ABSTRACT: Mercury is a pervasive global pollutant which, as methylmercury, bioaccumulates in the food web and is highly toxic to humans and other organisms. Methylmercury is produced in natural environments from inorganic mercury, predominantly by anaerobic microorganisms. Sulfate-reducing bacteria are the main producers of methylmercury, although iron-reducing bacteria and methanogens can also be involved. Mercury methylation is an enzyme-catalyzed process proposed to be associated with the reductive acetyl-CoA (Wood-Ljungdahl) pathway and potentially linked to corrinoid proteins involved in this pathway. However, no direct evidence firmly connects the acetyl-CoA pathway and the ability of bacteria to methylate Hg. Furthermore, phylogenetic analyses have not revealed any distinctive trends or clustering of methylating versus non-methylating microorganisms. Thus, despite substantial effort, the genetic and biochemical basis of microbial mercury methylation has remained elusive for over 40 years.

A combination of chemical reasoning, genomics, and microbiology lead to the discovery of a two-gene cluster, \( hgcA \) and \( hgcB \), required for mercury methylation by \emph{Desulfovibrio desulfuricans} ND132 and \emph{Geobacter sulfurreducens} PCA. In either bacterium, deletion of \( hgcA \), \( hgcB \) or both genes abolishes mercury methylation. The genes encode a putative corrinoid protein, HgcA, and a \([4\text{Fe}-\text{4S}]\) ferredoxin, HgcB, consistent with roles as a methyl carrier and an electron donor required for corrinoid cofactor reduction, respectively. This two-gene cluster is present in all known methylating bacteria and archaea but absent in non-methylators. Homologs have been found in the genomes of more than 50 diverse microorganisms, suggesting a common mercury methylation pathway among bacteria and archaea with sequenced genomes. The identification \( hgcA \) and \( hgcB \) is a critical step toward identifying sources of microbial methylmercury production in the environment.