BIOGRAPHICAL SKETCH

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NAME: Kreiswirth, Barry N.

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POSITION TITLE: Professor of Medicine

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Hamiton College, Clinton, New York	BFA	06/1976	Biology
New York University, New York, New York	PHD	06/1986	Microbiology

A. Personal Statement

I am the founding and current Director of PHRI TB Center which opened in 1992 when the laboratory was created in response to the multidrug resistance outbreak in New York City and the resurgence of tuberculosis in the US. Since that time the laboratory has had a rich history in studying the genotyping of *M. tuberculosis* and in developing resistance diagnostics to improve the speed in treating patients. The TB Center was involved in vitro analysis of the development PA-824, a compound that is used to treat XDR patients. But the laboratory is multifaceted with a rich history in MRSA research and public health tools, including the invention of *spa* typing and the development of a 12 hospital network in New York where we defined the local molecular epidemiology of MRSA. natural progression of the laboratory to whole genome sequencing and building bioinformatic expertise, we re-focused our efforts to unraveling the molecular epidemiology of carbapenem resistant *K. pneumoniae* and this work led to a significant PNAS paper on the characterization of ST258 *K. pneumoniae*; the global CRE clone that emerged in the NYC/NJ region.

1. Bifani PJ, Plikaytis BB, Kapur V, Stockbauer K, Pan X, Lutfey ML, Moghazeh SL, Eisner W, Daniel TM, Kaplan MH, Crawford JT, Musser JM, **Kreiswirth BN**. Origin and interstate spread of a New York City multidrug-resistant Mycobacterium tuberculosis clone family. JAMA. 1996 Feb 14;275(6):452-7. PubMed PMID: 8627966.
2. Stover, C.K., Warrener, P., VanDevanter, D.R., Sherman, D.R., Arain, T.M., Langhorne, M.H., Anderson, S.W., Towell, J.A., Yuan, Y., McMurray, D.N., **Kreiswirth, B.N**., Barry, C.E., Baker, W.R. A small-molecule nitroimidazopyran drug candidate for the treatment of tuberculosis. Nature 2000;405:962-6. PubMed PMID: 10879539.
3. Roberts, R.B., de lencastre, A., Eisner, W., Severina, E.p., Shopsin, B., **Kreiswirth, B.N.**, Tomasz, A. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in 12 New York hospitals. MRSA Collaborative Study Group. JID 1998;178:164-171. PubMed PMID: 9652436.
4. Deleo FR, Chen L, Porcella SF, Martens CA, Kobayashi SD, Porter AR, Chavda KD, Jacobs MR, Mathema B, Olsen RJ, Bonomo RA, Musser JM, **Kreiswirth BN**. Molecular dissection of the evolution of carbapenem-resistant multilocus sequence type 258 *Klebsiella pneumoniae*. Proc Natl Acad Sci U S A. 2014 Apr 1;111(13):4988-93. PubMed PMID: 24639510; PubMed Central PMCID: PMC3977278.

B. Positions and Honors

Positions and Employment

1976 - 1976 Research Technician, Michigan Breast Cancer Clinic, Detroit, MI

1977 - 1979	Predoctoral Research Fellow, University of Western Ontario, London
1986 - 1988	Predoctoral Research Fellow, Public Health Research Insitute, New York, NY
1988 - 1990	Research Scientist, Public Health Research Institute, New York, NY
1990 - 1992	Chief, Phage and Typing and Antibiotic Susceptibility Testing Laboratory, New York City Department of Health, New York, NY
1992 -	Director, Public Health Research Institute Tuberculosis Center, Public Health Research Institute, Newark, NJ
1994 -	Adjunct Assistant Professor of Medicine, New York University, New York, NY
2005 -	Professor of Medicine, Rutgers University, Newark, NJ

Other Experience and Professional Memberships

1981 -	Member, The New York Academy of Sciences
1982 -	Member, American Society for Microbiology
1993 -	Editorial Board, J Clinical Microbiology
1996 -	Chairperson, New York Academy of Sciences Microbiology Advisory Board
1996 -	Member, Defense Advanced Research Projects Agency (DARPA) review board.
1996 - 2002	Editorial Board, J Clinical Microbiology
1998 -	Editorial Board, Drug Resistance Updates.
1999 -	Member, NARSA Advisory Board
1999 -	Member, Henry L. Stimson Center working session on “Biological Wepons Proliferation”
2001 -	Advisor, NCCLS subcommittee: Molecular Methods for Bacterial Strain Typing
2003 -	Member, Veterans Biomedical Research Institute Board of Directors
2004 -	Chair Elect, ASM Division A: Antimicrobial Chemotherapy
2005 -	Chair, ASM Division A: Antimicrobial Chemotherapy
2006 -	Scientific Advisory Board, GangaGen Life Sciences Inc
2007 -	Editorial Board, Microbes and Infections
2008 -	Scientific Advisory Board, Innovative Biosensors, Inc.
2011 -	Chair, Gordon Conferece, Staphylococcal Diseases
2014 -	Editorial Board, Antimicrobial Agents and Chemotherapy
2014 -	Consultant, European Centre for Disease Prevention and Control

Honors

1984	Predoctoral Training Grant #5T3, NIH
1984	Graduate ASM Scholarship Award from the New York City Branch, ASM
1999	TV interview: Tuberculosis in Russia, 60 Minutes
2000	Microbiology Fellow, ASM
2004	The Genetic Revolution photo shoot, National Geographic
2008	System and method for tracking and controlling infections, US Patent: #7349808 - System and method for tracking and controlling infections
2011	System and method for tracking and controlling infections, US Patent:#8046172
2011	Invited Scientist, Museum of Natural History
2015	Waksman Award, Theobald Smith Society

C. Contribution to Science

1. My scientific career started in 1978 when I joined Dr. Richard Novick’s laboratory to study plasmid biology in *Staphylococcus aureus* and a later the next year started as a graduate student at New York University. The Novick laboratory had many talented students and post-doctoral fellows with diverse research interests and when isolates from cases of toxic shock syndrome came to the laboratory from the CDC, I was given the project to identify the toxin. The cloning and characterization of the *S. aureus* toxic shock syndrome toxin-1 became the focus of my research, the basis of my thesis and a first author Nature publication. More importantly, this project steered me toward the nascent field of molecular epidemiology

with a focus on developing genotyping methods and target regions to sub-speciate pathogens. The development of *spa* typing, which is now a standard method to discriminate *S. aureus*, was used to describe the recent evolution of MRSA strains in a *Science* publication. The molecular epidemiology of *S. aureus* is now driven by whole genome sequencing and we adopted this strategy to unravel the evolutionary history of the CC30 strains and this experience using genomics has become the basis of the recent laboratory efforts.

a. **Kreiswirth BN**, Löfdahl S, Betley MJ, O'Reilly M, Schlievert PM, Bergdoll MS, Novick RP. The toxic shock syndrome exotoxin structural gene is not detectably transmitted by a prophage. Nature. 1983 Oct 20-26;305(5936):709-12. PubMed PMID: 6226876.

b. Shopsin B, Gomez M, Montgomery SO, Smith DH, Waddington M, Dodge DE, Bost DA, Riehman M, Naidich S, **Kreiswirth BN**. Evaluation of protein A gene polymorphic region DNA sequencing for typing of Staphylococcus aureus strains. J Clin Microbiol. 1999 Nov;37(11):3556-63. PubMed PMID: 10523551; PubMed Central PMCID: PMC85690.

c. **Kreiswirth B**, Kornblum J, Arbeit RD, Eisner W, Maslow JN, McGeer A, Low DE, Novick RP. Evidence for a clonal origin of methicillin resistance in Staphylococcus aureus. Science. 1993 Jan 8;259(5092):227-30. PubMed PMID: 8093647.

d. DeLeo FR, Kennedy AD, Chen L, Bubeck Wardenburg J, Kobayashi SD, Mathema B, Braughton KR, Whitney AR, Villaruz AE, Martens CA, Porcella SF, McGavin MJ, Otto M, Musser JM, **Kreiswirth BN**. Molecular differentiation of historic phage-type 80/81 and contemporary epidemic Staphylococcus aureus. Proc Natl Acad Sci U S A. 2011 Nov 1;108(44):18091-6. PubMed PMID: 22025717; PubMed Central PMCID: PMC3207694.

2. Although the laboratory still maintains *S. aureus* research projects, the research focus changed in 1991 in response to the tuberculosis epidemic in New York City. With the intent of developing a genotyping laboratory to provide molecular analysis in support of public health TB control efforts. As the founding and current Director, the goal has been to maintain the multifaceted biosafety level III PHRI TB Center to support TB control. Since its opening in January 1992, the Center has genotyped over 31,000 M. tuberculosis cultures, including the isolates from all New York City and New Jersey tuberculosis patients. Molecular epidemiological studies have included a large focus on outbreak investigations and the genotyping of drug resistance targets and the development of diagnostic tools to improve treatment and public health efforts.

   a. Gutacker MM, Smoot JC, Migliaccio CA, Ricklefs SM, Hua S, Cousins DV, Graviss EA, Shashkina E, **Kreiswirth BN**, Musser JM. Genome-wide analysis of synonymous single nucleotide polymorphisms in Mycobacterium tuberculosis complex organisms: resolution of genetic relationships among closely related microbial strains. Genetics. 2002 Dec;162(4):1533-43. PubMed PMID: 12524330; PubMed Central PMCID: PMC1462380.

   b. Sullivan, E.A., **Kreiswirth, B.**, Palumbo, L., Musser, J., Kapur, V., Ebrahimzadeh, A., Frieden, T.R. Emergence of fluoroquinolone-resistant tuberculosis in New York City. Lancet 1995;345:1148-1150. PubMed PMID 7723548

   c. Post FA, Willcox PA, Mathema B, Steyn LM, Shean K, Ramaswamy SV, Graviss EA, Shashkina E, **Kreiswirth BN**, Kaplan G. Genetic polymorphism in Mycobacterium tuberculosis isolates from patients with chronic multidrug-resistant tuberculosis. J Infect Dis. 2004 Jul 1;190(1):99-106. PubMed PMID: 15195248.

   d. Shah NS, Auld SC, Brust JC, Mathema B, Ismail N, Moodley P, Mlisana K, Allana S, Campbell A, Mthiyane T, Morris N, Mpangase P, van der Meulen H, Omar SV, Brown TS, Narechania A, Shaskina E, Kapwata T, **Kreiswirth B**, Gandhi NR. Transmission of Extensively Drug-Resistant Tuberculosis in South Africa. New Engl J Med. 2017;19:376:243-253. PubMed PMID: 28099825

3. Similar to the emergence of the MDR tuberculosis epidemic in the early 1990s, the carbapenem resistant *K. pneumo*niae (CRKp) epidemic blossomed in high-risk patients in hospitals in the NYC metropolitan area and in 2010 we again changed focus in the laboratory to study CRKp. As we did with both *S. aureus* and **M. tuberculosis**, we took a whole genome approach to unravel the epidemic and we discovered that the global spread of ST258 is made up of two genetically conserved clades that differ in a highly

recombinagenic region that switches the capsular and lipopolysaccharide gene clusters. We also showed that ST258 is a recent clone evolved from a gross recombination between ST11 and ST442. Sequencing of *bla*$_{KPC}$ plasmid identified more than 10 different incompatibility types and we identified 3 major conjugative plasmids that are successfully spreading with *K. pneumoniae* and among other species in Enterobacteriaceae. The genetic dissection of ST258 led to the development of numerous molecular beacon assays to rapidly genotype ST258, the CPS type and the battery of beta-lactamase genes harbored by these multidrug resistant Enterobacteriaceae.

a. Chen L, Chavda KD, Mediavilla JR, Zhao Y, Fraimow HS, Jenkins SG, Levi MH, Hong T, Rojtman AD, Ginocchio CC, Bonomo RA, **Kreiswirth BN**. Multiplex real-time PCR for detection of an epidemic KPC-producing Klebsiella pneumoniae ST258 clone. Antimicrob Agents Chemother. 2012 Jun;56(6):3444-7. PubMed PMID: 22450983; PubMed Central PMCID: PMC3370784.
b. Chen L, Mathema B, Pitout JD, DeLeo FR, **Kreiswirth BN**. Epidemic Klebsiella pneumoniae ST258 is a hybrid strain. MBio. 2014 Jun 24;5(3):e01355-14. PubMed PMID: 24961694; PubMed Central PMCID: PMC4073492.
c. Chen L, Chavda KD, Findlay J, Peirano G, Hopkins K, Pitout JD, Bonomo RA, Woodford N, DeLeo FR, **Kreiswirth BN**. Multiplex PCR for identification of two capsular types in epidemic KPC-producing Klebsiella pneumoniae sequence type 258 strains. Antimicrob Agents Chemother. 2014 Jul;58(7):4196-9. PubMed PMID: 24733470; PubMed Central PMCID: PMC4068549.

b. Bulman ZP, Chen L, Walsh TJ, Satlin MJ, Qian Y, Bulitta JB, Peloquin CA, Holden PN, Nation RL, Li J, **Kreiswirth BN**, Tsuji BT.Polymyxin Combinations Combat *Escherichia coli* Harboring *mcr-1* and *bla*$_{NDM-5}$: Preparation for a Postantibiotic Era.MBio. 2017;8:e00540-17.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/barry.kreiswirth.1/bibliography/45301625/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

R01 AI090155, National Institute of Allergy and Infectious Diseases (NIAID)
Kreiswirth, Barry (PI)
03/15/11-11/30/21
THE MOLECULAR BASIS OF THE CARBAPENEM RESISTANCE EPIDEMIC
Our studies proposed herein are designed to decipher the nature of an expanding epidemic, both from a local/global epidemiological and biologic perspective, and identify genetic and/or phenotypic traits catalyzing this epidemic.
Role: PI

5UM1AI104681, National Institute of Allergy and Infectious Diseases (NIAID)

Fowler, Vance G. (PI)
06/01/13-11/30/19
ANTIBACTERIAL RESISTANCE LEADERSHIP GROUP (ARLG)
The Antibacterial Resistance Leadership Group (ARLG) develops, designs, implements, and manages a clinical research agenda to increase knowledge of antibacterial resistance (AR).
Role: Co-I

1U19AI109713-01 National Institute of Allergy and Infectious Diseases (NIAID)
David, Perlin (PI)
03/01/2014 – 02/28/2019
Center to develop therapeutic countermeasures to high-threat bacterial agents
This program will develop and evaluate new antibacterial agents against ESKAPE and biodefense-related pathogens.
Role: Co-I

R21 AI135250, National Institute of Allergy and Infectious Diseases (NIAID)
Kreiswirth, Barry (PI)
01/15/18-12/31/19
Unraveling colistin resistance in Klebsiella pneumoniae
The aim of this study is to correlate the genomic changes with colistin resistance in K. pneumoniae
Role: PI