G. Lynn Miesel, Ph.D.

Education:

1994	Ph.D.	Biology, University of Utah
1987	B.S.	Biology, University of California at Irvine

Research experience:

2007–present — Merck Research Laboratories, Infectious Diseases
Title: Senior Research Fellow
Supervisor: Dr. Phil Youngman

- Oversee a team of seven microbiologists, including three Ph.D.s, engaged in research to discover novel antibacterial agents for gram-positive and gram-negative infections. Supervise new lead discovery efforts that include screening and optimization campaigns with natural products and synthetic compounds. Responsibilities include project conception, design, coordination and presentation.
- Principal biologist, collaboration with Ranbaxy Pharmaceuticals. Supervise the development and implementation of target-specific whole cell and enzyme assays for high throughput screening and hit characterization. Communicate data and assay methods with our international collaborators.
- Project leader, hit-to-lead effort to develop a therapy for MRSA infections. Projects include microbiological evaluation of compound potency, resistance frequency, target identification, and evaluation of *in vivo* efficacy.
- Oversee a collaborative effort with BioTrove to develop a mass-spectrometry–based assay for a target pathway.
- Department representative on the Merck Rahway recruiting committee that establishes hiring guidelines for Ph.D. scientists and evaluates candidates.

2004–2006 — Schering-Plough Research Institute, Dept. of Infectious Diseases
Title: Principal Scientist

1998–2004 — Schering-Plough Research Institute, Dept. of Infectious Diseases
Title: Associate Principal Scientist
Supervisor: Dr. Todd Black

- Supervised a group of five biologists in antibacterial drug discovery. My responsibilities included project design, presentation, and laboratory work. The group performed many aspects of new lead discovery: target validation, gene cloning and protein purification, biochemical assay development, moderate throughput screening, biochemical and microbiological characterization of hit compounds, and mechanism of action and resistance studies. Biochemical assays included radiometric, fluorescence (FRET and direct), spectrophotometric and mass-spectrometric methods.
- Coordinated biological studies to support exploratory lead optimization efforts for peptide deformylase and a DNA replication target. My group evaluated compounds in biochemical and cell-based assays.
- Departmental representative on a preclinical lead licensing review team.
- Member of a strategic review team for Schering-Plough products Avelox and Ciprofloxacin. Evaluated research proposals submitted by external organizations.

- Member of FDA submission team for Garenoxacin. Assisted with editing and presenting the microbiology data.

1994–1998 Albert Einstein College of Medicine, Howard Hughes Medical Institute
Title: Postdoctoral research associate
Advisor: Professor William R. Jacobs, Jr.

- Researched mechanisms of antimicrobial resistance in *Mycobacterium smegmatis* using genetic and biochemical methods.

1987–1994 University of Utah, Department of Biology
Title: Graduate assistant
Advisor: Professor John R. Roth
Ph.D. thesis: Studies of chromosomal and transductional recombination in *Salmonella typhimurium.*

- Developed genetic methods for characterizing the mechanisms of transduction and chromosomal recombination.

Professional Activities:

2003–present	NIH study section, *ad hoc* member: review small business grant applications for the development of ID therapies (ZRG1 IDM-Q(10)).
2004	NIAID study group, *ad hoc* member: reviewed contract proposals on *in vitro* and animal models for emerging infectious diseases (RFP-NIH-NIAID-DMID-04-40)).
2003	*Ad hoc* manuscript reviewer: *Pharmacogenomics.*
2002	*Ad hoc* manuscript reviewer: *Genetics.*
2002	Co-organizer: Analytical Genetics Conference. Santorini Greece.
2002	Convener: Session on Genome Plasticity. ASM 102nd General Meeting.
2001	Convener: Session on Antibiotics and Vaccines. Conference on Microbial Pathogenesis and Host Response. Cold Spring Harbor Laboratories.
1998	*Ad hoc* manuscript reviewer: *Infection and Immunity.*
1994–present	Member: American Society for Microbiology, American Association for the Advancement of Science.

Awards and fellowship:

2000, 2006	Excellence Awards, Schering-Plough Research Institute.
1991–1994	Genetics Training Grant, National Institutes of Health.

Publications:

Research articles

Langsdorf, E., A. Malikzay, W. Lamarr, D. Daubaras, C. Kravec, R. Zhang, R. Hart, F. Monsma, T. Black, C. Ozbal, **L. Miesel** and C.A. Lunn. Screening for antibacterial inhibitors of the UDP-3-O-(R-3-hydroxymyristoyl)-N-acetylglucosamine deacetylase (LpxC) using a high throughput mass spectrometry assay. *In preparation.*

Miesel, L., S. Ma, C. Kravec, N. Brown, and T. Black. A high frequency of resistance emergence to inhibitors of bacterial DNA ligase. *In preparation.*

Miesel, L., C. Kravec, A. T. Xin, P. McMonagle, S. Ma, J. Pichardo, B. Feld, E. Barrabee, and R. Palermo. A high throughput assay for the adenylation reaction of bacterial DNA ligase. 2007. *Analytical Biochemistry.* 366: 9–17.

Madison, V., J. Duca, F. Bennett, S. Bohanon, A. Cooper, M. Chu, J. Desai, V. Girijavallabhan, R. Hare, A. Hruza, S. Hendrata, Y. Huang, C. Kravec, B. Malcolm, J. McCormick, **L. Miesel**, L. Ramanathan, P. Reichert, A. Saksena, J. Wang, P.C. Weber, H. Zhu, and T. Fischmann. Binding affinities and geometries of various metal ligands in peptide deformylase inhibitors. 2002. *Biophys. Chem*. 101–102: 239–47.

Chu, M., R. Mierzwa, L. He, L. Xu, F. Gentile, J. Terracciano, M. Patel, **L. Miesel**, S. Bohanon, C. Kravec, C. Cramer, T. Fischmann, A. Hruza, L. Ramanathan, P. Shipkova, and T. M. Chan. Isolation and structure elucidation of two novel deformylase inhibitors produced by *Streptomyces sp*. 2001. *Tetrahedron Lett*. 42: 3549–3551.

McNicholas, P.M., P.A. Mann, D.J. Najarian, **L. Miesel**, R.S. Hare, and T.A. Black. Effects of mutations in ribosomal protein L16 on susceptibility and accumulation of evernimicin. 2001. *Antimicrob. Agents Chemother*. 45: 79–83.

Miesel, L., T. Weisbrod, J.A. Marcinkeviciene, R. Bittman, and W.R. Jacobs, Jr. NADH dehydrogenase defects confer isoniazid resistance and conditional lethality in *Mycobacterium smegmatis*. 1998. *J. Bacteriol*. 180: 2459–2467.

Miesel, L. and J.R. Roth. Evidence that SbcB and "RecF pathway" functions contribute to RecBCD-dependent transductional recombination. 1996. *J. Bacteriol*. 178: 3146–3155.

Miesel, L., A.M. Segall, and J.R. Roth. Construction of chromosomal rearrangements in *Salmonella* by transduction: inversion of nonpermissive segments are not lethal. 1994. *Genetics* 137: 919–932.

Miesel, L. and J.R. Roth. *Salmonella recD* mutations increase recombination in a "short sequence" transduction assay. 1994. *J. Bacteriol*. 176: 4092–4103.

Review articles

Miesel, L., J. Greene, and T.A. Black. Genetic strategies for antibacterial drug discovery. 2003. *Nat. Rev. Genet*. 4: 442–456.

Miesel, L., D.A. Rozwarski, J.C. Sacchettini, and W.R. Jacobs, Jr. Mechanisms of isoniazid action and resistance. 1998. *Novartis Found. Symp*. 217: 209–220.

Roth, J.R., N. Benson, T. Galitski, K. Haack, J.G. Lawrence, and **L. Miesel**. Rearrangements of the bacterial chromosome: formation and applications. 1996. In *Escherichia coli and Salmonella: Cellular and Molecular Biology*. Ed. Frederic C. Neidhardt. (ASM Press, Washington D.C.) pp. 2256–2276.

Selected presentations:

Screening LpxC (UDP-3-O-(R-3-hydroxymyristoyl)-GlcNAC deacetylase) using BioTrove RapidFire HTS Mass Spectrometry. Coauthor on poster. SBS conference. Seattle, WA. 2006.

Genetic strategies for antibacterial drug discovery. Speaker. Analytical Genetics Conference. Aegean Conferences. Santorini, Greece. 2002.

A high-throughput assay of bacterial DNA ligase for antibacterial drug discovery. Coauthor on poster. The 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA. 2002.

Peptide deformylase of Staphylococcus aureus: a kinetic and structural comparison to the E. coli deformylase. Poster. The 14th Symposium of the Protein Society. San Diego, CA. 2000.

How does isoniazid kill mycobacteria? Invited speaker. University of Illinois at Urbana-Champaign. 1998.

Mechanisms for drug resistance in mycobacteria. Invited speaker. Microbial genomes II: Sequencing, Functional Characterization and Comparative Genomics. Hilton Head Island, SC. 1998.

Functional analysis of the mycobacterial genome. Speaker. Novartis Foundation Open Meeting: Genetics and Tuberculosis. Cape Town, South Africa. 1997.

NADH dehydrogenase defects confer conditional lethality and coresistance to isoniazid and ethionamide in mycobacteria. Speaker and poster. American Society for Microbiology. Tuberculosis: Past, Present, and Future. Copper Mountain, CO. 1997.

Transductional recombination in Salmonella. Speaker. Cold Spring Harbor Laboratory: Molecular Genetics of Bacteria and Phages. Cold Spring Harbor, NY. 1993.