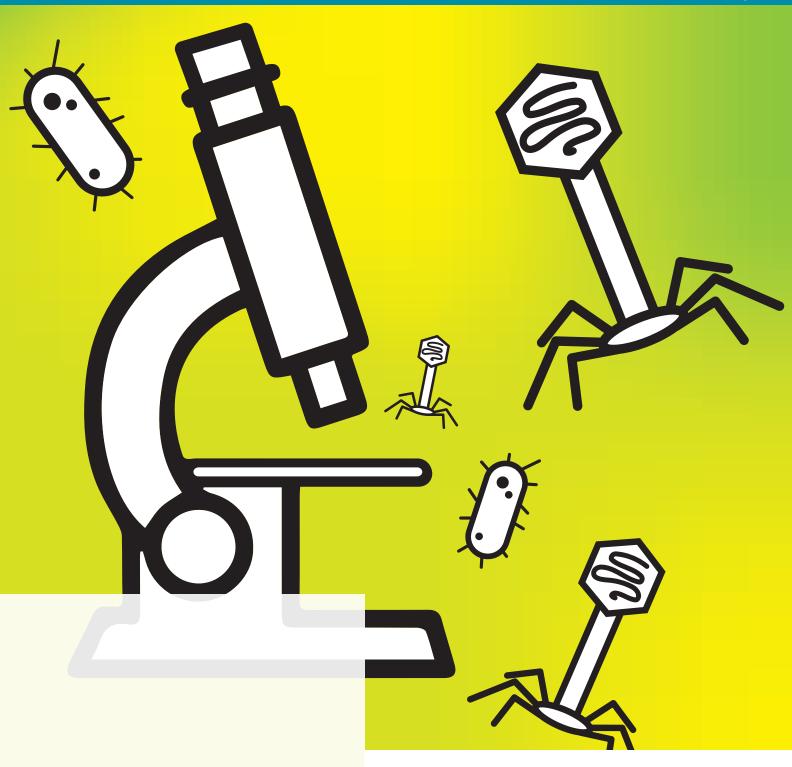
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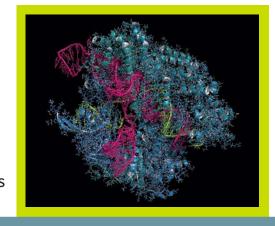




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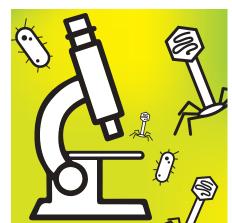
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- 5. Enhance the value of membership in the Society for both individual and corporate members.
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Newsworthy

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Public Comments Sought: Draft 5th National Climate Assessment

On November 7, 2022 the Administration released a draft of the Fifth National Climate Assessment for public comment. The National Climate Assessment is a congressionally mandated report that is prepared every four years by scientists from 13 federal agencies. The report, led by the U.S. Global Change Research Program (USGCRP), assesses the science of climate change, its impacts, and approaches for reducing present and future risk.

The fourth installment, which was published in 2018, concluded that "Earth's climate is now changing faster than at any point in the history of modern civilization, primarily as a result of human activities."

The latest iteration finds that the global average temperatures over the past decade were about 1.1 degrees Celsius warmer than the preindustrial era. Notably, over the past half-century, the United States has warmed "68 percent faster than the planet as a whole." Since 1970, the continental United States has experienced 2.5 degrees Fahrenheit of warming, which is about two-thirds faster than the average for the planet.

Rising land and water temperatures are also shrinking wildlife habitats, the draft report finds. This could have dire consequences for biodiversity. "Without emissions reductions, drastic changes to ecosystems are expected to pass a tipping point by mid- to late century, where rapid shifts in environmental conditions lead to irreversible ecological transformations," the authors argue.

Despite the grim outlook, the draft report suggests that immediate action could still mitigate the worst impacts of climate change. In addition to significant reductions in emissions, it calls for systemic, long-term, and transformational changes "to create a healthier, more just, and more resilient nation."

The fifth assessment will likely be finalized in 2023 after a period of public comment and peer review.

To review the draft assessment and submit comments, reviewers will need to register with the USGCRP Review and Comment System. Comments will be accepted until January 27, 2023.



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Zhang S, Guo F, Yan W, Dai Z, Dong W, Zhou J, Zhang W, Xin F and Jiang M (2020) Recent Advances of CRISPR/Cas9-Based Genetic Engineering and Transcriptional Regulation in Industrial Biology. *Front. Bioeng. Biotechnol.* 7:459. doi: 10.3389/fbioe.2019.00459

Recent Advances of CRISPR/Cas9-Based Genetic Engineering and Transcriptional Regulation in Industrial Biology

Industrial biology plays a crucial role in the fields of medicine, health, food, energy, and so on. However, the lack of efficient genetic engineering tools has restricted the rapid development of industrial biology. Recently, the emergence of clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9 (CRISPR/Cas9) system brought a breakthrough in genome editing technologies due to its high orthogonality, versatility, and efficiency. In this review, we summarized the barriers of CRISPR/Cas9 and corresponding solutions for efficient genetic engineering in industrial microorganisms. In addition, the advances of industrial biology employing the CRISPR/Cas9 system were compared in terms of its application in bacteria, yeast, and filamentous fungi. Furthermore, the cooperation between CRISPR/Cas9 and synthetic biology was discussed to help build complex and programmable gene circuits, which can be used in industrial biotechnology.



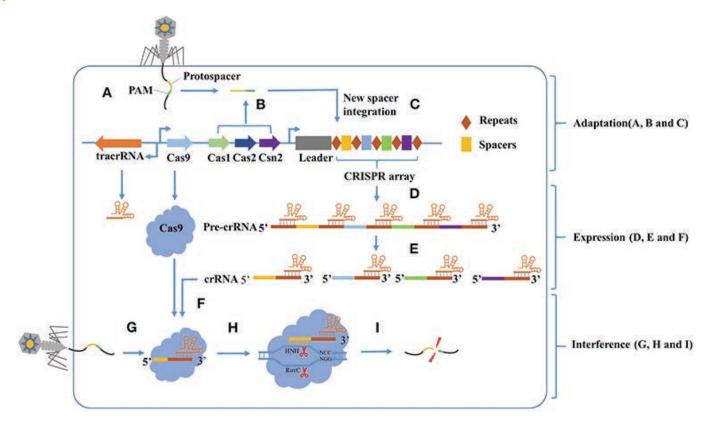


Figure 1: The CRISPR-Cas9 mediated adaptive immunity is divided into three phases: Adaptation, expression, and interference

INTRODUCTION

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Industrial biotechnology has advanced significantly in recent years due to the improvement of genomic engineering tools. Genetic engineering is a complex technology that manipulates genes at molecular level. The recombined exogenous genes can be replicated, transcribed, translated, and expressed in receptor cells to produce various valuable chemicals. During the long-time evolution of microorganisms, a unique adaptive immune system, named as clustered regularly interspaced short palindromic repeat sequences and CRISPR-associated protein 9 (CRISPR/Cas9), was employed by bacteria and archaea to defend against foreign-invading DNA (Figure 1; Horvath and Barrangou, 2010). This system is consisted of a Cas9 nuclease, a target-recognizing CRISPR RNA (crRNA), and auxiliary non-coding transactivating crRNAs (tracrRNAs) (Jiang and Doudna, 2017). The precursor crRNA (pre-crRNA) is able to combine with several tracrRNAs, and can be recognized and processed by RNase III into mature crRNA::tracrRNAs (dual RNA hybrid). A single-guide RNA (sgRNA) can be constructed by fusing a crRNA containing the targeting

guide sequence to a tracrRNA and then combines to Cas9 protein, generate DNA double-strand breaks (DSBs), and then alter the target gene by cellular DNA repair mechanisms (Cong et al., 2013). The DSBs can be repaired through two different ways: non-homologous end-joining (NHEJ) and homologous repair (HR) (Capecchi, 1989). NHEJ can introduce insertion and deletion at the target site. HR uses a foreign DNA donor template to recombine with the target site for introducing a specific point mutation or insertion of the desired sequence.

Previous methods of manufacturing targeted DSBs relied on protein–DNA recognition systems, such as zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs). However, these systems were limited due to their complex and expensive operation. On the contrary, the CRISPR/Cas9 system has been widely employed in various fields owing to its high efficiency, low cost, and convenience (Gaj et al., 2013; Hsu et al., 2014). Hence, in this review, the potential of CRISPR/Cas9 in industrial biotechnology was demonstrated by introducing its applications in bacteria, yeasts, and filamentous fungi. The future prospect of cooperation

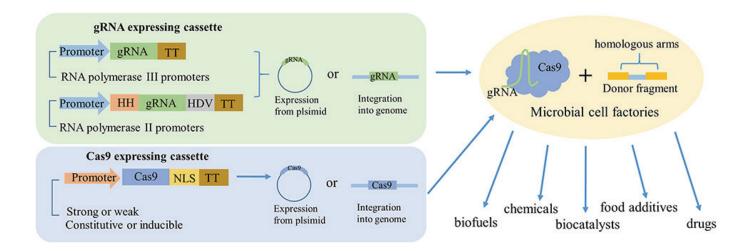


Figure 2. Schematic to illustrate how gRNA and Cas9 expressed in industrial microorganisms

between CRISPR/Cas9 and synthetic biology to build complex and programmable gene circuits was also summarized.

VERSATILE DESIGNS OF CRISPR/CAS9 FOR HIGHLY EFFICIENT GENE EDITING

Although the CRISPR/Cas9 system has been successfully used in bacteria, yeasts, and fungi, its gene editing efficiency is still unsatisfactory. How to improve the gene editing efficiency has been the focus in this filed. Several strategies employed to improve genome editing efficiency with CRISPR/Cas9 were accordingly summarized.

Improvement of Homologous Recombination Efficiency

The mechanism of gene editing is repairing the DSBs generated by CRISPR/Cas9 through NHEJ or HR. Once DSBs occurs, most industrial microorganisms prefer the NHEJ pathway over HR even with exogenous donors, which retards the precise genome editing. In order to increase the frequency of HR, two main strategies were employed: (1) coupling the CRISPR/Cas9 system to lambda Red oligonucleotide recombineering and (2) deleting KU70 or KU80 heterodimer involved in NHEJ repair. For instance, Jiang et al. established a two-plasmid-based CRISPR/Cas9 system in *Escherichia coli*, in which Streptococcus pyogenes Cas9 and crRNA array were expressed in the low-copy plasmid (pCas) and high-copy plasmid (pCRISPR) series (Jiang et al., 2013; Mali et

al., 2013). Although this novel genetic engineering tool had a better performance than did the traditional one, it still needed further modifications to obtain higher efficiency. Based on this system, a triple-plasmid strategy was designed with the third plasmid carrying the λ -Red genes expressed from ParaB. In contrast, this threeplasmid system increased the percentage of mutant cells from 19 to 65%. In another study, a CRISPR/Cas9 system, which had 94% efficiency toward single-gene non-sense mutations, was accordingly established in Komagataella pastoris. However, the integration efficiency was really low (2%), when a donor template with 1-kbp homologous arms was provided (Weninger et al., 2016). To improve the integration efficiency with markerless donor cassettes, the KU70 gene was accordingly knocked out and improved the knock-in efficiency up to nearly 100% (Weninger et al., 2018).

Adoption of Optimal Promoter for Expression of Cas9 and gRNA

In most studies, Cas9 protein and gRNA were separated into independent vectors. The Cas9 protein was commonly expressed in a low-copy plasmid with constitutive promoters because high-level expression of Cas9 will lead to negative influence on microbial growth. In contrast, the expression of gRNA should choose high-copy plasmids with a strong promoter. The RNA polymerase III (pol III) promoters had been successfully employed in many cases; however, it was difficult to find suitable RNA pol III promoters. Thus, the



sgRNA was flanked with two ribozyme sequences, 5' end hammerhead (HH) and 3' end hepatitis delta virus (HDV) to express under a strong RNA polymerase II promoter (Figure 2; Nødvig et al., 2015). In addition, synthesized hybrid promoters provide another feasible substitute for gRNA expression (Cai et al., 2019). For instance, the gene editing efficiency by harnessing the common RNA pol III promoter SNR52 to express sgRNA in oleaginous yeast Yarrowia lipolytica only reached 26%. In order to optimize the expression of sgRNA, Schwartz et al. constructed an RNA polymerase II (Pol II) TEF promoter for sgRNA with HH and HDV ribozymes in 5' end and 3' end, and fused the Pol III promoters RPR1, SCR1, and SNR52 with a glycine tRNA (tRNA^{Gly}) (Schwartz et al., 2015). Finally, the highest disruption efficiency of 92% reached with synthetic SCR1'tRNA^{Gly} promoter. In addition, the disruption efficiency using the SNR52'-tRNA^{Gly} promoter was improved by 28% than the initial SNR52 promoter.

Other Methods

Optimization of Cas9 Protein Codons

The importance of codon optimization of Cas9 is different in different strains. For example, the natural *S. pyogenes* Cas9 has shown high targeting efficiency in *Saccharomyces cerevisiae* (Bao et al., 2015). However, the targeting efficiency was unsatisfactory when using native *S. pyogenes* Cas9 in K. pastoris. By employing the human codon optimized Cas9 (*Hs*Cas9), the targeting efficiency improved from 32 to 73%, indicating that optimization of Cas9 protein codons plays a crucial role in improving the targeting efficiency. Hence, when the performance of the CRISPR/Cas9 system was unsatisfactory, optimization of Cas9 codons may be a good solution.

Adoption of suitable sgRNA binding sites

For industrial microorganisms, the sgRNA binding site is crucial in terms of the targeting efficiency. In order to improve the efficiency, different sgRNAs targeting sites should be tested. For instance, Peng et al. found that the targeting efficiency was distributed between 13 and 100% when using six different sgRNAs targeting six different sites of *mepA* gene, and the sgRNAs with the GC content under 60% had better performance. This result showed

that different sgRNAs had great influence on editing efficiency and adoption of suitable sgRNA is important for a high success rate. A series of website tools had been set for sgRNA design and summarized in previous literature (Chuai et al., 2017).

Prolongation of Incubation

The targeted chromosomal region could escape sgRNA/Cas9 endonuclease activity in some cases. The effective solution is to prolong the incubation under the appropriate selection pressure to generate iterative DSBs until mutagenic repair occurs. To confirm the effect of prolonged incubation on the mutation efficiency, So et al. introduced two plasmids that contained same sgRNA sequence and different length of homologous arms (30 and 500 bp) to the targeted gene into *Bacillus subtilis*, respectively (So et al., 2017). The mutation efficiencies were improved from 85% to almost 100% after incubation for 9 h. Results demonstrated that the mutation efficiency can be maximized by prolonging incubation.

CRISPR/CAS9-MEDIATED GENETIC ENGINEERING IN INDUSTRIAL BIOLOGY

Industrial microorganisms can produce various value-added chemicals from low-cost feedstock including renewable biomass and organic wastes (Yao et al., 2018). To enhance the performances of industrial microorganisms, genetic modifications were usually implemented to construct desired microbial cell factories. Although various methods are available for genetic modifications, it is time-consuming and labor-intensive. Fortunately, as a surprising "gift," the CRISPR/Cas9 system greatly improved the efficiency of genetic engineering. Here, we reviewed the applications of the CRISPR/Cas9 system in bacteria, yeasts, and filamentous fungi with special emphasis on *E. coli* and *S. cerevisiae*, which were the most commonly used cell factory.

The Application of CRISPR/Cas9 in Bacteria

Escherichia coli is often used to produce a variety of valuable chemicals, drugs, and biofuels in industrial biotechnology. A traditional method of gene knockout in E. coli was to adopt the Red homologous recombination system to mediate the homologous recombination of DNA. However, it is inefficient and especially not



Species	Cassettes for CRISPR/Cas9		Editing efficiency	Advances in genetic modification using CRISPR/Cas9	Strategies for improving efficiency	References
	Cas9 protein	gRNA	-			
Bacillus subtilis	lacA5'-Cas9- tracRNA-lacA3'	thrC5'-P _{xy4} ,Sphl+1* gRNA-thrC3'	100and 85% for single, double gene mutations, and 69% for chromosomal insertion of a 2.9 kb hyaluronic acid (HA) biosynthetic operon	Multiplex knockout	Choose optimal homology lengths (1,000 bp) for editing template, optimize PAM site	Westbrook et al., 2016
	Pgrac-SpCas9	Para-sgRNA-donor DNA	Point mutation (68%), single-gene deletion in spoOA (100%), and gene insertion (97%)	Traceless, high efficient	Incubation for longer periods to generate iterative DSB	So et al., 2017
Clostridium autoethanogenum	Cas9 was introduced into plasmid pLZtet3no and pIPL12	sgRNA was introduced into plasmid pMTL83157	Over 50% for gene deletion	Construct a small library of tetracycline-inducible promoters for efficient gene deletion	Construct variants of inducible promoter to control the expression of Cas9. Cas9 protein was codon adapted to <i>C. autoethanogenum</i>	Nagaraju et al., 2016
Clostridium cellulolyticum	Optimized SpCas9 was introduced into plasmid pLyc017	gRNA was introduced into plasmid pCR8/GW/TOPO TA	High editing efficiency (>95%)	High editing efficiency even using short homologous arms (0.2 kb), deliver foreign genes into the genome in a single step without a marker	Generate single-nick triggered homologous recombination and choose optimal homology lengths for editing template	Xu T. et al., 2015
Corynebacterium glutamicum	P _{tac} -SD-SpCas9 was introduced into plasmid pXMJ19	P _{trc} -sgRNA was introduced into plasmid pEC-XK99E	Deletion efficiencies were almost 100% for porB, mepA, clpX, and Ncgl0911 genes	High editing efficiency even using short homologous arms (0.3 kb)	Choose strong promoters for the expression of Cas9 and sgRNA	Liu J. et al., 2017
Clostridium Ijungdahlii	P _{thi} -SpCas9	P _{araE} -sgRNA	Deletion efficiencies were 100%, >75%, 100%, and >50% for pta, adhE1, ctf, and pyrE	More rapid, no added antibiotic resistance gene, scarless, and minimal polar effects	Choose strong promoters for the expression of Cas9 and sgRNA	Park et al., 2019
Clostridium pasteurianum	P _{thl} -SpCas9	P _{sRNA} -gRNA	Deletion efficiencies were 100% for <i>cpaAIR</i>	High efficient	Inducible expression of cas9 was recommended to mitigate toxicity for high editing efficiency	Pyne et al., 2016
Lactobacillus reuteri	tracrRNA, cas9, and CRISPR arrays derived from pCAS9 were introduced into plasmid pNZ9530		100% for genes mutations	High efficient	Employ oligonucleotide- mediated recombineering (RecT)	Jee-Hwan and Jan-Peter, 2014
Streptomyces albus	P _{rpsLp} -Cas9-T _{fd}	P _{gapahp} -gRNA-T _{ra}	Multiplex gene deletions with editing efficiency ranging from 70 to 100%	Reduce the time and labor needed to perform precise genome manipulation	Choose strong promoters for the expression of Cas9 and gRNA; Cas9 gene was optimized to favor the <i>Streptomyces</i> codon bias	Wang et al., 2016
Streptomyces coelicolor						Wang et al., 2016
Streptomyces lividans						Wang et al., 2016
Streptomyces viridochromogenes						Wang et al., 2016

Table 1. Applications of the CRISPR/Cas9 system in bacteria

n feature

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suitable for recombination of multiple sites (Murphy and Campellone, 2003). To improve the genetic engineering efficiency, Jiang et al. construct a triple-plasmid system as mentioned above. This novel genetic engineering tool significantly improved the efficiency of genetic modification and thus accelerated the development of industrial biology. In previous studies, Cas9 and gRNA were expressed in two plasmids, respectively, as the simultaneous expression would burden the organism metabolism and cause cell death. Hence, Cas9 or gRNA should be repressed before a genome editing event. Cas9 and gRNA can be assembled into one plasmid containing a pBAD promoter, which is repressed by glucose and induced by arabinose and a temperaturesensitive replicon repA101ts, so that transformed E. coli could grow on glucose-amended plates and be edited under the induction with 2 g/L of arabinose. This fast and easy procedure for genome editing could perform continuously, as multiple loci only required one plasmid construction and one step of transformation. To further improve the simultaneous editing efficiency of multiple loci, a CRISPR/Cas9-assisted multiplex genome editing technique was developed. The CRISPR/ Cas9-assisted multiplex genome editing technique contained three plasmids: pRedCas9 containing both λ-Red recombineering and Cas9 system under the control of pBAD promoter, pMgRNAs containing gRNAs, and pDonorDNAs carrying multiple donor DNA cassettes (Feng et al., 2018). In another versatile study, Li et al. firstly coexpressed a plasmid containing a gRNA targeting the bla gene and Cas9 with the λ -Red recombineering system into E. coli (Li et al., 2015). Then, the genetic editing started with cotransformation of donor DNA and gRNA plasmid into preceding cells. Comparing to the previously established system, this optimized system has a higher gene editing efficiency and less operating time, almost 100% for codon replacements and knockout genes within 2 days. It was noteworthy that using a double-strand DNA as a donor template has a better performance than a single-strand DNA in gene deletions. Subsequently, this optimized system was employed to strengthen the MEP pathway by substituting the promoters and ribosome binding sites, inserting a heterologous β-carotene biosynthetic pathway and optimizing the central carbon metabolism (Li et al., 2015). Finally, the best producer yielded 2.0 g/L β -carotene in fed-batch fermentation. This extensive work can hardly be completed without

employing CRISPR-based tools, revealing their great potential for efficient and diverse manipulation of genomic DNA. The Cas9-recombineering method was further exploited with the development of the CRISPR-enabled trackable genome engineering (CREATE) tool (Garst et al., 2017). Application of this tool in *E. coli* allowed for simultaneous transformation of multiple libraries of plasmid-borne recombined templates (Garst et al., 2017). The CREATE strategy was employed to construct genome libraries of isopropanol pathway by introducing multiple ribosome binding site variations in *E. coli*, leading to the construction and testing of ~1,000 strains in a few days. The best performer reached a titer of 7.1 g/L isopropanol within 24 h (Liang et al., 2017).

Besides the versatile applications in E. coli, the CRISPRbased tools also had satisfactory performances in other bacteria (Table 1). For instance, genetic engineering technologies for solventogenic Clostridium were still immature due to low transformation efficiency, inadequate endogenous homologous recombination, and poorly understood physiology and metabolism (Papoutsakis, 2008; Pyne et al., 2014; Bruder et al., 2016). Recently, CRISPR/Cas9 for Clostridium saccharoperbutylacetonicum N1-4, a hyperbutanol-producing strain, was developed. The genome engineering efficiency was improved from 20 to 75% by selecting optimized promoter PJ₂₃₁₁₀ from *E. coli* for gRNA expression. After deleting two essential genes of phosphotransacetylase (PTA) and butyrate kinase (BUK) for acetate and butyrate production, the butanol production reached 19.0 g/L, which is one of the highest levels ever reported from batch fermentations (Wang et al., 2017). This Cas9-based editing tool could be easily adapted for use in closely related microorganisms, paving the way for elucidating the mechanism of solvent production and constructing robust strains with desirable butanol-producing features. In addition, the Cas9-based editing tools have also been successfully employed for the production of bulk chemicals, such as succinate in Synechococcus elongatus (Li et al., 2016), isopropanolbutanol-ethanol in Clostridium acetobutylicum (Wasels et al., 2017), and γ-amino-butyric acid (GABA) in Corynebacterium glutamicum (Cho et al., 2017). The wide application of the CRISPR/Cas9 system in a variety of bacteria genera demonstrates that it plays a critical role in the prosperous development of bioindustrial.



Species	Cassettes for CRISPR/Cas9		Editing efficiency	Advances in genetic modification using CRISPR/Cas9	Strategies for improving efficiency	References
	Cas9 protein	gRNA				
Kluyveromyces lactis	P _{FBA1} -ScCAS9- CYC1TT	P _{SNR52} -gRNA- SUP4TT	Multiple-gene cassette insertion into multiple-gene loci: 2.1%	Multiplex knock-in	Delete KU80 gene to increase the frequency of HR	Horwitz et al., 2015
Komagataella pastoris	P _{HTA1} -HsCAS9- DAS1TT	P _{HTB1} -HH ribozyme-gRNA-HDV ribozyme-AOX1TT	87–94% for single-gene disruption and 69% for double-gene disruptions	Multiplex knockout	Choose optimal promoters for the expression of Cas9 and gRNA	Walter et al., 2016
Kluyveromyces marxianus	P _{Tef1p} -Cas9-CYC1TT	P _{RPR1-tRNAGly} -sgRNA	66% for single-gene disruption	High editing efficiency	Choose optimal promoters for the expression of sgRNA	Löbs et al., 2017
Ogataea polymorpha	P _{TDH3} -Cas9	P _{IRNA} -sgRNA	45% for single-gene disruption	High editing efficiency	Modify system using a tRNA-sgRNA fusion gene to increase the mutation efficiency	Numamoto et al., 2017; Wang et al. 2018
Schizosaccharomyces pombe	P _{ADH1} -HsCAS9- CYC1TT	P _{RRK1} -rrk1 leader-gRNA-HH ribozyme	Single-gene disruption (allele swap): 85%–90%	Highly efficient knockout	Add the leader RNA from rrk1 gene between the promoter and the gRNA sequence	Jacobs et al., 2014
Yarrowia lipolytica	Puasi88-TEF(136)- YICas9	P _{SCR1'-IRNAGIy} -gRNA-poly T	Single-gene disruptions (NHEJ/HR): 90–100%/64–88%	Highly efficient knock out	Choose optimal promoters for the expression of sgRNA; delete <i>KU70</i> gene to increase the frequency of HR	Schwartz et al., 2015
	P _{TEFin} -HsCAS9- CYC1TT	P _{TEFn} -HH ribozyme-gRNA-HDV ribozyme-MIG1TT	Single-gene disruption (NHEJ/HR): 62%—98%/72%; multiple-gene disruptions (NHEJ):19–37%	Highly efficient, scarless, single or multigene editing	Choose strong promoters for the expression of Cas9; delete <i>KU70</i> gene to increase the frequency of HR;	Gao et al., 2016

Table 2. Applications of CRISPR/Cas9 system in yeast

The Application of the CRISPR/Cas9 System in Yeasts

Yeasts play critical roles in industrial biology, as a wide range of products can be produced by yeasts, including biopharmaceuticals, biocatalysts, food additives, fine chemicals, and renewable biofuels (Raschmanova et al., 2018). Due to their robust physiology, yeasts could be cultivated in harsh growth conditions, such as low pH and elevated temperatures. Furthermore, yeasts can be introduced in complex eukaryotic post-translational modification systems, which are absent in bacterial hosts and often vital for biopharmaceuticals production (Thomas et al., 2013). Until now, a series of genetic engineering tools based on CRISPR/Cas9 had been exploited in yeast to improve the efficiency of genetic modification (Mitsui et al., 2019).

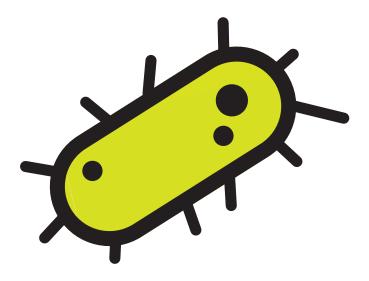
For decades, *S. cerevisiae* has been a well-known model organism in research and application areas (Jakočiunas

et al., 2016). To verify the efficiency of the CRISPR/Cas9 system in S. cerevisiae, the endogenous genomic negative selectable marker CAN1 (encoding arginine permease) can be chosen as a target gene (Dicarlo et al., 2013). To further improve the gene knockout efficiency, 90-bp double-strand oligonucleotides (dsOligo) including homologous arms to the target site and an internal stop codon as the HR template were designed. The recombined frequency of mutations selected from the medium containing canavanine (a toxic arginine analog that can kill cells containing functional CAN1 gene) was almost 100%, providing foundations for simple and powerful genome engineering tools in yeasts. This system can be used to knock out LEU2, TRP1, URA3, and HIS3 in polyploid industrial yeast S. cerevisiae ATCC 4124 with efficiency of up to 60%, and a quadruple-deficient strain $(\Delta ura3, \Delta trp1, \Delta leu2, \Delta his3)$ was successfully constructed (Zhang et al., 2014). In order to further improve the genetic editing efficiency of the CRISPR/Cas9 system, the

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USER cloning technology was accordingly employed to assemble multiple sgRNAs in one plasmid for efficient gene disruption and promoter engineering of one to five target loci in one step (Jakočiunas et al., 2015a). This onestep maker-free genome editing approach achieved high efficiencies of 50–100% from single to quintuple edits. However, the low efficiency of cotransformation of gRNA plasmids and corresponding HR donors hindered largescale genome engineering applications (Lian et al., 2018). To solve this problem, a homology-integrated CRISPR (HI-CRISPR) system by fusing a 100-bp HR template to the 5' end of the crRNA sequences was constructed, leading to 87% efficiency of multiplex knockout of CAN1, ADE2, and LYP1 (Bao et al., 2015). This HI-CRISPR system further improved the efficiency of multiplex genome editing and genome-scale engineering.

In addition to gene knockout, the CRISPR/Cas9 system can also mediate gene insertion using the homologous arm of donor DNA to the target gene. To better control cellular levels of correctly folding sgRNA, HDV ribozyme was fused to the 5^{\prime} end of sgRNA to protect the 5^{\prime} end of the sgRNA from 5^{\prime} exonucleases. This HDV-gRNA expression strategy significantly increased the efficiency of multiplex genome editing in diploid yeast strains, in which the heterologous cellodextrin transporter (cdt-1) and endogenous β -glucosidase (gh1-1) were inserted. As a result, the efficiency of utilizing cellobiose was increased by 10 times through site-directed mutagenesis of cdt-1 and gh1-1 genes via the multiplexed CRISPR/ Cas9 system (Ryan et al., 2014). Meanwhile, Ronda et al.



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cotransformed one episomal vector expressing three gRNAs with three donor DNAs containing β-carotene synthesis genes of BTS1, crtYB, and crt1 into S. cerevisiae, enabling it to synthesize β -carotene (Ronda et al., 2015). Similarly, three exogenous genes (XYL1, XYL2, and XYL3) encoding for xylose reductase, xylitol dehydrogenase, and xylulokinase from Scheffersomyces stipites were integrated into the loci of PHO13 and ALD6 in S. cerevisiae by employing the CRISPR/Cas9 system (Tsai et al., 2015). The refactored strains achieved the ability of utilizing xylose and could be readily used for large-scale fermentations, as no antibiotic-resistant markers were adopted. In addition, a more versatile genome engineering tool, Cas9facilitated multiloci integration of in vivo assembled DNA parts (CasEMBLR), was constructed by combining DNA assembly, HR of DSBs using donor DNAs, and multiplex gRNA expression cassettes (Jakočiunas et al., 2015b). As a proof of concept, this CasEMBLR was employed to assemble and integrate the gene expression cassettes (upstream homology arm, promoter, structural gene, terminator, and downstream homology arm) of CrtYB, Crtl, and CrtEinto the loci of ADE2, HIS3, and URA3, with a marker-free engineering efficiency of 31%.

CRISPR/Cas9 was also implemented in many other industrial yeasts (Table 2). For example, to construct more suitable promoters for sgRNA in Schizosaccharomyces pombe, Jacobs et al. constructed an expression cassette by adding the leader RNA from rrk1 gene between the promoter and sgRNA sequence, and fused the HH ribozymes with 3' end of the mature sgRNA to achieve correct 3' sgRNA processing. This system achieved a high efficiency of 98% when a donor template was cotransformed. To further simplify the operation of the CRISPR/Cas9 system in S. pombe, Zhang et al. developed a cloning-free procedure including a gapped Cas9-encoding plasmid and a PCR-amplified sgRNA insert. Ura4 and rrk1 promoter-leader was just between the gap of Cas9-encoding plasmid. The PCRamplified sgRNA insert was consisted of sgRNA target sequence and scaffold, and flanked with the homologous arms of ura4 and promoter-leader. Accordingly, a circular plasmid including Cas9 and sgRNA could generate two gap-repairing fragments. This cloning-free procedure could change the sgRNA target sequence only using an 83-bp sgRNA premier instead of cloning the whole sgRNA plasmid.

The Applications of the CRISPR/Cas9 System in Filamentous Fungi

Due to the considerable economic value of their metabolites, filamentous fungi have been applied to produce antibiotics, organic acids, pigments, polyunsaturated fatty acids, and so on (Dufossé et al., 2014; Ji et al., 2014; Xu X. et al., 2015). However, challenges of delivery through fungal cell wall and lack of available promoters and plasmids hindered the development of genetic engineering tools in filamentous fungi. In addition, the low editing efficiency and consequent large amount of labor time impeded the further application of filamentous fungi in the industry. The emerged CRISPR/Cas9 has brought a breakthrough for genetic manipulation in filamentous fungi.

Conventional genetic engineering strategies to improve the efficiency of HR were to delete KU70 or KU80heterodimer (Weld et al., 2006). However, if KU70 or KU80 is interrupted, the filamentous fungi will become more sensitive to growth environments with specific requirements for some chemicals, such as phleomycin, bleomycin, and methyl/ethyl methanesulfonate (Liu et al., 2015). To overcome this obstacle, the CRISPR/Cas9 system in the filamentous fungus of Trichoderma reesei using specific optimized codon and in vitro RNA transcription was established (Hao and Su, 2019). The highest frequency of single HR in *T. reesei* using a pair of ≥600-bp homology arms was almost 100%. Subsequently, a microhomologymediated end-joining system based on CRISPR/Cas9 in Aspergillus fumigatus was also established by flanking the sgRNA with HH and HDV. This system achieved accurate target gene editing with a high efficiency of 95–100% via very short (~35-bp) homology arms, indicating that it can function as a powerful and versatile genome editing tool in A. fumigatus (Zhang et al., 2016). In addition to the successful application in different species of Aspergillus, this evolved system has also been employed in several different filamentous fungal species, broadening the application of the CRISPR/Cas9 system (Hao and Xia, 2015; Weber et al., 2016; Weyda et al., 2017).

Taken together, the CRISPR/Cas9-mediated gene editing technology not only efficiently edited individual target gene but also showed satisfactory performances

in multigene editing, which greatly promoted the development of genetic manipulations in filamentous fungi.

COMBINATION OF CAS9-MEDIATED TRANSCRIPTIONAL REGULATION WITH SYNTHETIC BIOLOGY

In addition to the overexpression or deletion of genes, which occur in desired metabolite pathways, regulation of gene expression at the transcription levels is also very important to obtain high yields of metabolites (Mougiakos et al., 2018). Conventional methods to regulate gene expression were to use different promoters with desired strength or RNA interference (Crook et al., 2014). However, with the increased numbers of target genes, the task of testing promoters with suitable strength was timeconsuming and labor-intensive. In addition, in order to achieve transcriptional control in terms of level and timing, a complex and sophisticated genetic circuit including activating and repressive transcription factors is indispensable. According to the unique features of the CRISPR/Cas9 system, Jinek et al. constructed a catalytically deactivated Cas9 (dCas9) by introducing inactivating mutations into two nuclease domains of the Cas9 endonuclease, one in the HNH nuclease domain (H840A) and the other in the RuvC-like (D10A) domain (Jinek et al., 2012). This dCas9 protein lost the activity of DNA cleavage but retained the ability to specifically bind to target DNA sequences complementary to the sgRNA. Soon after, this CRISPR/dCas9 system was employed to synthesize a transcriptional repressor. Qi et al. showed that RNA guiding of dCas9 to target genes or promoters would block RNA polymerase binding and genetic transcription, leading to the repression of gene expression (Qi et al., 2013). This CRISPR interference (CRISPRi) system subsequently was used to create efficient, programmable, and genome-wide scale transcriptional regulators (Gilbert et al., 2013, 2014; Silvana et al., 2015). Similarly, CRISPR activation (CRISPRa) was constructed through the fusion of dCas9 to transcriptional activators or activation domains, allowing for transcriptional upregulation of select genes (David et al., 2013). To investigate whether the system could activate the transcription of reporter gene, dCas9 with an omega (ω) protein was fused, which could improve RNA polymerase activity and activate the transcription in E. coli. As a result, the transcription level of the reporter gene was increased by 2.8 times (David et

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al., 2013). In order to broaden the application of CRISPRa, several transcription activator domains have been excavated, such as VP64 and p65AD (Farzadfard et al., 2013; Silvana et al., 2015). Therefore, CRISPRi/a was allowed for facile transcriptional modification of gene networks and satisfied as an important tool to control enzyme expression levels in endogenous or synthetic pathways (Donohoue et al., 2017).

The core concept of synthetic biology is to transform existing natural systems and construct gene circuits by building and integrating standardized components and modules (Dai et al., 2018). However, an ultimate challenge in the construction of gene circuits was lack of effective, programmable, secure, and sequence-specific gene editing tools. The CRISPRi/a system was poised to solve this problem owning to its programmable targeting, efficacy as activator or repressor, high specificity, and rapid and tight binding kinetics (Sternberg et al., 2014 Xu and Qi, 2019). The CRISPR/Cas9 transcriptional regulator (CRISPR-TF) has been developed to become an important component of scalable device libraries, which were essential in creating complex genetic circuits. Nissim et al. constructed a multi-RNA-mediated gene network regulatory toolkit including RNA-triple-helix structures, introns, microRNAs, ribozymes, Cas9-based CRISPR-TFs, and Cas6/Csy4-based RNA processing to perform tunable synthetic circuits (Nissim et al., 2014). Nielsen et al. also constructed multiple transcriptional logic gates by employing CRISPR/dCas9 and linked them to perform logical computations in living cells (Nielsen and Voigt, 2014). In specific applications, researchers constructed a set of NOT gates by designing five synthetic σ70 promoters in E. coli. These promoters were inhibited by the corresponding sqRNAs, and interrelationships between various components did not exhibit crosstalk. Furthermore, they used these NOT gates to build larger lines, including the Boolean-complete NOR gate and three gates, which were consisted of four-layered sgRNAs. The previously designed gene synthetic lines were ligated into the native regulatory network using an export sgRNA capable of targeting the transcriptional regulator (MalT) in E. coli. By using these methods, the output of synthetic lines can be converted into switches of various cell phenotypes, such as sugar utilization, chemotaxis, and phage resistance.

Comparing with traditional methods of regulating expression, these complex gene circuits based on CRISPRi/a could carry out more precise regulation in terms of levels and timing. In addition, a cascade of responses in these circuits could be triggered by only one signal, which is more advanced than complex promoter engineering. Implementation of CRISPRi/a to design precise gene circuits in biosynthesis pathways will facilitate an unprecedented level of control of metabolic flux and promote the rapid development of the bioindustry.

CONCLUSION AND FUTURE DIRECTIONS

In the past, non-model microbes have been greatly limited in product diversity and yield due to the lack of efficient genetic engineering tools. These problems could be solved under the wide application of the CRISPR/Cas9 system, which will bring a bright future in the industrial biotechnology. Comparing to the conventional markerbased genome editing tools, the CRISPR/Cas9 system enabled fast strain engineering of prototrophic wild and industrial strains, allowing for multiple genome editing simultaneously with marker cassette integration (Stovicek et al., 2017). The high-throughput screening of industrial strains was another bottleneck in industrial biology (Donohoue et al., 2017). Recently, droplet-based microfluidics technology attracted great attention in terms of strain isolation and characterization due to its high-throughput screening efficiency. The combination of the CRISPR/Cas9 system and droplet-based microfluidics technologies maybe bring new breakthroughs in industrial biology in the future.

Although CRISPR/Cas9-meditated genome editing techniques were increasingly used in biotechnology, some disadvantages still existed (Zhang et al., 2019). First, the off-target effect is still a main issue needed to be solved. The designed sgRNAs may form mismatches with non-target DNA sequences, resulting in unexpected gene mutations. These unexpected gene mutations may cause genomic instability and disrupt the function of other normal genes. Although a variety of methods have optimized off-target effects, further improvement is still needed. Hence, conformational changes associated with sgRNA and DNA recognition need to be further explored to obtain higher genome editing accuracy (Mir et al., 2017). In addition, time-dependent control of Cas9 protein activity and the ratio of Cas9 to sgRNA also require further



investigation. High expression of Cas9 protein, whether in gene knockout or gene insertion, will affect the growth and recovery rate of host bacteria after transformation, and cause fatal damage to cells in most cases. The existing methods to increase the HR frequency are not suitable to many non-conventional industrial microorganisms. Hence, exploitation of novel approaches to improve homologous recombination efficiency in these strains is critical for precise and efficient CRISPR/Cas9-mediated genetic engineering. Besides, the intellectual property and scientific ethics issues also hindered the wide application of CRISPR/Cas9. The patent dispute has come to an end in the United States, but the war is continuing in Europe and other countries, delaying its adaptation for industrial biotechnology and pharmaceutical applications. Just like the first test-tube baby that appeared in 1978, employing CRISPR/Cas9 for gene therapy also caused some controversies. Therefore, if the laws in the application of the CRISPR/Cas system were completed, it would promote rapid development in the fields of medicine, genomics, agriculture, and so on.

AUTHOR CONTRIBUTIONS

SZ conceived, designed, and drafted the paper. SZ and FG wrote the part of the application of CRISPR-Cas9 in bacteria. WY and ZD wrote the part of the application of CRISPR-Cas9 system in Yeast. JZ and WD wrote the part of the applications of CRISPR-Cas9 system in filamentous fungi. MJ, WZ, and FX wrote the part of Cas9-mediated transcriptional regulation and critically revised the manuscript. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

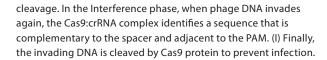
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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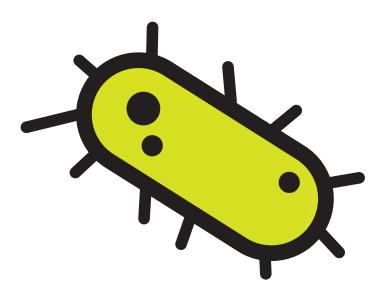
Figure and Table Legends for Zhang et. al., 2022

• Figure 1. The CRISPR-Cas9 mediated adaptive immunity is divided into three phases: Adaptation, Expression, and Interference. In the adaptation phase, (A) the host is invaded by phage DNA during infection. (B) Subsequently, the invading DNA is processed by various Cas genes into small DNA fragments (protospacer). The selection of protospacer depends in part on the specific recognition of protospacer adjacent motif (PAM) present within the viral genome. (C) The small DNA fragments is then incorporated into the CRISPR locus of the bacterial genome as a new spacer, flanked by a repeat sequence. In the expression phase, (D) the CRISPR locus is transcribed into a long precursor CRISPR RNA (pre-crRNA). (E) Then, the tracrRNA combine to pre-crRNA to a dual RNA hybrid, this dual RNA hybrid will be recognized and cut by RNase III with the existence of Cas9 protein, resulting in mature crRNA. (F) The mature crRNA will combine to Cas9 protein and guide the DNA





- Figure 2. Schematic to illustrate how gRNA and Cas9 expressed in industrial microorganisms. The gRNA was mainly expressed by two ways. One is directly derived by RNA polymerase III promoters. Another one is flanking the gRNA with HH and HDV ribozymes and then derived by RNA polymerase II promoters. The Cas9 could be expressed by a strong or weak, constitutive, or inducible promoter and fused with nuclear localization sequence (NLS). The two expressing cassettes can be expressed either from the same plasmid, separate plasmids, or integrated into the genome, most time with a donor fragment. So, after the genetic engineering, the industrial microorganisms could be transformed to high-powered microbial cell factories to product valuable production, such as biofuels, chemicals, biocatalysts, food additives, drugs, and so on.
- Table 1. Applications of the CRISPR/Cas9 system in bacteria.
- Table 2. Applications of CRISPR/Cas9 system in yeast.





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Natural Products: 4th International Conference on Discovery and Development in the Genomic Era

A JOINT CONFERENCE WITH THE SOCIETY FOR ACTINOMYCETES JAPAN AND THE KOREAN SOCIETY FOR MICROBIOLOGY AND BIOTECHNOLOGY

Manchester Grand Hyatt San Diego, CA January 8–12, 2023 www.simbhq.org/np

Onsite Registration Available for Conference and Limited Activities Program Chairs

Ben Shen, Scripps Florida Yi Tang, University of California, Los Angeles Alison Narayan, University of Michigan Kaity Ryan, University of British Columbia

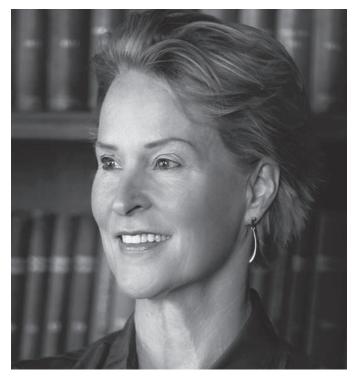
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Society for Actinomycetes

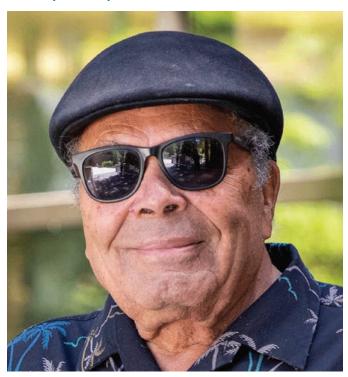
Jon Clardy, Harvard Medical School

Keynote Speaker



Frances Arnold, California Institute of Technology

Banquet Speaker



Phillip Crews, University of California, Santa Cruz

Program and Schedule

The program will consist of seven sessions over four and a half days, a poster session, networking receptions, two mid-week workshop tutorials for attendees only, a ticketed afternoon group outing to the Japanese Friendship Garden and Balboa or free evening to explore San Diego and more.

Topics covered throughout the conference and in every session:

- » Genome mining, metabolomics and synthetic biology
- » Natural product discovery
- » Natural product isolation and structural elucidation
- » Biosynthesis and enzymology
- » Biocatalysis and protein engineering
- » New modes of action and drug discovery





45th Symposium on Biomaterials, Fuels and Chemicals (SBFC)

Hilton Portland Portland, Oregon April 30-May 3, 2023 www.simbhq.org/sbfc

Abstract submissions Due: January 30

Registration and Housing Open Program Chair:

Carrie Eckert, Oak Ridge National Laboratory

Co-Chair:

Kevin Solomon, University of Delaware

2023 Program

TOPIC AREA 1

BIOFUELS, BIOPRODUCTS, AND SYNTHETIC BIOLOGY

Topics of interest involve lignocellulose (sugars and lignin) upgrading to fuels, chemicals, and material precursors via chemical and biological tools. Hybrid conversion technologies using ethanol or other bioinermediates to fuels are also encouraged.

Chairs:

Jay Fitzgerald – DOE- Bioenergy Technologies Office (BETO) Laura Jarboe – Iowa State University

TOPIC ARFA 2

ALTERNATIVE FEEDSTOCKS AND NOVEL BIO-BASED MATERIALS

Topics of interest include organic waste valorization, fermentation using CO2 and other C1 compounds, and the production of novel biomaterials and sustainable microbial food. This topic area places an emphasis on the use of non-model organisms to accomplish these goals.

Chairs:

Ben Woolston – Northeastern University John Yarbrough – National Renewable Energy Laboratory (NREL)

TOPIC AREA 3

ENGINEERING AND DECONSTRUCTION OF BIOMASS AND RECALCITRANT POLYMERS

Topics of interest involve engineering of bioenergy crops for fuels and bioproduct production, biomass deconstruction and fractionation, and biomass degrading enzymes and microbes.

Chairs:

Dawn Adin – DOE – Office of Biological and Environmental Research

Shing Kwok – DOE – Office of Biological and Environmental Research

Bryon Donohoe – National Renewable Energy Laboratory (NREL)

SPECIAL SESSION

BIOFUELS AND NEGATIVE EMISSIONS

Chair:

Lee Lynd – Dartmouth College

Keynote Speaker

John McGeehan, World Plastics Association Monaco



KEYNOTE PRESENTATION: "OUR PLASTIC CRISIS -BRINGING TOGETHER ACADEMIC, INDUSTRY AND GOVERNMENT RESEARCHERS TO ACCELERATE TECHNOLOGY SOLUTIONS"

Award Nominations

Nominations due January 30th

- » Diversity Travel Award
- » Charles D. Scott Award
- » Raphael Katzen Award





2022 SIMB Annual Meeting Recap

With the pandemic nearly over and vaccines, masks, and COVID treatments now widely available, things are starting to look more normal. In that spirit, the 2022 SIMB Annual Meeting was held in-person in San Francisco, California, from August 7–10, 2022. Between the return of many SIMB members and growth from new attendees discovering the value of SIMB, the Annual Meeting was a great success and was well attended with nearly 600 attendees.

This year's meeting featured three superlative Keynote talks. Dr. Jay Keasling of UC Berkeley kicked off the meeting on Sunday with a talk titled "Refactoring Natural Product Pathways in Yeast," sponsored by Curie Co. On Monday, we continued SIMB's commitment to our 2018 Memorandum of Understanding with the Korean Society for Microbiology and Biotechnology (KMB), in which we exchange speakers at our respective annual meetings, with a talk from KMB President Dr. Jung-Kee Lee titled "Quorum Quenching Bacteria and their Application for Controlling Biofilm Formation." On Tuesday, the 2022 Charles Thom Award winner Dr. Eleftherios "Terry" Papoutsakis presented his work on clostridia genetics

and metabolic engineering, with emphasis recently in syntrophic co-cultures for CO2 co-utilization with biomass carbohydrates to achieve supra-physiological product yields.

This year's program contained five topical tracks, with multiple sessions in each area. The Natural Products track featured five sessions, with foci on systems and synthetic biology, new modes of natural product activity, unusual enzymology, informatics and data science in natural products, and modern discovery of natural products. The Metabolic Engineering track consisted of five sessions, with topics highlighting automation and machine learning, engineering for production of commodity and specialty chemicals, use of alternate feedstocks, and domesticating and onboarding non-model organisms. The Biocatalysis track consisted of five sessions, including topics in cellfree and orthogonal chemistries, depolymerization and valorization of alternative feedstocks, enzyme engineering, biocatalysis at scale, and new-to-nature chemistries. The Cell Culture and Fermentation track featured five sessions, with topics including scale-up and scale-down, unconventional





fermentations and feedstocks, biomanufacturing of pharmaceuticals, Manufacturing 4.0, and tech transfer. Each session was well-received and highlighted excellent science and engineering being performed by members of the Society.

The Environmental track underwent a significant shift in its scope, leading to four sessions that were well-attended. The new Environmental track continues to cover traditional topics, such as biodegradation, bioremediation, and wastewater applications. A new emphasis on metal recovery and microbiomes in the natural and built environment reflects the importance of microbial communities throughout environmental applications.

This year's program also featured four special topics sessions. Three focused on emerging areas of science and engineering, and the other focused on Diversity, Equity, and Inclusion (DEI). The first highlighted cutting-edge research in animal products made by fermentation. A second special session focused on increasing biofoundry throughput while decreasing costs. A third special session focused on microbial and cell free approaches for protein secretion. The DEI session highlighted tools for dismantling white supremacy presented by the San Francisco United Way, plus a discuss about what how we can support diversity in STEM.

In addition to the excellent oral presentations, a poster session was also held on Sunday and Monday night, with 85

poster presenters in total. Posters were presented on topics from all five topical tracks. It was particularly great to see students and postdocs able to present their work to and receive direct feedback from the scientific community.

We would specifically like to thank our sponsors and exhibitors, the full list of which you can find in the SIMB Annual Meeting Resolutions later in this issue. Their support helped make the meeting possible.

It was an honor to serve as Program Chair for the 2022 SIMB Annual Meeting. I would especially like to thank all the SIMB team, including Haley Cox and Tina Hockaday, for all their assistance. This meeting could not have happened without their guidance, attention to detail, and patience. I would also like to thank each of the Program Committee members and Session Conveners, whose dedication and hard work were critical to the meeting's success.

I am already looking forward to the **2023 SIMB Annual Meeting being held July 30 – August 2 in Minneapolis, Minnesota**, and I welcome the new Program Chair, Dr.
Aindrila Mukhopadhyay from the Lawrence Berkeley
National Laboratory.

Mark Blenner University of Delaware 2022 Annual Meeting Program Chair





RAFT® 14 (2022 Recent Advances in Fermentation Technology) Meeting Recan

After the cancellation of the 2021 RAFT meeting due to a COVID surge and a relocation of the rescheduled 2022 meeting due to the devastation caused by Hurricane lan, it was a pleasure to hold the 2022 RAFT 14 meeting inperson in Orlando, from November 6th to 9th. Despite all of the challenges, and another impending hurricane, the conference was very well attended with 308 people from industry, government, and academia from 21 different countries.

We were privileged to open the symposium with a recently elected National Academy of Engineering Keynote Speaker, Dr. Michael V. Arbige, a 40-year veteran of the biotech community. Dr. Arbige led us through a detailed presentation of his career track and advice on how to launch and sustain successful biotechnology companies.

This year's program contained 5 scientific sessions

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including, Overcoming fermentation failure: Lessons learned, Alternative fermentation systems, Natural product biosynthesis, Alternative systems to animal cell culture, Model driven strain & fermentation process development, and Fermentation foods for today and tomorrow. All of the sessions were well attended and packed with very informative speakers, but sadly, due to hurricane Nicole, the Fermentation foods for today and tomorrow had to be moved to an online forum of recorded presentations and slides. The conference also included 2 poster sessions and a round table, Future faces of fermentation.

Attendees also had the ability to discuss their needs and learn about new technology with over 30 exhibitors in attendance (listed below) and listen to eight exhibitor showcases. Having attended multiple RAFT conferences, it is always a pleasure to see the friendly faces in the exhibitor hall, meet new people, and renew old acquaintances.





RAFT® 14 Exhibitors:

Aber Instruments

Ajinomoto. Co., Inc

Angel Yeast

BioIntelligence Technologies

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Bio-Technical Resources

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Scientific Bioprocessing, Inc.

Solabia Group

Tatua USA, Ltd.

Thermo Fisher Scientific

University of Georgia

I would also like to thank the RAFT® 14 sponsors: BioP2P Network, Corteva Agriscience, Applied Materials, and Kuhner Shaker for their generous support.

Overall, it was an honor to be the Program Chair of 2022 RAFT® 14 and I am thankful to have worked with such an experienced and dedicated team to make this in-person conference a reality: Kat Allikian (Co-Chair), Tina Hockaday, Jennifer Johnson, Haley Cox, Chris Lowe, and James Earle. In addition, I want to say a big thank you to the session conveners, who dealt with multiple last-minute changes and dropouts due to the pandemic and hurricanes. In many ways, the conveners almost had to plan two separate sessions, but they all came through to make RAFT® 14 such a success.

I am very much looking forward to the continued success of the RAFT® conference series. **RAFT® 15 will take place October 29–November 1, 2023 in Naples Florida**, where the Program Chair will be Kat Allikian.

My sincerest thanks and best wishes to all.

Mark Berge

2022 RAFT 14 Program Chair



Society for Industrial Microbiology and Biotechnology 2022 Resolutions

1. To the 2021-2022 Officers of the Society:

PresidentNoel Fong, NucelisPast PresidentSteve Decker, NREL

President-elect Nigel Mouncey, Joint Genome Institute
Secretary 2021-2024 Elisabeth Elder, Georgia State University
Treasurer 2020-2023 Laura Jarboe, Iowa State University

Directors Rob Donofrio, Neogen

Katy Kao, San Jose State University

Priti Pharkya, Genomatica

Ben Shen, UF Scripps Biomedical Research

Executive Director Haley Cox, SIMB

Christine Lowe, SIMB

2. To the outgoing members of the Board for their dedicated service:

Steve Decker, NREL Katy Kao, San Jose State University Priti Pharkya, Genomatica

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3. To the incoming members of the Board for 2022–2023, beginning August 10, 2022:

President Nigel Mouncey, Joint Genome Institute

President-elect Michael Resch, NREL

DirectorAdam Guss, Oak Ridge National LaboratoryDirectorBrian Pfleger, University of Wisconsin-Madison

- 4. To Ramon Gonzalez, Editor-in-Chief of the Journal of Industrial Microbiology and Biotechnology, for outstanding editorial services during the year and guiding JIMB to an increased impact factor of 4.258.
- 5. To the JIMB Editors: R. H. Baltz, T. W. Jeffries, T. D. Leathers, M. J. López López, S. Park, J. L. Revuelta, B. Shen, Y. Tang, E. J. Vandamme, and H. Zhao; and to Oxford University Press for producing a distinguished open access journal.
- 6. To Melanie Mormile, Editor-in-Chief of *SIMB News*, Kristien Mortelmans, PhD, Vanessa Nepomuceno, PhD and Elisabeth Elder, PhD, Associate Editors; and to Ms. Katherine Devins, Production Coordinator, for providing the membership with an attractive and professional publication throughout the year.
- 7. To Betty Elder, Placement Chair and SIMB co-photographer, for her valuable and committed efforts throughout the year on behalf of the Society.



- 8. To the Society's committee chairs and committee members for their dedicated service to the Society.
- 9. To Mark Berge for his efforts in leading the virtual Fermentation workshop and all his dedication throughout the years.
- 10. To the 2022 Quarter Century Club inductees Susan Bagley, Jonas Contiero, Mark Eiteman, and Ben Shen; and to the Class of 2022 SIMB Fellows Debbie Chadick and Mahendra Jain.
- 11. To the SIMB Headquarters Office Staff: Suzi Citrenbaum, Web Manager; Jennifer Johnson, Director of Member Services; Tina Hockaday, Meetings and Exhibits Coordinator, Al Trapal, Accountant; James Earle, Marketing and Communications Coordinator; and Todd Carlisle, IT and networking, for their patience with me, and their dedicated service to the Society this year.
- 12. And finally, to Christine Lowe for her caring guidance this past year transitioning the Society to a new Executive Director and steadfast stewardship of the Society throughout the years.

These Resolutions are respectfully submitted.

Haley Cox Executive Director December 2022

2022 SIMB ANNUAL MEETING RESOLUTIONS

Be it resolved that we, the members of the Society for Industrial Microbiology and Biotechnology, express our sincere appreciation and thanks to the following people and organizations who have made the 2022 Annual Meeting an outstanding success:

- 1. To the Headquarters Office staff for handling logistics, registration, local arrangements, and social activities for the annual meeting.
- 2. To the Annual Meeting program chair, Mark Blenner and the 2022 program committee for organizing an outstanding program.
- 3. To Tim Cooper, Marcello Fidaleo, and Peter D. Karp for presenting valuable workshops.
- 5. To the session conveners for developing and leading excellent technical sessions and to the invited speakers and poster presenters for their contributions.
- 6. To Jay Keasling for presenting the Keynote lecture.
- 7. To Jung-Kee Lee, Pai Chai University and President, KMB for presenting the Korean Society for Microbiology and Biotechnology plenary lecture "Quorum Quenching Bacteria and their Application for Controlling Biofilm Formation."
- 8. To Terry Papoutsakis, recipient of the Charles Thom Award, for his outstanding research contributions to industrial and applied microbiology, and for presenting the Charles Thom Award Lecture.
- 9 To Jan Westpheling, Charles Porter Award recipient, for her passionate and dedicated service to the Society.
- 10. To Kevin Solomon, worthy recipient of the Early Career Award (formerly the Young Investigator Award).

members

12. We congratulate the 2022 Diversity Travel Awardees: Taylor Andrzejak and Amanda Godar

13. We congratulate the 2022 Carol D. Litchfield student oral and poster presentation winners:

Best Student Oral Presentation: Efrain Rodriguez-Ocasio

Best Student Poster Presentations Biocatalysis: Efrain Rodriguez-Ocasio **Environmental:** Taylor Andrzejak

Cell Culture Fermentation: Amanda Godar **Metabolic Engineering:** Casey Hooker Natural Products: Stephanie Heard

14. To the following organizations for their sponsorship of the 2022 SIMB Annual Meeting:

Applied Materials Genomatica ARPA-E Ganymede Bio

Infinome Biosciences bitBiome, Inc. Kuhner Shaker Inc. Conagen

Lanzatech Corteva Curie Co Manus Bio

DSM Morrison Foerster

ExxonMobil **PivotBio POET** Frances Templeton Fund

15. To the commercial exhibitors and their representatives who recognize the value of their presence at the SIMB annual meeting:

Aber Instruments LTD. Igenbio

Agile BioFoundry **ILS Automation**

Infinome Biosciences Biolog

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BlueSens Corporation Kuhner Shaker, Inc.

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Global Bioingredients Oxford University Press Roche Custom Biotech **Hamilton Company**

Hiden Analytical Scientific Bioprocessing, Inc.

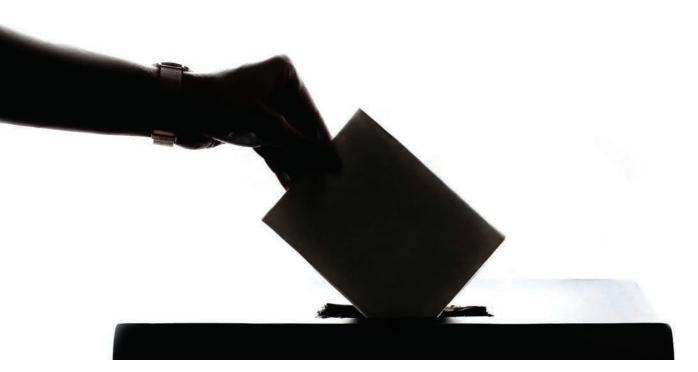
16. To Run Coordinator Betty Elder for continuing the 5K Fun Run-Walk tradition.

17. And Finally to all SIMB Members who attended the SIMB Business Meeting, discussing and voting on important issues that shape the future of the Society.

These Resolutions are respectfully submitted.

Haley Cox

Executive Director December 2022



2023 SIMB Election for Board of Directors

The SIMB Election for positions on the Board of Directors will commence March 1, 2023. The election will close at noon EDT on March 31, 2023, and members must join/renew by noon EDT, March 30 2023, to be eligible to vote.

Current members for 2023 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 15 far publication in the October-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.

members

Candidate for President-Elect Rob Donofrio



I am honored and humbled to be considered for the position of President of the Society of Industrial Microbiology and Biotechnology (SIMB). The Society has helped shape who I am as a scientist, professional and colleague. During

my 25+ years of membership I have volunteered for many roles: poster presenter (my first when I was a Masters of Science student at Duquesne University); session speaker; poster session judge; session organizer; conference planning committee; program chair of Recent Advances in Microbial Control; SIMB Board of Directors (two terms as Secretary and currently Director). Each experience provided insight into the inner workings of the Society and provided me with a genuine appreciation of the effort, collaborative spirit, and passion of my fellow SIMB members. My doctoral mentor at Michigan Technological University Dr. Susan Bagley (past SIMB President and all-around incredible person) instilled in me the mindset of servant leadership and the importance of volunteering. SIMB is truly a Society where everyone can (and should) get involved.

Professionally, I currently hold the position of chief scientific officer at Neogen where I am responsible for the global R&D strategic vision, resource management and coordination of product development activities for the 150+ scientists and researchers in our food safety, animal safety and genomics divisions. Prior to Neogen, I held multiple roles at NSF International over my 16-year tenure (director of microbiology, director of the Applied Research Center). My additional board and advisory commitments include AOAC's Global Council, International Fresh Produce Association Food Safety Council, National Institute of Antimicrobial Resistance Research and Education Advisory council, and the MichBio board of directors.

If I were fortunate enough to be selected at President, I would look to expand on the many impactful initiatives enacted by my predecessors. My vision for the term would be as follows:

- Plan for long term sustainment and growth of the Society
- Strategic planning sessions lead by Board of Directors and build on the input of key society stakeholders and members
- Emphasize adherence to core values while being fiscally responsibility
- Ensure that SIMB remains as the premiere industrial microbiology society
- Ensure that the Society continues to cultivate a diverse, equitable and inclusive group of scientists and professionals
- Evaluation of additional scientific tracks for inclusion into Annual Meeting or serving as special symposia
- Evaluation of society partnerships that align with core values and complements our scientific focus
- Increase Industry participation to drive corporate membership and sponsorship
- Establish key connections with corporate decision makers and define the value add of membership
- Evaluate and engage adjacent industry targets for potential membership
- Evaluate best practices for industry engagement by other societies and trade associations
- Expand recruitment of emerging scientists
- Mentorship engagement
- Develop SIMB emerging scientist support and development group
- Social media campaigns to raise awareness of Society meetings and local scientific gatherings; recognize member contributions and achievements
- Targeted local section engagements at universities

Thank you for your consideration and I look forward the opportunity to serve you.



Candidate for President-Elect Ramon Gonzalez



Dr. Ramon Gonzalez is a professor and Florida World Class Scholar in the department of chemical, biological, and materials engineering at the University of South Florida (USF) where he leads the laboratory for metabolic engineering and biomanufacturing. He currently serves as program director with the US National Science Foundation (NSF). Before joining USF, Dr. Gonzalez was a professor in the departments of chemical & biomolecular engineering and bioengineering at Rice University and the founding director of Rice's Advanced Biomanufacturing Initiative. From 2012 to 2015 he served as program director with the Advanced Research Projects Agency-Energy (ARPA-E) of the US Department of Energy. Dr. Gonzalez's work has been published in prestigious scientific journals and

has given more than 100 invited talks at institutions around the world. He is the lead inventor in 25 patents/patent applications, co-founded Glycos Biotechnologies Inc. and Creo Ingredients Inc., and has advised major companies in the biotechnology and chemical industries. Dr. Gonzalez has received numerous recognitions, including elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE), Discovery Series Lecture (BioDesign Institute, Arizona State University), Tiangong Forum Lecture (TIB-CAS, China), AIChE Division 15c Plenary Lecture, ASM Distinguished Lecturer, SDA/NBB Glycerine Innovation Research Award, and NSF CAREER Award.

Dr. Gonzalez has been actively engaged with SIMB for almost two decades, initially giving talks and chairing/co-chairing technical sessions at annual and specialized meetings, then served as the Program Chair of the 2011 Annual Meeting and as a member of the Board of Directors. He has also served as an Editor of the Journal of Industrial Microbiology and Biotechnology (JIMB) and since 2015 has been JIMB's Editor-in-Chief. Under his leadership, the Editorial Board was restructured, a highly coveted Special Issue Collection has been established, the visibility and quality of publications have reached new heights, and the impact factor increased to 4.258. Dr. Gonzalez also played a key role in the transition of JIMB to an open access journal with Oxford University Press. As SIMB President, Dr. Gonzalez will build upon these experiences to increase the visibility and impact of SIMB as the pre-eminent professional society that will shape the bioeconomy. These efforts will include working closely with leaders in academia, industry, non-profits, and public-private entities in the US and abroad. In addition, Dr. Gonzalez plans to make diversity, equity, inclusion, and accessibility an integral component of the SIMB community, an effort that will span both membership and leadership.

members

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Candidate for Treasurer Katy Kao



Katy Kao is a professor in the department of chemical and materials engineering at San Jose State University. Prior to joining San Jose State University in 2019, she was an Associate Professor in the Department of Chemical Engineering at Texas A&M University. Her work focuses on microbial adaptation for applications in biotechnology and microbial pathogenesis. Specifically, her lab is developing broadly applicable methods based on adaptive laboratory evolution for both strain development and to gain fundamental understanding of complex phenotypes in microbial systems. Her lab is also studying biofilm adaptation in human fungal pathogens.

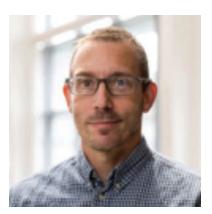
Katy has been an active member of the SIMB community since 2008. Her service

includes serving the chair of the 2019 SIMB Annual meeting in Washington, D.C. and as a director on the Board of Directors from 2019–2022, convening sessions, serving as a member of the Fermentation and Cell Culture program committee, and chairing the Fermentation and Cell Culture program committee. She also served as the Educational and Outreach Chair. Her vision for SIMB is to grow the membership, engage young scientists, and continue to bring together members from industry, academia, and national labs to address issues important in industrial biotechnology.

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Candidate for Treasurer Steven Van Lanen



Steven G. Van Lanen is a professor of pharmaceutical sciences within the College of Pharmacy at the University of Kentucky. His research is focused on the discovery and characterization of bioactive natural products with unique structures or distinct mechanisms of action relative to clinically used drugs. Another significant emphasis of the research is centered on the functional assignment and biochemical characterization of enzymes catalyzing highly unusual chemistry that enable the biosynthesis of these natural products. He earned a BS in molecular biology with honors from the University of Wisconsin-Madison and a PhD in chemistry from Portland State University. Following his graduate studies, he received a Ruth L. Kirschstein National Service Award for a postdoctoral fellowship under the guidance

of Professor Ben Shen at the University of Wisconsin-Madison. He joined the University of Kentucky in 2007, where he has instructed physiological chemistry, biochemistry, medicinal chemistry, and infectious disease courses within the College of Pharmacy. Dr. Van Lanen is a co-author of 80 refereed papers and the recipient of multiple extramural funding awards from the National Institute of Health. He has mentored more than 40 undergraduate, graduate, postdoctoral, and professional students and has co-organized and given lectures at multiple international conferences and venues.

members

Candidate for Director Jennifer Headman



Dr. Jennifer Headman holds the position of Fermentation Manager in Research at POET, the world's largest producer of biofuels. She has worked at multiple companies in the biofuels and biochemicals space, starting with two startup companies, EdeniQ and Verdezyne, before moving to global BioSolutions provider Novozymes, and finally to POET. During her career she has been involved in the development and scale up from laboratory to pilot, and eventually industrial scale fermentation of microbes and enzyme products. Jen prides herself in being able to effectively translate between the sometimes wildly different languages used within academia and industry. She was recently featured in the October 2022 edition of *Ethanol Producer* magazine in the Faces in Ethanol feature.

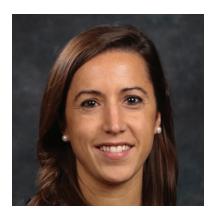
Jen earned a B.S. in Biotechnology from Worcester Polytechnic Institute in 2001. She then completed her PhD at the University of Wisconsin- Madison in 2009. During her PhD in the lab of past SIMB President Dr. Tom Jeffries, she spent a year as a Fulbright Scholar at the Technical University of Denmark, where she fell in love with all things fermentation related. It was during her time as a PhD student that Jen first became involved with SIMB. Jen has been helping to plan the SIMB annual meeting since 2016, first serving as a member of the bio-catalysis program committee and student poster session judge, serving as the 2020/2021 bio-catalysis program committee chair, and most recently helping to organize the student poster session and Science Slam. In her free time, Jen serves as a member of the national operations council for Alpha Phi Omega, the national coed service fraternity as the regional chair for the Carolinas, a role that will be ending in December 2023. This role has been rewarding as it works directly with college students and helps them in their own personal leadership development while serving as a role model to the next generation.

Jen values the impact that SIMB and its members has had on her personal career development and wishes to help bring that to others. If she is chosen as a director, Jen would like to focus on expanding knowledge of, and access to, the society to students and other young researchers, especially from underrepresented groups. This includes women and other groups who traditionally have less exposure to, and opportunity within, the scientific community. It also includes groups of people such as laboratory managers, laboratory technicians, and plant operators who have the potential to grow through interactions with the Society. She would also like to help facilitate more interactions between academic and government labs and industry as each bring unique resources to the table and effective collaborations can significantly advance discovery in the field of industrial microbiology.

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Candidate for Director Davinia Salvachúa



Davinia Salvachúa is a Senior Scientist and Distinguished Member of the Research Staff at the National Renewable Energy Laboratory (Golden, CO, USA). She received her PhD in biology with a specialization in microbiology from the University Complutense of Madrid in Spain. Her current work focuses on bioprocess development with bacteria and fungi to produce biofuels and biochemicals as well as on the use of systems biology and biochemistry to elucidate novel mechanisms of aromatic catabolism in white-rot fungi. Additionally, she currently serves as an Editor for *Microbial Biotechnology*. Davinia received an Early Career Award from the US Department of Energy's Biological and Environmental Research program and the Society of Industrial Microbiology (SIMB)'s Young Investigator Award, both in 2019.

Davinia has been an active member of the SIMB community since 2014. Her service has included convening sessions and speaking at the Annual SIMB Meeting, the Symposium on Biomaterials for Fuels and Chemicals (SBFC), and Recent Advances in Fermentation Technology (RAFT®). In addition, she also served as a Co-chair and Chair at the 43rd and 44th Symposium SBFC in 2021 and 2022, respectively.

"As a Director on the SIMB Board of Directors, and as an active researcher on industrial microbiology, one of my main goals will be enhancing the visibility of the society and growing the membership by engaging international scientists from academia, government research centers, and industry. The utilization of various social media platforms and continuous international outreach to researchers and societies with similar goals to SIMB will be key to continue exchanging knowledge and broadening the society. I also believe that promoting and supporting the diversity within the members of our society and sponsors will be also a major driver to build our community, to continue increasing the science quality in our meetings, and to expand professional opportunities for early career researchers. Reaching minority serving institutions, dedicating sessions to students, and building event apps to promote pre- and post-event networking are additional ideas to enrich the variety of expertise, views, and experiences to continue harnessing microbiology to promote human health and planet sustainability."



Upcoming SIMB Meetings

JAN. 8-12, 2023

4th International Conference on National Products Discovery & Development in the Genomics Era

Manchester Grand Hyatt • San Diego, CA

www.simbhq.org/np

APR. 30-MAY 3, 2023

45th Symposium on Biomaterials, Fuels and Chemicals (SBFC)

Hilton Portland • Portland, OR

www.simbhq.org/sbfc

JUL. 30-AUG. 2, 2023

SIMB Annual Meeting and Exhibition

Hyatt Regency Minneapolis • Minneapolis, MN

www.simbhq.org/annual

OCT. 29-NOV. 1, 2023

RAFT®15 – Recent Advances in Fermentation Technology

Naples Grande Hotel • Naples, FL

www.simbhq.org/raft

Upcoming Industry Meetings

MAR. 20-21, 2023

ICMA 2023: 17. International Conference on Microbiome Analysis

Tokyo, Japan

waset.org/microbiomeanalysis-conference-in-march-2023-in-tokyo

APR. 25-27, 2023

INTERPHEX 2023

Javits Center •New York City, NY

www.interphex.com/en-us. html

JUNE 14-15, 2023

3rd Edition of Chemistry
World Conference

Rome, Italy

chemistryworldconference. com/program/scientificsessions/natural-productschemistry

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SIMB Committee	Chair	r	Ema	il	Term expires	Members	Members		Staff liason
Annual Meeting 2023	Aindril Mukho	Irila amukho		hopadhyay@lbl.gov	2023	See Program Committee			Tina Hockaday, Haley Cox
Archives	(Currer	(Currently vacant. Interested in chairing this com			Email info@s	simbhq.org)			Jennifer Johnson
Audit Committee	Debbi	Debbie Yaver dyav		r@naturesfynd.com	2027	Tim Davies	Tim Davies		Haley Cox
Awards/Honors	Raj Bo	j Boopathy raman edu		raj.boopathy@nicholls. 2023		Gleason, Je Jeffries, The	Cathy Asleson Dundon, Stephanie Gleason, Jennifer Headman, Tom effries, Thomas Klasson, Sara Shields- Menard, Rajesh Sani		Haley Cox
Corporate Affairs	Steve	com		ien@persephonebiome.	2023	Yoram Barak, Andreas Schirmer, Priti Pharkya, Jonathan Sheridan, Lisa Lee, Melisa Carpio, Kevin McHugh, George Barringer		Jennifer Johnson, Haley Cox	
Diversity	Sheen	ena Becker sheen		a.becker@corteva.com	2023		Noel Fong, Laura Jarboe, Felipe Sarmiento, Vanessa Nepomuceno		Haley Cox
Education and Outreach	Noel F	el Fong <i>nfon</i>		@nucelis.com	2024	Katy Kao, Elizabeth Orchard, Torben Bruck, Neal Connors, Mark Blenner, Ian Wheeldon, Laura Jarboe, Benjamin Philmus, Linnea Fletcher		Haley Cox	
Elections	Kristie	tien Mortelmans kristie		n.mortelmans@sri.com	2023	2023 Melanie Mormile			Jennifer Johnson
Ethics Committee	Thoma	homas Klasson tho		thomas.klasson@usda.gov		In Develop	In Development		Haley Cox
Investment Advisory	Dick B	ick Baltz rbai		rbaltz923@gmail.com		George Ga	nrrity		Haley Cox
Meeting Sites	Haley	Haley Cox		haley.cox@simbhq.org		BOD and m	neeting chairs		
Membership Individual	Allen L	Allen Lee		ls1@usf.edu		Laura Jarbo Van Dien	Laura Jarboe, Thomas Klasson, Steve Van Dien		Jennifer Johnson
Nominations	Steve I	Steve Decker		Steve.Decker@nrel.gov		Richard Bal	tz, Susan Bagley, Ada	am Guss	Haley Cox
Placement	Elisabe	Elisabeth Elder		elisabeth.elder@gsw.edu		Lisa Lee			Jennifer Johnson
Planning	Michae	Michael Resch		michael.resch@nrel.gov		In Develop	ment		Haley Cox
Publications	Hal Alp	Hal Alper		halper@che.utexas.edu		George Garrity, Melanie Mormile			Haley Cox
JIMB	Ramor	Ramon Gonzalez		ramongonzale@usf.edu		JIMB Editors			
SIMB News	Melanie Mormile		mmormile@mst.edu		2023	Kristine Mortelmans, Vanessa Nepomuceno, Elisabeth Elder			Katherine Devins
Presidential Ad H	oc Con	nmittees							
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Student/Postdoc/ Early-Career	Nigel I	el Mouncey <i>njmou</i>		incey@gmail.com	2023	Noel Fong, Haley Cox, Michael Resch, Md. Azizul Haque, Sora Yu, Jay Huenemann, Allen Lee, Blake Rasor, Eric Eke, Aditya Kunjapur, Guangde Jiang, Bhargava Nemmaru, Lydia Rachbauer		Haley Cox	
SIMB Policy and Advocacy Working Group	Nigel I	gel Mouncey njmou		ıncey@gmail.com	2023	Tae Seok Moon, Thomas Alexander, Charles Isaac		Haley Cox	
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Co-chair	Kaity Ryan		ksryan@chem.ubc.ca			2023 Tina Hockaday			
Co-chair	Yi Tang		yitang@g.ucla.edu			2023 Tina Hockaday			
SBFC 2023 Chair	Carrie Eckert		eckertca@ornl.gov			2023 Tina Hockaday			
		Kevin Solomon				2023	Tina Hockaday		
		Davinia Salvach	-		l aov	2023	Tina Hockaday		
Past chair					901	2023	Tina Hockaday		
RAFT® 2023 Chair		Kat Allikian		kat@nourishing.io			,		
Co-Chair		Daniel Dong		daniel.dong@dsm.com		2023	Tina Hockaday		

October November December 2022



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

Visit www.simbhq.org/corporate-membership

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2023 SIMB Corporate Membership Application

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