Shinjinee Sengupta

SENIOR SCIENTIST- DBT WELLCOME TRUST EARLY CAREER FELLOW

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EDUCATION

PhD in Biotechnology
CSIR-Indian Institute of Chemical Biology
2008–2013

M.Phil. in Reproductive Biology
University of Delhi
2006-2007

M.Sc. in Botany
University of Delhi
2004-2006

SKILLS

- ***Synthetic Biology***: Genome editing tools such as CRIPSR Cas9, CRISPRi, circular polymerase extension cloning (CPEC), RT-PCR, Chromatin Immunoprecipitation (ChIP); Site directed Mutagenesis; Gene knockout; Molecular cloning.
- ***Biochemistry***: Protein purification from yeast, bacteria; fluorescence spectroscopy; enzyme assays; circular dichroism; HPLC, western blotting.
- ***Tissue Culture***: Mammalian adherent and non-adherent cell culture, electroporation, transfection
- ***Microscopic techniques***: Transmission electron microscopy, fluorescence microscopy,
- ***Bioinformatics***: Familiar with bioinformatics software and other computer applications

AWARDS

- DBT Wellcome Trust Early Career Award (2019)
- Travel Award from Department of Biotechnology, DBT (2019)
- DST Women Scientist award- Not availed (2016)
- Travel Award from Department of Biotechnology DBT (2016)
- Institute Postdoctoral Award, IIT Bombay (2014)
- Qualified (CSIR-UGC) National Eligibility Test and Awarded Lectureship (2007

PROFILE

Ph.D. in Biotechnology from CSIR-IICB, Kolkata with 7 years of postdoctoral experience in cellular and molecular/synthetic biology at IIT Bombay.

Received the most prestigious **DBT/Wellcome Trust Alliance Early Career Award**, 2019, comprising of a grant of INR 1.5 crores over 5 years, for my proposed project on "Establishing the relationship of p53 mutations and amyloid formation: A new insight in Cancer biology and therapeutics". https://www.indiaalliance.org/fellow/shinjinee-sengupta

PROFESSIONAL EXPERIENCE

DBT WELLCOME TRUST EARLY CAREER FELLOW
Indian Institute of Technology Bombay | Mumbai, Maharashtra | September 2019-Present

- Working on clinical samples obtained from Tata Memorial Hospital.
- My publications related to the field are acknowledged and sponsored by DBT Wellcome Trust.

SENIOR SCIENTIST
Indian Institute of Technology | Mumbai, Maharashtra | June 2017- August 2019

- Team leader of a synthetic biology group at DBT Pan IIT Center for Biofuels
- Production of biofuels and value-added products by engineering microbes
- Guiding PhD scholar, interns, project staff members
- Published numerous scientific articles in international journals

POSTDOCTORAL FELLOW
Indian Institute of Technology Bombay | Mumbai, Maharashtra | Jan 2014- April 2017

- Working on p53 amyloid formation and its implications in cancer
- Various cell and molecular biology tools such as RT PCR, Fluorescence microscopy were utilized.

SELECTED PUBLICATIONS (N=17)

Shinjinee Sengupta, Damini Jaiswal, Annesha Sengupta, Shikha Shah, Shruti Gadagkar and Pramod P. Wangikar, Metabolic engineering of a fast-growing cyanobacterium *Synechococcus elongatus* PCC 11801 for photoautotrophic production of succinic acid, **Biotechnology for Biofuels**, 2020, 13: 89.

Damini Jaiswal, Annesha Sengupta, Sujata Sohoni, **Shinjinee Sengupta**, Ambarish G. Phadnavis, Himadri B. Pakrasi & Pramod P. Wangikar, Genome Features and Biochemical Characteristics of a Robust, Fast Growing and Naturally Transformable Cyanobacterium Synechococcus elongatus PCC 11801 Isolated from India, 2018, ***Scientific Reports*** volume 8, Article number: 16632.

Saikat Ghosh[#], Shimul Salot[#], **Shinjinee Sengupta**[#], Ambuja Navalkar, Dhiman Ghosh, Reeba Jacob, Subhadeep Das, Rakesh Kumar, Narendra Nath Jha, Shruti Sahay, Surabhi Mehra, Santanu K. Ghosh, Mamata Kombrabail, G Krishnamoorthy, Pradip Chaudhari,and Samir K Maji[*]. p53 amyloid formation leading to its loss of function: Implication in cancer pathogenesis. ***Cell death and Differentiation.*** [#] **Equal contribution**. 24, 2017, pages 1784–1798.

PATENT

Indian Patent granted on "Amyloid mediated cell line transformation". Inventors: Samir K Maji, Saikat K Ghosh, **Shinjinee Sengupta**, Shimul Salot, Ambuja Navalkar, Subhadeep Das, Reeba S Jacob. **Patent file no. 201721014784**

List of Publications

Peer reviewed articles:

1. Vaibhav Srivastava, Ruth Amanna, Stephen J.L. Rowden, **Shinjinee Sengupta**, Swati Madhu, Christopher J. Howe, Pramod P. Wangikar, Adaptive laboratory evolution of the fast-growing cyanobacterium Synechococcus elongatus PCC 11801 for improved solvent tolerance, 2021, ***Journal of Bioscience and Bioengineering***, In Press.

2. **Shinjinee Sengupta**, Damini Jaiswal, Annesha Sengupta, Shikha Shah, Shruti Gadagkar and Pramod P. Wangikar, Metabolic engineering of a fast-growing cyanobacterium Synechococcus elongatus PCC 11801 for photoautotrophic production of succinic acid, 2020, ***Biotechnology for Biofuels***, 13, Article number 89.

3. Damini Jaiswal, Annesha Sengupta, **Shinjinee Sengupta**, Swati Madhu, Himadri Pakrasi, and Pramod Wangikar, A Novel Cyanobacterium Synechococcus elongatus PCC 11802 has Distinct Genomic and Metabolomic Characteristics Compared to its Neighbor PCC 11801, 2019, ***Scientific Reports***, 13, 10(1):191.

4. Damini Jaiswal, Annesha Sengupta, Sujata Sohoni, **Shinjinee Sengupta**, Ambarish G. Phadnavis, Himadri B. Pakrasi & Pramod P. Wangikar, Genome Features and Biochemical Characteristics of a Robust, Fast Growing and Naturally Transformable Cyanobacterium *Synechococcus elongatus* PCC 11801 Isolated from India, 2018, ***Scientific Reports*** volume 8, Article number: 16632

5. Saikat Ghosh[#], Shimul Salot[#], **Shinjinee Sengupta**[#], Ambuja Navalkar, Dhiman Ghosh, Reeba Jacob, Subhadeep Das, Rakesh Kumar, Narendra Nath Jha, Shruti Sahay, Surabhi Mehra, Santanu K. Ghosh, Mamata Kombrabail, G Krishnamoorthy, Pradip Chaudhari, and Samir K Maji[*]. p53 amyloid formation leading to its loss of function: Implication in cancer pathogenesis. ***Cell death and Differentiation.*** [#] **Equal contribution**. 2017, 24, pages 1784–1798.

6. Shakri Banerjee, Trina Dutta, Sagar Lahiri, **Shinjinee Sengupta**, Anushila Gangopadhya, Suresh Karri, Sandeep Chakraborty S, Debashish Bhattacharya and Anil K. Ghosh. 2015, ***Biochemistry and Biophysics Reports*** 4,59-75.

7. **Shinjinee Sengupta**, Shakri Banerjee, Sagar Lahiri, Trina Dutta, Tarun K. Dhar and Anil K. Ghosh, Purification, characterization, sequencing and molecular cloning of a novel cysteine methyltransferase that regulates trehalose-6-phosphate synthase from *Saccharomyces cerevisiae*. ***Biochimica et Biophysica Acta (BBA) - General Subjects***, 2014, 1840(6),1861-1871.

8. Sagar Lahiri, Shakri Banerjee, Trina Dutta, **Shinjinee Sengupta**, Sandip Dey, Rusha Roy, Devlina Sengupta, Krishnanendu Chattopadhyay and Anil K. Ghosh. Enzymatic and regulatory attributes of Trehalose-6-Phosphate Phosphatase from *Candida utilis* and its role during thermal stress, ***Journal of Cellular Physiology,*** 2014, 229(9),1245-55**.**

9. Sagar Lahiri, Arghya Basu, **Shinjinee Sengupta**, Shakri Banerjee, Trina Dutta, Krishnanendu Chattopadya and Anil K. Ghosh. Purification and characterization of trehalase-invertase dual activity enzyme from *Candida utilis*, ***Archives of Biochemistry and Biophysics***. 2012, 522(2), 90-99.

10. **Shinjinee Sengupta**, Sagar Lahiri, Shakri Banerjee, Trina Dutta and Anil K. Ghosh. Methylation dependent regulation of trehalose metabolism in *Candida utilis*. ***Carbohydrate Research*****,** 2012**,** 361(1), 175-181.

11. Trina Dutta, Shakri Banerjee, Dhananjay Soren, Sagar Lahiri, **Shinjinee Sengupta,** Juhi Rasquinha and Anil K. Ghosh. Regulation of enzymatic activity by edeamidation and their subsequent repair by protein L-isoaspartyl Methyl Transferase, 2 **Applied Biochemistry and Biotechnology**, 2012, 168(8), 2358-2375.

12. **Shinjinee Sengupta**, Sagar Lahiri, Shakri Banerjee, Bipasha Bashistha and Anil K. Ghosh. Arginine mediated purification of trehalose-6-phosphate synthase (TPS) from *Candida utilis*: it characterization and regulation. , **Biochimica et Biophysica Acta (BBA) - General Subjects**, 2011, 1810(12), 1346-1354

13. **Shinjinee Sengupta**, Paramita Chowdhury, Sagar Lahiri, Trina Dutta, Shakri Banerjee, Randhan Majhi and Anil K. Ghosh. Possible Regulation of Trehalose Metabolism by Methylation in *Saccharomyces cerevisiae**, Journal of Cellular Physiology***, 2010, 226(1), 158-164.

14. **Shinjinee Sengupta** and Rajesh Tandon. Assessment of ovule receptivity as a function of expected brood size in flowering plants, **International Journal of Plant Reproductive Biology** 2010, 2(1),1-13.

15. Paramita Chowdhury, Arghya Basu, **Shinjinee Sengupta**, Sagar Lahiri, Trina Dutta and Anil K. Ghosh. Studies on substrate specificity and activity regulating factors of trehalose-6-phosphate synthase of *Saccharomyces cerevisiae*, ***Biochimica et Biophysica Acta (BBA) - General Subjects***, 2009, 1790(5), 368-374.

Patents filed

1. Patent granted on "Amyloid mediated cell line transformation". Inventors: Samir K Maji, Saikat K Ghosh, **Shinjinee Sengupta**, Shimul Salot, Ambuja Navalkar, Subhadeep Das, Reeba S Jacob. Patent no. 361011.

2. Patent filled on "Method for photoautotrophic production of succinate using recombinant Synechococcus sp" Pramod Wangikar, **Shinjinee Sengupta**, Deepti Shrahastrabudhi, Swati Madhu and Damini Jaiswal. Patent application no. 202121022027.

Book Chapter

1. Arora, N., Jaiswal, D., **Sengupta, S**., Wangikar, P.P., 2020. Metabolic engineering of cyanobacteria for production of platform chemicals: A synthetic biology approach. In: Konur, O. (Ed.) The Handbook of Algal Science, Microbiology, Technology, and Medicine. Elsevier, Amsterdam, In Press.

Publications under review.

1. **Shinjinee Sengupta**, Deepti Sahasrabuddhe and Pramod P. Wangikar, Transporter Engineering for the development of Cyanobacteria as cell factories: A Text Analytics guided survey, ***Biotechnology Advances***, Under major review.

2. D. Chatterjee, R.S. Jacob, R. Kumar, N. Singh, P. Kadu, L. Gadhe, **S. Sengupta**, A. Navalkar, S. Mehra, N.N. Jha, A. Anoop, S. Kumar, D. G. Dastidar, P. S Singru, S. Senapati and S. K Maji, Synergistic aggregation and functional amyloid formation by prolactin and galanin for their secretory granule storage and release ***Journal of Chemical Biology***, Manuscript to be communicated.

3. Deepti Sahasrabuddhe, **Shinjinee Sengupta**, Annesha Sengupta, Vivek Mishra and Pramod Wangikar, Cyanobacteria as renewable resource for biofuel production book chapter, Advanced biofuels technologies - Present status, challenges and future prospects, Ms Elsevier

Biotechnology for Biofuels

RESEARCH Open Access

Metabolic engineering of a fast-growing cyanobacterium *Synechococcus elongatus* PCC 11801 for photoautotrophic production of succinic acid

Shinjinee Sengupta[1,2], Damini Jaiswal[1], Annesha Sengupta[1], Shikha Shah[1,2], Shruti Gadagkar[1] and Pramod P. Wangikar[1,2,3*]

Abstract

Background: Cyanobacteria, a group of photosynthetic prokaryotes, are being increasingly explored for direct conversion of carbon dioxide to useful chemicals. However, efforts to engineer these photoautotrophs have resulted in low product titers. This may be ascribed to the bottlenecks in metabolic pathways, which need to be identified for rational engineering. We engineered the recently reported, fast-growing and robust cyanobacterium, *Synechococcus elongatus* PCC 11801 to produce succinate, an important platform chemical. Previously, engineering of the model cyanobacterium *S. elongatus* PCC 7942 has resulted in succinate titer of 0.43 g l^{-1} in 8 days.

Results: Building on the previous report, expression of α-ketoglutarate decarboxylase, succinate semialdehyde dehydrogenase and phosphoenolpyruvate carboxylase yielded a succinate titer of 0.6 g l^{-1} in 5 days suggesting that PCC 11801 is better suited as host for production. Profiling of the engineered strains for 57 intermediate metabolites, a number of enzymes and qualitative analysis of key transcripts revealed potential flux control points. Based on this, we evaluated the effects of overexpression of sedoheptulose-1,7-bisphosphatase, citrate synthase and succinate transporters and knockout of succinate dehydrogenase and glycogen synthase A. The final construct with seven genes overexpressed and two genes knocked out resulted in photoautotrophic production of 0.93 g l^{-1} succinate in 5 days.

Conclusion: While the fast-growing strain PCC 11801 yielded a much higher titer than the model strain, the efficient photoautotrophy of this novel isolate needs to be harnessed further for the production of desired chemicals. Engineered strains of *S. elongatus* PCC 11801 showed dramatic alterations in the levels of several metabolites suggesting far reaching effects of pathway engineering. Attempts to overexpress enzymes deemed to be flux controlling led to the emergence of other potential rate-limiting steps. Thus, this process of debottlenecking of the pathway needs to be repeated several times to obtain a significantly superior succinate titer.

Keywords: Cyanobacteria, Succinic acid, Metabolites, Flux control

Background

Increasing concerns over the depletion of fossil fuels and the rise in the levels of atmospheric carbon dioxide have led to significant efforts toward a sustainable, bio-based economy. It is envisaged that biomass-derived fuels and commodity and specialty chemicals will replace those

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p53 amyloid formation leading to its loss of function: implications in cancer pathogenesis

Saikat Ghosh[1,7], Shimul Salot[1,7], Shinjinee Sengupta[1,7], Ambuja Navalkar[1,7], Dhiman Ghosh[1], Reeba Jacob[1], Subhadeep Das[1,2], Rakesh Kumar[1], Narendra Nath Jha[1], Shruti Sahay[1], Surabhi Mehra[1], Ganesh M Mohite[1], Santanu K Ghosh[1], Mamata Kombrabail[3], Guruswamy Krishnamoorthy[4,5], Pradip Chaudhari[6] and Samir K Maji*[,1]

The transcriptional regulator p53 has an essential role in tumor suppression. Almost 50% of human cancers are associated with the loss of p53 functions, where p53 often accumulates in the nucleus as well as in cytoplasm. Although it has been previously suggested that amyloid formation could be a cause of p53 loss-of-function in subset of tumors, the characterization of these amyloids and its structure-function relationship is not yet established. In the current study, we provide several evidences for the presence of p53 amyloid formation (in human and animal cancer tissues); along with its isolation from human cancer tissues and the biophysical characterization of these tissue-derived fibrils. Using amyloid seed of p53 fragment (P8, p53(250-257)), we show that p53 amyloid formation in cells not only leads to its functional inactivation but also transforms it into an oncoprotein. The *in vitro* studies further show that cancer-associated mutation destabilizes the fold of p53 core domain and also accelerates the aggregation and amyloid formation by this protein. Furthermore, we also show evidence of prion-like cell-to-cell transmission of different p53 amyloid species including full-length p53, which is induced by internalized P8 fibrils. The present study suggests that p53 amyloid formation could be one of the possible cause of p53 loss of function and therefore, inhibiting p53 amyloidogenesis could restore p53 tumor suppressor functions.

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p53 has been cast as a sentinel of the cell because it safeguards cells against stress and aberrancies, which threaten the cellular and genomic integrity.[1,2] Disruption in native p53 expression and activity, particularly due to mutation, has been linked to the incidence and progression of cancer.[2,3] Under cellular stress, p53 is primarily involved in transcriptional activity and hence found mostly in the nucleus.[1,4] However, cytoplasmic inclusions of wild-type (WT) and mutant p53 have been observed in several malignant cancers.[5,6] Sequestration of p53 in cytoplasm as large protein aggregates may lead to severe impairment of p53-mediated responses and might inevitably aggravate unregulated cell growth and subsequent tumorigenesis.[5,6] Several reports provide an account of abnormal p53 aggregation and amyloid formation in cancer cells/tissues.[7–11] Amyloid formation is a result of anomalous protein folding, and their consequent aggregation,[12,13] which results in impairment of their regular functions and can have dire consequences for the cell. Amyloid forms of proteins have also shown the ability to 'seed' or initiate the aggregation of corresponding native protein molecules in the cellular milieu.[14] More importantly, several amyloids possess prion-like 'infectious' properties[15] wherein they can amplify themselves and transmit between cells, thus resulting in an extensive dissemination of the disease.[16] In this context, it has been suggested that p53 aggregates possess prion-like properties in cancer.[17–19]

In this study, we present direct evidences of p53 amyloids in human and animal cancer tissues including its isolation and structural characterization. Using a cell model, we show functional inactivation as well as gain-of-tumorigenic functions upon p53 amyloid formation. Further, we observed prion-like properties of p53 amyloids in cells suggesting that this could be the probable mechanism of cancer propagation. Therefore, targeting p53 amyloid formation would be an important approach toward development of cancer therapeutics.

Results

Human and animal cancer tissues contain p53 amyloid. Previously, several reports have suggested the formation of p53 oligomers and amyloids in various tumor tissues[7,9,10,20] using amyloid oligomer-specific antibody A11.[21] Amyloid-specific antibody OC[22] and amyloid-specific dye Thio S, however, were used to detect p53 amyloids in basal cell carcinoma tissues sample.[7] In this study, we used OC and Thio S dye to detect p53 amyloid in cancer tissues of human breast, human lung, human urothelial, mouse colon carcinoma and rat hepatocarcinoma. The H&E staining further confirmed the nature of cancer tissues (Supplementary

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Genome Features and Biochemical Characteristics of a Robust, Fast Growing and Naturally Transformable Cyanobacterium *Synechococcus elongatus* PCC 11801 Isolated from India

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Cyanobacteria provide an interesting platform for biotechnological applications due to their efficient photoautotrophic growth, amenability to genetic engineering and the ability to grow on non-arable land. An ideal industrial strain of cyanobacteria would need to be fast growing and tolerant to high levels of temperature, light, carbon dioxide, salt and be naturally transformable. In this study, we report *Synechococcus elongatus* PCC 11801, a strain isolated from India that fulfills these requirements. The physiological and biochemical characteristics of PCC 11801 under carbon and light-limiting conditions were investigated. PCC 11801 shows a doubling time of 2.3 h, that is the fastest growth for any cyanobacteria reported so far under ambient CO_2 conditions. Genome sequence of PCC 11801 shows genome identity of ~83% with its closest neighbors *Synechococcus elongatus* PCC 7942 and *Synechococcus elongatus* UTEX 2973. The unique attributes of PCC 11801 genome are discussed in light of the physiological characteristics that are needed in an industrial strain. The genome of PCC 11801 shows several genes that do not have homologs in neighbor strains PCC 7942 and UTEX 2973, some of which may be responsible for adaptation to various abiotic stresses. The remarkably fast growth rate of PCC 11801 coupled with its robustness and ease of genetic transformation makes it an ideal candidate for the photosynthetic production of fuels and chemicals.

Cyanobacteria are the only group of prokaryotes that perform oxygenic photosynthesis. They play an important role in aquatic ecosystems as primary producers because of their ability to fix CO_2 into reduced carbon substrates using solar energy[1]. The cyanobacterial phylum comprises diverse groups of organisms capable of inhabiting extreme environmental niches with a high degree of success. Moreover, cyanobacteria can grow on non-arable land and wastewater thereby minimizing competition with food and feed. The short life cycle, minimal nutrient requirements, high photosynthetic efficiency and amenability to genetic modifications make this photoautotrophic group of prokaryotes an attractive platform for biotechnological applications[2,3]. In a future biorefinery, engineered cyanobacteria may be deployed for the production of biofuels and platform chemicals using CO_2 as feedstock and by harnessing solar energy. While such processes may not be commercially viable at present, significant promise lies in the proof of concept studies that demonstrate pathway engineering of cyanobacteria to produce a number of chemicals[4]. Indeed, laboratory strains of cyanobacteria such as *Synechococcus elongatus*

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Adaptive laboratory evolution of the fast-growing cyanobacterium *Synechococcus elongatus* PCC 11801 for improved solvent tolerance

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Background

Cyanobacteria are emerging as a promising host for the production of high-value chemicals and biofuels (1). The advancement of genome engineering techniques and synthetic biology toolkits have significantly improved the ability to engineer these photosynthetic organisms (2). However, the production of chemicals is often limited by product toxicity, bio-reactor design, light penetration in high density cultures etc. Increasing the product tolerance has proven to increase the product titers and also gain knowledge about the tolerance mechanisms.

Microbial tolerance towards the product of interest can be improved by genetic engineering or by adaptive laboratory evolution (ALE), the latter being the focus of this study. ALE involves the adaptation of culture towards the gradual increasing stress levels. The serial sub-culturing in ALE allows the culture to accumulate mutations which can improve the tolerance towards the applied stress. Moreover, performing parallel ALE experiments helps in identifying common mutations in the independently evolved cultures which can be correlated to the acquired trait of increased tolerance. ALE has proven to increase the tolerance towards cadmium (from 4.6 µM to 9 µM) (3) and n-butanol (from 1.6 g/L to 4 g/L) (4) in *Synechocystis* PCC 6803 (hereafter *Synechocystis*).

In this study, the fast growing and naturally transformable cyanobacterium, *Synechococcus elongatus* PCC 11801 (hereafter PCC 11801) was evolved to tolerate higher concentrations of n-butanol and 2,3-butanediol (hereafter 2,3-BD).

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Purification, characterization, sequencing and molecular cloning of a novel cysteine methyltransferase that regulates trehalose-6-phosphate synthase from *Saccharomyces cerevisiae*

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ABSTRACT

Background: In *Saccharomyces cerevisiae* methylation at cysteine residue displayed enhanced activity of trehalose-6-phosphate synthase (TPS).
Methods: The cysteine methyltransferase (CMT) responsible for methylating TPS was purified and characterized. The amino acid sequence of the enzyme protein was determined by a combination of N-terminal sequencing and MALDI-TOF/TOF analysis. The nucleotide sequence of the CMT gene was determined, isolated from *S. cerevisiae* and expressed in *E. coli*. Targeted disruption of the CMT gene by PCR based homologous recombination in *S. cerevisiae* was followed by metabolite characterization in the mutant.
Results: The purified enzyme was observed to enhance the activity of TPS by a factor of 1.76. The 14 kDa enzyme was found to be cysteine specific. The optimum temperature and pH of enzyme activity was calculated as 30 °C and 7.0 respectively. The K_m V_{max} and K_{cat} against S-adenosyl-L-methionine (AdoMet) were 4.95 μM, 3.2 U/mg and 6.4 s^{-1} respectively. Competitive inhibitor S-Adenosyl-L-homocysteine achieved a K_i as 10.9 μM against AdoMet. The protein sequence contained three putative AdoMet binding motifs. The purified recombinant CMT activity exhibited similar physicochemical characteristics with the native counterpart. The mutant, Matα, *cmt*:: *kan*^{r} exhibited almost 50% reduction in intracellular trehalose concentration.
Conclusion: A novel cysteine methyltransferase is purified, which is responsible for enhanced levels of trehalose in *S. cerevisiae*.
General significance: This is the first report about a cysteine methyltransferase which performs S methylation at cysteine residue regulating TPS activity by 50%, which resulted in an increase of the intercellular stress sugar, trehalose.

1. Introduction

Trehalose is an important multifunctional, non-reducing disaccharide found in nature [1]. It is accumulated during periods of nutrient starvation, desiccation and heat shock [2]. This sugar serves as a stabilizer of cellular structures under stress conditions besides having an exceptional capacity to protect biological membranes and enzymes from the adverse effects of freezing or drying [3]. In *Saccharomyces cerevisiae*, trehalose pathway involves the transfer of glucose from uridine diphosphate glucose (UDPG) to glucose-6-phosphate (G-6-P) to form trehalose-6-phosphate (T-6-P) and uridine diphosphate (UDP) [4]. This step is catalyzed by the enzyme trehalose-6-phosphate synthase (TPS). Trehalose-6-phosphate is subsequently dephosphorylated in the next step by trehalose-6-phosphate phosphatase (TPP) to yield inorganic phosphate and trehalose [5].

Post-translational modifications of proteins like methylation play an important role in regulating protein functions [6]. Protein methylation has an important role in cellular signaling events [6]. Biological transmethylation reactions utilizing S-adenosyl methionine (AdoMet) as a methyl donor have attracted the attention of many biochemists. The reaction can be catalyzed by three major categories. N-methylation involved methylation of arginine, lysine, histidine side chains. O-methylation of either the internal carboxyl group of glutamate and isoaspartate residues or the C-terminal of the cysteine residue and S-Methylation of either cysteine or methionine residues [7,8].

Regulation of trehalose metabolism by Oxidized Adenosine (Adox) and AdoMet in *S. cerevisiae* was observed in this laboratory as evident from the previous report [9]. Recent reports from this laboratory have confirmed that methylation of trehalose-6-phosphate synthase (TPS) in the presence of AdoMet resulted in enhanced activity and subsequently increased trehalose production [10]. It was observed that the TPS methylation occurred at the cysteine residue thus suggesting a

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A Novel Cyanobacterium *Synechococcus elongatus* PCC 11802 has Distinct Genomic and Metabolomic Characteristics Compared to its Neighbor PCC 11801

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Cyanobacteria, a group of photosynthetic prokaryotes, are attractive hosts for biotechnological applications. It is envisaged that future biorefineries will deploy engineered cyanobacteria for the conversion of carbon dioxide to useful chemicals via light-driven, endergonic reactions. Fast-growing, genetically amenable, and stress-tolerant cyanobacteria are desirable as chassis for such applications. The recently reported strains such as *Synechococcus elongatus* UTEX 2973 and PCC 11801 hold promise, but additional strains may be needed for the ongoing efforts of metabolic engineering. Here, we report a novel, fast-growing, and naturally transformable cyanobacterium, *S. elongatus* PCC 11802, that shares 97% genome identity with its closest neighbor *S. elongatus* PCC 11801. The new isolate has a doubling time of 2.8 h at 1% CO_2, 1000 µmole photons.m^{-2}.s^{-1} and grows faster under high CO_2 and temperature compared to PCC 11801 thus making it an attractive host for outdoor cultivations and eventual applications in the biorefinery. Furthermore, *S. elongatus* PCC 11802 shows higher levels of key intermediate metabolites suggesting that this strain might be better suited for achieving high metabolic flux in engineered pathways. Importantly, metabolite profiles suggest that the key enzymes of the Calvin cycle are not repressed under elevated CO_2 in the new isolate, unlike its closest neighbor.

Cyanobacteria are a group of prokaryotes that are capable of carrying out oxygenic photosynthesis. These microorganisms have gained attention in the field of biotechnology due to their efficient photoautotrophy, genetic amenability, and the potential for direct conversion of carbon dioxide (CO_2) to useful products. Engineered cyanobacteria have been reported for the production of a wide variety of chemicals, albeit at titers that are well below those needed for commercial production[1–9]. Majority of these studies have employed model strains such as *Synechocystis* sp. PCC 6803, *Synechococcus elongatus* PCC 7942, and *Synechococcus* sp. PCC 7002 (henceforth referred to as PCC 6803, PCC 7942, and PCC 7002, respectively, for brevity). Substantial information is now available on transcriptome, proteome, metabolome, and synthetic biology tools of these model cyanobacteria[10–15]. Thus, these strains and other closely related cyanobacteria would be favorable choices as hosts for chemical production. Further, it is believed that fast-growing strains that afford more efficient photoautotrophy will be better suited as hosts for metabolic engineering[16–18]. Moreover, organisms that are tolerant to high temperatures, light, and CO_2 levels are desirable as industrial strains considering the eventual outdoor utilization in biorefineries.

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