Peter J. Myler

POSITION TITLE
Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION			
University of Queensland, Brisbane, QLD, Australia	B.Sc.(Hons)	1978	Biochemistry
University of Queensland, Brisbane, QLD, Australia	Ph.D.	1979-1982	Biochemistry
Issaquah Health Research Institute	Post-doc	1982-1983	Molecular Parasitology
Washington State University	Post-doc	1984-1985	Molecular Parasitology
Seattle Biomedical Research Institute	Post-doc	1985-1989	Molecular Parasitology

A. Personal Statement

I have extensive (over 30 years) experience in parasite molecular biology, genomics and bioinformatics and, more recently, structural biology and drug development. After graduate work on Plasmodium falciparum (malaria) antigen identification, I undertook post-doctoral training in molecular biology; studying antigenic variation in African trypanosomes (Trypanosoma brucei) and Anaplasma mariginale. During my final post-doctoral period (at Seattle BioMed), I began to study Leishmania gene expression and developed expertise in DNA sequencing and bioinformatics. This led to my directing the L. major and T. cruzi genome sequencing projects; and I am currently an active participant in several trypanosomatid genomic sequencing and annotation projects. During this time, I have also been at the forefront of applying genomic technologies such as microarray-based expression profiling and proteomics to increase our understanding of molecular mechanisms underlying trypanosomatid transcription and regulation of gene expression during differentiation. About 10 years ago, I became actively involved in structural genomics, and I am currently PI and Director of the Seattle Structural Genomics Center for Infectious Disease (SSGCID), which is funded under a contract from NIAID. The mission of SSGCID is to use X-ray crystallography and NMR spectroscopy to solve the structure of proteins targets in emerging and re-emerging infectious disease organisms, primarily to facilitate development of new therapeutics using structure-based drug design. My laboratory has recently started making extensive use of high throughput sequencing technology for genome re-sequencing, mRNA profiling (RNA-seq) and chromatin immunoprecipitation using sequencing (ChIP-seq) in several Leishmania species; once again being at the forefront of technology development for this field. We have recently adapted the ribosome profiling approach approach, developed in yeast by Dr. Nicholas Ingolia, for use in trypanosomatid parasites. This technique is particularly suited to genome-wide quantification of the number and position of ribosomes on mRNA, and can therefore be used to compare the relative translation rates of particular mRNAs. The goal of the current project is use ribosome profiling technology to assess the role of translational regulation of gene expression during T. brucei and L. donovani development and response to environmental cues. We believe that the data generated, which will be disseminated to the research community as soon as possible, will greatly enhance other

genome-scale data currently available and faciliate comprehensive systems biology approaches to unraveling the complex biology of these organisms.

B. Positions and Honors

Positions and Employment

1990-1996 Associate Scientist, Seattle Biomedical Research Institute, Seattle, WA
1993-1997 Assistant Professor, Department of Pathobiology, University of Washington, Seattle, WA
1996-2000 Staff Scientist, Seattle Biomedical Research Institute, Seattle, WA.
1997-2004 Research Associate Professor, Department of Pathobiology, University of Washington, Seattle, WA
2000-2003 Associate Member, Seattle Biomedical Research Institute, Seattle, WA
2001-2004 Adjunct Research Associate Professor, Department of Medical Education and Biomedical Informatics, University of Washington, Seattle, WA
2004-presentFull Member/Professor, Seattle Biomedical Research Institute, Seattle, WA
2004-2008 Research Professor, Department of Pathobiology, and Department of Medical Education and Biomedical Informatics, University of Washington, Seattle, WA
2007-2008 Adjunct Research Professor, Department of Global Health, University of Washington, Seattle, WA
2008-presentAffiliate Professor, Department of Global Health and Department of Biomedical Informatics & Medical Education, University of Washington, Seattle, WA
2010-presentFaculty Member, Molecular and Cellular Biology Interdisciplinary Program, University of Washington, Seattle, WA

Other experience and Professional Memberships

1991-presentScientific Advisor, DNA Sequencing Core Facility, Seattle Biomedical Research Institute
2007-present Scientific Advisor, Protein Production Core, Seattle Biomedical Research Institute
2007-present Scientific Advisor, Bioinformatics Core, Seattle Biomedical Research Institute
2007-present Director, Seattle Structural Genomics Center for Infectious Disease (SSGCID)
2012-presentChair, Seattle BioMed Global Health and Biotechnology Center Steering Committee
1978-1981 Australian Biochemical Society
1995-presentAmerican Association for the Advancement of Science
1996-presentThe Society of Protozoologists
2004-presentAmerican Society for Microbiology
2007-2008 American Society of Tropical Medicine and Hygiene
1988-1992 USAID/AIBS, Malaria program review panel
1994-1995 NIH, Shared Instrumentation Grants Special Study Section
1999-2001 USDA, Sustaining Animal Health and Well-being Study Section
2003 Leishmaniasis Review panel for Military Infectious Diseases Research Program of the US Army, Navy, and Air Force; Joint Medical Technology Workshop.
2001-2008 Editorial board, Kinetoplastid Biology and Disease

2004-2009 NIH/NLM Grant review panel (ad hoc)
2008-2010 NIH Drug Design and Resistance Study Section (ad hoc)
2010-present Editorial board, Journal of Pharmacogenomics & Pharmacoproteomics

Honors

1986-present Invited speaker at 39 international meetings and session chair at 17 meetings
2008-2009 Member, Scientific Committee for 4th World Congress on Leishmaniasis
2011-2112 Chair-Elect, American Society for Microbiology, Division AA
2011-2013 Member, Scientific Committee for 5th World Congress on Leishmaniasis

C. Selected peer-reviewed publications
(from 145 publications in peer-reviewed journals, 13 reviews, 18 book chapters and 1 edited book)

Most relevant to the current application

1. El-Sayed NM, Myler PJ, Blundin G, Berriman M, Crabtree J, Aggarwal G, Caler E, Renauld H, Worthey EA, Hertz-Fowler C, Ghedin E, Peacock C, Bartholomeu DC, Haas BJ, Tran AN, Wortman JR, Alsmark UC, Angiuoli S, Anupama A, Badger J, Bringaud F, Cadag E, Carlton JM, Cerqueira GC, Creasy T, Delcher AL, Djikeng A, Embley TM, Hauser C, Ivens AC, Kummerfeld SK, Pereira-Leal JB, Nilsson D, Peterson J, Salzberg SL, Shallom J, Silva JC, Sundaram J, Westenberger S, White O, Melville SE, Donelson JE, Andersson B, Stuart KD & Hall N (2005) Comparative genomics of trypanosomatid parasitic protozoa. Science. 309:404-409. PMID: 16020724

2. Ivens AC, Peacock CS, Worthey EA, Murphy L, Aggarwal G, Berriman M, Sisk E, Rajandream MA, Adlem E, Aert R, Anupama A, Apostolou Z, Attipoe P, Bason N, Bauser C, Beck A, Beverley SM, Bianchettin G, Borzym K, Bothe G, Bruschi CV, Collins M, Cadag E, Ciarloni L, Clayton C, Coulson RM, Cronin A, Cruz AK, Davies RM, De Gaudenzi J, Dobson DE, Duesterhoeft A, Fazelina G, Fosker N, Frasch AC, Fraser A, Fuchs M, Gabel C, Goble A, Goffeau A, Harris D, Hertz-Fowler C, Hilbert H, Horn D, Huang Y, Klages S, Knights A, Kube M, Larke N, Litvin L, Lord A, Louie T, Marra M, Masuy D, Matthews K, Michaeli S, Mottram JC, Muller-Auer S, Munden H, Nelson S, Norbertczak H, Oliver K, O'Neil S, Pentony M, Pohl TM, Price C, Purnelle B, Quail MA, Rabbinowitsch E, Reinhardt R, Rieger M, Rinta J, Robben J, Robertson L, Ruiz JC, Rutter S, Saunders D, Schafer M, Schein J, Schwartz DC, Seeger K, Seyler A, Sharp S, Shin H, Sivam D, Squares R, Squares S, Tosato V, Vogt C, Volckaert G, Wambutt R, Warren T, Wedler H, Woodward J, Zhou S, Zimmermann W, Smith DF, Blackwell JM, Stuart KD, Barrell B, Myler PJ. (2005) The genome of the kinetoplastid parasite, Leishmania major. Science. 309:436-42. PMCID: PMC1470643

3. Rosenzweig D, Smith D, Myler PJ, Olafson RW, Zilberstein D. (2008) Post-translational modification of cellular proteins during Leishmania donovani differentiation. Proteomics. 8:1843-50. PMID: 18398879

4. Jensen BC, Sivam D, Kifer CT, Myler PJ, Parsons M. (2009) Widespread variation in transcript abundance within and across developmental stages of Trypanosoma brucei. BMC Genomics. 10:482. PMCID: PMC2771046

5. Thomas S, Green A, Sturm NR, Campbell DA, Myler PJ. (2009) Histone acetylations mark origins of polycistronic transcription in Leishmania major. BMC Genomics. 10:152. PMCID: PMC2679053

6. Lahav T, Sivam D, Volpin H, Ronen M, Tsigankov P, Green A, Holland N, Kuzyk M, Borchers C, Zilberstein D, Myler PJ. (2011) Multiple levels of gene regulation mediate differentiation of the intracellular pathogen Leishmania. FASEB J. 25:515-25. PMID: 20952481
7. Parsons M, Myler PJ, Berriman M, Roos DS, Stuart KD. (2011) Identity crisis? The need for systematic gene IDs. Trends Parasitol. 27:183-4. PMID: 21474380
8. van Luenen H., Farris C., Jan S, Genest P-A., Tripathi P, Velds A, Kerkhoven RM, Haydock A, Ramasmay G, Vainio S, Heidebrecht T, Perrakis A, Pagie L, van Steensel B, Myler PJ, Borst P. (2012) Glucosylated hydroxymethyluracil, DNA Base J, prevents transcriptional readthrough in Leishmania. Cell 150:909-921. PMID: 22939620. PMCID: pending.
9. Mittra B, Cortez M, Haydock A, Ramasamy G, Myler PJ, Andrews NW. (2013) Iron uptake controls the generation of Leishmania infective forms through regulation of ROS levels. J Exp Med [Feb 4 Epub ahead of Print].PMID: 23382545

Additional recent publications (in chronological order)

1. Edwards TE, Phan I, Abendroth J, Dieterich SH, Masoudi A, Guo W, Hewitt SN, Kelley A, Leibly D, Brittnacher MJ, Staker BL, Miller SI, Van Voorhis WC, Myler PJ, Stewart LJ. (2010) Structure of a Burkholderia pseudomallei trimeric autotransporter adhesin head. PLoS One. 5. PMCID: PMC2942831
2. Yamada S, Hatta M, Staker BL, Watanabe S, Imai M, Shinya K, Sakai-Tagawa Y, Ito M, Ozawa M, Watanabe T, Sakabe S, Li C, Kim JH, Myler PJ, Phan I, Raymond A, Smith E, Stacy R, Nidom CA, Lank SM, Wiseman RW, Bimber BN, O'Connor DH, Neumann G, Stewart LJ, Kawaoka Y. (2010) Biological and structural characterization of a host-adapting amino acid in influenza virus. PLoS Pathog. 6:e1001034. PMCID: PMC2916879
3. Jaffe EK, Shanmugam D, Gardberg A, Dieterich S, Sankaran B, Stewart LJ, Myler PJ, Roos DS. (2011) Crystal structure of Toxoplasma gondii porphobilinogen synthase: insights on octameric structure and porphobilinogen formation. J Biol Chem. 286:15298-307. PMCID: PMC3083160
4. Yates SP, Edwards TE, Bryan CM, Stein AJ, Van Voorhis WC, Myler PJ, Stewart LJ, Zheng J, Jia Z. (2011) Structural basis of the substrate specificity of bifunctional isocitrate dehydrogenase kinase/phosphatase. Biochemistry. 50:8103-8106. PMCID: PMC3354702
5. Stacy R, Begley DW, Phan I, Staker BL, Van Voorhis WC, Varani G, Buchko GW, Stewart LJ, Myler PJ. (2011) Structural genomics of infectious disease drug targets: the SSGCID. Acta Cryst F. 67:979-84. PMCID: PMC3169389
6. Edwards TE, Abramov AB, Smith ER, Baydo RO, Leonard JT, Leibly DJ, Thompkins KB, Clifton MC, Gardberg AS, Staker BL, Van Voorhis WC, Myler PJ, Stewart LJ. (2011) Structural characterization of a ribose-5-phosphate isomerase B from the pathogenic fungus Coccidioides immitis. BMC Struct Biol. 11:39. PMCID: PMC3212906
7. Edwards TE, Liao R, Phan I, Myler PJ, Grundner C. (2012) Mycobacterium thermoresistibile as a source of thermostable orthologs of Mycobacterium tuberculosis proteins. Protein Sci. 21:1093-6. PMCID: PMC3403447
8. Cadag E, Tarczy-Hornoch P, Myler PJ. (2012) Learning virulent proteins from integrated query networks. BMC Bioinformatics 13:321. PMCID: PMC3560104

9. Baugh L, Gallagher LA, Patrapuvich R, Clifton M, Gardberg AS, Edwards TE, Armour B., Begley DW, Dieterich SH, Dranow D, Abendroth J, Fariman JW, Fox DF III, Staker BL, Phan I, Gillespie A, Choi A, Hewitt SN, Nguyen MT, Napuli A, Barrett L, Buchko GW, Stacy R, Myler PJ, Stewart LJ, Manoil C, and Van Voorhis WC (2013) Combining functional and structural genomics to sample the essential Burkholderia structome. PLoS One 8:e53851. PMCID: PMC3561365.

D. Research Support

Ongoing Research Support

HHSN2722012200025C Myler (PI) 09/28/2012 – 09/27/2017
NIH/NIAID
Center for Structural Genomics of Infectious Diseases
The overall aim of this project is to apply state-of-the-art structural genomics technologies to characterize the three dimensional structures of proteins from NIAID Category A-C pathogens and organisms causing emerging or re-emerging infectious diseases, in order to advance our understanding of these targets and help guide structure-based drug development.

2009226 Myler (co-PI) 10/01/2010 – 09/30/2014
United States-Israel Binational Science Foundation (BSF)
Molecular dissection of the early events involved in the differentiation of the intracellular pathogen Leishmania donovani
The overall goal of this project is to uncover the signaling pathway(s) and the cellular processes that initiate differentiation of Leishmania inside its host. This will be accomplished by using high throughput phosphoproteomics and reverse genetic analysis of selected phosphoproteins.

R21 AI094129 Myler (PI) 03/01/2011 – 05/28/2013 (NCE)
NIH/NIAID
Ribosome profiling of Trypanosoma brucei
The parasite Trypanosoma brucei causes fatal human African trypanosomiasis (sleeping sickness) and drugs to treat the disease are toxic and facing resistance. Generating new drugs requires knowledge of which proteins are expressed in the disease-causing stages of parasite development. This project will apply a new technology to measure the initial steps of protein synthesis for all genes in the infective as compared to non-infective stages, thereby providing new information on candidate drug targets.

Completed Research Support

Grant #71129 Myler (PI) 04/01/2009 – 03/30/2010
Seattle BioMed Institutional grant
A novel approach to genetic validation in Leishmania
This project will adapt a novel system for regulating protein expression in mammalian cells, and determine its utility in Leishmania. Obtaining a good regulation system will allow the genetic validation of potential drug targets in Leishmania, as well as the examination of the role(s) of specific genes in infectivity and growth within the macrophage.

R01 AI053667 Myler (PI) 01/01/2003 – 04/30/2011
NIH/NIAID

Transcription of Protein-coding Genes in Leishmania
The major goals of this project are to characterize the components of the RNA polymerase II transcription complex in Leishmania major and to elucidate the molecular mechanisms involved in RNAPII-mediated transcription of protein-coding genes.
Grant Number 50097 Roos (PI) 11/1/2008 – 09/30/2011
Bill & Melinda Gates Foundation

TrypDB: A Bioinformatics Tool for Target Discovery Research on Trypanosomatid Parasites
The purpose of the grant is to leverage infrastructure and tools via the ApiDB project to rapidly and economically improve access to genomic-scale datasets for kinetoplastid researchers.
HHSN27220070005C Myler (PI) 09/28/2007 – 09/27/2012
NIH/NIAID

Seattle Structural Genomics Center for Infectious Disease
The primary goal of this project is to determine the structure of 75-100 protein targets from NIAID Category AC and emerging/re-emerging infectious disease organisms each year for a period of five years. This will be accomplished by employing a high-throughput gene-to-structure pipeline involving a multi-pronged serial escalation approach to protein expression followed by structure solution using X-ray crystallography and NMR spectroscopy.