BIOGRAPHICAL SKETCH

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NAME: Zeisel, Steven H.

POSITION TITLE: Professor

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

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
Harvard Medical School	M.D.	06/1975	Medicine
Yale – New Haven Hospital	Resident	06/1977	Pediatrics
Massachusetts Institute of Technology	PhD	06/1980	Nutrition
Children's Hospital, Boston	Fellow	06/1981	Human Nutrition
Massachusetts Institute of Technology	Postdoc	06/1981	Neurochemistry

A.Personal Statement

I am PI and founding Director of the UNC NORC. I have overseen its growth from 55 members in 1999 to its current membership of nearly 150 members spanning 35 departments. I also served as Chair of the UNC-CH Nutrition department for fifteen years and am now Director of the UNC-CH Nutrition Research Institute.

I have studied the nutrient choline and 1-carbon metabolism for 35 years and am one of the world's recognized experts in the field with over 250 publications. My research team was the first to demonstrate a human dietary requirement for choline, and our work set the basis for the Institute of Medicine-defined Adequate Intake. We have published extensively on nonalcoholic fatty liver disease (NAFLD) that is induced by choline deficiency, and are currently determining the molecular mechanisms by which alteration of 1-carbon metabolism through deletion of the *Bhmt* gene causes hepatocarcinoma. By taking advantage of the big data revolution in genomics, we are also actively pushing the frontiers of personalized nutrition and metabolism research.

1. Watkins, S.M., Zhu, X., and **Zeisel, S.H.** (2003) Phosphatidylethanolamine-N-methyltransferase activity and dietary choline regulate liver-plasma lipid flux and essential fatty acid metabolism in mice. *Journal of Nutrition* 133(11):3386-3391. PMID: 14608048.
2. da Costa, K-A., Kozyrez, O.G., Song, J., Galanko, J.A., Fischer, L.M., and **Zeisel, S.H.** (2006) Common genetic polymorphisms affect the human requirement for the nutrient choline. *FASEB Journal* 20:1336-1344. PMCID: PMC1574369.
3. Teng, Y-W, Mehedint, M.G., Garrow, T.A., **Zeisel, S.H.** (2011) Deletion of betaine-homocysteine *S-m*ethyltransferase in mice perturbs choline and 1-carbon metabolism, resulting in fatty liver and hepatocellular carcinoma. *Journal of Biological Chemistry* 286(42): 36258 – 67. PMCID: PMC3196139.
4. Corbin, K.D., Abdelmalek, M.F., Spencer, M.D., da Costa, K-A, Galanko, J.A., Sha, W., Suzuki, A., Guy, C., Cardona, D.M., Torquati, A., Diehl, A.M., **Zeisel, S.H.** (2013) Genetic signatures in choline and 1-carbon metabolism are associated with the severity of hepatic steatosis. *FASEB Journal*. 1674 – 89. PMCID: PMC3606533.

B. Positions and Honors

Positions and Employment

1982-1987 Assistant Professor, Boston University School of Medicine
1987-1990 Associate Professor, Boston University School of Medicine

1990-1990	Professor of Pathology and Pediatrics, Boston University School of Medicine
1990-2005	Professor and Chair, Department of Nutrition, School of Medicine and School of Public Health, University of North Carolina
1990-present	Professor, Department of Pediatrics, University of North Carolina
1999-2007	Associate Dean for Research, School of Public Health, University of North Carolina
2005-present	Kenan Distinguished University Professor, University of North Carolina
2006-present	Director, Nutrition Research Institute, University of North Carolina

Other Experiences and Professional Memberships

1987-present	American Society for Nutritional Sciences, (President 2002), Long Range Planning Chair, 2003-2005; Strategic Planning Committee 2055-present).
1998-present	International Society for Neurochemistry
1996-1998	Panel on Recommended Dietary Intake of Folate and B-vitamins, National Academy of Sciences
2000-2009	Chairman NIH Integrative Nutrition and Metabolic Processes study section
2001-2005	FDA Food Advisory Committee, Center for Food Safety & Applied Nutrition, Dietary Supplements
2005-2008	Member, Editorial Committee, Annual Review of Nutrition
2005-present	Member, Editorial Board, FASEB Journal
2010	Specialty Chief Editor, Frontiers in Nutrigenomics

Honors

1986	Future Leader Award, International Life Sciences Institute-Nutrition Foundation
1991	American College of Nutrition, Grace Goldsmith Award for Teaching & Research in Nutrition
1996-present	Who's Who in America
2001	American Society for Clinical Nutrition - Dannon Institute Award for Excellence in Medical/Dental Nutrition Education
2006	Bristol-Meyers Squibb Award for Distinguished Achievement in Nutrition Research
2007	The American College of Nutrition, Award for Outstanding Achievements in Nutrition
2008	The American Society for Nutrition, Osborne and Mendel Award
2009	W.O. Atwater Lecturer - U.S. Department of Agriculture's Agricultural Research Service
2010	Hans Falk Memorial Lecturer, National Institute of Environmental Health Sciences
2013	The Bernard G. Greenberg Alumni Endowment Award, The University of North Carolina at Chapel Hill

C. Contribution to Science

1. My research team focuses on the nutrient choline and related 1-carbon metabolism. We were the first to demonstrate a human dietary requirement for choline. Our findings have had a direct impact on global nutrition policies:

    a. **Zeisel, S.H.**, da Costa, K-A., Franklin, P.D., Alexander, E.A., LaMont, T.J., Sheard, N.F., and Beiser, A. (1991) Choline is an essential nutrient for humans. *FASEB Journal* 5: 2093-2098. PMID: 2010061.
    b. Fischer, L., da Costa, K-A., Kwock, L., Stewart, P., Lu, T, Stabler, S., Allen, R., and **Zeisel, S.H.** (2007) Sex and menopausal status influence human dietary requirements for the nutrient choline. *American Journal of Clinical Nutrition* 85(5):1275-85. PMCID: PMC2435503.
    c. Resseguie, M., Song, J., Niculescu, M., da Costa, K-A., Randall, T., and **Zeisel, S.H.** (2007) Phosphatidylethanolamine N-methyltransferase (PEMT) gene expression is induced by estrogen in human and mouse primary hepatocytes. *FASEB Journal* 10:2622-2632. PMCID: PMC2430895.
    d. Fischer, L.M., da Costa, K-A, Kwock, L., Galanko, J., **Zeisel, S.H**. (2010) Dietary choline requirements of women: effects of estrogen and genetic variation. *American Journal of Clinical Nutrition.* 92(5):1113-19. PMCID: PMC2954445.

2. We showed that perinatal availability of choline is important for normal brain development:

a. Niculescu, M., Yamamuro, Y., and **Zeisel, S.H. (**2004) Choline availability modulates human neuroblastoma cell proliferation and alters the methylation of the promoter region of the Cyclin-dependent Kinase Inhibitor 3 gene. *Journal of Neurochemistry* 89:1252-1259. PMCID: PMC1592524.
b. Albright, C.D., Mar, M-H., Craciunescu, C.N., Song, J., and **Zeisel, S.H.** (2005) Maternal dietary choline availability alters the balance of netrin-1 and DCC neuronal migration proteins in fetal mouse brain hippocampus. *Brain Research* 159:149-154. PMCID: PMC1592522.
c. Niculescu, M., Craciunescu, C.N., and **Zeisel, S.H.** (2006) Dietary choline deficiency alters global and gene-specific DNA methylation in the developing hippocampus of mouse fetal brains. *FASEB Journal* 20:43-49. PMCID: PMC1635129.
d. Mehedint, M.G., Craciunescu, C.N., **Zeisel, S.H.** (2010) Maternal dietary choline deficiency alters angiogenesis in fetal mouse hippocampus. *Proceedings of the National Academy of Sciences USA.* 107(29): 12834-39. PMCID: PMC2919920.

3. We have identified genetic polymorphisms that modify the human dietary requirement for choline. Many of these polymorphisms are surprisingly common – a finding that signifies wide-scale importance of our research:

a. Kohlmeier, M., da Costa, K-A., Fischer, L., and **Zeisel, S.H.** (2005) Genetic variation of folate-mediated one-carbon transfer pathway predicts susceptibility to choline deficiency in humans. *Proceedings of the National Academy of Sciences* 102(44): 16025-16030. PMCID: PMC1276051.
b. da Costa, K-A., Kozyrez, O.G., Song, J., Galanko, J.A., Fischer, L.M., and **Zeisel, S.H.** (2006) Common genetic polymorphisms affect the human requirement for the nutrient choline. *FASEB Journal* 20:1336-1344. PMCID: PMC1574369.
c. Johnson, A.R., Lao, S., Wang, T., Galanko, J.A., **Zeisel, S.H.,** (2012) Choline dehydrogenase polymorphism rs12676 is a functional variation and is associated with changes in human sperm cell function. *PLoS ONE.* 7(4): e36047. PMCID: PMC3338626.
d. da Costa, K-A, Corbin, K., Niculescu, M., Galanko, J., Zeisel, S.H. (2014) Identification of new genetic polymorphisms that alter the dietary requirement for choline and vary in their distribution across ethnic and racial groups. *FASEB Journal*. 28: 2970 – 2978. PMCID: PMC4062831.

4. We showed that decreased availability of choline results in fatty liver and hepatic carcinomas:

a. **Zeisel, S.H.**, Albright, C.D., Shin, O-H., Mar, M-H., Salganik, R.I., and da Costa, K-A. (1997) Choline deficiency selects for resistance to p53-independent apoptosis and causes tumorigenic transformation of rat hepatocytes. *Carcinogenesis* 18(4):731-738. PMID: 9111207
b. da Costa, K-A., Garner, S.C., Chang, J., and **Zeisel, S.H.** (1995) Effects of prolonged (1 year) choline deficiency and subsequent re-feeding of choline on 1,2,-sn-diradylglycerol, fatty acids and protein kinase C in rat liver. *Carcinogenesis* 16(2):327-334. PMID: 7859365.
c. Teng, Y-W, Mehedint, M.G., Garrow, T.A., **Zeisel, S.H.** (2011) Deletion of betaine-homocysteine *S-m*ethyltransferase in mice perturbs choline and 1-carbon metabolism, resulting in fatty liver and hepatocellular carcinoma. *Journal of Biological Chemistry.* 286(42): 36258 - 67. PMCID: PMC3196139.

5. We have developed novel mouse models for identifying the function of choline:

a. Johnson, A.R., Craciunescu, C.N., Guo, Z., Teng, Y-W., Thresher, R.J., Blusztajn, J.K., **Zeisel, S.H.** (2010) Deletion of murine choline dehydrogenase results in diminished sperm motility. *FASEB Journal.* 24(8):2752-61. PMCID: PMC2909292.
b. Teng, Y-W, Mehedint, M.G., Garrow, T.A., **Zeisel, S.H.** (2011) Deletion of betaine-homocysteine *S-m*ethyltransferase in mice perturbs choline and 1-carbon metabolism, resulting in fatty liver and hepatocellular carcinoma. *Journal of Biological Chemistry.* 286(42): 36258 - 67. PMCID: PMC3196139.
c. Tsuchiya, H., da Costa, K-A, Lee, S., Renga, B., Zhang, Y., Jaeschke, H., Smalling, R., **Zeisel, S.H.**, Fiorucci, S., Wang, L. (2015) Interactions between nuclear receptor SHP and FOXA1 maintain oscillatory homocysteine homeostasis in mice. *Gastroenterology*. 148(5):1012-1023. PMCID: PMC4409521.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=steven+zeisel

D. Research Support

Ongoing Research Support

P30 DK56350 Zeisel (PI) 09/30/99 - 03/31/16
NIH / NIDDK
UNC-Nutrition Obesity Research Center
The major goal of this center is to provide expertise and core services that increase and enhance conduct of human nutrition research.

1235-52000-051-17S Zeisel (PI) 09/15/05 - 08/31/15
US Department of Agriculture
Choline Content of Commonly Eaten Foods
The major goal of this project is to analyze the foods used by the USDA to provide nutrient database information to investigators and consumers. The USDA will provide UNC homogenized food samples and we will perform analyses.

No Grant Number (Zeisel) 02/01/12 - 01/31/17
Nestle
Develop a screening platform using cell culture and mouse models that will identify bioactives in milk, foods and plants that have potential to enhance brain development and function.

WS2307649 (Cheatham) 04/01/12 – 03/31/17
Nestle
Effects of choline, docosahexaenoic acid, tocopherol, and lutein on human infant cognition with assessment of the effects of genetic variation.
The proposed studies will examine whether a mixture of DHA, choline, tocopherol and lutein enhances cognitive development in humans and whether there are genotype-definable responders and non-responders to these treatments.
Role: Investigator

R25 GM103802-01 (Kohlmeier/Zeisel) 09/18/12 – 08/31/17
NIH
Online learning platform: introducing clinicians and researchers to metabolomics
The goal of this grant is to being metabolomics science to researchers and clinicians, preparing them to decode reports of metabolomics research and start thinking about using current metabolomics technology and resources for their bench and clinical research.

Completed Research Support

No Grant Number (Zeisel)
Dole
A new approach for identification of functionally active phytochemicals identified in the “Tail-of-the-Kite” project.
Proposal for a new approach for identifying antioxidant phytochemicals.

R25 CA134285 Zeisel (PI) 07/01/08 - 06/30/13
NIH / NCI
Nutrition Education for Practicing Physicians
The major aim of this study is to deliver a web-based medical nutrition training program for medical residents and other postgraduate physician learners.

No Number Zeisel (PI) 01/01/12 – 06/30/13
American Egg Board (No cost extension)
Determining Whether Egg Ingestion Increases Plasma TMAO and Activates LDL Oxidation in Humans

The major goal of this grant is to study whether humans eating eggs generate TMAO (trimethylamine oxide) and if so, does this only occur at a high intake of eggs. This grant will also determine whether there is a minimum threshold level of TMAO needed to cause increased oxidation of low density lipoprotein (LDL).

No Grant Number Zeisel (PI) 04/01/12 - 09/30/13
Bill and Melinda Gates Foundation
Grand Challenges Round 8: Choline and Optimal Development
The goal of this study is to establish methods to conduct a full scale choline-intervention study in a representative region of Gambia.

R01 DK55865 Zeisel (PI) 09/01/00 - 01/31/13
NIH / NIDDK (no cost extension)
Human Requirements for the Nutrient Choline
The major goals of this project is to better understand the how genetic polymorphisms influence the dietary requirements for choline.

R01 CA109753 Chen (PI) 06/26/06 – 04/30/12
NIH/NCI (No cost extension)
Dietary methyl content, epigenetics and etiology of breast cancer (Gammon, PI of subcontract at UNC)
Investigate whether the methyl content of the diet and methyl metabolism influences pathogenesis of breast cancer through epigenetic mechanisms.
Role: Investigator

09/30/05 - 03/31/11
NIH / NIDDK
Obesity in Asians Supplement - UNC Nutrition Obesity Research Center Parent Grant
Examine Asians living in China and Whites and Blacks living in the United States.