

Supplementary Data

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Fig. S9. ISOLIQ titer and HPLC-MS results of strain PN01 in 5-L bioreactor .

Table S1. Primers used in this study.

Table S2. The DNA sequence of *Ge2-HIS*, *crCPR*, *GmHID* and *PIUGT43*.

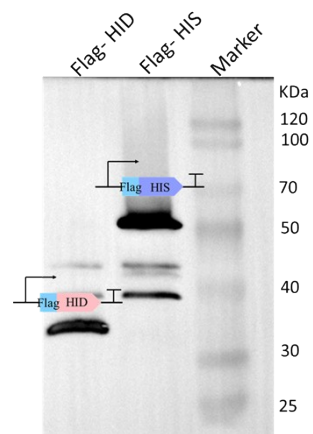


Fig. S1. Western Blot analysis of HID and 2-HIS Genes.

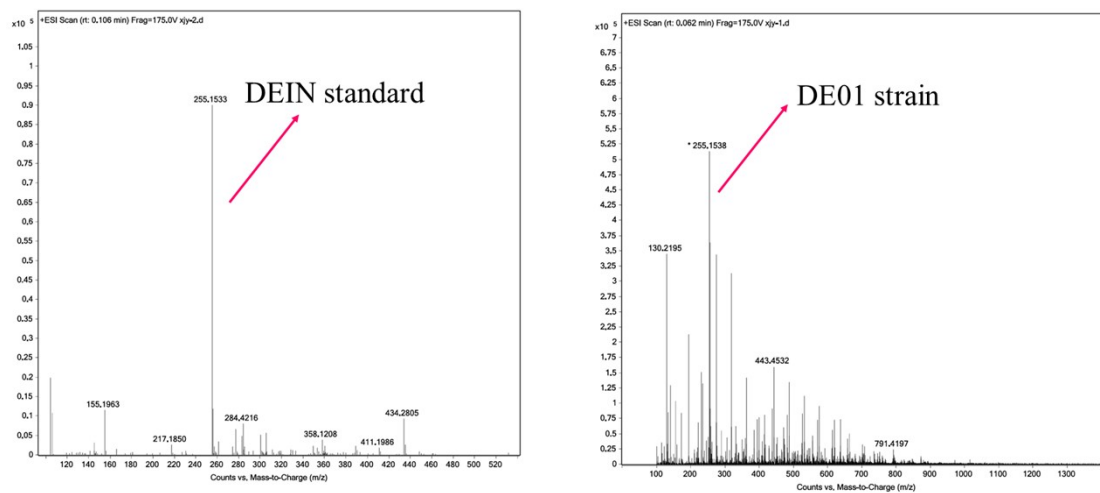


Fig. S2. HPLC-MS results of DEIN standard and strain DE01.

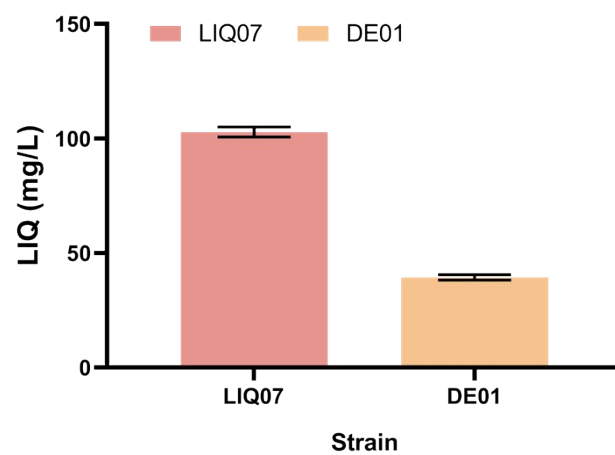


Fig. S3. LIQ of strains LIQ07 and DE01 at 120 h.

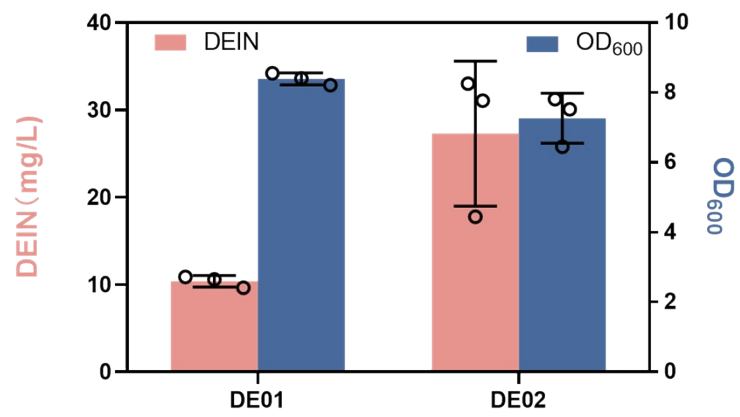


Fig. S4. DEIN and OD₆₀₀ of strains DE01 and DE02 at 48 h.

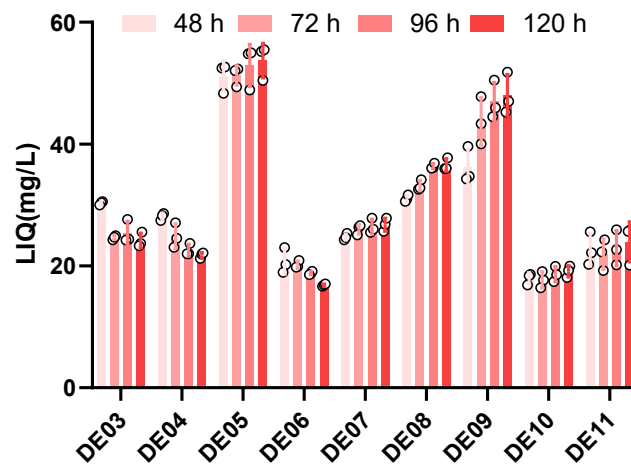


Fig. S5. LIQ of strains DE03, DE04, DE05, DE06 DE07, DE08, DE09, DE10 and DE11.

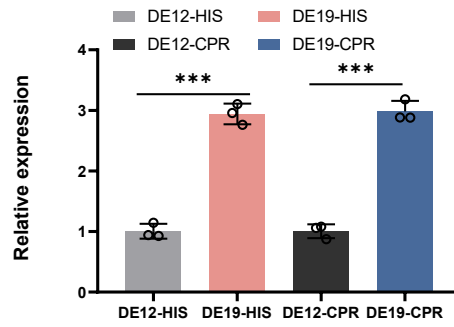


Fig. S6. Quantitative PCR analysis of the 2-HIS and CPR genes in DE12 and DE19 strains.

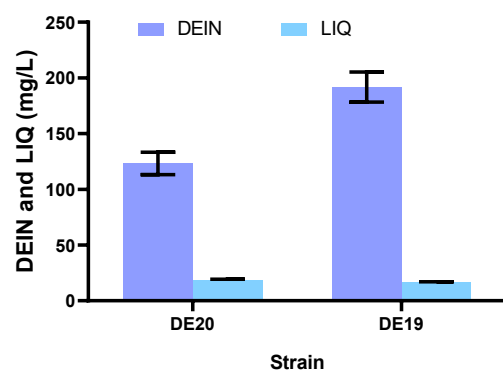


Fig. S7. DEIN and LIQ production of strains DE19 and DE20.

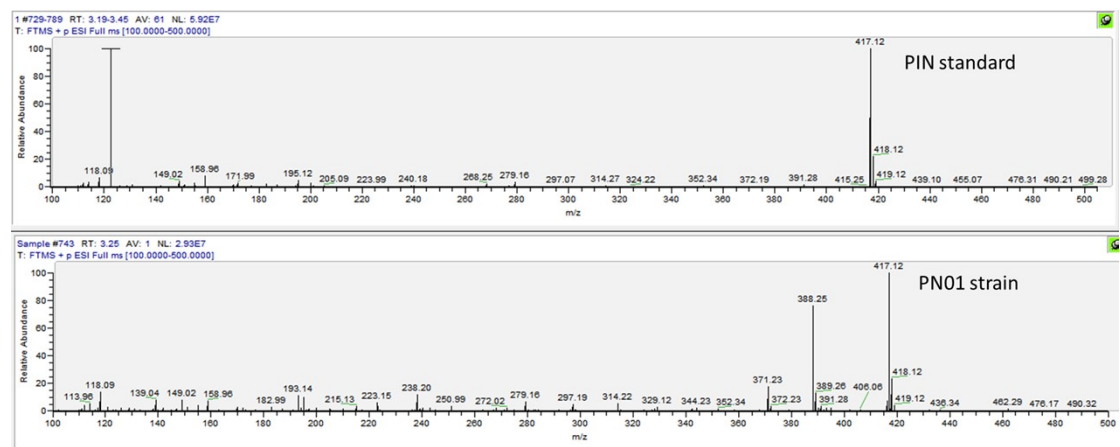


Fig. S8. HPLC-MS results of PIN standard and strain PN01.

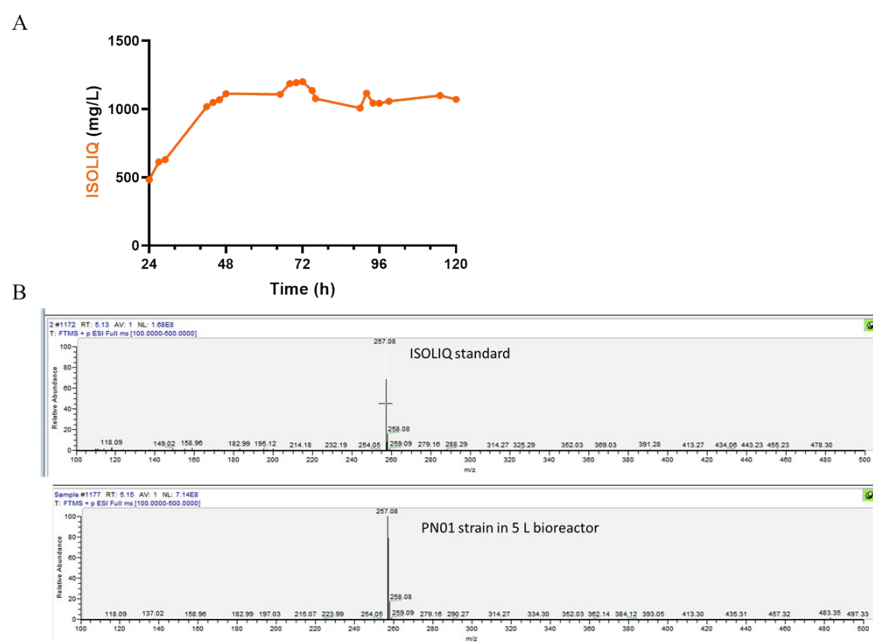


Fig. S9. (A) ISOLIQ titer of strain PN01 in 5-L bioreactor. (B) HPLC-MS results of ISOLIQ standard and strain PN01 in 5-L bioreactor.

Table S1. Primers used in this study.

Plasmids	Primers	DNA sequence (5' to3')
p1312-HIS-HID	F1R	cacaccacatcacacatacaaccacacacatccacgtgATGCTGGTTGAGCTGG CCATC
	F1R	aagaccggcaacgtggggacaggccatggaggtaccCTAAGAAGAGAACAG CTTAGGC
	F2F	caaagcacttgctagatagagtcgacaaaggaataaatttagtctgcagcccaagct
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1269-CPR	F3F	ccacatcacacatacaaccacacacatccacgtgatggactcgtcgagcgagaagctc
	F3R	gaccggcaacgtggggacaggccatggaggtacettaccacacgtctctcaggtagcg
p1269-HID	F4F	accacatcacacatacaaccacacacatccacgtgATGGCCAAAGAGATCGTC AAAGA
	F4R	ggcaagaccggcaacgtggggacaggccatggaggtacCTAGACCAGAAACG AAGCCAG
p1312-P _{hp4d} -HIS	F1F	cacaccacatcacacatacaaccacacacatccacgtgATGCTGGTTGAGCTGG CCATC
	F1R	aagaccggcaacgtggggacaggccatggaggtaccCTAAGAAGAGAACAG

CTTAGGC

p1312-P _{hp4d} -HIS-	F5F	cacaaagcactttgctagatagagtcgacaaaggctgactgggtgaaggctctcaag
P _{hp4d} -CPR		
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1312-P _{hp4d} -HIS-	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCGTTTTT
P _{exp1} -CPR		TCGAGC
	F6R	gggggagagcttctcgctcgacgagtcctTGCTGTAGATATGTCTTGTGT GTAAGGG
	F7F	CCAACCCCCTTACACACAAGACATATCTACAGCAatggactcgt cgagcgagaagctc
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1312-P _{hp4d} -HIS-	F8F	aaagcactttgctagatagagtcgacaaaggCAGTGTACGCAGTACTATAG
P _{fbain} -CPR		AGGAACA
	F8R	gggggagagcttctcgctcgacgagtcctCTGGGTTAGTTTGTGTAGAGA GTGTGTG
	F9F	atggactcgtcgagcgagaagctctccc
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1312-P _{hp4d} -CPR	F3F	ccacatcacacatacaaccacacacatccacgtgatggactcgtcgagcgagaagctc
	F3R	gaccggcaacgtggggacaggccatggaggtaccttaccacacgtctctcaggtagcg

p1312-P _{hp4d} -CPR-	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCGTTTTT
P _{exp1} -HIS		TCGAGC
	F10R	CAGAAGAGTGATGGCCAGCTCAACCAGCATTGCTGTAGAT ATGTCTTGTGTGTAAGGG
	F11F	ATGCTGGTTGAGCTGGCCATCACT
	F2R	gctctgtacaccgagaaacaggggagtgtgggagggttaagagaattatcaccggca
p1312-P _{hp4d} -CPR-	F8F	aaagcactttgctagatagagtcgacaaaggCAGTGTACGCAGTACTATAG
P _{fbain} -HIS		AGGAACA
	F12R	AGAAGAGTGATGGCCAGCTCAACCAGCATCTGGGTTAGTT TGTGTAGAGAGTGTGTGT
	F11F	ATGCTGGTTGAGCTGGCCATCACT
	F2R	gctctgtacaccgagaaacaggggagtgtgggagggttaagagaattatcaccggca
CasURA-A1-	F13F	tctgtggatcatagggaaactcttcgacactagtGGAGTTTGGCGCCCGTTTTTT
P _{hp4d} -CPR- P _{exp1} -		CGAG
HIS		
	F13R	tcagTTTGAAAAAATTTATTTCTAGACAGTTATATACTAAGA AGAGAACAGCTTAGGC
	F14F	TAGTATATAACTGTCTAGAAATAAATTTTTTCAAActgactggg ttgaaggctctcaa
	F14R	taacagtctcttggttttctgtctctggagtgtgggagggttaagagaattatcacc

pNew1312-P _{hp4d} -	F15F	ggtacctccatggcctgtccccacgtt
CPR-P _{exp1} -HIS		
	F15R	acgcgtatcgataagctagcttgggct
	F16F	tagtctgcagcccaagctagcttatcgatacgcgtGGAGTTTGGCGCCCCGTTTT
		TTCG
	F16R	gaccggcaacgtggggacaggccatggaggtagcttaccacacgtctctcaggtagcg
pNew1312-P _{hp4d} -	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCCGTTTTT
CPR-P _{exp1} -HIS-		TCGAGC
P _{hp4d} -CPR-P _{exp1} -		
HIS		
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1312-P _{hp4d} -CPR-	F5F	cacaaagcactttgctagatagagtcgacaaaggctgactgggtgaaggctctcaag
P _{hp4d} -CPR		
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
p1312-P _{hp4d} -CPR-	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCCGTTTTT
P _{hp4d} -CPR-P _{exp1} -		TCGAGC
HIS		
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcaccggca
pNEW1312-	F15F	ggtacctccatggcctgtccccacgtt
P _{exp1} -HIS		

	F15R	acgcgtatcgataagctagcttgggct
	F17F	tagtctgcagcccaagctagcttatcgatacgcgtGGAGTTTGGCGCCCGTTTT TTCG
	F1R	aagaccggcaacgtggggacaggccatggaggtagcCTAAGAAGAGAACAG CTTAGGC
pNEW1312- P _{exp1} -HIS-P _{exp1} - HIS	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCGTTTTT TCGAGC
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcacggca
pNEW1312- P _{exp1} -HIS- P _{hp4d} - CPR-P _{exp1} -HIS	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCGTTTTT TCGAGC
	F2R	gctctgtacaccgagaaacaggggagtggtgggaggttaagagaattatcacggca
p1269-ylGND- ylZWF1	F18F	ccacatcacacatacaaccacacacatccacgtgATGactgacactcaaacatcaag
	F18R	AAAAAATTTATTTCTAGACAGTTATATATtaagcatcgtaagtgaag aagaaacctc
	F19F	TATATAACTGTCTAGAAATAAATTTTTTCAAAAGAGACCG GGTTGGCGGCGCATTTGTG

	F19R	gaccggcaacgtggggacaggccatggaggtacctcacaggagcccttggtgacaggc
p1269-UGT43	F20F	cacatcacacatacaaccacacacatccacgtgATGACACGATACGAGGTCTG TCTTCAT
	F20R	aacgtggggacaggccatggaggtaccttaCTAAGAGGTCAGCTCTTGGAT CAGAGAC
p1269-UGT43- ylPGM2- ylUDPG1	F21F1	caccgaaacgcgcgaggcagcagatccactagtTTTGAAAAAATTTATTTCT AGACAG
	F21F2	TTTGAAAAAATTTATTTCTAGACAGTTATATAttaatgctccagaat actgagagatc
	F21R	CCGACCAGCACTTTTTGCAGTACTAACCGCAGatgtccaagcacc atctgaagaccc
	F22F	gcactctgggtcttcagatgggtgcttgacatCTGCGGTTAGTACTGCAAAAA GTGCT
	F22R	acgcgtatcgataagctagcttggAAAAGTCTCTACAAGTAGTCTTGTA A
	F23F	GAATGTTTTTACAAGACTACTTGTAGAGACTTTTccaagctagct tatcgatacgcgt
	F23R	tttaccgcagcagatccgcggccgcataggccggagtggtgggaggttaagagaattat
pNEW1312- P _{exp1} -HIS-P _{exp1} -	F6F	caaagcactttgctagatagatcgacaaaggGGAGTTTGGCGCCCGTTTTT TCGAGC

CPR

	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcaccggca
pNEW1312-	F8F	aaagcactttgctagatagagtcgacaaaggCAGTGTACGCAGTACTATAG
P _{exp1} -HIS-P _{fbain} -		AGGAACA

CPR

	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcaccggca
pNEW1312-	F15F	ggtacctccatggcctgtccccacgtt
P _{fbain} -HIS-		
	F15R	acgcgtatcgataagctagcttgggct
	F24F	ctgcagcccaagctagcttatcgatacgcgtCAGTGTACGCAGTACTATAGA GGAACA
	F24R	cggcaacgtggggacaggccatggaggtaccCTAAGAAGAGAACAGCTTA GGCACGG
pNEW1312-	F8F	aaagcactttgctagatagagtcgacaaaggCAGTGTACGCAGTACTATAG
P _{fbain} -HIS-P _{fbain} -		AGGAACA

CPR

	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcaccggca
pNEW1312-	F6F	caaagcactttgctagatagagtcgacaaaggGGAGTTTGGCGCCCGTTTTT
P _{fbain} -HIS-P _{exp1} -		TCGAGC

CPR

	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcaccggca
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p1312-P _{hp4d} -HIS-	F25	caaagcactttgctagatagagtcgacaaaggaataaatttagtctgcagcccaagct
P _{hp4d} -Flag CPR		
	F25R	CTTGTCGTCGTCGTCCTTGTAGTCCATcacgtggatgtgtgtggtgtat gtgtgatgt
	F26F	GACTACAAGGACGACGACGACAAGGGCTCTGGCTCTATG GCCAAAGAGATCGTCAAAG
	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcacggca
p1312-P _{hp4d} -CPR-	F25	caaagcactttgctagatagagtcgacaaaggaataaatttagtctgcagcccaagct
P _{hp4d} -Flag HIS		
	F25R	CTTGTCGTCGTCGTCCTTGTAGTCCATcacgtggatgtgtgtggtgtat gtgtgatgt
	F27F	CTACAAGGACGACGACGACAAGGGCTCTGGCTCTATGCTG GTTGAGCTGGCCATCACT
	F2R	gctctgtacaccgagaaacaggggagtgtgggaggttaagagaattatcacggca
	Q-actin-R	ggggagagagaaaccagag
	Q-actin-F	agtccaaccgagagaagatg
	Q-HIS-F	AGTGTGAGGTGGACGGTTACG
	Q-HIS-R	CAGGTCGGAACCTCGGTAGGTC
	Q-CPR-F	CCTCGCATGGCTCCGTCTC

Table S2. The DNA sequence of *Ge2-HIS*, *crCPR*, *GmHID* and *PIUGT43*.

Ge2-HIS	ATGCTGGTTGAGCTGGCCATCACTCTTCTGGTCATCGCTCTG TTCATCCACCTGCGACCTACTCTGTCCGCTAAGTCCAAGTCT CTGCGACACCTGCCTAACCCTCCATCGCCTAAGCCTCGACTT CCATTCGTCGGTCATCTGCACCTGCTGGACAAGCCTCTTCTG CACTACTCTCTCATCGACCTGTCCAAGCGATACGGACCTCTC TACTCTCTGTACTTCGGTTCCATGCCTACCGTCGTCGCTTCC ACTCCAGAGCTGTTCAAGCTGTTTCTGCAGACACATGAGGCT TCTTCTTTCAACACACGATTCCAGACCTCTGCTATCCGACGA CTGACCTACGACAACCTCCGTCGCTATGGTGCCTTTCGGACCT TACTGGAAGTTCATCCGAAAGCTGATCATGAACGACCTGCT GAACGCTACCACCGTCAACAAGCTGCGACCTCTGCGATCTC AAGAGATCCGAAAGGTTCTGCGAGTCATGGCTCAGTCTGCT GAGTCTCAGGTGCCTCTGAACGTGACCGAAGAACTGCTGAA GTGGACCAACTCCACCATCTCTCGAATGATGCTGGGTGAAG CTGAAGAGATTCGAGACATCGCACGAGATGTGCTCAAGATC TTCGGCGAGTACTCTCTGACCGACTTCATCTGGCCTCTGAAG AAGCTCAAGGTCGGTCAGTACGAGAAGCGAATCGACGACA TCTTCAACCGATTTCGACCCTGTCATCGAGCGAGTCATCAAG AAGCGACAAGAAATCCGAAAGAAGCGAAAGGAGCGAAAC GGTGAGATCGAAGAGGGTGAGCAGTCTGTCGTCTTTCTGGA CACACTGCTGGACTTTGCCGAAGACGAGACAATGGAGATCA AGATCACCAAAGAGCAGATCAAGGGTCTGGTCGTTGACTTC TTCTCCGCTGGAACCGACTCCACTGCTGTCGCCACCGACTG GGCACTTTCCGAGCTGATCAACAACCCTCGTGTCTTCCAGA
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	AGGCCAGAGAAGAGATCGACGCCGTTGTCGGCAAAGACCG ACTGGTTGACGAGGCTGACGTTTCAAGACCTGCCTTACATCC GATCCATCGTCAAAGAGACATTCCGAATGCACCCTCCACTT CCAGTCGTCAAGCGAAAGTGCGTCCAAGAGTGTGAGGTGG ACGGTTACGTCATTCCAGAGGGTGCTCTGATTCTGTTCAACG TCTGGGCTGTTGGCCGAGATCCAAAGTACTGGGACCGACCT ACCGAGTTCCGACCTGAGCGATTTCTGGAGAACGTCGGTGA GGGAGATCAGGCTGTCGATCTGCGAGGTCAGCACTTCCAGC TGCTGCCTTTCGGTTCTGGACGACGAATGTGCCCTGGTGTCA ACCTGGCTACCGCTGGTATGGCTACACTGCTCGTTCTGTCA TCCAGTGCTTCGACCTCTCTGTCTCGTCCGACCTCAGGGTAAG ATTCTGAAGGGTAACGACGCCAAGGTCAGCATGGAAGAAC GAGCCGGTCTGACCGTTCCACGAGCACACAACCTGATCTGC GTTCCAGTCGCACGATCTTCTGCCGTGCCTAAGCTGTTCTCT TCTTAG
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GmHID	ATGGCCAAAGAGATCGTCAAAGAGCTTCTTCCACTGATTCG AGTCTACAAAGACGGTTCTGTGGAACGACTGCTGTCTTCCG AGAACGTTGCAGCTTCTCCAGAAGATCCACAGACAGGTGTC TCTTCCAAAGACATCGTCATCGCTGATAACCCTTACGTCTCT GCTCGAATCTTTCTGCCTAAGTCTCACCACACCAACAACAA GCTGCCTATCTTTCTGTACTTCCACGGTGGTGCATTCTGTGT CGAGTCTGCCTTCTCGTTCTTCGTCCATCGATACCTGAACAT TCTGGCTTCTGAAGCCAACATCATCGCCATCTCTGTGGACTT

	TCGACTTCTGCCTCATCATCCAATCCCTGCTGCTTACGAAGA CGGTTGGACTACGCTGAAGTGGATCGCTTCTCATGCCAACA ACACCAACACCACTAACCCTGAACCTTGGCTTCTCAACCAT GCTGACTTCACCAAGGTCTACGTTGGTGGTGAAACCTCTGG TGCAAACATCGCTCACAACCTTCTGCTTCGAGCTGGTAACG AGTCTCTGCCTGGTGATCTGAAGATTCTGGGTGGTCTTCTTT GCTGCCCTTTCTTCTGGGGTTCTAAGCCTATCGGTTCTGAAG CTGTTGAAGGTCACGAACAGTCTCTTGCCATGAAGGTCTGG AACTTCGCTTGTCCAGATGCACCTGGTGGTATCGACAACCC TTGGATCAACCCTTGTGTTCCAGGTGCACCATCTCTGGCAAC TCTGGCTTGTTCCAAGCTGCTGGTCAACCATCACCGGTAAAG ACGAGTTCCGAGACAGAGACATTCTGTACCACCACACTGTT GAGCAGTCTGGTTGGCAAGGTGAACTTCAGCTGTTTCGATGC TGGTGATGAAGAACACGCATTCCAGCTGTTCAAGCCTGAGA CACACCTTGCTAAGGCCATGATCAAGCGACTGGCTTCGTTT CTGGTCTAG
PIUGT43	ATGACACGATACGAGGTCGTCTTCATCGCCATTCCAACCTCT GGGTAACCTGGTTCCACAGGTCGAGTTCGCTAACCTGCTGA CCAAGCACGATCCACGATTCTCTGCCACCATTCTGACCGTCT CCATGCCTCAGCGACCTCTGATGAACACCTACGTTCAAGCA CGAGCCTCTTCTGCCGCTAACATCAAGCTTCTGCAGCTGCCT ATCGTGGACCCTCCAGCTCCAGAGCAGTACCAGACTCTGGT CGGCTTTCTGTCTCTGCACATGCAGAATCACAAGCACCACG TCAAGCACGCTCTGCTGAACCTGATGAAGACCACCGAGTCC AACTCTTCCAACCTCCGTCCGACTGGCCGCTATCTTCGTGGAC ATGTTCTCCACCACTCTGATCGACGTTGCTGCTGAGCTTGCT GTGCCTTGCTACCTGTTCTTCGCCTCTCCAGCCTCTTGTCTG GGCTTCACTCTGGATCTGCCACGATTCGACCTGGCTGAGTCC

AAGTCCGAGTTCACCGTGCCTTGCTTCAAGAACCTGCTGCCT CGATCTGTCTTCCCTAACCTGGTGCTGGACGCTAAAGACGG AACCTTCTGGCTGTCTTACCATGCCAGACGATACAAAGAGA CGAAGGGTATCGTCATCAACACTCTGCAAGAGCTGGAGACT CATGCTCTGCAGTCTCTCCACAACGACTCTCAGCTGCAGCG AGTCTACCCTATCGGACCTATTCTGGACCTTGTCGGTTCTGC TCAGTGGGACCCTAATCCAGCTCAGTACAAGCGAATCATGG AGTGGCTGGATCAGCAGCCTCTGTCTTCTGTCGTGCTGCTGT GCTTCGGCTCTATGGGTTCTCTGGAGGCTAACCAGGTGCGAA GAGATCGCCATCGGACTGGAACGAGCCGGTGTCCGATTTCT GTGGGCTCTGCGAGAGTCGCCTAAGGCTCAGCTGGAGTATC CACGAGACTACGAGAACCACAAGGACGTGCTGCCTGATGG CTTTCTGGAGCGAACCAACAACATCGGTCTGGTCTGTGGCT GGGTGCCTCAAGCTGTCGTTCTGGCTCACAAGGCCGTTGGT GGTTTCGTCTCTCACTGCGGTTGGA ACTCCATTCTGGAGTCT CTGTGGCATGGTGTGCCTGTCGCTACCTGGCCTCTGTACTCT GAGCAGCAGATGAACGCCTTCCAGATGGTCCGAGATCTGGG TCTGGCCGTCGAGATCTCCGTGGACTACCGAGTTGGTGCTG ACCTTGTTTCGAGCTGAAGAGGTGCGAGAACGGTCTGCGATCT CTCATGAAGGGTGGTGACGAGATCCGACGAAAGGTCAAAG AGATGTCCGACACCTGTCGAGGTGCTCTGCTGGAGAACGGC TCTTCTTACTCCAACCTGGTGTCTCTGATCCAAGAGCTGACC TCTTAG
