Iron-sulfur (Fe-S) clusters act as cofactors of various Fe-S proteins that are widely distributed in nature and required to maintain fundamental life processes. Recent studies revealed that the assembly of Fe-S clusters in several bacteria as well as eukaryotic mitochondria is achieved by a multicomponent system, called ISC machinery. This machinery is generally encoded, in bacteria, by the iscSUA-hscBA-fdx operon, and consists of six ISC proteins. Among them, the components playing central roles in de novo Fe-S cluster biogenesis are IscS and IscU. IscS is a cysteine desulfurase that catalyzes the sulfur atom abstraction from cysteine substrate and provides it for biosynthesis. IscU directly accepts the sulfur atoms from IscS and serves as a scaffold for the assembly of a nascent Fe-S cluster, prior to its delivery to target Fe-S protein. We have so far determined the unique trimeric structure of the [2Fe-2S] cluster-bound form of IscU from the hyperthermophilic bacterium Aquifex aeolicus (Aa) [1]. This structural information provided mechanistic implications that the dynamic association/dissociation of IscU must be the critical events to interact with the other ISC components in the assembly for the nascent Fe-S clusters. Here we focus on the protein-protein interactions among ISC proteins, to clarify the detailed mechanism of de novo Fe-S cluster biogenesis.

Comprehension of Aa IscS and Aa IscU in E. coli resulted in formation of a binary complex, and it was purified and crystallized. A data set was collected to 3.6 Å resolution on beamline BL38B1 at SPring-8. The structure of IscS moiety was solved with the MR method using a model of the dimeric protein-protein interactions in ISC machinery.

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