BIOGRAPHICAL SKETCH

NAME: Simin Nikbin Meydani

eRA COMMONS USER NAME (credential, e.g., agency login): SMEYDANI1

POSITION TITLE: Senior Scientist; Director, Nutritional Immunology Laboratory

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 Tehran, Tehran, Iran	DVM	06/1975	Veterinary Medicine
Colorado State University, Fort Collins, CO	MS	06/1977	Nutrition
Iowa State University, Ames, IA	PhD	06/1981	Nutrition
Marine Biology Laboratory, Woods Hole, MA	Cert.	04/1985	Molecular Immunology
Drexel University, Philadelphia, PA	Fellowship	4/2006	Executive Leadership in Academic Medicine

A. Personal Statement

I am a Senior Scientist, Professor of nutrition and immunology and have been the Director of the Nutritional Immunology Laboratory (NIL) at the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University for over 25 years. I have more than 30 years of experience conducting cell and molecular, human and animal studies in nutrition, aging, oxidative stress, inflammation, immunity, and infection. My colleagues and I have made key contributions to demonstrate the importance of nutrition in maintaining the immune response and resistance to infectious diseases, and thus, the health status of the elderly. Moreover, we have furthered our knowledge of the underlying mechanisms of nutrient-induced modulation of the immune and inflammatory responses as well as the molecular changes that lead to age-associated immune dysregulation. I have served on several training grants and have mentored many graduate students, postdoctoral fellows, visiting and junior scientists, all of whom have achieved their career goals. Given my broad, lengthy training experience as a program Faculty member on several NIH-funded training grants, federal and non-federal advisory boards, and leadership of key nutrition and aging professional organizations, I will be able to provide the appropriate expertise as a member of the advisory committee on Drs. Allan Walker and Walter Willett's training grant "Training Grant in Academic Nutrition" (T32-DK-007703) at the Harvard School of Public Health. Several of my trainees have received awards from nutrition and aging professional societies, and I am a mentor on 3 K awards for early career investigators and two postdoctoral fellows. In particular, my expertise in immunology, aging research and age-driven dysregulation of immune and inflammatory responses provides me with the multi-faceted experience relevant to support a broad range of trainees. Until recently, I served as the director of JMUSDA Human Nutrition Research Center on Aging, which provided me with the opportunity to facilitate research and the advancement of investigators at different stages of their careers. My recent appointment as vice provost for research at Tufts University has broadened my experience with different modes of research and afforded me a better understanding of the research environment available to young investigators from different disciplines. Given my broad, lengthy and diverse experience in research and research administration, I can contribute to different components of this training grant by working in close collaboration with Dr. Allan Walker and Co-PI Dr. Walter Willet, both of whom I have known for many years as colleagues.

1. Wu D, Ren Z, Pae M, Guo W, Cui X, Merrill AH, **Meydani SN**. Aging up-regulates expression of inflammatory mediators in mouse adipose tissue. J. Immunol., 179 4829-39, 2007.
2. Dao MC, Sen S, Iyer C, Klebenov D, **Meydani SN**. Obesity during pregnancy impairs fetal iron status: is hepcidin the link? Journal of Perinatology Journal, 2012 Jun 21. doi: 10.1038/jp.2012.81.

3. Sen S, Iyer C, Klebenov D, Histed A, Aviles J, **Meydani SN**. Obesity impairs cell mediated immunity during the second trimester of pregnancy. Am J Obstetrics and Gynecology, 2013, 208:139.e1-8.
4. Sen S, Iyer C, **Meydani SN**. Obesity during pregnancy alters maternal oxidant balance and micronutrient status. J Perinatology, 2013, doi: 10.1038/jp.2013.15; 2014; 34, 105–111.

B. Positions and Honors

Positions and Employment

1981-1983 Postdoctoral Research Fellow in Nutrition, School of Public Health, Harvard University
1984-1989 Scientist II, USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University
1989-1994 Scientist I, HNRCA at Tufts University
1989-1994 Assoc. Professor, Nutrition, Friedman School of Nutrition Science & Policy, Tufts University
1990-Present Director, Nutritional Immunology Laboratory, USDA HNRCA at Tufts University
1994-Present Professor of Nutrition, Friedman School of Nutrition Science and Policy, Tufts University
1994-Present Senior Scientist, Jean Mayer USDA HNRCA at Tufts University
1996-Present Professor of Immunology, Sackler Graduate School of Biomedical Sciences, Tufts University
2005-2009 Associate Director, Jean Mayer USDA HNRCA at Tufts University
2009-2016 Director, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University
2016-Present Vice Provost for Research, Tufts University

Other Experience and Professional Memberships

1994-2000 NIA Geriatric Rehabilitation Study Section
2007-2009 Cellular Mechanism of Aging and Development (CMAD) Study Section
2009-2011 Aging Systems and Geriatrics (ASG) Study Section
2012-2014 Co-Chair NIH INSPIRE Scientific Steering Committee for Biomarkers of Nutrition and Inflammation
2014-15 President, American Society for Nutrition
2015 White House Conference on Aging, White House, Washington DC (invited participant)
2015 World Economic Forum, Davos Switzerland (invited speaker)

Section Editor

2013-Present Aging Cell

Editorial Board Member:

1991-1995 Journal of Nutrition
2000-2003 Journal of Experimental Biology and Medicine
2001-2009 Journal of Nutritional Biochemistry
2003-2009 American Journal of Clinical Nutrition
2015-Present AGE Journal

Honors

1998 The Lederle Award in Human Nutrition, American Society of Nutrition
1998 Wellcome Visiting Professorship, Iowa State University
1995; 1997 Tufts University Faculty Recognition for Outstanding Achievement
2001 Grace Goldsmith Award, American College of Nutrition
2003 Denham Harman Lifetime Achievement Research Award, American Aging Association
2005-2006 Fellow, Executive Leadership in Academic Medicine, Drexel University College of Medicine
2008 Robert H. Herman Award in Clinical Nutrition, American Society of Nutrition
2011 Helen LeBaron Hilton Distinguished Alumni Award, Iowa State University
2011 Food Science and Human Nutrition Alumni Impact Award, 2011, Iowa State University
2013-14 Life Time Achievement Alumni Award, Iowa State University

C. Contribution to Science

1. In 1990, my colleagues and I published the results of a clinical intervention trial on vitamin E supplementation. This was one of the first well-controlled studies to demonstrate the immunostimulatory effect of a single nutrient in humans. We demonstrated that vitamin E enhances T cell-mediated function in healthy elderly, thus reversing a major age-related biological defect. Further, we showed that the effect of vitamin E is due to reduction of an immunosuppressive, inflammatory lipid mediator, prostaglandin E_2 (PGE_2), which confirmed our earlier work in aged mice. We then conducted a second controlled clinical trial to determine the optimal level of vitamin E for the immune response of the aged. In this study, we demonstrated that 200 international units (IU)/day of vitamin E provided the optimal immune response in the elderly as demonstrated

by enhancement of *in vivo* measures of cell mediated immune response including response to hepatitis B vaccine, without any adverse effects. We provided evidence for the clinical benefit of these observations using an animal model of influenza as well as a large (617 elderly nursing home residents), randomized, double-blind, placebo-controlled clinical trial in which they demonstrated that supplementation with 200 IU vitamin E for a year reduced the risk of acquiring upper respiratory tract infections in the elderly. These findings have significant implications for the health of the elderly since they have a high rate of upper respiratory tract infections, which are responsible for substantial morbidity and burden on health care cost. Further, we showed that polymorphisms of cytokine genes may determine the effect of vitamin E on cytokine production as well as susceptibility to lower respiratory tract infection in the elderly, enhancing the body of evidence for significance of gene/nutrient interaction in determining nutrient requirement.

1. **Meydani SN**, Barklund MP, Liu S, et al. Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects. Am J Clin Nutr 1990 Sep;52(3):557-63.
2. **Meydani SN**, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, Thompson C, Pedrosa MC, Diamond RD, Stollar BD. Vitamin E supplementation and in vivo immune response in healthy elderly subjects: A randomized controlled trial. JAMA; 277:1380-1386, 1997.
3. **Meydani SN**, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF, Hamer DH. Vitamin E and respiratory infections among elderly nursing home residents: a randomized controlled trial. JAMA, 292:828-836, 2004.
4. Belisle SE. Leka LS, Lista JD, Jacques PF, Ordovas JM, **Meydani SN**. Polymorphisms at cytokine genes may determine the effect of vitamin E on cytokine production in the elderly, doi: 10.3945/jn.109.112268. . J Nutr. 2009, 139: 1855-1860. PMCID: PMC2744609

2. While studying the mechanisms of the immunostimulatory effects of vitamin E, my colleagues and I made important discoveries related to molecular changes associated with aging. In both animal and human studies, we reported an age-associated increase in the production of PGE_2. Further, we demonstrated that it is the increase in PGE_2 production that specifically contributes to the decline of T cell-mediated function in the aged. Subsequently, we showed that the increase in PGE_2 with aging is due to increased activity of the enzyme cyclooxygenase (COX-2). We then showed that the increase in COX-2 upregulation was mediated by higher levels of ceramide in old macrophages, which leads to higher NFκB activation and thus COX-2 expression. In a series of animal studies, we demonstrated that vitamin E exerts its immunostimulatory effect through two different mechanisms by: 1) indirectly decreasing PGE_2 production by macrophages and 2) directly increasing the ability of naïve T cells to go through cell cycle division and produce interleukin 2. Finally, using confocal microscopy at the single cell level, we showed that the vitamin E-induced effect on cell proliferation is mediated through improving formation of effective immune synapses at the site of antigen presenting and T cell conjugation. These novel observations were the first demonstration of a nutrient influencing early key signaling events in T cells. In addition, our work helped to refocus attention on the importance of macrophages in describing the age-associated changes of the immune response, rather than the traditional emphasis on T cells only, thereby pointing to new cellular targets for intervention. Related to this, using a model virus, we demonstrated that passage of an avirulent virus through old host resulted in mutation of the virus into a virulent form. These results have introduced a new paradigm to explain the higher susceptibility of an old host to viral infections, which has significant public health implications.

1. Beharka AA, Wu D, Han SN, **Meydani SN**. Macrophage prostaglandin production contributes to the age-associated decrease in T cell function which is reversed by the dietary antioxidant vitamin E. Mech. Ageing Dev. 1997;93:59-77.
2. Wu D, Marko M, Claycombe K, Paulson KE, **Meydani SN**. Ceramide-induced and age-associated increase in macrophage COX-2 expression is mediated through up-regulation of NF-kappa B activity. J Biol Chem 2003;278:10983-92.
3. Gay RT, Belisle S, Beck MA, **Meydani SN**. An aged host promotes the evolution of avirulent coxsackievirus into a virulent strain. Proc Natl Acad Sci U S A 2006;103:13825-30.
4. Marko, GM, Ahmed, T, Bunnell, SC, Wu, D, Chung, H, Huber, BT, **Meydani SN.** Age-associated decline in effective immune synapse formation of CD4+ T cells is reversed by vitamin E supplementation. J. Immunol. 178: 1443-1449. 2007.

3. We investigated the effect of fats, particularly fish oil, on immune response. My colleagues and I were the first to demonstrate that increased consumption of fish oil or fish by older adults can reduce T cell-mediated immune response, in addition to decreasing the production of pro-inflammatory cytokines. This study is unique in that it clearly demonstrated that the effect observed following consumption of fish oil was due to n-3 PUFA,

and not PUFA in general. These studies have been crucial in focusing the attention of scientists on the possible harmful effects associated with high intakes of fish oil. In subsequent work, my colleagues and I provided evidence that the suppressive effect of fish oil can be attributed to changes to tocopherol status and that adequate supplementation with tocopherol can prevent this adverse effect.

1. **Meydani SN**, Endres S, Woods MM, et al. Oral (n-3) fatty acid supplementation suppresses cytokine production and lymphocyte proliferation: comparison between young and older women. J Nutr 1991;121:547-55.
2. **Meydani SN**, Lichtenstein AH, Cornwall S, et al. Immunologic effects of national cholesterol education panel Step-2 diets with and without fish-derived n-3 fatty acid enrichment. J Clin Invest 1993;92:105-113. 3.
3. Wu D, **Meydani SN**, Meydani M, Hayek MG, Huth P, Nicolosi RJ. Immunological effects of marine- and plant-derived (n-3) polyunsaturated fatty acids in non-human primates. Am. J. Clin. Nutr. 1996;63:273-280.
4. Wu D, Han SN, Meydani M, **Meydani SN**. Effect of concomitant consumption of fish oil and vitamin E on T cell mediated function in the elderly: a randomized double-blind controlled trial, JACN, 25: 300-306, 2006.

4. We have evaluated the impact of several nutrients, diets and dietary components on the immune and inflammatory responses of older adults. For example, my colleagues and I have evaluated the effect of vitamin B6 on immune function in what is perhaps the first controlled study evaluating the requirements of a nutrient in the elderly based on a meaningful biologic indicator: the immune response. Our findings supported a recommendation to have higher requirements for B6 in the elderly age category. In addition, we showed that long term calorie restriction reduces inflammation in humans. We recently extended our work to the role of nutrition in immune response and health status of elderly in developing countries. Through these publications, we have brought attention to understudied populations in developing countries.

1. **Meydani SN,** Ribaya-Mercado J, Russell RM, Sahyoun N, Morrow FD, Gershoff SN. Vitamin B_6 deficiency impairs interleukin 2 production and lymphocyte proliferation of older adults. Am. J. Clin. Nutr.; 53:1275-1280, 1991.
2. Hamer DH, Sempertegui F, Estrella B, Tucker KL, Rodriguez A, Egas J, Dallal GE, Selhub J, Griffiths JK, **Meydani SN**. Micronutrient deficiencies are associated with impaired immune response and higher burden of respiratory infections in elderly Ecuadorians. J Nutr. 2009 Jan, 139(1):113-119. PMCID: PMC2646211.
3. Sempertegui F, Estrella B, Tucker K, Hamer D, Narvaez X, Sempertegui M, Griffiths J, Noel S, Dallal G, Selhub J, **Meydani SN**. Metabolic syndrome in elderly living in marginal peri-urban communities in Quito, Ecuador, Public Health Nutr. 2010, 14(5):758-767. PMCID: PMC3025090.
4. **Meydani SN**, Das SK, Pieper, CF, Lewis MR, Klein S., Dixit W, Gupta AK, Villareal DT, Bhapkar M, Huang M, Fuss P, Roberts SR, Holloszy JO,Fontana, L. Long-term moderate calorie restriction inhibits inflammation without impairing cell-mediated immunity: a randomized controlled trial in non-obese humans. Aging, 2016, Jul;8(7):1416-31. doi: 10.18632/aging.100994. PMCID:PMC4993339

5. We have conducted further experiments to demonstrate the clinical significance of nutrients, foods and food components on inflammation, induced changes in immune response and gut microbiota. Related to this, a noteworthy accomplishment among our recent work is the observation that 30% of elderly nursing home residents in the U.S. have low serum zinc levels, which is associated with higher incidence and longer duration of pneumonia and higher antibiotic use in this population. Further, in recent studies, my colleagues and I demonstrated that adding a preparation of wolfberries to the diet of older adults increases antibody response to flu vaccine as well as its efficacy to protect against a subsequent flu infection. These findings can have significant implications for older adults given that the current flu vaccines are only 40% effective in older adults. In addition, in a series of studies, my colleagues and I focused on the impact of green tea catechins on T-regulatory cells and autoimmune encephalomyelitis and demonstrated that epigallocatechin (EGCG) significantly reduces the clinical signs and symptoms of autoimmune encephalomyelitis in mice by impacting molecular events regulating T-regulatory cells development and function. Further, we showed consumption of whole grains compared to refined grains has a moderate impact on immune and inflammatory responses and gut microbiota.

1. **Meydani SN**, Barnett JB, Dallal GE, Fine BC, Jacques PF, Leka LS, Hamer DH. Serum zinc and pneumonia in nursing home elderly. Am J Clin Nutr. 2008 Apr; 87(4) 1167-73. PMCID: PMC2323679.

2. Wang J, Ren Z, Xu Y, Xiao S, **Meydani SN**, Wu D. Epigallocatechin-3-gallate ameliorates experimental autoimmune encephalomyelitis by altering balance among CD4+ T-cell subsets. Am J Pathol. 2012 Jan;180(1):221-34. PMCID: Not applicable.
3. Du, X, Wang, J, Niu, X, Smith, D, Wu, D, and **Meydani, SN**. Dietary wolfberry supplementation enhances protective effect of flu vaccine against influenza challenge in aged mice, J. Nutrition, 2014, 144: 224–229. PMCID: Not applicable.
4. Vanegas S, Meydani M., Barnett JB, Goldin B, Kane A., Rasmussen H, Brown, C, Vangay P., Knights D, Jonnalagadda SS, Koecher K, Karl J.P, Thomas M, Dolnikowski G, Li L., Saltzman E, Wu D, **Meydani SN.** Substituting whole grains for refined grains in a 6-week randomized trial has a modest effect on gut microbiota, and immune and inflammatory markers of healthy adults. AJCN, 2017, Advance online publication. DOI: 10.3945/ajcn.116.146928.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/simin.meydani.1/bibliography/41156119/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

USDA/ARS 8050-51000-090-01S Meydani SN (PI) 10/1/14-09/15/19
Immunity affected by diet and obesity
This project will 1) determine the impact/underlying mechanisms of obesity during pregnancy on newborn's life-long immune/inflammatory responses and resistance to infectious diseases in animal models and 2) determine the effect/ mechanisms of food components (fruits, vegetables, or whole grains) and their interaction with, age on immune and inflammatory responses and related diseases in both animal models and human studies.

Bill and Melinda Gates Foundation (Combs-Meydani, Co-PIs) 11/1/16-11/30/19
OPP1139998
Safe and effective delivery of supplemental iron to healthy volunteers
This project has three main objectives: 1) to demonstrate that children and older adults respond similarly to ferrous sulfate supplementation and 2) to determine whether two novel organic forms of iron, a nano-particulate form, iron hydroxide adipate tartrate (IHAT), and a fungal form, Aspiron, are safer than the inorganic iron ferrous sulfate, presently the major form of supplemental iron, and 3) to determine whether the two novel iron forms, IHAT and Aspiron, have comparable bioavailability of iron compared to ferrous sulfate by measuring the indicators of body iron status.

Completed Research Support

USDA/ARS1950-51000-067-01S Meydani S (PI) 10/1/09-09/30/14
Nutrition, aging, and immune and inflammatory responses in health and disease
The purpose of this project was to study the effects of nutrients on the immune response of the aged.

General Mills Meydani SN (Co-PI with Meydani M) 04/5/11-04/30/16 (NCE)
The addition of whole grains to the diets of adults: A study of digestive health and natural defenses.
The objective of the proposed study is to understand the effect of a diet rich in a variety of whole grains, which are rich sources of fibers, micronutrients and bioactive compounds on energy intake, and energy regulation, digestive health including gut microbiota, immune, oxidative stress and inflammatory markers in healthy adults.

Tufts Collaborates Leong J (PI) 07/1/12-06/30/13
Impact of age and vitamin E on *Streptococcus Pneumoneae* colonization
The project was a pilot animal study aimed to develop preliminary data on supplementing older mice with vitamin E to support their immune system against a bacterial infection that commonly causes pneumonia.
Role: Co-Investigator

Consejo Superior de Investigaciones Cientificas Meydani S (PI) 06/01/10-10/14/13
Effect of olive oil supplementation on immune and inflammatory responses of elderly
The major goal of this project was to determine the impact of high levels of olive oil consumption on immune system function and the inflammatory response in elderly humans.