BIOGRAPHICAL SKETCH

NAME: Sterling, Timothy R.

eRA COMMONS USER NAME: SterlingT

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colgate University Hamilton, NY	B.A.	05/1985	Chemistry, German
Columbia University College of Physicians & Surgeons New York, NY	M.D.	05/1989	Medicine
Columbia Presbyterian Medical Center New York, NY		06/1992	Internal Medicine
Johns Hopkins University School of Medicine Baltimore, MD		06/1998	Infectious Diseases

A. Personal Statement

I am an infectious disease physician-scientist with expertise in the epidemiology and treatment of tuberculosis and HIV. A special area of interest has been drug-resistant *M. tuberculosis*, particularly fluoroquinolone resistance. I have conducted epidemiological studies of fluoroquinolone exposure prior to tuberculosis diagnosis, and its effect on fluoroquinolone-resistant *M. tuberculosis*. I have also conducted laboratory-based studies of phenotypic and genotypic fluoroquinolone resistance in *M. tuberculosis*. I have ongoing research collaborations in this area at Stellenbosch University in South Africa, and more recently at the Center for Infectious Disease Research in Seattle, WA. I am well-qualified to oversee the conduct of this study, with work in Tennessee and South Africa, and its epidemiologic and laboratory-based components. Of my 186 publications, the following are some of my recent publications on fluoroquinolone-resistant *M. tuberculosis*.

1. Devasia R, Blackman A, Eden S, Li H, Maruri F, Shintani A, Alexander C, Kaiga A, Stratton CW, Warkentin J, Tang YW, **Sterling TR**. High proportion of fluoroquinolone-resistant *M. tuberculosis* isolates with novel gyrase polymorphisms and a *gyrA* region associated with fluoroquinolone susceptibility. J Clin Microbiol. 2012; 50:1390-6. PMCID: PMC3318526
2. van der Heijden YF, Maruri F, Blackman A, Holt E, Warkentin JV, Shepherd BE, **Sterling TR**. Fluoroquinolone exposure before tuberculosis diagnosis and risk of death. Int J Tuberc Lung Dis. 2012 Sep;16(9):1162-7. PMCID: PMC3981533
3. van der Heijden YF, Maruri F, Blackman A, Mitchel E, Bian A, Shintani AK, Eden S, Warkentin JV, **Sterling TR**. Fluoroquinolone susceptibility in *Mycobacterium tuberculosis* after pre-diagnosis exposure to older- versus newer-generation fluoroquinolones. Int J Antimicrob Agents. 2013 Sep; 42(3): 232-7. PMCID: PMC3780576
4. Eilertson B, Maruri F, Blackman A, Herrera M, Samuels DC, **Sterling TR**. High proportion of heteroresistance in gyrA and gyrB in fluoroquinolone-resistant *Mycobacterium tuberculosis* clinical isolates. Antimicrob Agents Chemother. 2014; 58(6):3270-5. PMCID: PMC4068501

B. Positions and Honors

Positions and Employment

1992-1996 Staff Physician, U.S. Air Force Medical Center Keesler, Keesler AFB, MS.
1998-2002 Assistant Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine

2002-2003 Associate Professor of Medicine & Epidemiology, Johns Hopkins University School of Medicine
1998-2003 Medical Director, Baltimore City Tuberculosis Clinic
2003-2008 Associate Professor of Medicine, Vanderbilt University School of Medicine
2003-present Director, Epidemiology Research, Division of Infectious Diseases
Director, Epi / Outcomes Working Group, Vanderbilt Comprehensive Care Clinic HIV Cohort
Director, Tuberculosis Research, Metro-Davidson Health Department
2008-2011 Professor of Medicine, Vanderbilt University School of Medicine
2011-present David E. Rogers Professor of Medicine, Vanderbilt University School of Medicine
2012-present Visiting Scientist, KwaZulu Natal Research Institute for Tuberculosis and HIV (K-RITH).Durban
2012-present Director, Vanderbilt Tuberculosis Center

Other Experience and Professional Memberships

- Centers for Disease Control and Prevention (CDC): Guidelines for the Use of Rifamycins for the Treatment of TB Among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. January 2004. Updated September 2007, January 2012, July 2013.
- CDC: Adult/Adolescent HIV/AIDS Surveillance Case Definition and Clinical Staging Consultation. 2005.
- American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA)/Centers for Disease Control (CDC): Diagnostic Standards and Classification of Tuberculosis in Adults and Children. 2007-2011.
- CDC: Expert consultation:3 months of rifapentine+isoniazid for treatment of latent *M. tuberculosis*. 2011.
- Tuberculosis Trials Consortium: Chair, Core Science Group. May 2011-present
- ATS/IDSA/CDC. Guidelines for Treatment of Latent Tuberculosis Infection. Co-chair. 2011-present
- World Health Organization. Guidelines Development Group: Latent Tuberculosis. May 2014
- World Health Organization. Latent Tuberculosis Task Force. April 2015-present
- U.S. Dept of Health and Human Services Adult HIV OI Guidelines, TB section. October 2015-present

Honors (last 5 years)
2011 Robert Koch Award for TB Prevention Research—National TB Controller's Association
2011 Excellence in Public Health Impact Award—Centers for Disease Control and Prevention
2012 Charles C. Shepard Science Award—Centers for Disease Control and Prevention
2014 Fellow, Infectious Diseases Society of America

C. Contributions to Science

1. Drug-resistant TB, with a focus on fluoroquinolone resistance

I have studied drug-resistant TB for more than 20 years. Recently, our focus has been on the role that fluoroquinolone exposure prior to TB diagnosis—for indications other than TB—plays on phenotypic and genotypic fluoroquinolone resistance. The identification of novel resistance mutations and mechanisms could improve the sensitivity of diagnostic tests for fluoroquinolone-resistant *M. tuberculosis*.

a. Frieden TR, **Sterling T**, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. N Engl J Med. 1993; 328:521-6. PMID: 8381207
b. Ginsburg AS, Woolwine SC, Hooper N, Benjamin WH, Dorman SE, Bishai WR, **Sterling TR**. The rapid development of fluoroquinolone resistance in *M. tuberculosis*. N Engl J Med. 2003; 349:1977-8. PMID: 14614180
c. Devasia RA, Blackman A, Gebretsadik T, Griffin M, Shintani A, May C, Smith T, Hooper N, Maruri F, Warkentin J, Mitchel E, **Sterling TR**. Fluoroquinolone resistance in *Mycobacterium tuberculosis*: the effect of duration and timing of fluoroquinolone exposure. Am J Respir Crit Care Med. 2009; 180(4):365-70. PMCID: PMC2731810
d. Eilertson B, Maruri F, Blackman A, Guo Y, Herrera M, van der Heijden Y, Shyr Y, **Sterling TR**. A novel resistance mutation in eccC5 of the ESX-5 secretion system confers ofloxacin resistance in Mycobaterium tuberculosis. J Antimicrob Chemother 2016 Jun 3. Epub ahead of print. PMID:27261264.

2. Treatment of HIV-related TB

I have led a series of studies of HIV-related TB that have characterized risk factors for TB relapse, acquired rifamycin resistance, immune reconstitution inflammatory syndrome (IRIS), and mortality. These studies have

helped inform the optimal timing of antiretroviral therapy initiation in TB patients, and the optimal duration of TB therapy in HIV-infected persons.

a. Pettit AC, Jenkins CA, Stinnette SE, Rebeiro PF, Blackwell RB, Raffanti SP, Shepherd BE, **Sterling TR**. Tuberculosis risk before and after highly active antiretroviral therapy initiation: does HAART increase the short-term TB risk in a low incidence TB setting? J Acquir Immune Defic Syndr. 2011; 57(4):305-10. PMCID: PMC3141096
b. **Sterling TR**, Lau B, Zhang J, et al, for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Risk factors for tuberculosis after highly active antiretroviral therapy initiation in the United States and Canada: implications for tuberculosis screening. J Infect Dis. 2011; 204(6):893-901. PMCID: PMC3156918
c. Cortes CP, Wehbe FH, McGowan CC, Shepherd BE, Duda SN, Jenkins CA, Gonzalez E, Carriquiry G, Schechter M, Padgett D, Cesar C, Madero JS, Pape JW, Masys DR, **Sterling TR** and the Caribbean, Central American, South American network for HIV research (CCASA-net) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). Duration of anti-tuberculosis therapy and timing of antiretroviral therapy initiation: association with mortality in HIV-related tuberculosis. PLoS ONE. 2013; 8(9):e74057. PMCID: PMC3774609.
d. Pettit AC, Mendes A, Jenkins C, Napravnik S, Freeman A, Shepherd BE, Dowdy D, Gill J, Rachlis A, Moore R, **Sterling TR**; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Timing of antiretroviral treatment, immunovirologic status and TB risk: implications for test and treat. J Acquir Immune Defic Syndr. 2016 Apr 5. [Epub ahead of print] PMCID: PMC4942351

3. Outcomes of HIV infection

I have led several observational studies of HIV outcomes that have provided insights into optimal management of HIV, as well as HIV pathogenesis. This has included studies of the sex difference in HIV-1 RNA, the association between pregnancy and improved HIV outcomes, the optimal timing of antiretroviral therapy initiation, and the relationship between body mass index and immune restoration on antiretroviral therapy.

a. **Sterling TR**, Vlahov D, Astemborski J, Hoover DR, Margolick JB, Quinn TC. Initial plasma HIV-1 RNA and progression to AIDS in women and men. N Engl J Med. 2001; 344:720-5. PMID: 11236775
b. Kitahata MM, Gange SJ, Abraham A, et al, **Sterling TR**, et al, Moore RD, for The North American AIDS Cohort Collaboration on Research and Design. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med. 2009; 360(18):1815-26. PMCID: PMC2854555
c. Koethe JR, Grome H, Jenkins CA, Kalams SA, **Sterling TR**. The metabolic and cardiovascular consequences of obesity in persons with HIV on long-term antiretroviral therapy. AIDS. 2015 Sep 28. PMID: 26418084.
d. Castilho JL, Shepherd BE, Koethe J, Turner M, Bebawy S, Logan J, Rogers WB, Raffanti S, **Sterling TR**. CD4+/CD8+ ratio, age, and risk of serious non-communicable diseases in HIV-infected adults on antiretroviral therapy. AIDS 2016 Mar 27;30(6):899-908. PMCID: PMC4785819

4. Immunogenetic factors associated with TB risk, particularly extrapulmonary disease

In a series of studies we have identified subtle immune defects among HIV-uninfected persons who have completed treatment for extrapulmonary TB. These abnormalities include decreased CD4+ counts, low unstimulated and stimulated cytokine production, increased regulatory T-cell frequency, and increased CD4+ activation. We also identified genetic polymorphisms associated with extrapulmonary TB. This suggests that an underlying host defect could predispose to extrapulmonary TB. This provides insight into TB pathogenesis, in which only a small sub-set of persons infected with *M. tuberculosis* progress to TB.

a. **Sterling TR**, Dorman SE, Chaisson RE, Ding L, Hackman J, Moore K, Holland SM. Human immunodeficiency virus-seronegative adults with extrapulmonary tuberculosis have abnormal innate immune responses. Clin Infect Dis. 2001; 33(7):976-82. PMID: 11528568
b. Antas PR, Ding L, Hackman J, Reeves-Hammock L, Shintani AK, Schiffer J, Holland SM, **Sterling TR**. Decreased CD4+ lymphocytes and innate immune responses in adults with previous extrapulmonary tuberculosis. J Allergy Clin Immunol. 2006;117(4):916-23. PMID: 16630952
c. **Sterling TR**, Martire T, de Almeida AS, Ding L, Greenberg DE, Moreira LA, Elloumi H, Torres AP, Sant'Anna CC, Calazans E, Paraguassu G, Gebretsadik T, Shintani A, Miller K, Kritski A, Lapa e Silva JR,

Holland SM. Immune function in young children with previous pulmonary or miliary/meningeal tuberculosis and impact of BCG vaccination. Pediatrics. 2007; 120(4):e912-21. PMID: 17908747

d. Motsinger-Reif AA, Antas PR, Oki NO, Levy S, Holland SM, **Sterling TR**. Polymorphisms in IL-1beta, vitamin D receptor Fok1, and Toll-like receptor 2 are associated with extrapulmonary tuberculosis. BMC Med Genet. 2010;11:37. PMCID: PMC2837863

5. Short-course treatment of latent *M. tuberculosis* infection

I led a large multi-center clinical trial which demonstrated that a 3-month once-weekly regimen of isoniazid + rifapentine given under direct observation was as effective and well-tolerated as the gold-standard 9-month daily self-administered isoniazid regimen. The higher completion rate of the short-course regimen could improve the effectiveness of TB prevention efforts, and contribute to a decrease in the global TB burden.

a. **Sterling TR**, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies D, Kerrigan A, Weis SE, Weiner M, Wing D, Conde MB, Bozeman L, Horsburgh CR, Chaisson RE, and the TB Trials Consortium. Three months of once-weekly rifapentine and isoniazid for the treatment of latent *M. tuberculosis* infection (PREVENT TB). N Engl J Med. 2011; 365:2155-66. PMID: 22150035.
b. Villarino ME, Scott NA, Weis SE, Weiner M, Conde MB, Jones B, Nachman S, Oliveira R, Moro RN, Shang N, Goldberg SV, **Sterling TR**; IMPAACT, TB Trials Consortium. Treatment for preventing tuberculosis in children and adolescents: a randomized clinical trial of a 3-month, 12-dose regimen of a combination of rifapentine and isoniazid. JAMA Pediatr. 2015; 169(3):247-55. PMID: 25580725
c. **Sterling TR**, Moro RN, Borisov AS, Phillips E, Shepherd G, Adkinson NF, Weis S, Ho C, Villarino ME; TB Trials Consortium. Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT TB Study. Clin Infect Dis. 2015 Aug 15;61(4):527-35. PMID: 25904367. PMCID: PMC4560029
d. **Sterling TR**, Scott NA, Miro JM, Calvet G, La Rosa A, Infante R, Chen MP, Benator DA, Gordin F, Benson CA, Chaisson RE, Villarino ME, the Tuberculosis Trials Consortium, and the AIDS Clinical Trials Group. Three months of weekly rifapentine and isoniazid for treatment of *M. tuberculosis* infection in HIV co-infected persons. AIDS 2016 June 19;30(10):1607-15. PMCID: PMC4899978

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/timothy.sterling.1/bibliography/40632070/public/?sort=date&direction=descending

D. Research Support

Current

NIAID R56 AI118361 — Multi- PI: Sterling TR (contact PI) — 08/01/16-07/31/17
National Institutes of Health
Fluoroquinolones and efflux-mediated cross-resistance in HIV-related TB
This project studies novel fluoroquinolone resistance mutations and mechanisms in *M. tuberculosis*, their contribution to resistance to other drugs, and the role of HIV infection.

NIH R01 AI120790 — PI: Sterling TR — 08/12/16-07/31/20
Predictors of treatment toxicity, failure, and relapse in HIV-related tuberculosis
This project seeks to identify pharmacogenomic predictors of TB/HIV treatment toxicity and effectiveness in Brazil.

CDC10FED TB Trials Consortium, — PI: Sterling TR; Peru PI: Gotuzzo E — 09/30/09-09/29/19
Universidad Cayetano Heredia, Lima, Peru
Centers for Disease Control and Prevention
This consortium conducts programmatically relevant studies of tuberculosis treatment and prevention.

NIAID 5 U01 AI069923 — Project PI: Sterling TR — 07/01/16-06/30/17

National Institutes of Health
Regional Prospective Observational Research for TB (RePORT)-Brazil
Supplement to Caribbean, Central and South America network for HIV epidemiology (CCASAnet)
With joint funding from the NIH and the Brazilian Ministry of Health, this is a prospective, multi-center cohort of TB cases and close contacts in Rio de Janeiro, Salvador, and Manaus, Brazil. There is a biorepository of *M. tuberculosis* isolates, cells, DNA, and RNA. Studies will be performed of host and pathogen determinants of TB treatment response, recurrence, acquiring *M. tuberculosis* infection, and progressing to TB disease.

RePORT South Africa PI: Pym A and Sterling TR 01/01/2016 - 12/31/2018
U.S. Civilian Research and Development Foundation
This study site is a collaboration between the Africa Health Research Institute (Durban) and Vanderbilt
Role: Vanderbilt PI

TB Epidemiologic Studies Consortium PI: Stout JE -Duke 09/30/11-09/29/21
Centers for Disease Control and Prevention
This consortium conducts studies of the diagnosis and treatment of latent *M. tuberculosis* infection.
Role: Co-investigator

NIAID P30AI110527 PI: Mallal S 04/01/15 – 03/31/20
National Institutes of Health
Tennessee Center for AIDS Research
Vanderbilt-Meharry-Tennessee Department of Health
Role: Associate Director, Developmental Core

NIAID U01AI069918 PI: Moore RD -Johns Hopkins 07/01/16-06/30/21
National Institutes of Health: Interntional Epi Databases to Evaluate AIDS
North America (NA-ACCORD)
Role: Vanderbilt PI

NIAID U01AI069923 PI: McGowan C 07/01/16-06/30/21
National Institutes of Health: International Epi Databases to Evaluate AIDS
South America and the Caribbean (CCASAnet)
Role: Co-investigator

Completed (past 3 years)

Biomarker Discovery for TB Infection and Disease PI: Sterling 04/01/15-06/30/16
NIH / Brazilian Ministry of Health (CNPq)
Role: Vanderbilt PI

NIAID K24 AI65298 PI: Sterling TR 05/01/05-04/30/16
Mentoring In HIV and Tuberculosis Research
National Institutes of Health
Dr. Sterling's research is focused on the following areas: 1) fluoroquinolone resistance in *M. tuberculosis*; 2) outcomes of HIV infection that influence timing of antiretroviral therapy initiation; 3) immunogenetic risk factors for tuberculosis infection and disease; 4) novel strategies to treat *M. tuberculosis* infection and disease; and 5) optimizing effectiveness of treatment of tuberculosis in HIV-infected persons. The K24 award allows Dr. Sterling to mentor young investigators in these areas of HIV and tuberculosis research.

NIAID 5 U01 AI069924 PI: Sterling TR 1/1/2013-06/30/15
National Institutes of Health
Bringing K-RITH into IeDEA and the IeDEA TB Data Collection Form Project
Supplement to the International Epidemiologic Databases to Evaluate AIDS- Southern Africa (IeDEA-SA) study (M Egger- University of Bern, PI), to study TB epidemiology in Durban, South Africa.

Traveling Scientist Award PI: Sterling TR 11/01/12-12/31/14
KwaZulu Natal Research Institute for TB and HIV (K-RITH). Howard Hughes Medical Institute + University of KwaZulu Natal. Novel fluoroquinolone resistance mutations and mechanisms in *M. tuberculosis*