

Studying the Evolution and Pathogenicity of Novel Bacteria in Humans

Hank Seifert, PhD, the John Edward Porter Professor of Biomedical Research and professor of Microbiology-Immunology



Hank Seifert, PhD, is the John Edward Porter Professor of Biomedical Research and a professor of [Microbiology-Immunology](#). His laboratory studies how various species of bacteria cause disease in humans and how the process of gene conversion occurs in a bacterial chromosome. He is also a member of the [Center for Genetic Medicine](#), Northwestern University Clinical and Translational Sciences (NUCATS) Institute and the [Simpson Querrey Institute for Epigenetics](#).

Q&A

What are your research interests?

My laboratory group studies the human-restricted *Neisseria* species, with a concentration on the pathogenic species *Neisseria gonorrhoeae* (the gonococcus or Gc) and *Neisseria meningitidis* (the meningococcus or Mc). While there are 10 *Neisseria* species that only live within humans, only Gc and Mc can cause pathology resulting in sexually transmitted infection: gonorrhea (Gc), bacterial meningitis (Mc) or bacteremia (both Mc and Gc). Most of our work revolves around the Type IV pilus, which is a proteinaceous organelle that is essential for colonization and pathogenicity. We study the mechanisms and biology behind the pilus antigenic variation system of Gc and Mc, which is a complex diversity-generation system that uses DNA recombination to alter the amino acid sequence of the major subunit of the pilus, pilin. We are determining how the pilus protects against host-derived, oxidative and nonoxidative antimicrobial mechanisms. We are also determining how the pilus fiber is expressed on the bacterial cell surface and what regulates the pilus extension and retraction cycle. Finally, we have begun a project to mutate every non-essential gene in the Gc chromosome to provide a resource for the broader research community.

What is the ultimate goal of your research?

We are trying to understand how these bacteria cause disease in otherwise healthy people, how high-frequency gene conversion can occur in a bacterial chromosome and what evolutionary paths allowed the pathogenic *Neisseria* to derive from a commensal progenitor.

How did you become interested in this area of research?

As a graduate student at Penn State, I heard my postdoctoral advisor Magdalene So give a talk on the early description of the pilus antigenic variation system. Immediately after her talk, I asked if she had any open postdoctoral positions, and after checking my referees and an interview in La Jolla, California, I started my studies on the pilus antigenic variation system.

What types of collaborations are you engaged in across campus (and beyond)?

We do a lot of different techniques within the laboratory, but we collaborate in areas where we do not have the expertise. We have an ongoing collaboration with James Garnett and Joseph Atherton of King's College London who are structural biology experts to study a new pilus associate protein we discovered. We have a collaboration with biophysicist Berenike Maier at the University of Cologne to measure pilus dynamics. We have collaborations with several Northwestern faculty including Chi-Hao Luan and [Gary Schlitz](#) to conduct a small molecule screen and to make derivatives of lead compounds as potential antivirulence antimicrobial agents.

Where have you recently published papers?

In the past five years our papers were published in [mBio](#), [Biochemistry](#), [mSphere](#), [Molecular Microbiology](#), [Journal of Bacteriology](#), [mSystems](#), [PLoS Genetics](#), [Journal of Biological Chemistry](#) and the [Journal of Proteome Research](#).

Who inspires you? Who are your mentors?

I've had many mentors over my career. My PhD advisor, Ron Porter, at Penn State accepted a raw student with little research experience into this lab and let me explore and learn without pressuring me for immediate results. My postdoctoral mentor, Maggie So, at the Scripps Research Institute provided a rich intellectual environment and resources to develop a research portfolio that allowed me to obtain a faculty position at Northwestern. [Pat Spear](#) hired me and always had sage advice. Over the past 33 years, I have leaned on many senior and junior faculty, both at Northwestern and beyond, for mentoring and am always learning from my laboratory group.