Neilands J B. Iron absorption and transport in microorganisms.
Annu. Rev. Nutr. 1:27-46, 1981.
[Department of Biochemistry, University of California, Berkeley, CA]

The review surveyed the topic of microbial iron assimilation in diverse microbial species as regards its mechanism, regulation, and relation to virulence. [The *SCI*® indicates that this paper has been cited in over 100 publications.]

J.B. Neilands
Department of Biochemistry
University of California
Berkeley, CA 94720

March 24, 1988

In 1949 I was a newly minted PhD starting a postdoctoral sojourn in the laboratory of Hugo Theorell in Stockholm. Sven Paleus and I devised a method for isolation of cytochrome *c*, although my principal discovery was the identification of multiple forms of lactic dehydrogenase, now called isozymes. Back in Wisconsin as an instructor in 1951, I applied the new method for isolation of cytochrome *c* to the fungus *Ustilago sphaerogena*. This led to the disclosure of a novel iron compound, which was crystallized and christened ferrichrome. In the following year, I took up my present post at Berkeley, where my first graduate student, John A. Garibaldi, found that yields of the metal-free species could be greatly enhanced by starvation of the cells for iron.[1] This seemed to nail down a role for ferrichrome-type compounds, now known to be widely distributed in microorganisms and generically termed siderophores,[2] to a role in iron assimilation.

Over the years a succession of unusually gifted students and collaborators have determined the structure and function of a number of siderophores. Lately, we have focused on the molecular mechanism of regulation of siderophore synthesis and transport in *Escherichia coli*.[3] A repressor protein, ferric uptake regulation (FUR) complexes Fe(II) and the holoprotein then binds operator DNA to negatively regulate transcription of operons and gene clusters involved in iron assimilation. This may be the only mode whereby *E. coli* regulates uptake of iron,[4] an element that is essential but toxic in excess. It remains to be seen if the *E. coli* model can be extended to other bacteria as well as to fungi, plants, and animals.

The review has been well cited because it affords a background reference for both siderophores, compounds that have become important in medicine and agriculture, and for a newly active field, namely, metal ion mediated regulation of gene expression.

In 1952 Linus Pauling had been summoned to give an inaugural address at the opening of the new biochemistry department. I came early, hoping for a moment with the great chemist and humanitarian. I sidled up, displayed my vial of ferrichrome crystals, and asked if it could be analyzed by X-ray diffraction. He whipped out a lens and opined that the crystals were rather small. Then I asked: "Is a compound like this worthy of study?" The reply: "Any natural compound containing iron should be studied."

Obviously, I could have achieved more in science if I had devoted myself exclusively to iron in biology. In 1960 I organized a committee to block construction of a nuclear power reactor on the coast 50 miles upwind of San Francisco. We won that battle with a little help from the San Andreas Fault! Perceiving the media to be the main impediment to social action, I then tried, and failed, to found a reader-owned daily newspaper in Berkeley. During the Free Speech Movement I was on cloud nine and in 1967 visisted Hanoi as an investigator for the Bertrand Russell War Crimes Tribunal.

I grew up in Canada in a social democratic family and find no real distinction between the Democrats and Republicans, except that one is in and the other is out. Now I am a follower of Earth First! and the Sea Shepherd Society. We scientists who do basic research often find ourselves and our endeavors exploited by governments, drug companies, agribusiness, and whomever else may have self-serving interests. Instead of pursuing status and awards we should devote ourselves to more important tasks such as the elimination of nuclear weapons and reduction of the human population. Clearly, the science-based industrialized society must be discarded in favor of a lifestyle that is benign, sustainable, and less rapacious of the rest of the planet, animate and inanimate.

1. **Garibaldi J A & Neilands J B.** Formation of iron binding compounds by microorganisms. *Nature* 177:526-7, 1956. (Cited 55 times.)
2. **Lankford C E.** Bacterial assimilation of iron. *Crit. Rev. Microbiol.* 2:273-331, 1973. (Cited 170 times.)
3. **Bagg A & Neilands J B.** Molecular mechanism of regulation of siderophore mediated iron assimilation. *Microbiol. Rev.* 51:509-18, 1987.
4. **Hantke K.** Ferrous iron transport mutants in *Escherichia coli* K12. *FEMS Microbiol. Lett.* 44:53-7, 1987.

182

©1988 by ISI® CURRENT CONTENTS®