Ackert Hall, Room 120
Wednesday, May 14, 2025
4:00 P.M.

Coffee and Cookies
Chalmers Hall, Room 168
3:45 P.M.

Biochemistry & Molecular Biophysics Seminar

How to Build a Dynamic Pathogen-Host Interface: Lipoprotein Sorting and Secretion in the Lyme Disease Spirochete *Borrelia burgdorferi*

Wolfram Zueckert

Microbiology, Molecular Genetics and Immunology
University of Kansas Medical Center

Bacterial protein secretion is a fundamental physiological process that generates the cell envelope and maintains its integrity throughout the bacterial life cycle. In bacterial pathogens, a variety of protein secretion systems have been shown to deploy important virulence factors to the bacterial surface, into the milieu, or even directly into eukaryotic cells or other bacteria. *Borrelia* spirochetes, the causative agents of tick-borne Lyme disease and relapsing fever, have a unique double-membrane (diderm) envelope with periplasmic flagella. The *Borrelia* surface lacks lipopolysaccharide (LPS), and we and others previously showed that the Lyme disease spirochete *Borrelia burgdorferi* is instead covered by subsets of more than 80 different lipoproteins that serve as linchpins for transmission and pathogenesis throughout the infectious cycle. Our recent studies have begun to define lipoproteome sorting and secretion determinants, revealing dichotomous roles of two pathways found in other diderm bacteria: a classical, yet variant Lol pathway responsible for periplasmic lipoprotein homeostasis, and a distant variant of the Lpt LPS transport pathway, which in *Borrelia* seems to have switched from secreting lipidated sugars to transporting lipidated proteins. Our ongoing studies focus on determining cargo specificity, spatiotemporal distribution, and structure-function relationships of the Lol and Lpt pathways using multiomics, time-lapse microscopy, X-ray crystallography, Cryo-EM, and a CRISPRi-PAM* knockdown/complementation platform.