

# PRACTICAL SCIENCE BRING ABOUT A NEW BREAKTHROUGH

## Industrial Microbiology

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Previously, the scientists in USA and Europe have been amazed at the progress of bioscience and biotechnology in Japan. This was mainly due to the achievements of our former leaders who carried out substantially innovative works in practical science. Many of their innovative findings were successfully translated into industrial production of useful compounds for human welfare. Unfortunately, however, the scientists in USA are currently showing overwhelming power to lead the field of bioscience based on their fundamental research. In order to compete with such a big power, it would be more and more important to reinforce our capability through the investigation with originality since we do not have enough resources without intellectual one. Our new laboratory was established in 2006 for expanding the practical science aiming at contribution to the development of industry. In pursuit of innovative breakthrough, we would like to construct the unique laboratory ranked as the core of applied microbiology.

### Bring unnoticed phenomena to valuable common knowledge

It is important to find out something new while closely looking at nature without prejudice. From a viewpoint of industrial microbiology, this mean the finding of novel and useful potential being involved in microorganisms. Through finding of new phenomena, we can establish a new concept and theory leading to further original research, and create new seeds for industrial breakthrough. In other words, our aim is to bring unnoticed phenomena to valuable common knowledge.

成功例の一つに「抗エイズ薬」が挙げられる。一九八七年に研究をスタートさせ、八九年に工業化した。副作用が少なく、延命効果のある二種（DDI、DDI）のエイズ治療物質は米国プリストルマイヤーズ社が独占使用権を所有しているが、難関の量産技術を湯川、横関らのグループが開発したのだ。横関は感慨をこめて言う。 . . .

徹底したスクリーニングによる発見が先決。理論の組立てはその後だ、というのが横関の姿勢。

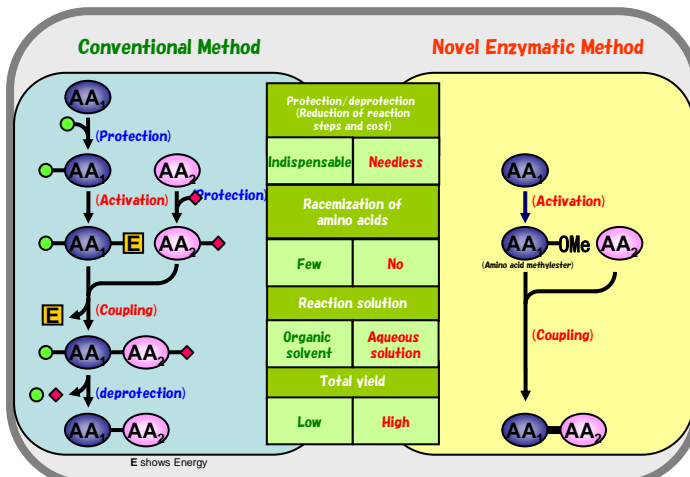
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An extract from a newspaper

### Impact of new potential in enzyme

Our laboratory aims at creating industrial innovation by the application of novel functions being involved in microorganisms. Recently, we successfully developed a new enzymatic method producing peptides from unprotected starting materials. Our newly developed system brought about a simple and high yield process without protection and deprotection steps, and is applied to industrial production. Our recent discovery of enzyme potential would create innovation beyond common knowledge and attract big attention.



A novel enzymatic method for peptide production

## Key words

*Industrial microbiology, applied microbiology, microbiology, enzyme, microbial conversion, enzymatic conversion, screening, stereospecificity, regioselectivity, genetic engineering, genetic modification of enzyme*

## Recent publications

**A novel L-isoleucine metabolism in *Bacillus thuringiensis* generating (2S,3R,4S)-4-hydroxyisoleucine, a potential insulinotropic and anti-obesity amino acid.**

Ogawa J, Koder T, Smirnov SV, Hibi M, Samsonova NN, Koyama R, Yamanaka H, Mano J, Kawashima T, Yokozeki K, Shimizu S (2011)  
Appl. Microbiol. Biotechnol., 89: 1929-1938

**Linoleic acid isomerase in *Lactobacillus plantarum* AKU1009a proved to be a multi-component enzyme system requiring oxidoreduction cofactors.**

Kishino S, Ogawa J, Yokozeki K, Shimizu S (2011)  
Biosci. Biotechnol. Biochem., 75: 318-322

**Metabolic engineering of *Escherichia coli* to produce (2S,3R,4S)-4-hydroxyisoleucine.**

Smirnov SV, Koder T, Samsonova NN, Kotlyarova VA, Rushkevich NY, Kivero AD, Sokolov PM, Hibi M, Ogawa J, Shimizu S (2010)  
Appl. Microbiol. Biotechnol., 88:719-726

**Two laccase isoenzymes and a peroxidase of a commercial laccase-producing basidiomycete, *Trametes* sp. Ha1.**

Nakatani M, Hibi M, Minoda M, Ogawa J, Yokozeki K, Shimizu S (2010)  
New Biotechnol., 27:317-323

**Microbial production of conjugated  $\gamma$ -linolenic acid from  $\gamma$ -linolenic acid by *Lactobacillus plantarum* AKU 1009a.**

Kishino S, Ogawa J, Ando A, Yokozeki K, Shimizu S (2009)  
J. Appl. Microbiol., 108: 2012-2018

**Microbial production of conjugated fatty acids.**

Kishino S, Ogawa J, Yokozeki K, Shimizu S (2009)  
Lipid Technol., 21: 177-181

**Novel l-isoleucine hydroxylating enzyme, l-isoleucine dioxygenase from *Bacillus thuringiensis*, produces (2S,3R,4S)-4-hydroxyisoleucine.**

Koder T, Smirnov SV, Samsonova NN, Kozlov YI, Koyama R, Hibi M, Ogawa J, Yokozeki K, Shimizu S (2009)  
Biochem. Biophys. Res. Commun., 390: 506-510

**Screening, purification, and identification of the enzyme producing N-(L- $\alpha$ -L-aspartyl)-L-phenylalanine methyl ester from L-isoasparagine and L-phenylalanine methyl ester.**

Kira I, Asano Y, Yokozeki K (2009)  
J. Biosci. Bioeng., 108: 190–193

**Enantioselective ester hydrolase from *Sphingobacterium* sp. 238C5 useful for chiral resolution of  $\beta$ -phenylalanine and for its  $\beta$ -peptide synthesis.**

Ogawa J, Mano J, Hagishita T, Shimizu S (2009)  
J. Mol. Catal., B Enzym., 60: 138-144

**Synthesis of Optically Active  $\alpha$ -Methyl Amino Acids using Biotransformation as a Key Step. ACS Symposium Series, 1009 (Asymmetric Synthesis and Application of  $\alpha$ -Amino Acids),**

Yatagai M, Hamada T, Nozaki H, Kuroda S, Yokozeki K, Izawa K (2009)  
American Chemical Society, p. 394-406

**Metabolic diversity in biohydrogenation of polyunsaturated fatty acids by lactic acid bacteria involving conjugated fatty acid production**

Kishino S, Ogawa J, Yokozeki K, Shimizu S (2009)  
Appl. Microbiol. Biotechnol., 84: 87-97

**Hyperproduction of 3,4-dihydroxyphenyl-L-alanine (L-Dopa) using *Erwinia herbicola* cells carrying a mutant transcriptional regulator TyrR**

Koyanagi T, Katayama T, Suzuki H, Onishi A, Yokozeki K, Kumagai H (2009)  
Biosci. Biotechnol. Biochem., 73: 1221-1223

**Fatty acid desturation and elongation reactions of *Trichoderma* sp. 1-OH-2-3**

Ando A, Ogawa J, Kishino S, Ito T, Shirasaka N, Sakuradani E, Yokozeki K, Shimizu S (2009)  
J. Am. Oil Chem. Soc., 86: 227-233

**Selective production of cis-9,trans-11 isomer of conjugated linoleic acid from trans-vaccenic acid methyl ester by *Delacroixia coronata***

Ando A, Ogawa J, Sugimoto S, Kishino S, Sakuradani E, Yokozeki K, Shimizu S (2009)  
J. Appl. Microbiol., 106: 1697-1704

**Gene cloning, purification, and characterization of  $\alpha$ -methylserine aldolase from *Bosea* sp. AJ110407 and its applicability for the enzymatic synthesis of  $\alpha$ -methyl-L-serine and  $\alpha$ -ethyl-L-serine**

Nozaki H, Kuroda S, Watanabe K, Yokozeki, K (2008)  
J. Mol. Catal., B Enzym., 59: 237-242

**Gene cloning of  $\alpha$ -methylserine aldolase from *Variovorax paradoxus* and purification and characterization of the recombinant enzyme**

Nozaki H, Kuroda S, Watanabe K, Yokozeki, K (2008)  
Biosci. Biotechnol. Biochem., 72: 2580-2588

**Purification and gene cloning of  $\alpha$ -methylserine aldolase from *Ralstonia* sp. strain AJ110405 and application of the enzyme in the synthesis of  $\alpha$ -methyl-L-serine**

Nozaki H, Kuroda S, Watanabe K, Yokozeki, K (2008)  
Appl. Environ. Microbiol., 74: 7596-7599

**Cloning of the gene encoding  $\alpha$ -methylserine hydroxymethyltransferase from *Aminobacter* sp. AJ110403 and *Ensifer* sp. AJ110404 and characterization of the recombinant enzyme**

Nozaki H, Kuroda S, Watanabe K, Yokozeki, K (2008)  
Biosci. Biotechnol. Biochem., 72: 3002-3005

**Screening of microorganisms producing  $\alpha$ -methylserine hydroxymethyltransferase, purification of the enzyme, gene cloning, and application to the enzymatic synthesis of  $\alpha$ -methyl-L-serine**

Nozaki H, Kuroda S, Watanabe K, Yokozeki, K (2008)  
J. Mol. Catal., B Enzym., 56: 221-226

**An enzymatic breakthrough in the industrial production of oligopeptides**

Yokozeki K (2007)  
Speciality Chemicals Magazine, 27: 44-45

**Highly diastereoselective chemoenzymatic synthesis of (2'R)- and (2'S)-2'-deoxy[2'-2H]guanosines**

Kawashima E, Terui Y, Kodama R, Yokozeki K (2006)  
Tetrahedron. Lett., 47: 3161-3165

**Screening and industrial application of unique microbial reactions involved in nucleic acid and lipid metabolisms**

Ogawa J, Soong CL, Kishino S, Li QS, Horinouchi N, Shimizu S (2006)  
Biosci. Biotechnol. Biochem., 70: 574-582