Synthetic biology to engineer *E. coli* as more industrially applicable host

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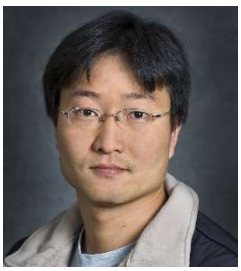

Abstract

The following five host characteristics would be keys to bring a microbe closer to industrial application: i) deep understanding of the host metabolism, ii) availability of genetic tools, iii) capacity to grow on inexpensive carbon sources with a short doubling time, iv) an autonomous, inducer-free expression system that does not allow accumulation of toxic metabolites, and v) chromosomally integrated pathway operons to avoid genetic instability and the use of expensive antibiotics required to maintain plasmids.

Escherichia coli has been the organism of choice for the production of different chemicals by engineering native and heterologous pathways. However, there are several issues to using *E. coli* as an industrial host, including i) susceptibility to phage contamination, ii) inefficiency in growing on certain desirable carbon sources (especially sucrose), and iii) low recombination capacity of DNA into its chromosome. The first two issues have been previously addressed. Countermeasures for bacteriophage contamination have been developed, and engineering approaches to introduce effective sucrose utilization capabilities are now available even though most industrial strains cannot grow on sucrose.

In this talk, we report our recent synthetic biology efforts to engineer *E. coli* as an industrially more applicable host. Our attempts include sucrose utilization, stress-responsive control of the biosynthetic pathway, autonomous inducer-free expression of the biosynthetic pathway using Quorum-sensing system, redirecting metabolic flux via combinatorial multiplex CRISPRi-mediated repression, and advanced method of chromosomal integration and expansion of the biosynthetic pathway.

Brief Biography

Dr. Taek Soon Lee is a Staff Scientist at Biological Systems and Engineering Division of LBNL and serving as a Director of Pathway and Metabolic Engineering at Joint BioEnergy Institute. Dr. Lee earned a B.S. in Chemistry at Seoul National University (Korea) and a Ph.D. in Chemistry at Stanford University studying type II aromatic polyketide synthases with

Professor Chaitan Khosla. After a postdoctoral training at University of California, Berkeley with Professor Jay D. Keasling, Dr. Lee started his own career as a Scientist at Lawrence Berkeley National Laboratory (LBNL) and joined as a Director of Metabolic Engineering at the Joint BioEnergy Institute (JBEI), one of three US Department of Energy (DOE)'s Bioenergy Research Centers. Dr. Lee's work at JBEI includes the application of synthetic biology and multiple omics tools to engineer metabolic pathways for production of biofuels and biochemicals. Dr. Lee has co-authored over 50 papers and 6 patents.

Brief CV

Taek Soon Lee, PhD

Staff Scientist, Biological Systems and Engineering Division, Lawrence Berkeley National Laboratory, USA

Education:

Ph.D., Chemistry, Stanford University, Stanford, CA
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Professional Career:

2016-current Staff Scientist, Biological Systems and Engineering (BSE) Division, Lawrence Berkeley National Laboratory (LBNL), Director of Pathway and Metabolic Engineering, Biofuels and Bioproducts Division, Joint BioEnergy Institute (JBEI), Emeryville, CA

2016-2018 Deputy Vice President, Fuels Synthesis Division, Joint BioEnergy Institute (JBEI), Emeryville, CA

2012-2016 Research Scientist, Physical Biosciences Division, LBNL, Director of Metabolic Engineering, Fuels Synthesis Division, JBEI

2008-2012 Project Scientist, Physical Biosciences Division, LBNL, Director of Metabolic Engineering, Fuels Synthesis Division, JBEI

2006-2008 Postdoctoral researcher, Physical Biosciences Division, LBNL

Research Interests:

1. Metabolic Engineering and Synthetic Biology
2. Isoprenoid biosynthesis
3. New pathways for biofuels and bioproducts

Selected publications

1. Kang, A., et al. *Metabol. Eng*. **2019**, (doi: 10.1016/j.ymben.2019.09.003)
2. Tian, T., et al. *ACS Synth Biol.* **2019**, (doi: 10.1021/acssynbio.8b00429)
3. Goyal, G., et al. *ACS Synth Biol.* **2018**, (doi: 10.1021/acssynbio.8b00243)
4. George, K.W., et al. *Metabol. Eng*. **2018**, *47*, 60-72 (doi: 10.1016/j.ymben.2018.03.004)
5. Alonso-Gutierrez, J., et al. *Biotechnol Bioeng*, **2017**, (doi: 10.1002/bit.26530)
6. Kim, E.M., et al. *Metabol. Eng*. **2017**, *44*, 325-336 (doi: 10.1016/j.ymben.2017.11.004)
7. Kang, A., et al. *Metabol. Eng*. **2017**, *41*, 125-134 (doi: 10.1016/j.ymben.2017.03.010)