Stanford



Robert W. Shafer

Professor (Research) of Medicine (Infectious Diseases) and, by courtesy, of Pathology

Medicine - Infectious Diseases

CLINICAL OFFICE (PRIMARY)

- **Stanford AIDS Clinical Trial Unit**

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  Palo Alto, CA 94304

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Bio

BIO

Dr. Robert Shafer specializes in the treatment of infectious diseases. He has practiced for more than 25 years. Dr. Shafer has a special interest in acute and chronic viral infections.

CLINICAL FOCUS

- Infectious Disease

ACADEMIC APPOINTMENTS

- Professor-Research, Medicine - Infectious Diseases
- Professor-Research (By courtesy), Pathology
- Member, Bio-X

PROFESSIONAL EDUCATION

- Medical Education: New York University School of Medicine (1983) NY
- Fellowship: Stanford University School of Medicine (1993) CA
- Board Certification: Infectious Disease, American Board of Internal Medicine (1988)
- Fellowship: SUNY at Brooklyn School Of Medicine (1988) NY
- Board Certification: Internal Medicine, American Board of Internal Medicine (1986)
- Residency: Lenox Hill Hospital (1986) NY
- Internship: Lenox Hill Hospital (1984) NY

LINKS

- HIV Drug Resistance Database: http://hivdb.stanford.edu

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My group's research is on the mechanisms and consequences of virus evolution with a focus on HIV therapy and drug resistance. We maintain a public HIV drug resistance database (http://hivdb.stanford.edu) as a resource for HIV drug resistance surveillance, interpreting HIV drug resistance tests, and HIV drug development. These three disciplines – epidemiology, clinical management, and basic science – reflect the interdisciplinary nature of antiviral drug resistance research and represent the range of our group's activities.

HIV drug resistance, once the main challenge to the very concept that antiretroviral therapy would be possible, has been countered in a striking success of modern medicine. However, HIV drug resistance persists as the main threat to the long-term effectiveness of antiretroviral therapy in the under-resourced parts of the world with the highest numbers of HIV-infected people. The paramount goal of our group's work is to inform HIV treatment and prevention policies by identifying the most important factors responsible for the emergence and spread of drug resistance.

Additional interests of our group include sequence analyses that provide insight into viral pathogenesis, open source informatics approaches that facilitate the use of genomic data in clinical practice, and new sequencing technologies.

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biomedical Data Science (PhD Program)
- Immunology (PhD Program)

Publications

PUBLICATIONS

- **Genotypic challenges in implementing broadly neutralizing antibody-based long-acting HIV-1 therapies.** *Communications medicine*
  Tao, K., Herschhorn, A., Fera, D., Lynch, R. M., Julg, B. D., Korber, B., Shafer, R. W.
  2026
- **Combating antimicrobial resistance in malaria, HIV and tuberculosis.** *Nature reviews. Drug discovery*
  Duffey, M., Shafer, R. W., Timm, J., Burrows, J. N., Fotouhi, N., Cockett, M., Leroy, D.
  2024
- **Prevalence of Emergent Dolutegravir Resistance Mutations in People Living with HIV: A Rapid Scoping Review.** *Viruses*
  Chu, C., Tao, K., Kouamou, V., Avalos, A., Scott, J., Grant, P. M., Rhee, S. Y., McCluskey, S. M., Jordan, M. R., Morgan, R. L., Shafer, R. W.
  2024; 16 (3)
- **Recommendations on data sharing in HIV drug resistance research.** *PLoS medicine*
  Inzaule, S. C., Siedner, M. J., Little, S. J., Avila-Rios, S., Ayitewala, A., Bosch, R. J., Calvez, V., Ceccherini-Silberstein, F., Charpentier, C., Descamps, D., Eshleman, S. H., Fokam, J., Frenkel, et al
  2023; 20 (9): e1004293
- **Treatment Emergent Dolutegravir Resistance Mutations in Individuals Naïve to HIV-1 Integrase Inhibitors: A Rapid Scoping Review.** *Viruses*
  Tao, K., Rhee, S. Y., Chu, C., Avalos, A., Ahluwalia, A. K., Gupta, R. K., Jordan, M. R., Shafer, R. W.
  2023; 15 (9)
- **Genotypic Resistance Testing of HIV-1 DNA in Peripheral Blood Mononuclear Cells.** *Clinical microbiology reviews*
  Chu, C., Armenia, D., Walworth, C., Santoro, M. M., Shafer, R. W.
  2022: e0005222

- **Susceptibility of SARS-CoV-2 Omicron Variants to Therapeutic Monoclonal Antibodies: Systematic Review and Meta-analysis.** *Microbiology spectrum*
  Tao, K., Tzou, P. L., Kosakovsky Pond, S. L., Ioannidis, J. P., Shafer, R. W.
  2022: e0092622

- **Public availability of HIV-1 drug resistance sequence and treatment data: a systematic review.** *The Lancet. Microbe*
  Rhee, S., Kassaye, S. G., Jordan, M. R., Kouamou, V., Katzenstein, D., Shafer, R. W.
  2022; 3 (5): e392-e398

- **Coronavirus Resistance Database (CoV-RDB): SARS-CoV-2 susceptibility to monoclonal antibodies, convalescent plasma, and plasma from vaccinated persons.** *PloS one*
  Tzou, P. L., Tao, K., Pond, S. L., Shafer, R. W.
  2022; 17 (3): e0261045

- **The biological and clinical significance of emerging SARS-CoV-2 variants.** *Nature reviews. Genetics*
  Tao, K., Tzou, P. L., Nouhin, J., Gupta, R. K., de Oliveira, T., Kosakovsky Pond, S. L., Fera, D., Shafer, R. W.
  2021

- **SARS-CoV-2 Antiviral Therapy.** *Clinical microbiology reviews*
  Tao, K., Tzou, P. L., Nouhin, J., Bonilla, H., Jagannathan, P., Shafer, R. W.
  2021: e0010921

- **Virological Failure and Acquired Genotypic Resistance Associated With Contemporary Antiretroviral Treatment Regimens.** *Open forum infectious diseases*
  Rhee, S. Y., Clutter, D. n., Hare, C. B., Tchakoute, C. T., Sainani, K. n., Fessel, W. J., Hurley, L. n., Slome, S. n., Pinsky, B. A., Silverberg, M. J., Shafer, R. W.
  2020; 7 (9): ofaa316

- **Analysis of unusual and signature APOBEC-mutations in HIV-1 pol next-generation sequences.** *PloS one*
  Tzou, P. L., Kosakovsky Pond, S. L., Avila-Rios, S. n., Holmes, S. P., Kantor, R. n., Shafer, R. W.
  2020; 15 (2): e0225352

- **Coronavirus Antiviral Research Database (CoV-RDB): An Online Database Designed to Facilitate Comparisons between Candidate Anti-Coronavirus Compounds.** *Viruses*
  Tzou, P. L., Tao, K. n., Nouhin, J. n., Rhee, S. Y., Hu, B. D., Pai, S. n., Parkin, N. n., Shafer, R. W.
  2020; 12 (9)

- **Multiplex Solid-Phase Melt Curve Analysis for the Point-of-Care Detection of HIV-1 Drug Resistance** *JOURNAL OF MOLECULAR DIAGNOSTICS*
  Clutter, D. S., Mazarei, G., Sinha, R., Manasa, J., Nouhin, J., LaPrade, E., Bolouki, S., Tzou, P. L., Hannita-Hui, J., Sahoo, M. K., Kuimelis, P., Kuimelis, R. G., Pinsky, et al
  2019; 21 (4): 580–92

- **Trends in the Molecular Epidemiology and Genetic Mechanisms of Transmitted Human Immunodeficiency Virus Type 1 Drug Resistance in a Large US Clinic Population** *CLINICAL INFECTIOUS DISEASES*
  Rhee, S., Clutter, D., Fessel, W., Klein, D., Slome, S., Pinsky, B. A., Marcus, J. L., Hurley, L., Silverberg, M. J., Pond, S., Shafer, R. W.
  2019; 68 (2): 213–21

- **Trends in the Molecular Epidemiology and Genetic Mechanisms of Transmitted HIV-1 Drug Resistance in a Large U.S. Clinic Population.** *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*
  Rhee, S., Clutter, D., Fessel, W. J., Klein, D., Slome, S., Pinsky, B. A., Marcus, J. L., Hurley, L., Silverberg, M. J., Kosakovsky Pond, S. L., Shafer, R. W.
  2018

- **Mutational Correlates of Virological Failure in Individuals Receiving a WHO-Recommended Tenofovir-Containing First-Line Regimen: An International Collaboration.** *EBioMedicine*
  Rhee, S., Varghese, V., Holmes, S. P., van Zyl, G. U., Steegen, K., Boyd, M. A., Cooper, D. A., Nsanzimana, S., Saravanan, S., Charpentier, C., de Oliveira, T., Etiebet, M. A., Garcia, et al
  2017; 18: 225-235

- **Evolution of gag and gp41 in Patients Receiving Ritonavir-Boosted Protease Inhibitors.** *Scientific reports*

Manasa, J. n., Varghese, V. n., Pond, S. L., Rhee, S. Y., Tzou, P. L., Fessel, W. J., Jang, K. S., White, E. n., Rögnvaldsson, T. n., Katzenstein, D. A., Shafer, R. W.
2017; 7 (1): 11559

- **HIV-1 drug resistance and resistance testing.** *Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases*
  Clutter, D. S., Jordan, M. R., Bertagnolio, S., Shafer, R. W.
  2016
- **HIV-1 Protease, Reverse Transcriptase, and Integrase Variation** *JOURNAL OF VIROLOGY*
  Rhee, S., Sankaran, K., Varghese, V., Winters, M. A., Hurt, C. B., Eron, J. J., Parkin, N., Holmes, S. P., Holodniy, M., Shafer, R. W.
  2016; 90 (13): 6058-6070
- **Response to Therapy in Antiretroviral Therapy-Naive Patients With Isolated Nonnucleoside Reverse Transcriptase Inhibitor-Associated Transmitted Drug Resistance** *JAIDS-JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES*
  Clutter, D. S., Fessel, W. J., Rhee, S., Hurley, L. B., Klein, D. B., Ioannidis, J. P., Silverberg, M. J., Shafer, R. W.
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- **Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study** *LANCET INFECTIOUS DISEASES*
  Gregson, J., Tang, M., Ndembi, N., Hamers, R. L., Rhee, S., Marconi, V. C., Diero, L., Brooks, K., Theys, K., de Wit, T. F., Arruda, M., Garcia, F., Monge, et al
  2016; 16 (5): 565-575
- **More effective drugs lead to harder selective sweeps in the evolution of drug resistance in HIV-1.** *eLife*
  Feder, A. F., Rhee, S., Holmes, S. P., Shafer, R. W., Petrov, D. A., Pennings, P. S.
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- **Modifying Antiretroviral Therapy in Virologically Suppressed HIV-1-Infected Patients** *DRUGS*
  Collins, S. E., Grant, P. M., Shafer, R. W.
  2016; 76 (1): 75-98
- **Geographic and Temporal Trends in the Molecular Epidemiology and Genetic Mechanisms of Transmitted HIV-1 Drug Resistance: An Individual-Patient- and Sequence-Level Meta-Analysis.** *PLoS medicine*
  Rhee, S., Blanco, J. L., Jordan, M. R., Taylor, J., Lemey, P., Varghese, V., Hamers, R. L., Bertagnolio, S., de Wit, T. F., Aghokeng, A. F., Albert, J., Avi, R., Avila-Rios, et al
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- **HIV-1 Drug Resistance Mutations: Potential Applications for Point-of-Care Genotypic Resistance Testing.** *PloS one*
  Rhee, S., Jordan, M. R., Raizes, E., Chua, A., Parkin, N., Kantor, R., van Zyl, G. U., Mukui, I., Hosseinipour, M. C., Frenkel, L. M., Ndembi, N., Hamers, R. L., Rinke de Wit, et al
  2015; 10 (12)
- **A uniquely prevalent nonnucleoside reverse transcriptase inhibitor resistance mutation in Russian subtype A HIV-1 viruses** *AIDS*
  Kolomeets, A. N., Varghese, V., Lemey, P., Bobkova, M. R., Shafer, R. W.
  2014; 28 (17): F1-F8
- **Non-nucleoside reverse transcriptase inhibitor (NNRTI) cross-resistance: implications for preclinical evaluation of novel NNRTIs and clinical genotypic resistance testing** *JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY*
  Melikian, G. L., Rhee, S., Varghese, V., Porter, D., White, K., Taylor, J., Towner, W., Troia, P., Burack, J., deJesus, E., Robbins, G. K., Razzeca, K., Kagan, et al
  2014; 69 (1): 12-20
- **Prototypical Recombinant Multi-Protease-Inhibitor-Resistant Infectious Molecular Clones of Human Immunodeficiency Virus Type 1** *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*
  Varghese, V., Mitsuya, Y., Fessel, W. J., Liu, T. F., Melikian, G. L., Katzenstein, D. A., Schiffer, C. A., Holmes, S. P., Shafer, R. W.
  2013; 57 (9): 4290-4299
- **Trends in Genotypic HIV-1 Antiretroviral Resistance between 2006 and 2012 in South African Patients Receiving First- and Second-Line Antiretroviral Treatment Regimens** *PLOS ONE*
  van Zyl, G. U., Liu, T. F., Claassen, M., Engelbrecht, S., de Oliveira, T., Preiser, W., Wood, N. T., Travers, S., Shafer, R. W.

2013; 8 (6)

- **Nucleoside reverse transcriptase inhibitor resistance mutations associated with first-line stavudine-containing antiretroviral therapy: programmatic implications for countries phasing out stavudine.** *journal of infectious diseases*
  Tang, M. W., Rhee, S., Bertagnolio, S., Ford, N., Holmes, S., Sigaloff, K. C., Hamers, R. L., de Wit, T. F., Fleury, H. J., Kanki, P. J., Ruxrungtham, K., Hawkins, C. A., Wallis, et al
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- **Low-Level Persistence of Drug Resistance Mutations in Hepatitis B Virus-Infected Subjects with a Past History of Lamivudine Treatment** *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*
  Margeridon-Thermet, S., Svarovskaia, E. S., Babrzadeh, F., Martin, R., Liu, T. F., Pacold, M., Reuman, E. C., Holmes, S. P., Borroto-Esoda, K., Shafer, R. W.
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- **HIV-1 Antiretroviral Resistance: Scientific Principles and Clinical Applications** *DRUGS*
  Tang, M. W., Shafer, R. W.
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- **The efficacy of an anti-CD4 monoclonal antibody for HIV-1 treatment** *ANTIVIRAL RESEARCH*
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  2011; 92 (3): 484-487

- **HIV-1 Integrase Inhibitor Resistance and Its Clinical Implications** *JOURNAL OF INFECTIOUS DISEASES*
  Blanco, J., Varghese, V., Rhee, S., Gatell, J. M., Shafer, R. W.
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- **Comparison of the Mechanisms of Drug Resistance among HIV, Hepatitis B, and Hepatitis C** *VIRUSES-BASEL*
  Margeridon-Thermet, S., Shafer, R. W.
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- **HIV-1 Protease Mutations and Protease Inhibitor Cross-Resistance** *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*
  Rhee, S., Taylor, J., Fessel, W. J., Kaufman, D., Towner, W., Troia, P., Ruane, P., Hellinger, J., Shirvani, V., Zolopa, A., Shafer, R. W.
  2010; 54 (10): 4253-4261

- **Minority Variants Associated with Transmitted and Acquired HIV-1 Nonnucleoside Reverse Transcriptase Inhibitor Resistance: Implications for the Use of Second-Generation Nonnucleoside Reverse Transcriptase Inhibitors** *JAIDS-JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES*
  Varghese, V., Shahriar, R., Rhee, S., Liu, T., Simen, B. B., Egholm, M., Hanczaruk, B., Blake, L. A., Gharizadeh, B., Babrzadeh, F., Bachmann, M. H., Fessel, W. J., Shafer, et al
  2009; 52 (3): 309-315

- **Predictive Value of HIV-1 Genotypic Resistance Test Interpretation Algorithms** *JOURNAL OF INFECTIOUS DISEASES*
  Rhee, S., Fessel, W. J., Liu, T. F., Marlowe, N. M., Rowland, C. M., Rode, R. A., Vandamme, A., Van Laethem, K., Brun-Vezinet, F., Calvez, V., Taylor, J., Hurley, L., Horberg, et al
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- **Ultra-Deep Pyrosequencing of Hepatitis B Virus Quasispecies from Nucleoside and Nucleotide Reverse-Transcriptase Inhibitor (NRTI)-Treated Patients and NRTI-Naive Patients** *15th Conference on Retroviruses and Opportunistic Infections*
  Margeridon-Thermet, S., Shulman, N. S., Ahmed, A., Shahriar, R., Liu, T., Wang, C., Holmes, S. P., Babrzadeh, F., Gharizadeh, B., Hanczaruk, B., Simen, B. B., Egholm, M., Shafer, et al
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- **Drug Resistance Mutations for Surveillance of Transmitted HIV-1 Drug-Resistance: 2009 Update** *PLOS ONE*
  Bennett, D. E., Camacho, R. J., Otelea, D., Kuritzkes, D. R., Fleury, H., Kiuchi, M., Heneine, W., Kantor, R., Jordan, M. R., Schapiro, J. M., Vandamme, A., Sandstrom, P., Boucher, et al
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- **Characterization of mutation spectra with ultra-deep pyrosequencing: Application to HIV-1 drug resistance** *GENOME RESEARCH*
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  2007; 17 (8): 1195-1201

- **HIV-1 subtype B protease and reverse transcriptase amino acid covariation** *PLOS COMPUTATIONAL BIOLOGY*
  Rhee, S., Liu, T. F., Holmes, S. P., Shafer, R. W.
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- **Rationale and uses of a public HIV drug-resistance database** *Symposium on Bridging Generations Toward an Understanding of Infectious Disease Pathogenesis*
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  Gonzales, M. J., JOHNSON, E., Dupnik, K. M., Imamichi, T., Shafer, R. W.
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