

Celebrating ten years of nutrition discoveries

Dear Friends.

With this report, I am pleased and proud to let you know that the UNC Nutrition Research Institute is celebrating its tenth anniversary this year. As we look back at the impact we have made in precision nutrition this past year – which your generosity has made possible – we also make note of our first decade of progress.

From inception to today, the NRI has been home to some of the most experienced and innovative scientists in the world who, daily, explore the human genome, brain, metabolism and environment in search of the how's and why's of individualized nutritional needs. Their discoveries in nutrition science are leading to successes in preventing or mitigating the negative effects of chronic diseases and aging, and in improving human development, even prior to conception.

Use this report for a glimpse into the myriad ways in which your contributions to our institute are put to work advancing nutrition science for everyone. Thank you for your support.

Sincerely,

Saure & Spin



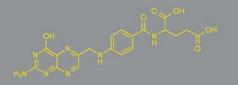
Steven H. Zeisel, MD, PhD

Director

Nutrition Research Institute

University of North Carolina at Chapel Hill

Guiding Scientific Premise



Each of us is metabolically unique. The NRI is dedicated to finding out how these differences affect an individual's health so that current one-size-fits-all dietary guidelines can be replaced with customized nutritional

recommendations and actions to improve a person's health and quality of life. With NRI's discoveries, physicians and dietitians will soon be able to create diet and exercise plans customized to your unique needs.

Mission

The NRI is leading research in precision nutrition by developing an understanding of how our genes, the bacteria in our gut, and our environment create differences in our metabolism that affect our individual requirements for and responses to nutrients.



FUNDAMENTALS

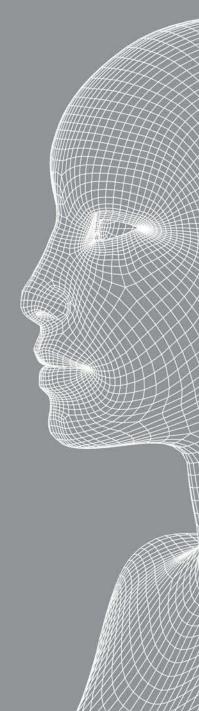
Nutrigenomics and Metabolomics

In Nutrigenomics, we study common variations in the spelling of our genetic code and in the "switches" that turn our genes on and off, and relate these to differences in our metabolism and nutrition needs. The gene tests we are developing will allow gene-guided recommendations for individual nutrition.

With Metabolomics, we can measure thousands of metabolites in blood or other tissues using a single, small sample. This makes possible a complete view of our metabolism that was not possible before. Now, we can add to

gene tests the ability to see what the changes in genes are doing to our metabolism, and use this to make metabolomic-guided recommendations for individual nutrition.

The Nutrition Research Institute is an international leader in both of these new fields of science.



FACULTY



Precision Nutrition & Health/Disease

Emma H. Allott, PhD Carol L. Cheatham, PhD John E. French, PhD Stephen D. Hursting, PhD, MPH Natalia Surzenko, PhD

Katie Mever, ScD

Nutrigenomics

Martin Kohlmeier, MD, PhD Saroja Voruganti, PhD

Metabolomics

Wimal Pathmasiri, PhD Delisha Stewart, PhD

Appointments

Carol L. Cheatham, PhD

- Member, External Advisory Committee, Division of Nutrition Sciences, University of Illinois, Urbana-Champaign, Champaign, IL
- Fellow, Frank Porter Graham Child Development Institute, University of North Carolina - Chapel Hill, Chapel Hill, NC

Martin Kohlmeier, MD, PhD

- Founding editor-in-chief of BMJ Nutrition, Prevention & Health, a new nutrition journal
- President, International Society of Nutrigenetics/ Nutrigenomics
- Co-editor of Principles of Nutrigenetics and Nutrigenomics, published by Elsevier

Philip A. May, PhD

- Faculty member of Delta Omega, The Honorary Public Health Society, Theta Chapter, Gillings School of Global Public Health, University of North Carolina at Chapel Hill
- ·International Ambassador, National Organization for Fetal Alcohol Spectrum Disorders, Australia

Presentations

Carol L. Cheatham, PhD. "Assessing Neonatal Cognitive Development in the Human" (Summer 2017). Origins and Benefits of Biologically Active Components in Human Milk, FASEB Science Research Conference, Lisbon, Portugal

Carol L. Cheatham, PhD. "DHA and the Science of Delivering More to the Brain" (Summer 2017). Power of Three Congress: Leading the Future with Faster Learning, Manila, Philippines

Philip A. May, PhD. "FASD Prevalence in the U.S.A. and Maternal Risk Factors" webinar (June 2018). National Institutes of Health, (NIH) National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Susan J. Sumner, PhD. "Technologies to Capture Influences of Exposome and Diet" (June 25, 2018). Precision Medicine Workshop, Metabolomics 2018, Seattle, WA

Steven H. Zeisel, MD, PhD. "Choline is an essential nutrient" (December 2017) Symposium Neonatology, Tubingen, Germany

Discoveries in the News

Stephen D. Hursting, PhD, MPH featured in "The connection between diet, obesity, and cancer: Nutrition experts explore the evidence" at Medical Xpress.com (March 2018)

Martin Kohlmeier, MD, PhD, quoted in "23andMe for Weight loss" in Prevention magazine (April 2018)

Philip A. May's findings that prevalence of fetal alcohol spectrum disorders may be as high as 5 percent in US communities covered by worldwide media including Forbes, Time, New York Times, and Daily Mail.

Prevalence of fetal alcohol spectrum disorders in 4 U.S. communities. May, PA, Chambers, CD, Kalberg, WO, Zellner, J, Feldman, H, Buckley, D, et al. JAMA 319:474-482, 2018. PMID: 29411031

Steven H. Zeisel, MD, PhD interviewed in Carolina Public Health magazine in "What's essential for the prenatal brain?" (October 2017)

DISTINCTIONS

Martin Kohlmeier, MD, PhD. "How to make the most of high-density genetic data for nutrition research" (October 2017). Keynote presentation at the IUNS International Congress of Nutrition, Buenos Aires, Argentina

Philip A. May, PhD. "The Prevalence and Select Characteristics of FASD in Four Regional Communities of the United States" (June 2018). FASD Study Group of the Research Society on Alcoholism, San Diego, CA

Steven H. Zeisel, MD, PhD featured in "Choline: The essential but forgotten nutrient" in The Seattle Times (November 2017)



KEY FINDINGS

NUTRITION, OBESITY AND CANCER

Obesity and diet are known to alter cancer outcomes, but exactly how is often not understood. Research conducted by NRI faculty is providing answers that will help in prevention and treatment.

For example, folate (vitamin B9) is important in early pregnancy to prevent neural tube defects in babies because it is needed by rapidly dividing cells (e.g., those of a developing embryo) for DNA synthesis and cellular energy production. However, aggressive cancers are also defined, in part, by their rapidly dividing cells, and antifolate drugs such as methotrexate are first-line chemotherapeutics. Whether dietary folate, either through vitamin supplements or fortified foods, could contribute to cancer progression is unclear, as existing studies of the effects of low-folate diets on cancer have produced conflicting results.

Several NRI faculty collaborated to clarify the folate-cancer

connection. Sergey Krupenko, PhD, and Stephen Hursting, PhD, MPH, along with NRI visiting scholar Mirko Hennig, PhD, and their laboratories looked at the effects of folate restriction on the metabolic properties of three breast cancer cell lines (Ashkavand et al., 2017). They compared macroscopic cell properties including proliferation, migration, and invasion, and also looked at cellular levels of specific



metabolites in order to understand molecular changes within the cells that were caused by folate-restricted feeding. They found that folate restriction causes changes in certain metabolite levels and the expression of specific genes. Folate restriction also causes change in cellular energy metabolism, and decreases cells' invasiveness. Overall, folate restriction shifted cancer cells toward less aggressive phenotypes.

This study shows that folate restriction does alter the



In another example, researchers in Hursting's laboratory (Bowers et al., 2018) sought to identify differences Stephen D. Hursting, PhD, MPH in tumors growing in normal-weight

properties of cancer cells, but that the specific cellular changes are dependent on the cancer subtype. This means that the decision to

target the folate pathway, either through dietary or pharmaceutic

an individual's cancer.

means, will depend on the nature of

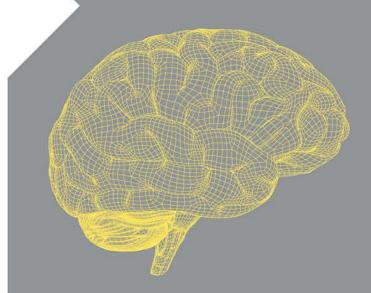
versus obese mice in order to better understand how obesity contributes to breast cancer development. They profiled the tumors and identified groups of genes whose expression was markedly different between the two tumor types. Several of these gene groups that were related to tumor growth were also associated with obesity. Further analysis identified leptin as a master regulator of the metabolic pathways defined by these genes.

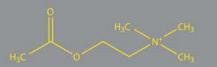
Leptin is a hormone that signals satiety. Resistance to leptin signaling is often found in obesity, and leptin levels are elevated in the obese. This study confirms a role for leptin in pro-tumorigenic potential, and through its use of RNA sequencing and pathway analysis, also identifies genes downstream of leptin that need to be investigated as more direct effectors of obesity-induced susceptibility to breast cancer, with the ultimate goal of identifying druggable targets (Smith et al, 2018).

Metabolic reprogramming by folate restriction leads to a less aggressive cancer phenotype. Ashkavand, Z. O'Flanagan, C., Hennig, M, Du, X, Hursting, SD, Krupenko, SA (2017). *Mol Cancer Res* 15: 189-200.

Leptin signaling mediates obesity-associated CSC enrichment and EMT in preclinical TNBCmodels. Bowers, LW, Rossi, EL, McDonell, SB, Doerstling, SS, Khatib, SA, Lineberger, CG, Albright, JE, Tang, X, deGraffenried, LA and Hursting, SD (2018). Mol Cancer Res 16: 869-879.

Translating mechanism-based strategies to break the obesity-cancer link: A narrative review. Smith, L.A., O'Flanagan, CH, Bowers, LW, **Allott,** EH and Hursting, SD (2018). J Acad Nutr Diet 118: 652-667.





NUTRITION AND ALCOHOL DURING PREGNANCY

NRI scientists Susan Smith, PhD, Philip May, PhD, and Sandra Mooney, PhD, study how alcohol causes

behavioral deficiencies associated with FASD is much May's group uses, which include in-person interviews the societal costs of FASD will be higher than previously assumed, and highlight a need for new approaches to reduce

Research in the Smith and Mooney laboratories looks at how this discrepancy is maternal nutrition: A healthy maternal diet may protect an infant from the effects of alcohol, while a poor maternal diet worsens the effects of alcohol. But what, in terms

are iron deficient and drink alcohol (note that, regardless worse cognitive outcomes than babies from mothers who away from the brain. Thus, maternal alcohol consumption the babies than if the mother is iron deficient.







Prevalence of fetal alcohol spectrum disorders in 4 US communities. May, PA, Chambers, CD, Kalberg, WO, Zellner, J, Feldman, H, Buckley, D, Kopald, D, Hasken, JM, Xu, R, Honerkamp-Smith, G, Taras, H, Manning, MA, Robinson, LK, Adam, MP, Abdul-Rahman, O, Vaux, K, Jewett, T, Elliott, AJ, Kable, JA, Akshoomoff, N, Falk, D, Arroyo, JA, Hereld, D, Riley, EP, Charness, ME, Coles, CD, Warren, KR, Jones, KL and Hoyme, HE (2018). JAMA 319: 474-482.

Maternal iron nutriture as a critical modulator of fetal alcohol spectrum disorder risk in alcohol-exposed pregnancies. Helfrich, KK, Saini, N, Kling, PJ and Smith, SM (2018). Biochem Cell Biol 96: 204-212.

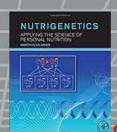
Dietary iron fortification normalizes fetal hematology, hepcidin, and iron distribution in a rat model of prenatal alcohol exposure. Huebner, SM, Helfrich, KK, Saini, N, Blohowiak, SE, Cheng, AA, Kling, PJ and Smith, SM (2018). Alcohol Clin Exp Res 42: 1022-1033.

Time quotes Dr. Oz calling NRI "a leader in the growing field of individualized nutrition." "The Oz Diet." TIME 12 Sept. 2011:48-58



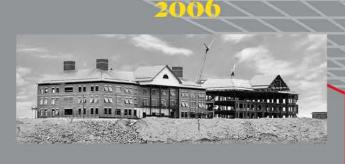
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Nutrigenetics by Martin Kohlmeier, MD, PhD, the first comprehensive textbook on the topic, published



90 participants from around the world attend first NGx Workshop to learn the latest in nutrigenetics, nutrigenomics and precision nutrition







Grand opening with 2 faculty and 9 staff



Free, online "Nutrition in Medicine" training modules launched, giving physicians access to up-to-date nutrition information



2,300 elementary school students participate in interactive science projects at NRI



FINDING: Maternal obesity during pregnancy related to permanent developmental delays in children



FINDING: Omega-3 fatty acids reduce the risk of developing cancer and may prevent the spread of some types



Looking forward with 16 faculty and 68 science and admin staff



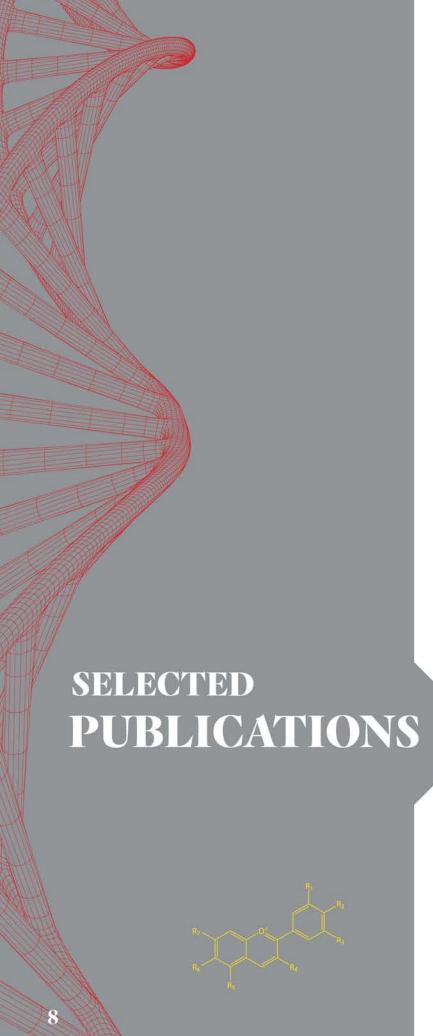
FINDING: Responsiveness of gut microbes related to heart health are influenced by a person's genetics



FINDING: Cognitive performance in children depends on ratios as well as quantities of essential fatty acids

A DECADE OF DISCOVERY





BRAIN DEVELOPMENT & COGNITION

Latent profile and cluster analysis of infant temperament: Comparisons across person-centered approaches. Gartstein, MA, Prokasky, A, Bell, MA, Calkins, S, Bridgett, DJ, Braungart-Rieker, J, Leerkes, E, **Cheatham, CL**, Eiden, RD, Mize, KD, Jones, NA, Mireault, G and Seamon, E (2017). *Dev Psychol* 53: 1811-1825.

Milk intake at midlife and cognitive decline over 20 years. The Atherosclerosis Risk in Communities (ARIC) study. Petruski-Ivleva, N, Kucharska-Newton, A, Palta, P, Couper, D, Meyer, K, Graff, M, Haring, B, Sharrett, R and Heiss, G (2017). *Nutrients* 9: 1134.

Reduced brain volume and impaired memory in betaine homocysteine S-methyltransferase knockout mice. Prieur, EAK, Pjetri, E, Zeisel, SH and Jadavji, NM (2017). *Appl Physiol Nutr Metab* **42**: 1228-1231.

CANCER & METABOLOMICS

Correlated metabolomic, genomic, and histologic phenotypes in histologically normal breast tissue. Sun, X, Stewart, DA, Sandhu, R, Kirk, EL, Pathmasiri, WW, McRitchie, SL, Clark, RF, Troester, MA and Sumner, SJ (2018). *PLoS One* 13: e0193792.

Antibiotic-induced acceleration of type I diabetes alters maturation of innate intestinal immunity. Zhang X, Li J, Krautramer KA, Badri M, Battaglia T, Borbet TC, Koh H, Ng S, Sibley RA, Li Y, Pathmasiri W, Jindal S, Shields-Cutler RR, Hillmann B, Al-Ghalith GA, Ruiz VE, Livanos A, Wout A, Nagalingam N, Rogers AB, Sumner SJ, Knights D, Denu JM, Li H, Ruggles KV, Bonnneau R, Williamson AR, Rauch M, Blaser MJ (2018). *eLife* 7:e37816.

NUTRIGENETICS

Guide for current nutrigenetic, nutrigenomic, and nutriepigenetic approaches for precision nutrition involving the prevention and management of chonic chronic diseases associated with obesity.

Ramos-Lopez, O, Milagro, FI, Allayee, H,
Chmurzynska, A, Choi, MS, Curi, R, De Caterina,
R, Ferguson, LR, Goni, L, Kang, JX, **Kohlmeier,**M, Marti, A, Moreno, LA, Perusse, L, Prasad, C,
Qi, L, Reifen, R, Riezu-Boj, JI, San-Cristobal, R,
Santos, JL and Martinez, JA (2017). *J Nutrigenet*Nutrigenomics 10: 43-62.

Serum lipid concentrations and *FADS* genetic variants in young Mexican college students: The UP-AMIGOS Cohort Study. Vazquez-Vidal, I, Voruganti, VS, Hannon, BA, Andrade, FCD, Aradillas-Garcia, C, Nakamura, MT and Teran-Garcia, M (2018). *Lifestyle Genom*: 11:40-48.

Introduction to mammalian genome special issue: The combined role of genetics and environment relevant to human disease outcomes. Rusyn, I, Kleeberger, SR, McAllister, KA, French, JE and Svenson, KL (2018). *Mamm Genome* 29: 1-4.

OUR TEAM



The NRI's 13 administrative staff members support the institute and its scientific staff—from operations and personnel to finance and fundraising—throughout the year. Also supporting our 18 faculty members in FY18 were 3 research scientists, 3 research associates, 10 postdoctoral fellows, 12 research associates and technicians, 5 doctoral students, and 4 interns.

Administration



Eduardo Serrano Deputy Director for Research Administration



Suzanne Dane Director of Development and Community Outreach



Ryan Dayvault Facilities and Special Projects Coordinator



Brandi Childers Assistant Director for Training, Programs and Partnerships



Scott Jaworski Applications Analyst and IT Consultant

NRI employees come from all over the country and across the globe to pursue their passion for the study and understanding of precision nutrition. All are employees of the University of North Carolina at Chapel Hill

EDUCATION & ENGAGEMENT



On May 1 and 2, 2018, the NRI hosted 96 participants at a Defining Precision Nutrition Symposium. Eight expert speakers from universities across the country and around the world delved into the tools and approaches needed to study and practice Precision Nutrition—from early discoveries based on genetics to powerful new methods like



metabolomics, and developments in our understanding of gut microbes that absorb and metabolize nutrients.

Results of their work in these fields were brought together for examination and instruction.

Professor Jeremy Nicholson of Imperial College London delivered the keynote address, "Understanding Gene-Environment-Diet and Lifestyle Interactions in Human Health." Presentations included "Metabotyping for Optimal Nutrition" and "Genetic Testing for Personalized Nutrition."

Scientists and nutrition and medical professionals from academia, government, and industry attended. A panel of government and industry leaders discussed "The Future of Precision Nutrition."

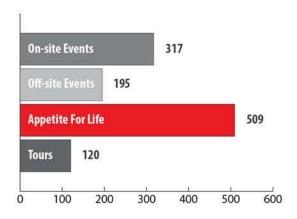
The NRI organized and produced this symposium because, says Director Steven H. Zeisel, MD, PhD, "We predict Precision Nutrition will become the standard for evidence-based professional practice of nutrition and it is important for health practitioners to understand responses to nutrition interventions."

Nutrigenetics, Nutrigenomics and Precision Nutrition Short Course

The NRI is dedicated to answering questions of how our genes and diet interact (the science fields of nutrigenetics and nutrigenomics), and how we can use these answers to develop a precision nutrition approach that maximizes each individual's health. Such "NGx" research spans scientific concepts ranging from cell biology to dietetics. Staying abreast of current developments in all of these various fields is difficult for researchers and practitioners, creating barriers that impede translation of research results from laboratories to populations.

The NRI's third annual NGx Workshop, June 4-7, 2018 enabled interdisciplinary communication in Nutrigenetics, Nutrigenomics, and Precision Nutrition by bringing together graduate students, health professionals and nutrition scientists from academia and industry. Sixteen presenters led 76 participants through the 4-day short course, which provided fundamental concepts through cutting-edge presentations and hands-on experiences using the latest tools to analyze participants' genetic data and understand their nutrigenetic profiles.

FY18 Engagement



TOTAL PEOPLE ENGAGED: 1,141

APPETITEFORLIFE

Our research is complex but our purpose is very human. To help make NRI science accessible and relatable, we offer opportunities for community involvement because, ultimately, our science is about you. Free Appetite For Life programs provide helpful information through educational and interactive lectures, demonstrations and events. Speakers, experts in their fields, present programs to help you understand what precision nutrition is and the advanced methods of research we are using to investigate how your genetics and metabolism play critical roles in your health.

In the past year, audiences learned about:

Vitamin D and Human Health from Folami Ideraabdullah, PhD

Navigating Holiday Cooking from Susan M. Smith, PhD

Whole Foods and Nutrient Synergy from Carol L. Cheatham, PhD

Effects of Genes and Environment on Our Health

from John E. French, PhD

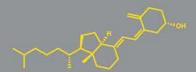
Using Biochemical Fingerprints to Understand Individual Health and Response

from Susan J. Sumner, PhD

Diet and Prostate Cancer from Emma H. Allott, PhD



Appetite For Life at Restaurant Forty-Six in Kannapolis



In our partnership with **Johnson & Wales University** in Charlotte, North Carolina, two Appetite For Life programs featured cooking demonstrations and nutrition talks focusing on fall and spring cooking to promote good health.



Johnson & Wales University - Charlotte

NRI SEMINAR SERIES

The NRI invites faculty from UNC-Chapel Hill, across the U.S. and around the world to give lectures on their research discoveries to faculty at the NRI. Guest speakers presented seven seminars this past year on such topics as:

Glucose and amino acid metabolism in cancer. Jason Locasale, PhD, Duke University

MicroRNA mediators of prenatal alcohol effects: From bench to bedside and back

Rajesh Miranda, PhD, Texas A&M University

Polyphenols and health: the good (science), the bad (science), and the ugly (truth)

Daniel Del Rio, PhD, University of Parma, Italy

N-3 fatty acid derived metabolite deficiencies impair immunological and metabolic responses in obesity

Raza Shaikh, PhD, UNC-Chapel Hill

Assessing neonatal brain and cognitive development in the preclinical piglet model

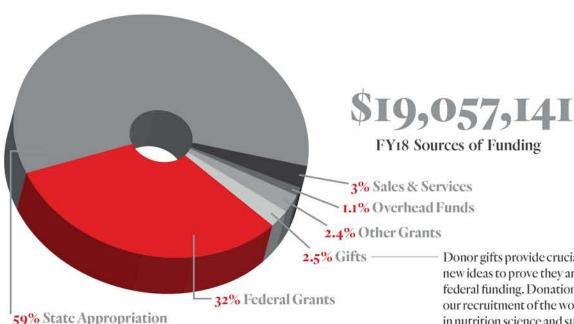
Rvan Dilger, PhD, University of Illinois

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FUNDING FY18

"I work as an obesity medicine physician and also as a hospice physician. I am also a rheumatologist, I see the role nutrition has to play in people's health and disease, and I support your efforts to help change people's lives for the better."

-Dr. Sally Nicks



Donor gifts provide crucial funds for exploring new ideas to prove they are worthy of larger federal funding. Donations also make possible our recruitment of the world's best minds in nutrition science and support hands-on education and mentoring of students. Your gifts make all the difference to our success. Thank you.

Corporate & Foundation Funding



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PHILANTHROPY 2008-2018

Thank you to those who have supported our research over the last decade, helping make precision nutrition discoveries possible.

Diane Laval

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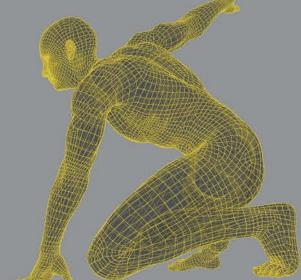
\$250 - \$499

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Brenda Roman Donand Kay Scott Charles D. Taylor Jr. Mildred P. Turner Tyler Warmack Jack E. Wilson

"I continue to be inspired with the research and work being done at NRI. Supporting their mission to understand the benefits of personalized nutrition will help to ensure their contributions to improving health and changing lives for the better."

Rina K. Shah



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