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Structure Determination of the HgcAB Complex Using Metagenome Sequence Data

Sarah J. Cooper[1], Sergey Ovchinnikov[2], Georgios A. Pavlopoulos[3], Nikos C. Kyrpides[3], Stephen W. Ragsdale[4], Alexander Johs[5], Mircea Podar[5], and Jerry M. Parks[5*]

[1] University of Tennessee, Knoxville, TN
[2] Harvard University, Cambridge, MA
[3] DOE Joint Genome Institute, Walnut Creek, CA
[4] University of Michigan, Ann Arbor, MI
[5] Oak Ridge National Laboratory, Oak Ridge, TN

Contact: parksjm@ornl.gov

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Project Website: http://www.esd.ornl.gov/programs/rsfa/

Bacteria and archaea possessing the *hgcAB* gene pair can methylate inorganic mercury to form highly toxic methylmercury. Previous sequence analyses revealed that HgcA consists of a corrinoid binding domain and a transmembrane domain, and HgcB is a ferredoxin with two 4[Fe-4S] clusters. However, the detailed structure and function of these proteins are not well understood. Recent advances have enabled highly accurate structural models of proteins to be generated by combining metagenome sequence data, coevolution analysis, and ab initio structure calculations. We use this approach to generate a complete structural model of the assembled HgcAB complex. The model confirms many previously predicted structural features and reveals new insights into the structure and function of these two proteins. Surprisingly, the coevolution analysis revealed that the two domains of HgcA do not interact with each other, but HgcB binds to both of these domains in the assembled complex. In addition, there is evidence for dynamic movement of individual domains relative to each other, which likely plays an important role in methyl transfer. These findings expand the repertoire of known corrinoid methyltransferase folds, provide structural and mechanistic insight, and form the basis for identifying additional proteins involved in mercury methylation.