

Jason D. Limberis

Personal Information



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Profile

As an accomplished infectious disease researcher, I have dedicated my career to investigating the causative agent of tuberculosis, *Mycobacterium tuberculosis*, using a combination of wet lab work and bioinformatics. I focus on understanding the genomic and transcriptional correlates of drug resistance, clinical outcomes, and patient infectiousness. Growing up in South Africa, I witnessed firsthand the devastating impact of tuberculosis, which fuels my passion for this field.

I am currently a postdoctoral fellow in the Department of Experimental Medicine at the University of California, San Francisco (UCSF). Prior to joining UCSF, I led the Bioinformatics and Drug Resistance Group at the Center for Lung Infection and Immunity at the University of Cape Town, where I published several papers on treatment outcomes, patient infectiousness, and transmission of drug-resistant tuberculosis. Additionally, I developed bioinformatics and statistical analysis tools for non-bioinformaticians and lectured the group on genomic and transcriptomic analyses and machine learning approaches. I continue to collaborate with this group on several ongoing projects.

I work in two capacities in my current role. First, I perform bioinformatic analyses for the Ernst Lab in the Department of Experimental Medicine at UCSF. For example, I recently analyzed RNAseq data from cell subsets obtained from *M. tuberculosis*-infected mice to investigate the killing ability of various immune cells. Second, I work with John Metcalfe on *M. tuberculosis* drug resistance diagnostics. I have developed a pipeline to analyze UMI tagged amplicons sequenced on the Oxford Nanopore MiniON, and have explored novel differential lysis of *M. tuberculosis* in sputum to allow for rapid, cost-effective sequencing directly from patient sputum without the need for culture.

I am an experienced manuscript writer and have contributed to numerous grant applications, including several submissions to the NIH, MRC, EDCTP, and Royal Society. I have also managed several grants and written progress reports. As head of the Bioinformatics and Drug Resistance group, I managed a team, trained M.Sc. and Ph.D. students, and held regular meetings. One member of my team was a Ph.D. candidate that I mentored in the investigation of the impact of new anti-TB drugs on patient-important outcomes, leading to several high-impact publications.

My rare combination of wet lab and bioinformatics abilities and experience has allowed me to conceptualize ideas, perform lab work, optimize techniques, and develop the computational methods necessary to analyze the data I generate. I am skilled in laboratory, statistical, and bioinformatic techniques and am biohazard level 3 certified. Additionally, I have a robust knowledge of infectious diseases, bioinformatics, statistics, machine learning, and molecular biology. I am an effective leader and mentor, dedicated to disseminating the knowledge I have gathered through the tutelage of my mentors.

Work experience

10/2019 – present
San Francisco,
United States

Postdoctoral Researcher **Department of Experimental Medicine, University of California, San Francisco**

- Conducted extensive literature reviews to identify gaps in existing knowledge and inform research hypotheses.
- Designed and executed experiments, analyzing data to draw conclusions and make recommendations for further study.
- Collaborated with colleagues to publish research findings in peer-reviewed journals and present at conferences.
- Mentored graduate students and guided experimental design, data analysis, and scientific writing.

07/2017 – 09/2019
Cape Town, South Africa

Postdoctoral Researcher **Center for Lung Infection and Immunity, University of Cape Town**

- Developed and implemented computational pipelines for analyzing genomic and transcriptomic data.
- Conducted statistical analyses and created visualizations to identify significant gene expression patterns.
- Designed and executed experiments and interpreted results.
- Published research findings in peer-reviewed journals and presented at scientific conferences.

01/2017 – 06/2017
Barcelona, Spain

Internship **Novartis-CRG mobility program, Centre for Genomic Regulation**

01/2011 – 11/2012
Cape Town, South Africa

Internship **Cereal Genomics Laboratory, University of Stellenbosch**

Education

02/2014 – 06/2017
Cape Town, South Africa

PhD Med Medicine **University of Cape Town, Cape Town** Upgraded MSc to PhD in 2015

01/2013 – 12/2013
Cape Town, South Africa

BSc Honours Medical Molecular Biology **University of Stellenbosch**

01/2008 – 06/2012
Stellenbosch, Cape Town

BSc Molecular Biology with Biotechnology **University of Stellenbosch, Cape Town**

Skills

BIOINFORMATICS

BASH

Python

R

LABORATORY TECHNIQUES

-Biohazard Level 3 certified

-Mycobacterial, bacterial and yeast cell culture

-DNA, RNA, and plasmid isolation (manual methods)

-PCR, qPCR, digital PCR, and RT-PCR

-Library preparation and sequencing

-Cloning

-PAGE

-Protein expression

-Southern and Western blotting

-Scanning electron microscopy

-Confocal microscopy

Skills

STATISTICAL TECHNIQUES

-Basic descriptive stats	-Regression and classification analyses	-Survival models (Cox, Kaplan-Meier)	-Geneome wide association
-Machine learning techniques (SVM, XGBoost, rf, BST)	-Population genetics	-Graph theory	

MISCELLANEOUS

-3D printing	-Laser cutting	-Soldering	-Illustrator/Photoshop
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Awards

2017	Best oral presentation SATS conference
2018	Best postgraduate publication Faculty of Health Sciences, UCT

Certificates

Genetic data analysis using R
PRstatistics, Scotland

Bioinformatics Training (2 x 2 weeks)
LSHTM, London

Gene Expression Biomarker Masterclass
UCT, Cape Town

Next Generation Sequencing
CAF, Cape Town

Digital and RT-PCR
CAF, Cape Town

Good Clinical Laboratory Practice
HVTN, Cape Town

Machine Learning
Stanford University, Online

Writing in The Sciences
Stanford University, Online

Game Theory
Stanford University, Online

Deep Learning Specialization (4 courses)
Deeplearning.ai, Online

Data Science Specialization (10 courses)
Johns Hopkins University, Online

Genomic Data Science Specialization (8 courses)
Johns Hopkins University, Online

Statistical Reasoning for Public Health 1

Johns Hopkins University, Online

Statistical Reasoning for Public Health 2

Johns Hopkins University, Online

Statistical Inference

Johns Hopkins University, Online

Biostatistics in Public Health Specialization (4 courses)

Johns Hopkins University, Online

Phylogenetics: An Introduction

EMBL-EBI, Online

IBM Cognitive Class

Big Data University, Online

Epidemics - the Dynamics of Infectious Disease

Pennsylvania State University, Online

📄 Web Applications

Demonstration available at

http://drdx.me/index_webVersion.html

2022

DrDx.Me – Amplicon Data Analysis Server

www.DrDx.Me

2021

SeqCals – Sequencing Calculators

<https://semiquant-sq.shinyapps.io/SeeK>

2019

Sscalculator – Comprehensive Sample Size and Power Calculator with range graphs

<https://semiquant.shinyapps.io/SampleSizeCalculator/>

2019

DEAD – Diagnostic Estimates and Disease with ROC curves

<https://semiquant.shinyapps.io/DEAD>

📁 Analysis pipelines

2022

cloneArmyInterrogate– identify haplotypes from Illumina paired end sequencing of a specific amplicon

<https://github.com/SemiQuant/cloneArmyInterrogate>

2022

Hasan – bacterial population reconstruction from short read sequencing

<https://github.com/SemiQuant/Hasan>

2022

RCAAnalysis – Analyze long read rolling circle amplified amplicons

<https://github.com/SemiQuant/RCAAnalysis>

2021

pipeline-umi-amplicon – Generate high accuracy single molecule reads using unique molecular identifiers (UMIs) from nanopore amplicon data

<https://github.com/SemiQuant/pipeline-umi-amplicon>

Full Publication Record

<https://tinyurl.com/JasonLimberisPublications>

H-index: 13 | Citations: 646

Limberis JD, Nalyvayko A, Ernst JD, Metcalfe JZ. Circularization of rv0678 for Genotypic Bedaquiline Resistance Testing of Mycobacterium tuberculosis. Microbiol Spectr. 2023 Mar 6;;e0412722. doi: 10.1128/spectrum.04127-22. [Epub ahead of print] PubMed PMID: 36877083.

Whitfield MG, Engelthaler DM, Allender C, Folkerts M, Heupink TH, **Limberis J**, Warren RM, Van Rie A, Metcalfe JZ. Comparative Performance of Genomic Methods for the Detection of Pyrazinamide Resistance and Heteroresistance in Mycobacterium tuberculosis. J Clin Microbiol. 2022 Jan 19;60(1):e0190721. doi: 10.1128/JCM.01907-21. Epub 2021 Nov 10. PubMed PMID: 34757831; PubMed Central PMCID: PMC8769725.

Ismail N, Rivière E, **Limberis J**, Huo S, Metcalfe JZ, Warren RM, Van Rie A. Genetic variants and their association with phenotypic resistance to bedaquiline in Mycobacterium tuberculosis: a systematic review and individual isolate data analysis. Lancet Microbe. 2021 Nov;2(11):e604-e616. doi: 10.1016/s2666-5247(21)00175-0. Epub 2021 Aug 31. PubMed PMID: 34796339; PubMed Central PMCID: PMC8597953.

Naidoo CC, Nyawo GR, Sulaiman I, Wu BG, Turner CT, Bu K, Palmer Z, Li Y, Reeve BWP, Moodley S, Jackson JG, **Limberis J**, Diacon AH, van Helden PD, Clemente JC, Warren RM, Noursadeghi M, Segal LN, Theron G. Anaerobe-enriched gut microbiota predicts pro-inflammatory responses in pulmonary tuberculosis. EBioMedicine. 2021 May;67:103374. doi: 10.1016/j.ebiom.2021.103374. Epub 2021 May 8. PubMed PMID: 33975252; PubMed Central PMCID: PMC8122180.

Textbook of tuberculosis & non-tuberculous mycobacterial diseases. Medknow; 2021. 0971-5916.

Rudd S, **Limberis JD**, Rescheneder P. pipeline-umi-amplicon – A pipeline for generating high accuracy single molecule reads using unique molecular identifiers (UMIs) from ONT nanopore amplicon sequence data. [Internet]. 2020 September. Available from: <https://github.com/SemiQuant/pipeline-umi-amplicon>.

Theron G, **Limberis J**, Venter R, Smith L, Pietersen E, Esmail A, Calligaro G, Te Riele J, de Kock M, van Helden P, Gumbo T, Clark TG, Fennelly K, Warren R, Dheda K. Bacterial and host determinants of cough aerosol culture positivity in patients with drug-resistant versus drug-susceptible tuberculosis. Nat Med. 2020 Sep;26(9):1435-1443. doi: 10.1038/s41591-020-0940-2. Epub 2020 Jun 29. PubMed PMID: 32601338; PubMed Central PMCID: PMC8353872.

Tomasicchio M, **Limberis J**, van der Merwe R, Jacobson R, Meldau R, Theron G, Nicol M, Warren R, Dheda K. Differential RD-1-specific IFN-γ host responses to diverse Mycobacterium tuberculosis strains in HIV-uninfected persons may be explained by genotypic variation in the ESX-1 region. Int J Infect Dis. 2020 Jul;96:240-243. doi: 10.1016/j.ijid.2020.04.053. Epub 2020 Apr 24. PubMed PMID: 32339714.

Davids M, Pooran A, Hermann C, Mottay L, Thompson F, Cardenas J, Gu J, Koeuth T, Meldau R, **Limberis J**, Gina P, Srivastava S, Calder B, Esmail A, Tomasicchio M, Blackburn J, Gumbo T, Dheda K. A Human Lung Challenge Model to Evaluate the Safety and Immunogenicity of PPD and Live Bacillus Calmette-Gurin. American Journal of Respiratory and Critical Care Medicine. 2020 May; 201(10):1277-1291. doi: 10.1164/rccm.201908-1580OC.

Klopper M, Heupink TH, Hill-Cawthorne G, Streicher EM, Dippenaar A, de Vos M, Abdallah AM, **Limberis J**, Merker M, Burns S, Niemann S, Dheda K, Posey J, Pain A, Warren RM. A landscape of genomic alterations at the root of a near-untreatable tuberculosis epidemic. BMC Med. 2020 Feb 4;18(1):24. doi: 10.1186/s12916-019-1487-2. PubMed PMID: 32014024; PubMed Central PMCID: PMC6998097.

Olayanju O, Esmail A, **Limberis J**, Dheda K. A regimen containing bedaquiline and delamanid compared to bedaquiline in patients with drug-resistant tuberculosis. European Respiratory Journal. 2020 January; 55(1):1901181-. doi: 10.1183/13993003.01181-2019.

Publications

Meldau R, Randall P, Pooran A, **Limberis J**, Makambwa E, Dhansay M, Esmail A, Dheda K. Same-Day Tools, Including Xpert Ultra and IRISA-TB, for Rapid Diagnosis of Pleural Tuberculosis: a Prospective Observational Study. J Clin Microbiol. 2019 Sep;57(9). doi: 10.1128/JCM.00614-19. Print 2019 Sep. PubMed PMID: 31270183; PubMed Central PMCID: PMC6711909.

Dheda K, Gumbo T, Maartens G, Dooley K, Murray M, Furin J, Nardell E, Warren R, Dheda K, Gumbo T, Maartens G, Dooley K, Esmail A, Murray M, Furin J, Nardell E, London L, Lessem E, **Limberis J**, Theron G, McNerney R, Niemann S, Dowdy D, Van Rie A, Pasipanodya J, Rodrigues C, Clark T, Sirgel F, Schaaf H, Chang K, Lange C, Nahid P, Fourie B, Ndjeka N, Nunn A, Migliori G, Udwadia Z, Horsburgh C, Churchyard G, Menzies D, Hesselting A, Seddon J, Low M, Keshavjee S, Nuermberger E, McIlleron H, Fennelly K, Jindani A, Jaramillo E, Padayatchi N, Barry C, Warren R. The Lancet Respiratory Medicine Commission: 2019 update: epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant and incurable tuberculosis. The Lancet Respiratory Medicine. 2019 September; 7(9):820-826. doi: 10.1016/S2213-2600(19)30263-2.

Olayanju O, Esmail A, **Limberis J**, Gina P, Dheda K. Linezolid interruption in patients with fluoroquinolone-resistant tuberculosis receiving a bedaquiline-based treatment regimen. Int J Infect Dis. 2019 Aug;85:74-79. doi: 10.1016/j.ijid.2019.04.028. Epub 2019 May 14. PubMed PMID: 31100421.

Olayanju O, **Limberis J**, Esmail A, Oelofse S, Gina P, Pietersen E, Fadul M, Warren R, Dheda K. Long-term bedaquiline-related treatment outcomes in patients with extensively drug-resistant tuberculosis from South Africa. Eur Respir J. 2018 May;51(5). doi: 10.1183/13993003.00544-2018. Print 2018 May.

Dheda K*, **Limberis JD***, Pietersen E, Phelan J, Esmail A, Lesosky M, Fennelly KP, Te Riele J, Mastrapa B, Streicher EM, Dolby T, Abdallah AM, Ben-Rached F, Simpson J, Smith L, Gumbo T, van Helden P, Sirgel FA, McNerney R, Theron G, Pain A, Clark TG, Warren RM. Outcomes, infectiousness, and transmission dynamics of patients with extensively drug-resistant tuberculosis and home-discharged patients with programmatically incurable tuberculosis: a prospective cohort study. Lancet Respir Med. 2017 Apr;5(4):269-281. doi: 10.1016/S2213-2600(16)30433-7. Epub 2017 Jan 19. PubMed PMID: 28109869.

Dheda K, Esmail A, **Limberis J**, Maartens G. Selected questions and controversies about bedaquiline: a view from the field. Int J Tuberc Lung Dis. 2016 Dec 1;20(12):24-32. doi: 10.5588/ijtld.16.0065. Review. PubMed PMID: 28240569.

Theron G, Venter R, Calligaro G, Smith L, **Limberis J**, Meldau R, Chanda D, Esmail A, Peter J, Dheda K. Xpert MTB/RIF Results in Patients With Previous Tuberculosis: Can We Distinguish True From False Positive Results?. Clin Infect Dis. 2016 Apr 15;62(8):995-1001. doi: 10.1093/cid/civ1223. Epub 2016 Feb 16. PubMed PMID: 26908793; PubMed Central PMCID: PMC4803105.

Patents

WO 2023/060138

Limberis JD, Metcalfe JZ. Methods For Producing Circular Deoxyribonucleic Acids

Novel Protocols

Full Record

www.protocols.io/researchers/jason-limberis1

easyDB – Circularization of rv0678 for genotypic bedaquiline resistance testing of *Mycobacterium tuberculosis*
Limberis JD, Nalyvayko A, Ernst JD, Metcalfe JZ.

uDumBell – Circularization of rv0678 for genotypic bedaquiline resistance testing of *Mycobacterium tuberculosis*
Limberis JD, Nalyvayko A, Ernst JD, Metcalfe JZ.

Rapid Ribosome (polysome) Profiling

Limberis JD, Chen, Y.

☰ Novel Protocols

se/Seq: A method for the enrichment of non-polyadenylated RNAs including enhancer and long non-coding RNAs for sequencing

Limberis JD, Nalyvayko A, Ernst JD, Metcalfe JZ.

🔧 Major Projects

A novel cartridge-based sequencing solution for decentralized *M. tuberculosis* resistance detection (2023-2028; National Institutes of Health)

My role: As laboratory lead I am designing, optimizing and validating novel sequencing strategies to facilitate early, appropriate drug-resistant TB treatment under programmatic conditions in collaboration with Cepheid.

Pragmatic Use of Next-generation Sequencing for Management of Drug-resistant Tuberculosis (TSELIOT; 2022-2027; National Institutes of Health)

My role: Develop the DNA extraction methods to be used for isolating *M. tuberculosis* DNA for targeted and whole genome sequencing in the clinical trial. Assist and support the laboratory team.

Enabling dual single cell RNA sequencing of host and intracellular pathogens (PBRR; 2021-2022)

My role: As laboratory lead I designed and tested several novel devices built on the principles underlying electroporation. I also developed methods to selectively deplete host RNA from pathogen infected cells.

Host and microbiological determinants of infectiousness in patients with drug sensitive-, multi- and extensively drug resistant tuberculosis (2014 – 2018; National Institutes of Health)

My role: Project management and laboratory lead; development of new methods to interrogate and analyze the bacterial transcriptome in complex clinical samples; perform data analysis and interpretation.

Diagnosis, spread, and management of incurable tuberculosis in the Western Cape Province of South Africa (2014 – 2017; Oppenheimer Foundation)

My role: Project manager and laboratory lead; perform culture, DNA extraction, and analyze clinical and whole genome sequence data to determine the risk factors and transmission of incurable tuberculosis.

TESA Networks of Excellence for the evaluation of new diagnostics and interventions for tuberculosis (TESA; 2017 – 2020; EDCTP)

My role: Project manager. To coordinate exchange programmes and courses within the TESA network and to assist in the development of mentoring programmes.

⚙ References

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