BIOGRAPHICAL SKETCH

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NAME: BERG, Anders Hayden

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

POSITION TITLE: Co-Director of Clinical Chemistry and Core Laboratory at Cedars-Sinai Medical Center

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
University of Iowa, Iowa City, IA	B.A.	06/1996	Physics
Albert Einstein College of Medicine, NY, NY	M.D.	06/2004	Medicine
Albert Einstein College of Medicine, NY, NY	Ph.D.	06/2004	Cell Biology
Brigham and Women's Hospital, Boston, MA	Residency	10/2007	Clinical Pathology

A. Personal Statement

I am an Associate Professor of Pathology at Cedars-Sinai. My scientific interests focus on the metabolic pathophysiology and diagnostic challenges of kidney disease, diabetes mellitus, and their complications. My laboratory is engaged in translational research, using animal models to study the pathophysiology of uremia, and developing mass spectrometric diagnostic tests for kidney disease and the pathophysiology of vitamin D deficiency. My lab investigates the chemical mechanisms of cellular toxicity of uremia and discovery of clinically useful assays that are mechanistically tied to this pathophysiology. My primary project focuses on the pathology associated with urea-induced protein carbamylation, amino acid deficiencies, and cardiovascular risk in patients with kidney disease and chronic uremia. This project has wide-ranging implications for the management of patients with kidney disease and may lead to a pathway for optimization of dialysis, nutritional supplements, and carbamylation-scavenging therapies in order to improve the quality of life and survival for kidney patients. My laboratory also uses metabolomic assays to ask fundamental questions regarding the roles of metabolic intermediates (such as niacinamide and NAD deficiency) in the pathogenesis of uremic cardiac toxicity and kidney injury, and we have developed clinical assays for serum free and bioavailable 25-hydroxyvitamin D, which may be superior indicators of vitamin D sufficiency when compared to standard clinical assays for total 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D. Our focus is development of clinically relevant biomarker assays that are directly and mechanistically related to the pathophysiology of kidney disease and its sequelae.

B. Positions and Honors

Positions and Employment

2004-2007 Resident, Clinical Pathology, Brigham and Women's Hospital, Boston, MA
2006-2007 Research Fellow, Clinical Chemistry, Brigham and Women's Hospital, Boston, MA
2007-2018 Associate Medical Director, Clinical Chemistry, Beth Israel Deaconess Medical Ctr, Boston, MA
2007-2013 Instructor in Pathology, Harvard Medical School, Boston, MA
2013-2018 Assistant Professor of Pathology, Harvard Medical School, Boston, MA
2018- Associate Professor of Pathology, Cedars-Sinai, Los Angeles, CA
2018- Pathologist III, Beverly Pathology, Los Angeles, CA

Other Experience and Professional Memberships

2007-	Full medical license, Massachusetts Board of Registration in Medicine
2007-	Board certification in clinical pathology, American Board of Pathology
2007-	Member, American Association of Clinical Chemists (AACC)
2007-	Member, American Diabetes Association
2005-13	Member, Continuing Medical Education advisory committee for the AACC
2008-	Member of American Diabetes Association Research Grant Review Committee
2011-	Member of American Society of Nephrology
2015	Ad hoc reviewer, NIH Special Emphasis Panel ZDK1 GRB-S (M2)
2018	Full medical license, Medical Board of California

Honors

2015	Harold Dvorak Young Investigator Award (BIDMC)
2007	ACLPS Paul E. Strandjord Young Investigator Award (Academy of Clinical Laboratory Physician Scientists)
2001	Interviewed on CNBC television news program "Newsfront" in connection with recently published Nature Medicine article on the insulin-sensitizing properties of the serum protein adiponectin
1997	Albert Einstein College of Medicine Medical Student Cancer Research Fellowship

C. Contribution to Science

1. The primary project in my lab focuses on the pathophysiology of kidney disease, urea-induced protein carbamylation, and resulting uremia-associated heart disease. In the past several years we have published the discovery of a novel clinical biomarker of protein carbamylation (carbamylated albumin, or C-Alb) which is elevated in patients with kidney disease and correlates with time-averaged urea concentrations. We have shown that protein carbamylation is promoted by the combination of chronically elevated urea and amino acid deficiencies that are universally present in patients with kidney disease. We have demonstrated that high serum concentrations of C-Alb are strongly associated with decreased mortality in patients with chronic kidney disease both before and after initiating hemodialysis, and are specifically associated with death due to heart failure and sudden cardiac arrhythmias in these patients. Protein carbamylation is associated with amino acid deficiencies, and we have demonstrated in a pilot human clinical trial that protein carbamylation may be ameliorated by treatment with intravenous amino acid supplements. Protein carbamylation is also the result of chronically elevated blood urea concentrations, and we have recently obtain evidence that C-Alb can be reduced by more frequent or longer duration hemodialysis treatments, and that reductions of C-Alb correlate with reductions in dialysis patient's left ventricular mass. These discoveries have important translational implications for the monitoring and treatment of kidney disease, and we are actively engaged in studies to determine whether measurement of C-Alb predicts whether patients have improved outcomes with dialysis dose intensification and amino acid therapy.

    a. Berg AH (corresponding author), Drechsler C, Wenger J, Buccafusca R, Hod T, Kalim S, Ramma W, Parikh SM, Steen H, Friedman DJ, Danziger J, Wanner C, Thadhani R, Karumanchi SA. Carbamylation of serum albumin as a risk factor for mortality in patients with kidney failure. Science Translational Medicine. 2013 Mar 6;5(175):175ra29. doi:10.1126/scitranslmed.3005218. PMID: 23467560. PMCID: PMC3697767.
    b. Drechsler C, Kalim S, Wenger J, Suntharalingam P, Hod T, Thadhani R, Karumanchi SA, Wanner C, Berg AH. Protein carbamylation is associated with heart failure and mortality in diabetic patients with end stage kidney disease. Kidney Int. 2015 Feb 11. doi: 10.1038/ki.2014.429. PMCID: PMC4449819.
    c. Kalim S, Ortiz G, Trottier CA, Deferio JJ, Karumanchi SA, Thadhani RI, Berg AH. The Effects of Parenteral Amino Acid Therapy on Protein Carbamylation in Maintenance Hemodialysis Patients. J Ren Nutr. 2015 Mar 5. pii: S1051-2276(15)00042-4. doi: 10.1053/j.jrn.2015.01.019. PMCID: PMC4469570.
    d. Kalim S, Trottier CA, Wenger JB, Wibecan J, Ahmed R, Ankers E, Karumanchi SA, Thadhani R, Berg AH. Longitudinal Changes in Protein Carbamylation and Mortality Risk after Initiation of Hemodialysis. Clin J Am Soc Nephrol. 2016. Epub 2016/07/23. doi: 10.2215/CJN.02390316. PubMed PMCID: PMC5753089.

2. There is growing evidence that deficiency of vitamin D contributes to disorders of calcium homeostasis bone mineralization, cardiovascular disease, cancer, and other disorders. There is controversy, however, whether or not measurement of serum 25-hydroxyvitamin D using the current standard clinical assays provides accurate information regarding which patients are truly deficient. One source of this controversy is the fact that people of African descent have much lower 25(OH)D concentrations than whites, but actually have decreased risk of osteoporosis and bone fractures. 25-hydroxyvitamin D in circulation binds tightly to vitamin D binding protein (DBP). Our group has proposed the hypothesis that DBP-bound vitamin D is biologically unavailable, and that only the non-bound bioavailable fraction is clinically predictive of true deficiency. I have developed assays for serum measurements of calculated and directly measured bioavailable 25(OH)D. In collaboration with Drs. Ananth Karumanchi and Ravi Thadhani and others, our collaborative group has used these assays to demonstrate that bioavailable 25(OH)D is more strongly correlated with bone mineral density and plasma parathyroid hormone concentrations than are measurements of total serum 25(OH)D. Using samples from HANDLS clinical study, we have also found that due to significant differences in DBP concentrations between African Americans and white Americans, average concentrations of calculated bioavailable 25(OH)D are equivalent between these groups, despite significant difference in total 25(OH)D concentrations. These findings have had a significant impact on the vitamin D field, with many experts calling for a re-evaulation of current practices, and new studies looking to extend the studies of bioavailable vitamin D as a clinical test for vitamin D sufficiency.

    a. Powe CE, Evens MK, Wenger J, Zonderman AB, Berg AH, Nalls M, Tamez H, Bhan I, Karumanchi SA, Thadhani R. Vitamin D Binding Protein and Vitamin D Status of Black and White Americans. New England Journal of Medicine 2013 Nov 21;369(21):1991-2000. PMCID: PMC4030388.
    b. Berg AH, Powe CE, Evans MK, Wenger J, Ortiz G, Zonderman AB, Suntharalingam P, Lucchesi K, Powe NR, Karumanchi SA, Thadhani RI. 24,25-dihydroxyvitamin D3 and Vitamin D Status of Community-dwelling Black and White Americans. Clin Chem 2015 Jun; 61(6):877-884. PMID 25922442. PMCID: PMC4686255.
    c. Bhan I, Powe CE, Berg AH, Ankers E, Wenger JB, Karumanchi SA, Thadhani RI. Bioavailable vitamin D is more tightly linked to mineral metabolism than total vitamin D in incident hemodialysis patients. Kidney Int. 2012 Mar 7. doi: 10.1038/ki.2012.19. PMID: 22398410. PMCID: PMC3376220.
    d. Powe CE, Ricciardi C, Berg AH, Erdenesanaa D, Collerone G, Ankers E, Wenger J, Karumanchi SA, Thadhani R, Bhan I. Vitamin D binding protein modifies the vitamin D-bone mineral density relationship. J Bone Miner Res. 2011 Jul;26(7):1609-16. doi: 10.1002/jbmr.387. PMID: 21416506. PMCID: PMC3351032

3. I previously worked with Dr. Philipp Scherer on a project focused on the role of adiponectin in insulin sensitivity and the development of obesity-associated type 2 diabetes mellitus. Dr. Scherer discovered adiponectin, and in his lab I developed the first immunoassays for adiponectin and produced the first animal model and human clinical correlation studies showing that adiponectin played a role in liver insulin sensitivity. Adiponectin stimulates the AMPK/Akt pathways in the liver and muscle and other metabolic organs, sensitizing these tissues to insulin. Adiponectin concentrations are low in many insulin resistant states, and deficiency has been implicated as playing a causal role in development of obesity-associated insulin resistance and may mediate part of the insulin sensitizing effects of PPAR gamma agonists. Our manuscripts are some of the most-cited papers in the adiponectin field. This story is still developing and small molecule agonists of the adiponectin receptors have recently shown promise as novel therapies of type 2 diabetes mellitus.

    a. Berg AH, Combs TP, Du X, Brownlee M, Scherer PE. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med. 2001 Aug;7(8):947-53. PubMed PMID: 11479628.
    b. Combs TP, Berg AH, Obici S, Scherer PE, Rossetti L. Endogenous glucose production is inhibited by the adipose-derived protein Acrp30. J Clin Invest. 2001 Dec;108(12):1875-81. PubMed PMID: 11748271; PubMed Central PMCID: PMC209474.
    c. Qi Y, Takahashi N, Hileman SM, Patel HR, Berg AH, Pajvani UB, Scherer PE, Ahima RS. Adiponectin acts in the brain to decrease body weight. Nat Med. 2004 May;10(5):524-9. Epub 2004 Apr 11. PubMed PMID: 15077108.

d. Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism. Trends Endocrinol Metab. 2002 Mar;13(2):84-9. Review. PubMed PMID: 11854024. PubMed Central PMCID: N/A.

Complete List of Published Work:
http://www.ncbi.nlm.nih.gov/sites/myncbi/12wyTL5t7jzQk/bibliography/47854517/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01 HL133399 Berg (PI) 3/29/2018 – 3/29/2022
Protein carbamylation and uremic cardiomyopathy in chronic kidney disease
This continuation of award R56 HL133399 will evaluate the association between serum carbamylated albumin and mortality risk in non-dialyzed participants from the German Chronic Kidney Disease (GCKD) study, and will utilize mouse models to test whether high urea combined with PGC-1 alpha deficiency have synergistic effects on loss of cardiac function in uremia.
Role: PI

Completed Research Support

R01 DK095072 Parikh (PI) 9/27/2012–07/30/2018
Mitochondrial Biogenesis in Kidney Disease
The major goal of this project is to understand the role of the mitochondrial biogenesis regulator PGC1 in different forms of kidney injury.
Role: Co-Investigator

K08 HL121801 Berg (PI) 9/1/2014 – 5/31/2018
The role of carbamylation in uremia associated heart disease
The aim of this project is to test the effects of urea and cyanate-induced protein carbamylation on cardiac pathology in the 5/6 nephrectomy mouse model of uremia.
Role: PI

R56 HL133399 Berg (PI) 9/16/2016 – 3/31/2018
Protein carbamylation and uremic cardiomyopathy in chronic kidney disease
This project will evaluate the association between serum carbamylated albumin and mortality risk in non-dialyzed participants from the German Chronic Kidney Disease (GCKD) study, and will utilize mouse models to test whether high urea combined with PGC-1 alpha deficiency have synergistic effects on loss of cardiac function in uremia.
Role: PI

R21 HD088004 Karumanchi (PI) 4/1/2016 – 2/28/2018
Role of ADAMTS13 in Maternal Complications of Preeclampsia
The goal of this project is to evaluate the biological role of ADAMTS13 and VWF in the maternal complications of preeclampsia, and whether they are critical determinants of maternal complications of preeclampsia such as the HELLP syndrome.
Role: Co-Investigator

7-14-IN-02 Berg (PI) 1/1/2015 – 12/31/2016
Carbamylated Albumin May Predict Which Patients Benefit from Intensive Hemodialysis
The aim of this American Diabetes Association project is to determine whether intensive intermittant hemodialysis reduces protein carbamylation and associated mortality risk.
Role: PI