

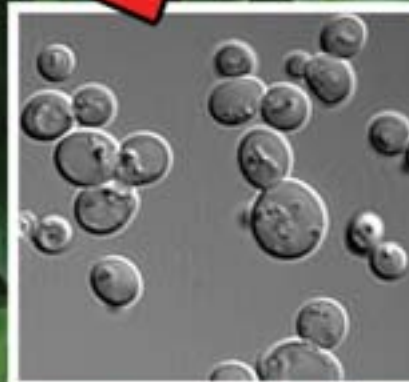
# SIMB News

News Magazine of the Society for Industrial Microbiology and Biotechnology  
January/February/March 2021 v.71 n.1 • [www.simbhq.org](http://www.simbhq.org)



## Adventures in Brewing

Exotic Japanese Alcoholic  
Beverages with  
“Amino Acid-rich Yeast”





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On the cover  
Hibiscus flower and the yeast  
*Saccharomyces cerevisiae*

Sake fermentation tank and paddling  
work for managing sake mash ‘moromi’  
(Courtesy of Gekkeikan Sake Co., Ltd.)



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# Letter from the Editor-in-Chief

We have a new cover design for *SIMB News*! It is in the style of the *Journal of Industrial Microbiology and Biotechnology (JIMB)*. You are probably asking yourself, why is this so? Commencing January 1, 2021, *JIMB* is published by Oxford University Press (OUP) and *SIMB News* is commemorating the change with the new cover design. The change in publishers enables *JIMB* to be published as open access. As stated by Dr. Ramon Gonzalez, Editor-in-Chief of *JIMB*, "The excellent digital capabilities and publishing experience of OUP will undoubtedly lead to an increase in the visibility, influence, and impact of the research being published by *JIMB*. We very much look forward to leveraging OUP resources to better serve authors, readers, reviewers, editors, and the *SIMB* community at large." With *JIMB*'s open access format, this will indeed increase the visibility of your peer-reviewed research.

Along with publishing your research in *JIMB*, please consider sending informative articles for possible publication in *SIMB News*. This issue's feature article is a great example provided by Professor Hiroshi Takagi. His peer reviewed article, "Effects of a novel variant of the yeast  $\gamma$ -glutamyl kinase Pro1 on its enzymatic activity and sake brewing", appeared in the October 2020 issue of *JIMB*. This work was performed in close collaboration with the Gekkeikan Sake Company. Because not all of the research accomplished through this partnership could be included in his *JIMB* article, Professor Takagi first proposed preparing a press release to be published in *SIMB News*. However, on further discussion, it was decided that there was plenty of information to develop a wonderful feature article for inclusion in this issue of *SIMB News*. I think you will agree.

Sincerely,

**Melanie R. Mormile**

Editor-in-Chief, *SIMB News*  
[mmormile@mst.edu](mailto:mmormile@mst.edu)

## Corrections

October-December 2020 issue

Hal Alper is a candidate for President-elect

Yoram Barak and Ben Shen are candidates for Director



# *SIMB Strategic Plan*

## **Vision**

To be the leading international professional society in industrial microbiology and biotechnology

## **Mission**

Empower our members and others to address current and future challenges facing humanity using industrial microbiology and biotechnology.

## **Core values**

Scientific excellence (innovation, rigor, multi-disciplinary science and engineering, translational technology)

Leadership (collaboration, continuity, advocacy)

Diversity (promotion, inclusion, openness, internationality)

Responsibility (ethics, integrity, transparency, societal impact)

Communication (education, information, outreach, responsiveness)

Passion for science (fun, inspiration)

## **Goals**

1. Provide information to increase global knowledge, understanding, and application of industrial microbiology and biotechnology.
2. Organize preeminent meetings in our core scientific disciplines.
3. Publish the leading journal in industrial microbiology and biotechnology.
4. Promote and increase diversity in all aspects of the Society, with membership open to anyone interested in our vision and mission.
5. Enhance the value of membership in the Society for both individual and corporate members.
- 6 Offer educational/professional development opportunities for the membership and the general public.
7. Communicate our activities and accomplishments in industrial microbiology and biotechnology to both the global scientific community and the general public.
8. Expand our global reach.
9. Ensure the financial and operational stability of the Society.





# TIME TO RENEW!

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for 2021 are due!

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## Science Coalition Urges Congress to Provide Emergency Relief to NSF

The Coalition for National Science Funding (CNSF)—an alliance of more than 130 professional organizations, scientific societies, universities, and businesses that advocate for the National Science Foundation (NSF) — has called on congressional leadership to include \$3 billion in emergency relief for the NSF while providing relief to all federal science agencies.

The groups note, in part: “Though our nation’s scientists and research institutions have risen to the challenge of the pandemic, they are facing enormous strains on their operations and infrastructure. NSF needs additional funding to support research grants, students and post-docs, early-career faculty, and scientific facilities. Federally funded scientists and engineers are experiencing significant negative impacts to their work during the pandemic, such as delays or cessation of their research projects, an extremely challenging academic and research job market, lab closures, and uncertainty about continuing to pay salaries, extend timelines, access needed lab equipment, and more. These impacts have disproportionately affected students, trainees, and early-career researchers, who make up an important segment of NSF award recipients. Without emergency relief, we risk many early-career researchers and STEM students leaving science altogether, losing a generation of diverse talent that is the bedrock of our national competitiveness.”

President Biden’s \$1.9 trillion COVID-19 relief plan, called American Rescue Plan, includes funding to expand testing and vaccinations; \$1,400 direct payments to individuals; extension of federal unemployment benefits; state and local government aid; and funding for K-12 and higher education institutions, among other provisions. The package, however, does not include emergency supplemental funding for research.

## White House Orders Review of Federal Scientific Integrity Policies

On January 27, 2021, the Biden Administration issued a memorandum ordering a government-wide review of the effectiveness of existing scientific integrity policies.

The directive, “Memorandum on Restoring Trust in Government Through Scientific Integrity and Evidence-Based Policymaking,” builds on a 2009 memo from President Obama and a 2010 memo from the White House Office of Science and Technology Policy (OSTP), which called for ensuring a culture of scientific integrity in the government, strengthening the credibility of government research, facilitating the free flow of scientific information, and establishing principles for conveying information to the public.

“Scientific findings should never be distorted or influenced by political considerations,” reads Biden’s memo. “Improper political interference in the work of Federal scientists or other scientists who support the work of the Federal Government and in the communication of scientific facts undermines the welfare of the Nation, contributes to systemic inequities and injustices, and violates the trust that the public places in government to best serve its collective interests.”

The directive orders the OSTP Director to convene an interagency task force to conduct a 120-day review of existing scientific integrity policies across the government. The task force will consider whether existing policies “prevent improper political interference” in scientific research; “prevent the suppression or distortion” of research data and findings; and support researchers of all genders, races, ethnicities, and backgrounds. Once the review concludes, a report synthesizing the task force’s findings, including an assessment of agencies’ strengths and weaknesses regarding scientific-integrity policies and a description of best practices, will be published on the OSTP website.

The memo directs agencies to identify chief science officers to serve as principal advisors to agency heads on scientific issues; conduct a 90-day review of federal advisory committees that provide independent scientific advice to the government; and determine whether any science advisory panels disbanded under the Trump Administration need to be re-established. It also calls on agencies to review and update within 60 days any website content and within 300 days any reports and data published during the Trump administration that are “inconsistent” with Biden’s directive.

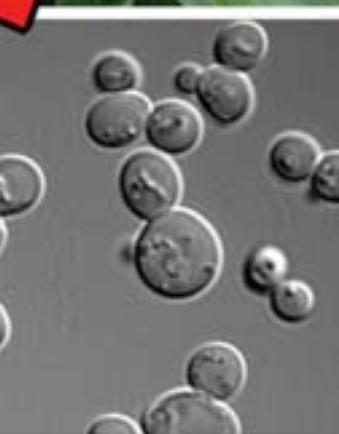
The memo has been welcomed with cautious optimism by research and advocacy groups. Lauren Kurtz, Executive Director of the Climate Science Legal Defense Fund notes the memo is “considerably more detailed than Obama’s” but that there is “quite a tall task order for the Biden [A]dministration.” According to Science Insider, Roger Pielke Jr., a policy specialist at the University of Colorado, Boulder argued that the memo “is very good, but legislation is still needed.” Andrew Rosenberg, Director of the Center for Science and Democracy at the Union of Concerned Scientists, stated, “Over the next four years, scientists, public health experts and community advocates will be watching closely to make sure that the Biden administration upholds its promise to heed the science.”



## Hiroshi Takagi

(Division of Biological Science, Graduate School of Science and Technology, Nara Institute of Science and Technology, Nara, Japan)

# Adventures in Brewing Exotic Japanese Alcoholic Beverages with “Amino Acid-rich Yeast”



## Abstract

*The yeast *Saccharomyces cerevisiae* is an important microorganism in basic science as a model for higher eukaryotes. For example, Dr. Yoshinori Ohsumi was awarded the 2016 Nobel Prize in Physiology or Medicine for his discoveries of mechanisms for autophagy in *S. cerevisiae* cells\*1. Also, yeasts are useful microbes in fermentation industries, such as breweries and bakeries, due to extremely high ethanol productivity and gassing power.*

In terms of biotechnological applications, there are two major purposes for breeding of industrial yeasts, improvement of fermentation ability with enhanced stress tolerance and diversity of product taste and flavor with modified metabolic pathways. Amino acids are one of the key factors affecting yeast fermentation. In yeast, amino acid metabolism and its regulatory mechanisms vary under different growth environments by regulating anabolic and catabolic processes, including uptake and export. The control of amino acid composition and content is expected to contribute to an improvement in productivity, and to add to the value of alcoholic beverages and fermented foods. In this article, I will introduce our research outcomes by an industrial-government-academic collaboration that includes construction of brewer's yeast strains with high functionality, focused on the metabolic regulatory mechanisms and physiological roles of "functional amino acids" and their application in brewing the Japanese alcoholic beverages, sake and awamori.

### What are sake and awamori?

There are two types of alcoholic beverages produced by lovely yeasts, specifically *Saccharomyces cerevisiae*. Among them, sake and shochu are unique Japanese alcoholic beverages by a collaboration of fungus and yeast (Figure 1). Sake is a traditional Japanese alcoholic beverage made from steamed rice by multiple parallel fermentations of the fungus *Aspergillus oryzae* and the *S. cerevisiae* yeast to produce saccharification enzymes and ethanol from glucose, respectively. The yeast strains used in sake brewing (sake yeast) can produce ethanol to a concentration of approximately 20% (v/v). During sake fermentation, yeast cells are exposed to high concentrations of ethanol which drastically inhibit the growth, viability and fermentation of yeast cells. Therefore, increased tolerance to ethanol in sake yeast strains could improve ethanol productivity and reduce fermentation time. We expected that sake yeast cells have specific genes or mutations to enhance ethanol stress tolerance, like a superhero. However, to our surprise, sake yeast cells are like workaholics, because they gave up the genes to protect themselves, such as MSN4 and RIM15, which inhibit ethanol production (Watanabe

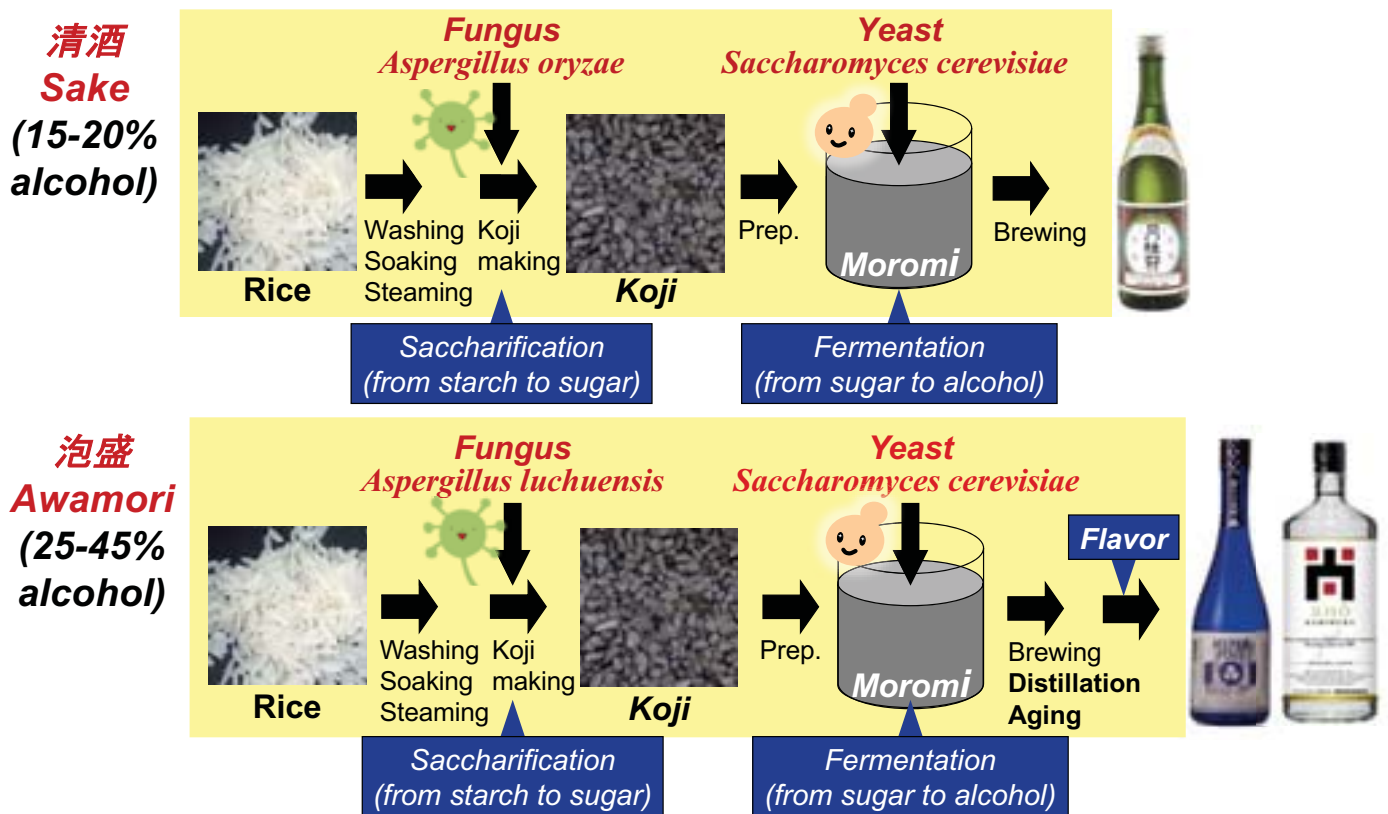


Figure 1: How to brew Japanese alcoholic beverages, sake and awamori, through collaborations with fungus and yeast

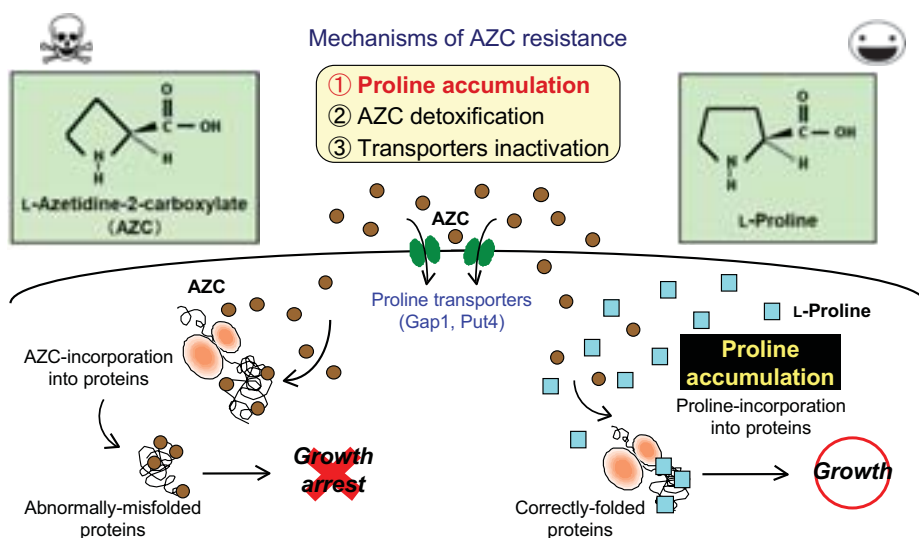


Figure 2: How to isolate yeast mutants with Pro accumulation

The toxic Pro analogue AZC causes misfolding of the proteins into which it is incorporated competitively with Pro, and thereby inhibits cell growth. However, Pro-accumulating cells are resistant to AZC

et al., 2012; 2016; 2019). Awamori, which is one type of shochu, is a traditional spirit (distilled alcoholic beverage) made from steamed rice in subtropical Okinawa, Japan. Its brewing process is quite different from that of other distilled spirits such as whiskey made from grain mash where the malt enzyme and yeast convert starch to sugar to alcohol. During awamori brewing, the fungus *Aspergillus luchuensis* and the yeast *S. cerevisiae* are widely used for preparing the fermented mash (moromi) and producing alcohol, respectively, by multiple parallel fermentations (simultaneous saccharification and fermentation). After the fermentations, the alcohol is mainly distilled under atmospheric pressure and is put in barrels for aging that develops a rich and strong flavor. Thus, awamori has a unique aroma that is clearly distinguishable from the profiles of other types of shochu, to which the vacuum distillation brings about a clear and light taste.

## How to isolate or construct brewer's yeast strains with higher amino acid content

I focused on the metabolic regulatory mechanisms and physiological roles of amino acids which are key factors affecting yeast fermentation ability and the flavor of yeast products including sake and awamori. How can we isolate yeast mutants with the specific amino acid accumulation? For example, Figure 2 shows the mechanism of resistance

for L-proline (Pro) toxic analogue L-azetidine-2-carboxylate (AZC). It is said that the amino acid analogues are transported into cells via the amino acid transporters on plasma membranes. Some AZC analogues could cause misfolding of the proteins into which they are incorporated competitively with the corresponding amino acid (Pro) and thereby inhibit the growth of the cells. However, the cells that accumulate large quantities of Pro are tolerant to AZC. Thus, we can isolate the toxic amino acid analogue-resistant mutants derived from the parent yeast strain. Basically, the parent cells cannot grow in the presence of a high concentration of AZC due to its

toxicity. However, after introduction of random mutagenesis into the genome of many cells with ethyl methanesulfonate (EMS), several colonies appeared on agar plates containing AZC. Subsequently, AZC-resistant mutants were collected and measured for intracellular Pro content.

For the application of recombinant yeasts, self-cloning yeast (SC), is more acceptable for consumers than genetically modified (GM) yeast. According to the Japanese government guidelines, SC yeast does not have to be treated as GM yeast, because SC processes are considered to be the same as naturally occurring gene conversions. However, the food industry has not yet accepted SC yeast. To overcome this obstacle, we constructed brewer's yeast strains by conventional mutagenesis using EMS, which is a widely acceptable method of yeast breeding for food industries and consumers.

## Improvement of taste of light-bodied sake by higher L-proline and lower succinate levels [collaboration with Gekkeikan Sake Co., Ltd.\*2]

The taste of sake is determined by a combination of many compounds such as sugars, organic acids, amino acids, nucleotides, and inorganic salts. In particular, since sugars are sweet and organic acids are sour, it is possible to make sake of various tastes by changing the balance of sugars

and organic acids. On the other hand, amino acids with sweet, bitter, or umami taste may impact some sensory qualities of sake, but a high amino acid content is often thought to produce an unfavorable taste in sake. In sake mash, amino acids are mainly derived from the digestion of rice proteins by sake koji enzymes; however, yeast cells also synthesize them during fermentation. In sake, amino acids in addition to other taste components originate mainly from *S. cerevisiae* cells, and a variety of yeast strains have been constructed to develop differentiated sake products. Recently, Gekkeikan Sake Co., Ltd. isolated mutants resistant to AZC, derived from a diploid sake yeast strain. Some of the mutants produced a greater amount of Pro in the brewed sake. Among them, one mutant (K-9-AZC) was found to

produce higher Pro and lower succinate levels than those of its parent strain Kyokai no. 9 (K-9) in sake mash, leading to the potential for low-carbohydrate sake (Kotaka et al., 2019). However, the molecular mechanisms involved in both higher Pro and lower succinate production in K-9-AZC have not been yet clarified. Recently, we identified a novel gene mutation which increases intracellular Pro levels, in strain K-9-AZC. We also analyzed the fermentation and metabolite profiles of strain K-9-AZC during sake brewing (Murakami et al., 2020).

Some AZC-resistant mutants were found to accumulate larger amounts of intracellular Pro than the parent strain. Pro-accumulating *S. cerevisiae* strains usually have a mutation in the PRO1 gene which encodes  $\gamma$ -glutamyl kinase (Pro1; GK). Glutamylkinase(GK) is the rate-limiting enzyme of proline biosynthesis from l-glutamate (Glu), and its activity is regulated allosterically by the end product Pro (Sekine et al, 2007). The majority of Pro-accumulating strains have been obtained by expressing GK variants, such

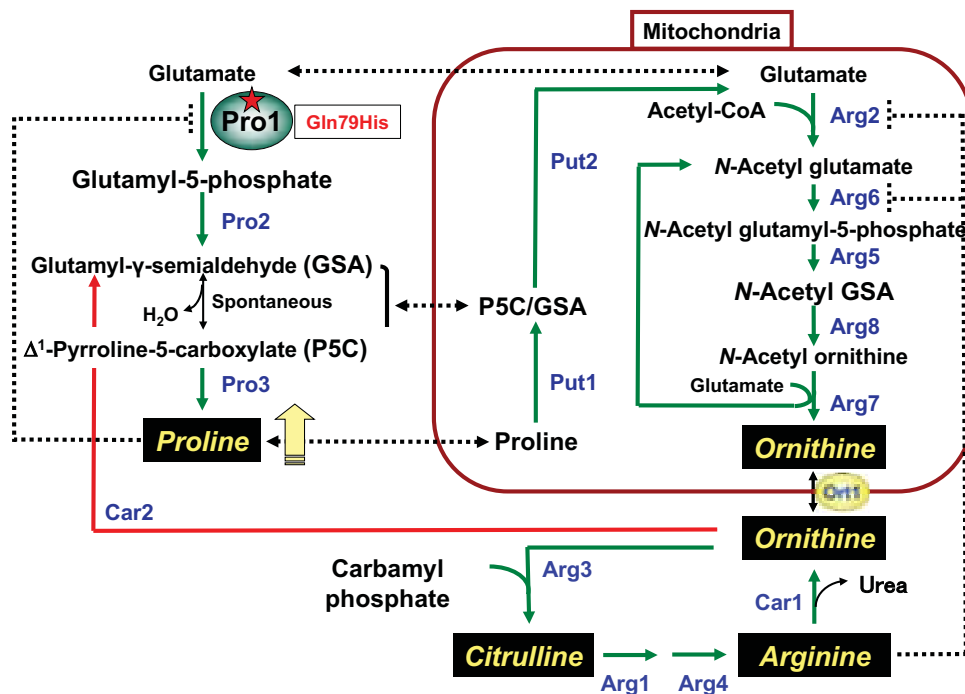


Figure 3: Synthetic pathway of l-proline [Pro] and l-arginine [Arg] in *S. cerevisiae*  $\gamma$ -Glutamyl kinase [GK; Pro1] is the key enzyme that controls Pro synthesis by feedback inhibition. We found a heteroallelic mutation in the PRO1 gene encoding the Gln79His variant GK in strain K-9-AZC. Enzyme activity of the variant was insensitive to feedback inhibition by Pro, leading to Pro overproduction.

as Asp154Asn and Ile150Thr, which are less sensitive to feedback inhibition by Pro (Figure 3) (Morita et al., 2003; Sekine et al., 2007). We found that strain K-9-AZC carried a novel mutation in the PRO1 gene encoding the Gln79His variant of GK (Figure 3). This mutation resulted in extreme desensitization to feedback inhibition by Pro, leading to Pro overproduction. The amino acid residue at position 79 is highly conserved in GK among other microorganisms. Interestingly, sake brewed with K-9-AZC contained 3.7-fold more Pro but only 25% less succinate than sake brewed with K-9. It was shown that the acidity was reduced to about 70% compared with K-9, although there were no significant differences in the sake meter value, alcohol, and amino acid contents between strains K-9 and K-9-AZC. Moreover, the sensory test revealed that the sourness in sake brewed with K-9-AZC was suppressed. Thus, we were able to brew sake with a lower acidity based on both analytical data and sensory evaluation. Metabolome analysis suggests that the decrease in succinate was attributable to a lower level of 2-oxoglutarate which is converted into Glu. The approach



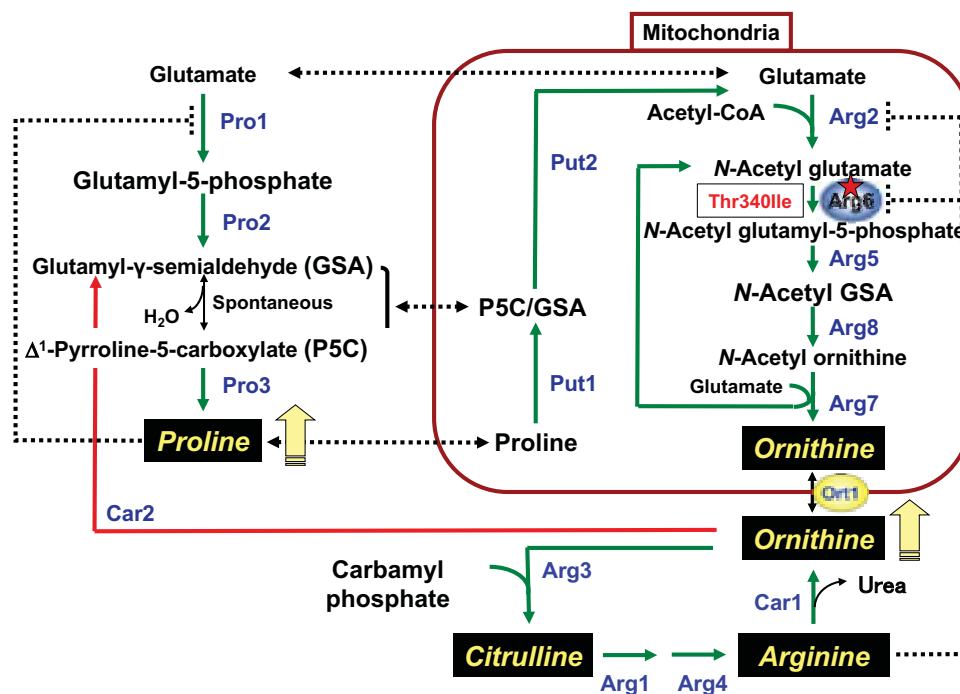


Figure 4: Synthetic pathway of l-proline [Pro] and l-ornithine [Orn] in *S. cerevisiae*. N-Acetylglutamate kinase [NAGK; Arg6] is the key enzyme that controls Arg and Orn synthesis by feedback inhibition. We found a homoallelic mutation in the ARG6 gene encoding the Thr340Ile variant NAGK in strain A902-4. Enzyme activity of the variant was insensitive to feedback inhibition by Arg, leading to Orn and Pro overproduction.

here could be a practical method for breeding yeast strains involved in the diversity of sake taste.

### Enhanced l-ornithine synthesis mediated by l-proline/l-arginine metabolism and application to brewing a “healthy image” sake [collaboration with Nara Prefecture Institute of Industrial Development\*3]

Increased tolerance to ethanol in sake yeast strains would potentially improve ethanol productivity and reduce the time required for fermentation. We previously reported that Pro confers an increased tolerance for ethanol by yeast cells (Takagi et al., 2005; 2007). Recently, we constructed diploid sake yeast strains expressing the N-acetyltransferase Mpr1 which protects yeast cells from oxidative stresses by possibly activating a novel l-arginine (Arg) biosynthesis (Nasuno et al., 2016). We found that a stable Asn203Lys variant of Mpr1 increased the fermentation rate of yeast cells under laboratory scale sake brewing conditions (Ohashi

et al., 2019). To improve the ethanol productivity of sake, we successfully isolated several Pro-accumulating mutants derived from diploid sake yeast by conventional mutagenesis. Interestingly, one of them, A902-4, produced more than 10-fold greater amounts of l-ornithine (Orn) and Pro compared to the parent strain (K901). However, the molecular mechanisms involved in both higher Pro and Orn production in A902-4 have not yet been clarified. Recently, we identified and analyzed a novel gene mutation which increases intracellular Pro and Orn levels (Ohashi et al., 2020).

Ornithine is a non-proteinogenic amino acid and a precursor of both Arg and Pro. It has some physiological functions such as amelioration of negative states such as lassitude and improvement of sleep quality.

We identified a homo-allelic mutation in the ARG5,6 gene encoding the Thr340Ile variant N-acetylglutamate kinase (NAGK; Arg6) in strain A902-4 (Figure 4). The NAGK activity of the Thr340Ile variant was extremely insensitive to feedback inhibition by Arg, leading to intracellular Orn accumulation. This is the first report of the removal of feedback inhibition of NAGK activity in an industrial yeast. Based on the structure of the yeast NAGK, Arg interacts with these amino acid residues. Thr340 was conserved in NAGKs that are sensitive to feedback inhibition by Arg, suggesting that this residue is involved in Arg recognition. Also, local conformation around Thr340 forming the Arg-binding cavity is highly conserved among NAGKs that are sensitive to feedback inhibition by Arg. On the other hand, Arg-insensitive NAGKs exhibited different local folding. The difference of this local structure is one of the most important mechanisms for explaining the Arg sensitivity of NAGKs. Therefore, we concluded that the substitution of Thr340 for Ile disrupts the local structure via the intramolecular interaction, leading to removal of

the Arg-feedback inhibition.

This variant is not inhibited by Arg, but N-acetyl glutamate is regenerated with Orn production by transferring the acetyl group from N-acetyl Orn to glutamate in the cyclic pathway, resulting in Orn overproduction in the mutant. On the other hand, there are no mutations in the PRO1 gene associated with Pro accumulation in the mutant. However, yeast cells can synthesize Pro from Orn mediated by the Orn transaminase Car2 so this mutant could accumulate Pro from excess Orn via Car2 and Pro3. Finally, we brewed laboratory-scale sake and analyzed the fermentation profiles of the parent and mutant strains. After fermentation, this mutant produced a slightly higher amount of ethanol (20.4%) than the parent strain (19.5%), also sake and sake cake brewed with this mutant contained 4-5 time more Orn and Pro than those brewed with the parent strain. This “healthy image” sake containing a high level of Orn has been commercialized by local breweries in Nara. This approach could be a practical method for the development of superior yeast strains for Orn overproduction.

### Enhanced key flavor synthesis mediated by l-leucine metabolism and application to brewing “aromatic” awamori [collaboration with BioJet Co., Ltd.\*4]

Isoamyl acetate (IAA) is known as a banana-like flavor and ginjoko in Japanese sake. In yeast, IAA is converted from *a*-ketoisocaproate, which is an intermediate of l-leucine (Leu) pathway, in two steps catalyzed by *a*-keto acid decarboxylase and alcohol dehydrogenase. Regarding Leu synthesis, *a*-isopropylmalate synthase (IPMS; Leu4) is the key enzyme that controls the intracellular Leu level and its activity is subjected to feedback inhibition by Leu. In order to increase the contents of fruity flavor, such

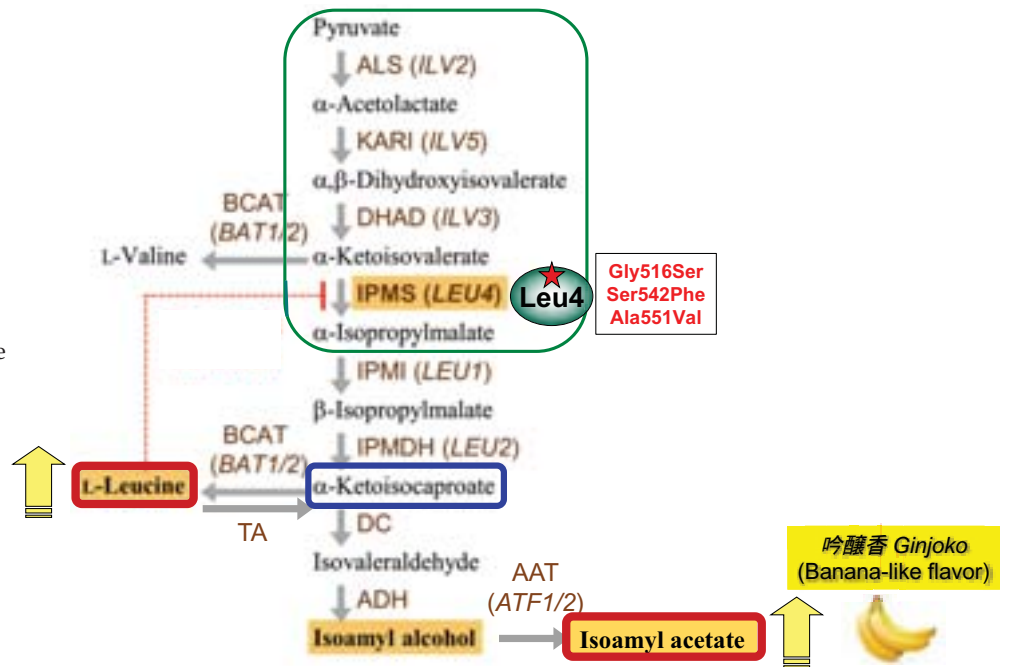
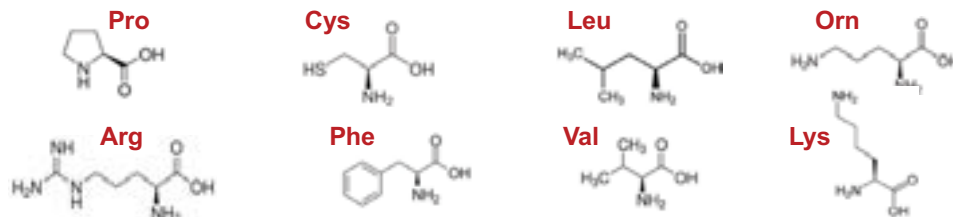


Figure 5: Synthetic pathway of l-leucine [Leu] and isoamyl acetate [IAA] in *S. cerevisiae* –Isopropylmalate synthase [IPMS; Leu4] is the key enzyme that controls Leu synthesis by feedback inhibition. We found a heteroallelic mutation in the LEU4 gene encoding the Ser542Phe, Ala551Val, or Gly516Ser variant IPMS in strains 18-T55 and H25. Enzyme activity of the variant was less sensitive to feedback inhibition by Leu, leading to Leu and IAA overproduction.

as IAA, in awamori, we tried to isolate awamori yeast mutants that accumulate Leu in the cell by conventional mutagenesis (Takagi et al., 2015). Thus, we isolated TFL-resistant mutants derived from the diploid awamori yeast strain (101-18). Among many TFL-resistant mutants, we successfully obtained a mutant 18-T55 with increased Leu content in the cell and found heteroallelic mutations in the LEU4 gene encoding the Ser542Phe and Ala551Val variant IPMS (Figure 5). The Leu content in cells expressing the IPMS variants was higher than cells expressing the wild-type IPMS. IPMS activity in wild-type cells was markedly inhibited by Leu, but IPMS activity in the mutant was insensitive to feedback inhibition, leading to Leu over synthesis. Homology modeling suggested that Leu binding was drastically inhibited in the IPMS variants due to steric hindrance at the activation site. Yeast strains were cultured and the flavor content from the volatile substances were measured by using gas chromatography coupled with mass spectrometry. In proportion to the intracellular Leu level, yeast cells expressing the IPMS variants produced higher

## Functional Amino Acids

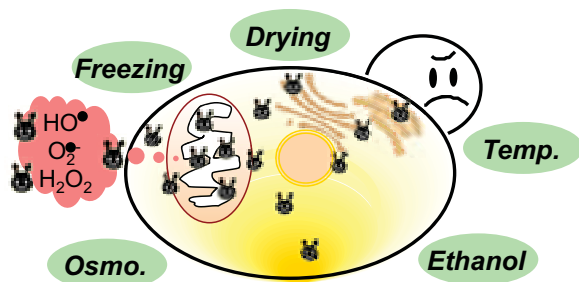


Improvement of  
fermentation ability

Diversity of  
taste and flavor

Addition of healthy image  
Improvement of nutritional value

### Stress tolerance



### Metabolism modification

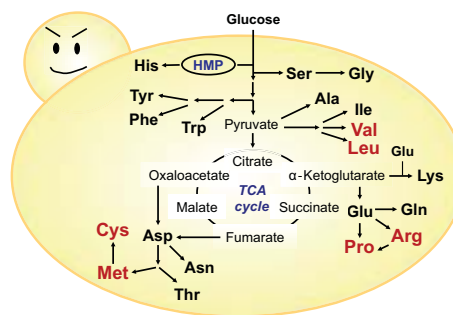


Figure 6: Concept of “functional amino acids engineering”

This is a new breeding technology for industrial yeast strains which contributes to improvement of fermentation ability, diversity of product taste and flavor, addition of a healthy image or improvement of nutritional value.

IAA than cells expressing the wild-type IPMS. These results demonstrated that the IPMS variants with desensitization to feedback inhibition cause intracellular accumulation of Leu and extracellular hyperproduction of IAA in awamori yeast. This study is the first to report the isolation of diploid awamori yeast mutant that overproduces IAA. The approach described here could be a practical method for the breeding of novel awamori yeasts to expand the diversity of awamori taste and flavor. Finally, awamori brewed with 18-T55 was successfully commercialized by the oldest brewery in Okinawa, Shinzato Shuzo, as the brand name HYPER YEAST 101.

BioJet Co., Ltd. recently isolated a novel *S. cerevisiae* from hibiscus flowers (HC02-5-2; HB yeast) in Okinawa that produces high levels of ethanol and 4-vinyl guaiacol (4-VG) which is a precursor of vanillin known as a key flavor of aged awamori. However, the IAA concentration observed in HB yeast was lower than that observed in

awamori yeast (101-18) (Abe et al., 2019). The whole genome information revealed that HB yeast is contiguous to wine yeast and different clades with classical awamori yeast in a phylogenetic tree, suggesting that HB yeast does not share ancestry with sake or shochu yeast strains. Although conventional awamori yeast which possesses the FDC1 pseudogene does not produce 4-VG, HB yeast which has the intact PAD1 and FDC1 genes encoding phenylacrylic acid decarboxylase and ferulic acid decarboxylase that are involved in the decarboxylation of aromatic carboxylic acids has an advantage for use in a novel kind of awamori. To increase the IAA content, we obtained a mutant T25 with Leu accumulation by conventional mutagenesis. In this mutant, a heteroallelic mutation was found in the LEU4 gene encoding the Gly516Ser variant IPMS that was less sensitive to feedback inhibition by Leu, leading to intracellular Leu accumulation (Figure 5). Homology modeling of IPMS also suggested that Leu binding was drastically inhibited in this variant due to steric hindrance in the activation

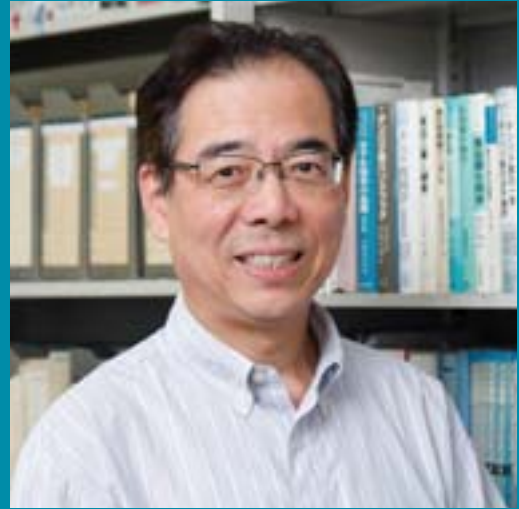
site. In a laboratory scale test, awamori brewed with strain T25 showed higher concentrations of IAA than that brewed with HB yeast. Finally, this aromatic awamori has been commercialized last year by Kamimura Shuzo, a local brewery in Okinawa under the brand name SHŌ KAMIMURA. This combinatorial approach to yeast isolation from nature and its breeding is applicable to the variation of the quality of alcoholic beverages in the fermentation industry.

## Conclusions

We propose a combinatorial approach for industrial yeast breeding – combining yeast isolation from nature with whole genome analysis and metabolism focused mutations that possess great potential to improve the quality or increase the added value of alcoholic beverages. *S. cerevisiae* is reliable and safe in food production and thus the development of novel strains that overproduce functional amino acids such as Pro, Orn, and Leu, would greatly contribute to food related industries. Moreover, breeding other industrial yeast strains to overproduce functional amino acids could lead to improvements in fermentation ability, diversity of product taste and flavor, addition of healthy images, or improvement of nutritional value. To emphasize these improvements, I named this new breeding technology “functional amino acids engineering” (Figure 6) (Takagi et al., 2019). ◆

## Acknowledgments

I am grateful to Daisuke Watanabe, Ryo Nasuno, Akira Nishimura, Yoichi Toyokawa, Shota Isogai, Keiko Ashida, Keisuke Hashida, and Yukiko Sugimoto (Nara Institute of Science and Technology, Nara, Japan), Masataka Ohashi (Nara Prefecture Institute of Industrial Development, Nara, Japan), Atsushi Kotaka, Naoyuki Murakami, Kengo Matsumura, Yoji Hata, and Hiroki Ishida (Gekkeikan Sake Co., Ltd., Kyoto, Japan), Masatoshi Tsukahara, Takayuki Abe, Maiko Nezu, Tomoya Iha, Haruna Azuma, and Keiko Tsukahara (BioJet Co., Ltd., Okinawa, Japan) for their contributions and collaborations. The preparation of this article was supported in part by a grant from the Project of the NARO Bio-oriented Technology Research Advancement Institution (30017B).



About the author: Professor Hiroshi Takagi is the Director of the Division for Industry-Government-Academia Collaboration of the Nara Institute of Science and Technology. He can be reached at his email address: hiro@bs.naist.jp

## Footnotes

- \*1 <https://www.nobelprize.org/prizes/medicine/2016/summary/>
- \*2 <https://www.gekkeikan.co.jp/english/>, <https://www.gekkeikan.co.jp/RD/sake/sake18/>
- \*3 [https://www.nara-sangyoshinko.or.jp/about/pdf/guiding\\_principles\\_e.pdf](https://www.nara-sangyoshinko.or.jp/about/pdf/guiding_principles_e.pdf)
- \*4 <http://www.biojet.jp/English%20index.html>

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## Figure legends

- Cover image:
  - Hibiscus flower and the yeast *Saccharomyces cerevisiae*  
We propose a combinatorial approach for industrial yeast breeding, such as yeast isolation from nature, whole genome analysis and metabolism focused mutation, which has great potential to improve the quality or to increase the added value of alcoholic beverages.
  - Sake fermentation tank and paddling work for managing sake mash 'moromi' (Courtesy of Gekkeikan Sake Co., Ltd.). Sake brewing is a fermentation technology that Japan is proud of.
- Figure 1: How to brew Japanese alcoholic beverages, sake and awamori, through collaborations with fungus and yeast
- Figure 2: How to isolate yeast mutants with Pro accumulation  
The toxic Pro analogue AZC causes misfolding of the proteins into which it is incorporated competitively with Pro, and thereby inhibits cell growth. However, Pro-accumulating cells are resistant to AZC.
- Figure 3: Synthetic pathway of L-proline (Pro) and L-arginine (Arg) in *S. cerevisiae*  $\gamma$ -Glutamyl kinase (GK; Pro1) is the key enzyme that controls Pro synthesis by feedback inhibition. We found a heteroallelic mutation in the PRO1 gene encoding the Gln79His variant GK in strain K-9-AZC. Enzyme activity of the variant was insensitive to feedback inhibition by Pro, leading to Pro overproduction.
- Figure 4: Synthetic pathway of L-proline (Pro) and L-ornithine (Orn) in *S. cerevisiae* N-Acetylglutamate kinase (NAGK; Arg6) is the key enzyme that controls Arg and Orn synthesis by feedback inhibition. We found a homoallelic mutation in the ARG6 gene encoding the Thr340Ile variant NAGK in strain A902-4. Enzyme activity of the variant was insensitive to feedback inhibition by Arg, leading to Orn and Pro overproduction.
- Figure 5: Synthetic pathway of L-leucine (Leu) and isoamyl acetate (IAA) in *S. cerevisiae*  $\alpha$ -Isopropylmalate synthase (IPMS; Leu4) is the key enzyme that controls Leu synthesis by feedback inhibition. We found a heteroallelic mutation in the LEU4 gene encoding the Ser542Phe, Ala551Val, or Gly516Ser variant IPMS in strains 18-T55 and H25. Enzyme activity of the variant was less sensitive to feedback inhibition by Leu, leading to Leu and IAA overproduction.
- Figure 6: Concept of "functional amino acids engineering"  
This is a new breeding technology for industrial yeast strains which contributes to improvement of fermentation ability, diversity of product taste and flavor, addition of a healthy image or improvement of nutritional value.



# *Symposium on Biomaterials, Fuels & Chemicals (SBFC)*

Virtual Symposium

April 26–28, 2021

[www.simbhq.org/sbfc](http://www.simbhq.org/sbfc)

## 2021 Symposium Chair

Scott Baker, PNNL

### Co-chairs:

Davinia Salvachua, NREL

Claus Felby, Novo Nordisk Foundation

## Keynote Speakers

- » Bernard Henrissat, U Marseilles
- » Linda Broadbelt, Northwestern U
- » Jens Nielsen, Chalmers U,
- » Claudia Schmidt-Dannert, U Minnesota
- » Blake Simmons, DOE Joint BioEnergy Institute/LBL.

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Non-members \$300

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### New plastics from renewable monomers

**Conveners:** Maria Auxiliadora Prieto – Biological Research Center-CSIC, Spain; Nick Wierckx – Institute of Bio- and Geosciences, Germany

### Biomaterials

**Conveners:** Yasuo Yoshikuni – DOE Joint Genome Institute; Seema Singh – Lawrence Berkeley National Lab

## Track 2: Biofuels, bioproducts, synthetic biology

### One-carbon metabolism

**Conveners:** Calvin Henard – University of North Texas; Marina Kalyuzhnaya – San Diego State University

### Performance-advantaged bioproducts and separations

**Conveners:** Brent Shanks – Iowa State University; Jean-Philippe Tessonier – Iowa State University

### Advanced biofuels

**Conveners:** Scott Baker – Pacific Northwest National Laboratory; Aindrila Mukhopadhyay – Lawrence Berkeley

National Laboratory

### Speeding up synthetic biology

**Conveners:** Jay Fitzgerald – Department of Energy – Bioenergy Technologies Office; Nathan Hillson – Lawrence Berkeley National Laboratory

### Lignin upgrading

**Conveners:** Davinia Salvachua – National Renewable Energy Laboratory; Kristiina Hilden – University of Helsinki, Finland

### Waste valorization

**Conveners:** Violeta Sanc – National Renewable Energy Laboratory; Steve Singer – Lawrence Berkeley National Laboratory

## Track 3: Feedstocks, deconstruction and biomass active enzymes

### Bioenergy crops and plant genetics

**Conveners:** Jenny Mortimer – Lawrence Berkeley National Laboratory; Wellington Muchero – Oak Ridge National Laboratory

### Enzyme discovery and engineering for biomass deconstruction and biofuels and chemical production

**Conveners:** Michelle O'Malley – University of California Santa Barbara; Kevin Solomon – Purdue University

### Feedstock variability and impacts on conversion

**Conveners:** Beau Hoffman – Department of Energy-Bioenergy Technologies Office; Sunkyu Park – North Carolina State University



Photo by Denys Kostyuchenko on Unsplash

# RAFT<sup>®</sup> 14

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- » Mark Berge, AstraZeneca
- » Kat Allikian, Mythic Mushrooms

## Call for Abstracts

- » March 2021

## Exhibitors

- » Prospectus Available May 2021

## Topics and Sessions

### Pre-RAFT<sup>®</sup> Workshops

- » Advanced Fermentation Concepts – in person and virtual  
Friday, November 5, 2021  
Organizer: Tim Cooper, Novozymes
- » Quality and Design of Experiment – in person only  
Saturday, November 6, 2021  
Organizers: Tiffany Rau, Rau Biotech and Philip Ramsey, University of New Hampshire



## Session Topics

### *OVERCOMING FERMENTATION FAILURE: LESSONS LEARNED*

Conveners: Tim Cooper, Novozymes; Chris Stowers, Corteva

### *ALTERNATIVE FERMENTATION SYSTEMS*

Conveners: Jason Brown, Thermofisher.com; Silas Villas-Boas, Luxembourg Inst. Of Science and Technology

### *FERMENTATION FOODS OF TODAY AND TOMORROW*

Conveners: Maria Marco, UC Davis;

### *NATURAL PRODUCT BIOSYNTHESIS*

Conveners: Nigel Mouncey, Joint Genome Inst.; Esha Khullar, Corteva

### *ALTERNATIVE SYSTEMS TO ANIMAL CELL CULTURE*

Conveners; Sushil Machhi, Astra Zeneca; David Dietz, Lonza

### *MODEL DRIVEN STRAIN & FERMENTATION PROCESS DEVELOPMENT*

Conveners: Philip Ramsey, University of New Hampshire; Steve Van Dien, Persephone Biome

### *FUTURE FACES OF FERMENTATION: ROUND TABLE*

Ayden Barenjian, University of Waikato; Ehsan Medina, Albany College of Pharmacy and Health Sciences

## Poster Session

Poster Session Chairs

Nancy Dowe, NREL and Karen Esmonde-White, Endress+Hauser

# 2021 SIMB WORKSHOPS

## Fermentation Basics

Sunday August 8, 2021

## Fermentation-Advanced Concepts

Friday, November 5, 2021

## Modern DOE and Quality by Design

Saturday, November 6, 2021



# Call for SIMB Award Nominations

Nominations for the following SIMB awards and honors will be presented at the 2021 SIMB Annual Meeting.

Access [www.simbhq.org/awards](http://www.simbhq.org/awards) for nomination forms and instructions or contact Mahendra Jain, SIMB Awards and Honors Chair ([mahendra3950@gmail.com](mailto:mahendra3950@gmail.com))

- » Charles Thom Award
- » Charles Porter Award
- » SIMB Fellowship
- » SIMB Young Investigator Award
- » Waksman Outstanding Teaching Award



## *2021 SIMB Election for Board of Directors*

The SIMB Election for positions on the Board of Directors will commence March 1, 2021. The election will end at noon EDT on March 31, 2021, and members must join/renew by March 30, 2021, noon EDT, to be eligible to vote.

Current members for 2021 will receive login instructions for accessing the voting module.

The first step in the election process is the identification of the Nominations Committee (NC) consisting of the chair and least two members. The committee members are approved by the Board and serve only for the current year and cannot be reappointed within a three-year period. The NC proposes a slate of candidates (usually at least two candidates for each position) with input from the membership. The candidates must be current SIMB members with a demonstrated interest and involvement in SIMB. Upon acceptance of the nomination, the NC informs the candidates of the duties and responsibilities required by each position. In addition to the NC, candidates can be identified via Article 5, Section 4 in the SIMB Constitution using a petition process.

The final slate of candidates is due to the president by the first board meeting during the annual meeting. Candidates must submit a biography and photograph by October 1, for publication in the October-November-December issue of *SIMB News* and for posting on the website. After voting ends, the Election Committee, consisting of a minimum of two SIMB members, receives access to the voting module and certifies counts from online voting, as well as any paper ballots previously requested and postmarked no later than the deadline date for electronic voting ballots, and delivers the results to the SIMB President and SIMB Secretary for announcement.

The election process and ballots are available for inspection for at least 30 days following the annual meeting. Ballots and records are destroyed six months after the election (unless otherwise directed by the Board) and final tabulation of the votes is preserved.



by Elisabeth Elder

### **The State of Science: What the Future Holds and the Scientists Making It Happen**

Marc Zimmer

ISBN: 9781633886391 [cloth]; ISBN: 9781633886407 [epub]

2020

Prometheus Books

Lanham, Maryland, USA

In light of full disclosure, this review was a challenge to write. Melanie Mormile recommended to book to me and I am very glad she did. Once I started reading, the book was hard to put down. Once I started writing the review, deciding on the information to include and the information to leave for you to read on your own was difficult. The review became longer and longer. The length was dictated by it being long enough to encourage you to read the book and short enough to not take over the newsletter issue.

*The State of Science: What The Future Holds And The Scientists Making it Happen* was written by Marc Zimmer. He has also written *Glowing Genes* (2005); *Illuminating Diseases* (2015); *Solutions for a Cleaner, Greener Planet* (2020); and three books for young adults. He is the Jean C. Tempel '65 Professor of Chemistry at Connecticut College.

*The State of Science* is divided into six parts. Part One is Science including Chapter One that covers The Big Picture. In this chapter Zimmer uses the Merriam-Webster Dictionary definition of science which is "the state of knowing" and the anecdotal story of the role of William Whewell in the development of the term scientist to initially describe Mary Somerville. Zimmer then points out the importance of science in our lives and in

our impacts on Earth and the ongoing development of the concept of the Anthropocene era. He explores the importance of science in economics and equity along with the ethical and safety challenges of scientific growth. Zimmer covers current challenges to science including increasing impacts of deregulation, the lack of understanding of science by elected officials as well as the general population; and fake news/pseudoscience. Chapter Two covers The Professional Scientist in which Zimmer points out the inequities that exist for women and people of color in science. The information provided will be of particular interest to members involved in, and following the work of, the SIMB Diversity Committee and to those searching for information to support writing grants. This chapter also points out problems in balancing scientific careers and family life; implicit biases in recommendation letters as well as reviews of publications and presentations; discrimination based on race and gender; and rewarding of masculine (white American) confidence. Based on the figures there is a need to increase the proportions of people of color and women in science.

NOTE: As this review was being written, four female Nobel laureates were announced in 2020. The three in STEM fields were Jennifer Doudna and Emmanuelle Charpentier in Chemistry and Andrea Ghez in Physics along with Louise Glück

in Literature. Chapter Three covers Do-It-Yourself Science undertaken by amateur scientists who do scientific research for the love of science. Historic examples of amateur scientists covered included Michael Faraday, Charles Darwin, Henrietta Swan Leavitt, and Robert Evans. While the activities of amateur scientists can be limited by funding, the need for high tech equipment, the need for graduate students and postdocs, and the need for graduate degrees, the internet, computer and telephone technologies, and mail-order kits have resulted in more citizen scientists. With his background in computational chemistry, Zimmer started with examples of amateur scientists assisting professional scientists through the use of folding@home, Poem@home, Rosetta@home, SETI@home, Global Biodiversity Information Facility (GBIF), and iNaturalist with which you may be familiar and are worth investigating. Zimmer moved to scientific art with his focus of Eduardo Kac, a professor in the Art and Technology Department at the School of the Art Institute of Chicago, whose projects are pioneering examples of transgenic art. The remainder of this chapter covers community lab spaces and biohacking.

Part Two is Doing Science in which Chapter Four covers “The Nuts and Bolts.” This chapter explains whether published data can be trusted, how peer-review works, and funding.

Part Three is Old Science in which Chapter Five covers “Recognizing a Breakthrough in Science.” In this chapter, Zimmer discusses the DNA double helix, chlorination to disinfect water, and green fluorescent proteins in terms of how these breakthroughs provide context for the current state of science.

Part Four is New Science in which Chapter Six covers “LIGO and Virgo,” immense projects for detecting gravitational waves. LIGO is Laser Interferometer Gravitational-Wave Observatory, the largest project ever funded by NSF, and Virgo is the Italian counterpart. Chapter Seven covers “Deep Learning” which uses algorithms to pull information from massive data sets to solve questions, develop games, drive autonomous cars, recognize voices and faces, and make medical diagnoses and determine treatments. A potential problem with deep learning is that a mistake could impact multiple people. Chapter Eight covers “Optogenetics” in which neurons are modified to produce fluorescent proteins. Exposure of the neurons to pinpoint lasers allows pinpoint accuracy and repeat firings of the neurons. Potential applications of optogenetics in humans include curing retinitis pigmentosa, Alzheimer’s disease, and Parkinson’s disease in humans. Chapter Nine, “CRISPR,” covers the history plus the applications in plants, animals, and medicine of the gene editing tool CRISPR (Clustered Regularly Interspaced

Palindromic Repeats). It also covers combining CRISPR with gene drives to force a genetic trait through a population plus the ethical considerations of the processes.

In Part Five Zimmer covers Bad Science by which he means doing sloppy science, misrepresenting science, or misusing science. Chapter Ten, “This Is Not Science; It Is Fake Science,” covers the origins of fake news and post-science. This chapter focuses on the impacts of fake news, predatory publishers, and the efforts of some companies to undermine science. Chapter Eleven is “This Is Science, Not Politics” which focuses on people who, as results of their political and cultural identities, do not believe the science associated with climate change, vaccinations, and genetically modified foods. Chapter Twelve is “Quackery” covering the sales of fake medicines and treatments that include stem cell injections and health supplements. Zimmer warns readers to be aware of treatments/cures/wellness claims such as cinchona bark mixtures for malaria; jellyfish proteins for memory problems; applications of stem cells for which efficacy or safety studies have not been done; parabiosis (using blood from younger organisms/people to fight ageing in older organisms/people); and ingesting activated charcoal to cure hangovers, detoxification, preventing ageing, and reducing bloating.

In Part Six, “Some Thoughts on Keeping Science Healthy in a Sustainable Future,” Zimmer points out that while we need to admire the advances brought about by science we also need to curb potential abuses/excesses. He acknowledges that science is growing very quickly which is leading to a greater knowledge gap between experts and nonexperts and that we need to rely on each other. Zimmer uses a quote attributed to Dr. Jonas Salk, “Are we being good ancestors?” to acknowledge that we are in charge of our own evolution and the health of the planet. That is a lot of responsibility.

This book will appeal to a broad audience. As the title indicates, the book is about science. While an interest in science will draw readers, the concepts covered such that in-depth knowledge of any area is not essential. In fact, encouraging middle school/high school students to read the book might enhance their interest in science. Encouraging adults with limited interest in science might make them realize the importance of science in the future. As Zimmer says in the conclusion of the last chapter, “THE FUTURE OF SCIENCE IS BRIGHT.”

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**AUG. 8–11, 2021**

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Hotel Palomar • San Diego, CA

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For assistance with job postings at all SIMB meetings, the Career Workshop held during the SIMB Annual Meeting, navigating the Career Center site, or Resume Review during the year, contact SIMB Placement Chair Bob Berber, [bbberg@att.net](mailto:bbberg@att.net)

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Awards/Honors	Mahendra Jain	<a href="mailto:mahendra3950@gmail.com">mahendra3950@gmail.com</a>	2021	Kathy Asleson Dundon, Tom Jeffries, Dale Monceaux, Raj Boopathy, Susn Bagley	Chris Lowe
Audit Committee	Jeff Schwartz	<a href="mailto:JLSmicro@aol.com">JLSmicro@aol.com</a>	2021	Debbie Yaver	Chris Lowe
	Herb Ward	<a href="mailto:wardch@rice.edu">wardch@rice.edu</a>	2020		
Corporate Outreach/ Exhibits	Steve Van Dien	<a href="mailto:svandien@persephonebiome.com">svandien@persephonebiome.com</a>	2023	Bob Berger, Lisa Lee	Jennifer Johnson, Tina Hockaday
Corporate Sponsorship	Andreas Schirmer	<a href="mailto:aschirmer@genomatica.com">aschirmer@genomatica.com</a>	2020	Jonathan Sheridan	Jennifer Johnson
	Yoram Barak	<a href="mailto:yoram.barak@basf.com">yoram.barak@basf.com</a>	2020		
Diversity	Sara Shields-Menard	<a href="mailto:sara.shieldsmenard@gmail.com">sara.shieldsmenard@gmail.com</a>	2021	Noel Fong, Laura Jarboe, Felipe Sarmiento, Vanessa Nepomuceno	
	Sheena Becker	<a href="mailto:sheena.becker@corteva.com">sheena.becker@corteva.com</a>	2023		
Education and Outreach	Katy Kao	<a href="mailto:kao.katy@gmail.com">kao.katy@gmail.com</a>	2022	Mark Berge, Steve Van Dien, Noel Fong, Laura Jarboe, Katy Watts	Chris Lowe
Elections	Kristien Mortelmans	<a href="mailto:kristien.mortelmans@sri.com">kristien.mortelmans@sri.com</a>	2022	Badal Saha	Jennifer Johnson
Ethics Committee	Susan Bagley	<a href="mailto:sthabagley@mtu.edu">sthabagley@mtu.edu</a>	2022	Scott Baker, Neal Connors	
Investment Advisory	Dick Baltz	<a href="mailto:rbaltz923@gmail.com">rbaltz923@gmail.com</a>	2022	George Garrity	
Meeting Sites	Chris Lowe	<a href="mailto:chris.lowe@simbhq.org">chris.lowe@simbhq.org</a>	-	BOD and meeting chairs	
Membership-individual	Michael Resch	<a href="mailto:michael.resch@nrel.gov">michael.resch@nrel.gov</a>	2022	Laura Jarboe, Thomas Klasson, Steve Van Dien	Jennifer Johnson
Nominations	Steve Van Dien	<a href="mailto:svandien@persephonebiome.com">svandien@persephonebiome.com</a>	2021	Mark Blenner, Taraka Dale	Chris Lowe
Placement	Bob Berger	<a href="mailto:bbberg@att.net">bbberg@att.net</a>	2021	Sara Dorman	Jennifer Johnson
Planning	Noel Fong	<a href="mailto:nfong@nucelis.com">nfong@nucelis.com</a>	2021	-	
Publications	Nigel Mouncey	<a href="mailto:njmouncey@gmail.com">njmouncey@gmail.com</a>	2020	George Garrity, Herb Ward	Chris Lowe
	<i>JIMB</i>	Ramon Gonzalez	<a href="mailto:ramon.gonzalez@usf.edu">ramon.gonzalez@usf.edu</a>	2025	<i>JIMB</i> Editors
<i>SIMB News</i>	Melanie Mormile	<a href="mailto:mmormile@mst.edu">mmormile@mst.edu</a>	2023	Kristine Mortelmans, Vanessa Nepomuceno, Elisabeth Elder	Katherine Devins
<b>Presidential Ad Hoc Committees</b>					
International Outreach	Susanne Kleff	<a href="mailto:kleff@msu.edu">kleff@msu.edu</a>	2020	Scott Baker, Tim Davies, George Garrity, Peter Punt, Thomas Klasson, Erick Vandamme, Michael Resch	

Special Conferences			Term
<b>SBFC 2021 Chair</b>	Scott Baker	<a href="mailto:scott.baker@pnl.gov">scott.baker@pnl.gov</a>	2021
Co-chair	Davinia Salvachua	<a href="mailto:davinia.salvachua@nrel.gov">davinia.salvachua@nrel.gov</a>	2021
Past chair	Claus Felby	<a href="mailto:cfe@novo.dk">cfe@novo.dk</a>	2021
<b>RAFT® 2021 Chair</b>	Mark Berge	<a href="mailto:mark.berge@astrazeneca.com">mark.berge@astrazeneca.com</a>	2021
Co-chair	Kat Allikian	<a href="mailto:kat@mythicmushrooms.co.nz">kat@mythicmushrooms.co.nz</a>	2021
<b>IMMM 2022 Chair</b>	Debbie Yaver	<a href="mailto:dsy@novozymes.com">dsy@novozymes.com</a>	2022
Co-chair	Yoram Barak	<a href="mailto:yorambarak@basf.com">yorambarak@basf.com</a>	2022
Co-chair	George Garrity	<a href="mailto:garrity@msu.edu">garrity@msu.edu</a>	2022
<b>Natural Products 2023 Chair</b>	Ben Shen	<a href="mailto:shen@scripps.edu">shen@scripps.edu</a>	2023



# Become a SIMB Corporate Member

## **Member Benefits:**

- Meeting Registration Discounts (Each \$500 voucher is good toward any SIMB meeting registration fee)

Silver - 1 \$500 voucher

Gold – 2 vouchers

Diamond - 3 vouchers

## **Other Current Benefits:**

- Recognition and corporate profile in *SIMB News*
- Discounted exhibit booths
- Discounted advertisements and job postings

**Choose Your Corporate Level:**

<input type="checkbox"/> Institutional Level \$700	<input type="checkbox"/> Bronze Level \$500	<input type="checkbox"/> Silver Level \$1000	<input type="checkbox"/> Gold Level \$1,500	<input type="checkbox"/> Diamond Level \$2,500
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Name of Company: \_\_\_\_\_

Company Website: \_\_\_\_\_

Company Description (50 words or less): \_\_\_\_\_

Social Media Handle(s): \_\_\_\_\_

\*\* Gold and Diamond Levels - Send company logo to [membership@simbhq.org](mailto:membership@simbhq.org)

How Did You Hear About SIMB?		
<input type="checkbox"/> Colleague/Networking	<input type="checkbox"/> SIMB Local Section	
<input type="checkbox"/> SIMB Meeting Announcement	<input type="checkbox"/> SIMB Member	
<input type="checkbox"/> Direct Mail	<input type="checkbox"/> <i>JIMB</i>	
<input type="checkbox"/> <i>SIMB News</i>	<input type="checkbox"/> SIMB Website	
<input type="checkbox"/> Social Networking	<input type="checkbox"/> SIMB Meeting Attendance	
Choose Your Industry Segment:		
<input type="checkbox"/> Fermentation (non-food or beverage)	<input type="checkbox"/> Microbiome Research/ Metagenomic	<input type="checkbox"/> Systems Biology, Omics, Computational Biology, and Bioinformatics
<input type="checkbox"/> Cell Culture	<input type="checkbox"/> Microbial Control/Biocides and Disinfectants/Clinical & Medical Microbiology	<input type="checkbox"/> Process Development & Biochemical Engineering
<input type="checkbox"/> Metabolic Engineering/Strain Engineering	<input type="checkbox"/> Environmental Microbiology/ Bioremediation	<input type="checkbox"/> Agriculture/Plant Biology
<input type="checkbox"/> Molecular Biology/Synthetic Biology Tools Development	<input type="checkbox"/> Food Microbiology and Safety	<input type="checkbox"/> Marine, Aquatic Biology & Algae
<input type="checkbox"/> Biocatalysis/Enzymology/Biochemistry/Enzyme Engineering	<input type="checkbox"/> Brewing, Winemaking, and Fermented Foods	<input type="checkbox"/> Mycology/Fungal Biotechnology
<input type="checkbox"/> Biomass Pretreatment, Deconstruction, and Conversion		<input type="checkbox"/> Analytical Chemistry, QA/QC
<input type="checkbox"/> Antibiotics/Secondary Metabolites/Natural Products/Pharmaceuticals		<input type="checkbox"/> Regulatory Affairs, IP, and Sustainability

**Payment**

Federal Tax ID# 35-6026526

**Total Amount Enclosed \$** \_\_\_\_\_

Invoice my company  Check enclosed (payable to SIMB). Check must be drawn from a US bank.

Charge to:  Visa  MC  AMEX

Wire Transfer (Additional Fees Apply)

Card #: \_\_\_\_\_

Exp. Date: \_\_\_\_\_

Signature: \_\_\_\_\_

Name on Card: \_\_\_\_\_

**Authoring Officer who is to receive all billing information:**

Name: \_\_\_\_\_

Title: \_\_\_\_\_

Address: \_\_\_\_\_

City/State/Zip: \_\_\_\_\_

Country: \_\_\_\_\_

P: \_\_\_\_\_ F: \_\_\_\_\_

Email: \_\_\_\_\_

(see page 2 for company representative form)

**Send Payment To:**

Society for Industrial Microbiology & Biotechnology • 3929 Old Lee Highway Suite 92A • Fairfax VA 22030-2421  
 P: 703.691.3357 x23 • F: 703.691.7991 • E: [membership@simbhq.org](mailto:membership@simbhq.org) • [www.simbhq.org](http://www.simbhq.org)

**Company Representative who will receive membership including publications:**

<input type="checkbox"/> Please do not send me SIMB information via email <input type="checkbox"/> Please do not include me on any SIMB mailing lists <input type="checkbox"/> Please do not include my information in the SIMB online membership directory	<b>Please Select a Delivery Method for SIMB News</b> <input type="checkbox"/> SIMB News MAIL Print Copy <input type="checkbox"/> SIMB News Online Access ONLY
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Name: \_\_\_\_\_

Title: \_\_\_\_\_

Address: \_\_\_\_\_

City/State/Zip: \_\_\_\_\_

Country: \_\_\_\_\_

P: \_\_\_\_\_ F: \_\_\_\_\_

Email: \_\_\_\_\_

**Additional Company Representative (Gold and Diamond Level only)**

<input type="checkbox"/> Please do not send me SIMB information via email <input type="checkbox"/> Please do not include me on any SIMB mailing lists <input type="checkbox"/> Please do not include my information in the SIMB online membership directory	<b>Please Select a Delivery Method for SIMB News</b> <input type="checkbox"/> SIMB News MAIL Print Copy <input type="checkbox"/> SIMB News Online Access ONLY
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Name: \_\_\_\_\_

Title: \_\_\_\_\_

Address: \_\_\_\_\_

City/State/Zip: \_\_\_\_\_

Country: \_\_\_\_\_

P: \_\_\_\_\_ F: \_\_\_\_\_

Email: \_\_\_\_\_

**Additional Company Representative (Gold and Diamond Level only)**

<input type="checkbox"/> Please do not send me SIMB information via email <input type="checkbox"/> Please do not include me on any SIMB mailing lists <input type="checkbox"/> Please do not include my information in the SIMB online membership directory	<b>Please Select a Delivery Method for SIMB News</b> <input type="checkbox"/> SIMB News MAIL Print Copy <input type="checkbox"/> SIMB News Online Access ONLY
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Name: \_\_\_\_\_

Title: \_\_\_\_\_

Address: \_\_\_\_\_

City/State/Zip: \_\_\_\_\_

Country: \_\_\_\_\_

P: \_\_\_\_\_ F: \_\_\_\_\_

Email: \_\_\_\_\_

**Additional Company Representative (Diamond Level only)**

<input type="checkbox"/> Please do not send me SIMB information via email <input type="checkbox"/> Please do not include me on any SIMB mailing lists <input type="checkbox"/> Please do not include my information in the SIMB online membership directory	<b>Please Select a Delivery Method for SIMB News</b> <input type="checkbox"/> SIMB News MAIL Print Copy <input type="checkbox"/> SIMB News Online Access ONLY
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Name: \_\_\_\_\_

Title: \_\_\_\_\_

Address: \_\_\_\_\_

City/State/Zip: \_\_\_\_\_

Country: \_\_\_\_\_

P: \_\_\_\_\_ F: \_\_\_\_\_

Email: \_\_\_\_\_

Your company and its corporate representative(s) have reviewed and agree with the SIMB Code of Conduct  (form will not be processed if box is not checked)