

SUPPLEMENTARY MATERIAL

Global response of *Phaeobacter inhibens* DSM 17395 to deletion of its 262 kb chromid encoding antibiotic synthesis

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The compound and enzyme names (alphabetic order) as used in Fig. 2 in the manuscript are as follows:

2-ABz, 2-aminobenzoate; 2-ABz-CoA, 2-aminobenzoyl-CoA; 2-OG, 2-oxoglutarate; 3-OxoSubCoA, 3-oxosuberoyl-CoA; aatA, aspartate aminotransferase; AcCoA, acetyl-CoA; acdA1, acyl-CoA dehydrogenase; acnA, aconitate hydratase; Ala, alanine; ald, alanine dehydrogenase; Asp, aspartate; bhbA, methylmalonyl-CoA mutase; c00380, maleylacetoacetate isomerase; c01220, 3-hydroxybutyryl-CoA dehydrogenase; c09350, class III aminotransferase; c16590, transketolase; c17080, pyruvate ferredoxin/flavodoxin oxidoreductase; c23440, benzoate-CoA ligase; c23490, NADH:flavin oxidoreductase/NADH oxidase; c27870, CoA-transferase-family III; c29640, predicted arylformamidase; c33040, aldehyde dehydrogenase; c33180, acetyl-CoA acetyltransferase; c33640, 2-oxoisovalerate dehydrogenase; c34400, class III aminotransferase; c36210, L-asparaginase II; c36500, enoyl-CoA hydratase/isomerase; Cit, citrate; fadJ, fatty acid oxidation complex; fah, fumarylacetoacetate; Fum, fumarate; fumC, fumarate hydratase class II; gcdH, acyl-CoA dehydrogenase; gcvH, glycine cleavage system protein; gcvP, glycine dehydrogenase; gcvT, aminomethyltransferase; gltA1, citrate synthase; Glu, glutamate; gluD, glutamate dehydrogenase; Gly, glycine; glyA, serine hydroxymethyltransferase; Hibch, 3-hydroxyisobutyryl-CoA hydrolase; His, histidine; hmgA, homogentisate 1,2-dioxygenase; hpd, 4-hydroxyphenylpyruvate dioxygenase; hutF, formiminoglutamate deiminase; hutG, *N*-formylglutamate deformylase; hutH, histidine ammonia-lyase; hutI, imidazolonepropionase; hutU, urocanate hydratase; icd, isocitrate dehydrogenase; iCit, isocitrate; Ile, isoleucine; ilvE, branched-chain amino acid aminotransferase; iorAB, indolepyruvate oxidoreductase; ivd, isovaleryl-CoA dehydrogenase; ivd, isovaleryl-CoA dehydrogenase; kbl, 2-amino-3-ketobutyrate-CoA ligase; kynA, tryptophan 2,3-dioxygenase; kynU, kynureninase; Ldc, lysine/ornithine decarboxylase; Leu, leucine; lpd2, dihydrolipoyl dehydrogenase 2; lpdA1-2, dihydrolipoyl dehydrogenase; Lys, lysine; Mal, malate; mccA, methylcrotonoyl-CoA carboxylase; mce, methylmalonyl-CoA epimerase; mdeA, methionine gamma-lyase; mdh, malate dehydrogenase; Met, methionine; mgh, enoyl-CoA hydratase; mmsA, methylmalonate-semialdehyde dehydrogenase; mmsB, 3-hydroxyisobutyrate dehydrogenase; mvaB, hydroxymethylglutaryl-CoA lyase; mvvB, methylcrotonoyl-CoA carboxylase subunit beta; OxAc, oxaloacetate; paaA-D, phenylacetic acid degradation protein; paaE, phenylacetic acid degradation NADH oxidoreductase; paaG, enoyl-CoA hydratase; paaJ, beta-ketoacidipyl-CoA thiolase; paaZ, phenylacetic acid degradation protein; pccA, propionyl-CoA carboxylase subunit alpha; pccB, propionyl-CoA carboxylase subunit beta; pdhA, pyruvate dehydrogenase E1 component subunit alpha; pdhB, pyruvate dehydrogenase E1 component subunit beta; pdhC, dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex; phaB, acetoacetyl-CoA reductase; phbA, acetyl-CoA acetyltransferase; Phe, phenylalanine; PhePyr, phenylpyruvate; PropCoA, propanoyl-CoA; Pyr, pyruvate; scoA, succinyl-CoA:3-ketoacid-coenzyme A transferase subunit A; scoB, succinyl-CoA:3-ketoacid-coenzyme A transferase subunit B; sdhA, succinate dehydrogenase flavoprotein subunit; sdhB, succinate

dehydrogenase iron-sulfur subunit; sdhC, succinate dehydrogenase cytochrome b_{556} subunit; sdhD, succinate dehydrogenase hydrophobic membrane anchor subunit; sucA, 2-oxoglutarate dehydrogenase E1 component; sucB, dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex; Succ, succinate; sucC, succinyl-CoA ligase subunit beta; Succ-CoA, succinyl-CoA; sucD, succinyl-CoA ligase; tdcG, L-serine dehydratase; tdh, L-threonine 3-dehydrogenase; Thr, threonine; Trp, tryptophan; Tyr, tyrosine; tyrB, aromatic-amino-acid aminotransferase; Val, valine.

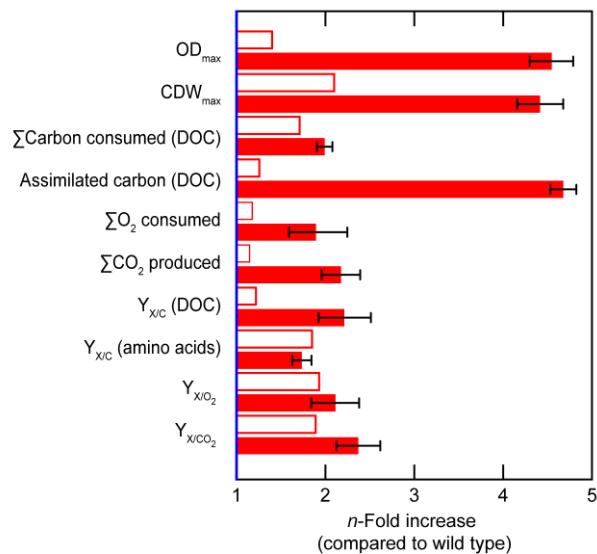


Fig. S1. Comparison of selected growth parameters of *P. inhibens* DSM 17395 in process-controlled bioreactors with Casamino Acids as substrate. The wild type serves as reference state, which is indicated by the blue colored y-axis. Bars represent the performance of $\Delta 262$ mutant: open bars, data previously reported (fig. 2b in Trautwein et al. [2016]); filled bars, data generated in this study (from four biological replicates).

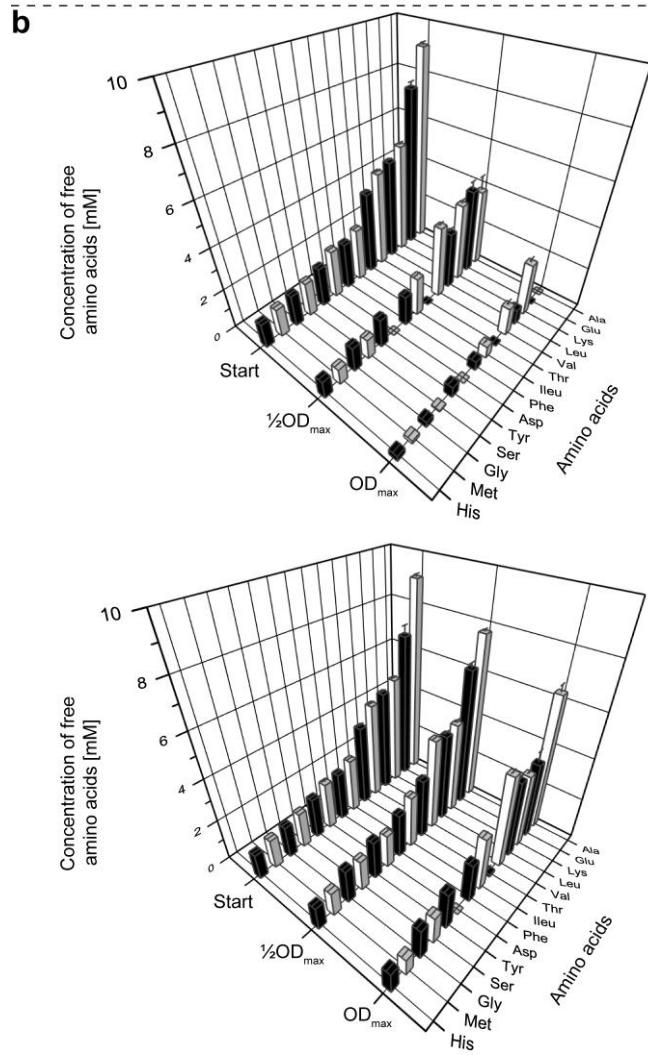
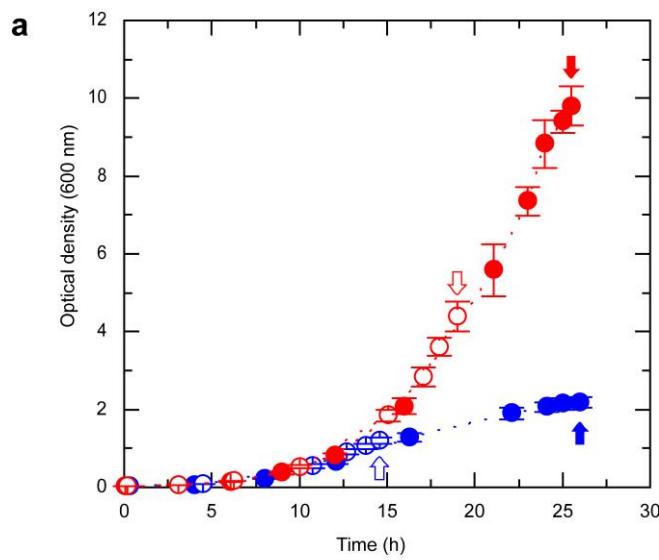


Fig. S2. Growth of *P. inhibens* DSM 17395 in process-controlled bioreactors with Casamino Acids as substrate. **a** Growth curves of $\Delta 262$ mutant (red) and wild type (blue). Time points used for harvesting are at $\sim \frac{1}{2} OD_{max}$ (open arrows/circles) and OD_{max} (filled arrows/circles). Mean value deviations of biological replicates are indicated. **b** Profiles of amino acid consumption from casamino acids as determined for the $\Delta 262$ mutant (upper panel) and the wild type (lower panel). Please note that substrate consumption is here absolutely quantified, while the previously determined consumption profiles reflected relative changes only (Fig. 2c in Trautwein et al. [2016]).

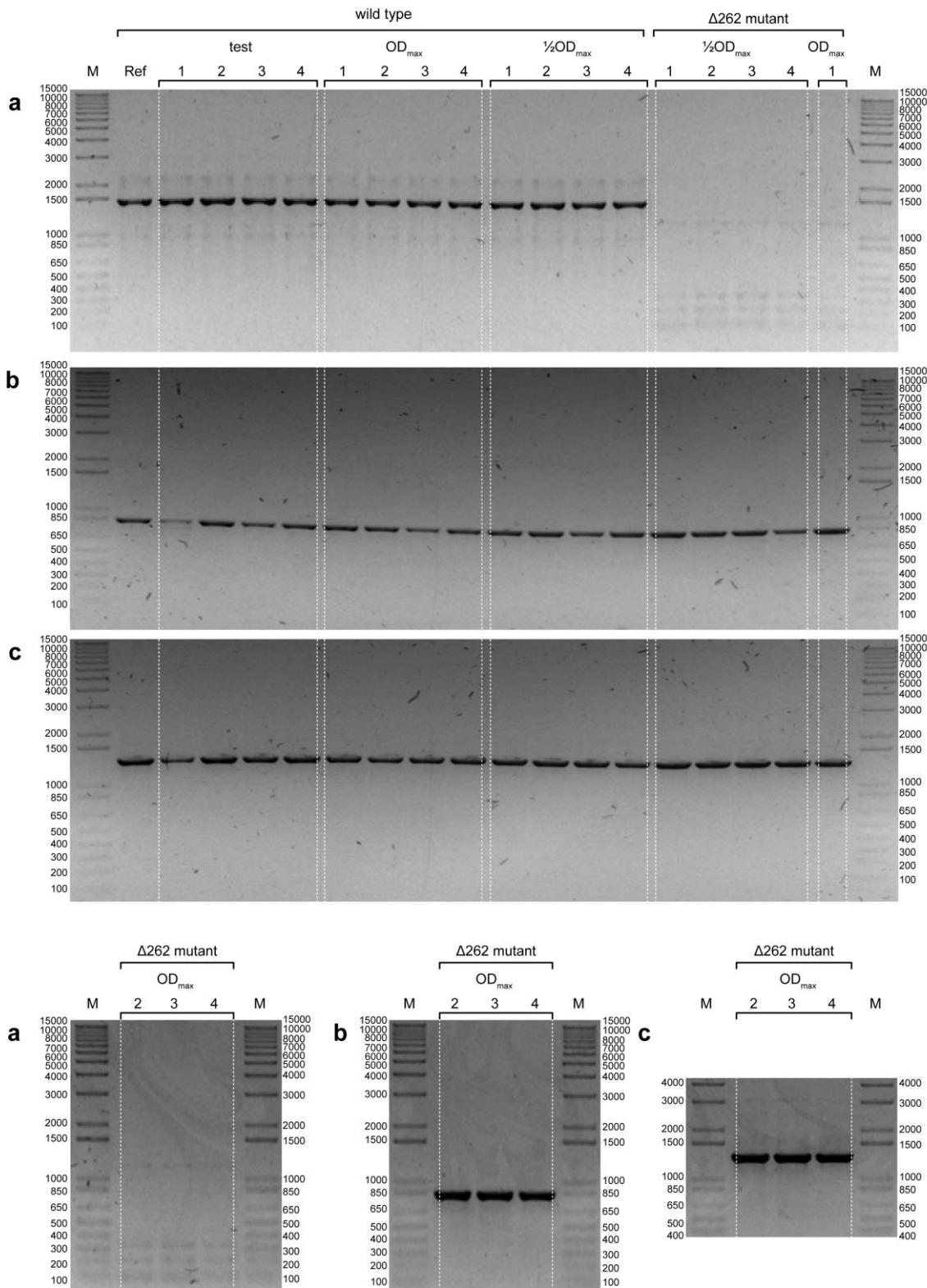


Fig. S3. Chromid profiling of *P. inhibens* DSM 17395 and *P. inhibens* DSM 17395 Δ 262/1. Size of DNA-ladder is in bp. **a** 262-kb chromid (PCR-primer: P100/P105; annealing 65°C; extension 1'10"). **b** 78-kb chromid (PCR-primer: P737/P738; annealing 60°C; extension 45"). **c** 65-kb chromid (PCR-primer: P258/P259; annealing 65°C; extension 1'10"). Primer for plasmid PCR-profiling: P100: AACACCTTCGTGCCGCTTGTGA; P105: CCCAGTTGGAGGATGAGG; P737: GCTCTGCACCATTCTTTCG; P738: CGAGGCGGTTGGTGTAGT; P258: GCCAGAGCGCACCCACATCGT; P259: TGCGGCCTTGTGATGATA

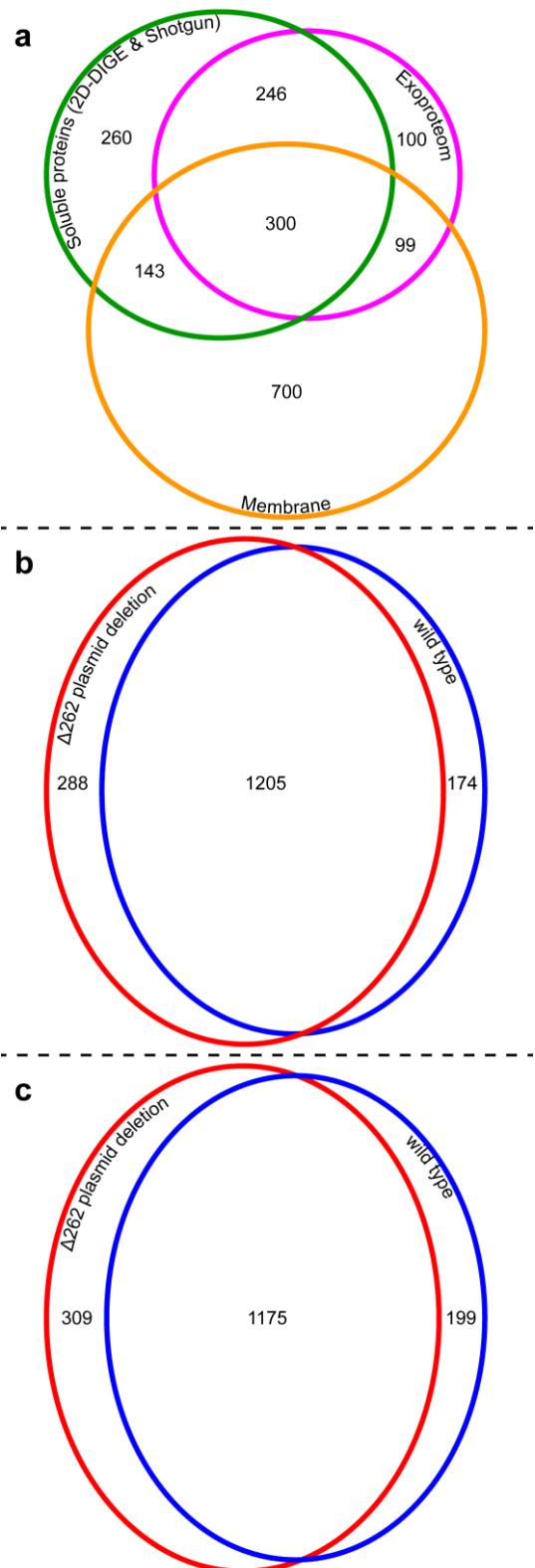


Fig. S4. Complementarity of the different applied approaches used to study the differential proteome of *P. inhibens* DSM 17395 wild type vs. $\Delta 262$ mutant. **a** Complete data set of 1,848 identified proteins. **b** at $\sim \frac{1}{2} OD_{max}$. **c** at OD_{max} .

Table S1. Functional predictions for genes of the heterogenic insert in *P. inhibens* DSM 17395 ($\Delta 65/1$)

Scheme of the heterogenic insert at ~ 0.5 Mb of the chromosome						
DSM17395d65_c00				with assigned function	unknown function	1 kb
509	510	511 512	513	514	515	516

<i>Phaeobacter inhibens</i> DSM 17395 $\Delta 65/1$		Relevant BLAST hits (tRNAscan-SE database)						
Locus tag	Predicted protein function	Length (bp)	tRNAscan-SE entry	Identity (%)	Length (aa)	Function	Organism	
DSM17395d65_c00	509	tRNA-Ser (GTC)	90	chr.tRNA13	100.0	90	tRNA-Ser (GCT)	<i>Roseobacter litoralis</i> Och 149

<i>Phaeobacter inhibens</i> DSM 17395 $\Delta 65/1$		Relevant BLASTP hits (Swiss-Prot database)							
Locus tag	Predicted protein function	Length (aa)	UniProt entry	Identity (%)	E-value (-)	Length (aa)	Function	Organism	
DSM17395d65_c00	510	site-specific integrase	340	A0A3L9XXN0	97.4	0.0E+00	340	site-specific integrase	<i>Rhodobacteraceae bacterium MA-7-27</i>
	511	DNA-binding protein	154	A0A3L9XWL8	91.2	2.5E-84	146	DNA-binding protein	<i>Rhodobacteraceae bacterium MA-7-27</i>
	512	DNA-binding protein	66	A0A3L9YDE7	95.5	1.4E-46	66	DNA-binding protein	<i>Rhodobacteraceae bacterium MA-7-27</i>
	513	DUF4817 domain-containing protein	271	A0A3L9XWU9	81.5	5.7E-154	272	DUF4817 domain-containing protein	<i>Rhodobacteraceae bacterium MA-7-27</i>
	514	hypothetical protein	406	A0A3L9Y190	91.6	0.0E+00	380	hypothetical protein	<i>Rhodobacteraceae bacterium MA-7-27</i>
	515	predicted helicase	1621	A0A1M7FRU5	82.3	0.0E+00	1629	predicted helicase	<i>Roseovarius pacificus</i> DSM 29589
	516	prophage CP4-57 integrase	391	A0A1X6Z6C3	79.5	0.0E+00	398	prophage CP4-57 integrase	<i>Roseivivax jejudonensis</i>

Table S2. Genome comparison of two *Phaeobacter inhibens* DSM 17395 strains with the GenBank reference (GCA_000154765.2). Genomes of highest quality were obtained by *de novo* PacBio RS II sequencing followed by Illumina (HiSeq PE200) correction. The comparison of complete genomes documented the absence

of any large scale flip-flop inversions and deletions. The presence of SNPs and InDels was validated by the respective Illumina *de novo* assembly. Authentic mutations that were independently validated by PCR-amplification and Sanger sequencing are highlighted in green, three sequence errors in the reference genome that were revealed via genome resequencing [see (01)] are shown in red and an insertion of 10 kb that is present in a subpopulation of the wild type, but lacking in the Δ262 mutant, is shown in blue

(a) <i>Phaeobacter inhibens</i> DSM 17395 (JP03alt [PacBio], JP45 [Illumina])									
	Replicon	Position	Gene	Mutation	Nucleotide	Protein	Illumina-Validation	Gene	Comment
1	262-kb chromid	37	intergenic	Insertion	3xT => 4xT	non-coding	yes (4xT)	x	Sequence error in reference genome
2	262-kb chromid	153,515	PGA1_262p01410	Insertion	3xC => 4xC	real gene	yes (4xC)	frame shift	Frame shift correction; protein with 335 aa instead of 145 aa (now identical to Ldh family oxidoreductase <i>P. inhibens</i> P10 [WP_102804152.1])
3	78-kb chromid	78,175-78,198	intergenic	Deletion	24 nt	non-coding	yes (24nt missing)	x	Sequence error in reference genome
4	chromosome	498,971 to 509331		10,361 bp Insertion				6 additional ones	Low Illumina coverage of about 20% shows that the insertion is only present in a subpopulation of the <i>P. inhibens</i> DSM 17395 wild type.

Validation of InDels in <i>P. inhibens</i> DSM 17395 wild type via Sanger-sequencing of PCR amplicates				
2IndDel	PCR-Primer 1	PCR-Primer 2	Sequencing Primer	Sequence – wild type
1	P1701 (ATGGCTGCCTCTGCGCTCA)	P1702 (TCAGCGATTGCGATTACTT)	P1703 (CTCTGCAAACACCACCGAATC)	Seq3517 - TTTT
2	P1707 (GCCGGATCAACTGCGACGAAG)	P1708 (CCCGCCCCGCTGTGGTAGCTG)	P1709 (AATGCCGACCCCTTGTAGCC)	Seq3519 - CCCC

(b) SNPs & GAPs in <i>Phaeobacter inhibens</i> DSM 17395 curing mutant ($\Delta 262/1$; B01 [PacBio], JP50 [Illumina])									
	Replicon	Position	Gene	Mutation	Nucleotide	Protein	Illumina & Sanger*-Validation	Gene	Comment
1	chromosome	1,386,542	ATG GCG <u>CAG</u> GAC GGG	SNP1	C => T	Q => STOP	yes (C => T)	PGA1_c13430	authentic SNP (<i>dctB1</i> ; EC 2.7.13.3; C4-dicarboxylate transport sensor protein DctB)
2	chromosome	2,085,584	CTC GCA <u>GCG</u> GCA GCG	SNP2	G => T	G => V	yes (G => T)	PGA1_c20110	authentic SNP (hypothetical protein)
3	chromosome	2,085,596	GGC GCA <u>GCG</u> GCA GGC	SNP3	G => T	G => V	yes (G => T)	PGA1_c20110	authentic SNP (hypothetical protein)
4	chromosome	2,085,602	GGC GCA <u>GCG</u> GCA GTC	SNP4	G => T	G => V	yes (G => T)	PGA1_c20110	authentic SNP (hypothetical protein)
5	chromosome	2,504,573	GAA AGC <u>GCC</u> TGA TCA	SNP5	G => A	A => T	yes (G => A)	PGA1_c23990	authentic SNP (hypothetical protein)
6	78-kb chromid	78,176-78,199	intergenic	Deletion	24 nt	non-coding	yes (24nt missing)	x	Sequence error in reference genome

Validation of SNPs in <i>P. inhibens</i> DSM 17395 $\Delta 262/1$ via Sanger-sequencing of PCR amplicates					
SNP	PCR-Primer 1	PCR-Primer 2	Sequencing Primer	Sequence – wild type	Sequence - $\Delta 262/1$
1	P1641 (GCGGTGGCTTGCCTTAGGTTT)	P1642 (CCAGTCGCATCACCGCCTCAC)	P1643 (TTACCGAAAGCACCCGCAACC)	Seq3495 - C	Seq3572 - T
2, 3, 4	P1656 (TTGGCGCGCTATGACTTGAT)	P1657 (AAAGGAAAGAGCCCCGAGGAAA)	P1658 (CTGCATACCGCTCTCATCTGG)	Seq3500 - G, G, G	Seq3555 - T, T, T
5	P1674 (AGCAAGAACAAAAAGGAAGCA)	P1675 (ATCATTGATTGCCGACATTG)	P1676 (GATGCCGATGACAAGAAATA)	Seq3508 - G	Seq3530 - A

Aminoacyl-tRNA-synthases/etc.										
c00520	trmD	tRNA (guanine-N(1))-methyltransferase TrmD	-0.1	-0.8	-1.0					
c04900	pth	peptidyl-tRNA hydrolase Pth	0.0	-1.2	-1.2					
c05710	ileS	isoleucyl-tRNA synthetase IleS	-0.1	-0.6	-0.6	0.0	0.0	0.0	0.0	0.0
c06470	glyQ	glycyl-tRNA synthetase subunit alpha	0.0	-1.6	-1.4	0.0	0.0	0.0	0.0	0.0
c06500	glyS	glycyl-tRNA synthetase subunit beta	0.0	-1.1	-0.8	0.0	0.0	0.0	0.0	0.0
c07010	pheS	phenylalanyl-tRNA synthetase subunit alpha	-0.2	-1.9	-1.9	0.0	0.0	0.0	0.0	0.0
c07030	pheT	phenylalanyl-tRNA synthetase subunit beta	0.0	-0.5	-0.7	0.0	0.0	0.0	0.0	0.0
c08340	metG	methionyl-tRNA synthetase MetG	0.1	-1.3	-1.1	0.0	0.0	0.0	0.0	0.0
c11140	argS	arginyl-tRNA synthetase ArgS	-0.2	0.0	-0.4	0.0	0.0	0.0	0.0	0.0
c11340	tyrS	tyrosyl-tRNA synthetase TyrS	0.7	-0.8	-1.5					
c11630	valS	valyl-tRNA synthetase ValS	0.0	-0.5	-0.7	0.0	0.0	0.0	0.0	0.0
c13970	-	threonyl/alanyl-tRNA synthetase-like protein	-0.6	-0.1	0.2	0.0	0.0	0.0	0.0	0.0
c15270	alaS	alanyl-tRNA synthetase AlaS	-0.1	-0.3	-0.6	0.0	0.0	0.0	0.0	0.0
c16090	-	tRNA-processing ribonuclease	-0.2	-0.1	-0.5					
c16960	gluX1	glutamyl-tRNA synthetase	-0.2	-0.4	-1.0	0.0	0.0	0.0	0.0	0.0
c18960	serS	seryl-tRNA synthetase SerS	0.4	-0.2	-0.9	0.0	0.0	0.0	0.0	0.0
c19230	dusA	tRNA-dihydrouridine synthase A	0.1	0.4	-0.3	0.0	0.0	0.0	0.0	0.0
c20990	thrS	threonyl-tRNA synthetase ThrS	0.2	-0.7	-0.6	0.0	0.0	0.0	0.0	0.0
c21420	proS	prolyl-tRNA synthetase ProS	0.0	-0.7	-0.9	0.0	0.0	0.0	0.0	0.0
c21970	gatA	glutamyl-tRNA(Gln) amidotransferase subunit A	-0.1	-1.1	-1.4	0.0	0.0	0.0	0.0	0.0
c23960	-	tRNA-modifying protein ygZ-like protein	-0.1	0.1	0.3	0.0	0.0	0.0	0.0	0.0
c26430	gluX2	glutamyl-tRNA synthetase	-0.4	-1.5	-1.4	0.0	0.0	0.0	0.0	0.0
c26770	trpS	tryptophanyl-tRNA synthetase TrpS	0.1	-1.1	-1.1	-1.1	-1.1	0.0	0.0	0.0
c29890	hisS	histidyl-tRNA synthetase HisS	-0.1	-0.3	-0.5	0.0	0.0	0.0	0.0	0.0
c33400	leuS	leucyl-tRNA synthetase	0.3	0.2	-0.5	0.0	0.0	0.0	0.0	0.0
Ribosome										
c00540	rimM	16S rRNA processing protein RimM	0.1	0.1	-0.2	0.0	0.0	0.0	0.0	0.0
c00900	fmr	methionyl-tRNA formyltransferase Fmr	0.3	0.1	-0.1					
c01510	fusA	elongation factor G	-0.3	-2.2	-0.7	-1.1	-1.6	-1.5		
c05820	prmA	ribosomal protein L11 methyltransferase PrmA	-0.7	-1.6	-0.9					
c14220	frr	ribosome-recycling factor Frr	-0.1	-0.1	-0.6	1.1	1.3	1.3		
c15580	tsf	elongation factor Ts	-0.5	-2.2	-1.7	-1.1	-1.5	-1.8		
c01320	tufL	elongation factor Tu	-0.1	-2.0	-0.8	1.1	-1.2	-1.5		
c16080	rrmJ	ribosomal RNA large subunit methyltransferase J	-0.1	0.2	0.1					
c20840	infC	translation initiation factor IF-3	0.4	-1.4	-1.0	0.0	0.0	0.0	0.0	0.0
c23980	efp	translation elongation factor P	0.1	0.3	-0.1	0.0	0.0	0.0	0.0	0.0
c29260	rsmD	ribosomal RNA small subunit methyltransferase D	0.5	-0.6	-0.4	0.0	0.0	0.0	0.0	0.0
c31130	infA	translation initiation factor IF-1	-1.0	-1.7	-0.1	0.0	0.0	0.0	0.0	0.0
c32930	rfaB	ribosome-binding factor A	0.7	0.9	1.2	0.0	0.0	0.0	0.0	0.0
c34620	infB	translation initiation factor IF-2	-0.4	-0.9	-0.6	0.0	0.0	0.0	0.0	0.0
c32880	-	ribosomal RNA small subunit methyltransferase B	-0.3	-0.9	-0.5					
c35090	rsmG	ribosomal RNA small subunit methyltransferase G	0.6	0.3	0.0	0.0	0.0	0.0	0.0	0.0
c36240	rmlN	ribosomal RNA large subunit methyltransferase N	-0.6	-1.8	-0.6	0.0	0.0	0.0	0.0	0.0
c00500	rpmE	50S ribosomal protein L31	-0.3	-1.3	-0.6	0.0	0.0	0.0	0.0	0.0
c00510	rplS	50S ribosomal protein L19	-0.3	-1.6	-0.6	0.0	0.0	0.0	0.0	0.0
c00570	rpsP	30S ribosomal protein S16	-0.4	-0.8	-0.6	0.0	0.0	0.0	0.0	0.0
c01380	rplK	50S ribosomal protein L11	-0.9	-3.5	-2.2	0.0	0.0	0.0	0.0	0.0
c01400	rplA	50S ribosomal protein L1	-0.7	-2.9	-2.0	-1.2	-1.4	-1.5		
c01410	rplJ	50S ribosomal protein L10	-1.0	-5.2	-2.7	-1.2	-1.6	-1.6		
c01420	rplL	50S ribosomal protein L7/L12	-0.5	-4.2	-2.1	-1.1	-1.6	-1.7		
c01490	rpsL	30S ribosomal protein S12	-0.8	-3.7	-1.8	0.0	0.0	0.0	0.0	0.0
c01500	rpsG	30S ribosomal protein S7	-0.7	-2.9	-1.5	0.0	0.0	0.0	0.0	0.0
c01540	rpsJ	30S ribosomal protein S10	-0.6	-4.1	-1.9	0.0	0.0	0.0	0.0	0.0
c01550	rplC	50S ribosomal protein L3	-0.5	-3.3	-1.5	0.0	0.0	0.0	0.0	0.0
c01560	rplD	50S ribosomal protein L4	-0.3	-3.1	-1.4	0.0	0.0	0.0	0.0	0.0
c01570	rplW	50S ribosomal protein L23	-0.2	-2.8	-1.3	0.0	0.0	0.0	0.0	0.0
c01590	rplB	50S ribosomal protein L2	-0.5	-3.7	-1.5	0.0	0.0	0.0	0.0	0.0
c01600	rpsS	30S ribosomal protein S19	-0.5	-3.8	-1.6	0.0	0.0	0.0	0.0	0.0
c01610	rplV	50S ribosomal protein L22	-0.4	-3.3	-1.3	0.0	0.0	0.0	0.0	0.0
c01620	rpsC	30S ribosomal protein S3	-0.4	-3.2	-1.3	0.0	0.0	0.0	0.0	0.0
c01630	rplP	50S ribosomal protein L16	-0.3	-2.4	-1.1	0.0	0.0	0.0	0.0	0.0
c01680	rpmC	50S ribosomal protein L29	-1.0	-2.8	-1.2	0.0	0.0	0.0	0.0	0.0
c01700	rplN	50S ribosomal protein L14	-0.8	-3.0	-1.4	0.0	0.0	0.0	0.0	0.0
c01710	rplX	50S ribosomal protein L24	-0.7	-2.3	-0.9	0.0	0.0	0.0	0.0	0.0
c01720	rplE	50S ribosomal protein L5	-0.5	-1.8	-0.8	0.0	0.0	0.0	0.0	0.0
c01730	rpsN	30S ribosomal protein S14	-0.3	-1.6	-0.8	0.0	0.0	0.0	0.0	0.0
c01740	rpsH	30S ribosomal protein S8	-0.2	-1.6	-0.5	0.0	0.0	0.0	0.0	0.0
c01750	rplF	50S ribosomal protein L6	-0.1	-1.6	-0.5	0.0	0.0	0.0	0.0	0.0

Table S4. Literature data for K_M - and K_{cat} --values of enzymes constituting the catabolic network of *P. inhibens* DSM 17395

Catabolic enzyme		K_M (mM) ^{a)}	K_{cat} (s ⁻¹) ^{a)}	Catabolic enzyme		K_M (mM) ^{a)}	K_{cat} (s ⁻¹) ^{a)}				
<i>Leucine (4.88 ± 0.06 mM^{b)} in casamino acids)</i>											
c34110	IlvE	0.2 - 25	8.1 - 898	c16600	MdeA	0.0013 - 98	0.03 - 48.6				
c10280	Ivd	0.0013 - 0.9	0.17 - 10	c21540/600	PccAB	0.035 - 2.6	44045				
c10320/30	MccAB	0.0098 - 31	0.43-4	c24490	Mce	0.08	2-8				
c10360	Mgh	0.01	138	c21510	BhbA	0.0279 - 0.364	0.003 - 255				
c10340	MvaB	0.02 - 62	0.0004 - 158	<i>Valine (4.65 ± 0.06 mM^{b)} in casamino acids)</i>							
c06200/10	ScoBA	0.0002 - 0.44	9.17 - 98.3	c34110	IlvE	0.22 - 143	3.8 - 1236				
c34350	PhbA	0.0038 - 0.18	0.0767 - 5000000	c10280	Ivd	0.5 - 0.79	-				
<i>Tryptophan (not quantifiable^{b)} in casamino acids)</i>											
c09970	KynA	0.02 - 1.531	0.01 - 1071	c17350	Hibch	0.006	15				
c29640	-	0.05 - 5	26.4 - 161	c17360	MmsB	0.12 - 0.652	7.1 - 80.79				
c09980	KynU	0.0067 - 1	0.0058 - 16	c17300	MmsA	0.006 - 0.215	0.003				
c23440	-	0.013 - 0.02	21.7 - 267	<i>Isoleucine (2.62 ± 0.03 mM^{b)} in casamino acids)</i>							
c23490	-	0.02 - 0.025	70.8	c34110	IlvE	0.15 - 22.2	7.6 - 1075				
<i>Alanine (9.11 ± 0.12 mM^{b)} in casamino acids)</i>											
c30420	Ald	0.018 - 30	6.1 - 228	c10280	Ivd	0.0019 - 0.0035	0.3				
c17550/60/70	PdhABC	0.0002 - 50	0.05 - 486	<i>Phenylalanine (2.33 ± 0.03 mM^{b)} in casamino acids)</i>							
c02180	LpdA1	0.3 - 0.48	-	c29420	TyrB	0.05 - 16.6	152 - 1200				
<i>Threonine (3.96 ± 0.09 mM^{b)} in casamino acids)</i>											
c34320	Tdh	0.01129 - 221	0.55 - 551.7	c04490	IorAB	0.018 - 1.4	-				
<i>Glycine (1.55 ± 0.03 mM^{b)} in casamino acids)</i>											
78p00310	GcvP	0.0003 - 40	0.0001 - 0.047	c04090	PaaJ	0.15	7.8				
c11870	GlyA	0.68	5	<i>Tyrosine (1.96 ± 0.03 mM^{b)} in casamino acids)</i>							
<i>Serine (1.71 ± 0.02 mM^{b)} in casamino acids)</i>											
c23770	tdcG	0.00258-420	0.033 - 585	c29420	TyrB	0.042 - 15	72 - 500				
<i>Histidine (1.22 ± 0.01 mM^{b)} in casamino acids)</i>											
c36340	HutH	0.2 - 20	86 - 255	c07610	Hpd	0.0043 - 54	0.03 - 9.9				
c36320	HutU	0.005 - 0.7	-	c00440	HmgA	0.009 - 0.6	10.1 - 79.5				
c36350	HutI	0.1 - 1.54	-	c00380	-	0.068 - 0.64	2.1 - 464				
c36360	HutF	0.0012 - 19	0.005 - 31	c00430	Fah	0.0014	-				
c36330	HutG	14	-	<i>Lysine (5.29 ± 0.09 mM^{b)} in casamino acids)</i>							
c08740	GluD	0.24 - 31	2 - 121.2	c11650	Ldc	1.59 - 10.3	0.09 - 0.57				
<i>Aspartic acid (2.33 ± 0.08 mM^{b)} in casamino acids)</i>											
c36210	-	0.00016 - 100	0.0027 - 5721	c15710	GcdH	0.0012 - 3.8	0.004 - 13.2				
c21250	AatA	0.09 - 37	0.13 - 530	c15710	GcdH	0.003 - 0.011	2.04 - 5.5				

^{a)} data taken from BRENDA database [Placzek et al., 2017]

^{b)} data from Fig. S2 in the supplementary material

Table S5. Absolute quantitation of tropodithietic acid (TDA) during cultivation of *P. inhibens* DSM 17395 wild type with Casamino Acids in process-controlled bioreactors ^{a)}

Bioreactor replicate	TDA [μM]	
	$\sim \frac{1}{2}OD_{max}$	OD_{max}
1	31.77	51.20
2	37.57	55.72
3	39.67	51.92
4	29.01	46.04
Av (AvDev)	34.51 (± 4.12)	51.22 (± 2.60)

^{a)} no TDA was detected for cultivations with the $\Delta 262$ mutant

References

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