

Mihai Dinu Niculescu, MD, PhD

Assistant Professor

Nutrition Research Institute at Kannapolis
School of Public Health and School of Medicine
University of North Carolina at Chapel Hill

Experience, Professional

2008 Nutrition Research Institute at Kannapolis, Assistant Professor, UNC Department of Nutrition

- Developing new research on the roles that maternal diet has on the epigenetic regulation of fetal brain development. Specific interests include α -linolenic acid, high-fat diets and maternal obesity, and soy isoflavones.

2006-2008 University of North Carolina at Chapel Hill, Research Assistant Professor, Department of Nutrition

- Collaborate with the principal investigator in designing and writing grant proposals, and implementing approved grants.
- Supervise and coordinate scientific activity within Zeisel Lab.
- Implementing new research techniques (laser-capture micro-dissection, statistical analysis for gene expression arrays and real-time RT-PCR, etc.).
- Supervise and coordinate graduate and undergraduate students, in collaboration with Steven H. Zeisel.
- Invited member in the dissertation committee for the PhD candidates within the UNC School of Dentistry.

2005-2006 University of North Carolina at Chapel Hill, Research Associate, Department of Nutrition

- Design and manage animal and cell culture studies with a research team.
- Develop assays using DNA-modifying techniques, gene expression using micro-arrays and polymerase chain reaction (PCR), protein expression and other molecular biology techniques.
- Manage and coordinate laboratory activity.
- Collaborate with the principal investigator in designing, writing and implementing approved grants and grant proposals.

2001-2005 University of North Carolina at Chapel Hill, Ph.D. Candidate, Nutrition Laboratory of Dr. Steven H. Zeisel, Department of Nutrition

- Completed *in vitro* and animal studies to determine the mechanisms by which dietary choline deficiency alters brain development during fetal life.
- Used and developed biochemical and molecular biology assays (DNA methylation, gene and protein expression, laser-capture micro-dissection, siRNA transfection, liquid chromatography, etc.).

2000-2001 University of North Carolina at Chapel Hill, Postdoctoral Fellow, Department of Nutrition

- Conducted research on the effects of choline deficiency on fetal brain development.

1996-2000 Transilvania University in Brasov, Romania, Assistant Professor, School of Medicine, Department of Human Physiology

- Taught and designed selected courses in Human Physiology for medical students (Digestion, Excretion, Blood, Cardiovascular, and Neuro-endocrine systems).
- Taught and designed laboratory classes in Human Physiology.
- Directed student research; organized and hosted student research seminars.

1997-1999 The “MiroMedica” Family Practice and Medical Laboratory, Brasov, Romania, co-founder and manager

- Coordinated the activity of six doctors and three staff members.
- Conducted medical activity.

Education

**2001-2005, Doctor of Philosophy, Nutrition
University of North Carolina at Chapel Hill**

**1996-2000, Family Practice Resident
Brasov County Hospital, Romania**

**1989-1995, Doctor of Medicine
Carol Davila University of Medicine, Bucharest, Romania**

Honors

- ASNS – Gerber Foundation Fellowship for Outstanding Research, 2003
- The Graduate School UNC: Dean’s Award for Graduate Student Research Benefiting North Carolina, 2003
- ASNS – Procter & Gamble Abstract Competition, 2003

Membership in Professional Societies

- American Society of Nutrition (ASN); 2003-present

Grant Support – Current

- NIH, P01 AG09525, Parent Program – Brain Aging: Effects of Perinatal Nutrition (J. Blusztajn, Program Director), Daughter project – Biochemistry of Supplemental Choline in Neonatal Rats (S. Zeisel, PI), 04/01/05-03/31/10. \$1,300,000.
- UNC-CH, University Research Council. Genistein alters the DNA methylation and the phenotype of mouse neural progenitors (M. Niculescu, PI), 12/01/07-11/30/09. \$5,000.
- UNC-CH CNRC, P30 DK056350. Maternal high-fat diet alters the fetal brain development by epigenetic mechanisms (M. Niculescu, PI), 04/01/08-03/31/09. \$22,000.
- CECN-Mead Johnson. Maternal availability of alpha-linolenic acid during lactation alters postnatal brain development (M. Niculescu, PI). \$70,000.

Grant Support – History

- NIH, P01 AG09525, Parent Program – Brain Aging: Effects of Perinatal Nutrition (J. Blusztajn, Program Director), Daughter project – Biochemistry of Supplemental Choline in Neonatal Rats (S. Zeisel, PI), 4/01/92-3/31/05. \$693,441.
- USDA, 2005-3520015247, Dietary Choline and Folic Acid and Optimal Brain Development (S. Zeisel, PI), 7/1/04-6/30/06. \$425,000.

- NIEHS, R21 ES012997, Diethanolamine Alters Brain Development (S. Zeisel PI), 04/01/04-03/31/07. \$438,000.

**Publications
Peer Reviewed**

1. **Niculescu MD**, Yamamuro Y, Zeisel SH. (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(5):1252-1259.
2. **Niculescu MD**, Craciunescu CN, Zeisel SH. (2005) Gene expression profiling of choline-deprived neural precursor cells isolated from mouse brain. *Brain Research - Molecular Brain Research*, 134(2):309-322.
3. **Niculescu MD**, Craciunescu CN, Zeisel SH. (2006) Dietary choline deficiency alters global and gene specific DNA methylation in the developing hippocampus of mouse fetal brains. *The FASEB Journal*, 20(1):43-49.
4. da Costa KA, **Niculescu MD**, Craciunescu CN, Fischer LM, Zeisel SH. (2006) Choline deficiency increases lymphocyte apoptosis and DNA damage in humans. *The American Journal of Clinical Nutrition*, 84:88-94.
5. **Niculescu MD**, Pop EA, Fischer LM, Zeisel SH. (2007) Dietary isoflavones differentially induce gene expression changes in lymphocytes from postmenopausal women who form equol as compared with those who do not. *The Journal of Nutritional Biochemistry*, Jun 18(6):380-90. Epub 2006 Sep 8.
6. **Niculescu MD**, Wu R, Guo Z, da Costa KA, Zeisel SH. (2007) Diethanolamine Alters Proliferation and Choline Metabolism in Mouse Neural Precursor Cells. *Toxicol Sci*, 96(2):321-326.
7. Strauss KA, Morton DH, Puffenberger EG, Hendrickson C, Robinson DL, Wagner C, Stabler SP, Allen RH, Chwatko G, Jakubowski H, **Niculescu MD**, Mudd SH. (2007) Prevention of brain disease from severe 5,10-methylenetetrahydrofolate reductase deficiency. *Mol Genet Metab*, 91(2):165-75. Epub 2007 Apr 3.
8. Resseguie M, Song J, **Niculescu MD**, da Costa KA, Randall TA, Zeisel SH. (2007) Phosphatidylethanolamine N-methyltransferase (PEMT) gene expression is induced by estrogen in human and mouse primary hepatocytes. *FASEB J*, Apr 21(10):2622-32. Epub 2007 Apr 24.
9. **Niculescu MD**, da Costa KA, Fischer LM, Zeisel SH. (2007) Lymphocyte gene expression in subjects fed a low-choline diet differs between those who develop organ dysfunction and those who do not. *Am J Clin Nutr*, 86(1):230-9.
10. Mehedint MG, **Niculescu MD**, Craciunescu CN, Zeisel SH. (**in preparation**) Choline deficiency alters global histone methylation and chromatin remodeling on RE1 site of the calbindin 1 gene.

**Publications
Non-Peer Reviewed**

1. **Niculescu MD**, Zeisel SH. (2002) Diet, methyl donors and DNA methylation: interactions between dietary folate, methionine and choline. *Journal of Nutrition*, 132(8 Suppl):2333S-2335S.
2. Zeisel, S.H., **Niculescu, M.D.** (2006) Perinatal choline influences brain structure and function. *Nutrition Reviews*, 64(4):197-203.

Book Chapters

1. Zeisel, S.H., **Niculescu, M.D.** (2005) Choline and Phosphatidylcholine. In *Modern Nutrition in Health and Disease* (M.E. Shils, M. Shike, A.C. Ross, B. Caballero, R.J. Cousins, eds) Lippincott Williams & Wilkins, Philadelphia, pp. 525-536.
2. **Niculescu, M.D.**, Zeisel, S.H. (2008) Choline and Neural Development. In *Nutrition in the Prevention and Treatment of Disease*, 2nd Edition (Coulston, A. and Boushey, C., Eds.) Elsevier Inc., Boston, pp. 241-

Abstracts

1. **Niculescu, M.D.**, Zeisel, S.H., Meeker, R.B. (2002) Extracellular choline availability alters DNA-methylation and apoptosis in embryonic brain neurons from the rat. *The FASEB Journal*, 16(4):A643.
2. **Niculescu, M.D.**, Yamamuro, Y., Zeisel, S.H. (2003) Choline Deficiency Inhibits Cell Proliferation and is Associated with Hypomethylation of CDKN3 Promoter in IMR-32 Cells. *The UNC Graduate School Centennial*, Chapel Hill, NC, *The FASEB Journal*, 17(5):A1092.
3. da Costa, K., **Niculescu, M.D.**, Zeisel, S.H. (2003) Micro array analysis of changes in gene expression in choline deficient humans. *The FASEB Journal*, 17(5):A1157.
4. da Costa, K., **Niculescu, M.D.**, Badea, M., Craciunescu, C.N., Zeisel, S.H. (2003) Choline deficiency induces apoptosis and DNA damage in human lymphocytes *in vivo*. *The FASEB Journal*, 17(5):A1157.
5. **Niculescu, M.D.**, Craciunescu C.N., Zeisel S.H. (2006) Dietary choline deficiency alters global and gene specific DNA methylation in the developing hippocampus of mouse fetal brains. *Environmental Epigenomics Conference*, Durham, NC. *The FASEB Journal*, 20(4):A609.
6. Pop, E.A., **Niculescu, M.D.**, Fischer, L.M., Zeisel, S.H. (2006) Isoflavone-induced gene expression changes in lymphocytes from postmenopausal women. *The FASEB Journal*, 20(4):A612.
7. **Niculescu, M.D.**, Craciunescu, C.N., Wu, R., Mehedint, M.G., Zeisel, S.H. (2006) Diethanolamine treatment and choline deficiency induce similar alterations of neurogenesis in fetal mouse hippocampus. *The Neuroscience 2006 Conference*, Atlanta, GA.
8. Mehedint, M.G., **Niculescu, M.D.**, Craciunescu, C.N., Zeisel, S.H. (2008) Choline deficiency influences the interaction between REST, chromatin methylation and altered fetal neurogenesis. *The FASEB Journal*, 22:689.5.
9. Mehedint, M.G., Craciunescu, C.N., **Niculescu, M.D.**, Sin, K.M., Zeisel, S.H. (2008) Choline deficiency alters angiogenesis in the fetal brain. *The FASEB Journal*, 22:1122.19.

Courses Taught

- Human Physiology: year I, School of Medicine, Transilvania University in Brasov, Romania. 1996-2000.
- Human Physiology: year II, School of Medicine, Transilvania University in Brasov, Romania. 1996-2000.
- Human Physiology – Laboratory Practice: year I & 2, School of Medicine, Transilvania University in Brasov, Romania. 1996-2000.
- NUTR 40 Introduction in Human Nutrition – UNC Chapel Hill, Niculescu guest lecture on antioxidants. 2004.
- NUTR 885 Doctoral Seminar – UNC Chapel Hill. 2007-2008.
- NUTR 620 Micronutrients – UNC Chapel Hill, Niculescu guest lecture on B₁₂, Folate, Choline, S-adenosylmethionine & DNA methylation. 2007.
- NUTR 868 Nutrients and Disease: Brain Function and Development – UNC Chapel Hill, Niculescu faculty leader on Choline and Brain. 2008.
- NUTR 845 Nutritional Metabolism – UNC Chapel Hill. Invited expert on Trans-generational epigenetics. 2008.

Ph.D. Candidacy Committees

- Shaoping Zhang, Oral Biology Program, UNC School of Dentistry, 2007