

# Iron–sulfur-protein biogenesis in eukaryotes

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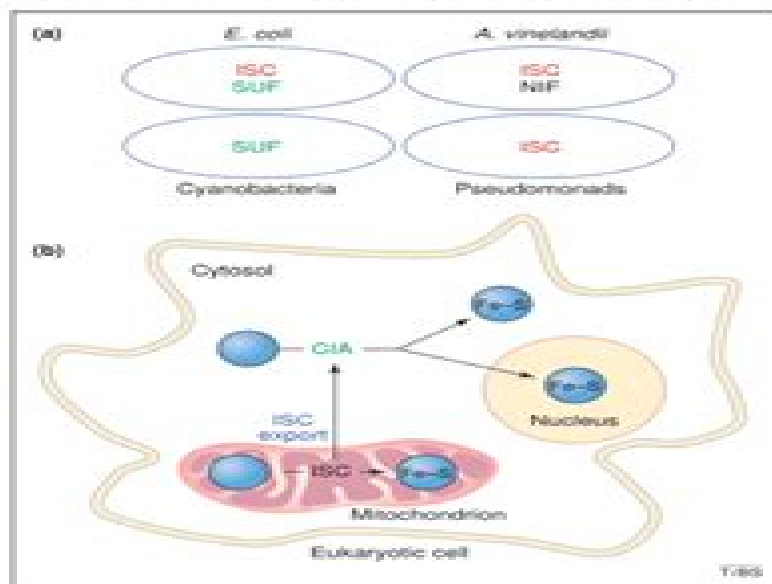
Iron–sulfur (Fe–S) clusters (ISCs) are versatile, ancient co-factors of proteins that are involved in electron transport, enzyme catalysis and regulation of gene expression. The synthesis of ISCs and their insertion into apoproteins involves the function of complex cellular machineries. In eukaryotes, the mitochondrial ISC-assembly machinery is involved in the maturation of all cellular iron–sulfur proteins. A mitochondrial export machinery and a recently discovered cytosolic assembly system specifically participate in the maturation of cytosolic and nuclear iron–sulfur proteins. Of the ~20 assembly components, more than ten are encoded by essential genes, which indicates that the process is indispensable for life. Mutations in two of the assembly components lead to neurological diseases. The essential character of Fe–S-protein biogenesis in eukaryotes and its importance for human disease identifies this evolutionary ancient process as one of the most important biosynthetic pathways of life.

## Introduction

Iron–sulfur (Fe–S) clusters (ISCs) were discovered by Helmut Beinert and others in the early 1960s [1–3]. Until the late 1990s, the complexity of the *in vivo* assembly process of the ISC from its constituents,  $\text{Fe}^{2+}/\text{Fe}^{3+}$  and sulfide ( $\text{S}^{2-}$ ), and its incorporation into an apoprotein was not anticipated. It is now known that bacteria possess three distinct biosynthetic systems to generate Fe–S proteins (for a review, see Ref. [4]). The first discovered system, termed nitrogen-fixation (NIF) machinery, is dedicated to the assembly of the complex Fe–S protein nitrogenase, which is responsible for the conversion of  $\text{N}_2$  to  $\text{NH}_3$  in nitrogen-fixing bacteria [5,6] (Figure 1a). The second system, the ISC-assembly machinery, is required for generation of the majority of cellular Fe–S proteins and, thus, might perform a general ‘house-keeping’ biosynthetic function [7]. The ISC-assembly machinery consists of approximately ten proteins. Finally, the SUF (sulfur-mobilization) machinery was discovered as an independent assemblage that might be used predominantly under iron-limiting or oxidative-stress conditions [8–11]. Although many bacteria contain both the ISC and SUF machineries, others harbour just one of these systems (Figure 1a). Strikingly, the NIF system of the eukaryotic parasite *Endamoeba histolytica* can replace both the ISC and SUF systems in *Escherichia coli* under

anaerobic conditions, which shows that, in principle, these systems are interchangeable [12].

In eukaryotes, Fe–S proteins are present in the mitochondria, the cytosol and the nucleus (Table 1).



**Figure 1.** Distinct systems support cellular Fe–S-protein biogenesis in bacteria and eukaryotes. (a) In bacteria, three systems have been identified that are capable of assembling Fe–S proteins. The ISC and SUF systems are responsible for general assembly of Fe–S proteins, whereas the NIF system present in nitrogen-fixing bacteria (e.g. *Acetobacter vinelandii*) is specialized in assembling the ISCs of nitrogenase, a complex metalloprotein [5,6]. Components of all these systems are usually encoded by operons. When both the ISC and SUF systems are present in one species, such as *Escherichia coli*, the ISC system is responsible for biogenesis of house-keeping Fe–S proteins, in particular, in low oxygen concentrations. The SUF system is used preferentially under oxidative stress and iron-limiting conditions [8]. Some of the SUF genes have been identified in archaeobacterial genomes but, so far, nothing is known about Fe–S-protein biogenesis in Archaea. (b) In eukaryotes, such as the yeast *Saccharomyces cerevisiae*, mitochondria contain a machinery that shares similarity with the bacterial ISC system. This machinery is required for maturation of almost all Fe–S proteins in non-photosynthetic eukaryotes. The mitochondrial ISC-export machinery contributes an unknown factor to biogenesis of cytosolic and nuclear Fe–S proteins. The cytosolic CIA machinery functions downstream of mitochondrial to accomplish Fe–S-protein assembly. Note that the situation in photosynthetic eukaryotes (plants and algae) might be similar but, in addition, they contain SUF proteins in their plastids, thus, resembling the situation in cyanobacteria. Fe–S apoproteins are shown as blue circles.

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# Iron Sulfur Protein Research

**Albert A Gayle**



## **Iron Sulfur Protein Research:**

**Iron-Sulfur Protein Research** Hiroshi Matsubara, Yukiteru Katsube, Keishiro Wada, 1987 *Iron-Sulfur Protein Research* Hiroshi Matsubara, Yukiteru Katsube, Keishiro Wada, 1987 *Iron-Sulfur Proteins*, 1999-06-07 Advances in Inorganic Chemistry presents timely and informative summaries of the current progress in a variety of subject areas within inorganic chemistry ranging from bioinorganic to solid state This acclaimed serial features reviews written by experts in the area and is an indispensable reference to advanced researchers Each volume of Advances in Inorganic Chemistry contains an index and each chapter is fully referenced [Iron-Sulfur Proteins—Advances in Research and Application: 2013 Edition](#), 2013-06-21 Iron Sulfur Proteins Advances in Research and Application 2013 Edition is a ScholarlyBrief that delivers timely authoritative comprehensive and specialized information about Ferredoxins in a concise format The editors have built Iron Sulfur Proteins Advances in Research and Application 2013 Edition on the vast information databases of ScholarlyNews You can expect the information about Ferredoxins in this book to be deeper than what you can access anywhere else as well as consistently reliable authoritative informed and relevant The content of Iron Sulfur Proteins Advances in Research and Application 2013 Edition has been produced by the world's leading scientists engineers analysts research institutions and companies All of the content is from peer reviewed sources and all of it is written assembled and edited by the editors at ScholarlyEditions and available exclusively from us You now have a source you can cite with authority confidence and credibility More information is available at <http://www.ScholarlyEditions.com> [Iron-Sulfur Proteins—Advances in Research and Application: 2012 Edition](#), 2012-12-26 Iron Sulfur Proteins Advances in Research and Application 2012 Edition is a ScholarlyBrief that delivers timely authoritative comprehensive and specialized information about Iron Sulfur Proteins in a concise format The editors have built Iron Sulfur Proteins Advances in Research and Application 2012 Edition on the vast information databases of ScholarlyNews You can expect the information about Iron Sulfur Proteins in this eBook to be deeper than what you can access anywhere else as well as consistently reliable authoritative informed and relevant The content of Iron Sulfur Proteins Advances in Research and Application 2012 Edition has been produced by the world's leading scientists engineers analysts research institutions and companies All of the content is from peer reviewed sources and all of it is written assembled and edited by the editors at ScholarlyEditions and available exclusively from us You now have a source you can cite with authority confidence and credibility More information is available at <http://www.ScholarlyEditions.com> [Iron-Sulfur Proteins: Advances in Research and Application: 2011 Edition](#), 2012-01-09 Iron Sulfur Proteins Advances in Research and Application 2011 Edition is a ScholarlyBrief that delivers timely authoritative comprehensive and specialized information about Iron Sulfur Proteins in a concise format The editors have built Iron Sulfur Proteins Advances in Research and Application 2011 Edition on the vast information databases of ScholarlyNews You can expect the information about Iron Sulfur Proteins in this eBook to be deeper than what you can access anywhere else as well as consistently reliable

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Biochemistry of Nonheme Iron Anatoly Bezkorovainy, 2012-12-06 Atomic biology has come of age Interest in the role of chemical elements in life processes has captured the imagination of a wide spectrum of research scientists ranging from the nutritionist to the biochemist the inorganic chemist and even to some biophysicists This series Biochemistry of the Elements is a recognition of this increasing interest When complete the books will assemble the hard facts concerning the biochemistry of each element singly or in a logical grouping The series will provide a permanent reference for this active and growing field Each volume shall represent an integrated effort by one or several authors to describe the current knowledge of an element s or the methods by which it is studied Iron is the only element to which we have devoted two volumes because its biological and chemical role is so versatile and complex These two volumes will treat the two main structural categories of iron heme and nonheme iron In this volume on nonheme iron the first in the series Anatoly Bezkorovainy provides what we believe is the most comprehensive treatment of this important topic **Chemistry and Properties of Biomolecular Systems** E. Rizzarelli, T. Theophanides, 2013-04-17

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### **Table of Contents Iron Sulfur Protein Research**

1. Understanding the eBook Iron Sulfur Protein Research
  - The Rise of Digital Reading Iron Sulfur Protein Research
  - Advantages of eBooks Over Traditional Books
2. Identifying Iron Sulfur Protein Research
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Iron Sulfur Protein Research
  - User-Friendly Interface
4. Exploring eBook Recommendations from Iron Sulfur Protein Research
  - Personalized Recommendations

- Iron Sulfur Protein Research User Reviews and Ratings
- Iron Sulfur Protein Research and Bestseller Lists
- 5. Accessing Iron Sulfur Protein Research Free and Paid eBooks
  - Iron Sulfur Protein Research Public Domain eBooks
  - Iron Sulfur Protein Research eBook Subscription Services
  - Iron Sulfur Protein Research Budget-Friendly Options
- 6. Navigating Iron Sulfur Protein Research eBook Formats
  - ePub, PDF, MOBI, and More
  - Iron Sulfur Protein Research Compatibility with Devices
  - Iron Sulfur Protein Research Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Iron Sulfur Protein Research
  - Highlighting and Note-Taking Iron Sulfur Protein Research
  - Interactive Elements Iron Sulfur Protein Research
- 8. Staying Engaged with Iron Sulfur Protein Research
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Iron Sulfur Protein Research
- 9. Balancing eBooks and Physical Books Iron Sulfur Protein Research
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Iron Sulfur Protein Research
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine Iron Sulfur Protein Research
  - Setting Reading Goals Iron Sulfur Protein Research
  - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Iron Sulfur Protein Research
  - Fact-Checking eBook Content of Iron Sulfur Protein Research



- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks
- 14. Embracing eBook Trends
  - Integration of Multimedia Elements
  - Interactive and Gamified eBooks

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