Redox linked flavin sites in extracellular decaheme proteins involved in microbe-mineral electron transfer

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Outer membrane multi-heme cytochromes (OMMC) play a key role in electron transfer between bacteria and extracellular electron acceptors, but it is debated whether flavins play a role as an additional cofactor of these proteins. The x-ray crystal structures of the *Shewanella* OMMC family, added to here by decaheme MtrC, reveal a conserved disulfide bond in a C-terminal β-barrel domain. Reduction of the disulfide bond of MtrC by glutathione in the presence of flavin mononucleotide (FMN) resulted in the formation of a stable flavocytochrome complex that rapidly dissociated when exposed to air. All ten hemes and the bound FMN cofactor of the MtrC flavocytochrome remained oxidized, showing that FMN binding was dependent only on the reduction of the disulfide cysteines. Similar results were also observed with other members of the OMMC family. Mutant *S. oneidensis* strains in which the MtrC disulfide cysteines were converted to alanines were able to grow normally under anaerobic conditions, but were severely attenuated in their ability to grow aerobically. The data suggest that members of the Shewanella OMMC family can transition between highly reactive flavocytochromes or less reactive cytochrome, and that this is controlled by a redox active disulfide that responds to the presence of oxygen in the environment.