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CBCB SEMINAR
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BIOINFORMATICS SEMINAR

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COLUMBIA UNIVERSITY

METABOLIC HETEROGENEITY AND ANTIBIOTIC TOLERANCE IN BACTERIAL BIOFILMS

Cells in assemblages, ranging from microbial aggregates to developing tumors, are subject to gradients of resources that lead to metabolic heterogeneity. This heterogeneity also itself contributes to gradient formation, and the ensuing physiological differentiation contributes to resilience and exacerbates the challenges of treating infections and cancer. We use biofilms, which are microbial assemblages held together by an excreted matrix, of the bacterial pathogen Pseudomonas aeruginosa to study the interplay between metabolic differentiation, multicellular development, and antibiotic tolerance. P. aeruginosa colony biofilms contain gradients of oxygen. However, they also produce redox-active pigments called phenazines and studies in homogeneous liquid cultures and of phenazine-null mutants indicate that these endogenous compounds have the potential to act as alternate metabolic electron acceptors. Using microsensors and microelectrodes, we have observed that oxygen decreases and that phenazines become more reduced, with depth in biofilms. To directly test whether phenazines support metabolism in oxygen-limited zones, we developed a technique that relies on stable isotope labeling and stimulated Raman scattering (SRS) microscopy and found that the production of phenazines and specific respiratory complexes supports metabolic activity at depth. Importantly, this metabolic heterogeneity also contributes to the survival of cells in biofilms treated with the antibiotic ciprofloxacin. We are now coupling SRS microscopy to a thin-sectioning technique that enables profiling of metabolic activity and gene expression in the same sample. Through these diverse approaches, we are defining the complex interactions between bacterial products, their roles in metabolically differentiated biofilms, and the antibiotics we use to treat infections.

BIOGRAPHY

Lars Dietrich earned a Diploma in Biology from Konstanz University and a doctoral degree from Heidelberg University studying membrane fusion in eukaryotes. He then worked as a postdoc with Dianne Newman at Caltech and MIT on bacterial signaling and Pseudomonas aeruginosa physiology. In 2010 he joined the Department of Biological Sciences at Columbia University.

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