

Lectures in Chemical and Biological Engineering

From iron oxides to infections: physiological roles for redox-active "antibiotics"



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Iron is an essential cofactor for growth and function of key metabolic enzymes in most bacteria. However, under aerobic, circum-neutral pH conditions, biologically available iron is extremely limiting because iron in nature is present as highly insoluble Fe(III) minerals, and in mammalian hosts is tightly bound to various host Fe(III) sequestering proteins. Consequently, bacteria need to develop strategies to acquire iron over a distance; this may be particularly relevant for bacteria in multicellular, or biofilm, communities. One strategy some bacteria use is to produce diffusible iron-binding siderophores. Alternatively, some bacteria produce diffusible redox-active small molecules (e.g., phenazines), which are traditionally thought to merely serve as antibiotics to inhibit competitors, may function as electron shuttles to facilitate iron acquisition by reductively dissolving Fe(III) and hence liberating Fe(II). Here we characterize the ability of phenazine natural products to reduce Fe(III) minerals and reveal that reactivity can be predicted based on phenazine redox properties and structure. Using a genetic approach, we further show that phenazine and siderophore production promotes *Pseudomonas aeruginosa* biofilm development. By examining the parent and mutants defective in iron transport or acquisition along with phenazine effects, we reveal that phenazine-promoted biofilm development is indeed via its ability to facilitate Fe(II) uptake. Such promotion in biofilm development leads to a drastically enhanced resistance to killing by antimicrobial agents in *P. aeruginosa* by compromising the host Fe(III)-withholding defense against infections. Because phenazines are versatile redox-active molecules, we study their roles as oxidants as well as reductants in the context of biofilm formation. Our findings imply that redox-active "antibiotics" may play primary roles in iron acquisition and microbial physiology for the cells that produce them.

Thursday October 29th at 4:00PM in Tech LR4

The Technological Institute

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Refreshments will be served at 3:45 PM