

# BIOLOGICAL SYSTEMS IN MICROORGANISMS

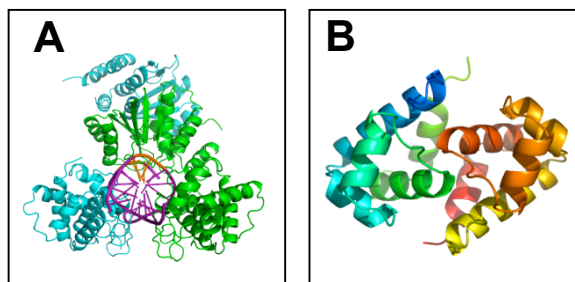
**Molecular Microbiology**

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Microorganisms are always challenged with a variety of stresses in the natural environment. However, they undertake all exquisite strategies to survive under such stressful conditions. For instance, bacteria have the restriction endonucleases to specifically cleave the phage DNA but not their own genomic DNA, which is one of the self-defense systems of bacteria against phage infection. On the other hand, yeast has a very complex system like human cells to respond to the endogenous stressors such as reactive oxygen species. We aim to clarify the entire mechanisms of adaptation to environmental changes of microorganisms by analyzing the molecular structure and function of proteins, gene expression, and signal transduction systems involved in the self-defense system.

## Restriction-Modification System of Bacteria

Bacteria have a restriction-modification system to distinguish their own genomic DNA from the foreign DNA. The restriction endonuclease is an enzyme that recognizes and cuts the specific base sequence of the foreign DNA, which is also an essential tool for the gene engineering. We are taking many approaches to study the mechanism of the base sequence recognition as the specific DNA-binding protein, as well as the mechanism of molecular evolution that results in developing various enzymes. Moreover, we are also analyzing the regulation of the expression of genes involved in the restriction-modification system, because the restriction endonuclease acts as a kind of “poison” in bacterial cells.

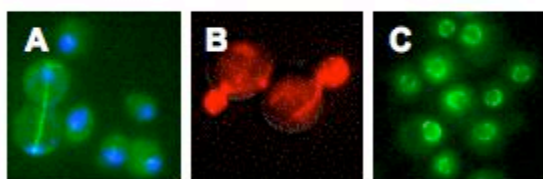


**Structures of proteins for the restriction-modification system**

A, restriction endonuclease-DNA complex  
B, transcriptional regulator

## Cellular Mechanism of Adaptation to Environment: Yeast as a Model System

The cellular structure of yeast is similar to that of higher eukaryotes like the human cell. Additionally, various biological events that occur in the cell also resemble each other. In fact, thus far, the detailed mechanisms of many important biological events have been clarified using yeast as a model organism. We are trying to determine what kind of gene is expressed when yeast cells are exposed to environmental changes, how such genes are regulated, and also how mRNAs and gene products derived from such genes are trafficked and functioning in the cell.



**Staining of cellular components**

A, microtubule; B, actin; C, nuclear envelope.

## Key words

*Bacteria, yeast, virus, protein, DNA, interaction, signal transduction, molecular evolution, gene expression, cell biology, molecular biology, reactive oxygen species, ethanol*

## Recent publications

### **Crystallization and X-ray diffraction studies of DNA-free and DNA-bound forms of EcoO109I DNA methyltransferase**

Iwamoto M, Hishiki A, Shimada T, Imasaki T, Tsuda J, Kita K, Shimizu T, Sato M, Hashimoto H (2010)

Acta Cryst F66:1528-1530

### **Calcineurin/Crz1 destabilizes Msn2 and Msn4 in the nucleus in response to Ca<sup>2+</sup> in *Saccharomyces cerevisiae***

Takatsume Y\*, Ohdate T\*, Maeta K, Nomura W, Izawa S, Inoue Y (2010)

Biochem J 427:275-287

\* Equally contributed.

### **Regulatory mechanism for expression of *GPX1* in response to glucose starvation and Ca<sup>2+</sup> in *Saccharomyces cerevisiae*: Involvement of Snf1 and Ras/cAMP pathway in Ca<sup>2+</sup> signaling**

Ohdate T, Izawa S, Kita K, Inoue Y (2010)

Genes Cells 15:59-75

### **Methylglyoxal activates Gcn2 to phosphorylate eIF2 $\alpha$ independently of the TOR pathway in *Saccharomyces cerevisiae***

Nomura W, Maeta K, Kita K, Izawa S, Inoue Y (2010)

Appl Microbiol Biotechnol 86:1887-1894

### **Post-transcriptional regulation of gene expression in yeast under ethanol stress**

Izawa S, Inoue Y (2009)

Biotechnol Appl Biochem 53:93-99

### **Role of Gcn4 for adaptation to methylglyoxal in *Saccharomyces cerevisiae***

### **Methylglyoxal attenuates protein synthesis through phosphorylation of eIF2 $\alpha$**

Nomura W, Maeta K, Kita K, Izawa S, Inoue Y (2008)

Biochem Biophys Res Commun 376:738-742

### **Heat shock and ethanol stress provoke distinctly different responses in 3'-processing and nuclear export of HSP mRNA in *Saccharomyces cerevisiae***

Izawa S, Kita T, Ikeda K, Inoue Y (2008)

Biochem J 414:111-119

### **Release of thioredoxin from *Saccharomyces cerevisiae* with environmental stimuli: solubilization of thioredoxin with ethanol**

Takeuchi Y, Nomura W, Ohdate T, Tamasu S, Masutani H, Murata K, Izawa S, Yodoi J, Inoue Y (2007)

Appl Microbiol Biotechnol 75:1393-1399

**Improvement of tolerance to freeze-thaw stress of baker's yeast by cultivation with soy peptides**

Izawa S, Ikeda K, Takahashi N, Inoue Y (2007)  
Appl Microbiol Biotechnol 75:533-538

**Efficient extraction of thioredoxin from *Saccharomyces cerevisiae* with ethanol**

Inoue Y, Nomura W, Takeuchi Y, Ohdate T, Tamasu S, Kitaoka A, Kiyokawa Y, Masutani H, Murata K, Wakai Y, Izawa S, Yodoi J (2007)  
Appl Environ Microbiol 73:1672-1675

**Green tea polyphenols function as prooxidants to activate oxidative stress-responsive transcription factors in yeasts**

Maeta K, Nomura W, Takatsume Y, Izawa S, Inoue Y (2007)  
Appl Environ Microbiol 73:572-580

**Msn2p/Msn4p-activation is essential for the recovery from freezing stress in yeast**

Izawa S, Ikeda K, Ohdate T, Inoue Y (2007)  
Biochem Biophys Res Commun 352:750-755

**Formation of the cytoplasmic P-bodies in sake yeast during Japanese sake brewing and wine making**

Izawa S, Kita T, Ikeda K, Miki T, Inoue Y (2007)  
Biosci Biotechnol Biochem 71:2800-2807

**Modulation of Spc1 stress-activated protein kinase activity by methylglyoxal through inhibition of protein phosphatase in the fission yeast**

***Schizosaccharomyces pombe***

Takatsume Y, Izawa S, Inoue Y (2007)  
Biochem Biophys Res Commun 363:942-947

**Methylglyoxal as a signal initiator for activation of the stress-activated protein kinase cascade in the fission yeast *Schizosaccharomyces pombe***

Takatsume Y, Izawa S, and Inoue Y (2006)  
J Biol Chem 281:9086-9092

**GPX2, encoding a phospholipid hydroperoxide glutathione peroxidase homologue, codes for an atypical 2-Cys peroxiredoxin in *Saccharomyces cerevisiae***

Tanaka T, Izawa S, and Inoue Y (2005)  
J Biol Chem 280:42078-42087

**The glycolytic metabolite methylglyoxal activates Pap1 and Sty1 stress responses in *Schizosaccharomyces pombe***

Zuin A, Vivancos AP, Sansó M, Takatsume Y, Ayté J, Inoue Y, Hidalgo E (2005)  
J Biol Chem 280:36708-36713

**Crystal structures of type II restriction endonuclease EcoO109I and its complex with cognate DNA**

Hashimoto H, Shimizu T, Imasaki T, Kato M, Shichijo N, Kita K, Sato M (2005)  
J Biol Chem 280:5605-5610

**Methylglyoxal, a metabolite derived from glycolysis, functions as a signal initiator of the high osmolarity glycerol-mitogen-activated protein kinase cascade and calcineurin/Crz1-mediated pathway in *Saccharomyces cerevisiae***

Maeta K, Izawa S, Inoue Y (2005)

J Biol Chem 280:253-260

**X-ray structures of NADPH-dependent carbonyl reductase from *Sporobolomyces salmonicolor* provide insights into stereoselective reductions of carbonyl compounds**

Kamitori S, Iguchi A, Ohtaki A, Yamada M, Kita K (2005)

J Mol Biol 352:551-558

**Gle2p is essential to induce adaptation of the export of bulk poly (A)<sup>+</sup> mRNA to heat shock in *Saccharomyces cerevisiae***

Izawa S, Takemura R, Inoue Y (2004)

J Biol Chem 279:35469-35478

**Stress response in the yeast mRNA export factor: reversible change in the localization of Rat8p is caused by ethanol stress but not heat shock**

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**Activity of the Yap1 transcription factor in *Saccharomyces cerevisiae* is modulated by methylglyoxal, a metabolite derived from glycolysis**

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