Siderophores – potential candidate in the therapy of neonatal meningitis

The mortality and morbidity associated with neonatal meningitis remain significant in spite of advances in antimicrobial chemotherapy (Kim, 2003). *Escherichia coli* k1 is a successful pathogen capable of invading the brain despite the protective effect of physiological barriers between the blood stream and the central nervous system. Inadequate knowledge regarding the pathophysiology of this organism along with poor drug delivery to the brain has resulted in a lack of success following therapy of this infection. Investigations regarding neonatal meningitis have focused on the determination of resistance to antibiotics, but alternate therapies exploiting the modulation of the environment for invading bacteria have not been explored (Nigrovic et al., 2004; Shah et al., 2004; Kumar, 2004).

Iron supply for many microbes plays a decisive role in the infection process. Acquiring iron from the environment has a significant effect on the establishment of infection in the host, and microbial pathogens have evolved different mechanisms to overcome iron restriction. The role of iron chelation in virulence has been evaluated for microbial organisms (Dale et al., 2004). Iron facilitates the progression of high-level *E. coli* bacteremia to meningitis. Indeed, it has been shown elsewhere that the ferric-siderophore receptor IroN, but not the high-affinity siderophore receptor IroN, is the most likely mechanism of iron restriction for invasion of invading bacteria. We have previously shown that a plant-based siderophore will reduce invading bacteria (Negre et al., 2004). Negre et al. (2004) showed that the ironN gene plays a key role in the virulence of *E. coli* and an ironN mutant lacking siderophore receptors differs from the wild-type strain in its ability to cause bacteraemia, suggesting that iron acquisition by a siderophore is the most likely mechanism of the ironN-associated virulence. Thus, stress generated by the acquisition of iron by a siderophore will reduce invading *E. coli* burden. The role of different siderophores in reducing the *E. coli* burden, and therefore their role in therapy, remains to be determined and justifies further studies in this regard. An understanding of this process could result in a novel therapeutic strategy for management of neonatal meningitis.

**Tapen Dam**
Room no. 1133, Ross Building, 720 Rutland Avenue, Division of Infectious Diseases, Department of Pediatrics, School of Medicine, Johns Hopkins University, Baltimore, MD 21205, USA

Correspondence: Tapen Dam (tdam1@jhmi.edu)


