Efficient Production of Value-added Chemicals in Cyanobacteria by Metabolic Regulation Using Light Sensor Proteins

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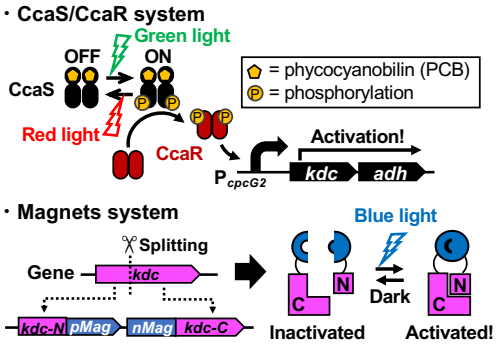
Cyanobacteria have been engineered by integrating heterologous biosynthetic pathways to produce value-added chemicals from CO_2. As the timings of gene expression and/or enzyme activation are critical factors for efficient production, the chemical inducer-dependent production has been demonstrated. However, the use of the chemical inducers is not ideal for scale-up production because of its high operation costs. In this study, to avoid the use of chemical inducers, we attempted the light-induced production of valuable alcohols in *Synechocystis* sp. PCC 6803 (PCC 6803) using two light sensor proteins, CcaS and Magnets (Fig.). The green light sensor protein CcaS regulates the ON/OFF of gene expression by green/red light, coworking with transcription factor CcaR[1]. Whereas the Magnets consisting of pMag and nMag forms heterodimer by blue light[2].



Isobutanol and 3-methyl-1-butanol (3MB) are valuable alcohols as alternatives to gasoline and can be produced by integrating two enzymes, keto-acid decarboxylase (KDC) and alcohol dehydrogenase (ADH), into the amino acid biosynthesis pathway[3]. When the *kdc* and *adh* were expressed under the control of CcaS/CcaR system, we found that the production of alcohols was induced under red and green light illumination and repressed under red light illumination alone. Production titers of isobutanol and 3MB reached 238 mg L^{-1} and 75 mg L^{-1}, respectively, and these values are comparable to those reported in previous studies using chemical inducers. Then, after splitting KDC into two fragments, we designed a blue light responsive KDC (OptoKDC) by fusing pMag and nMag to the N- and C-terminal fragment of the split KDC, respectively (Fig.). When the OptoKDC was expressed in *E. coli*, we found that isobutanol production was induced by blue light and repressed by dark or red light, suggesting that the OptoKDC has a potential for application in PCC 6803. This study demonstrates the potential use of the light sensor proteins for production of valuable chemicals in cyanobacteria.

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