

PUBLICATIONS

* Denotes Co-first author

Anita S. Iyer*, Noor M. Khaskhely*, David J. Leggat, Jennifer A. Ohtola, Jessica L. Saul-McBeth, Sadik A. Khuder and M.A. Julie Westerink "Serum Inflammatory markers and surface expression of Tumor Necrosis Factor Receptors in pneumococcal polysaccharide-specific B cells of HIV-positive and HIV-negative adults" Manuscript in preparation.

Anita S. Iyer*, David J. Leggat*, Jennifer A. Ohtola, Joan M. Duggan, Claudiu A. Georgescu, Adeb A. Al Rizaiza, Noor M. Khaskhely, Sadik Khuder and M. A. Julie Westerink "Response to pneumococcal polysaccharide vaccination in newly diagnosed HIV-positive individuals On Long Term Highly Active Antiretroviral Therapy (HAART)" J AIDS Clin Res 2015,6: 421

Anita S. Iyer*, Jennifer A. Ohtola* and M.A. Julie Westerink "Age-related immune response to pneumococcal polysaccharide vaccination: lessons for the clinic", Expert Rev Vaccines, 2015 Jan; 14(1):85-97.

David J. Leggat*, **Anita S. Iyer***, Jennifer A. Ohtola, Sneha Kommoori, Joan M. Duggan, Noor M. Khaskhely and M.A. Julie Westerink "Response to pneumococcal polysaccharide vaccination in newly diagnosed HIV-positive individuals" J AIDS Clin Res 2015,6: 419

Anita S. Iyer* Research work featured in local newspaper Toledo Blade, November 2014. <http://www.toledoblade.com/A-E/2014/11/03/HIV-The-deck-is-stacked-in-fight-vs-pneumonia.html>

Jennifer A. Ohtola, Jessica L. Saul-McBeth, **Anita S. Iyer**, David J. Leggat, Sadik A. Khuder, Noor M. Khaskhely and M. A. Julie Westerink "Quantitative and Functional Antibody Responses to the 13-Valent Conjugate and/or 23-Valent Purified Polysaccharide Vaccine in Aging HIV-Infected Adults" Manuscript in preparation

"Jennifer A. Ohtola*, Noor M. Khaskhely*, Jessica L. Saul-McBeth, **Anita S. Iyer**, David J. Leggat, Sadik A. Khuder, and M. A. Julie Westerink "Alterations in Serotype-specific B Cell Responses to the 13-Valent Pneumococcal Conjugate Polysaccharide Vaccine in Aging HIV-Infected Adults" Manuscript in preparation

David J. Leggat, Noor M. Khaskhely, **Anita S. Iyer**, Jason Mosakowski, Rebecca S. Thompson, John D. Weinandy, and M.A. Julie Westerink. "Pneumococcal polysaccharide vaccination induces polysaccharide-specific B cells in adult peripheral blood expressing CD19+CD20+CD3-CD70-CD27+IgM+CD43+CD5+/-", Vaccine, 2013

David Leggat, Noor Khaskhely, Rebecca Thompson, **Anita Iyer**, M A Julie Westerink, "The elderly immune response to pneumococcal polysaccharides 14 and 23F consists predominantly of switched memory B cells", J Infect Dis, 2013

DISSERTATION COMMITTEE

M.A. Julie Westerink, M.D., Major Advisor

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The University of Toledo College of
Medicine

Infection, Immunity & Transplantation (IIT)
Track

Department of Medicine



THE UNIVERSITY OF
TOLEDO
1872

**DISSERTATION
PRESENTATION**

Anita Sridhar Iyer

May 15, 2015

**Response to
Pneumococcal
Polysaccharide Vaccine
PPV23 in HIV-positive
individuals on long term
highly active anti-
retroviral therapy
(HAART)**

Ph.D. in
Biomedical Sciences

ABSTRACT

SELECT PRESENTATIONS

Anita S. Iyer*, David J. Leggat, Jennifer A. Ohtola, Claudiu A. Georgescu, Adeeb A. Al Rizaiza, Noor M. Khaskhely, and M. A. Julie Westerink. Effectiveness of PPV-23 Revaccination in HIV-Positive Individuals on Long-Term Highly active anti-retroviral therapy (HAART). 2014 American Society for Microbiology (ASM) General Meeting, Boston, MA (Poster).

Anita S. Iyer*, David J. Leggat, Jennifer A. Ohtola, Claudiu A. Georgescu, Adeeb A. Al Rizaiza, Noor M. Khaskhely, and M. A. Julie Westerink. Effectiveness of PPV-23 Revaccination in HIV-Positive Individuals on Long-Term Highly active anti-retroviral therapy (HAART). 2014 ASM Branch meeting, Columbus, OH (Poster).

Anita S. Iyer*, David J. Leggat, Jennifer A. Ohtola, Claudiu A. Georgescu, Adeeb A. Al Rizaiza, Noor M. Khaskhely, and M. A. Julie Westerink. Effectiveness of PPV-23 Revaccination in HIV-Positive Individuals on Long-Term Highly active anti-retroviral therapy (HAART). 2014 Graduate Research Forum, The University of Toledo, Toledo, OH (Poster).

Anita S Iyer*, David J Leggat, Noor M Khaskhely, M.A. Julie Westerink "Impact of PPV-23 vaccine in HIV patients on long term highly active antiretroviral therapy (HAART)", 2013 American Association of Immunologists (AAI), Honolulu, HI (Poster).

Streptococcus pneumoniae accounts for significant morbidity and mortality in individuals suffering from Human Immunodeficiency Virus (HIV) infections. The Advisory Committee on Immunization Practices (ACIP) recommended PPV23 vaccination for all HIV-positive individuals as close to HIV-diagnosis as possible followed by re-vaccination after 5 years. Evidence to support these recommendations were however scarce. Herein, we investigated the response to vaccine serotypes 14 and 23F post PPV23 immunization at the total, functional antibody and pneumococcal polysaccharide (PPS)-specific B cell level in long term HAART cohorts, stratified based on the degree of immune reconstitution as Group A (CD4>200 cells/mm³) and Group B (CD4<200 cells/mm³). In addition, signals speculated to be critical in PPS responses were characterized and potential anomalies in their expression between HIV-positive and -negative adults were investigated.

Post-immunization, both group A and B showed significant increases in opsonophagocytic titers (OPT) against serotype 14 and 23F concomitant with significant increases in PPS14- and 23F-specific memory B cells. Percentages of PPS-specific IgM memory B cells but not other subsets correlated with OPT indicating its pivotal role in PPS response. Together, these findings highlight the benefits of PPV23 re-immunization in long term HAART cohorts. However, OPT and PPS-specific IgM memory B cell responses were significantly diminished in HIV-positive compared to HIV-negative individuals despite long term HAART. These findings highlight damage to critical PPS-responding B cell subsets early on during HIV-infection that fail to recover with HAART regardless of recovery in CD4+ T cells. Further, it emphasizes the need for evidence based vaccination strategies and alternate robust vaccination approaches for high risk populations.

We next investigated factors that could plausibly influence diminished PPV23 response in HIV-positive individuals. In the recent years, chronic inflammation, defined by elevated levels of pro-inflammatory cytokines has been associated with impaired antibody response. However, its influence on PPV23 response remains to be investigated. Consistent with literature, we noted elevated levels of pro-inflammatory markers C-reactive protein (CRP), sCD27 and sCD30 in HIV-positive compared to HIV-negative individuals. However, this did not correlate with PPV23 response indicating response to each vaccine is different and not always adversely influenced by generalized inflammatory status.

Ligand and receptors of the tumor necrosis family (TNF) have been speculated to contribute towards PPS-response in murine models. However, its expression on total and PPS-specific B cells of immunized HIV-negative and -positive adults remains to be elucidated. Assessment of these signals revealed significantly higher expression of tumor necrosis factor receptor transmembrane activator and calcium-modulator and cytophilin ligand interactor (TACI) on PPS-specific B cells of HIV-positive and HIV-negative adults compared to total B cells indicating a potential role for TACI in PPS response consistent with its role in murine studies. Although, surface TACI expression was similar between HIV-positive and -negative adults, soluble sTACI was significantly lower in HIV-positive adults. Improved understanding of these cytokines, receptors and downstream signaling will be useful while considering the design of new robust pneumococcal vaccines.

AWARDS

Graduate Research Award for the proposal on "Role of B1 cells in immune defense against *Streptococcus pneumoniae*" from the Graduate Student Association (GSA) at the University of Toledo (2015)

Semi-finalist, Graduate Research forum, held by the Council of Biomedical Graduate students (CBGS) at the University of Toledo (2014)

Award for academic excellence during Bachelor's in Microbiology, Vivekananda College, University of Mumbai (2004)

SELECTED ACTIVITIES

Vice President, Council of Biomedical Graduate Students (CBGS), University of Toledo (June 2014-May 2015)

College of Medicine and Life Science Representative, Graduate Student Association (GSA), University of Toledo (June 2014-May 2014)

Infection, Immunity and Transplantation Track Representative, CBGS (June 2013-May 2014)

FUTURE PLANS

Anita has accepted a temporary research assistant position in the laboratory of Dr. Joan Duggan at the Department of Medicine, University of Toledo .