BIOGRAPHICAL SKETCH

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NAME: James Lawrence Wynn, MD

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POSITION TITLE: Associate Professor of Pediatrics, and Pathology, Immunology, and Laboratory Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Florida Atlantic University	BS	05/1998	Biology: Microbiology
University of Florida	MD	05/2002	Medicine
Shands Teaching Hospital-University of Florida		06/2005	Pediatrics
Shands Teaching Hospital-University of Florida		06/2008	Neonatal Critical Care
University of Florida, Laboratory of Inflammation Biology and Surgical Science, Lyle Moldawer, PhD		06/2008	Inflammatory Biology

A. Personal Statement

Since 2005, I have focused on increasing our knowledge of the neonatal-specific immune response to sepsis. My efforts are directed at improving the accuracy of diagnostic methods, identification of prognostic and clinical stratification markers, and discovery of potential opportunities for translational interventions aimed at improving infection-related outcomes for neonates.

B. Positions and Honors

2002-2008 Resident (2002-2005, Pediatrics), Fellow (2005-2008, Neonatal-Perinatal Medicine) Department of Pediatrics, University of Florida
2005-2008 Fellow, Laboratory of Inflammation Biology and Surgical Science (Director: Dr. Linc Moldawer), Department of Surgery, University of Florida
2008-2010 Medical Instructor, Division of Neonatal-Perinatal medicine, Department of Pediatrics, Duke University
2010-2012 Assistant Professor (effective July 1, 2010), Division of Neonatal-Perinatal medicine, Department of Pediatrics, Duke University
2012-2015 Assistant Professor (effective July 2, 2012), Division of Neonatal-Perinatal medicine, Department of Pediatrics, Vanderbilt University
2015-present Associate Professor, Division of Neonatal-Perinatal Medicine, Department of Pediatrics, University of Florida
2015-present Associate Professor, Department of Pathology, Immunology, and Laboratory Medicine, University of Florida
2015-present Associate Director, Neonatal-Perinatal Medicine Fellowship Program

Other Experience and Professional Memberships

2008-2014 Fellow, American Academy of Pediatrics
2008-2014 Section on Perinatal Pediatrics
2011-present Elected, *Society for Pediatric Research*
2012-present Elected, *Perinatal Research Society*, Associate Member
2013-present Immunology Basic Science III committee at the American Heart Association
2014-present *The Shock Society*
2015-present *The American Association of Immunologists*
2015-present University of Florida representative for the AAMC Council of Faculty and Academic Societies
Served as ad hoc reviewer for over 30 scientific journals and funding agencies including NIH (NICHD/NIAID)

Honors

1998	Bachelor of Science, *Summa cum laude*
2004 & 2005	Society of Teaching Scholars: Resident Teaching Award for Outstanding Medical Student and House-staff Teaching-Department of Pediatrics, University of Florida
2005	Pediatric Resident Teaching Award: Most outstanding teacher for University of Florida Class of 2005
2007	Children's Miracle Network (CMN) Travel Award for travel to Trauma, Shock, and Inflammation Society meeting 2007, Munich, Germany
2007	Douglas J. Barrett Academic Fellowship Physician Award ($50,000)
2007 & 2008	Pediatric Academic Society Young Investigator's Travel Award for travel to PAS meeting 2007 Toronto, Canada, 2008 Hawaii
2008	Induction into Chapman Society, Gold Humanism Honor Society
2008	University of Florida, Department of Pediatrics, *Henry Kokomoor* Outstanding Pediatric Fellow Research Award
2011-2015	NIH Loan Repayment Award: "*Evaluation of Peripheral Blood Neutrophil Gene Expression During Neonatal Sepsis*"
2011	Induction into *Society for Pediatric Research*
2012	Perinatal Research Society, NIH R13 Young Investigator
2012	Perinatal Research Society, President's *Cassady* Award for Young Investigator
2014	Accepted for participation in the Early Career Reviewer (ECR) program at the Center for Scientific Review (CSR), NIH
2014	Chairperson: NIH/NICHD 2014/05 ZHD1 DSR-A (51) 1 - Pediatric Critical Care and Trauma Scientist Development Program (PCCTSDP)

C. Contribution to Science

1. My early publications directly addressed the deficit in mechanistic studies of neonatal-specific sepsis pathophysiology. First, we developed and characterized a model of polymicrobial sepsis that recapitulates the pathophysiology of septic peritonitis. The availability of this model allowed a direct comparison of the neonatal and adult host response. We showed neonates manifest a markedly reduced inflammatory response to sepsis as compared to adults. We next demonstrated that the adaptive immune system does not play a significant role in neonatal sepsis highlighting a dependence on innate immunity. Using specific TLR agonists, we demonstrated that innate immune priming (trained immunity) was associated with enhanced innate immune function and reduced neonatal sepsis mortality. We demonstrated that neonates, in contrast to adults, are dependent upon TRIF signaling for survival to Gram negative sepsis. Most recently, we showed murine neonatal CD71+ erythroid cells, although immunomodulatory *ex vivo*, had no impact on murine neonatal sepsis survival.
    a. **Wynn JL**, Scumpia PO, Delano MJ, O'Malley K, Abouhamze A, Ungaro R, Moldawer LL. (2007) Increased mortality and altered immunity in neonatal sepsis produced by generalize peritonitis. Shock. 2007 Dec;28(6):675-683. PMID: 17621256
    b. **Wynn, JL**, Scumpia, PO, Winfeld, RD, Delano, MJ, Barker, T, Satoh, M, Levy, O, Moldawer, LL. (2008). Defective innate immunity predisposes neonates to poor sepsis outcome, but is reversed by TLR agonists. Blood. 2008 Sep 1;112(5):1750-8. PMCID: PMC2518883
    c. Cuenca AG, **Wynn JL**, Kelly-Scumpia KM, Scumpia PO, Vila L, Delano MJ, Mathews CE, Wallet SM, Reeves WH, Behrns KE, Nacionales DC, Efron PA, Kunkel SL, Moldawer LL. (2011). Critical role for CXC Ligand 10 (IP-10)/CXCR3 signaling in the murine neonatal response to sepsis. Infect Immun. 2011 Jul;79(7):2746-54. PMCID: PMC3191971
    d. Cuenca AG, Joiner DN, Gentile LF, Cuenca AL, **Wynn JL**, Kelly-Scumpia KM, Scumpia PO, Behrns KE, Efron PA, Nacionales D, Wallet SM, Reeves WH, Mathews CE, Moldawer LL. TRIF-Dependent Innate Immune Activation Is Critical for Survival to Neonatal Gram-Negative Sepsis. *J Immunol. 2015 Feb 1;194(3):1169-77.* PMID: 25548220, PMCID: PMC4297742.
    e. **Wynn JL**, Scumpia PO, Stocks BT, Romano-Keeler J, Alrifai MW, Liu JH, Kim AS, Alford CE, Matta P, Weitkamp JH, Moore DJ. Neonatal CD71+ Erythroid Cells Do Not Modify Murine Sepsis Mortality. *J Immunol. 2015 Aug 1;195(3):1064-70.* PMID: 26101326, PMCID PMC4506905.
2. In parallel with the novel mechanistic investigations into the pathophysiology of sepsis in murine neonates described above, I have also led several studies of human neonates that have significantly improved our understanding neonatal-specific sepsis pathophysiology. Using genome-wide expression profiling on peripheral blood, we showed that human neonates manifest a unique host immune response among

pediatric patients with septic shock. Our examination of the impact of candiduria in extremely low birth weight infants led to a change in practice. In a series of three investigations, we presented evidence that neonates do not manifest clinically-apparent immunoparalysis as seen in older children and adults after sepsis and that neonates with sepsis have altered vaccine responses manifested months after the episode. We demonstrated an effective method to safely reduce antimicrobial exposure in preterm infants. We have worked to align the efforts of neonatal sepsis investigators by working towards a consensus definition. In parallel and important precedent for the implementation and success of the studies described in this application, we showed that timing of sepsis after birth is a critical determinant of the host response to sepsis in preterm neonates.

a. **Wynn JL**, Cvijanovich NZ, Allen GL, Thomas NJ, Freishtat RJ, Anas N, Meyer K, Checchia PA, Lin R, Shanley TP, Bigham MT, Wong HR. The influence of developmental age on the early transcriptomic response of children with septic shock. *Mol Med. 2011;17(11-12):1146-56. PMID: 21738952, PMCID: PMC3321808*
b. **Wynn JL**, Tan S, Gantz MG, Das A, Goldberg RN, Adams-Chapman I, Stoll BJ, Shankaran S, Walsh MC, Auten KJ, Miller NA, Sánchez PJ, Higgins RD, Cotten CM, Smith PB, Benjamin Jr DK, Neonatal Research Network. Outcomes following candiduria in extremely low birth weight infants. *Clin Infect Dis. 2012 Feb 1;54(3):331-9. PMID: 22144537, PMCID: PMC3258271*
c. **Wynn JL**, Hansen NI, Das A, Cotton CM, Goldberg RN, Sanchez PJ, Bell EF, Van Meurs KP, Carlo WA, Laptook AR, Higgins RD, Benjamin Jr DK, and Stoll BJ for the NICHD Neonatal Research Network (NRN). Early sepsis does not increase the risk of late sepsis in very low birth weight neonates. *J Pediatr. 2013 May;162(5):942-8.e1-3. PMID: 23295144, PMCID: PMC3622770*
d. Lin CB, Hornik CP, Clark R, Cotten CM, Benjamin Jr. DK, Cohen-Wolkoweiz M, Smith PB, **Wynn JL**. Very low birth weight neonates who survive early-onset sepsis do not have an increased risk of developing late-onset sepsis. *Early Hum Dev. 2012 Nov;88(11):905-9. PMID: 22840605, PMCID: PMC3462255*
e. **Wynn JL**, Li L, Cotten CM, Phelps DL, Shankaran S, Goldberg RN, Carlo WA, Van Meurs KP, Das A, Vohr BR, Higgins RD, Stoll BJ, and D'Angio CT for the NICHD NRN. Blood stream infection is associated with altered heptavalent pneumococcal conjugate vaccine immune responses in very low birth weight infants. *J Perinatol. 2013 Aug;33(8):613-8. PMID: 23370608, PMCID: PMC3722279*
f. Coggins SA*, **Wynn JL***, Hill ML, Slaughter JC, Ozdas-Weitkamp A, L. Waitman LR, Carnevale RJ, Matta A, Weitkamp JH. Use of a computerized C-reactive protein based sepsis evaluation in the NICU: A five-year experience. *PLoS One. 2013 Nov 11;8(11):e78602. PMID: 24244325, PMCID: PMC3823853* ***co-first authors***
g. **Wynn JL**, Wong HR, Shanley TP, Bizzarro M, Saiman L, Polin RA. Time for a neonatal–specific consensus definition for sepsis. *Pediatr Crit Care Med.* 2014 Apr 18. PMID: 24751791, PMCID: PMC4087075.
h. Benitz WE, **Wynn JL**, Polin RA. Reappraisal of Guidelines for Management of Neonates with Suspected Early-Onset Sepsis. *J Pediatr. 2015 Apr;166(4):1070-4.* PMID: 25641240. PMCID pending.
i. **Wynn JL**, Guthrie SO, Wong HR, Lahni P, Ungaro R, Lopez MC, Baker HV, Moldawer LL. Post-natal age is a critical determinant of the neonatal host response to sepsis. Mol Med. 2015 Jun 2. PMID: 26052715, PMCID pending.

3. In addition to the contributions described above, with a team of collaborators led by Dr. Moldawer, I directly addressed the impact of multiple facets of the immune system on the outcome of sepsis including $CD4^+$ T cells, T regulatory cells, B cells, myeloid suppressor cells, and type I interferon signaling.

a. Scumpia PO, Delano MJ, Kelly-Scumpia KM, Weinstein JS, **Wynn JL**, Winfield RD, Xia C, Chung CS, Ayala A, Atkinson MA, Reeves WH, Clare-Salzler MJ, Moldawer LL. Treatment with GITR agonistic antibody corrects adaptive immune dysfunction in sepsis. *Blood*. 2007 Nov 15;110(10):3673-81. *PMCID: PMC2077315*
b. Scumpia PO, Delano MJ, Kelly KM, O'Malley K, Efron PA, McAuliffe PF, Brusko T, Ungaro R, Barker T, **Wynn JL**, Atkinson MA, Reeves WH, Clare Salzler MJ, and Moldawer LL. Increased natural $CD4^+CD25^+$ regulatory T cells and their suppressor activity does not contribute to mortality in murine polymicrobial sepsis. *J Immunol* 2006 Dec 1;177(11):7943-9. *PMID: 17114466*

c. Kelly-Scumpia KM, Scumpia PO, Weinstein JS, Delano MJ, Cuenca AG, Nacionales DC, **Wynn JL**, Lee PY, Kumagai Y, Efron PA, Akira S, Wasserfall C, Atkinson MA, and Moldawer LL. B cells enhance early innate immune responses during bacterial sepsis. *J Exp Med. 2011 Aug 1;208(8):1673-82.* *PMCID: PMC3149216*
d. Delano MJ, Scumpia PO, Weinstein JS, Coco D, Nagaraj S, Kelly-Scumpia K, O'Malley K, **Wynn JL**, Antonenko S, Al-Quran S, Swam R, Chung C, Atkinson MA, Ramphal R, Gabrilovich D, Reeves W, Ayala A, Philips J, Laface D, Heyworth P, Clare-Salzer M, Moldawer LL. MyD88-Dependent expansion of an immature $Gr1^{+}CD11b^{+}$ population induces T-cell suppression and T_H2 polarization in sepsis. *J Ex Med*. 2007 Jun 11;204(6):1463-74. PMCID: PMC2118626
e. Kelly-Scumpia KM, Scumpia PO, Delano MJ, Weinstein J, Cuenca AG, **Wynn JL**, Moldawer LL. Type I interferon signaling in hematopoietic cells is required for survival in murine polymicrobial sepsis by regulating CXCL10. *J Exp Med*. 2010 Feb 15;207(2):319-26. *PMCID: PMC2822595*

Complete List of Published Work in MyBibliography (37 publications):
http://www.ncbi.nlm.nih.gov/sites/myncbi/1LCw54GQP2E/bibliography/9815252/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

K08 GM106143 PI: Wynn 4/2013-4/2018
NIGMS/NIH
The Role of the Inflammasome in Neonatal Sepsis
The goal of this application is to determine the role of the inflammasome in neonatal host response to sepsis and the potential of immunotherapy with downstream inflammasome products (IL-1β, IL-18).

Completed Research Support

Children's Miracle Network Grant PI: Wynn 12/2005-12/2006
Evaluation and Characterization of Immunological Changes in Murine Neonatal Sepsis.
The overall goal of this award ($12,500) was to support the development of a murine model of neonatal sepsis and to compare the neonatal response to the adult response.

Douglas J. Barrett Academic Fellowship Award PI: Wynn 7/2007-7/2008
Evaluation and Characterization of Immunological Changes in Murine Neonatal Sepsis.
The overall goal of this award was salary support ($50,000) for Dr. Wynn.

Thrasher Research Fund PI: Cohen (Wynn Site PI) 10/2010-12/2011
Safety and Pharmacokinetics of Multiple Dose Metronidazole in Premature Infants
The goal of this award is to determine the pharmacokinetics of Metronidazole in premature infants.

The Gerber Foundation PI: Wynn 1/2011-12/2013
Evaluation of Peripheral Blood Neutrophil Gene Expression during Neonatal Sepsis
The goal of this award is to characterize the host response to sepsis in the preterm infant.

R01 GM096994 PI: Wong 4/2011-3/2015
NIGMS/NIH
MMP-8 As a Novel Therapeutic Target in Sepsis
The goal of this award is to elucidate the role for MMP-8 expression and activity in sepsis pathology.

NIH Loan Repayment Award-Pediatric Research PI: Wynn 7/2011-7/2015
Evaluation of Peripheral Blood Neutrophil Gene Expression During Neonatal Sepsis
The goal of this award is to characterize the host response to sepsis in the preterm infant.

Thrasher Research Fund PI: Wynn 2/2013-11/2015
Effect of Colostrum on Innate Mucosal Immunity in Very Preterm Infants
The goal of this application is to determine key antimicrobial proteins and peptides on mucosal surfaces and in human milk and the effect of oral colostrum priming on these proteins.