BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Jörn-Hendrik Weitkamp, MD	Assistant Professor of Pediatrics
eRA COMMONS USER NAME (credential, e.g., agency login) weitkah	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Graf-Adolf-Gymnasium, Tecklenburg, Germany	Baccalaureate	06/1985	Biology
University of Ulm, Ulm, Germany	MD	07/1995	Medicine / Gastroenterology
Vanderbilt University, Nashville, TN	Postdoctoral	06/2002	Pediatric Infectious Diseases
Vanderbilt University, Nashville, TN	Postdoctoral	10/2006	Neonatal-Perinatal Medicine

A. Personal Statement.

My laboratory focuses on the development of mucosal immune regulation in preterm infants. Premature infants are at high risk for long-lasting complications following a fetal inflammatory response. I am an Early Stage Investigator seeking to attain my first R01 grant. I am a board-certified Pediatrician with additional post-doctoral training in Pediatric Infectious Diseases and Neonatal-Perinatal Medicine. I am therefore well versed in the specific inflammatory/immune complications that arise in the newborn following chorioamnonitis and maternal immune activation. As post-doctoral fellow in the laboratory of Dr. James E. Crowe, Jr. at Vanderbilt, I created new technologies allowing for the first time to compare the genetic antibody repertoire in virus-specific B cells between infants and adults (e.g. Weitkamp et al. *J Immunol Methods* 2003, Weitkamp et al. *J Immunol* 2003 and 2005, Weitkamp et al. *Hum Immunol* 2005 and 2006). Of high relevance to this application, I expanded my research experience as a faculty member to study the development of T regulatory cells (Tregs). As part of my NIH K08 award, I developed tools for pioneer studies on the ontogeny and function of immune effector and suppressor cells in the premature intestine (e.g. Weitkamp et al. *Pediatr Dev Pathol* 2009, Weitkamp et al. *Gut* 2013, Weitkamp et al. *PONE* 2014). To overcome the ethical and technical limitations of human immunology research in this population, we customized multicolor flow cytometry protocols (which will be utilized in this proposal) and T cell assays from small number of lymphocytes isolated from peripheral blood and surgically resected intestinal tissue specimens from preterm infants. Work from these projects has resulted in several independent and peer-reviewed manuscripts and we have used a combination of these methodologies to obtain the preliminary data for this application (e.g. Weitkamp et al. *Gut* 2013, Weitkamp et al. *PONE* 2014, Van Kaer et al. *Immunity* 2014). I laid the groundwork for the proposed research by establishing a large metadata-linked repository of prospectively collected peripheral blood and intestinal mucosa lymphocytes from preterm infants admitted at Vanderbilt and built the collaborative infrastructure for a comprehensive analysis of the molecular mechanisms and clinical outcomes of fetal immune priming. Because of my background and experience, I am fully prepared to carry out the research proposed in this application, which is a logical extension of the work I initiated during my K-funding period.

B. Positions and Honors.

Positions and Employment

1995-1998 Medical Residency, Pediatrics, University of Bonn, Bonn, Germany
1998-2002 Medical Fellowship, Pediatric Infectious Diseases, Vanderbilt University, Nashville, TN
2002-2004 Medical Residency, Pediatrics, Vanderbilt University, Nashville, TN
2004-2006 Medical Fellowship, Neonatal-Perinatal Medicine, Vanderbilt University, Nashville, TN
2006-Present Assistant Professor, Department of Pediatrics, Vanderbilt University, Nashville, TN

Other Experience and Professional Memberships

2002-Present Member, Fellow, American Academy of Pediatrics
2006-Present Member, Perinatal Section of the American Academy of Pediatrics
2009-Present Member, Perinatal Research Society (elected)

2010-Present Member, Society for Pediatric Research (elected)
2010 Peer Review Panel (ad hoc) Medical Research Council (United Kingdom),
2011 Special Emphasis Panel NIH/NICHD Loan Repayment Project (LRP)
2012 Special Emphasis Panel NIH/NICHD Loan Repayment Project (LRP)
2013 Special Emphasis Panel NIH/NICHD Loan Repayment Project (LRP)
2012 Session Chair, *Intestinal Epithelial Defense: Role in Pediatric Diseases,* Topic Symposium, Annual Meeting of the American Pediatric Society and Society for Pediatric Research, Boston, MA, May 2012
2012 Peer Review Panel (ad hoc) American Diabetes Association
2013-Present Study Section (ad hoc) National Institute of Health (NIH) Cellular and Molecular Immunology-B (CMIB)
2013 Session Chair, *Chorioamnionitis and the Fetal Response to Inflammation: Effects for the Developing Infant,* Topic Symposium, Annual Meeting of the American Pediatric Society and Society for Pediatric Research, Washington, DC, May 2013
2013 Workshop Leader, *A Practical Guide to Understanding the Techniques and Tools for Human Microbiome Studies,* Annual Meeting of the American Pediatric Society and Society for Pediatric Research, Washington, DC, May 2013
2014 Session Chair, *Nanotechnology and Organs-on-a-Chip: Emerging Technologies to Study Physiology and Test Therapies in Human Infants,* Topic Symposium, Annual Meeting of the American Pediatric Society and Society for Pediatric Research, Vancouver, Canada, May 2014
2013-2015 Chair, Society for Pediatric Research Student Research and House Officer Awards Selection Committee
2013-Present Academic Editor PLoS ONE
2014-Present Chair, Research Committee, Section on Perinatal Pediatrics, American Academy of Pediatrics
2014-Present Member, Vanderbilt Kennedy Center

Honors

2001 Infectious Diseases Society of America & Bayer/Harold Neu Postdoctoral Fellowship Award
2002 Young Investigator Travel Award from the Society for Mucosal Immunology
2002 Special Citation Award for the abstract submitted to the 40th Annual meeting of the Infectious Diseases Society of America
2005 Marshall Klaus Perinatal Research Award
2006 Vanderbilt Infection Prevention Award
2007 NIH Young Investigator Travel Award: Perinatal Research Society
2007 Vanderbilt Physician Scientist Development Award
2008 Vanderbilt DDRC Young Investigator Award
2009 Vanderbilt DDRC Young Investigator Award
2009 Induction into the *Perinatal Research Society*
2010 Induction into the *Society for Pediatric Research*

C. Peer-reviewed publications (selected from 42 total, * corresponding author)

Most relevant to the current application

1. **Weitkamp JH**, Kallewaard N, Kusuhara K, Feigelstock D, Feng N, Greenberg H, Crowe JE Jr. Generation of recombinant human monoclonal antibodies to rotavirus from single antigen-specific B cells selected with fluorescent viruslike-particles. J Immunol Methods 2003; 275:223-237.
We developed a new technology to study genetic antibody repertoires in virus-specific B cells from human infants.

2. **Weitkamp JH**, Kallewaard N, Kusuhara K, Bures E, Williams JV, LaFleur B, Greenberg H, Crowe JE Jr. Infant and adult human B cell responses to rotavirus share common immunodominant variable gene repertoires. J Immunol 2003; 171(9):4680-4688.
We defined for the first time the genetic antibody repertoire for rotavirus in infected children and adults.

3. **Weitkamp JH**, Kallewaard NL, Bowen AL, Lafleur BJ, Greenberg HB, Crowe JE Jr. VH1-46 is the dominant immunoglobulin heavy chain gene segment in rotavirus-specific memory B cells expressing the intestinal homing receptor alpha4beta7. J Immunol 2005; 174(6):3454-3460.
We identified a critical antibody gene segment for mucosal immunity against rotavirus.

4. **Weitkamp JH***, Lafleur BJ, Greenberg HB, Crowe JE Jr. Natural evolution of a human virus-specific antibody gene repertoire by somatic hypermutation requires both hotspot-directed and randomly-directed processes. Hum Immunol 2005; 66(6):666-676.
We performed a molecular analysis of the human virus-specific antibody repertoire.

5. **Weitkamp JH***, Lafleur BJ, Crowe JE Jr. Rotavirus-specific CD5+ B cells in young children exhibit a distinct antibody repertoire compared to CD5- B cells. Hum Immunol 2006; 67(1-2):33-42.
We analyzed $CD5^+$ rotavirus-specific B cells in children.

6. **Weitkamp JH***, Rudzinski E, Koyama T, Correa H, Matta P, Alberty, JB, Polk DB. Ontogeny of FOXP3+ regulatory T cells in the postnatal human small intestinal and large intestinal lamina propria. Pediatr Dev Pathol 2009; 12(6):443-449 *(Journal Cover)*, PMCID: PMC2844857.
We reported for the time the ontogeny of mucosal T regulatory (Tregs) in the intestine of human infants.

7. McElroy S, Hobbs S, Kallen M, Rosen MJ, Grishin A, Matta P, Upperman J, Ford H, Polk DB, **Weitkamp JH*.** LPS transactivation of EGFR stimulates COX-2 expression in enterocytes, PLoSOne 2012, 7(5) e38373, doi: 10.1371/journal.pone.0038373. PMCID: PMC 3364993.
This publication stimulated our interest in the cellular signaling pathways initiated by endotoxin (LPS).

8. Rosen MJ, Chaturvedi R Washington MK, Kuhnheim LA, Moore PD, Coggeshall SS, McDonough EM, **Weitkamp JH,** Singh AB, Coburn LA, Williams CS, Van Kaer L, Peebles RS, Wilson KT. STAT6 deficiency ameliorates severity of oxazolone colitis by decreasing expression of claudin-2 and Th2-inducing cytokines, J Immunol, 2013; 190(4):1849-1858. PMCID: PMC 3563924.
We collaborated by assisting in experiments and data interpretation regarding function and regulation of Th2-type CD4 T helper cells.

9. **Weitkamp JH***, Koyama T, Rock MT, Correa H, Goettel JA, Matta P, Kyra Oswald-Richter K, Rosen MJ, Engelhardt BG, Moore DJ, Polk DB. Necrotizing enterocolitis is characterized by disrupted immune regulation and diminished mucosal regulatory ($FOXP3^+$) / effector ($CD4^+$, $CD8^+$) T cell ratios, Gut, 2013, 62:73-82. PMCID: PMC 3606820.
Here we established for the first time the significant deficiency of functional Tregs in the intestinal mucosa of preterm infants with necrotizing enterocolitis (NEC) compared to gestational age matched surgical controls.

10. **Weitkamp JH***, Rosen MJ, Zhiguo Z, Koyama T, Denning T, Rock MT, Moore DJ, Matta P, Denning PW. Small intestinal intraepithelial TCR$\gamma\delta$ lymphocytes are present in the premature intestine but selectively reduced in surgical necrotizing enterocolitis, *PLoS One,* 9(6):e99042, **2014**. PMCID: PMC 4048281.
We characterize for the first time these relatively poorly described unusual T cells cells in the premature intestine.

11. Van Kaer L, Algood HMS, Singh K, Parekh VV, Greer MJ, Piazuelo MB, **Weitkamp JH**, Matta P, Chaturvedi R, Wilson KT, Olivares-Villagómez D. CD8αα+ innate-type lymphocytes in the intestinal epithelium mediate mucosal immunity, *Immunity*, 41(3):451-464, **2014**. PMC: *in progress*.
This work demonstrates our experience in human immunology and our success in working with challenging sample sizes.

Additional recent publications of importance to the field

1. Ullrich T, Tang YW, Correa H, Hill M, Matta P, **Weitkamp JH***. Absence of gastrointestinal pathogens in ileum tissue resected for necrotizing enterocolitis. Pediatr Infect Dis J 2012; 31(4):413-414. PMCID: PMC 3305842.

2. Zhang C, Sherman MP, Prince LS, Bader D, **Weitkamp JH**, Slaughter JC, McElroy SJ. Paneth cell ablation in the presence of *Klebsiella pneumoniae* induces necrotizing enterocolitis (NEC)-like injury in immature murine small intestine, Dis Model Mech 2012; 5(4):522-532. *(Journal Cover).* PMCID: PMC 3380715.

3. Engelhardt BG, Griffith ML, Crowe, JE, Jr., Savani BN, Kassim AA, Lu P, **Weitkamp JH**, Moore DJ, Yoder SM, Rock MT, Jagasia SM, Jagasia M. Predicting post-transplant diabetes mellitus by regulatory T cell phenotype: Implication for metabolic intervention to modulate alloreactivity. *Blood* 119:2417-2421, 2012. PMCID: PMC 3311262.

4. Romano-Keeler J, Moore DJ, Brucker R, Lovvorn H, Wang C, Tang YW, Bordenstein S, George AL, **Weitkamp JH*** Early life establishment of site-specific microbial communities in the gut, *Gut Microbes,* 2014, 5(2):192-201. PMCID: PMC 4063844.
Cumulatively, these publications demonstrate the PI's training, experience and productivity in human immunology research.

D. Research Support During the Last 3 years

Ongoing Research Support

1) RFA-TR-13-002 Peters (PI) 07/01/14-06/30/19
NIH Rare Diseases Clinical Research Consortia (RDCRC) for Rare Diseases Clinical Research Network (U54)
As a permanent clinical data site, Vanderbilt University enrolls and evaluates patients with Rett Syndrome, *MECP2* duplication syndrome, and Rett-related disorders. We bio-bank all samples, perform immune response testing and assist with interpretation of immune and inflammatory changes associated with disease progression.
Role: Co-Investigator (0% effort)
Total annual direct amount: $224,700

2) Vanderbilt University Discovery Grant Wikswo (PI) 03/01/12-10/15/14
Molecular effects of maternal immune activation: The story of placental, glial and neuronal interactions.
This interdisciplinary internally competitive grant tests the hypothesis that maternal immune activation by interleukin 6 stimulates placental cells to release humoral factors that alter glial and neuronal development in the fetus.
Role: Co-Investigator (0% effort)
Total annual direct amount: $50,000

3) Division of Neonatology Weitkamp (PI) 01/11/06-06/30/15
Vanderbilt University
Start-up funding
Establishing of techniques and models to study the development and function of immunoregulatory cells in the premature intestinal mucosa and their role in the pathophysiology of necrotizing enterocolitis.
Role: Principal Investigator

Completed Research Support

1) 1K08HD061607-01 Weitkamp (PI) 5/01/09-4/30/14 (no cost extension to 6/30/2014)
NICHD/NIH
Development of Intestinal Immune Regulation in Human Infants
The main objective of this research career development award is to study the development and role of $FOXP3^+$ T cells and other regulatory cells in the gut of preterm infants.
Role: Principal Investigator

2) Pilot and Feasibility Translational Research Grant George/Weitkamp (Co-PI) 05/01/11-04/30/13
Vanderbilt Digestive Disease Research Center (VDDRC)
Intestinal microbiota as a risk factor in necrotizing enterocolitis (NEC)
This study uses next-generation deep sequencing of bacterial 16S ribosomal RNA genes in fecal and tissue samples to examine if differences exist in bacterial phyla and taxa between samples from infants with NEC and non-NEC controls.
Role: Co-Principal Investigator

3) PF298 Mani (PI) 10/01/09-09/31/12
Vanderbilt Institute for Clinical and Translational Research (VICTR) Grant
A diagnostic test for neonatal sepsis (DTNS) based on gene expression profile

This pilot study combines expertise in machine learning and clinical neonatology to investigate whether profiles of differentially expressed genes can be used as an early marker for diagnosing neonatal sepsis.
Role: Co-Investigator