

**BIOGRAPHICAL SKETCH**

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NAME David S. Newburg, Ph.D.		POSITION TITLE Associate Professor of Pediatrics, Harvard Medical School Glycobiologist, Mass. General Hospital	
eRA COMMONS USER NAME davidnewburg			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Massachusetts (Amherst)	B.S.	1970	Chemistry
Boston University Graduate School	Ph.D.	1976	Biochemistry & Nutrition

**A. Positions and Employment**

1974-1976 Res Assoc, Dept of Nutritional Sciences, Boston University Medical Center  
 1976-1982 Asst Prof, Dept of Nutrition & Food Science, University of Kentucky, Lexington  
 1982-1986 Assoc Prof, Dept of Nutrition & Food Science, University of Kentucky  
 1986-1992 Assoc Biochemist, Dept of Biochemistry, E.K. Shriver Center, Waltham, MA  
 1988-1991 Res Fellow in Neurology, Faculty of Medicine, Harvard University  
 1988-1993 Asst Biochemist in Neurology, Massachusetts General Hospital  
 1991-2000 Instructor in Neurology, Faculty of Medicine, Harvard University  
 1992-2000 Senior Scientist (Biochemist), Dept of Biomedical Sciences, E.K. Shriver Center  
 1993-2000 Assoc Biochemist in Neurology, Massachusetts General Hospital  
 1998-2004 Director, Program in Glycobiology, E.K. Shriver Center  
 2000-2004 Professor of Biochem & Molec Pharmacol, Univ of Mass Med School, Worcester, MA  
 2001-2004 Professor, Grad Sch of Biomedical Sciences, Univ of Mass Med School  
 2004-pres Glycobiologist, Pediatric Gastroenterology & Nutrition, Massachusetts General Hospital  
 2004-pres Director, Program in Glycobiology, Massachusetts General Hospital  
 2004-pres Director, Cell Biology Core, Clinical Nutrition Research Center at Harvard  
 2006-pres Associate Professor of Pediatrics, Harvard Medical School

**Other Experience and Professional Memberships**

International Society for Research on Human Milk and Lactation: 1989-90 Nominating  
 Committee; 1993-96 Executive Committee; 1997 Chair, International Meeting  
 Society for Glycobiology: 1996 Symposium Chair  
 Boston Glycobiology Discussion Group: 1994-pres, President  
 American Society for Nutritional Sciences (ASNS): 1991, 1993-1995 Minisymposium co-chair;  
 2004 Symposium co-chair  
 American Pediatrics Society, 2006

**B. Selected Peer-reviewed Publications**

Yolken RH, Peterson JA, Vonderfecht SL, Fouts ET, Midthun K, Newburg DS. Human milk mucin inhibits rotavirus replication and prevents experimental gastroenteritis. *J Clin Invest* 1992;90:1984-1991.

Chaturvedi P, Warren CD, Ruiz-Palacios GM, Pickering LK, Newburg DS. Milk oligosaccharide profiles by reversed-phase HPLC of their perbenzoylated derivatives. *Anal Biochem* 1997;251:89-97.

Newburg DS, Peterson JA, Ruiz-Palacios GM, Matson DO, Morrow AL, Shults J, Guerrero ML, Chaturvedi P, Newburg SO, Scallan CD, Taylor MR, Ceriani RL, Pickering LK. Role of human milk lactadherin in protection against symptomatic rotavirus infection. *Lancet* 1998;351:1160-1164.

Newburg DS. Oligosaccharides in human milk and bacterial colonization. *J Pediatr Gastroenterol Nutr* 2000;30:S8-S17.

Dai D, Nanthakumar NN, Newburg DS, Walker WA. Role of oligosaccharides and glycoconjugates in intestinal host defense. *J Pediatr Gastroenterol Nutr* 2000; 30:S23-S33.

Shen Z, Warren CD, Newburg DS. High-performance capillary electrophoresis of sialylated oligosaccharides of human milk. *Anal Biochem* 2000;279:37-45.

Bulik DA, van Ophem P, Manning JM, Shen Z, Newburg DS, Jarroll EL. UDP-*N*-acetylglucosamine pyrophosphorylase, a key enzyme in encysting *Giardia*, is allosterically regulated. *J Biol Chem* 2000;275:14722-14728.

Chaturvedi P, Warren CD, Altaye M, Morrow AL, Ruiz-Palacios GM, Pickering LK, Newburg DS. Fucosylated human milk oligosaccharides vary among individuals over the course of lactation. *Glycobiology* 2001;11:365-372.

Shen Z, Warren CD, Newburg DS. Resolution of structural isomers of sialylated oligosaccharides by capillary electrophoresis. *J Chromatogr A* 2001;921(2):315-321.

Newburg DS, Editor. *Bioactive Components of Human Milk*. NY: KluwerAcad/Plenum, 2001.

Dai D, Nanthakumar NN, Savidge TC, Newburg DS, Walker WA. Region-specific ontogeny of  $\alpha$ 2,6 sialyltransferase during normal and cortisone-induced maturation in the mouse intestine. *Am J Physiol Gastrointest Liver Physiol* 2002;282:G480-G490.

Nanthakumar NN, Dai D, Newburg DS, Walker WA. *The role of indigenous microflora in the development of murine intestinal fucosyl- and sialyltransferases*. *FASEB J* (November 15, 2002) 10.1096/fj.02-0031fje (summary: *FASEB J* 2003; 17: 44-46).

Ruiz-Palacios GM, Cervantes LE, Ramos P, Chavez-Munguia B, Newburg DS. *Campylobacter jejuni* binds intestinal H(O) antigen (Fuc $\alpha$ 1,2Gal $\beta$ 1,4GlcNAc), and fucosyloligosaccharides of human milk inhibit its binding and infection. *J Biol Chem* 2003;278:14112-20.

Huang P, Farkas T, Marionneau S, Zhong W, Ruvoën-Clouet N, Morrow AL, Altaye M, Pickering LK, Newburg DS, LePendou J, Jiang X. Noroviruses bind to human ABO, Lewis and secretor histo-blood group antigens: Identification of four distinct strain-specific patterns. *J Infect Dis* 2003;188:19-31.

Newburg DS, Ruiz-Palacios GM, Altaye M, Chaturvedi P, Meinzen-Derr J, Guerrero ML, Morrow AL. Innate protection conferred by fucosylated oligosaccharides of human milk against diarrhea in breastfed infants. *Glycobiology* 2004;14:253-263.

Morrow AL, Ruiz-Palacios GM, Altaye M, Jiang X, Guerrero ML, Meinzen-Derr JK, Farkas T, Chaturvedi P, Pickering LK, Newburg DS. Human milk oligosaccharides are associated with protection against diarrhea in breastfed infants. *J Pediatr* 2004;145:297-303

Jiang X, Huang P, Zhong W, Tan M, Farkas T, Morrow AL, Newburg DS, Ruiz-Palacios GM, Pickering LK. Human milk contains elements that block binding of Noroviruses to human histo-blood group antigens in saliva. *J Infect Dis* 2004;190:1850-9.

Nanthakumar NN, Dai D, Meng D, Chaudry N, Newburg DS, Walker WA. Regulation of intestinal ontogeny: Effect of glucocorticoids and luminal microbes on galactosyltransferase and trehalase induction in mice. *Glycobiology* 2005;15(3):221-232.

Newburg DS, Morrow AL, Ruiz-Palacios GM. Human milk glycans protect infants against enteric pathogen. *Annu Rev Nutr* 2005;25:2537-58.

Stepans MBF, Wilhelm SL, Hertzog M, Rodehorst TKC, Blaney S, Clemens B, Polak JJ III, Newburg DS. Early consumption of human milk oligosaccharides and infant diseases. *Breastfeeding Medicine* 2006;1:207-215.

Newburg DS, Walker WA. Protection of the neonate by the innate immune system of developing gut and of human milk. *Pediatr Res* 2007;61:2-8.

## C. Research Support

### Ongoing Research Support

PO1 HD13021 (Morrow) 04/01/03 - 03/31/08  
NIH, NICHD

#### *Role of Human Milk in Infant Nutrition and Health: Glycobiology Core*

The purpose of this program project is to study the bioactive components of human milk. The aim of the Glycobiology Core is to isolate and characterize carbohydrate-containing compounds of human milk that protect the infant from enteric disease, including *Campylobacter jejuni*, *Vibrio cholerae*, caliciviruses, noroviruses, and rotavirus; measure concentrations of milk oligosaccharides and glycoconjugates in individual milk samples; and, synthesize bioactive oligosaccharides and neoglycoproteins.

Role: PI of this core

PO1 HD13021 (Morrow) 04/01/03 - 03/31/08  
NIH, NICHD

#### *Role of Human Milk in Infant Nutrition and Health: Stable Toxin*

The purpose of this program project is to study the bioactive components of human milk. The aim of the ST project is to isolate and characterize the milk oligosaccharide that protects against the toxicity of stable toxin of *E. coli* and to determine the mechanism of this inhibition, its distribution in human milk, and its efficacy in human population. Developing a method for the synthesis of this oligosaccharide is also a goal of this project.

Role: PI of this subproject

RO1 DK070260 (Walker) 05/01/05-04/30/10  
NIH-NIDDK

#### *Ontogeny of the Human Intestinal Mucosal Barrier and NEC*

The major goals of this project are to study: 1) bacterial colonization and its pattern in NEC patients 2) the developmental regulation of antibacterial products of Paneth cells at various ages (fetal - childhood and in NEC patients) 3) the functional significance of the human fetal intestinal Fc receptor for human IgG and 4) selective aspects of intestinal inflammatory responses and immune function.

Role: Investigator

2 PO1 DK33506-21 (Pothoulakis) 9/30/05-08/31/10  
NIH-NIDDK

Project 5 – (Kelly)

#### *Barrier Function of the GI Tract in Health and Disease*

The major goals of this project are: 1) to define the developmental response of the immature human intestine to inflammatory stimuli, including endotoxin and IL-1 $\beta$ , using IL-8 secretion as an effector response including: a) defining the role of toll-like receptors (TLR), CD14, and lipopolysaccharide binding protein (LBP) molecules; b) determining if IL-1 $\beta$  postreceptor signal transduction steps leading to NF $\kappa$ B expression are involved; c) characterizing the effects of butyrate, including histone acetylation and d) finally determining if known maturational (trophic) factors such as cortisone, EGF, etc., can modulate developmental differences. 2) To define the developmental response of the immature human intestine to exotoxins (CT/LT) using chloride secretion as the effector response including: a) determining the number and affinity of toxin binding sites; b) characterizing postreceptor signal transduction events including: (1) ADP-ribosylation of GTP-

stimulatory protein alpha ( $G_s\alpha$ ) and (2) expression of ADP-ribosylation factor; c) defining toxin effector responses including: quantitation of CFTR expression and phosphorylation; d) characterizing the role of serotonin (5-hydroxytryptamine, 5HT) and prostaglandin E2 ( $PGE_2$ ) and e) finally determining if known maturational (trophic) factors including cortisone, EGF, etc. can modulate developmental differences.

Role: Investigator

P30 DK40561-10S1 (Walker)

09/30/99-03/31/11

NIH/NIDDK

*Clinical Research Nutrition Center*

Specific aims of project: The major specific aims are: 1) to provide research in basic areas of biology relevant to problems in clinical nutrition; 2) to promote the study of clinical nutrition and application of knowledge derived there from within the HMS, MIT and HSHP community; 3) to promote interactions among scientists and clinical investigators to show relevance to advancing the science of clinical nutrition; and 4) to attract "basic" investigators into the domain of clinical nutrition to promote an environment and mechanism to develop new investigator-initiated research.

Role: Director, Cell Biology Core

Hong Kong Association for HealthCare 1/1/2007–12/31/2009

*Activity of T. versicolor (PSP) intestinal digestion products in mucosal immunity and against cancer*

The goal of this project is to isolate and define the biologically active glycans from an extract of *Trametes versicolor*, a traditional East Asian botanical whose oral ingestion is reported to inhibit cancer and enteric inflammation.

Role: Principal Investigator

**Completed**

PO1 HD13021 (Morrow)

04/01/98 - 03/31/03

NIH, NICHD

*Role of Human Milk in Infant Nutrition and Health: Biochemical Core*

Role: PI of this core

*Role of Human Milk in Infant Nutrition and Health: Stable Toxin*

Role: PI of this subproject

Pilot Feasibility Project (Newburg)

9/1/02-8/31/03

Clinical Nutrition Research Center at Harvard

*Human Milk Oligosaccharides and Fluid Homeostasis of Gut*

The purpose of this application was to test the hypothesis that the human milk oligosaccharide fraction contains a component that inhibits intestinal guanylin and uroguanylin, thereby contributing to fluid and electrolyte homeostasis in the breastfed infant.

Role: PI

RO1DK59811 (Newburg)

09/30/00 – 07/31/05

NIH/NIDDK

*Endothelial Gb<sub>3</sub> Species Involved in HUS Pathogenesis*

The goal of this project is to better understand the involvement of CNS in many cases of HUS by comparing microvascular endothelial cells from human brain with endothelial cells from the kidney glomerulus.

Measuring the relative amounts of Gb<sub>3</sub>, any increase in Gb<sub>3</sub> induced by cytokines, and relative sensitivity of these two types of endothelial cells to Shiga toxin before and after cytokine stimulation will help to understand the relative sensitivities of these two types of cells. In each of these types of endothelial cell, the species of Gb<sub>3</sub> that relates most strongly to toxin sensitivity will be ascertained.

Role: PI