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Applied Microbiology and Biotechnology

ISSN 0175-7598

Appl Microbiol Biotechnol
DOI 10.1007/s00253-013-5100-x

Springer

Appl Microbiol Biotechnol
DOI 10.1007/s00253-013-5100-x

MINI-REVIEW

Inducible cell lysis systems in microbial production of bio-based chemicals

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Received: 1 April 2013 / Revised: 4 July 2013 / Accepted: 5 July 2013

Abstract The release of products from microbial cells is an essential process for industrial scale production of bio-based chemicals. However, traditional methods of cell lysis, e.g., mechanical disruption, chemical solvent extraction, and immobilized enzyme degradation, account for a large share of the total production cost. Thus, an efficient cell lysis system is required to lower the cost. This review has focused on our current knowledge of two cell lysis systems, bacteriophage holin–endolysin system, and lipid enzyme hydrolysis system. These systems are controlled by conditionally inducible regulatory apparatus and applied in microbial production of fatty acids and polyhydroxyalkanoates. Moreover, toxin–antitoxin system is also suggested as alternative for its potential applications in cell lysis. Compared with traditional methods of cell disruption, the inducible cell lysis systems are more economically feasible and easier to control and show a promising perspective in industrial production of bio-based chemicals.

Keywords Cell lysis systems · Inducible regulatory apparatus · Holin–endolysin system · Lipid enzyme system · Toxin–antitoxin system

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Introduction

Metabolic pathway engineering has driven the development of commercially viable processes for production of bio-based chemicals (Millard et al. 1996). So far, a variety of bio-based chemicals including aromatic compounds, carbohydrates, organic acids, alcohols, and other secondary metabolites has been produced by microbial fermentation. Of all these bio-products, some are easy to be released from the host cells, such as amino acids (Berry 1996; Ikeda and Katsumata 1999; Ito et al. 1990), succinic acid (Millard et al. 1996), lactic acid (Zeikus 1980), ethanol (Moniruzzaman and Ingram 1998), glycerol (Albertyn et al. 1994; Ben-Amotz and Avron 1979; Steinbüchel and Müller 1986), and 1,3-propanediol (Biebl et al. 1992). However, others like fatty acids and polyhydroxyalkanoates (PHAs) cannot be released from the cell.

Fatty acids are important precursors for biodiesel synthesis and can be converted to biodiesel by esterification with methanol or ethanol. For fatty acid production on a large scale, the most efficient way is to cultivate and extract fatty acids from oil-rich cyanobacteria and microalgae which can directly convert solar energy and CO_2 into fuels (Peralta-Yahya and Keasling 2010). PHAs are a family of structurally diverse polyesters accumulated by many bacteria and can be applied in the fields of bioplastics, fine chemicals, implant biomaterials, medicines, and biofuels (Chen 2009). To extract fatty acids and PHAs from their hosts, cell disruption is often a necessary step (Mendes-Pinto et al. 2001). The mechanical methods for cell disruption, like high-speed agitator bead mill and high-pressure homogenizers, are popular for industrial production due to their convenience without chemical interaction between cells and media (Zhang et al. 1999). Ultrasonication is one of the favorite physical methods employed for cell disruption especially at a laboratory scale (Feliu et al. 1998; Ho et al. 2006). It can lyse a wide range of bacteria cells according to the power of acoustic waves and

Published online: 20 July 2013

the physical strength of the cell walls (Choonia and Lele 2011). Iida et al. (2008) combined ultrasonication and mechanical homogenization for baker's yeast cell disruption and obtained a better protein release than either of them. Of all these physical methods, grinding in liquid nitrogen is the quickest method that only needs 2 min to process 500 ml microalgae cells for the lipids release (Zheng et al. 2011). There are also some other physical methods of cell disruption such as bead-beater pulsed electric field and laser treatment in oil extraction from microalgae (McMillan et al. 2013; Sheng et al. 2011). However, low energy efficiency owing to the dissipation by generating high temperature is the most obvious disadvantage of these methods.

Chemical methods including organic solvent extraction, alkali or detergent treatment of cells, also have been widely applied for intracellular substances extraction (Numanoğlu and Sungur 2004). For instance, chloroform was usually used to extract PHAs from dry biomass. Combined with acetone pretreatment and ethanol precipitation, chloroform extraction recovered poly(β-hydroxybutyrate) (PHB) with a purity of 95 % from lyophilized *Cupriavidus necator* cells (Ramsay et al. 1994). For large-scale production of poly(3-hydroxyoctanoate) (PHO), the precipitation solvent containing 70 % (*v*/*v*) methanol and ethanol with a ratio of 1:1 was employed and led to 94 % recovery and 99 % purity of PHO (Elbahloul and Steinbuchel 2009). Organic solvent extraction is also used to isolate lipids from cyanobacteria and microalgae; furthermore, cell membrane electroporation can improve the penetration of organic solvent through cell barrier and extracting efficiency (Hamilton and Sale 1967; Weaver and Chizmadzhev 1996). Besides mechanical and chemical methods, enzyme digestion is another useful way to disrupt the bacterial cells, but it is rather expensive when dealing with large amount of samples (Fu et al. 2010).

The product recovery from bacterial cells using traditional methods has been claimed to contribute to 20–30 % of the total production cost (Gudin and Thepenier 1986). Compared with bacteria, the cost of microalgae downstream processes is even higher and accounts for 70–80 % of the total production cost because the cell walls containing hemicellulose and saccharides are much thicker than that of bacteria (Molina Grima et al. 2003). To cut down the production cost, strains secreting the fermentation products automatically were designed and constructed by genetic modification. When *tesA* gene encoding thioesterase from *Escherichia coli* was introduced to *Synechocystis* sp. PCC 60803, the cellular acyl-acyl carrier proteins (ACPs) were converted into free fatty acids, relieving the inhibition of fatty acid synthesis by long-chain acyl-ACP and resulting in overproduction of cellular free fatty acids which promoted the fatty acid secretion to culture medium (Liu et al. 2011b; Fell 1997). Furthermore, weakened cell walls had a synergistic effect on fatty acid secretion (Liu et al. 2011b). In addition, the production of extracellular fatty acids had also been achieved in *E. coli* by TesA overexpression and deleting *fadL* gene to inhibit the β-oxidation pathway or reabsorbance of extracellular fatty acids (Liu et al. 2012). But the fatty acid-secreting strains still had some disadvantages, such as low growth rate and increased cell fragility which even caused cell damage at low cell density (Liu et al. 2011b). Simplified PHA extraction process based on osmotic lysis in the presence of alkali/detergent was performed using a novel moderately halophilic bacteria strain *Halomonas* sp. SK5 which could grow and accumulate PHA granules only in high-salinity environment (Rathi et al. 2013). In the presence of distilled water, the osmotic pressure difference between inside and outside cell will cause cell rupture and PHA release. This method resulted in approximately 90–100 % recovery of PHA with purity as high as 90 %; however, the use of high-salinity medium and alkali/detergent brought some economic and environmental issues. Thus, current work has focused on developing economically feasible mechanisms to release valuable bio-products by lysing host cells in a genetically-regulated manner.

Up to now, two strategies using bacteriophage holin–endolysin and lipid enzyme, respectively, have been tested for controllable cell lysis. The cell lysis systems were controlled by conditionally inducible regulatory apparatus and could be expressed with the presence of specific inducer or environmental condition, such as isopropyl β-D-thiogalactoside (IPTG), arabinose, xylose, and CO_2 depletion. Moreover, toxin–antitoxin system is also suggested as alternative for its potential applications in cell lysis.

Holin–endolysin system

The lysis process of *E. coli* phage λ has been regarded as the model to study the holin–endolysin lysis system (Fig. 1) (São-José et al. 2007). When separated from antiholin which has an inhibitory effect on the function of holin (Young 2002), the hydrophobic domain of holin monomer will insert into cell membrane and then oligomerize to form higher-order assembled holins (Grundling et al. 2000), developing into a hole large enough for about 500-kDa proteins to get though the cell membrane (Savva et al. 2008; Wang et al. 2003). Then accumulated endolysin in cytoplasm can be released into the periplasm, degrading the peptidoglycan in the cell wall (Loessner 2005). Four enzyme activities are associated with the endolysin: the glucosaminidase hydrolyzing the glycosyl–oxygen bond (Drulis-Kawa et al. 2012), the transglycosylase attacking the same bond but forming a muramic acid product (Blackburn and Clarke 2000), the amidase hydrolyzing the amide bond in the oligopeptide cross-linking chains (Low et al. 2005), and the endopeptidase attacking the cross-linking peptide

bonds (Donovan et al. 2006). In addition, Rz/Rz1 complex of phage λ can promote the fusion of inner membrane (IM) and outer membrane (OM), thus pushing the OM away from the murein layer and eliminating the last barrier (Young 1992; Berry et al. 2010; Berry et al. 2008).

To reduce the cost of PHB recovery from engineered *E. coli* strain, an autolysis system was developed using the lysis cassette of phage λ and the promoter of *Salmonella typhimurium* magnesium transporter gene *mgtB* (P_{mgtB}), which is activated only in the Mg^{2+}-depletion condition (Zhang et al. 2009). During fermentation, magnesium sulfate was added into the culture medium to inhibit the expression of lysis genes and promote the PHB accumulation. When the cells were harvested and resuspended in water or low ionic strength buffer, the promoter P_{mgtB} was activated and started the expression of phage λ lysis genes, resulting in immediate cell lysis (Zhang et al. 2009). Additionally, Resch et al. (1998) integrated the lysis gene *E* of bacteriophage ΦX174 downstream of the phage λ P_R promoter into the plasmid pSH2, controlled by the thermosensitive repressor CI857 encoded by the same plasmid. The protein E can complement phage λ *S* and *R* dysfunction for host cell lysis (Roof and Young 1993) and can introduce a transmembrane tunnel in the cell envelope complex with a diameter of 40–200 nm (Witte and Lubitz 1989; Witte et al. 1990). When the growth temperature was upshifted from 28 to 42 °C, the gene *E* was expressed with inactivation of CI857 repressor, leading to the collapse of cell membrane and the release of PHB granules.

Inducible holin–endolysin lysis system to release PHA was also achieved in other hosts. For example, the holin and endolysin genes of *Bacillus amyloliquefaciens* phage were inserted into the *amyE* locus of chromosomal DNA of *Bacillus megaterium*, a PHB-producing strain (Hori et al. 2002). The expression of holin–endolysin system was controlled by the regulatory system P_{xylA}-XylR, which is induced by xylose but inhibited by glucose (Rygus et al. 1991; Dahl et al. 1995). For PHB accumulation, the recombinant strain was grown in a medium containing glucose as carbon source in the presence of xylose. When the glucose in culture medium was exhausted, cell disruption was spontaneously induced, releasing intracellular PHB into culture broth (Hori et al. 2002). To construct a self-disruptive strain of medium-chain-length PHAs producer *Pseudomonas putida* KT2440, two strategies were applied simultaneously: the holin gene *ejh* and endolysin gene *ejl* from the pneumococcal bacteriophage EJ-1 (Díaz et al. 1996) integrated into the bacterial chromosome DNA and the *tolB* gene mutant exhibiting outer membrane integrity defect and lysis hypersensitivity. The expression of genes *ejh* and *ejl* was under the control of P_m-XylS monocopy expression system, and 3-methylbenzoate was used as inducer molecule to promote cell lysis (Martinez et al. 2011).

The holin–endolysin system was also used in microbial fatty acid production. A series of *Synechocystis* sp. PCC 6803 strains containing controllable lysis systems were designed and constructed in three strategies (Fig. 2) (Liu and Curtiss 2009). In strategy 1, the lysis genes from *Salmonella* phage P22 (*13 15 19*) and phage λ (*S R Rz*), respectively, were inserted into the chromosome of *Synechocystis* PCC 6803 downstream of the promoter P_{nrsB}, which is activated by addition of Ni^{2+}. The P22 lysis cassette could lyse the strains much faster after induction of Ni^{2+} than that of phage λ. In strategy 2, the P22 endolysin and the auxiliary

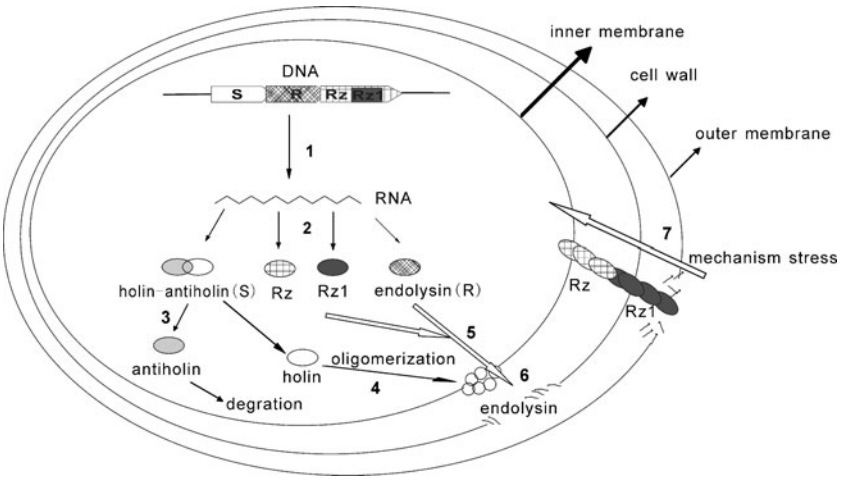

Fig. 1 The cell lysis process of phage λ holin–endolysin system. *1* Transcription: the genes of holin, endolysin, and Rz/Rz1 transcribe into corresponding messenger RNA (mRNA); *2* translation: the holin and antiholin is co-expression, forming holin–antiholin complex; *3* the antiholins are degraded by specific proteinase, and functional holins are released; *4* holins accumulate in the cell membrane, forming the hole for 500-kDa protein to get through; *5* the endolysin and Rz and Rz1 are released into periplasm and Rz and Rz1 are located to the IM and OM, respectively; *6* enzymolysis: the endolysin hydrolyzes the peptidoglycan, degrading the cell wall; and *7* the Rz and Rz1 proteins link the IM and OM, transmitting mechanical stress from IM and forcing the disruption of OM

lysis factor genes *19* and *15* were overexpressed under a constitutive promoter P_{psbAII}, while expression of the holin gene *13* was regulated by P_{nrsB}. Before Ni^{2+} induction, the lysis enzymes were accumulated in the cytosol. When Ni^{2+} was added into the culture, the holin protein was synthesized, thus helping the accumulated lysis enzymes to cross the cytoplasmic membrane and collapse the cell wall. As expected, strain SD123 constructed using strategy 2 exhibited a significantly faster lysis rate than strain SD121 in strategy 1. Strategy 3 was to incorporate the lysis genes from λ with P22 lysis genes. The endolysin and the auxiliary lysis factor genes, P22 *19 15*, and λ *R Rz*, were inserted downstream of the promoter P_{psbAII}. At the same time, the holin genes, P22 *13*, and λ *S*, were controlled by the P_{nrsB} promoter. The strategy 3 strain SD127 performed successful inducible cell lysis; however, its growth rate was slower than strain SD123. Due to the fact that all strains constructed using three strategies grew much slower than the wild-type strain, which might be caused by the basal transcription of P_{nrsB} promoter before Ni^{2+} induction (López-Maury et al. 2002), further studies should focus on screening for a strain with both higher growth rate and faster lysis rate.

Lipid enzyme system

As been well known, the cell membrane is generally comprised of proteins and membrane lipids, such as glycerides, phospholipids, and glycolipids, and the lipolytic enzymes can hydrolyze the carboxylic ester bonds to release fatty acids from acylglycerols. For example, galactolipase catalyzes the hydrolysis of galactolipids by removing one or two fatty acids (Helmsing 1969), and phospholipase B presenting both activities of phospholipase A1 and phospholipase A2 cleaves acyl chains from both the sn-1 and sn-2 positions of a phospholipid (Kohler et al. 2006). So cell lysis could be achieved using some proper lipid enzyme genes.

In cyanobacterium *Synechocystis* sp. PCC 6803 strain, Green Recovery strategy utilizing lipolytic enzymes was employed to convert membrane lipids into fatty acids and

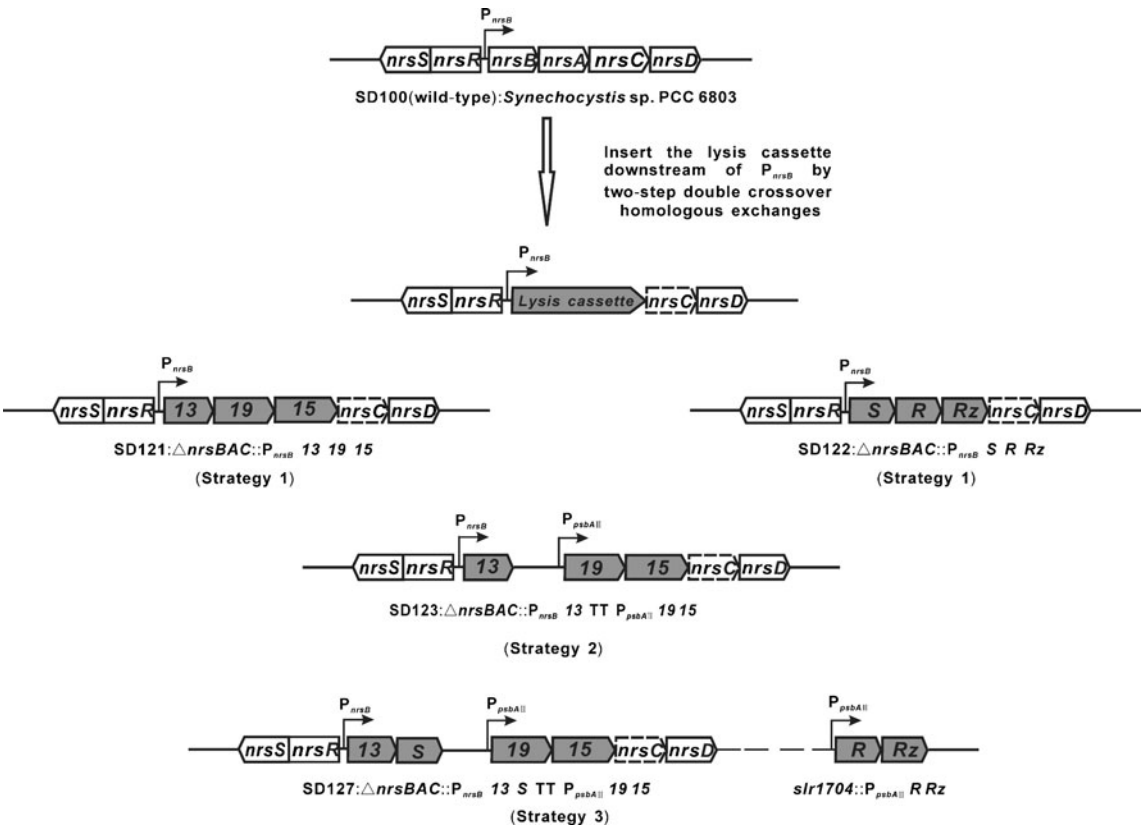

Fig. 2 The strategies used in Green Recovery process of *Synechocystis* sp. PCC 6803. The lysis cassette (*shaded area*) was inserted downstream of P_{nrsB} by two-step double crossover homologous exchanges, deleting the *nrsB* and *nrsA* fragments in the chromosome at the same time. *nrsR* and *nrsS*, nickel-sensing and -responding genes; *nrsA*, *nrsB*, *nrsC*, and *nrsD*, nickel-resistance genes; P_{psbAII}, a constitutive promoter of *Synechocystis* gene *psbAII*; P_{nrsB}, the nickel inducible promoter; *13* holin, *19* endolysin, and *15* auxiliary lysis enzyme are the cell lysis genes from *Salmonella* phage P22; *S* holin, *R* endolysin, and *Rz* auxiliary lysis enzyme are the lysis genes from *E. coli* phage λ; TT transcriptional terminator from cyanophage Pf-WMP4

destroy the cell (Liu et al. 2011a). As CO_2 is the raw material of photosynthesis, CO_2-containing air was used to bubble the culture medium and the concentration of CO_2 is controlled exactly. To induce the expression of lipid enzymes efficiently and economically after fatty acid accumulation, the promoter P_{cmp} activated by CO_2 limitation (McGinn et al. 2003) was selected to control the lipid enzyme genes. When lowering the CO_2 concentration in the culture medium to near zero level by aeration with CO_2-free air for 30 min, the lipolytic enzyme genes started to express, increasing cell membrane permeability and releasing fatty acids. Three lipolytic enzymes were tested for their ability to hydrolyze membrane lipids, including the bacterial lipase from *Staphylococcus hyicus* (Shl) (Rosenstein and Gotz 2000), the modified fungal phospholipase from *Fusarium oxysporum* (Fol) (Rapp 1995), and the guinea pig lipase (Gpl) from the digestive juice of guinea pig (Andersson et al. 1996). Although Gpl was reported to show the highest galactolipase activity (Andersson et al. 1996), three strains carrying various lipid enzymes produced fatty acids at a similar level, and the Gpl resulted in a membrane damage rate much lower than Shl and Fol (Liu et al. 2011a). Green Recovery strategy is clearly an efficient and effective method for lipid recovery from biomass; however, there is still a problem in this system. The lipase synthesis requires adequate light to provide the energy while the concentrated cultures create a self-shading environment, making that Green Recovery had to be applied on unconcentrated cultures, which lowers efficiency. To solve this problem, thermorecovery system was developed, in which genes encoding thermophilic lipases were inserted into *Synechocystis* chromosome under the control of both the CO_2-depletion-inducible promoter P_{cmp} and the constitutive promoter P_{trc} (Liu and Curtiss 2012). During growth in an unconcentrated culture with plenty of light at ambient temperature, the thermophilic lipase was synthesized and accumulated due to the basal activity of promoter P_{trc} without affecting cell growth. Then the CO_2 limitation pretreatment boosted the synthesis of thermophilic lipase, which was activated by the subsequent temperature elevation of concentrated culture. In this study, the lipase Fnl from *Fervidobacterium modosum* Rt17-B1 (Yu et al. 2010) released the most fatty acids. Compared with Green Recovery, the biomass volume to be processed in thermorecovery was significantly reduced because of light-independence, resulting in the cost-decrease. It is expected that the efficiency of thermorecovery could be further improved by introducing additional thermophilic lipases with different substrate specificities to recover a greater fraction of the total membrane lipids.

Toxin–antitoxin system

For the possible applications in cell lysis, toxin–antitoxin system is suggested as an alternative to construct a self-disruption strain. Comparing with the holin–endolysin and lipid enzyme systems, toxin–antitoxin systems show a quite different mechanism of cell lysis, that can kill the host cells or cause apoptosis by inhibiting the replication of DNA, digesting mRNA, restraining the synthesis of proteins and so on (Chang et al. 1989; Sandvig and van Deurs 1992). In the cell death process, one key event is increasing of cell membrane permeability (Tsujimoto and Shimizu 2007), which will contribute to the release of intracellular substrates.

Genes encoding toxins and antitoxins are widespread in most prokaryotic chromosomes (Hayes 2003). The toxin–antitoxin system is generally comprised of two components: a comparable stable toxin protein targeting different cellular processes and inducing cell growth arrest or death and a labile antitoxin counteracting the action of toxin protein. The antitoxin protein is usually degraded by a specific intracellular protease such as Lon or ClpPA (Buts et al. 2005; Short et al. 2012; van Melderen et al. 1996). To construct an inducible cell lysis system, a conditionally inducible regulatory device is needed to prevent the expression of antitoxin or to elevate the toxin level in the cell.

Inducible regulatory apparatus

Due to the fact that the lysis systems above can cause growth inhibition or cell death, the expression of the cell lysis systems must be controlled by conditionally inducible regulatory apparatus strictly. We can choose the suitable promoter according to the different host cells and end products. Besides the conditionally inducible regulatory apparatus discussed above, some other regulatory devices were also used to control the cell lysis systems (Table 1). In cheese fermentation strain *Lactococcus lactis*, the promoter P_{nisA} induced by antimicrobial peptide nisin, was employed to control the expression of the lytic genes *lytA* (lysin) and *lytH* (holin) from lactococcal bacteriophage ΦUS3. The nisin-induced cell lysis led to releasing of intracellular proteolytic and esterolytic enzymes, accelerating cheese ripening and contributing to the flavor development (de Ruyter et al. 1997). The regulatory systems having been used to control the cell lysis process also include P_{BAD}-AraC system sensing L-arabinose (Guzman et al. 1995; Lim et al. 2012), P_{lac}-LacI system responsible to lactose and its derivative IPTG (Lubitz et al. 1981; Henrich et al. 1982), and chloride-inducible system P_{gad}-GadR (Sanders et al. 1997). In addition, some tight regulatory systems, like tetracycline-inducible system P_{tetA}-TetR (Skerra 1994; Wirtz et al. 1999), are also the alternatives to control the cell lysis.

However, there are still some problems in the currently used regulatory devices. First, the addition of inducers is mandatory and brings some economic and environmental concerns. IPTG is relatively expensive and has toxic effect

Table 1 Conditionally-inducible systems and their applications

Inducible regulatory systems			Lysis systems		Remarks	References
Name	Source	Inducer	Lysis genes	Source		
P_{xylA}-XylR system	*B. megaterium*	Xylose	Holin and endolysin genes	*B. amyloliquefaciens* phage	The expression is inhibited by glucose, and the regulation is more effective in strains not utilizing xylose	(Hori et al. 2002)
P_{nrsB}-NrsRS system	*Synechocystis* sp. PCC 6803	Ni^{2+}	*13 19 15* *S R Rz*	*Salmonella* phage P22 phage λ	The inducer nickel compound is relatively expensive and toxic to the environment	(Liu and Curtiss 2009)
P_{cmp} promoter	*Synechocystis* sp. PCC 6803	CO_2 limitation	Lipase gene *shl* Lipase gene *fol* Lipase gene *gpl*	*S. hyicus* *F. oxysporum* Guinea pig	Limiting CO_2 concentration is an ideal method to initiate cell lysis of cyanobacteria as aeration to photobioreactor is necessary and easy to control. Releasing fatty acids from membrane lipids further improves the fatty acids production	(Liu et al. 2011a)
P_{BAD}-AraC system	*E. coli*	L-abinose	Holin, endolysin, and Rz/Rz1-like protein	*Salmonella* phage SPN1S	The expression of genes controlled by P_{BAD}–AraC system is tightly regulated corresponding to the intracellular L-arabinose concentration. The regulation is more effective in strain not utilizing L-arabinose	(Lim et al. 2012)
P_{gad}-GadR system	*L. lactis*	chloride ions	Holin–lysin genes *lytPR* Autolysin gene *acmA*	*L. lactis* phage r1t *L. lactis*	The activation of promoter P_{gad} need large amount of NaCl, which can reduce salt-sensitive microorganism contamination and meanwhile produce high-salinity waste water	(Sanders et al. 1997)
P_R-CI857 system	phage λ	42 °C	Lysis gene *E*	*E. coli* phage ΦX174	The thermosensitive mutant of CI repressor is used in this system. High temperature can inactivate CI857 repressor and start the expression of genes controlled by P_R promoter	(Resch et al. 1998)
P_m-XylS system	*P. putida*	3-methylbenzoate	Holin gene *ejh* and endolysin gene *ejl*	pneumococcal phage EJ-1	It is a two-step induction process. The inducer 3-methylbenzoate activates the expression of gene *xylS* and then XylS gene induces the transcription of P_m promoter. The inducer 3-methylbenzoate is toxic	(Martinez et al. 2011)
P_{lac}-LacI system	*E. coli*	IPTG	Lysis gene *E*	*E. coli* phage ΦX174	The inducer IPTG is too expensive	(Henrich et al. 1982)
P_{mgtB} promoter	*S. typhimurium*	Mg^{2+}-depletion	*S R Rz*	phage λ	It does not need addition of inducer, and is an economical and environmental-friendly method to start the cell lysis process	(Zhang et al. 2009)
P_{nisA} promoter	*L. lactis*	nisin	Lysine gene *lytA* and holin gene *lytH*	lactococcal phage ΦUS3	The inducer nisin is an antimicrobial peptide and natural preservative, reducing the contamination of bacteria. But it is too costly	(de Ruyter et al. 1997)

on cell growth (Baneyx 1999), and the use of nickel increases production cost and causes environmental pollution as well as the high-salinity medium to activate the promoter P_{gad}. So the cell lysis systems need to be regulated economically and environment-friendly. In this issue, the CO_2-limitation-inducible promoter in fatty acids recovery and the Mg^{2+}-depletion sensing promoter in PHA production are the best choices for regulation of the cell lysis systems. Second, some chemical induction systems cause rapid accumulation of target proteins within a short period (van den Berg et al. 1999), resulting in the inclusion bodies without native biological activities. Therefore, the appropriate expression intensity is another criterion for selecting the regulatory apparatus.

Differently from that the cell lysis systems are controlled by inducible regulatory devices in most cases, automatic cell lysis also can be realized by downstream operation or chemical reagent. Yu et al. (2000) constitutively expressed the phage λ lysis genes with an *S* amber mutation (*S*⁻*RRz*) in a recombinant *E. coli* strain producing PHB. By introduction of the *S* amber mutation, the encoding of the *S* gene was unable to damage the cell membrane, and the endolysin R and auxiliary lysis factor Rz were synthesized and accumulated in the cytoplasm without restraining the growth of the host strain. At the end of fermentation, both EDTA and high-temperature treatment could cause the cell membrane damage, releasing R Rz to the periplasm and resulting in the cell wall degradation (Yu et al. 2000; Yu et al. 2003).

Conclusion

Conditionally inducible cell lysis system is an efficient and economical strategy to simplify the downstream purification and extraction process of some bio-based chemicals that fail to release from the cells. At present, the holin–endolysin system and the lipid enzyme system have been successfully used to release fatty acids and PHAs from their host cells. Another system, the toxin–antitoxin system, is discussed about its potential use in cell lysis. It is believed that more lysis systems with different mechanisms and suitable regulatory apparatus will be used in this field in the future. Currently, the usage of conditionally inducible lysis systems is still restricted on the laboratory pilot scale. The principle task is to exploit the applications of conditionally inducible cell lysis systems in industrial production of bio-based chemicals for cost reduction.

Acknowledgment This research was financially supported by 100-Talent Project of CAS (for GZ), Director Innovation Foundation of QIBEBT, CAS (Y112141105), National Natural Scientific Foundation of China (31200030), National Science and Technology Program (2012BAD32B06), and National 863 Project of China (SS2013AA050703-2).

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