Dear Friends,

As we launch our second decade of nutrition discoveries, I’m pleased to share with you in this report the successes we realized in FY19 (July 1, 2018 – June 30, 2019). In particular, we are proud of the achievements of our faculty and their research teams in winning highly competitive federal grants that assure these investigators’ continued exploration of precision nutrition science. This past year, our researchers’ excellence was further demonstrated by their publications in peer-reviewed journals, appearances as guest speakers, and honors bestowed on them. Our outstanding scientists are the engines that fuel the NRI’s innovations in precision nutrition, leading the world toward a better understanding of how to make personalized nutrient advice work for each of us.

With the generosity of people like you who understand the significance of our mission to the overall improvement of human well-being and healthcare, we have closed our most successful year to date. I extend my sincere and humble thanks for your support, and hope that you’ll enjoy reading about how your contributions advanced our work this past year.

Sincerely,

Steven H. Zeisel, MD, PhD
Institute Director
Professor of Nutrition and Pediatrics
Nutrition Research Institute
University of North Carolina at Chapel Hill

ADVANCED APPROACHES TO OUR SCIENCE

Nutrigenetics
Identifying the genetic blueprint that makes each of us respond uniquely to nutrition and what it means for our personal health.

Epigenetics
Studying chemical marks on genes that turn them on or off, and are often affected by nutrition early and for the rest of life.

Nutrigenomics
Using molecular tools to understand how nutrients may affect the expression of genes.

Metabolomics
Measuring thousands of small molecules (metabolites) to better understand how nutrition affects our metabolism, performance and health.

Microbiotics
Studying how each of the many microbe species in our gut affects our nutritional health in different ways and makes us respond uniquely to nutrition.

A leader in the Precision Nutrition space, the NRI is developing and applying cutting-edge methods to determine why metabolism and nutrition requirements differ between individuals.

We seek to understand nutrient metabolism and its relationship to human development and disease with the goal of increasingly replacing general dietary guidance with more customized nutrition recommendations.

This is Precision Nutrition.
NRI principal investigators hold faculty appointments in the departments of Nutrition and Psychology at UNC Chapel Hill. Their research includes studies on the role of nutrients in preventing disease, diet-related health behaviors and risk factors for disease, the effects of the environment and genes on disease outcomes, and the impact of gene-nutrient interactions.

**FACULTY**

Carol L. Cheatham, PhD  
John E. French, PhD  
Stephen Hoving, PhD, MPH  
Martin Kohlmeier, MD, PhD  
Natalia Krupenko, PhD  
Sergey Krupenko, PhD

Philip May, PhD  
Karen Meyer, Ed.D  
Sandra Morvey, PhD  
Wimal Palanisamy, PhD  
Susan Smith, PhD, Deputy Director  
Debora Smoyer, PhD

Susan Sumner, PhD  
Natalia Sumonko, PhD  
Sanja Vranez, PhD  
Steven Zeisel, MD, PhD, Director

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**HONORS**

**Stephen Hursting, PhD, MPH**
- Vice chair of program committee, 2019 American Association for Cancer Research Annual Meeting in Atlanta, GA, March 29-April 3, 2019
- Co-chair of 2019 American Institute for Cancer Research Conference in Chapel Hill, NC, May 15-17, 2019
- 2019 Excellence in Nutrition Education Award from American Society for Nutrition presented at its annual meeting in Baltimore, MD, June 9, 2019

**Martin Kohlmeier, MD, PhD**
- President of the International Society of Nutrigenetics/Nutrigenomics

**Philip May, PhD**
- Mark Keller Honorary Lecture Award for the National Institute of Alcohol Abuse and Alcoholism of the National Institutes of Health, "presented for advancing our understanding of fetal alcohol spectrum disorders," in Washington, DC, November 29, 2018

**Susan Smith, PhD**
- External Advisory Council for the National Institute of Alcohol Abuse and Alcoholism

**Susan Sumner, PhD**
- Elected Co-chair 2021 Metabolomics Gordon Research Conference
- Elected Chair 2023 Metabolomics Gordon Research Conference
- Organizer of Precision Medicine/Precision Nutrition Workshop: 2019 Metabolomics Society Meeting, The Hague, Netherlands, June 23, 2019

**Steven Zeisel, MD, PhD**
- American Institute for Cancer Research Distinguished Service Award for his contribution to the field of nutrition and cancer, May 16, 2019

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**In the News**

Carol L. Cheatham, PhD, featured in “Choline in human milk plays a crucial role in infant memory,” by SPLASH™ Milk Science Update (October 2018)

Martin Kohlmeier, MD, PhD, featured in “What should I eat on my night shift?” by Abi Rimmer at The BMJ 2019;365:l1413 (May 16, 2019)

Steven H. Zeisel, MD, PhD and Martin Kohlmeier, MD, PhD, quoted in “The DNA diet: How knowing your genes can help you fit into your jeans” by Melina Jampolis, MD for CNN (May 27, 2019)
KEY FINDINGS

Nutrient stress, cell death, and cancer treatments
Nutrient availability regulates cell metabolism, growth, and survival. Nutrient deprivation can stall cell growth, causing severe negative effects if it happens during certain critical growth periods such as early brain development. In contrast, harnessing the innate ability of cells to enter programmed cell death is an important strategy in cancer treatment. However, our current understanding of the molecular mechanisms linking nutrient deficiency with programmed cell death is incomplete.

NRI assistant professor Natalia Krupenko is researching how nutrient stress regulates cell metabolism and survival. Her laboratory found that deprivation of the nutrient folate causes increased levels of the molecule C16-ceramide. This molecule enhances activity of a protein known as p53, which regulates cell death/survival. p53 activity is decreased in many cancers; finding ways to increase its activity is a goal of cancer treatment researchers.

The findings from the Krupenko laboratory that low folate can induce C16-ceramide and thereby promote cell death could lead to new strategies for cancer treatment. Many drugs work by activating or deactivating existing cellular stress response mechanisms to either kill or protect cells as necessary. Clarification of the role of C16-ceramide and p53 in the nutrient starvation response provides increased details on how cells respond to stress.


The gut microbiome affects blood pressure
Animal studies suggest that activity of the gut microbiome plays a role in regulating hypertension. However, translating the results of controlled animal studies to diverse human populations continues to be difficult. NRI assistant professor Katie Meyer is interested in nutritional risk factors for cardiometabolic disease. She has published a study that investigated associations between the gut microbiome and blood pressure in 539 participants in the ongoing CARDIA (Coronary Artery Risk Development in Young Adults) study. This is the largest study to date associating hypertension with gut microbiome composition. Her research group found that people with lower blood pressure when they had a more diverse population of bacteria in their microbiome.

Diet and genetics impact both the microbiome composition and its activity. Diets rich in fiber typically increase microbial diversity and, at least in animal models, prevent hypertension. The study from the Meyer group suggests that similar processes may be found in humans.


Energy balance affects cancer progression and treatment
Obesity is now the second leading cause of cancer after smoking. Obesity increases the risk of gastrointestinal (GI) cancer and worsens disease outcomes. While one might expect that, for obese patients diagnosed with GI cancer, weight loss would be beneficial for patient survival, results to date are ambiguous. A significant contributing factor to this uncertainty is lack of clarity as to how obesity contributes to cancer initiation, aggressiveness, and resistance to treatment.

NRI professor Stephen Hursting is a leader in nutrition, obesity, metabolism and cancer research with a focus on the molecular and metabolic mechanisms underlying obesity-cancer associations and the impact on response to chemotherapy. In a recent comprehensive review article, Hursting and colleagues describe the state of knowledge regarding the link between energy balance (i.e., diet and physical activity) and GI cancer. There are many mechanisms by which obesity can impact cancer, and treatment will therefore differ across patients. The authors conclude that there is a need to integrate mechanistic approaches with preclinical and human studies to develop effective, personalized diet and exercise interventions to reduce the burden of obesity on gastrointestinal cancer.


Choline is required for retinal development
It is well established that adequate maternal intake of choline is crucial for proper fetal brain development. However, the impact of low dietary choline during gestation on the development of most other tissues and organs is not known. NRI assistant professor Natalia Surzenko is interested in how maternal choline intake affects retinal development and how offspring together with NRI professor Steven Zeisel and their laboratories, she has determined that low maternal intake of choline results in abnormal development of the retina in the eye and disrupts normal vision in a mouse model.

In 2018 the American Academy of Pediatrics listed key nutrients that are needed during pregnancy to build a healthy baby, including protein, zinc, iron, choline, folate, iodine, long-chain polyunsaturated fatty acids and vitamins A, D, B6, and B12. This study at the NRI reiterated the importance of choline and identifies its importance in the development of the visual system.


“...our work depends on a variety of sources of funding, and I’m grateful for all the support we receive—from major federal grants to the donations of generous individuals. We do our research because we want to help people, when they, in turn, support our work, it is most gratifying.”

- Natalia Krupenko, PhD
Assistant Professor
UNC Nutrition Research Institute

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.
SELECTED PUBLICATIONS & PRESENTATIONS

Carol L. Chcchatam, PhD
• (Poster) Fetal alcohol effects on Morris Water Maze performance ameliorated by maternal choline: relation with BDNF promoter methylation. 42nd Annual Meeting of the Research Society on Alcoholism, Minneapolis, MN. June 22-26, 2019

John E. French, PhD
• Diet-diverse Diversity Outbred mice weight gain followed by calorie restriction weight loss quantitative traits. The Complex Traits Consortium/ Rat Genomics 5th Annual Meeting, University of California at San Diego. June 8-11, 2019

Stephen Hurting, PhD, MPH
• Breaking the obesity cancer link: New targets and strategies. 2019 National Cancer Institute-Stars in Nutrition & Cancer Lecture Series, Bethesda, MD. March 12, 2019

Martin Kohlmier, MD, PhD
• Genotype-specific vitamin D guidelines. Inaugural Meeting of the ISNN Vitamin D Working Group, ISNN Congress, Cambridge, UK. July 13, 2019

Natalia Krupenko, PhD
• Cs6-ceramide modulates p53 function via direct binding to the protein. 59th International Conference on the Oxidation of Lipids, Helsinki, Finland. September 4-7, 2018

Sergey Krupenko, PhD
• Role of ALDH1A1 folate enzyme in cancer. 19th International Carbohydrate Conference, Breckenridge, CO. July 17-22, 2018

Phil May, PhD
• Health disparities in fetal alcohol spectrum disorders: Under diagnosis of a common disorder. American Public Health Association, San Diego, CA. November 12, 2018

Katie Meyer, ScD
• Gut microbiome and blood pressure in CARDIA. CHARGE Consortium Meeting, Baltimore, MD. Oct 11, 2018

Sandra Mooney, PhD
• Functional connectivity in a rat model of fetal alcohol spectrum disorder (FASD). Pilot study using resting state functional MRI. 6th International Conference on Fetal Alcohol Spectrum Disorder, Vancouver, BC, Canada. March 6-9, 2019

Susan Smith, PhD
• Exon-level machine learning elucidates novel candidate miRNA targets in an avian model of fetal alcohol exposure. 42nd Annual Meeting of the Research Society on Alcoholism, Minneapolis, MN. June 22-26, 2019

Delisha Stewart, PhD
• Metabolomics approaches to cancer research. American Institute for Cancer Research Conference on Diet, Obesity, Physical Activity and Cancer, Chapel Hill, NC. May 15-17, 2019

Susan Sumner, PhD

Saroja Voruganti, PhD
• Genetics primer for nutrition researchers. Nutrigenetics, Nutrigenomics and Precision Nutrition, Karnaplag, NC. June 2019

Steven Zeisel, MD, PhD
• Choline intake during early life and neurodevelopment and cognition. One Carbon Metabolism Conference, Catalunya, Spain. June 9-13, 2019

49 Peer-Reviewed Publications

World-wide Presentations
Our research is complex, but our purpose is very simple. To help make NRI science accessible and reliable, we offer opportunities for community involvement because, ultimately, our science is about you. Free Appetite for Life programs offer helpful information through educational and interactive lectures, demonstrations, and events. Expert speakers 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.

Nutrigenetics, Nutrigenomics and Precision Nutrition Short Course
To help prepare for a future when precision nutrition is used to manage everyone’s health, the NRI held the fourth annual Nutrigenetics, Nutrigenomics and Precision Nutrition Short Course (NGs) in Kannapolis, NC, June 3-6, 2019. An international gathering of graduate students, health professionals, and nutrition scientists from academia and industry attended the short course to gain understanding of diet-genome interactions through lectures and applied sessions.

Community Talks
Faculty, research staff, and administrators from the NRI are often invited to speak to community groups about the exciting research we are doing in precision nutrition. Last year we presented at five events including a county career day and a regional nutrition summit.

NRI SEMINAR SERIES
Each year, the NRI invites faculty from other research universities to present their discoveries to the science teams at the NRI and across the NC Research Campus. Twelve guest scientists presented topics such as the impact of gut microbes on cancer risk, and environmental and genetic factors in congenital abnormalities.
CLINICAL STUDIES

NRI nutrition research starts in the laboratory then, sometimes, moves into clinical studies. These studies rely on people who volunteer to be a part of scientific discovery to find new ways to detect, treat, or even prevent disease. When you participate in a clinical study you provide opportunity to researchers and hope to so many people worldwide.

Children’s Health Study
Dr. Saroja Voruganti is working to identify genes and lifestyle factors that affect children’s health status and overall well-being.

Fructose-Liver Fat Study
Dr. Saroja Voruganti is identifying genetic and dietary factors that affect the risk for non-alcoholic fatty liver disease.

Choline Status Study
Dr. Steven Zeisel’s study is determining which biomarkers in the blood most accurately reflect a person’s choline status.

Infant Cognition & Nutrition Study
Dr. Carol L. Cheatham is testing whether eating an egg for five out of seven days each week while breastfeeding will improve infant cognitive development.

FASD Epidemiological Study
In addition to studies recruiting participants in our local community, Dr. Phil May’s research reaches far beyond and includes cohorts of women and their children in the Western Cape Province of South Africa. These participants are in a longitudinal study on child growth and development and maternal risk factors for fetal alcohol spectrum disorders.

LOCAL IMPACT

At the NRI, research focuses on the intersection of nutrition and genetics and, therefore, each clinical study has different requirements. In FY19 the following studies were underway, offering opportunities for many community members to be further involved in our mission.

In the past year, downtown Kannapolis, adjacent to the campus, has been under expansive renovation through both public and private investment. A major anchor in this development is a new baseball stadium and event venue.

It is important to us that our location in Kannapolis means that many people in this town, which experienced the single greatest one-day layoff of workers in state history when the Cannon Mills closed, now have the opportunity to find local employment again. Our presence on the research campus also means that, along with our sister institutions, we have attracted many new residents to Rowan, Cabarrus and surrounding counties, all of whom shop locally and contribute to the revitalization of our beautiful community.

As a proud member of the North Carolina Research Campus in Kannapolis, the NRI is pleased that our participation as a member of the local business community contributes to the economic development of our hometown.

FY19 NRI Local Expenditures

<table>
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<tr>
<th>Operations</th>
<th>Laboratory supplies &amp; services</th>
<th>Property tax</th>
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<td>$1,219,879</td>
<td>$863,101</td>
<td>$149,203</td>
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NRI²

The NRI’s Neighborhood Resource Initiative (NRI²) brings our faculty, students and staff together in community service. Last year we helped with gardening, painting and cleaning at a local elementary school and contributed 70 pounds of canned food to a local food bank.

FY19

3.2M
FUNDING FY19

The Impact of Donor GIFTS
Donor gifts from individuals, corporations, and foundations 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.

$20,533,910

“It was very interesting to see what is taking place at NRI, how it is benefiting the community and how our support helps continue this important scientific investigation.”

—Jason C. Holt

Corporate & Foundation Gifts

Dole Food Company, Inc.
Balchem
NC Biotechnology Center
Metabolon
DNA Genotek
North Carolina Research Campus

F & M Bank
Genetic Direction
Brothers Tire Sales, Inc.
Castle & Cooke
Arcadia University Physician Assistant Program

We are grateful for the people who have contributed throughout the years and now, supporting our efforts to make lasting change in nutrition discovery.

$100,000+
Alan and Mary Anne Dickson
Toni L. Smith

$20,000 - $99,999
Jana Harrison and Jeffrey Hughes
Fred and Alice Stanback
Steven and Susan Zeisel

$10,000 - $19,999
Gregory and Melissa Alcorn
Broyen L. Bollard

$5,000 - $9,999
John and Jolee Fennerbrooke
Elka Enk
David and Karen Harper
Charles and Katherine Kinsey
Philpy and Dwayne Alby
David H. Murdock
Rona and Rimal Shah
Robert Steele

$1,000 - $4,999
Kenneth and Patricia Argo
Fred and Laura Brown
Molly Brocks
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Jane Liles
James and Dorothy Martin
Julia and Christopher Mills
Hugh and Mary Margaret Monitor
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Thomas and Ken Sears
Jo Anna Stephens
Susan L. Summar and Timothy F. Hannell
Sandi Thomas
Richard and Judith Vincent
Phyllis A. Wingate
James H. Woodward

$500 - $999
Jefferson and Kathleen Adams
Jim and Shanna Atkinson
Brooke Billingsley
Carol L. Cheatham
Linda and David Grembs
Suzanne G. Dino
Dell Wilcox
Joyce Brown
David and Dorothy Dearman
Peter Gilberts and Caroline Viles
Bryan G. Klein and
Susan A. Macias
Martin Kahne
Karen and J.P. McBride
Steven and Debra Medlin
Kendra M. Mooney
Heidi Holt Montana
Sally A. Nichols
Ninon O’Hara
David R. Patterson
James and Nancy Rutledge
Lynda and Walter Sahn
Thomas and Teresa Santis
Joseph and Leila Tresc
Sarja and Zarko Vankovskaja
Richard and Teresa Williams

$250 - $499
Ilie and Diane Apigoian
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Donald and Beverly Cameron
Donna and Jeff Childress
Troy and Pauline Day
Arun Dubey
James and Ina Elliott
Benzie E. Fuller
Douglas and Carolyn Galsgow
Leila and George Herzog
Frederic G. Hiyih
Linda P. Johnson
L. Christopher Kawaguchi and
Matthew Robbins
Sharon Sloop Leininger
Pam Levin

Welcome and thanks to our new friends in FY19!

Patricia Andrews
Linda Brown
Brandi M. Childers
Regina Craven
Sudan Evans
Reese E. Francis

Alison Gustafson
David A. Hentsch
David and Francesca Heyo
Sarah Heyo
Stephanie Hunter
Veron and Chester Inkos

Scott A. Jaworski
Anne Lippsomb
Mark L. Lohr
Lori Maguire
James Naughton
Courtney Parcell

Alina Pittman
Natalia Surzynko
Thomas Wilson
Linda Wenzlau
Chirstine Zimmerman

Donor Thank You Reception June 6, 2019

“Balchem considers it a privilege to support scientific research in general, but is particularly honored to support ongoing scientific endeavors by Dr. Steven Zeisel and his team. We are committed to supporting high-quality research, and Dr. Zeisel’s work on choline is world class.”

—Jonathan Bartz, MD
Senior Director Strategic Innovation, Human Nutrition and Pharma, Balchem