Comparative Genetic Analysis of the Three Distinct Systems Involved in the Assembly of Fe-S Clusters

Umechiyo Tokumoto, Seiichi Kitamura, Kei Suzuki, Kei Wada, Keiichi Fukuyama and Yasuhiro Takahashi*

Department of Biology, Graduate School of Science, Osaka University, Toyonaka, Osaka 560-0043, Japan

The assembly of Fe-S clusters, a key step in the post-translational maturation of Fe-S proteins, is mediated by a complex apparatus. In *E. coli*, this process involves two distinct systems called ISC and SUF encoded by the *iscRSUA-hscBA-fdx* operon and *sufABCDSE* operon, respectively. Another system, termed NIF (*nifSU*), is required for the maturation of nitrogenase in nitrogen-fixing bacteria. We have shown recently, using a mutant *E. coli* strain lacking both the *isc* and *suf* operons, that the NIF-like system of the non-diazotrophic bacterium *Helicobacter pylori* or the eukaryotic parasite *Entamoeba histolytica* can replace the ISC and SUF systems. Thus, the *in vivo* function of the Fe-S cluster assembly systems are basically interchangeable, suggesting that they do not have strict specificity toward the target apo-Fe-S proteins or the type of Fe-S clusters to be transferred. The heterologous complementation analysis also indicates that the NIF-like system is fully functional only under anaerobic conditions. The apparent sensitivity toward oxygen may explain why the NIF system is only found in a limited number of organisms (anaerobes, microaerophiles, and diazotrophs); however, most other organisms prefer the ISC and/or SUF systems. We are currently investigating the components required for the oxygen-resistant mission of the ISC machinery; such components would be responsible for stabilization of the oxygen-labile Fe-S cluster on the IscU scaffold or its transfer to target apo-Fe-S proteins in the presence of oxygen.