcif Tissue Int. 2004;74(2):208. PMID: 11683533 PMCID: N/A
    c. Schousboe JT, Taylor BC, Kiel DP, Ensrud KE, Wilson KE, McCloskey EV. Abdominal aortic calcification detected on lateral spine images from a bone densitometer predicts incident myocardial infarction or stroke in older women. J Bone Miner Res. 2008;23(3):409-16. PMID: 17956153 PMCID: N/A
    d. Samelson EJ, Miller PD, Christiansen C, Daizadeh NS, Grazette L, Anthony MS, Egbuna O, Wang A, Siddhanti SR, Cheung AM, Franchimont N, Kiel DP. RANKL inhibition with denosumab does not influence 3-year progression of aortic calcification or incidence of adverse cardiovascular events in postmenopausal women with osteoporosis and high cardiovascular risk. J Bone Miner Res. 2014 Feb;29(2):450-7. doi: 10.1002/jbmr.2043. PMID:23873632 PMCID: PMC3946983.

3. As the PI of the Framingham Osteoporosis Study, I directed the development of a research group that became one of the foremost genetic epidemiology groups studying musculoskeletal phenotypes in the United States. We began with investigations of single gene polymorphism associations with bone mineral density, expanded to describe gene by environment interactions (e.g., interactions between the MTHFR C677T and folate, variants in the LRP5 gene and physical activity, and variants in the PPARG and dietary fat intake), performed linkage analyses and progressed onto large scale genome wide association studies in large consortia that are now moving into targeted sequencing, whole exome sequencing, and whole genome sequencing.

    a. McLean RR, Karasik D, Selhub J, Tucker KL, Ordovas JM, Russo GT, Cupples LA, Jacques PF, Kiel DP. Association of a common polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene with bone phenotypes depends on plasma folate status. J Bone Miner Res. 2004;19(3):410-8. PMID: 15040829 PMCID: N/A
    b. Ackert-Bicknell CL, Demissie S, Marín de Evsikova C, Hsu YH, DeMambro VE, Karasik D, Cupples LA, Ordovas JM, Tucker KL, Cho K, Canalis E, Paigen B, Churchill GA, Forejt J, Beamer WG, Ferrari S, Bouxsein ML, Kiel DP, Rosen CJ. PPARG by dietary fat interaction influences bone mass in mice and humans. J Bone Miner Res. 2008;23(9):1398-408. PMID: 18707223 PMCID: PMC2683155
    c. Estrada K, Styrkarsdottir U,… Kiel DP, Rivadeneira F. Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture. Nat Genet. 2012;44(5):491-501. PMID: 22504420 PMCID: PMC3338864 NIHMS: 364577
    d. Kwan JS, Hsu YH, Cheung CL, Dupuis J, Saint-Pierre A, Eriksson J, Handelman SK, Aragaki A, Karasik D, Pramstaller PP, Kooperberg C, Lacroix AZ, Larson MG, Lau KS, Lorentzon M,

Pichler I, Sham PC, Taliun D, Vandenput L, Kiel DP, Hicks AA, Jackson RD, Ohlsson C, Benjamin EJ, Kung AW. Meta-analysis of genome-wide association studies identifies two loci associated with circulating osteoprotegerin levels. Hum Mol Genet. 2014 Jul 30. pii: ddu386. [Epub ahead of print] PMID: 25080503 [PubMed - in process]

4. Another major focus of my work has been the testing of interventions to prevent falls and fractures in older individuals. As such, I have led single site and multi-center randomized, placebo-controlled clinical trials that recruited seniors from a variety of settings including long term care and community settings. These trials have included the use of vitamin D to prevent falls, which has contributed to the understanding of dosing of vitamin D to prevent falls in the most vulnerable seniors, use of hip protectors to prevent fractures in nursing home residents, and most recently, the efficacy of low magnitude mechanical stimulation to enhance bone density.

    a. Broe, KE, Chen TC, Weinberg J, Bischoff-Ferrari HA, Holick MF, Kiel DP. A higher dose of vitamin D reduces the risk of falls in nursing home residents: A randomized, multiple-dose study. J Am Geriatr Soc. 2007;55(2):234-39. PMID: 17302660 PMCID: N/A
    b. Kiel DP, Magaziner J, Zimmerman S, Ball L, Barton BA, Brown KM, Stone JP, Dewkett D, Birge SJ. Efficacy of a hip protector to prevent hip fracture in nursing home residents: the HIP PRO randomized controlled trial. JAMA. 2007;298(4):413-22. PMID: 17652295 PMCID: N/A
    c. Kiel DP, Hannan MT, Barton BA, Bouxsein ML, Sisson E, Lang T, Allaire B, Dewkett D, Carroll D, Magaziner J, Shane E, Leary ET, Zimmerman S, Rubin C. Low Magnitude Mechanical Stimulation to Improve Bone Density in Persons of Advanced Age: A Randomized, Placebo-Controlled Trial J Bone Miner Res. 2015 Jan 8. doi: 10.1002/jbmr.2448. [Epub ahead of print] PMID: 25581217 [PubMed – in process]

5. The last area of research contributions is in the area of accidental falls. Early in my career I performed studies of risk factors and outcomes of falls in elderly individuals. Based on my expertise, I have been writing the “falls” chapters for multiple textbooks, including the Geriatric Review Syllabus, UpToDate, and the major Osteoporosis textbook in the field. Later I went on to study fall prevention (see above vitamin D intervention trial by Broe., et al.) I was a key investigator in the MOBILIZE Boston Study, which assembled a population based cohort from the Greater Boston area, and characterized novel risk factors for falls.

    a. Kiel DP, O'Sullivan P, Teno JM, Mor V. Health care utilization and functional status in the aged following a fall. Med Care. 1991; 29(3):221-8. PMID: 1997751 PMCID: N/A
    b. Kiely DK, Kiel DP, Burrows AB, Lipsitz LA. Identifying nursing home residents at risk for falling. J Am Geriatr Soc 1998;446(5):551-5. PMID: 9588366 PMCID: N/A
    c. Leveille SG, Jones RN, Kiely DK, Hausdorff JM, Shmerling RH, Guralnik JM, Kiel DP, Lipsitz LA, Bean JF. Chronic musculoskeletal pain and the occurrence of falls in an older population. JAMA. 2009;302(20):2214-21. PMID: 19934422 PMCID: PMC2927855 NIHMS: 218458
    d. Kelsey JL, Berry SD, Procter-Gray E, Quach L, Nguyen US, Li W, Kiel DP, Lipsitz LA, Hannan MT. Indoor and outdoor falls in older adults are different: the maintenance of balance, independent living, intellect, and zest in the Elderly of Boston Study. J Am Geriatr Soc. 2010;58(11):2135-41. PMID: 20831726 PMCID: PMC2975756 NIHMS: 222890

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/douglas.kiel.1/bibliography/40374222/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

NIAMS R01 AR041398-21, (Principal Investigator- Douglas P. Kiel) 06/01/15- 05/31/20
Risk Factors for Aged Related Bone Loss
This project investigates the role of visceral adipose tissue on bone microarchitecture and muscle density in the Framingham Generation 3 cohort.

NIDDK R01 DK092938 (Principal Investigator Shalendar Bhasin, MD, PhD) 1/1/13 – 12/31/16
Population-based Reference Ranges for Estradiol and Estrone in Men
This investigation uses state-of-the-art, LC-MS/MS method for the measurement of estradiol and estrone levels and a population-based reference sample from the Framingham Heart Study for generating reference limits for total and free estradiol and estrone levels in men. Long- term health consequences of low and high estradiol and estrone levels will be studied longitudinally. These steps will help us develop rational criteria for classifying men into estrogen-deficient and estrogen-replete, provide a standardized framework for the interpretation of serum estradiol and estrone levels, and enhance the comprehensibility of circulating estradiol and estrone values to practicing clinicians.
Role – Co-Investigator

NIAMS R01 AR061445-01 PI
Bone Microarchitecture: The Framingham Osteoporosis Study 5/1/12 – 4/31/17
After performing high resolution peripheral quantitative computed tomography scans on over 2,500 Framingham Study participants, the microarchitectural indices obtained from the images will be used to perform genome wide association studies, to study risk factors for bone microarchitecture, and to determine if bone microarchitecture predicts fracture.
Role: PI

NIA R01 AG041658 (Principal Investigator Elizabeth Samelson, PhD) 9/30/11 – 8/31/16
Mechanisms and Clinical Implications of Hyperkyphosis: The Framingham Study
The purpose of this project is to determine the natural history, risk factors and clinical outcomes of hyperkyphosis. A greater understanding of the factors that contribute to progression of kyphosis will help lead to interventions to prevent and treat this complex condition
Role – Co-Investigator

NIAMS R01 AR (Principal Investigator – Marian T. Hannan, DSc.) 4/1/13 – 3/31/16
Biomechanical Approach to Predicting Hip Fractures
This project will investigate the role of trochanteric soft tissue thickness on hip fracture risk, and include this in a biomechanical “Factor-of-Risk” model, to examine if they will predict hip fracture, and further, perform better than currently available prediction tools
Role – Co-Investigator

NIAMS R01 AR053986 (Principal Investigator – Mary L. Bouxsein, PhD) 9/18/13 – 8/31/17
Biomechanics of Vertebral Fractures: The Framingham QCT Study
This project will determine the contribution of 1) spinal curvature, 2) the size and quality of trunk muscles; and 3) the distribution of bone density within the vertebral body to VF.
Role – Co-Investigator

NIA R01 AG045441 (Principal Investigator – Sarah Berry, MD) 10/01/14 – 9/30/18
A Clinical Prediction Tool to Guide Treatment of Osteoporosis in the Nursing Home
This project will develop a fracture prediction tool for nursing home residents and evaluate the efficacy of pharmacologic therapy to prevent fractures in nursing home residents using a national sample of nursing home residents.
Role – Co-Investigator

NIA U24 AG051129-01 (Principal Investigator Steven R. Cummings, MD, Simon Melov, PhD, Nicholas Schork, PhD
Integrative Resource to Develop Translational Strategies to Promote Longevity
This grant will create a resource and infrastructure that integrates genomic and related data sources that will lead to the development of strategies for identifying targets for pharmacological intervention that will impact longevity based on genetic associations. This infrastructure will include information from longitudinal cohort studies with genome-wide genotype and sequencing data, computational methods for annotating genetic variants, information from tissue-specific studies of expression quantitative trait loci (eQTL), and datasets of chemical properties of small molecule compounds linked to protein targets.