

Viral lung disease/Influenza

Wilbur Chen (wchen@som.umaryland.edu):



Dr. Chen is the Chief of the Adult Clinical Studies section, University of Maryland Center for Vaccine Development (CVD), which focuses on the development and clinical testing of vaccines for the infectious diseases. Dr. Chen's research focuses on development and testing of vaccines including for the pulmonary pathogens, influenza and tularemia, and for enteric and other infections. The CVD is a global program that offers opportunities to test vaccines in third world settings.

Highlighted Publications:

1. Chen WH, Toapanta F, Shirey KA, Zhang L, Giannelou A, Page C, Frieman M, Vogel S, and Cross AS. Potential Role for Alternatively Activated Macrophages in the Secondary Bacterial infection During Recovery from Influenza. *Immunology Letters* 2012; 141:227-34.
2. Shirey KA, Lai W, Scott A, Lipsky M, Mistry P, Pletneva LM, Karp CL, McAlees J, Gioannini JL, Weiss J, Chen WH, Ernst R, Rossignol DP, Gusovsky F, Blanco JC, Vogel SN. The TLR4 Antagonist, Eritoran, Protects Mice from Lethal Influenza Infection. *Nature* 2013; 497:498-502.
3. Chen WH, Jackson LA, Edwards KM, Keitel WA, Hill H, Noah DL, Creech CB, Patel SM, Mangal B, Kotloff KL. Safety, Reactogenicity, and Immunogenicity of Inactivated Monovalent Influenza A/H5N1 Virus Vaccine Administered With or Without AS03 Adjuvant. *Open Forum Infect Dis* 2014; 1(3):ofu091.
4. Chen WH, Jackson LA, Edwards KM, Keitel WA, Hill H, Noah DL, Creech CB, Patel SM, Mangal B, Kotloff KL. Persistence of Antibody to Influenza A/H5N1 Vaccine Virus: Impact of AS03 Adjuvant. *Clin Vacc Immunol* 2015; 23:73-77.
5. Chen WH, Pasetti MF, Adhikari RP, Baughman H, Douglas R, El-Khorazaty J, Greenberg N, Holtsberg FW, Liao GC, Reymann MK, Wang X, Warfield KL, Aman MJ. The safety and

immunogenicity of a parenterally administered structure-based rationally modified recombinant Staphylococcal enterotoxin B protein vaccine, STEBVax. *Clin Vacc Immunol* 2016; 23: 918-25.

Links:

Med School faculty page: <http://www.medschool.umaryland.edu/profiles/Chen-Wilbur/>

PubMed

publications: <http://www.ncbi.nlm.nih.gov/sites/myncbi/wilbur.chen.1/bibliography/40322237/public/?sort=date&direction=ascending>

Matt Frieman (MFrieman@som.umaryland.edu):



Dr. Frieman's research focused on how respiratory viruses cause disease with a specific interest in Coronaviruses. The Frieman laboratory uses both *in vitro* and *in vivo* models of replication and pathogenesis to study the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The lab is currently focused on identifying the role of comorbidities in exacerbating MERS-CoV and a wide range of therapeutics against these and other highly pathogenic coronaviruses.

Highlighted Publications:

1. Pascal KE, Coleman CM, Mujica AO, Kamat V, Badithe A, Fairhurst J, Hunt C, Strein J, Berrebi A, Sisk JM, Matthews KL, Babb R, Chen G, Lai KM, Huang TT, Olson W, Yancopoulos GD, Stahl N, Frieman MB, Kyratsous CA. Pre- and postexposure efficacy of fully human antibodies against Spike protein in a novel humanized mouse model of MERS-CoV infection. *Proc Natl Acad Sci U S A*. 2015 Jul 14;112(28):8738-43. PubMed PMID: 26124093; PubMed Central PMCID: PMC4507189.
2. Dyall J, Coleman CM, Hart BJ, Venkataraman T, Holbrook MR, Kindrachuk J, Johnson RF, Olinger GG Jr, Jahrling PB, Laidlaw M, Johansen LM, Lear-Rooney CM, Glass PJ, Hensley LE, Frieman MB. Repurposing of clinically developed drugs for treatment of Middle East respiratory syndrome coronavirus infection. *Antimicrob Agents Chemother*. 2014 Aug;58(8):4885-93. PubMed PMID: 24841273; PubMed Central PMCID: PMC4136000.

3. Page C, Goicochea L, Matthews K, Zhang Y, Klover P, Holtzman MJ, Hennighausen L, Frieman M. Induction of alternatively activated macrophages enhances pathogenesis during severe acute respiratory syndrome coronavirus infection. *J Virol*. 2012 Dec;86(24):13334-49. PubMed PMID: 23015710; PubMed Central PMCID: PMC3503056.

4. Coleman CM, Sisk JM, Halasz G, et al. CD8+ T Cells and Macrophages Regulate Pathogenesis in a Mouse Model of Middle East Respiratory Syndrome. *Journal of Virology*. 2017;91(1):e01825-16. doi:10.1128/JVI.01825-16.

Links:

Med School faculty page: <http://www.medschool.umaryland.edu/profiles/Frieman-Matthew/>

PubMed publications:

<https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41149728/?sort=date&direction=ascending>

Don Milton (dmilton@umd.edu):

Dr. Milton's work focuses on the interrelated areas of infectious bioaerosols, exhaled breath analysis, and development and application of innovative methods for respiratory epidemiology. Fellows working in my lab will have the opportunity to participate in a variety of federally funded research projects. Currently the lab is working on development and testing of innovative non-invasive measurement of deep lung biomarkers with a transdisciplinary team of engineers, molecular biologists, and photonics experts. Dr. Milton is also performing molecular epidemiologic studies of the importance of the airborne mode in transmission of influenza and other respiratory viruses using whole genome sequencing of viruses from exhaled breath aerosols and NP swabs to identify the source of transmitted viruses.

Highlighted Publications:

1. Yan J, Grantham M, Pantelic J, Bueno de Mesquita PJ, Albert B, Liu F, Ehrman S, Milton DK. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci U S A*. 2018 Jan 30;115(5):1081-1086. PubMed PMID: 29348203; PMCID: PMC5798362.
2. Milton DK, Fabian MP, Cowling BJ, Grantham ML, McDevitt JJ. Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks. *PLoS Pathog*. 2013 Mar;9(3):e1003205. PubMed PMID: 23505369; PMCID: PMC3591312.
3. Fabian P, Brain J, Houseman EA, Gern J, Milton DK. Origin of exhaled breath particles from healthy and human rhinovirus-infected subjects. *J Aerosol Med Pulm Drug Deliv*. 2011 Jun;24(3):137-47. PubMed PMID: 21361786; PMCID: PMC3123971.
4. Shorter JH, Nelson DD, McManus JB, Zahniser MS, Sama SR, Milton DK. Clinical study of multiple breath biomarkers of asthma and COPD (NO, CO(2), CO and N(2)O) by infrared laser spectroscopy. *J Breath Res*. 2011 Sep;5(3):037108. PMCID: PMC3169766
5. Roy CJ, Milton DK. Airborne transmission of communicable infection--the elusive pathway. *N Engl J Med*. 2004 Apr 22;350(17):1710-2. PubMed PMID: 15102996.

Links:

Faculty webpage: <http://sph.umd.edu/people/donald-milton>

CATCH-the virus study page: <https://catch.umd.edu/>

Google Scholar Profile: <https://scholar.google.com/citations?user=35qhH0QAAAAJ&hl=en>

PHAB Lab page: <http://sph.umd.edu/laboratory-resources/public-health-aerobiology-virology-and-exhaled-biomarker-laboratory-phab-lab>

Justin Ortiz (jortiz@som.umaryland.edu):

Dr. Ortiz' research interests focus on respiratory virus surveillance, vaccine clinical trials, observational research, policy development, and clinical epidemiology and prevention of pneumonia.

Highlighted Publications:

1. Ortiz JR, Sotomayor V, Uez OC, Oliva O, Bettels D, McCarron M, Bresee JS, Mounts AW. Strategy to enhance influenza surveillance worldwide. *Emerg Infect Dis*. 2009 Aug;15(8):1271-8.
2. Madhi SA, Cutland CL, Kuwanda L, Weinberg A, Hugo A, Jones S, Adrian PV, van Niekerk N, Treurnicht F, Ortiz JR, Venter M, Violari A, Neuzil KM, Simões EA, Klugman KP, Nunes MC; Maternal Flu Trial (Matflu) Team. Influenza vaccination of pregnant women and protection of their infants. *N Engl J Med*. 2014 Sep 4;371(10):918-31. doi: 10.1056/NEJMoa1401480. PubMed PMID: 25184864.
3. Ortiz JR, Neuzil KM, Shay DK, Rue TC, Neradilek MB, Zhou H, Seymour CW, Hooper LG, Cheng PY, Goss CH, Cooke CR. The burden of influenza-associated critical illness hospitalizations. *Crit Care Med*. 2014 Nov;42(11):2325-32. doi: 10.1097/CCM.0000000000000545. PubMed PMID: 25148596.
4. Ortiz JR, Goswami D, Lewis KDC, Sharmeen AT, Mostaq A, Rahman M, Rahman MZ, Feser J, Neuzil KM, Brooks WA. Safety of Russian-backbone seasonal trivalent, live-attenuated influenza vaccine in a phase II randomized placebo-controlled clinical trial among children in urban Bangladesh. *Vaccine*. 2015 Apr 24. pii: S0264-410X(15)00512-5. doi: 10.1016/j.Vaccine.2015.04.048. [Epub ahead of print] PubMed PMID: 25917680.
5. Somayaji R, Goss CH, Khan U, Neradilek M, Neuzil KM, Ortiz JR. Cystic Fibrosis Pulmonary Exacerbations Attributable to Respiratory Syncytial Virus and Influenza: A Population-Based Study. *Clin Infect Dis*. 2017 Jun 15;64(12):1760-1767. doi: 10.1093/cid/cix203. PubMed PMID: 28329304.
6. Baxter RP, Lewis N, Fireman B, Hansen J, Klein NP, Ortiz JR. Live Attenuated Influenza Vaccination Prior To Age 3 Years and Subsequent Development of Asthma: A 14-Year Follow-Up Study. *Pediatr Infect Dis J*. 2017 Sep 12. doi:10.1097/INF.0000000000001783. [Epub ahead of print] PubMed PMID: 28914750.

Links:

Med School faculty page: <http://www.medschool.umaryland.edu/profiles/Ortiz-Justin/>

PubMed

publications: <https://www.ncbi.nlm.nih.gov/sites/myncbi/justin.ortiz.1/bibliography/40490877/public/?sort=date&direction=ascending>

Kari Ann Shirey (kshirey@som.umaryland.edu):

Dr. Shirey's research focuses on the ability of pathogens, e.g., *Francisella tularensis*, Respiratory Syncytial Virus (RSV), and influenza to modulate the host's innate immune response by altering macrophage differentiation (alternatively activated phenotype (M2)) and skewing toward a Th2-like phenotype (e.g., IL-4, IL-13, TSLP). A second aspect of Dr. Shirey's research focuses on host-oriented approaches as novel therapeutics for pathogens that induce acute lung injury by modifying expression of cytokines and endogenous danger-associated molecular pattern (DAMP) molecules. Working with Dr. Vogel, Dr. Shirey demonstrated that the TLR4 antagonist, Eritoran, blocks influenza-mediated acute lung injury even when given late in infection. More recently, this work has been followed up with other small molecule inhibitors or neutralizing antibodies that have effectively blocked viral-induced lethality in mice and cotton

rats.

Highlighted Publications:

1. Shirey KA, Nhu QM, Yim, KC, Roberts ZJ, Teijaro JT, Farber DL, Blanco JC, and Vogel SN. (2011). The anti- tumor agent, 5,6-dimethylxanthenone-4-acetic acid (DMXAA), induces IFN- γ mediated antiviral activity *in vitro* and *in vivo*. *J Leuk Biol.* 89:351-57. See accompanying editorial. PMC3040469
2. Shirey KA, Lai W, Scott AJ et al. (2013) The TLR4 antagonist, Eritoran, protects mice from lethal influenza infection. *Nature* 497:498-502. PMC3725830 See accompanying podcast interview.
3. K. A. Shirey, W. Lai, L. M. Pletneva et al. (2014) Agents that increase alternatively activated macrophage differentiation blunt Respiratory Syncytial Virus-mediated lung pathology. *J. Leukoc. Biol.* 96: 951-955. PMC4226793 See accompanying editorial.
4. Piao W, Shirey KA, Ru LW et al. (2015). A decoy peptide that disrupts TIRAP recruitment to TLRs protects mice in a murine model of influenza. *Cell Reports* 11: 1941-1952. PMC4490105
5. Shirey KA, Lai W, Patel MC et al. (2016). Novel strategies for targeting innate immune responses to influenza. *Mucosal Immunol.* 9:1173-82. PMC5125448

Links:

Med School faculty page: <http://www.medschool.umaryland.edu/profiles/Shirey-Kari-Ann/>
PubMed

publications: https://www.ncbi.nlm.nih.gov/sites/myncbi/1xQKiut_y7t5X/bibliography/48010950/public/?sort=date&direction=ascending

Stefanie Vogel (svogel@som.umaryland.edu):



Dr. Vogel's focuses on the innate immune response to infection, the mechanisms by which inflammatory responses are regulated, macrophage differentiation and disease outcome, and targeting TLR signaling pathways to blunt pathogen-mediated acute lung injury. Dr. Vogel's most recent work has identified novel strategies for treating influenza therapeutically by blocking Toll-like receptor 4 signaling, the role of metabolism in the differentiation of macrophages, the

cross-talk between innate immune signaling pathways, and other related topics. Innate immune responses to respiratory infections

Highlighted Publications:

1. K. A. Shirey, W. Lai, A. J. Scott, M. Lipsky, P. Mistry, L. M. Pletneva, C. L. Karp, J. McAlees, T. L. Gioannini, J. Weiss, W. H. Chen, R. K. Ernst, D. P. Rossignol, F. Gusovsky, J. C. Blanco, and S. N. Vogel. The TLR4 antagonist, Eritoran, protects mice from lethal influenza infection. *Nature* 497:498-502 (2013) PMC3725830
2. K. A. Shirey, W. Lai, L. M. Pletneva, F. D. Finkelman, D. J. Feola, J. C. G. Blanco, and S. N. Vogel. Agents that increase alternatively activated macrophage differentiation blunt Respiratory Syncytial Virus-mediated lung pathology. *J. Leukoc. Biol.* 96: 951-955. PMC4226793. (2014). See accompanying editorial.
3. K. A. Shirey, W. Lai, M. C. Patel, L. M. Pletneva, G. Pang, E. Kurt-Jones, M. Lipsky, T. Roger, T. Calandra, K. J. Tracey, Y. Al-Abed, A. G. Bowie, A. Fasano, C. A. Dinarello, F. Gusovsky, J. C. G. Blanco, S. N. Vogel. Novel strategies for targeting innate immune responses to influenza. *Mucosal Immunol.* 9: 1173-1182. (2016). PMC5125448
4. K. Richard, B. Mann, L. Stocker, A. Qin, E. M. Barry, R. K. Ernst, and S. N. Vogel. Monophosphoryl Lipid A enhances efficacy of a *Francisella tularensis* LVS-cationic nanoparticle subunit vaccine against *F. tularensis* Schu S4 challenge by augmenting both humoral and cellular immunity. *Clin Vaccine Immunol.* 24: pii: 300574-16 (2017) PMC5339645
5. K. A. Shirey, W. Lai, L. M. Pletneva, C. L. Karp, S. Divanovic, J. C. G. Blanco, and S. N. Vogel. Role of the lipoxygenase pathway in RSV-induced alternatively activated macrophages leading to resolution of lung pathology. *Mucosal Immunol* 7: 549-557. (2013) PMC3965659.
6. A. A. Awomoyi, P. Rallabhandi, T. I. Pollin, E. Lorenz, M. B. Sztejn, M. S. Boukhvalova, V. G. Hemming, J. C. G. Blanco, and S. N. Vogel. Association of TLR4 polymorphisms with symptomatic Respiratory Syncytial Virus infection in high-risk infants and young children. *J. Immunol.* 179: 3171-3177 (2007).

Links:

Med School faculty page: <http://www.medschool.umaryland.edu/profiles/Vogel-Stefanie/>

PubMed publications:

<http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40447249/?sort=date&direction=ascending>