# ABSTRACT

Advanced age and human immunodeficiency virus (HIV) infection are both risk factors for *Streptococcus pneumoniae* infections due to immunological dysfunction. The aging HIV-infected (HIV+) population may be at higher risk for pneumococcal disease due to the combination of these factors on humoral immunity. Current recommendations for pneumococcal vaccination in HIV+ adults include a priming dose of the 13-valent pneumococcal conjugate vaccine followed by one dose of the 23-valent pneumococcal polysaccharide vaccine 8 weeks later (PCV/PPV). We compared quantitative and qualitative antibody responses to PCV/PPV versus a single dose of PPV in HIV+ adults aged 50-65 years with CD4+ T cells/µl (CD4) >200 on antiretroviral therapy ≥1 year. We found that PCV/PPV did not demonstrate a clear immunological advantage to PPV alone, as serotype-specific IgG levels and functional titers postvaccination were similar between groups. In addition, these antibody responses were significantly reduced in HIV+ subjects vaccinated with PCV/PPV compared to age-matched, uninfected (HIV–) controls who received PCV/PPV. We also characterized the phenotype and surface expression of several receptors on serotype-specific B cells that may influence vaccine responses. HIV+ subjects vaccinated with PCV/PPV generated significantly reduced frequencies of circulating serotype-specific B cells postvaccination compared to those who received PPV only. However, phenotypic distributions of serotype-specific memory B cell subsets were similar between groups. Transmembrane activator and calcium-modulating cyclophilin ligand interactor (TACI)+ serotype-specific B cell percentages were significantly decreased in HIV+ PCV/PPV compared to PPV groups, indicating that prior PCV altered TACI expression. It remains unclear if this impact provides any benefit to vaccine responses. CD21+ serotype-specific B cells were also significantly reduced in HIV+ compared to HIV– PCV/PPV groups which may contribute to diminished antibody responses. Collectively, our findings suggest that continued efforts aimed at developing more effective vaccination strategies in susceptible adult populations are warranted, and further investigation into the immunological mechanisms that increase the risk of pneumococcal disease and induce potent vaccine responses are necessary.

## DISSERTATION COMMITTEE

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## DISSERTATION PRESENTATION

**Jennifer A. Ohtola**

**June 19, 2015**

# Pneumococcal vaccination in aging HIV-infected individuals

Ph.D. in
Biomedical Sciences

## PRESENTATIONS

**Ohtola JA**, Kommoori S, Khaskhely NM, Leggat DJ, Iyer AS, Westerink MAJ. Impact of pneumococcal vaccination on B cell responses in the aging HIV+ population. American Society for Microbiology 114th General Meeting (2014), Boston, Massachusetts. Poster presentation.

**Ohtola JA**, Kommoori S, Khaskhely NM, Leggat DJ, Iyer AS, Westerink MAJ. B cell responses to pneumococcal vaccination in the aging HIV+ population. 2014 Annual Graduate Research Forum, Toledo, Ohio. Poster presentation.

**Ohtola JA**, Takashima A. Discovery of neutrophil-targeted immunoregulatory drugs by unbiased screening. 2013 Annual Graduate Research Forum, Toledo, Ohio. Poster presentation.

## PUBLICATIONS

**Ohtola JA**, Saul-McBeth JL, Iyer AS, Leggat DJ, Khuder SA, Khaskhely NM, Westerink MAJ. Quantitative and functional antibody responses to the 13-valent conjugate and/or 23-valent purified polysaccharide vaccine in aging HIV-infected adults. Manuscript under review.

**Ohtola JA***, Khaskhely NM, Saul-McBeth JL, Iyer AS, Leggat DJ, Khuder SA, Westerink MAJ. Alterations in serotype-specific B cell responses to the 13-valent pneumococcal conjugate vaccine in aging HIV-infected adults. Manuscript under review.

Iyer AS, Khaskhely NM, Leggat DJ, **Ohtola JA**, Saul-McBeth JL, Khuder SA, Westerink, MAJ. Serum inflammatory markers and surface expression of tumor necrosis factor receptors in pneumococcal polysaccharide (PPS)-specific B cells of HIV-positive and HIV-negative adults. Manuscript under review.

Iyer AS, Leggat DJ, **Ohtola JA**, Duggan JM, Georgescu CA, Al Rizaiza AA, Khuder SA, Khaskhely NM, Westerink MAJ. Response to pneumococcal polysaccharide vaccination in HIV-positive individuals on long term highly active antiretroviral therapy. J AIDS Clin Res. 2015 Feb;6(2). PMID: 25908996.

Leggat DJ, Iyer AS, **Ohtola JA**, Kommoori S, Duggan JM, Georgescu CA, Khuder SA, Khaskhely NM, Westerink MAJ. Response to pneumococcal polysaccharide vaccination in newly diagnosed HIV-positive individuals. J AIDS Clin Res. 2015 Feb;6(2). PMID: 25908995.

Yao Y, Matsushima H, **Ohtola JA**, Geng S, Lu R, Takashima A. Neutrophil priming occurs in a sequential manner and can be visualized in living animals by monitoring IL-1β promoter activation. J Immunol. 2015 Feb 1;194(3):1211-24. PMID: 25527787.

Iyer AS, **Ohtola JA***, Westerink MAJ. Age-related immune responses to pneumococcal polysaccharide vaccination: lessons for the clinic. Expert Rev Vaccines. 2015 Jan; 14(1):85-97. PMID: 25269650.

Cortes C, **Ohtola JA**, Saggu G, Ferreira VP. Local release of properdin in the cellular microenvironment: role in pattern recognition and amplification of the alternative pathway of complement. Front Immunol. 2013 Jan 17;3:412. PMID: 23335922.

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## LEADERSHIP

**President**, University of Toledo Council of Biomedical Graduate Students. 2014-2015.

**Leader**, TH3 Infection, Immunity and Transplantation Student Group. 2013 -2014.

**M.D./Ph.D. Representative**, University of Toledo Council of Biomedical Graduate Students. 2012-2014.

## AWARDS

M.D./Ph.D. program full tuition scholarship.

## FUTURE PLANS

Jennifer will return to medical school to complete her M.D./Ph.D. training.