

UNC Nutrition Research Institute

IMPACT REPORT 2014-2015



THE UNIVERSITY of
NORTH CAROLINA
at CHAPEL HILL

**NUTRITION
RESEARCH
INSTITUTE**



Steve Zeisel, M.D., Ph.D., Institute Director, addressing faculty and staff in his lab.

Dear Friends,

In the past year scientists at the Nutrition Research Institute have made significant advances in our understanding of the roles genetics and nutrition play in determining our individual susceptibility and resistance to disease. This is our bold mission: to discover the mechanisms by which diet can prevent or lessen the negative effects of chronic diseases and aging, and improve human development, even prior to conception.

We are achieving these goals thanks to your generosity. Because of your support, we are making exciting progress. For instance, this year we learned that while Fetal Alcohol Spectrum Disorders are more prevalent in some U.S. populations than previously thought, there may be nutritional interventions to mitigate the risks. We now know that maternal nutrition at conception plays a significant role in memory function throughout the child's life. And we made greater strides than ever in understanding the relationship between our gut microbiome and a range of health conditions.

The NRI was represented across the globe by our esteemed faculty who were invited to speak at scientific conferences on such topics as nutrigenetics and nutrigenomics, cognitive development, cardiovascular disease, and epigenetics.

Many of our scientists competed successfully for grant funding from the National Institutes of Health and other federal agencies—grants that are awarded only to the most promising applicants. Your contributions, added to these essential government funds made it possible for us to test ground-breaking hypotheses and move toward clinical trials with some studies.

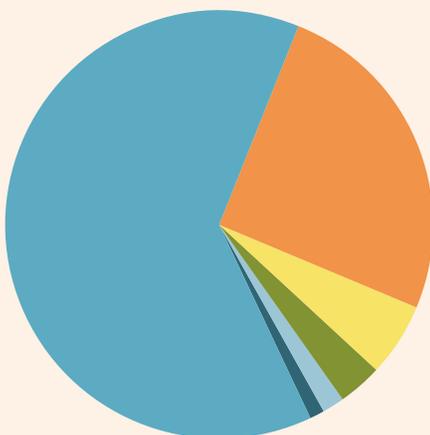
With progress there is growth. Recently, the NRI successfully incubated two companies that have spun out of the university and are in the early stages of capitalization here in Kannapolis. In the coming year we will hire several more senior scientists. We employ students, lab technicians and postdoctoral trainees from colleges and universities near and far. We take seriously our responsibility to bolster our local economy.

On behalf of the faculty and staff of the Nutrition Research Institute, I send sincere gratitude for the confidence you have placed in us and demonstrated through your gifts and other forms of support. I am certain that what we are discovering today at the NRI will dramatically improve our ability to personalize recommendations for better nutrition, and that soon this will allow you to target what you should eat based on your individual metabolism and health needs.

Steven H. Zeisel, M.D., Ph.D.
Institute Director

2014-2015 COMPONENTS OF SUPPORT

\$18.45 MILLION



- 63% State Appropriation
- 25% Federal Grants
- 6% Other Grants and Contracts
- 3% Overhead Funds
- 2% Sales and Services
- 1% Gifts/Donations

The Nutrition Research Institute is

- a nonprofit center for the study of nutrigenetics, a science that explores the interactions of our genes and the nutrients we consume
- replacing the outdated one-size-fits-all approach to nutrition with cutting-edge discoveries of unique differences in DNA and metabolism.
- located on the North Carolina Research Campus in Kannapolis with 70 staff members, including 14 principal investigators
- a unit of UNC Chapel Hill, the nation's first public university and a global higher education leader known for innovative teaching, research and public service
- funded through research grants awarded by the National Institutes of Health, the National Science Foundation and a variety of other national and regional foundations, as well as by individual philanthropic gifts



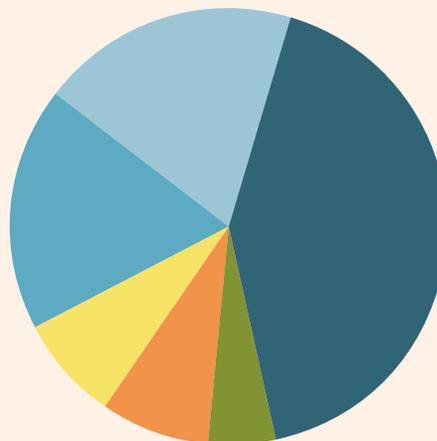
Heather Zhao, research technician, preparing samples for choline analysis.

PRIMARY AREAS OF RESEARCH

Birth Defects
 Brain Development
 Cancer
 Diabetes
 Eye Disease
 Fetal Alcohol Spectrum Disorders
 Gout
 Heart Disease
 Infertility
 Liver Disease
 Memory Loss
 Muscle Function
 Nutritional-environmental influences on disease risk
 Obesity

To learn more, visit UNCNRI.org

Research Staff	42%
Faculty	19%
Administrative Staff	18%
Doctoral Students	8%
Graduate Students	8%
Visiting Faculty/Scholars	5%



2014-2015 TEAM MEMBERS

* The NRI mentored 24 college and 9 high school interns in 2014-2015

Choline: An Essential Nutrient

Dr. Steven Zeisel is a world-renowned expert in choline metabolism and its importance to human health. His research set the stage for the Institute of Medicine to establish a recommended dietary level, the Adequate Intake (AI).¹

Your Genetics Influence What You Should Eat. In research published over the past decade, Dr. Zeisel and his coworkers have shown that alterations to certain genes can affect how well a person is able to process choline. People with a particular genetic variant are not able to process choline as efficiently, and thus require more in their diet, than people with a different genetic variant. Somewhat surprisingly, some of these variants, or polymorphisms, are quite common in the US population, often exceeding 40%.²

What You (and Your Ancestors) Eat Influences Your Genetics. These studies were carried out in US populations who have comparatively high dietary choline intake. In a 2015 paper published in *The Journal of the Federation of American Societies for Experimental Biology*, Dr. Zeisel and colleagues also studied a population in The Gambia that has traditionally eaten a low-choline diet. Notably, they found that this group was less than half as likely to have these same genetic polymorphisms. That is, multiple generations eating a low-choline diet has applied selectivity against polymorphisms that require higher dietary choline.³

What This Means. The fact that the general US population includes substantial subpopulations with different dietary requirements means that setting

singular USDAs or AIs can result in an excessive or insufficient intake, depending on which subpopulation are used for development of guidelines. The 2015 findings are particularly significant in this regard as they suggest that multigenerational ethnic/cultural/traditional diets can actually impact one's need for specific nutrients, and a knowledge of an individual's genetic makeup is important for determination of appropriate nutrient intake.

30% Choline in Pregnancy

The placenta is designed to deliver choline to babies in large amounts. Choline is also transported abundantly in breast-feeding. There is a critical period—before the third trimester—when a little extra choline in a mother's diet results in a 30% improvement in memory that lasts for the offspring's entire life.

25 weeks into pregnancy is when the memory center starts developing and continues through the first year after birth; thus it is crucial to consume choline prior to that development.

Choline is also critical for brain and spinal development.

Male Infertility

The tail of a sperm cell is made up with energy-producing units called mitochondria. The mitochondria make the energy the sperm needs to swim. A defect in choline metabolism may contribute to distorted mitochondria, contributing to infertility.

TOP SOURCES

from highest to lowest



BEEF LIVER



EGG, boiled



WHEAT GERM

Choline is needed for the formation of neurotransmitters and for strengthening cell walls.

Inadequate choline intake can result in fatty liver, which arises when the phospholipids required to transport fat away from the liver are in short supply. As the organ becomes congested with excess fat, severe liver damage occurs.

Too much choline can result in a dramatic drop in blood pressure, profuse sweating and diarrhea.

¹Zeisel, SH, da Costa, K-A, Franklin, PD, Alexander, EA, LaMont, TJ, Sheard, NF, and Beiser, A (1991) Choline is an essential nutrient for humans. *FASEB J.* 5: 2093-2098.

²da Costa, K-A, Kozyre, OG, Song, J, Galanko, JA, Fischer, LM, and Zeisel, SH (2006) Common genetic polymorphisms affect the human requirement for the nutrient choline. *FASEB J.* 20:1336-1344.

³Silver, M, Corbin, K, Hellenthal, G, da Costa, K-A, Dominguez-Salas, P, Moore, S, Owen, J, Prentice, A, Hennig, B, Zeisel, SH (2015) Evidence for negative selection of gene variants that increase dietary choline requirement in a Gambian cohort. *FASEB J.* 29:3426-3435

Genetics and Epigenetics

People vary in their susceptibility to disease. These variations arise in part from our internal, or genetic, makeup and in part from our exposure to external factors. A well-known example of genetic susceptibility is the BRCA1 gene mutation, which increases a woman's chance of developing breast cancer 5-fold and chance of developing ovarian cancer 30-fold. The BRCA1 mutation is an example of a heritable mutation because it can be passed from generation to generation, as children's genetic



Folami Ideraabdullah, Ph.D.,
Assistant Professor of Genetics

makeups are based on their parents' genetic makeups. Disease risk also can be passed across generations through mechanisms that do not involve changes in DNA sequence. This phenomenon is known as epigenetic inheritance to emphasize that the different traits or risks are not caused by differences in the underlying genes or DNA sequences, but in the way DNA sequence code is interpreted by the cell.

Dr. Folami Ideraabdullah, who joined the NRI in 2013, is working at the crossroads of genetics and epigenetics. She is trying to determine which genetic factors alter disease risk from toxic chemical exposure, and what mechanisms are involved in establishing these epigenetic conditions. To do this, she is studying a class of chemicals known as endocrine-disrupting compounds (EDCs) and their ability to create epigenetic defects. EDCs are widely found in daily life. They include certain pesticides and plasticizers, and are also found naturally occurring in food such as soy beans. Exposure to EDCs, especially during pregnancy, can cause epigenetic defects that can be passed through multiple generations. Exposure can thus affect not only your child, but also their children and even their children.

Link to Nutrition

How are genetics and epigenetics related to nutrition? It turns out that the biochemistry behind epigenetics is closely tied to diet. Importantly, the cell's ability to establish epigenetic conditions is directly related to dietary intake of methionine, choline, and folate, compounds of great interest to the NRI. Dietary deficiencies of choline and folate, in particular, are known to cause certain birth defects.

Impact

Identifying who is most at risk for a particular disease is an important component of disease prevention because it allows us to focus prevention efforts where they will be the most effective. Because EDCs are so common in our environment, total avoidance is not a realistic goal. Dr. Ideraabdullah's research will help identify who is most susceptible to EDC toxicity. Her research on the mechanisms of toxicity may also lead to additional treatment or prevention options. Because EDCs act in part by altering many of the epigenetic mechanisms regulated by nutrition, it is possible that adjusting one's diet could reduce disease risk across multiple generations.

Endocrine-Disrupting Chemicals

can be found in:

-  TOILETRIES
-  SYNTHETIC & NATURAL HORMONES
-  PESTICIDES/FUNGICIDES
-  HEAVY METALS
-  PHARMACEUTICAL DRUGS
-  INDUSTRIAL CHEMICALS

EDCs

Ideraabdullah FY, Thorvaldsen JL, Myers JA, Bartolomei MS. (2014). Tissue-specific insulator function at H19/Igf2 revealed by deletions at the imprinting control region. *Hum Mol Genet.* 23(23):6246-59.

<http://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet#q2>



Hayden Trayah, AFL tour participant demonstrating the use of the BOD POD®.

APPETITE FOR LIFE

Events

A series of community programs that bring the latest nutrition science research down to earth in educational and interactive lectures, demonstrations and events. Our 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 2015 audiences heard about a range of nutrition and health topics:

Diet and Cancer Prevention. Stephen Hursting, Ph.D., M.P.H., UNC NRI

Keeping A Hungry World Healthy. Patrick Stover, Ph.D., Cornell University

Vitamins and Healthy Diet. Natalia Krupenko, Ph.D., UNC NRI

The Longevity Diet. Bruce Ames, Ph.D., Children's Hospital Oakland Research Institute and University of California, Berkley

"Thanks for offering these seminars. The presenters are very knowledgeable and provide a lot of useful information in ways that are easy to understand." –Caitlyn Rogers, Kannapolis, NC

"Very enjoyable evening and beneficial topic for the health and wellness industry." –Mark Hall, Salisbury, NC

Tours

Many found out where scientific discovery takes place by touring the UNC Nutrition Research Institute during the 2015 summer. Points of interest included one of only a few whole-room calorimeters in the U.S., metabolic assessment lab, body composition lab with BOD POD® demonstration, and a research laboratory.

Learn about new Appetite for Life programs at UNCNRI.org/AFL

AFL ATTENDANCE

DIET AND CANCER PREVENTION

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KEEPING A HUNGRY WORLD HEALTHY

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VITAMINS AND A HEALTHY DIET

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THE LONGEVITY DIET

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NRI TOURS

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ACROSS THE WEB

Last year we launched a new website and revamped our social media to better communicate with you.

UNCNRI.org • Visit our website to learn about our pioneering research, state-of-the-art facilities, award-winning faculty, community outreach activities, job openings and opportunities to support our work.

 **/UNCkannapolis** • The UNC Nutrition Research Institute's Facebook page allows our scientists and researchers to share findings and calls for volunteers with the public. It also allows you to communicate with us. From photos and videos to links to our latest articles, Facebook keeps everyone up to date with the NRI.

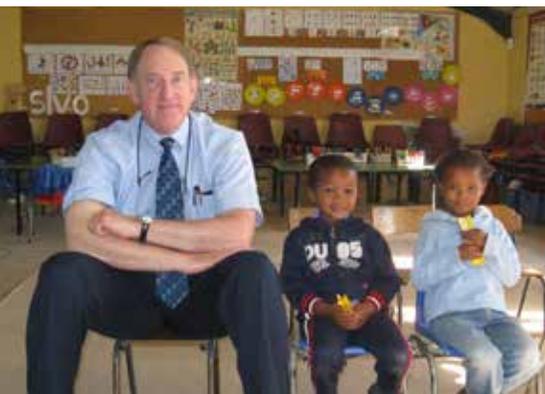
 **@UNC_NRI** • Visit our new Twitter page to find helpful nutritional facts and to stay current on all our recent information, including live tweeting during events and presentations.

SELECTED CONTRIBUTIONS TO SCIENCE (FY15)

PUBLICATIONS

Maternal nutrition at conception modulates DNA methylation of human metastable epialleles.

Dominguez-Salas P, Moore SE, Baker MS, Bergen AW, Cox SE, Dyer RA, Fulford AJ, Guan Y, Laritsky E, Silver MJ, Swan GE, **Zeisel SH**, Innis SM, Waterland RA, Prentice AM, Hennig BJ. *Nature Communications*. 2014; 5:3746.



Philip May, Ph.D., Research Professor studying FASD prevalence and characteristics in South Africa.

Prevalence and characteristics of Fetal Alcohol Spectrum Disorders.

May PA, Baete A, Russo J, Elliott AJ, Blankenship J, Kalberg WO, Buckley D, Brooks M, Hasken J, Abdul-Rahman O, Adam MP, Robinson LK, Manning M, Hoyme HE. *Pediatrics*. 2014; 134:855-66.

Responsiveness of cardiometabolic-related microbiota to diet is influenced by host genetics.

O'Connor A, Quizon PM, Albright JE, Lin FT, **Bennett BJ**. *Mammalian Genome*. 2014; 25:583-99.

Modulation of breast cancer risk biomarkers by high dose omega-3 fatty acids: phase II pilot study in post-menopausal women.

Fabian CJ, Kimler BF, Phillips TA, Nydegger JL, Kreutzjans AL, Carlson SE, Hidaka BH, Metheny T, Zalles CM, Mills GB, Powers KR, Sullivan DK, Petroff BK, Hensing WL, Fridley BL, **Hursting SD**. *Cancer Prevention Research (Phila)*. 2015; in press.

Rho GTPases RhoA and Rac1 mediate effects of dietary folate on metastatic potential of A549 cancer cells through the control of cofilin phosphorylation.

Oleinik NV, Helke KL, Kistner-Griffin E, **Krupenko NI, Krupenko SA**. *The Journal of Biological Chemistry*. 2014; 289:26383-94.

Global metabolomic profiling targeting childhood obesity in the Hispanic population.

Butte NF, Liu Y, Zakeri IF, Mohney RP, Mehta N, **Voruganti VS**, Göring H, Cole SA, Comuzzie AG. *American Journal of Clinical Nutrition*. 2015; 102:256-67.

INVITED ORAL PRESENTATIONS

Brian Bennett. "Towards Nutrigenomics: Studies to Identify Gene-Diet Interactions Affecting Susceptibility to Cardiovascular Disease." Federation of American Societies for Experimental Biology. San Diego, California. April 2014.

Carol Cheatham. "The Relation of Human Milk Lutein, Choline, and Docosahexaenoic Acid Content to Recognition Memory Abilities of 6-Month-Old Breastfed Infants." Recent Advances in Cognition and Nutrition Conference, Taipei, Taiwan. Summer 2015.

Carol Cheatham. "The Impact of Long-Chain Polyunsaturated Fatty Acids on Child Development." Second Indonesia – Southeast Asia Sharing on Child Health Challenges Summit. Denpasar, Bali, Indonesia. Summer 2015.

Stephen D. Hursting. "Epigenetic and Metabolic Targets for Breaking the Obesity and Breast Cancer Link." University of Manchester Cancer Center Grand Rounds. Manchester, England. 2015.

Natalia Krupenko. "Metabolic Cross-Talk: Folate and Sphingolipids." Third Alcohol and Cancer Conference, Crete, Greece. Spring 2014.

Philip May. "Active Case Ascertainment to Determine the Prevalence of FASD." U.S. Government Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders. Rockville, MD. April 2015.

Steven H. Zeisel. "Choline, Metabolic Signaling and Gene Expression/Epigenetics." Summer Research Conference of the Federation of American Societies for Experimental Biology, Big Sky, Montana. August 2014.

Steven H. Zeisel. "Nutrigenetics of the Nutrient Choline." National Institutes of Health, Office of Dietary Supplements, Bethesda, Maryland. February 2015.



Zackie Salmon, Director of the McNair Scholar's program at the University of Wyoming, **Carol Cheatham, Ph.D.**, of the UNC Nutrition Research Institute and **Susan Stoddard**, Assistant Director of the McNair Scholar's Program

BOOKS AND OTHER SCHOLARLY PRODUCTS

Martin Kohlmeier, M.D., Ph.D. (2015). *Nutrient Metabolism: Structures, Functions, and Genes* (Second ed.). London: Academic Press.

Martin Kohlmeier, M.D., Ph.D. Congress president and conference chair, 9th Congress of the International Society of Nutrigenetics and Nutrigenomics, Chapel Hill, NC. May 2015.

2014-2015 TEAM MEMBERS

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Carolyn Harris
Jana Harrison
David Horita, Ph.D.
Scott Jaworski
Tamara Marlowe
Tim Mills
Julie Pope
Joseph Squires



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1. Faculty and research staff gathered on NRI balcony.
2. Dr. Patrick Stover presenting his talk, "Keeping a Hungry World Healthy" in our Appetite for Life series.
3. Tamara Marlowe, medical lab technician, analyzing cell cultures in the NRI's Human Research Core.
4. Thomas Benton, research technician, preparing samples for choline analysis.
5. Participants in NRI's collaborative project with Eric Ryan, Ph.D., Assistant Professor in the Department of Exercise and Sport Science at UNC Chapel Hill, and the Kannapolis Fire Department.
6. Koyt Everhart, research technician and Geetha Chittoor, Ph.D., postdoctoral research associate, at work in the Voruganti Lab.
7. The UNC Nutrition Research Institute's home in Kannapolis on the North Carolina Research Campus.