## **Supporting Information**

# Selective oxidation of aliphatic C-H bonds in alkylphenols by a chemomimetic biocatalytic system

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#### **SI Methods**

**Strains and culture conditions.** The bacterial strains and plasmids used in this study are listed in Table S3. *Escherichia coli* strains were grown at 37 °C on LB agar (2% w/v) plates or LB liquid broth. *E. coli* DH5 $\alpha$  strain was used for vector construction and plasmid isolation. For protein expression and purification, *E. coli* BL21 (DE3) strain was cultured in Terrific Broth (TB) medium (1) with a rotary shaker (220 rpm). When required, kanamycin was added to a final concentration of 50 µg/ml.

**DNA isolation and manipulation.** Plasmids were isolated using the E.Z.N.A.<sup>TM</sup> Plasmid Miniprep Kit (Omega Biotek, Norcross, GA). DNA fragments were purified using the Wizard SV Gel and PCR Clean-up System (Promega, Madison, USA). Vector transformation, agarose gel electrophoresis and other standard techniques of molecular cloning were performed as previously described (2).

General protein expression, purification and concentration determination. For protein expression, *E. coli* BL21 (DE3) carrying a specific expression vector was grown in LB broth containing 50  $\mu$ g/ml kanamycin at 37 °C overnight. Terrific Broth (1 l) supplemented with 4% glycerol was inoculated with a 1:100 dilution of the overnight culture. The culture was then incubated on a rotary shaker (220 rpm) at 37 °C until the OD<sub>600</sub> reached ~0.6. Next, IPTG (final concentration of 0.2 mM) was added into the culture to induce protein expression. Cultivation continued for additional 20 h at 18 °C.

Protein purification was carried out as described elsewhere (3) with minor modifications. All procedures were performed at 4 °C. The cells were harvested by centrifugation (5000 × *g* for 5 min), washed with deionized water for 2 times, and re-suspended in 50 ml of lysis buffer (50 mM NaH<sub>2</sub>PO<sub>4</sub>, 300 mM NaCl, 10% glycerol and 10 mM imidazole, pH 8.0). After sonication on ice, the crude cell lysate was centrifuged at 12,000 × *g* for 30 min to collect the supernatant fraction. Subsequently, 1 ml of Ni-NTA resin (Qiagen, Germany) was added into the supernatant with subsequent incubation at 4 °C on a gentle rotator for 30 min. This slurry was loaded onto an empty column, and washed with ~100 ml wash buffer (50 mM NaH<sub>2</sub>PO<sub>4</sub>, 300 mM NaCl, 10% glycerol and 20 mM imidazole, pH 8.0) until no proteins were detectable in flow-through by Coomassie Brilliant Blue G-250 assays. Approximately 10 ml of elution buffer (50 mM NaH<sub>2</sub>PO<sub>4</sub>, 300 mM NaCl, 10% glycerol and 250 mM imidazole, pH 8.0) was used to elute target proteins from the Ni-NTA resin. The eluent was concentrated with an Amicon Ultra centrifugal filter (Merck KGaA, Darmstadt, Germany) ( $7500 \times g$  for 30 min) and buffer exchanged on a PD-10 column (GE Healthcare, Buckinghamshire, UK) with 5 ml desalting buffer ( $50 \text{ mM NaH}_2\text{PO}_4$ , 10% glycerol, pH 7.5). The desalted enzyme solution was again concentrated to about 1 ml using Amicon Ultra centrifugal filter. The protein aliquots were flash frozen by liquid nitrogen and stored at -80 °C.

Concentrations of non-P450 enzymes (CreH, CreI, CreE, CreF, CreD, CreG and CreC) were determined by the Bradford method using BSA as the standard (4). The concentration of P450 enzymes (wt and mutant CreJ enzymes) was determined according to the method described by Omura (5). Specifically, the CO-bound reduced difference spectrum was recorded by NanoDrop 2000 Spectrophotometer (Thermo Scientific). The concentration of functional P450 was calculated using the extinction coefficient ( $\epsilon_{450 \text{ nm}-490 \text{ nm}}$ ) of 91000 M<sup>-1</sup>·cm<sup>-1</sup>.

**Expression and purification of CreJ for crystallization procedures.** To facilitate heterologous expression of CreJ, the *creJ* gene with the first 84 nucleotides truncated was cloned into pET28a between *Bam*HI and *Hind*III restriction sites. The shortened protein containing an *N*-terminal His<sub>6</sub>-tag was expressed in *Escherichia coli* BL21 (DE3) and purified using a Ni<sup>2+</sup> Sepharose HP column (GE healthcare). The protein was further purified by anion exchange chromatography with a Q-sepharose column (GE healthcare) and gel filtration using a Superdex 75 column (GE healthcare). The gel filtration result indicates that the recombinant CreJ is monomeric in solution.

**CreJ mutagenesis and relative activity determination.** Mutation sites were introduced via PCR (Table S4). Specifically, complimentary primer pairs containing the mutated codon of interest were employed in PCR amplifications (35 cycles of 95 °C for 10 s, 55 °C for 15 s, and 72 °C for 2 min; FailSafe system from Epicentre) to yield a linear mutant plasmid from the original pET28a-*creJ* template DNA. Following gel purification, each linear mutant plasmid was treated with homologous recombinase (Hieff Clone TM One Step Cloning Kit, Yeasen, Shanghai, China) following vendor's protocols, followed by transformation into *E. coli* BL21(DE3). The incorporation of the mutated codon was confirmed via Sanger DNA sequencing (GENEWIZ, Suzhou, China).

Wild-type and mutant enzymatic activities were comparatively determined in reactions using **1'** as substrate, at 30 °C for 20 min. A standard reaction mixture contained 1  $\mu$ M CreJ (or CreJ mutant), 1  $\mu$ M CreE and 1  $\mu$ M CreF, 1 mM substrate, and 4 mM NADPH in 100  $\mu$ l of 50 mM Tris·HCl (pH 8.0). The substrate consumption ratio of each reaction was determined by high-performance liquid chromatography (HPLC). Relative enzymatic activity of each mutant was calculated by comparing substrate consumption ratios to that of CreJ, which was assigned 100% activity. All reactions were carried out in triplicate and the data was reported as the means  $\pm$  SD.

Substrate binding assays. Spectroscopic substrate binding assays were carried out at room temperature by employing a UV visible spectrophotometer (Infinite M200 pro, TECAN) (6). Protein dissolved in 1 mL of 50 mM sodium phosphate buffer containing 10% glycerol (pH 7.4) at concentration of 1  $\mu$ M was titrated with 100 mM stock solution of 4-cresol. The final concentration of substrate ranged from 0.2 to 0.8 mM. Data consisting of absorbance differences  $\Delta A$  ( $A_{390 \text{ nm}} - A_{420 \text{ nm}}$ ) and corresponding substrate concentration from duplicated experiments were plotted and fitted to the hyperbolic function  $\Delta A = A_{\text{max}} \cdot S/(K_D + S)$ , where *S* is the total substrate concentration,  $A_{\text{max}}$  is the maximal absorption shift at saturation, and  $K_D$  is the apparent dissociation constant for the enzyme-substrate complex.

**Chiral HPLC analysis of 2a and 7a.** The reaction sample was extracted with an equal volume of ethyl acetate. The organic phase was dried by nitrogen stream and re-constituted in an equal volume of methanol. The chiral column  $(250 \times 4.6 \text{ mm})$  was manually packed with the chiral stationary phase, which was prepared by coating chitosan bis(3-chlorophenylcarbamate)-(cyclohexyl urea) on the surface of 3-aminopropyl silica gel according to a previously published method (7).

Chiral analysis was carried out on an Agilent 1260 infinity HPLC system (Agilent Technologies, USA) equipped with a DAD detector. The two enantiomers of 2a and 7a were respectively separated on the chiral column described above using an isocratic mobile phase of hexane containing 10% isopropanol over 60 min. The flow rate was set to 1 ml/min and injection volume was 10  $\mu$ l. The detection wavelength was set to 275 nm. Optical configuration was determined via retention time comparison with the enantiomerically pure authentic standard.

Sources of substrates and authentic standard compounds. Except the phosphorylated compounds that were chemically synthesized (*see below*), all substrates and authentic standard compounds were purchased from different chemical suppliers. In details, **2** was bought from Tokyo Chemical Industry (TCI, Shanghai, China); **3**, **4b**, **6a**, **7b**, **11** and **12** from J&K Scientific Ltd. (Beijing, China); **4** from Acros Organics (Thermo Fisher Scientific, USA); **5**, **6** and **9** from AIKE REAGENT (Chengdu, China); **7** from Sigma-Aldrich (USA), **8** from Toronto Research Chemicals (TRC, Canada); **10** from Fluorochem (Derbyshire, UK), **5b** and racemic **2a** from Bide Pharmatech Ltd. (Shanghai, China); **5a** and the enantiomerically pure *S*-**2a** and *S*-**7a** from Enamine (Ukraine); **2b**, **3b**, **6b** and **6c** from Aladdin (Shanghai, China); racemic **7a** from Accela ChemBio (San Diego, CA, USA). **1**' was synthesized by following the chemical method with reference to the previous report (8).

**Chemical synthesis of 4-ethylphenyl phosphate (2').** Compound **2'** was synthesized through chemical methods with reference to previous reports by McKenna and Kenner (9, 10). The reaction scheme is as follow:



In details, to a solution of 4-ethylphenol (1.22 g, 10 mmol) dissolved in carbon tetrachloride (10 mL) was added diethyl phosphite (1.55 mL, 12 mmol) at 0 °C under argon atmosphere. Triethylamine (1.65 mL, 12 mmol) was carefully added drop-wise to the mixture by using a dropping funnel. The mixture was stirred overnight at room temperature. Water (30 mL) was added and the organic layer was separated. The organic layer was washed twice with dilute hydrochloric acid ( $2 \times 15$  mL), four times with dilute sodium hydroxide solution ( $4 \times 15$  mL), and twice with brine ( $2 \times 15$  mL) before being dried over anhydrous MgSO<sub>4</sub>. Removal of solvent on rotary evaporator gave a crude, which was further purified by silica gel column chromatography using a petroleum ether/ethyl acetate (4/1: v/v) mixture to afford diethyl (4-ethylphenyl) phosphate (2.51 g). Yield: 97 %.

Diethyl (4-ethylphenyl) phosphate (2.51 g, 9.7 mmol) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (50 mL). Then bromotrimethylsilane (12.8 mL, 10 equiv. to phosphate ester) was added to the solution and the mixture was heated to reflux for 18 h under argon atmosphere. The solvent was evaporated and the residue was dissolved in anhydrous methanol (50 mL). The solution was stirred for 30 min at 40 °C. Then the resulting solution was concentrated to give **2'** (1.8 g). Yield: 92%. Structure of synthetic **2'** was confirmed by HRMS (Fig. S42) and NMR (Fig. S43 and S44).

Chemical synthesis of 1-hexanol phosphate (11') and 4-methyl cyclohexanol phosphate (12'). Compound 11' was chemically synthesized using previously reported methods (11). The reaction scheme is as follow:



In details, **11'** was prepared by mixing **11** (5 mmol, 0.51 g) with the reagent phosphorus oxychloride (5 mmol, 0.77 g), by vigorous stirring for 1 h under aspirator vacuum to remove HCl (g), and then heated at 50 °C for 5 h. The reaction was quenched via a dropwise addition of the reaction mixture into excess cold water, and the resultant mixture was then stirred for 5 h at 30 °C. The product was extracted with Et<sub>2</sub>O multiple times. The combined extracts were dried with anhydrous MgSO<sub>4</sub>, and Et<sub>2</sub>O was removed under reduced pressure to afford a colorless oil 0.75 g (yield: 91 %).

Compound **12'** was accessed by following previously described methods (12). The reaction scheme is as follow:

HO 
$$+$$
 POCl<sub>3</sub>  $\xrightarrow{1.2,6-lutidine, CCl_4}$   $HO \xrightarrow{P} O$   
12  $HO \xrightarrow{H} O$   
2. *t*-BuOH, H<sub>2</sub>O  $HO \xrightarrow{H} O$   
 $OH$   
12  $12'$ 

Specifically, **12** (5 mmol, 0.57 g) and 2,6-lutidine (5.5 mmol, 0.59 g) in carbon tetrachloride (2 ml) were added to phosphorous oxychloride (5mmol, 0.77 g) in carbon tetrachloride (10 ml) at 0-10 °C. After an hour, the product was filtered from base hydrochloride and evaporated, yielding the dichloridate as a colorless oil. 4-Methyl cyclohexy1 phosphorodichloridate in carbon tetrachloride (5 ml) was treated with *tert*-butyl

alcohol (0.85 g) and water (0.1 ml) for 30 min at 50 °C. Removal of the solvent left an oil which was dissolved in 30 ml water, and extracted with Et<sub>2</sub>O several times. The combined extracts were dried with anhydrous MgSO<sub>4</sub>, and Et<sub>2</sub>O was removed *en vacuo* to give 0.3 g of a white solid (yield: 31 %). The chemical structures of synthetic **11**' and **12**' were confirmed by HRMS (Fig. S29 and S30) and NMR (Fig. S45-S48).

## SI Tables

Parameter	CreJ-1'	CreJ-2'
<b>Data collection</b> <sup><i>a</i></sup>		
Space group	C 1 2 1	P 43 21 2
<i>a,b,c</i> (Å)	125.54, 121.14, 125.61	86.07, 86.07, 125.04
α, β, γ	90.0, 90.96, 90.0	90.0, 90.0, 90.0
Wavelength	0.979	0.979
Resolution (Å)	34.56-2.0 (2.03-2.0)	35.45-1.70 (1.73-1.70)
Total reflections	454625 (17470)	687298 (36247)
Unique reflections	125653 (5928)	52282 (2731)
Completeness (%)	99.3 (94.4)	99.8 (100.0)
Multiplicity	3.6 (2.9)	13.1 (13.3)
Mean I/sigma (I)	8.5 (2.1)	20.1 (5.6)
$R_{merge}^{b}$	0.106 (0.516)	0.091 (0.505)
Refinement		
$R_{work}/R_{free}$ (%)	16.08/19.79	18.15/20.88
No. atoms		
Protein	12765	3252
Ligands	255	56
water	1825	552
<b>B-factors</b>		
Average B-factor	34.00	24.20
Proteins	33.70	22.40
Ligands	23.80	11.20
Solvent	38.10	35.80
r.m.s.d.		
Bond length (Å)	0.01	0.006
Bond angles	1.22	1.15
Ramachandran statistics		
Favored (%)	97	97
Outliers (%)	0.06	0

Table S1. Data collection and refinement statistics for CreJ structures.

<sup>*a*</sup> Numbers in parentheses refer to data in the highest-resolution shell.

<sup>b</sup>  $R_{\text{merge}} = \sum hkl \sum i |I(hkl)i-\langle I(hkl)\rangle| / \sum hkl \sum i \langle I(hkl)i\rangle$ , where *I* is the observed intensity,  $\langle I(hkl)\rangle$  represents the average intensity, and I(hkl)i represents the observed intensity of each unique reflection.

Alkylphenol	<b>CreHI</b> <sup>a</sup>	CreHI + CreJEF <sup>b</sup>	$CreHI + CreJEF + CreD^{c}$
p-cresol (1)	+	+	+
<i>p</i> -ethylphenol (2)	+	+	+
<i>p</i> -vinylphenol (3)	+	+	+
<i>p</i> -propylphenol (4)	+	+	+
<i>p</i> -isopropylphenol (5)	+	+	+
m-cresol (6)	+	+	+
<i>m</i> -ethylphenol (7)	+	+	+
<i>m</i> -vinylphenol (8)	+	-	+
<i>o</i> -cresol (9)	+	-	+
o-ethylphenol (10)	-	-	-

 Table S2. Reactivity of CreHI, CreJEF and CreD towards different alkylphenols (1-10).

<sup>a</sup>Each alkylphenol (1 mM) was phosphorylated by CreHI (10  $\mu$ M for each enzyme), in the presence of 20 mM MgCl<sub>2</sub>, 2 mM MnCl<sub>2</sub>, and 2 mM ATP, at 30 °C for 2 h;

<sup>b</sup>Following the first stage of phosphorylation by CreHI<sup>a</sup>, CreJEF (10  $\mu$ M for each protein) and 2 mM NADPH were added at 30 °C for 2 h;

 $^{\rm c}$  Following the reactions catalyzed by CreHIa and CreJEFb, CreD (10  $\mu M$ ) was added at 30  $^{\rm o}$ C for 2 h;

"+" represents that substrate consumption or product formation was detected;

"-" represents neither substrate consumption nor product formation was detected.

Strain, plasmid	Genotype/Phenotype	Source
E. coli BL21(DE3)		Novagen
<i>E. coli</i> DH5α		Invitrogen
pET28b	Expression vector	Novagen
pET28b-creC	Expression vector of CreC	Du L, et al., 2016
pET28a-creD	Expression vector of CreD	Li T, et al., 2014
pET28a-creE	Expression vector of CreE	Li T, et al., 2014
pET28a-creF	Expression vector of CreF	Du L, et al., 2016
pET28a-creG	Expression vector of CreG	Li T, et al., 2014
pET28b-creH	Expression vector of CreH	Du L, et al., 2016
pET28b-creI	Expression vector of CreI	Du L, et al., 2016
pET28a- <i>creJ</i>	Expression vector of CreJ	Li T, et al., 2014
pET28a- <i>creJ</i> -Q83A	Expression vector of CreJ-mutant (Q83A)	Present study
pET28a- <i>creJ</i> -S106A	Expression vector of CreJ-mutant (S106A)	Present study
pET28a- <i>creJ</i> -S109A	Expression vector of CreJ-mutant (S109A)	Present study
pET28a- <i>creJ</i> -R194A	Expression vector of CreJ-mutant (R194A)	Present study
pET28a- <i>creJ</i> -R194K	Expression vector of CreJ-mutant (R194K)	Present study
pET28a- <i>creJ</i> -R194E	Expression vector of CreJ-mutant (R194E)	Present study
pET28a- <i>creJ</i> -S261A	Expression vector of CreJ-mutant (S261A)	Present study
pET28a- <i>creJ</i> -W199A	Expression vector of CreJ-mutant (W199A)	Present study
pET28a- <i>creJ</i> -F264A	Expression vector of CreJ-mutant (F264A)	Present study
pET28a- <i>creJ</i> -I312A	Expression vector of CreJ-mutant (I312A)	Present study
pET28a-creJ-W315A	Expression vector of CreJ-mutant (W315A)	Present study
pET28a- <i>creJ</i> -F416A	Expression vector of CreJ-mutant (F416A)	Present study

Table S3. Strains and plasmids used in this study.

Mutant	Primer	Sequence
Q83A	Q83A-F	AAATGCAGCAGCCCCAGTCCGCAAG
	Q83A-R	CTGGGGC <b>TGC</b> TGCATTTTCAGAGGA
S106A	S106A-F	TGCATACGCAGGATTATCAGCTCGT
	S106A-R	ATAATCCTGCGTATGCAGTGAAGCC
S109A	S109A-F	CGGATTA <b>GCA</b> GCTCGTATTCCACCA
	S109A-R	TACGAGC <b>TGC</b> TAATCCGGAGTATGC
R194A	R194A-F	AGATTCCGCAGCGGCCATGACCTGG
	R194A-R	TGGCCGCTGCGGAATCTGACCACCG
R194K	R194K-F	AGATTCCAAAGCGGCCATGACCTGG
	R194K-R	TGGCCGCTTTGGAATCTGACCACCG
R194E	R194E-F	AGATTCCGAAGCGGCCATGACCTGG
	R194E-R	TGGCCGCTTCGGAATCTGACCACCG
S261A	S261A-F	GCTGTACGCACTGCTTTTTGCGGGGG
	S261A-R	AAAGCAGTGCGTACAGCAAAGAAGC
W199A	W199A-F	CATGACCGCAGGCGATCTTAGTGAT
	W199A-R	GATCGCCTGCGGTCATGGCCGCACG
F264A	F264A-F	CCTGCTT <b>GCA</b> GCGGGGGCACGAAACA
	F264A-R	GCCCCGCTGCAAGCAGGGAGTACAG
I312A	I312A-F	CGGCTCG <b>GCA</b> GTGGGGTGGCGTCGA
	I312A-R	ACCCCACTGCCGAGCCGGAGTACCG
W315A	W315A-F	CGTGGGGG <b>GCA</b> CGTCGAAAAGCATTA
	W315A-R	TTCGACG <b>TGC</b> CCCCACGATCGAGCC
F416A	F416A-F	CCTCTCCGCACGCGTCCCCACTTCT
	F416A-R	GGACGCGTGCGGAGAGGGTTCTCCCG

Table S4. Primers used for mutagenesis of CreJ.

Nucleotides in bold represent the mutated codons.

**SI Figures** 



Fig. S1. The P450 catalytic cycle. (Adapted from the previous publication (13))



Fig. S2. Steric positions of the residues interacting with the phosphate group (A) and benzyl moiety (B) of 4-cresol.



**Fig. S3. SDS-PAGE analysis of purified wild-type and mutant CreJ enzymes.** (*A*) Mutants of the residues interacting with the phosphate group of substrate. (*B*) Mutants of the residues surrounding the benzyl moiety of substrate. M, protein marker.



Fig. S4. The binding curve of 4-cresol to the R194A mutant.



Fig. S5. The binding curve of 4-cresol to the R194K mutant.



Fig. S6. The binding curve of 4-cresol to the R194E mutant.



Fig. S7. The binding curve of 4-cresol to wild-type CreJ.



Fig. S8. The binding curve of 4-cresol to the S106A mutant.



Fig. S9. The binding curve of 4-cresol to the S261A mutant.



Fig. S10. The binding curve of 4-cresol to the Q83A mutant.



Fig. S11. The binding curve of 4-cresol to the S109A mutant.



Fig. S12. The binding curve of 4-cresol to the W199A mutant.



Fig. S13. The binding curve of 4-cresol to the I312A mutant.



Fig. S14. The binding curve of 4-cresol to the F416A mutant.



Fig. S15. The binding curve of 4-cresol to the F264A mutant.



Fig. S16. The binding curve of 4-cresol to the W315A mutant.



Fig. S17. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 2 and its derivatives. Trace i, Negative control; trace ii, 2 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S18. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 3 and its derivatives. Trace i, Negative control; trace ii, 3 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$  indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S19. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 4 and its derivatives. Trace i, Negative control; trace ii, 4 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S20. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 5 and its derivatives. Trace i, Negative control; trace ii, 5 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S21. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 6 and its derivatives. Trace i, Negative control; trace ii, 6 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S22. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 7 and its derivatives. Trace i, Negative control; trace ii, 7 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S23. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 8 and its derivatives. Trace i, Negative control; trace ii, 8 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$  indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



Fig. S24. Preliminary reactivity determination of CreHI, CreJEF and CreD towards 9 and its derivatives. Trace i, Negative control; trace ii, 9 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.  $\blacklozenge$ indicates product generation compared to the upper trace.  $\blacktriangle$  indicates significant substrate consumption compared to the upper trace.



**Fig. S25.** Preliminary reactivity determination of CreHI, CreJEF and CreD towards 10 and its derivatives. Trace i, Negative control; trace ii, 10 + CreHI; trace iii, the post-CreHI reaction mixture + CreJEF; trace iv, the post-CreHI/CreJEF reaction mixture + CreD.



Fig. S26. Determination of the absolute configuration of 2a (A) and 7a (B) by chiral HPLC analysis. (A) Trace i, S-2a authentic standard; trace ii, racemic 2a standard; trace iii, the reaction mixture of 2 sequentially reacted with CreHI/CreJEF and CreD.  $\blacklozenge$  indicates only S-2a was produced. (B) Trace i, S-7a authentic standard; trace ii, racemic 7a standard; trace iii, the reaction mixture of 7 sequentially reacted with CreHI/CreJEF and CreD.  $\blacklozenge$  indicates only S-7a was produced.



**Fig. S27. Structural comparison of CreJ-1' (green, 5GWE) and CreJ-2' (orange, 5XJN).** (*A*) Superimposition of CreJ-1' and CreJ-2'. (B) Conformational alignment of the active site residues. Substrate 1' and 2' are shown in purple and cyan, respectively. "w" represents the water molecule observed only in the CreJ-1' structure.



Fig. S28. Structures of non-aromatic 11, 12, 11' and 12'.



**Fig. S29. LC-HRMS analysis of the CreJ reactivity towards 11'.** Trace i, the total ion chromatography (TIC) of the CreJEF catalyzed reaction with **11'** as substrate; trace ii, the extract ion chromatography at m/z 181; trace iii, the extract ion chromatography at m/z 197. The right panel shows the high resolution mass spectra of **11'** and **11'a-c**.



**Fig. S30. LC-HRMS analysis of the CreJ reactivity towards 12'.** Trace i, the total ion chromatography (TIC) of the CreJEF catalyzed reaction with **12'** as substrate; trace ii, the extract ion chromatography at m/z 193; trace iii, the extract ion chromatography at m/z 209. The right panel shows the high resolution mass spectra of **12'** and **12'a-d**.

				α1 β1	
CYP288A2	i 10	20	TT TT 30		
CYP288A2 WP_011013726.1		TGG <mark>CP</mark> FGHTSESTS	MHGYQPFDMH HHGYQPFDMH	N <mark>P</mark> F P A Y K E L <mark>R</mark> QE E P V M F D F N P F P A Y K E L RQE E P V M F D F	ARI ERI
WP_060564075.1	MTSQTSQQSTS.	TGG <mark>CP</mark> FGHTSESTS	HHGYQPFD MH	N <mark>P</mark> F P A Y K E L <mark>R Q E E P</mark> V M F D E N P F P A Y K E L R O F E P V M F D E	ARI CRI
WP_003860615.1	MTSQTSQQSTS.	TGGCPFGHTSESTS	HHGYQPFDMH	N P F P A Y K E L R Q E E P V M F D E	RI
WP_083967321.1 WP_038582779.1	MISQISQQSIS.		HHGYQPFDMH	N <mark>P</mark> FPAYKEL <mark>R</mark> QEEPVMFDE	SRI
WP_006287245.1 WP_044026924.1		TGG <mark>CP</mark> FGHTSESTS TGG <mark>CP</mark> FGHTSESTS	MHGYQPFDMH HHGYQPFDMH	N P F P A Y K E L R Q E E P V M F D E N P F P A Y K E L R Q E E P V M F D E	JRI SRI
WP_040966998.1 BAF53637.1		TGG <mark>CP</mark> FGHTSESTS	HHGYQPFD MH	N <mark>P</mark> F P A Y K E L <mark>R Q E E P</mark> V M F D E N P F P A Y K E L R OF E P V M F D E	SRI SRI
WP_003854399.1		TGGCPFGHTSESPS	HHGYQPFD MH	N <mark>P</mark> F P A Y K E L <mark>R</mark> Q E E <b>P</b> V M F D F	RI
WP_066564562.1		TGG <mark>CP</mark> FGHTASSDTDQ	YHGYQPFQME	N <mark>P</mark> FPAYQEL <mark>R</mark> REEPVMFDE N <mark>P</mark> FPAYQEL <mark>R</mark> REE <mark>P</mark> VMFDE	SRI
WP_035109760.1 EEW50177.1		SGGCPYGHGNPDATGTP SGGCPYGHGNPDATGTP	.GTSHHGYEPFNMT .GTSHHGYEPFNMT	N <b>P</b> F P A Y E E L <b>R R E E P</b> V M F D E N <b>P</b> F P A Y E E L <b>R R E E P</b> V M F D E	JRI SRI
BAC17372.1		SGG <mark>CP</mark> YGHGNPDATGTP	.GISHHGYEPFNMT	N <mark>P</mark> FPAYEEL <mark>R</mark> REE <mark>P</mark> VMFDE NPEPSYAELPREEPVMEDE	SRI FRT
WP_010144948.1	MT.TESTTAAPA	GQ.CPFGHGGPGAQDADAA	IPTDHHGYQPFQMK	DPFPSYAALRSEEPVMFDE	RI
WP_026196155.1 WP_062861371.1		QG. <mark>CP</mark> FGHG TGK <mark>CP</mark> YSGAAQGS	AEKSHHGYEPFQMK HHGYEPFDMK	N <b>P</b> F P A Y S E L <b>R K N E P</b> I M F D E N <b>P</b> F P A Y A E M <b>R</b> K E E <b>P</b> V M F D E	JRI SRV
WP_039207235.1	TLQSAAE	TGKCPYSGAAQGS	HHGYEPFD MK	N <mark>P</mark> FPAYAEM <mark>R</mark> KEEPVMFDE NPEPAYAEMRKEEPVMEDE	SRV
WP_011691841.1	SPSTET.	AGRCPFGHGAEAPAG	HHGYEPFQMK	DPFPAYAELRAEQPVMFDE	RV
WP_024367961.1 WP_005273409.1	SPSTET.	AGRCPFGHGAEAPAG		D P F P A Y A E L RAE OP V M F D E D <mark>P</mark> F P A Y A E L <mark>R</mark> A E Q P V M F D E	SRV SRI
WP_043481247.1 WP_055806675.1	SPSTET	AGRCPFGHGAEAPAG	HHGYEPFQ MK	DPFPAYAELRAEOPVMFDE DPFPAYAELRAEOPVMFDE	IRV ERV
WP_062289581.1	SSTRET	APGCPFGHGAQAPAG	HHGYEPFSMK	DPFPAYAELRAEOPVMFD	RI
WP_028276640.1	SSSIEI.	AGR <mark>CP</mark> FGHGAEAPTG	HHGYEPFQMK	D <mark>P F P A Y A E L R A E Q P</mark> V M F D F D <mark>P F P A Y A E L R A E Q P</mark> V M F D F	SRI
WP_026539569.1 WP_018775007.1		AGR <mark>CP</mark> FGHGAEAPAG	HHGYEPFQ MK	D P F S A Y A E L R A E Q P V M F D F D P F S A Y A E L R A E O P V M F D F	GRI GRI
WP_013600843.1	SPSTET	AGR <mark>CP</mark> FGYGAEAPAG	HHGYEPFQMK	D P F P A Y A E L R A E Q P V M F D F	RV
WP_028285717.1 WP_068734283.1		AGV <mark>CP</mark> MGHGATAPAD	HHGYEPFTME	N <mark>P</mark> F P S Y T N L <mark>R</mark> N E Q P V M F D E	SRV
WP_069950213.1 WP_007269721.1		AGR <mark>CP</mark> YGHGAEAPAG AGVCPMGHGATAPAD	HHGYEPFQ MK HHGYEPFT ME	N P F P A Y A E L R A E Q P V M F D E N P F P S Y S N L R D E Q P V M F D E	JRV ERV
AIS67786.2		CPMGHGATAPAD	HHGYEPFT ME	N <mark>P</mark> F P S Y S N L <mark>R</mark> D E Q P V M F D E N P F P S Y A K M P S F O P V M F D E	SRV ERT
WP_038992926.1		SGGCPMGFGAEAPAG	HHGYEPFAME	N <mark>P</mark> F P S Y A K M <mark>R</mark> S E Q P V M F D E	RT
WP_047120326.1 WP_053799000.1		SGG <mark>CP</mark> MGFGAQTPAD	HHGYEPFAME	N P F P A Y A RMR SE Q P V M F D E N <mark>P</mark> F P A Y A K M <mark>R</mark> SE Q P V M F D E	JRT SRT
WP_040795180.1	MTSTHSPAGP	ATGCP	VHHGYEPFAQN	D <mark>P</mark> FPAYAAL <mark>R</mark> AEE <mark>P</mark> VMFDE DPEPSYAELRTEAPVEEDE	SRI ERT
WP_045191440.1	SKTTEAPTA	QSGCP	VHHGYEPFKLD	D P F P A Y A E L R R E E P V M F D E	RI
WP_066501301.1 WP_052024002.1		QAG <mark>CP</mark> VPHGDT	AHHGYEPFQQN	N P F P A Y A A L RAE E P V M Y D E D <mark>P</mark> F P S Y A E L <mark>R</mark> T E A <mark>P</mark> V F F D E	SRI
WP_026453050.1 WP 067137052.1		GPG <mark>CP</mark>	VHHGYEPFRQF VHHGYEPFDON	D <mark>P</mark> FPAYAAL <mark>R</mark> AEEPVMYDE DPFPAYAALRSEEPVMFDE	SRI SRI
ELB90053.1	TODTOCADUDUSCETMUAA		AHHGYEPFDQN	D P F P S Y A E L R T E A P V F F D E	RI
WP_055597530.1		APG <mark>CP</mark>	IRHGYEPFAQD	D <mark>P</mark> F P S Y A A L <mark>R</mark> A E E P V M Y D E	RI
WP_066941537.1 WP_040168028.1		PRSCP	QN GHHGYEPFQMT	D P F P A Y A A L R SE E P V M F D E D <mark>P</mark> F P A Y E N L <mark>R R D A P</mark> V Y F D I	JRI DRT
WP_033293979.1 WP_061252837.1		. TG <mark>CP</mark>	VHHGYEPFAQD	D <mark>P</mark> FPAYAAL <mark>RAGEP</mark> VMYDE DPFPAYAALRSEEPVMEDE	SRI CRI
WP_006335139.1		. AGCP	VHHGYEPFNQN	N <b>P F V S Y A A L R A E E P V M Y D F</b>	RI
WP_020389625.1 WP_053447282.1	STEQGPS	PSK <mark>CP</mark> VAHGG.AA	EHHGYEPFDMH	DPFPSIALLRALEVMIDE D <mark>P</mark> FPAYAQL <mark>R</mark> EQE <mark>P</mark> VMYDE	SRI
WP_024368481.1 WP_022870166.1		SG.CPFGHGAEAPAG		N <mark>P</mark> F P A Y A E L <mark>R</mark> A E Q P V M F D E D P F P A Y A K M R H E O P V M F D I	JRV DRT
ODT11970.1	CPVDHT	AFTGAGTGDS	AHHGYEPFD MT	DPFPAYERLRTEEPVMYDE	SRI
WP_056728828.1	STVATRPPT.	ASACPVDHGT	GHHGYSPFDMD	DPFEAYAKLRSEHPVMYDE	RI
BAU99498.1 WP_035877878.1	MNAQPSVSAASADRAVATCPFPHS.	AAPESASTPESAA	YHGYEPFDMK PHADYAPFAMN	DPFPAYAELRREEPVMYDI D <mark>P</mark> FPSYAAL <mark>REHAP</mark> VMYDE	)RI SRI
SBT38743.1 KGA07700 1	GE	ARR <mark>CP</mark>	VTHGFDAFDLT	DPFPAYAQLRAGGPVLYDE NPFPSYAALREFAPVMWDI	RT
GAP56794.1	SPSTDT.	AGR <mark>CP</mark> FGHGAEAPAG	HHGYEPFQ MK	N <mark>P F P A Y A E L R A E Q P</mark> V M F D F	RI
WP_015030068.1		GCPIHQIR	LEFKPFDLI	N <mark>P</mark> F P F Y K Q A R E E E P I F F S F	EL
WP_009184779.1 WP_015664221.1		CPYHKELN	LT	N <mark>P</mark> F P F Y K E V R E K C P I F F S E D P F P F Y E WARAE A P V F F S I	JEL DEL
WP_009031006.1		CPYHDA	AKDFDPFEMR	D <mark>P</mark> FPFYEWARAEAPVFFSI DPFPFYEWARAEAPVFFSI	EL
WP_012041855.1		CPYHDA	ATDFDPFEMR	DPFPFYEWARAEAPVFFSI DPFPFYEWARAEAPVFFSI	EL
WP_067547936.1 WP_013926219.1		.SACPYHSQLS	LS KEFKPFDLT	APHAKWKELREDQPVFQDE D <mark>P</mark> FPVYKK <mark>AR</mark> EEE <mark>P</mark> VFYSE	'ES EL
WP_007204700.1			LG	APHPKWKQLREOKPVFHD APHAAWKALREFAPVYHD	ES
WP_064750566.1			FRPFELA	DPFAFYARARAEEPVFFSE	AL
wr_037664388.1 SCG02642.1	· · · · · · · · · · · · · · · · · · ·	TTGCP	VHHGFDPLGDEYIA VHHGFDPLGDEYIA	DE I FIHSAVREEAEAFYA D <mark>P</mark> YPIHSAV <mark>R</mark> EEAPAFYA	IA1
WP_030497796.1 WP 014158279.1			VHHGFDPLGDEYIA	DPYPIHTAVREEAPAFYAF DPYPIHSAVREEAPAFYA7	AI
WP_037831154.1		• • • • • • • • • • • • • • • • • • • •	HHSFDPLGEPYIA	DPYPIHSAVREEAPAFYA	AI
WP_030882035.1 WP_009951127.1			HHSFDPLGEPYIA	DETETHSAVREEAPAFYAA DEFEILAAIREETEVFYSS	A Í SE L

CYP288A2	β2 0.0	α2	β3	α3	TT	α4 000000000000000	α5
CIFZOORZ	60	70	80	90 100	110	120	130
CYP288A2	GYWVVTKYD	DIKTTFDDWE	T F S S E N A <mark>Q</mark> A	PVRKRGPQATQIMTDGGF	TAYSGL <mark>S</mark> ARI <mark>P</mark>	PEHTRIRAIAQKA	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_011013726.1	GYWVVTKYD GYWVVTKYD	DIKTTFDDWE	TFSSENAOA	PVRKRGPQATQIMTDGGF	TAYSGLSARIP	PEHTRIRAIAQKAE PEHTRIRAIAOKAE	TPRRYKALEP
WP_065366652.1	GYWVVTKYD	DIKTTFDDWE	TFSSENAOA	PVRKRGPQATQIMTDGGF	TAYSGLSARIP	PEHTRIRAIAOKA	TPRRYKALEP
WP_003860615.1	GYWVVTKYD	DIKATFDDWE	T F S S E N A <mark>Q</mark> A	<b>PVRKRGPQATQIMTDGGF</b>	TAYSGL <mark>S</mark> ARIP	PEHTRIRAIAQKAE	TPRRYKALEP
WP_063967321.1 WP 038582779.1	GYWVVTKYD	DIKATEDDWE	TFSSENAOA	V R K R G P Q A T Q I M I D G G F P V R K R G P O A T O I M I D G G F	TAYSGLSARIP	PEHTRIRAIAQKAE	TPRRYKALEP
WP_006287245.1	GYWVVTKYD	DIKATFDDWE	TFSSENAQA	PVRKRGPQATQIMTDGGF	TAYSGLSARIP	PEHTRIRAIAQKA	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_044026924.1	GYWVVTKYD	DIKATEDDWE	TFSSENAQA	PVRKRGPQATQIMTDGGF	TAYSGLSARIP	PEHTRIRAIAQKAE	TPRRYKALEP
WP_040966998.1 BAF53637.1	GYWVVIKID	DIKATEDDWE	TFSSENAOA	V R K R G P Q A T Q I M I D G G F	TAYSGLSARIP	PEHTRIRAIAOKA	TPRRYKALEP
WP_003854399.1	GYWVVTKYD	DIKATFDDWE	T F S S E N A <mark>Q</mark> A	PVRKRGPQATQIMTDGGF	TAYSGL <mark>S</mark> AR I P	PEHTRIRAIAQKA	TPR <mark>R</mark> YKALE <mark>P</mark>
BAU94954.1 WP 066564562 1	GYWVVTKYD GYWVVTKYD	DIKATEDDWE	TESSENAOA	PVRKRGPQATKIMNDGGF	TAYSGLSARIP	PEHTRIRAIAQKAB	TPRRYKALEP
WP_035109760.1	GYWVVTRYD	DIKATFDDWE	TFSSENAQA	PVRKRGPQATKIMEEGGF	TAYSGLSARIP	PEHTRIRAIAQKA	TPRRYKALEP
EEW50177.1	GYWVVTRYD	DIKATFDDWE	TFSSENA <mark>Q</mark> A	PVRKRGPQATKIMEEGGF	TAYSGLSARIP	PEHTRIRAIAQKAE	TPRRYKALEP
BAC17372.1 WP 015399966.1	GYWVVTRYD GYWVVTRYD	DIKATEDDWE	TFSSENAQA TFSSENAQA	V R K R G P Q A T K I MEE G G F V R E R G P O A K K I MEE G G F	TAYSGLSARIP	PEHTRIRALAQKAS	TPRRYKALEP
WP_010144948.1	GYWVVSRYD	DIKAVFDDWE	T F S S E N A <mark>Q</mark> A	PVRERGPLATQIMKDGGF	TAYSGL <mark>S</mark> ARVP	PEHTRIRAIAQKA	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_026196155.1	GYWVVSTYD CYWVVTOYD	DIKNVFDDWE	TFSSENAQA	PVRERGPQATQIMKDGGF	TAYSGLSARVP	PEHTRIRE IAQKAE	TPRRYKALEP
WP_039207235.1	GYWVVTQYD	DIKAVFEDWE	TFSSENAOA	PVRKRGPQATKIMNDGGF	TAYSGLSARIP	PEHTRIREIVOKA	TPRRFKKLEP
WP_062241641.1	GYWVVTRYD	DIKAVFEDWE	T F S S E N A <mark>Q</mark> A	<b>PVRKRGPQATKIMKDGGF</b>	TAYSGLSARIP	PEHTRIREIVQKAE	T P R <mark>R</mark> F K K L E P
WP_011691841.1 WP_024367961_1	GLYVVSRYD	DIKAVFEDWE	TESSENAQA	VRERGPAAKKIMEDGGE VRERGAAAKKIMEDGGE	TAYSGLSARRP	PEHTRIRAVVQKAB	TPRRYKALEP
WP_005273409.1	GYYVVTRYD	DIKAVFDDWE	TFSSENAQA	PVRERGPAAKKIMEEGGF	TAYSGLSARRP	PEHTRIRSVVQKA	TPRRFKVLEP
WP_043481247.1	GLYVVSRYD	DIKAVFEDWE	TFSSENAQA	PVRERGPAAKKIMEDGGF	TAYSGLSARRP	PEHTRIRAVVQKA	TPRRYKALEP
WP_055806675.1 WP 062289581.1	NYFVATRYD	DIKAVFEDWE	TFSSENAOA	PVRERGPAAKOIMTDGGF	TAYSGLSARVP	PEHTRIRAVVQKAL	TPRRYKALEP
WP_028269402.1	GLYVVSRYD	DIKAVFEDWE	T F S S E N A <mark>Q</mark> A	PVRERGAAAKKIMDDGGF	TAYSGLSARRP	PEHTRIRAVVQKA	TPRRYKALEP
WP_028276640.1	GLYVVSRYD	DIKAVFEDWE	TFSSENAQA	PVRERGAAAKKI MDDGGF	TAYSGLSARRP	PEHTRIRAVVQKAE DEHTRIRAVVQKAE	TPRRYKALEP TDBRYKALEP
WP_018775007.1	GLYVVSRYD	DIKAVFEDWE	TFSSENAOA	VRERGAAAKKI MDDGGF	TVYSGLSARRP	PEHTRIRAVVQKA	TPRRYKALEP
WP_013600843.1	GLYVVSRYD	DIKAVFEDWE	T F S S E N A <mark>Q</mark> A	PVRERGPAAKKIMVDGGF	TAYSGL <mark>S</mark> AR <mark>P</mark>	PEHTRIRAVVQKA	T P R <mark>R</mark> Y K A L E <mark>P</mark>
WP_028265717.1 WP_068734283_1	GLYVVSRYD	DIKAVFEDWE	TFSSENAQA TFSSENAQA	EVRERGAAAKKIMDDGGF	TAYSGLSARIP TTYSGLSARP	PEHTRIRAIVQKAB	TPRRYKALEP
WP_069950213.1	GLYIVSRYD	DIKAVFEDWE	TFSSENAQA	VRERGAAAKKIMEDGGF	TAYSGLSARRP	PEHTRIRAVVQKA	TPRRYKALEP
WP_007269721.1	GLYVVTRYD	DVKAVFEDWE	TFSSENAQA	VRKRGPQATQIMNDGGF	TTYSGLSARRP	PEHTRIRAIAQKA	TPRRFKALEP
WP 066143328.1	GLYVLTRYD	DVKAVFEDWE	TFSSENAOA	V R K R G P O A T K I M N D G G F	TTYSGLSARRP	PEHTRIRAIAOKA	TPRRFKALEP
WP_038992926.1	GLYVLTRYD	DVKAVFEDWE	TFSSENA <mark>Q</mark> A	PVRKRGPQATKIMNDGGF	TTYSGLSARRP	PEHTRIRAIAQKA	TPR <mark>R</mark> FKALE <mark>P</mark>
WP_047120326.1	GLYVITRYD	DVKSVFENWE	TFSSENAQA	PVRKRGPQATQIMTEGGF	TTYSGLSARRP	PEHTRIRAVAQKAE	TPRRFKALEP
WP_040795180.1	GYWVVTRYD	DIKAVFEDWE	TFSSENAOA	PVRERGPEAKRIMEEGGF	TAYSGLSARVP	PEHTRIRKVAAKA	TPRRYKVLEP
WP_064080112.1	GYWVVTRFD	DIKAVFEDWQ	T F S S E N A <mark>Q</mark> A	<b>P</b> VRERGAEATRIMTEGGF	TAYSGL <mark>S</mark> ARV <mark>P</mark>	PDHTRIRKIASKAE	TPR <mark>R</mark> YKVLE <mark>P</mark>
WP_045191440.1 WP_066501301.1	GYWVVTRYD	DVKAVFDDWE	TFSSENAQA TFSSENAQA	EVRERGPEAKRIMQEGGE VRKRGPOATOIMNEGGE	TAYSGLSARVP	PEHTRIRKVVAKAB	TPRRYKALEP
WP_052024002.1	GYWVVTRFD	DIKAVFEDWQ	TFSSENAQA	VRERGAEATRIMTEGGF	TAYSGLSARVP	PDHTRIRKIASKA	TPRRYKVLEP
WP_026453050.1	GYWVVTRYD	DIKRVFDDWE	TFSSENAQA	PVRERGPQAKRIMEEGGF	TAYSGLSARVP	PEHTRIRRVVAKA	TPRRYKALEP
ELB90053.1	GYWVVIRID	DIKAVFEDWO	TFSSENAOA	PVRERGAEATRIMTEGGF	TAYSGLSARVP	PDHTRIRKIASKA	TPRRYKVLEP
WP_029339819.1	GYWVVSRYD	DVKAVFEDWH	T F S S E N A <mark>Q</mark> A	PVRQRGPEAKRIMEEGGF	TAYSGL <mark>S</mark> ARV <mark>P</mark>	P D H T R I R K I V S R A B	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_055597530.1 WP_066941537.1	GCWVVSRYD	DIKAVFEDWE	TFSSENAQA TFSSENAQA	PVRERGPQAKQIMEEGGF PVRERGPEATRIMIDGGF	TAYSGLSARVP	PEHTRIRKVAAKAE	TPRRFKVLEP
WP_040168028.1	DLWVVTRWA	DVRAVFEDWE	TFSSENAQA	<b>VRPRGEAASRIMKDGGF</b>	TAYSGLSARIP	PDHTRLRAIAQRA	TPRRYKALEP
WP_033293979.1	GCWVVSRYD	DVKAVFEDWH	TFSSENAQA	PVRERGPQAKQIMADGGF	TAYSGLSARVP	PEHTRIRKVAAKA	TPRRFKVLEP
WP_001252837.1 WP 006335139.1	GYWVVIRID	DVKAVFEDWK	TFSSENAOA	PVRERGPEAKRIMEEGGF	TAYSGLSARVP	PEHTRIRKVAAKAE	TPRRYKALEP
WP_020389625.1	GYWVVTRYD	D VKAVFDDWE	TFSSENA <mark>Q</mark> A	PVRERGPQATRIMADGGF	TAYSGL <mark>S</mark> AR I P	PDHTRIRKVVÄKA	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_053447282.1	DCWVVTRHE	DVKQVFGDWE	TFSSENA <mark>Q</mark> A TFSSENAQA	PVRERGPEARRIMEEGGF	TAYSGL SARVP	PEHTRIRKIAQKAE	TPRRFKVMEP
WP_022870166.1	NLYVVSAYD	DVKAVFEDWE	TFSSENAQA	PVRSRGPQATQIMNDGGF	TVYSGLSARRP	PEHTRIRAVAQKA	TPRRFKVLEP
ODT11970.1	GYWVVTRWA	DVRAVFDDWE	TFSSENA <mark>Q</mark> A	PVRERGAEATRIMKEGGF	TAYSGLSARIP	PDHTRIRAIAQRAE	TPRRFKALEP
WP_043055803.1 WP 056728828.1	GYWVVSAYD	DVKAVFEDWE DVRAVFEDWE	TFSSENAOS	V TKRGP QATQIMKD GGF VRERGREASRIMKE GGF	TAYSGLSARRP	PEHTRIRAVAQKAS	TPRRFKVLEP
BAU99498.1	GYFVVSRYD	DVKAVFEDWE	TFSSENA <mark>Q</mark> A	PVRPMGAPAKKIMEEGGF	TAYSGLSARIP	PEHTRIRSIASKA	TPRRYKVLEP
WP_035877878.1	DCYVVSRYE	DVKAVFENWE DVRAVETDWE	TFSSENAQA TFSSANAQA	PVRPRGEVATRI MNDGGF	TAYSGLSARIP	PEHTRMRGIVQKEE PEHTRIRKVVOROE	TPRRYRKLEP CPPRYRALEP
KGA07700.1	GMFVVTRYD	DVKGVFDDWE	GFSSKDAQS	PIRPLGAAAKKVMADGEF	TTYSGLSARIP	PEHTRIREVATKA	TPRRYKVLEP
GAP56794.1	GLYVVSRYD	DIKTVFEDWE	T F S S E N A <mark>Q</mark> A	<b>PVRERGAAAKKIMEEGGF</b>	TAYSGLSARRP	PEHTRIRAVVQKAE	TPR <mark>R</mark> YKALE <mark>P</mark>
WP_019986768.1 WP_015030068.1	GYYVVTRYE	DIKAVFSNWK	TYTSENAOS VFTSENAOS	PFKPIAPKAKALMEAHGM PFKPIAPKAKALMEEGGI	TGLSGLSGRIP	PDHTRIRRIVSMAR	NVSRFKKLEP
WP_009184779.1	GYYVVSKYĚ	D V K A I F G N W Q	A F S S E N A <mark>Q</mark> S	PFKPIAPKAKALMDSAGL	VGLSGLSGRIP	PDHTRIRRIVSMA	NLARIKKLEP
WP_015664221.1	KYFVVARHA	DIKAVFDDWR	TFSSENAOA	PLRPMCEEGKRIMREGGF	TAYSGLSARVP	PDHTRIRKLVQGCE	GPRRFRAIEP CDDDFDAIEP
WP_006614257.1	KYYVVARHA	DIKAVFDDWR	TFSSENAOA	PLRPMCEEGKRIMREGGF	TAYSGLSARVP	PDHTRIRKLVQGC	GPRRFRAIEP
WP_012041855.1	KYFVVARHA	DIKAVFDDWR	TFSSENA <mark>O</mark> A	PLRPMCEEGRRIMREGGF	TAYSGL <mark>S</mark> ARVP	PDHTRIRKLVQGC	GPR <mark>R</mark> FRAIE <mark>P</mark>
WP_067547936.1 WP 013926219 1	GYWIVTRHA	DIKGVFDDWN	IFSSENAQA VFTSENAOT	PREPACED AGK QIMKD GGF PPKPVPD AVROIMVEGGT	TVYSGLSARIP VGLSGLSGRTP	P DHTRIKKLAQSAE P DHTRIRRIVTMA	GP RKFKAIQP TP KRLRKLEP
WP_007204700.1	GYWIITRHA	DIKAVFDDWK	TFSSENAOA	PMRPMCDAGKQIMKDGGF	TVYSGLSARVP	PDHTRIRKLAQSAE	GPRRFKAIQP
WP_009809975.1	GYWVVTAYD	DIKAVFDDYQ	TFSAEIAQE	TKPLCDEAKRIIAKGGF	T. SGLSARMP	PDHTRIRKVAQTAE	GPR <mark>R</mark> FKSIE <mark>P</mark>
WP_037664388.1	DMWVITRYD	DIEAVLKDPG	TFSAAVGOK	PVFPMSAEAODILKK GF	RAYPVMSDCDP	PRHTRIRKHNMTGE	SPRRIAALEP
SCG02642.1	DMWVITRYD	DIEAVLKDPG	T F S A A V G <mark>Q</mark> K	PVFPMSAEAQDILKK.GF	RAYPVMSDCDP	PRHTRIRKHNMTGE	SPR <mark>R</mark> IAALE <mark>P</mark>
WP_030497796.1 WP 014158279 1	DMWVITRYD	DIEAVLKDPG	TFSAQVG <mark>Q</mark> K TFSAAVGOR	EVEPLSEEAQEILKK.GF	RAYPVMSDCDP	PRHTRIRKHNMTG	SPRRIASLEP SPRRIATLEP
WP_037831154.1	DMWVITRYD	DIEAVLKDPG	TFSAAVGOR	PVFPMSEEAQGILKE.GF	HAYPVMSDCDP	PRHTRIRKHNMTG	SPRRIATLEP
WP_030882035.1	DMWVITRYD	DIEAVLKDPG	TFSAAVGOR	PVFPMSEEAQGILKE.GF	HAYPVMSDCDP	PRHTRIRKHNMTG	SPRRIATLEP
	DUME VINDE	E INNIE ID I E	T O OUT INT			A A A A A A A A A A A A A A A A A A A	O INDER DEE

CYP288A2	<u>α6</u> 22222222	000000 TT	$\xrightarrow{\beta4}$ $00000$ $0$	α7 <u>222222222</u>	η1 eeee	α8 2222222	وووووو	عع	يععد
	140	150	160 1	70	180	190	200	* 21	. <u>o</u>
CYP288A2 WD 011013726 1		RVEKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_060564075.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVDI	YKRWSDSI	RAAMTWGDLS	SDEEQIP	HAH
WP_065366652.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	P <mark>TITILTLI</mark>	GADISMVD1	Y <mark>K</mark> RWSDSI	RAAMTWGDLS	S D E E <mark>Q</mark> I P	? H <mark>A</mark> H
WP_003860615.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVD1	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_038582779.1	DIRAMVID	RVGKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVDI	YKRWSDSI	RAAMTWGDLS	SDEEQIP	HAH
WP_006287245.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVD1	Y <mark>K</mark> RWSDSI	RAAMTWGDLS	S D E E <mark>Q</mark> I P	₽H <mark>A</mark> H
WP_044026924.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	PTITILTLI	GADISMVDI	YKRWSDSI	RAAMTWGDLS	SDEEQIP	HAH
BAF53637.1	DIRAMVID	RVEKMLANDO	HVGDMVSDLAIDI	PTITILTLI	GADISMVDI	YKRWSDS	RAAMTWGDLS	SDEEOIP	HAH
WP_003854399.1	DIRAMVID	RVEKMLANDQ	HVGDMVSDLAYDI	P <mark>TITILTLI</mark>	GADISMVDI	YKRWSDS	RAAMTWGDLS	SDEE <mark>Q</mark> IP	≀H <mark>A</mark> H
BAU94954.1	DIRAMVVD	RVEKMLAHDQ	PVGDMVSDLAYDI	PTITILTLI	GADISMVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_0000304302.1 WP_035109760.1	DIRANVVA	RLETMLKOG	APADIVPALAYDI	PTITILTLI	GADUSMVDI	YKRWSDS	RAAMIWGDLS	SDEEOIP	HAH
EEW50177.1	DIRANVVA	RLETMLKQG	APADIVPALAYDI	PTITILTLI	GADVSMVD1	YKRWSDS	RAAMTWGDLS	SDEE <mark>Q</mark> IP	≀H <mark>A</mark> H
BAC17372.1	DIRANVVA	RLETMLKQG	APADIVPALAYDI	PTITILTLI	GADVSMVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_0103399968.1 WP_010144948.1	DIRANVAS	SRLEAVAAROD	RTGEMVODLAYEI	PTITILTLI	GADISQVDI GADVSKIDI	YKRWSDA	RAAMIWGDLS		HAH
WP_026196155.1	DIRQGVQQ	RLEAMLARDS	KEGEMVQDLAYDI	PTITILTLI	GADTSKIDI	YKKWSDS	RAAMTWGDLS	SDEE <mark>Q</mark> IP	H <mark>A</mark> H
WP_062861371.1	EIRENVVS	SRIEKMLERPD	KDGEIIRDLAYDI	PTITILTLI	GADISKVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	(HAH
WP_039207235.1 WP_062241641.1	EIRENVVS	SRIERMLERPD	KDGEIIRDLAIDI	PTITILILL	GADISKVDI	YKRWSDS	RAAMIWGDLS	SDEEQIP	HAH
WP_011691841.1	FIRQNVIE	LIEKMLARPE	HRGDMVKDLAYDV	PTITILTLI	GADVSQVD1	FKRWSDS	RAAMTWGDLS	SDEEQIP	H <mark>A</mark> H
WP_024367961.1	FIRQNVVE	LLEKMLARPE	HRGDMVKDLAYDV	PTITILTLI	GADVSQVDI	FKRWSDS	RAAMTWGDLS	SDEEQIP	' H <mark>A</mark> H
WP_003273409.1 WP_043481247.1	FIRONVVE	CLLEKMLARPE	HRGDMVKDLAYDV	PIVIILILI PTITILTLI	GADVEQVDQ GADVSOVDI	FKRWSDS	RAAMIWGDLS	SDEEQIP	HAH
WP_055806675.1	FIRQNVVE	LLEKMLARPE	HRGDMVKDLAYDV	PTITILTLI	GADVS. QVDI	FKRWSDS	RAAMTWGDLI	I D E E Q I P	HAH?
WP_062289581.1	DIRANVVE	RLESMLGRPE	RTGDMVADLAYDI	PTITILTLI	GADTAEIDF	YKRWSDS	RAAMTWGNL	NDEEQIP	/ H <mark>A</mark> H
WP_028269402.1 WP_028276640_1	FIRQNVVE	LLERMLARPE	SEGDMVKDLAYDV	PTITILTLI PTITILTLI	GADVS. QVD1 GADVA. OVD1	FKRWSDS	RAAMTWGDLS	SDEEQIP FDDEOTP	'НАН ЭНАН
WP_026539569.1	FIRQNVVE	LLEKMLARPE	HRGDMVRDLAYDV	PTITILTLI	GADVS. QVD1	FKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_018775007.1	FIRQNVVE	LLEKMLARPE	HRGDMVKDLAYDV	PTITILTLI	GADVSQVDI	FKRWSDSI	RAAMTWGDLS	S D E E <mark>Q</mark> I P	2 H <mark>A</mark> H
WP_013600843.1 WP_028265717_1	FIRQNVVA	LIEKMLARPE	RRGDLVKDLAYDV	PTITILTLI	GADVSQVDQ GADVS	FKRWSDS	RAAMTWGDLS	SDEDQIP SDEEQIP	НАН
WP_068734283.1	SIRANVID	SIQAMLARES	GTGDIVKDLAYAI	PTITILTLI	GADTAQVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_069950213.1	FIRQNVVG	GL <mark>LEKML</mark> ARPD	RHGDLVKDLAYDV	PTITILTLI	GADVSQVDI	FKRWSDSI	RAAMTWGDLS	SDEE <mark>Q</mark> IP	? H <mark>A</mark> H
WP_007269721.1 ATS67786.2	SIRANVVI	SIEAMLARES	AEGDIVKDLAYAI	PTITILTLI PTITILTLI	GADVIQVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_066143328.1	MIRENVRS	SAIEQMLARSD	GHAEIVADLAYSL	PTITIVTLI	GADISKVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_038992926.1	MIRENVRS	AIEQMLARGD	GHAEIVADLAYSL	PTITIVTLI	GADISKVDI	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH?
WP_04/120326.1 WP_053799000.1	MIRONVKD	SISAMLANGI	SHADIVADLAYAL	PTITILILI	GEDVGMVD1 GEDVTMVD1	YKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_040795180.1	QIRANVVR	LLETMLARPE	RRGDLVRDLAYDV	PTITILTLI	GADVNQIDI	FKRWSDS	RAAMTWGDLS	SDEEQIP	HAR
WP_064080112.1	SIRAQVVN	ILLENMLERPG	HEGDIVADLAYDV	PTVTILTLI	GADTSQVP1	FKRWSDS	RAAMTWGDLS	SDEEQIP	'H <b>A</b> H
WP_045191440.1 WP_066501301.1	FIRONVAD	RIDAMIARCODIA	. RRADLVRDLAYTV	PTVTILTLI PTTTTLTLT	GEDLA. KLDI	YKRWSDS	RAAMTWGDLS	SDEEQVE	HAH
WP_052024002.1	SIRAQVVN	ILLENLLERPG	HEGDIVADLAYDV	PTVTILTLI	GADTSQVP1	FKRWSDS	RAAMTWGDLS	SDEEQIP	HAH
WP_026453050.1	AIRANVVD	QLEQLLSKDS	RTGDLVRELAYQV	PTVTILTLL	GADTSQVDI	YKRWSDS	RSAMTWGDLS	SDEEQVP	HAH?
WP_06/13/052.1 ELB90053.1	SIRQHVVI	LLERMLARPE	HEGDIVADLAYDV	PIVIILILI PTVTILTLI	GADIG. QVDI GADIS. OVPI	FKRWSDS	RAAMIWGDLS	SDEEOIP	HAH
WP_029339819.1	AIRDHVVR	RE <mark>VE</mark> AMLQRPD	RTGDLVADLAYDV	PTVTILTLI	GADTSQVN1	YKRWSES	RAAMTWGDLS	SDEE <mark>Q</mark> IP	H <mark>a</mark> r
WP_055597530.1	DIRANVVR	RLLETMLARPE	RRGDLVRDLAYDV	PTITILTLI	GADVSQIDI	FKRWSDS	SAMTWGDLS	SDEE <mark>Q</mark> VP	HAH
WP_060941537.1 WP_040168028.1	TIRENTRA	ALAAMLANPE	RTGDFLAEIAYDI	PIVIILILI	GVDPAMVPI	YKKWSDS	RAAMIWGDLS		HAH
WP_033293979.1	EIRANVVR	RL <mark>LETML</mark> ARPE	HYGDLVRDLAYDV	PTITILTLI	GADIGQVG1	FKRWSDS	R <mark>SAMTWGDL</mark> S	SDDE <mark>Q</mark> VP	H <mark>a</mark> r
WP_061252837.1	SIRQHVVT	LLERMLARPK	ATGDFVRDLAYDV	PTVTILTLI	GADIGKVDI	FKRWSDSI	RAAMTWGDLS	S D Q E Q V P	HAH
WP_020389625.1	AIRANVVA	OLEGLLANPG	REGDLVKELAYOV	PTITILTLI	GADTSOVDI	YKRWSDS	RAAMTWGNLS		HAH
WP_053447282.1	EIRENVRR	RÎ <mark>lddml</mark> rnpe	AKGDIVRDLARDV	PTITILTLF	GEDVDQVDI	FKRWSDS	R <mark>GAMTWGDL</mark> S	SDEE <mark>Q</mark> IP	H <mark>A</mark> H?
WP_024368481.1	FIRQNVVH	ILVTNMLARPE	RRGDLFRDLAVDL	PTITILTLI	GADVAMIPS	YKRWSDS	RAAMTWGNLS	SDEEQIP	HAH
ODT11970.1	TIRENTRI	ALQRMLESPD	RQGDVLHDIAFDI	PTITILTLL	GVDPAMVP1	YKRWSDS	GAMTWGDLS	SDEQOVE	HAH
WP_043055803.1	MIRDNVRA	SIERMLAKDT	PHADILADVAYSL	PTITILTLI	GEDTDPETVDC	YKRWSDS	RAAMTWSNLS	SDEEQIP	HAH?
WP_056728828.1 BAU99498 1	AIRENTRI	MIDKMLAACE	RIGDFLMDVAYEI	PTVTILTLL	GVDPAMVP1 GVDTS PTPH	TKKWSDS	RAAMTWGDLS	SDDQQIP FDFFQTP	HAH
WP_035877878.1	TIRENTAR	LLQQMLAHPD	ARGDFLTDVAVDI	PTITILGLL	GVGPEMVP1	YKKWSDS	RAAMTWGNLS	SDEEQIP	HAH
SBT38743.1	QIRANVVR	RLLKRMLLRAE	RTGDLVSDLAIDV	PTITILTLL	GADPAMLSI	FKRWSASI	RAAMTWGDLS	S A E E <mark>Q</mark> V P	' H <mark>A</mark> H
KGA07700.1 GAP56794.1	FIRENADA	LIDAMVAKGG	HRGDMVKDLAYDL	PTITIFALI PTITIITI	GADVS. OVDI	FKRWSDS	RAAMTWGDLI	IDEEQVP SDEEQTP	HAH
WP_019986768.1	RIRELAIN	MIGQFQA.DG	. HAEMVRQLAYDL	PAFVIFMLL	GVPNEDVQC	VKSWAES	RLLMTWGDLT	FEDEQLV	/HAE
WP_015030068.1	KIRELAIN	IMIEDFAA.KG	.KTNIIKDLAYDL	PAYVIFMLL	GVPNEEVQC	VKSWAES	RLLLTWGDLS	SEDD <mark>Q</mark> LM	1H <mark>A</mark> Q
WP_009184779.1 WP_015664221.1	EIKNIAIR	ATDGFADRGH	.QAEMISELAIDL	PALVIFKLL	GVPDSDVAC	VKSWAES	RALLTWGDL	SDDEOTV	THAE 7HAH
WP_009031006.1	EIKAIVNQ	AIDAFAARGH	ADFFREFAYDV	PALVLFKLV	GIPNMDVPF	VKSWAVS	ALLTWGDLS	SDDEQVV	/HAR
WP_006614257.1	EIKAIVNQ	AIDAFAGRGH	ADFFREFAYDV	PALVLFKLV	GIPNMDVPF	VKSWAVS	RALLTWGDLS	SDDEQVV	/HAR
WP_012041855.1 WP_067547936_1	OIEATVDR	HLNKIAVAGE.		PALVLFKLV	GIPDE. DVPR	VKDWAASI	ALLIWGDLS	SDEEOLP	LAF
WP_013926219.1	DIRALAIE	MIEKFQD.KK	.HAELVKELVYDL	PAFVIFMLL	GVPKEEVTC	V K A W A I SI	RMMLTFSDTS	SEEE <mark>Q</mark> LF	HAR
WP_007204700.1	QIEAIIDR	HLTKIAAAGE	CDFFRDVAYDV	PALVLFALM	GIPDADVPF	V K D W A A SI	RALLTWGNLS	SDED <mark>Q</mark> LP	LAH
WP_009809975.1 WP_064750566_1	OIRELTTT	MIDREASEGU	ADLVEALTHEL	PALVLFIMM	GIPDEDVPF	VKEWAAS	VFLNFGDLS	VSEOVA	HAC
WP_037664388.1	<b>KV</b> WAK <b>A</b> TE	LVDAIK.PGQ	VDLVSALTYPL	PAYMIFTFI	GFPDEDMDM	IL <mark>K</mark> SWCGN	RIAFSWGRPS	GDE <mark>Q</mark> RE	IAT
SCG02642.1	KVWAKATE	LVDAIK.PGQ	VDLVSALTYPL	PAYMIFTFI	GFPDEDMDM	LKSWCGN	RIAFSWGRPS	G D E O R E	IAT
WP 014158279 1	KVWAKATE KVWAKATE	LVDAVE.PGO.	VDLVNALTYPL	PAYMIFTET	GFPDEDMDN	LKGWCGN	I AF SWGRPS	SADEORE	LIAT
WP_037831154.1	K <mark>VW</mark> AK <mark>A</mark> TE	LVDAVE.PGQ	VDLVAALTYPL	PAYMIFTFI	GFPDEDMDN	L <mark>K</mark> GWCGN	RIAFSWGRPS	S A D E <mark>Q</mark> R E	I <mark>A</mark> T
WP_030882035.1	KVWAKATE TIRA VUTE	LVDAVE.PGQ	VDLVAALTYPL	PAYMIFTFI	GEPES DMEN	LKGWCGN	A I AF SWGRPS	SAGEORE	IAT
	- <u></u>		· · · · · · · · · · · · · · · · · · ·			IN	THE FUCKO		IV

CYP288A2	α9 <u>220</u> 220	<u>230</u>	α10 <u>202020202</u> .2 <b>240</b> 21	α11 <u>0000000000000</u> 50 <b>260</b>	200000 270
CYP288A2	NLVE <mark>YW</mark> QE	CQRMVADAHAH	GGDNLTADLVRAQ. QEGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_011013726.1	N L V E <mark>Y W</mark> Q E	CQRMVADAHAH	GGDNLTADLVRAQ.QEGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_060564075.1	NLVEYWQE		GGDNLTADLVRAQ.QEGQ	EITDHEIASLLYSLLFAG	HETTTL
WP_005366652.1	NLVEYWOE		GGDNLTADLVRAQ. QEGQ	STIDHETASLLISLLFAG	HETTTL
WP 063967321.1	NLVEYWOE	CORMVADAHAH	GGDNLTADLVRAO. OEGOI	EITDHEIASLLYSLLFAG	HETTTL
WP_038582779.1	NLVE <mark>YW</mark> QE	CQRMVADAHAH	GGDNLTADLVRAQ. QEGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_006287245.1	NLVE <mark>YW</mark> QE	CQRMVAEAHEN	GGDNLTADLVRAQ.QEGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_044026924.1	NLVEYWQE	CQRMVAEAHEN	GGDNLTADLVRAQ.QEGQ	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_040966998.1	NLVEYWQE		GGDNLTADLVRAQ.QEGQ	SITDHEIASLLYSLLFAG	HETTTL
WP 003854399.1	NLVEYWOE		GGDNLTADLVRAQ. OFGO	ETTDHETASLLYSLLFAG	HETTTL
BAU94954.1	NLVEYWOE	CORMVADAHAH	GGDNLTADLVRAO. OEGOI	EITDHEIASLLYSLLFAG	HETTTL
WP_066564562.1	NLVE <mark>YW</mark> QE	CQRMVAHAHEH	GGDNLTADLVRAQ. ESGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_035109760.1	N L V E <mark>Y W</mark> Q E	CQRMVADAHAN	GGDNLTADLVRAQ.ESGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
EEW50177.1	NLVEYWQE	CQRMVADAHAN	GGDNLTADLVRAQ.ESGQI	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
BAC17372.1	NLVEYWQE		GGDNLTADLVRAQ. ESGQI	EITDHEIASLLYSLLFAG	HETTTL
WP_010399900.1	NLVEYWOE		GGDNLTADLVRTO OFGG	ETSDHETASLISLERAG	HETTTL
WP 026196155.1	NLVEYWAE	CORLVOEAKSN	PTDDLTSDLVRFO. SEGGI	EISDHEIASLLYSLLFAG	HETTTL
WP_062861371.1	NLVE <mark>YW</mark> QE	CLSIVADAHEN	GGDSMTADLVKAQ.SEGA	EISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_039207235.1	NLVE <mark>YW</mark> QE	CLSIVADAHEN	GGDSMTADLVKAQ.SEGA	EISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_062241641.1	NLVEYWQE	CLSIVADAHEN	GGDSMTADLVTAQ.SEGA	EISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_011691841.1	NLVEYWQE		GGDNLTADLVKSQ. QEGA	SISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP 005273409 1	NLVEYWOR		GGDNUTADLVKSQ. QEGA	SISUREIASVLISLLFAG	HETTTL
WP 043481247.1	NLVEYWOF	CLRLVOVAHEE	GGDNLTADLVKSO. OFGAN	EISDHEIASVLYSLLFAG	HETTTI
WP_055806675.1	NLVEYWOE	CLRLVRVAHEQ	GGDNLTADLVKSO. OEGA	EISDHEIASVLYSLLFAG	HETTTL
WP_062289581.1	NLVDYWQE	CQRLVQAAHEH	GGDNLTADLVAAQ. AGGA	EITDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_028269402.1	NLVE <mark>YW</mark> QE	CQRLVAEAKEK	GGDNLTADLVKAQ.QDGA	DISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_028276640.1	NLVEYWQE	CLRLVRVAHEE	GGDNLTADLVKAQ. QDGA	EISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_026539569.1	NLVEYWOE		GGDNITADLVKSQ.QEGA	SISDHEIASVLYSLLFAG	HETTTL
WP_013600843.1	NLVEYWOE		GGDNLTADLVKAQ. ODGA	ETSDHETASVLISLLFAG	HETTTL
WP 028265717.1	NLVEYWOE	CLRLVOVAHDD	GGDNLTADLVKSO. ODGA	EISDHEIASVLYSLLFAG	HETTTL
WP_068734283.1	NLVE <mark>YW</mark> ÃE	CLRLVÄHAHEH	GGDNLTADLVKAQ. SDGA	EITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_069950213.1	N L V E <mark>Y W</mark> Q E	CLRLVKVAHEE	GGDHLAADLVKSQ.QEGA	EISDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_007269721.1	NLVEYWAE	CLRLVAHAHKH	GGDNLTADLVKAQ. TEGA	EITDHEIASLLYSLLFAG	HETTTL
WP 066143328 1	NLVEYWDE		EGDSUTADLVKAO NEGA	STIDHETASLLISLLFAG	HETTIL
WP 038992926.1	NLVEYWDE	COKLVAEAHAT	EGDSLTADLVKAO. NEGA	EITDHEIASLLYSLLFAG	HETTTL
WP_047120326.1	NLVE <mark>YW</mark> NR	CQAQVAQAHAA	GGDSLTADLVQAQ.KDGA	DITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_053799000.1	N L V E <mark>Y W</mark> N R	CQAQVAQAHAA	GGDNLTADLVAAQ.RDGA	DITDHEIASLLYSLLF <mark>AG</mark>	HETTTL
WP_040795180.1	NLVEYWAE	CRRLVAEAHET	RPDSLVGDMIRMQ. ADGDI	PITDHEIASLCYSLLFAG	HETTTL
WP_064080112.1	NLVEYWTE		QPDSLIGDLVRAQ. AAGDI	SISDHEIASVGYSLLFAG	HETTTL
WP_066501301.1	NLVOYWOA		GGDNLIADLVTAO, KDGA	EISDHEIASVAYSLLFAG	HETTTL
WP_052024002.1	NLVEYWTE	CRRLVAEAHEK	QPDSLIGDLVRAQ. AAGDI	EISDHEIASVGYSLLFAG	HETTTL
WP_026453050.1	NLVE <mark>YW</mark> QE	CLRLVADAHGN	ERDSLVGDLVRAQ.RDGDI	PITDHEIASVCYSLLF <mark>AG</mark>	HETTTL
WP_067137052.1	NLVD <mark>YW</mark> QE	CLRLVADAHEH	ERGSLVGDLVRAQ.AAGDI	EITDHEIASVVYSLLF <mark>AG</mark>	HETTTL
ELB90053.1	NLVEYWIE		QPDSLIGDLVRAQ. AAGDI	EISDHEIASVGYSLLFAG	HETTTL
WP_029339819.1 WP_055597530_1	NLVEYWAE		EPDSLVGDMVRMO AEGDI	DISDHETASVCISLLFAG	HETTTL
WP 066941537.1	NLVDYWOE	CLRLVADAHEH	ERGSLVGDLVRAO. AAGDI	EISDHEIASVVYSLLFAG	HETTTL
WP_040168028.1	NLVD <mark>YW</mark> NE	CQRLVAVAHES	GGDNLVADLVEAQ.KAGA	EITDHEIASLCYSLLF <mark>AG</mark>	HETTTL
WP_033293979.1	N L V E <mark>Y W</mark> A E	CRRLVAEAHET	ERDSLVGDMVRMQ.AAGDI	PISDHEIASVCYSLLFAG	HETTTL
WP_061252837.1	NLVDYWQE		ERGSLVGDLVRAQ. AAGDI	EITDHEIASVVYSLLFAG	HETTTL
WP_0000335139.1	NLVEYWTE		DPDSLVGDLVRAQ, BDGD	DI TOHEIASVCISLIFAG	HETTTL
WP_053447282.1	NLVEYWOK	CLSLVEKAHRE	GGDNFVGDLVAAQ. QGGDI	EITDHEIASLCYSLLFAG	HETTTL
WP_024368481.1	NLVE <mark>YW</mark> QE	CQRLVEVAHEE	AGDSLTADLVKAQ.SEGA	ELSDHEIASVLYSLLF <mark>AG</mark>	HETTTL
WP_022870166.1	NLVEYWAR	CRELVAQAHEE	GGDNLTADMVRDQ.EAGA	EIDDHEIASLLYSLLFAG	HETTTL
UDT11970.1	NLVEYWQE		GONITADAVERO, GAGA	STIDHEIASLCYSLLFAG	HETTTL
WP_043033803.1	NLVEYWOF		GGDDLVADLVEAO DAGA	ETSDHETASLCYSLLEAG	HETTTL
BAU99498.1	NLVEYWNF	CQEIVANNKANP		EISDHEIASLLYSMLFAG	HETTTL
WP_035877878.1	NLVD <mark>YW</mark> NE	CLRLVSAAHEALAAHEALAAQKDAADDE	EAVGTDNLVADLVRAQ.LAGA	EISDHEIASVCYSLLF <mark>AG</mark>	HETTTL
SBT38743.1	RLVE <mark>YW</mark> HE	CLRLVAEAGQS	ERDSLVGDLVRAQ.RGGDI	PISDHEIASVCYSLLF <mark>AG</mark>	HETTTAL
KGA07700.1	NMVA <mark>YW</mark> SF	CQKLVADAKVT	PGDNLVTDLVNLQ.AAGE	KISDHEIASFLYSLLF <mark>A</mark> G	HETTTL
GAP56794.1	NLVEYWQE	CLRLVKVAHAE	GGDNLTADLVKSQ.QEGA	EISDHEIASVLYSLLFAG	HETTTL
WP_019986768.1	NMUKYWNI	COCLVAKRKEN	PTDDIPCDIVRLQ.ALGH	EISDREIAAMCISQLEAG	HETTISL
WP_009184779.1	NMIRYWNY	COKLVSDRKEK	MODDLPGDLVVLO. AEGH	EITDREIAAICYSOLFAG	HETTISL
WP_015664221.1	NMVE <mark>YW</mark> NY	CRELVRQRHDD.	PTDDLPGDLVRLQ.KDGA	EISDEEIAGVLYSVLF <mark>AG</mark>	HETTTL
WP_009031006.1	NMVD <mark>YW</mark> NY	CRDLVRQRHDD	PTDDLPGDLVRLQ.KEGA	EISDEEIAGVLYSALF <mark>AG</mark>	HETTTL
WP_006614257.1	NMVE <mark>YW</mark> NY	CRDLVRQRHDD	PTDDLPGDLVRLQ.KDGA	EISDEEIAGVLYSALF <mark>A</mark> G	HETTTL
WP_012041855.1	NMVEYWNY		PTDDLPGDLVRLQ. KDGA	EISDEEIAGVLYSALF <mark>AG</mark>	HETTTL
WF_U0/54/936.1	OVVKVWDY		LODERSDIVELO	STIDEETAGLMYSVLFAG	HETTTL
WP 007204700 1	KMVAYWSY	CRALVAARKET.	PGDDFPTDMVRTO AFCC	DITDEEIAGLMYSVLEAG	HETTTT
WP_009809975.1	GMVDYWAY	CRALVDARREN	PGDDFPSDLLKAQ. AEGA	DITDEEIAGLMYSTLFAG	HETTTL
WP_064750566.1	NLVR <mark>YW</mark> RY	CIELIEARKRE	PRDDLPSALVALD.DAS.	.ISLDEMAGLVYGQLT <mark>AG</mark>	HETTSAL
WP_037664388.1	NMTH <mark>YW</mark> EY	CENFVAERAAR	PVDDFTSDLIRIREENPE	ALSLEDITNVAYGLSFAG	HETTTSF
SCG02642.1	NMTHYWEY		FVDDFTSDLIRIREENPE	ALSLEDITNVAYGLSFAG	HETTTSF
WP 014158279 1	NMTHYWKY	CEDEVARRAAE	PVDDFTSDLVRIHLADPD	ALSLADITNVAIGLSFAG	HETTTSF
WP_037831154.1	NMTHYWKY	CEDFVARRAAE	PVDDFTSDLVRIHLADPD	ALSLADITNVAYGLSFAG	HETTTSF
WP_030882035.1	NMTH <mark>YW</mark> KY	CEDFVARRAAE	PVDDFTSDLVRIHLADPD	A L S L A D I T N V A Y G L S F <mark>A G</mark>	HETTTSF
WP_009951127.1	NQVDYWQY	CTEFVASRLAE	PKDDFTSDLIRTHLADPD	E L S V D E I T N V V H A L S F <mark>A G</mark>	HETTTNV

	α12	α13	η2	α14	β5	β6 β7	β8 α15	
CYP288A2	280	290	300	310	320		$T \longrightarrow 0000$	350
CYP288A2	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRD	EARFENGE
WP_011013726.1	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRD	EARFENGE
WP_060564075.1 WP_065366652_1	I SNCFRVLLD.	HPEQWQAILEN HPEOWOATLEN	PKLIPA	AVDEVLRYSGS	I VGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRE GDGVLLLMGSANRE	EARFENGE
WP_003860615.1	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRD	EARFENGE
WP_063967321.1	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRE	EARFENGE
WP_038582779.1 WP_006287245.1	I SNCF RVLLD	HPEQWQAILEN HPEOWOAILEN	PKLIPA	AVDEVLRYSGS AVDEVLRYSGS	IVGWRRKALKI	DIEIGGVAIKE DIEIGGVAIKE	GDGVLLLMGSANRE	EARFENGE
WP_044026924.1	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRD	EARFENGE
WP_040966998.1	ISNCFRVLLD	HPEQWQAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DIEIGGVAIKE	GDGVLLLMGSANRD	EARFENGE
WP 003854399.1	ISNCFRVLLD	HPEOWOAILEN	PKLIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRE	EARFENGE
BAU94954.1	ISNCFRVLLD	HPAQWÊAILEN	PKLIPA	AVDEVLRYSGS	I V <mark>G</mark> WRRKALKI	DTEIGGVAIKE	GDGVLLLMGSANRE	EARFENGE
WP_066564562.1	I SNCFRVLLD.	HPEQWAAITEN HPDOWEALTED	PKLIPG	AVDEVLRYSGS	I VGWRRKALKI	DTEIGGVSIKE	GDGVLLLMGSANRE	EERFENSE
EEW50177.1	ISNCFRVLLA	HRDQWEALIED	PKKIPA	AIDEVLRYSGS	IVGWRRKALRI	DTEIGGOPIKK	GDGVLLLMGSANRE	EARFDDGE
BAC17372.1	ISNCFRVLLA	HRDQWEALIED	ΡΚΚΙΡΑ	AIDEVLRYSGS	IVGWRRKALRI	DTEIGGQPIKK	GDGVLLLMGSANRD	EARFDDGE
WP_015399966.1	IANSFRULLG	HREQWETLIDN	PKKTGA	AVDEVLRYSGS	I VGWRRKALKI	DIEVGGVEIAK	GDGLLLLMGSANRE	ESRFENGE
WP_026196155.1	ISNCFRVLLA	HPDQWQELVEN	PKKIPS	AVDETLRYSGS	IVGWRRKALRI	DTEISGQKIKK	GDGLLLLMGSANRE	ESRFDEGE
WP_062861371.1	IGNTLRVLLA	HPDQWQAVIDD	EKKIPA	AVDEVLRYSGS	IVGWRRKALKI	DTEVGGVKIAE	GDELLLLMGSANRD	ESRFESGE
WP_039207235.1 WP_062241641_1	IGNTLRVLLA.	HPDQWQAVIDD HPDQWQAVIDD	EKKIPA	AVDEVLRYSGS	I VGWRRKALKI	DIEVGGVKIAE	GDELLLLMGSANRE	ESRFESGE
WP_011691841.1	ISNALRELLS	RPEQWQQLVED	PKKIPA	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVPIEE	GAQLLLLMGSANRD	EAKFNAGE
WP_024367961.1	ISNALRELLA	RPEQWKQLVED	ΡΚΚΙΡΑ	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVAIEE	GAQLLLLMGSANRD	ENKFNAGE
WP_005273409.1 WP_043481247_1	I SNAVRVLLA I SNALRELLA	HPEQWQQLVAE BPGOWKHLVED	PKKIPA	AIDEVLRYSGS AIDEVLRYAGS	I VGWRRKALTI I VGWRRKALKI	DTEVGGVPIPE	GGQLLLLMGSANRD	ESREADGE
WP_055806675.1	ISNALRELLA	RPEQWKQLVED	RKKIPA	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVAIEE	GAQLLLLMGSANRE	ANKFNDGE
WP_062289581.1	ISNCVRVLLA	HPEQWQQLVAE	PKKIPG	AIDEILRYSGS	IVGWRRKALKI	DTTIGGVTIPA	GAGVLLLMGSANRD	DARFEDGE
WP_028269402.1 WP_028276640_1	I SNALRELLA.	RPEQWQQLVAE RPEOWKOLVED	PKKIPA	AIDEVLRYAGS AIDEVLRYAGS	I VGWRRKALKI	DAEVGGVALEE	GAQLLLLMGSANRE	ENKEDAGE
WP_026539569.1	ISNALRELLA	RPEQWQQLVED	PKKIPA	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVAIAE	GSQLLLLMGSANRE	DTKFDAGE
WP_018775007.1	ISNALRELLA	RPEQWQQLVAD	ΡΚΚΙΡΑ	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVAIAE	GSQLLLLMGSANRD	DTKFDAAE
WP_013600843.1 WP 028265717 1	IANALRELLV.	RPGQWQQLVED RPAOWRTLVED	PKKIPA	AIDEVLRYAGS AIDEVLRYAGS	I VGWRRKALKI	DIEVGGVPIRE	GSQLLLLMGSANRE	DTKEDAGE
WP_068734283.1	ISNCVRVLLA	HQEAWDQVVEN	PKSIPA	AIDEVLRYAGS	IVGWRRKALKI	DTEVAGVKIPE	GAELLLLMGAANRD	ENRFEDPE
WP_069950213.1	ISNALRELLA	RPEQWKQLVED	PKKIPA	AIDEVLRYAGS	IVGWRRKALKI	DTEVGGVAIEE	GAQLLLLMGSANRD	ENKFSAGE
WP_007269721.1 ATS67786 2	I SNCVRVLLA I SNCVRVLLA	HREAWDQIVEN HREAWDOIVEN	PKSISA	AIDEVLRYAGS AIDEVLRYAGS	I VGWRRKALKI	DIEVAGVKIPE	GAELLLLMGAANRE GAELLLLMGAANRE	GDRFENPE
WP_066143328.1	ISNCVRVLLE	HRDAWDALVAE	PKQIPK	AIDEVLRYSGS	IVGWRRKALKI	DTEIAGVQIPQ	GAELLLLMGSANRD	ESRFENGE
WP_038992926.1	ISNCVRVLLE	HRDAWDALVAE	PKQIPK	AIDEVLRYSGS	IVGWRRKALKI	DTEIAGVQIPQ	GAELLLLMGSANRD	ESRFENGE
WP_047120326.1 WP_053799000.1	I SNCVRVLLE.	HREAWEAVVAD HREAWEAVVAD	PKQIPK	AIDEVLRYSGS AIDEVLRYSGS	I VGWRRKALAI I VGWRRKALAI	DTEVGGVQIPQ	GAELLLLMGSANRE GAELLLLMGSANRE	ESRFENGE
WP_040795180.1	ISNALRVLLS	HPDQWQQIVED	PSRIPA	AVDEVLRYSPS	IVGWRRKALRI	DTEIGGVTIPK	GADILLLMGSANRD	ETRFEDAD
WP_064080112.1	ISNAVRALLG	HPGQWQQLVDN	PSKIPA	AVDEVLRYSGS	ITAWRRKALTI	DATIGGVRIAA	GDQVLLVMGSANRD	ETKFADGE
WP_045191440.1 WP_066501301.1	I ANTLRVLLA.	HPDQWQQVVDE	PSKIAA	AVDEVLRYSPS	I VAWRRRATRI	DATIGGVDIPE	GADVLLVMGSANRL GSGTLLVMGSANRT	ESKEDDAE
WP_052024002.1	ISNAVRALLG	HPGQWQQLVDN	PSKIPA	AVDEVLRYSGS	ITAWRRKALTI	DATIGGVRIAA	GDQVLLVMGSANRD	ETKFADGE
WP_026453050.1	ISNLLRVLLD	HPGQWQQVVED	PKKIAG	AVDEVLRYSPS	IVAWRRKALAI	DTTVGGVDIPA	GAGLLLVMGSANRD	AEKFDDPD
ELB90053.1	ISNAVRALLG	HPGQWQSVVDR	PSKIPA	AVDEVLRYSGS	ITAWRRKALTI	DATIGGVRIAA	GDOVLLVMGSANRE	ETKFADGE
WP_029339819.1	ISNTLRVLLA	H P E Q W R K V V E D	PSQIPA	AVDEVLRYSPS	IVAWRRKATKI	DATVGGVAIPG	GAELLLVMGSANRD	DSHFEDPD
WP_055597530.1	I SNALRVLLS	HPDQWRQVVED	PRRIPG	AVDEVLRYSPS ATDEVIDUSCS	I VGWRRRALRI	DAEIGGVKVPE	GADILLLMGSANRE	AARFEDGE
WP_040168028.1	IANSVRVLLG	HREAWDAIVAD	PKRIPS	ATDEVLRYSGS	IVAWRRKATRI	DAEIAGVPIAE	GDGVLLVMGSANRE	ENVFANPD
WP_033293979.1	ISNALRVLLS	Y P E Q W Q Q V V E D	PKRIPA	AVDEVLRFSPS	IVGWRRRALRI	DVEIGGVAIPS	GADILLLMGSANRD	ESRFADGE
WP_061252837.1 WP_006335139_1	I SNALRVLLS	HRDQWRRVVDR	PSLIPA	AIDEVLRHSGS AVEEVLRYSPS	I VAWRRRALVI I VAWRRKALVI	DTRIGGVDIPK	GADILLVMGSANRE GAOLLLVMGSANRE	AAKFDDPE
WP_020389625.1	ISNTLRVLLA	HPDQWRHIVDD	PTKIAG	AVDEVLRFSPS	IVAWRRRATKI	DASIGGVSVPA	GADVLLVMGSANRD	DAKFDDPD
WP_053447282.1	IANSLRVLLG	HPDQWAQLRED	PKKVAA	ALDEVLRYSGS	IVSWRRKALKI	DAEVGGVSIPE	GAQLLLVMGSANRD	EAMFEDGE
WP_024368481.1 WP_022870166.1	I SNAVRVLLS	HRDOWKTIVEE	PKKIPA	AIEEVLRISGS	IVAWRRKALKI	DAVVGGVEIPK	GAELLLLMGSANRE	ESKEPDGE
ODT11970.1	IANSIRVLLS	HREAWEAIVAD	PSRIPS	AIDEVLRYSGS	IVAWRRKALRI	DAEIGGVKIPE	GAGILLVMGSANRD	EEVFAHPE
WP_043055803.1	ISNAVRVLLD	HREQWDAIVED	PKKISK	AIDEVLRYSGS	IVAWRRKALKI	DTEIGGVPIPE	GAELLLLMGSANRD	EERFEDGD
BAU99498.1	ISNSLRMLLS	NPETYOALVED	PEKIPG	AIDEVLRISGS	IVAWRRKAIRI	DAEIAGVKIPE	GANILLLMGSANRL	ASVFENPD
WP_035877878.1	ISNTIRVLLS	HAEQWQQLVDD	PSLIPA	AIDETLRYSPS	IVGWRRKALVI	DAEIAGTRIPR	GANLLLLMGSANRD	AAVFEEPE
SBT38743.1	I SNALSVLLA	HREQWDSLVAD	AGKIPG	AIDEVLRHSPA	VITWRRQARR	A A T I G G V E V P A	GANILLVLGSANRD	ERRFVDPD
GAP56794.1	ISNALRELLA	RPEQWKQLVED	PKKIPA	AIDEVLRYAGS	IVA			
WP_019986768.1	IGNGIRELLL	KRESWEAICAN	PALIPN	AIEEVLRYSPS	IVSWRRRALEI	DSIVGGVHIPA	GSNLLLVMGSANRD	EAQFEQGE
WP_015030068.1	LGNGIRELLI	HRKSWESLCTN	HEMIPN	AVEEVLRYSPS	IVSWRRRSTE	EATVGGITIPA	GSNILLVMGSGNRD	EAQFENGE
WP_015664221.1	MANGMRELLQ	RRENWEAIIĂE	PRLIPT	AVEESLRFSPS	IVAWRRRALKI	DARIGGMPVPK	DSNILLLIGSANRD	ETVFSAPA
WP_009031006.1	MANGMRELLQ	RRENWEAILAE	PQLIPN	AVE <mark>ESLR</mark> FSPS	IVAWRRRALKI	DAEIGGVPVPK	GSNILLLIGSANRD	ESVFSAPT
WP_006614257.1	MANGMRELLQ	RRENWEAIIAE	PQLIST	AVEESLRESPS	IVAWRRRALKI	DAEIGGVPVPK	DSNILLLIGSANRE	ESVESAPS
WP_067547936.1	MSNAIITLMA	NRDAWDAVCAD	PSLIPA	ATEEILRFEPS	IVSWRRRAKTI	DAEIGGVAIPE	GADILLVMGAGNRE	ADVFENAE
WP_013926219.1	MGNGIRELLK	YRHNWEKLCAD	ASLIPG	AIEEILRFNPS	VITWRRKATE	EATIGGETEPK	GADILLLMGSGNRD	EAVFENGE
WP_007204700.1	MSNAVITLMS MSNAVITLMU	NKGAWNAICAD	PGLIPA	ATEELLRFEPS ATEETLBVCDC	I VSWRRKAKM	JAKIGGIAIPE	GADILLVMGSGNRD	AAAFENAE ESVEDCCE
WP_064750566.1	LASGIKELLG	QRERWVELTRD	ESLIPT	AVEELLRLVAP	VFAWKRRVKQI	DTRIGEVTLPA	GANVLLLLGSANHD	DTVFADPE
WP_037664388.1	TGNAIRQLLA	NPEQWAAICSD	RGLISK	AVEELLRYDSS	IPAWRRVTTRA	AVDVGGVEIPA	EAKVLILLGAANRD	PKHFEDPE
SCG02642.1 WP 030497796 1	IGNAL ROLLA	NFEQWAAICSD NPEOWAAVCAD	RGLISK	AVEBLLRYDSS	IPAWRRVTTRA	AVDVGGVEIPA AVDVGGVETPF	EAKVLILLGAANRE RAKVLILLGAANPE	PKHFEDPE
WP_014158279.1	TGNAIRQLLS	NPEQWAAICAD	RSLIPK	AIEELLRYDSS	IPAWRRITTRA	AVDVGGVRVPA	EAKVLILLGAANRD	PKHFEEPE
WP_037831154.1	TGNAIRQLLS	NPEQWAAVCAD	RSLIPK	AIEELLRYDSS	I PAWRRITTRA	AVDVGGVRVPA	EAKVLILLGAANRD	PKHFEEPE
WP_009951127.1	SSSMIQRLLT	HREQWEELCAD	PALIPK	AIEEGLREDPS	LFTWRRITTKI	PVSIGGVEVPA	GAKLLLLVGSANHD	PAKFPDPE

CVD20032		η3	<b>~~</b>	<b>m</b> 0000000	α16	000	39					β1	0
CIFZOOAZ	360		370	380	390	400	-	4	10	4	20	_	-
CYP288A2	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRLVPSL	HLVAD	KAI	GFRE	NLSFRV	PTS	VPN	/TWNA
WP_011013726.1	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRLVPSL	H <mark>L</mark> VAD	KAI	GFRE	NLSFRV	PTS	۷P۱	/TWNA
WP_060564075.1	DFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TKLVPSLI	HLVAD	EAI	GFRE	NLSFRV	PTS	VPN	AWNA
WP_065366652.1	DEDISK	ANAREH	LSFGFGI	HICLGNMLAKLQ	AKICLEEV.	TKIVPSI	HLVAD HLVAD	EAI	GERE	NLSFRV	PIS		/ A W N A
WP 063967321.1	DFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLO	AKICLEEV	TKLVPSL	HLVAD	EAI	GFRE	NLSFRV	STS	VPN	AWNA
WP_038582779.1	DFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TKLVPSL	HLVAD	EAI	GFRE	NLSFRV	PTS	VPN	JAWNA
WP_006287245.1	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRL <mark>VPSL</mark> H	H <mark>l</mark> VAD	EAI	GFRE	NLSFRV	PTS	۷P۱	/TWNA
WP_044026924.1	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRLVPSL	HLVAD	EAI	GFRE	NLSFRV	PTS	VPV	/TWNA
WP_040966998.1	EFDISR.	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRLVPSLE	RLVAD	EAI	GFRE	NLSFRV	PTS		TWNA
WP 003854399.1	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLO	AKICLEEV	TRLVPSL	HLVAD	EAT	GFRE	NLSFRV	PIS	VPI	TWNA
BAU94954.1	EFDISR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TRLVPSL	LTAE	TPI	SFRE	NLSFRV	PTS	VPN	TWNA
WP_066564562.1	EFDIAR	TNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEV	TKLAPSL	Q <mark>l</mark> iqd	SPI	GFRE	NLSFRV	PTS	۷P۱	/TWNS
WP_035109760.1	TFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEA	TRLVPSL	ELADD	QS <mark>V</mark>	EFRE	NLSFRV	PVS	۷P۱	/TWS.
EEW50177.1	TFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLEEA	TRLVPSL	ELADD	QSV	EFRE	NLSFRV	PVS		TWS.
WP 015399966 1	EFDINR	PNAREH	LSFGFGI	HYCLGNMLAKLO	AKICLEEA	TKLAPSLE	RITDD	QSV		NLSFRV	PVA	VPN	TWDA
WP 010144948.1	DFDITR	SNAREH	LSFGFGI	HYCLGNMLAKLO	AKICLEEA	VKLLPGL	RLDDSGG	AADGSDI	EFRE	NLSFRV	PVA	VPI	TWAA
WP_026196155.1	EFDISR	KNAREH	LSFGYGI	HYCLGNMLAKLQ	AKICLEEA	TRLAPSME	RLTDT	DT	EFRE	NLSFRV	PIS	VPN	JTWDA
WP_062861371.1	DFDISR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLQEI	TRL <mark>AP</mark> NL	K <mark>l</mark> VGG	EDI	DFRE	NLSFRV	ΡKΤ	۷P۱	/т₩
WP_039207235.1	DFDIRR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLQEI	ARLAPNLE	KLVGG	EDI	DFRE	NLSFRV	PKT	VPV	/TW
WP_062241641.1	DFDIDR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKICLQEI	TRLAPNLE	KLVDG	ENI	DFRE	NLSFRV	PKT	VPN	TW
WP_011091041.1	DEDTIR	PNAREH	LSFGFGI	HYCLGNMLAKLO	AKIALEEV	ARLAPAL	JLENP	E A T	NFRE	NLSFRV	PES		JSWKA
WP 005273409 1	VFDISR	SNAREH	LSFGYGT	HYCLGNMLAKLO	AKIALEET	ARLAPNI	KLEDP.	EAT	GFRF	NLSFRV	PET	VPN	TWEA
WP_043481247.1	DFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEV	ARLAPEL	LEEP.	EAI	TFRE	NLSFRV	PET	VP	SWKA
WP_055806675.1	DFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEV	ARLAPEL	QLEAP	EA <mark>I</mark>	AFRE	NLSFRV	PES	VPV	/SWKA
WP_062289581.1	AFDISR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEI	TRLLPTL	FLTEP	ESI	TFRE	NLSFRV	PES	VP	AWKA
WP_028269402.1	NFDITR	PNAREH	LSFGFGI	HICLGNMLAKLQ	AKIALEEV	ARLAPELE	KLEEP	EAI	AFRE	NLSFRV	PET	VPN	/SWKA
WP 026539569 1	DEDITE	PNAREH	LSFGVGT	HYCLGNMLAKLQ	ARTALEEV	ARLAPEL	∠⊔слг Этемр	F AT	AFDT	NLSFDU	PFT		JSWKA
WP 018775007.1	DFDITR	PNAREH	LSFGYGI	HYCLGNMLAKLO	AKIALEEV	ARLAPELO	DLENP	EAI	AFRE	NLSFRV	PET	VPN	JSWKA
WP_013600843.1	DFDISR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEV	ARLAPKL	LEDP	EDI	AFRE	NLSFRV	PET	VPN	/ T W K A
WP_028265717.1	DFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	ARIALEEV	ARLAPEL	QLENP	EE <mark>I</mark>	TFRE	NLSFRV	ΡEΤ	۷P۱	/S <mark>W</mark> KA
WP_068734283.1	AFDIAR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEL	ASRIPGLE	E <mark>L</mark> IDG	EGI	EFRK	NLSFRV	ΡEΥ	VNV	/SWK.
WP_069950213.1	DFDITR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEV	ARLAPGL	2PENP	EAI	SFRE	NLSFRV	PET	VPN	SWKA
WP_00/269/21.1	AFDIIR	INAREH ANAREH	LSFGFGI	HICLGNMLAKLQ	AKIALEEL	SSRIPGLI	ELIDG	EDI	TERK	NISFRV	PEI		JSWK.
WP 066143328.1	DFDITR	ANARDH	LSFGFGI	HYCLGNMLAKLO	AKIALEEL	ASALPNLO	DLVDG.	DAI	TFRK	NISFRV	PDF	VNV	TLNA
WP_038992926.1	DFDITR	ANARDH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEL	ASALPNL	QLVDG	DAI	TFRK	NISFRV	PDF	VNV	JTLNA
WP_047120326.1	DFDITR	PNARDH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEL	AAALPNLI	E <mark>l</mark> VDG	GAI	TFRK	NLSFRV	PDF	VNV	/ELNA
WP_053799000.1	DFDITR	PNARDH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEL	AAALPNLH	ELVDG	GAI	TFRK	NLSFRV	PDF	VNV	/ELNA
WP_040795180.1	SFDITR	PNAREH	LAFGFGI	HYCLGNMLAKLQ	AKVAIEEV	ARLVPGLE	RLADD	ADI	RFGD	NLSFRA	PVA		TW
WP_045191440.1	SEDITR	PNAREH	LAFGFGI	HYCLGNMLAKLO	AKTAVEEV	ARLAPGLE	RPVOD.	EPV	HFGF	NLSFRV	PLA	VPI	ISWEA
WP_066501301.1	TFDIAR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	AKIALEEA	TAKLPHL	IVDDP	ESI	EFRE	NLSFRV	PVS	VPN	/SWT.
WP_052024002.1	TFDIDR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	TKIALEEL	VRLAPDL	R <mark>L</mark> RSG	ASI	TFRE	NLSFRV	PQD	۷P۱	/T <mark>W</mark> GG
WP_026453050.1	TFDISR	PNAREH	LSFGYGI	HYCLGNMLAKLQ	ARIAAEEV	ARLAPGIE	RLTDG	AAI	DFVD	NLSFRT	PVA	VPV	/TW
WP_06/13/052.1	TEDIDR	PNARDH	LSFGFGI	HICLGNMLAKLQ	ARIALEEL	ARLIPDVI VRIADDII	RLCED	EQ1		NLSFRS	POD		THCC
WP 029339819.1	VEDISB	PTAREH	LAFGEGI	HYCLGNMLAKLO	TKVAVEEV	ARLAPGLE	RIVDA.	EAT	RESE	NLSFRA	PVR	VPI	TWEA
WP_055597530.1	SFDIGR	ANAREH	LSFGFGI	HYCLGNMLAKLQ	AKITLEET	ARLAPGLE	RLADP	S G I	HFGD	NLSFRA	PAA	VR	JIW
WP_066941537.1	VFDIDR	PNAREH	LSFGFGI	HYCLGNMLAKLQ	ARIAIEEI	ARLIPDV	R <mark>l</mark> red	AR <mark>I</mark>	AFGÇ	NLSFRS	PVS	۷P۱	/EWEA
WP_040168028.1	AFDIDR	DDARNH	ISFGFGI	HYCLGNMLAKLQ	NRIVLEET	TALVPSLE	RLAE	GEI	GFRE	NLSFRV	ΡΤΤ	۷P۱	/TWEA
WP_033293979.1	SFDLAR	PNAREH	LAFGFGI	HYCLGNMLAKLQ	ARIAVEEV	ARLAPGVI	RLAAD	AEI	HFGD	NLSFRA	PAA	VPN	TWEA
WP_001252837.1 WP_006335139_1	SEDINR	ANARTH	LSFGFGI	HYCLGNMLAKLO	DKINVOEV	TNHAPRI	RLKED RITDP	<u>EQI</u>	TEGE	NLSERA	PIS		TWLA
WP 020389625.1	TFDIER	PNAREH	LAFGFGI	HYCLGNLLAKLO	AKIAVEEV	ARRAPGLE	ELVDG	DAI	EFGD	NLSFRG	PVA	VPI	JTW
WP_053447282.1	SFDIER	SNAREH	LSFGFGI	HYCLGNMLAKLQ	GRIVLEEV	LDR <mark>APGL</mark> E	ELEDS	EPI	A <mark>F</mark> G E	NLSFRA	PVA	۷P۱	/T <mark>W</mark> KA
WP_024368481.1	AFDIDR	KNAREH	LSFGFGI	HYCLGNKLAKLQ	AKIAVEEV	VRLAPQL	QVMNA	DDI	KFRE	NLSFRV	PET	۷P۱	/SWKA
WP_022870166.1	SFDISR	SNAREH	LSFGFGI	HYCLGNMLAKLQ	TKIALEEL	SSAIPSLE	ELDEP	EGI	PFRE	NISMRI	PEH	VH	TWN.
WP 043055803 1	TEDIAR	SNAREH	LSEGEGI	HYCLGNMLAKLO	TKIALEEL	TSATPTLE	RLIG	EGT		SISMRI	PIS	VPN	TWEA
WP 056728828.1	OFDIDR	TDARSH	MSFGFGI	HYCLGNMLAKLO	DRIVLEET	IAAVPSLE	RLAD	GPI	GFRE	NLSFRV	PTS	VAN	TWEA
BAU99498.1	<b>VFDIGR</b>	ENARNH	MSFGYGI	HFCLGNLLAKLQ	GKVALEEI	TKKIPTL	RLMPG	AD I	NFIE	NISFRV	PTS	VPN	/EW
WP_035877878.1	VFDLSR	PNARNH	LSFGFGI	HYCLGNLLAKMQ	DKIVVEET	IRA <mark>AP</mark> HLI	R <mark>I</mark> ITP	EK <mark>I</mark>	TFGD	NLSFRA	PTS	۷P۱	/TWEA
SBT38743.1	VFDIHR	GNAREH	LAFGFGI	HYCLGSVLAKTQ	AKIVVEEV	TRLCPHL	RLAPD	VPL	AYGA	NLSLRA	PLS	VPV	/TW
KGA07700.1	KFDIER.	ANARTH	LSFGFGI	HYCIGNMLGKLQ	VRVALEQL:	IKKLPSL	RVIKG	EDI	EFGD	NLSFRV	PLA	VPN	/TW
WP 019986768.1	TFDIER	ТNАКЕН	LSFGYGI	HFCLGSPLAKLE	SKIVLEEL	TRLIPNLE	RIKPD.	OAF	KFAF	NTSFRA	PVA	VEN	JEW.
WP_015030068.1	DFDIER	KNANQH	LSMGSGI	HFCLGAPLAKLE	AKVVLEEL	TKRLPSL	RLTPE	QTF	AFAÇ	NTSFRA	PVA	LEN	JEWDV
WP_009184779.1	SFDITR	GNAGTH	LSFGSGI	HFCLGSPLAKLE	FKVVLEEL	TDRIPNL	H <mark>L</mark> TPN	QTF	TFAP	NTSFRA	PQA	ΓQΙ	7QW
WP_015664221.1	RFDVRR	SDARSH	LAFGYGI	HTCVGQQLARIE	FAIALGEL	TRRLPGL	RLAAD	QSI	DFVH	NISFRV	ΡTΑ	LR1	ίΕWD.
WP_009031006.1	SFDVRR	TDARSH	LAFGYGI	HTCVGQQLARIE	FAIALGEL	TRRLPSL	RLAAD	QTI	DFVH	NISFRV	PTA	LRI	EWD.
WP_000014257.1	REDVER	SUARSH TDADGU	LAFGYGI	HTCVGQQLARIE	FATALGEL	TRRLPCT	RLAAD	QTI		NISFRV	PIA	LRI	LEWD.
WP 067547936 1	TFDIOR	KNARNH	LSFGYGT	HFCIGFOLAKME	FGIMLREL	TARFPNM	IMKPD.	OHT	EYLC	NISFRV	PNO	VMV	7
WP_013926219.1	TLDIER	KNAKEH	LSFGSGI	HYCLGAPLAKLE	FKIVLEEL	TQRIPNLO	LTPD	QTF	EFAY	NTSFRA	PVÃ	LEN	/EW
WP_007204700.1	AFDIER	HNSRNH	LSFGYGI	HFCIGFQLAKME	LGIMLREL	TARFPNM	TLKPD	QQI	DYLH	NISFRV	PNQ	VMV	7
WP_009809975.1	EFDIHR	ANARNH	LTFGYGI	HFCIGFQLAKME	FGIMLREL	IKRFPNM	ILTDG	QNI	D <mark>y</mark> lk	NISFRV	PLK	VEN	7
WP_064750566.1	AIDLRR	ENARGH	LAFGHGI	HFCLGASLARLE	ARVVLEEL	TARLPGL	ELVPG	····QIF	DYPA	NTTFRA	PAA	VHV	/RW
wr_03/664388.1 SCG02642 1	TEDIRR	GDSRRH	LAFGKGI	HYCTGAPLARME	ARIALDLL		RLIQD	QDF	UE PA	NVSFRG	PPC		/EW
WP 030497796 1	TFDIHR	GDARRH	LAFGKGT	HYCIGAPLARME	ARIALDLL	AERAPDM	RLVED.	ODF	DEPA	NVSFRG	PRS	Ĩ.,	ZEW.
WP_014158279.1	SFDITR	GDARRH	LAFGKGI	HYCIGAPLARME	ARIALDLL	AQRVPDL	RLVAD.	QDF	DFPA	NVSFRG	PRS	LL	JDW.
WP_037831154.1	SFDITR	GDARRH	LAFGKGI	HYCIGAPLARME	ARIALDLL	AQR <mark>VP</mark> DL	RLVAD	QDF	DFPA	NVSFRG	PRS	L L 7	7DW
WP_030882035.1	SFDITR	GDARRH	LAFGKGI	HYCIGAPLARME	ARIALDLL	AQRVPDL	RLVAD	QDF	DFPA	NVSFRG	PRS	L L V	/DW
wr_009951127.1	AF NIHR	SGAQAH	LIFGRGI	n SUFGAPLARLE	MUIMLEEL	IAKMPGLI	KLVED	QD <mark>V</mark>	ОПН∧	NACTRG	¥VE	<u>-</u>	J-11

Fig. S31. Protein sequence alignment of CreJ homologues from diverse genera of microorganisms. Conserved residues are highlighted in white display with red background.



**Fig. S32.** Phylogenetic tree of CreJ homologues with > 40% protein sequence identity. CreJ (*i.e.* CYP288A2) is highlighted with the symbol of star.



**Fig. S33. Representations of** *cre***-like gene clusters from diverse microorganisms.** Arrows in a same color represent the homologous genes. Genes without colors have no homology to any *cre* genes. The number below the arrow indicates the percentage of protein sequence identity between the specific gene with its homologous gene in the *cre* cluster of *C. glutamicum* ATCC13032.



Fig. S34. HRMS spectra of oxidative products from 2.



Fig. S35. HRMS spectra of oxidative products from 3.



Fig. S36. HRMS spectra of oxidative products from 4.



Fig. S37. HRMS spectra of oxidative products from 5.



Fig. S38. HRMS spectra of oxidative products from 6.



Fig. S39. HRMS spectra of oxidative products from 7.



Fig. S40. <sup>1</sup>H NMR spectrum of 2c in CD<sub>3</sub>CN.



Fig. S41. <sup>13</sup>C NMR spectrum of 2c in CD<sub>3</sub>CN.



Fig. S43. <sup>1</sup>H NMR spectrum of 2' in CD<sub>3</sub>CN.



Fig. S44. <sup>13</sup>C NMR spectrum of 2' in CD<sub>3</sub>CN.





Fig. S46. <sup>13</sup>C NMR spectrum of 11' in CDCl<sub>3</sub>.





Fig. S48. <sup>13</sup>C NMR spectrum of 12' in CDCl<sub>3</sub>.

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