

**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 Institute, 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 Weapons 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 Conference, 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.
  - 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, Shashkina 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.
3. Similar to the emergence of the MDR tuberculosis epidemic in the early 1990s, the carbapenem resistant *K. pneumoniae* (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 recombinogenic 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<sub>KPC</sub>* 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, Rojzman 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](https://pubmed.ncbi.nlm.nih.gov/22450983/); PubMed Central PMCID: [PMC3370784](https://pubmed.ncbi.nlm.nih.gov/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](https://pubmed.ncbi.nlm.nih.gov/24961694/); PubMed Central PMCID: [PMC4073492](https://pubmed.ncbi.nlm.nih.gov/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](https://pubmed.ncbi.nlm.nih.gov/24733470/); PubMed Central PMCID: [PMC4068549](https://pubmed.ncbi.nlm.nih.gov/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<sub>NDM-5</sub>*: Preparation for a Postantibiotic Era. *MBio.* 2017;8:e00540-17.

#### Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/myncbi/barry.kreiswirth.2/bibliography/45297152/public/?sort=date&direction=ascending>

## D. Research Support

### Current

1R01AI090155-01 Kreiswirth NIH	9/31/2010 – 02/29/2017 \$365,243	6.0 CM
The molecular basis of the <i>bla<sub>KPC</sub></i> gene in <i>Klebsiella pneumoniae</i> The goal of this project is study the molecular epidemiology of carbapenem resistant Enterobacteriaceae		
1UM1AI104681-01 Fowler NIH	12/01/2013 – 11/30/2019 \$167,303	3.0 CM
Antibacterial Resistance Leadership Resistance To support clinical trials and combat antibiotic resistance		
1U19AI109713-01 Perlin NIH	03/01/2014 – 02/28/2019	1.2 CM
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.		
5R01AI106398-03 Dartois NIH	08/01/2013 – 07/31/2017	0.6 CM
Lesion-centric imaging and PK-PD of pyrazinamide for TB/HIV co-infection		

5R21AI111037-02 Clancy 12/01/2014 – 11/30/2016 0.24 CM  
NIH \$10,000  
Evolution of KPC-K pneumonia that persist in patients on prolonged antibiotics

**Pending**

R21 AI128338 Nguyen 12/1/16-11/30/18 0.6 CM  
NIH \$50,500  
Chromosomal and plasmid contributions to colistin resistance and virulence in KPC-producing *Klebsiella pneumoniae*