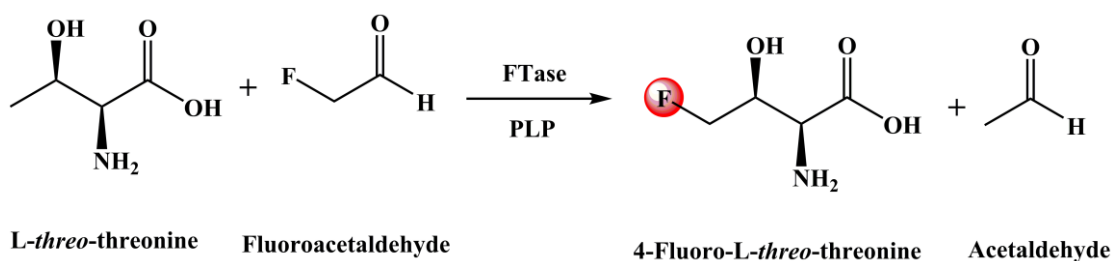


25

26 **Figure S1.** The selective fluorination process catalyzed by cytochrome
 27 P450 enzyme and diethylaminosulfur trifluoride (DAST).

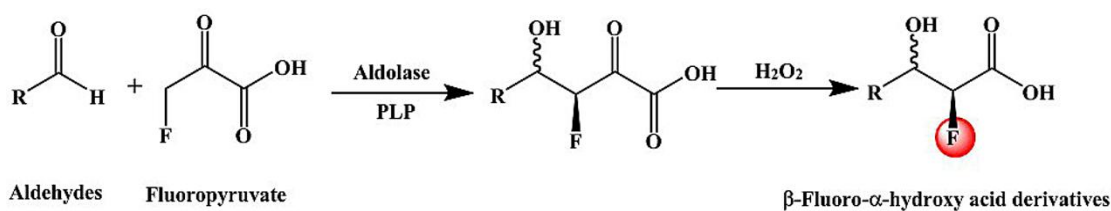
28



29

30 **Figure S2.** Synthesis of 4-fluoro-*L-threo-threonine* employing
 31 4-fluorothreonine transaldolase (FTase).

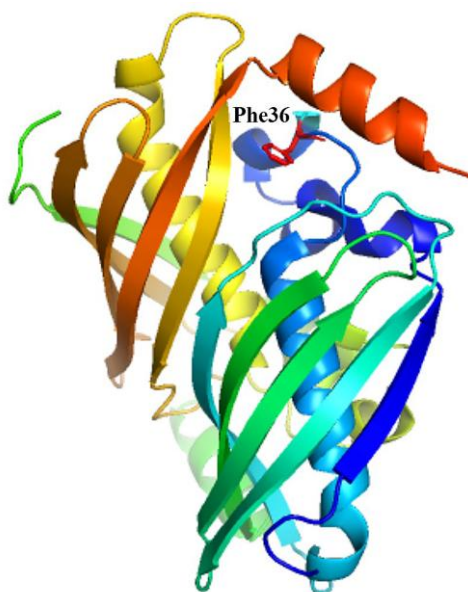
32



33

34 **Figure S3.** Chemo-enzymatic synthesis of β -fluoro- α -hydroxy acid
 35 derivatives catalyzed by aldolase and H₂O₂.

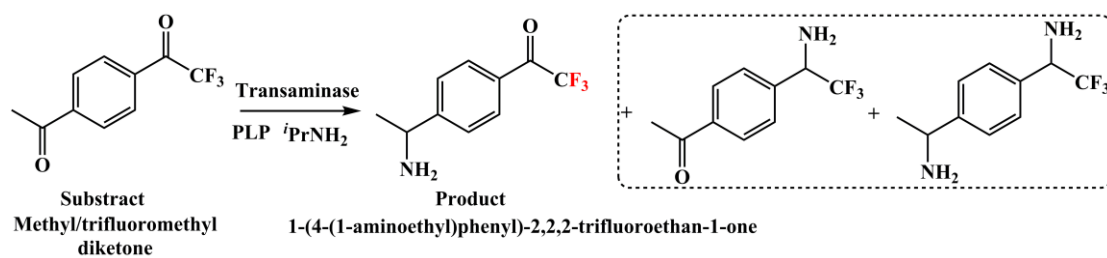
36



37

38 **Figure S4.** Structural of FLK. Phe36 is shown in red.

39

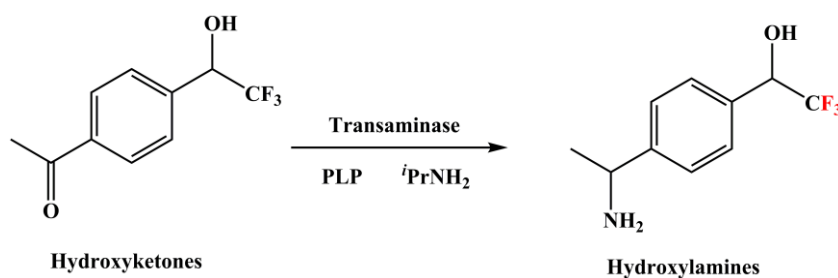


40

41 **Figure S5.** Selective amination catalyzed by transaminase. The dashed

42 box is the theoretical product but has not been generated in practice.

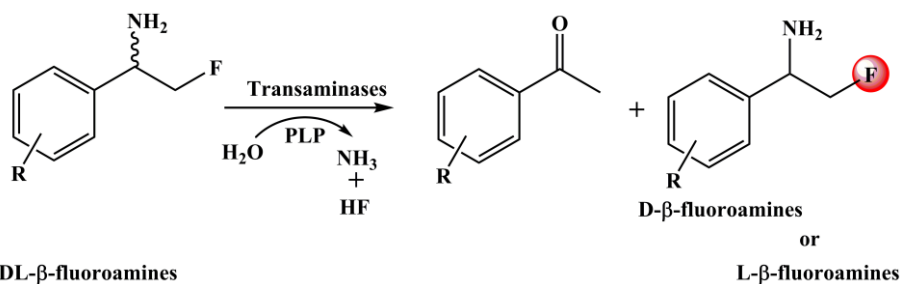
43



44

45 **Figure S6.** Fluorinated hydroxylamines were obtained by transaminase.

46



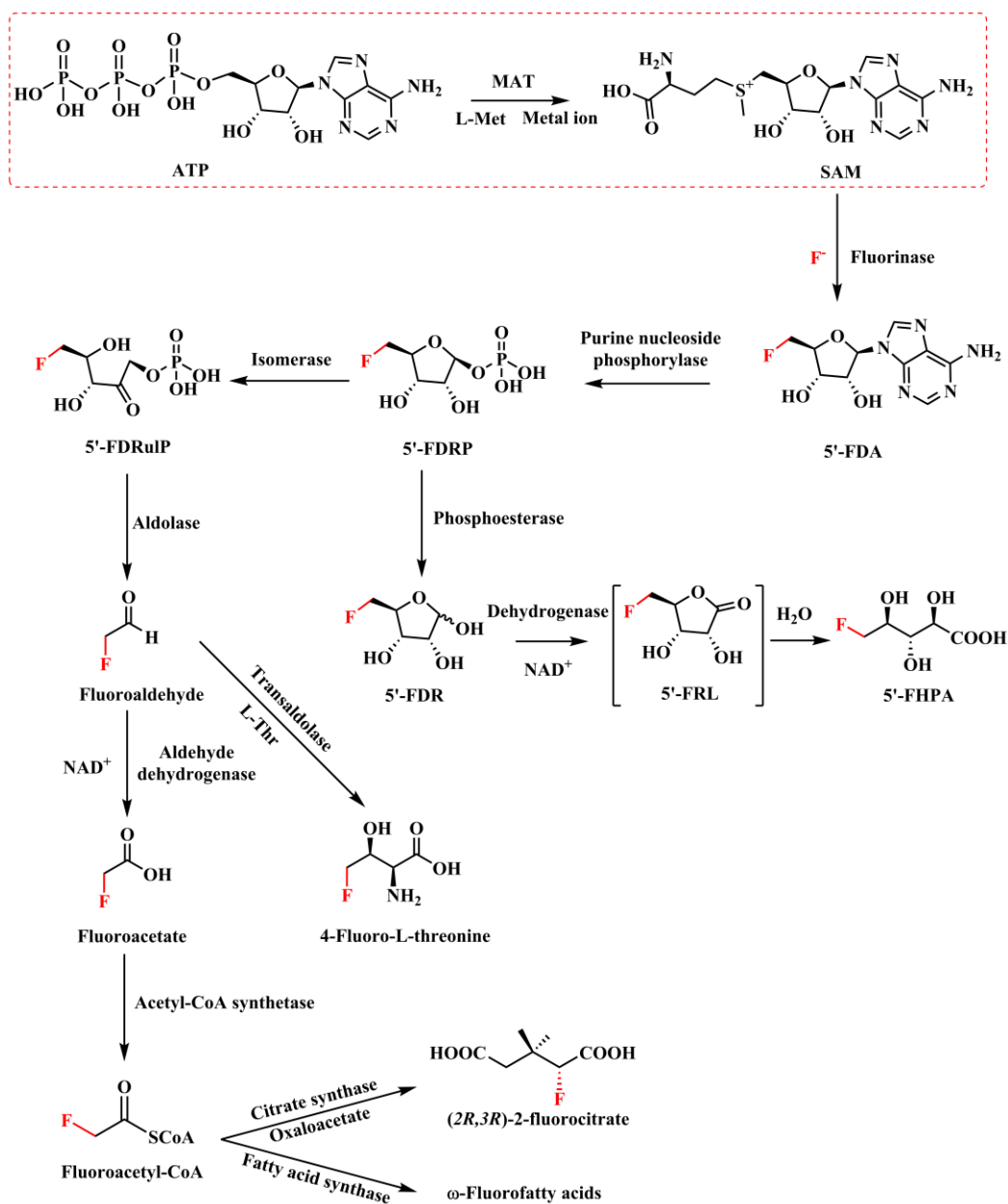
47

DL-β-fluoroamines

D-β-fluoroamines
or
L-β-fluoroamines

48 **Figure S7.** β-Fluoroamines were obtained by kinetic resolution through
49 transaminase-mediated hydrodefluorination/deamination reactions.

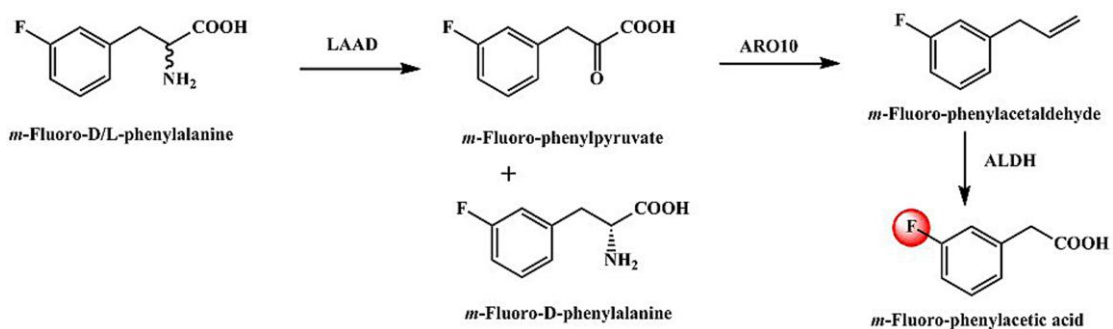
50



51

52 **Figure S8.** The biosynthetic pathway of fluorinated metabolites identified
 53 from *Streptomyces*. S-adenosyl-L-methionine (SAM);
 54 5'-fluoro-5'-deoxyadenosine (5'-FDA);
 55 5'-fluoro-5'-deoxy-ribose-1-phosphate (5'-FDRP);
 56 5'-fluoro-5'-deoxy-ribulose-phosphate (5'-FDRuIP);
 57 5'-fluoro-5'-deoxy-D-ribose (5'-FDR);
 58 5'-fluoro-5'-deoxy-D-ribo- γ -lactone (5'-FRL);
 59 (2R3S4S)-5'-fluoro-2,3,4-trihydroxypentanoic acid (5'-FHPA). The
 60 metabolic pathway in the red dashed box is a new pathway newly
 61 discovered in our laboratory. Related research results will be published
 62 elsewhere.

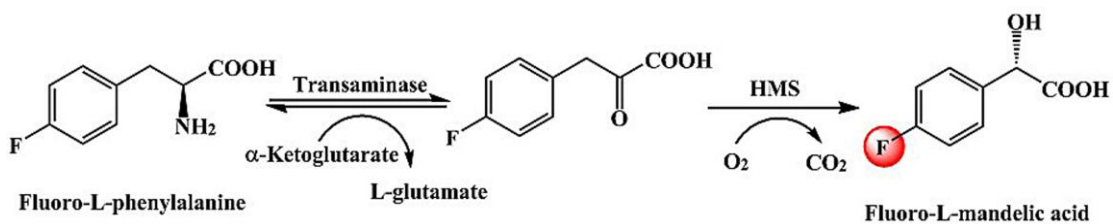
63



64

65 **Figure S9.** *m*-Fluoro-phenylacetic acid was synthesized by LAAD,
 66 ARO10, and ALDH.

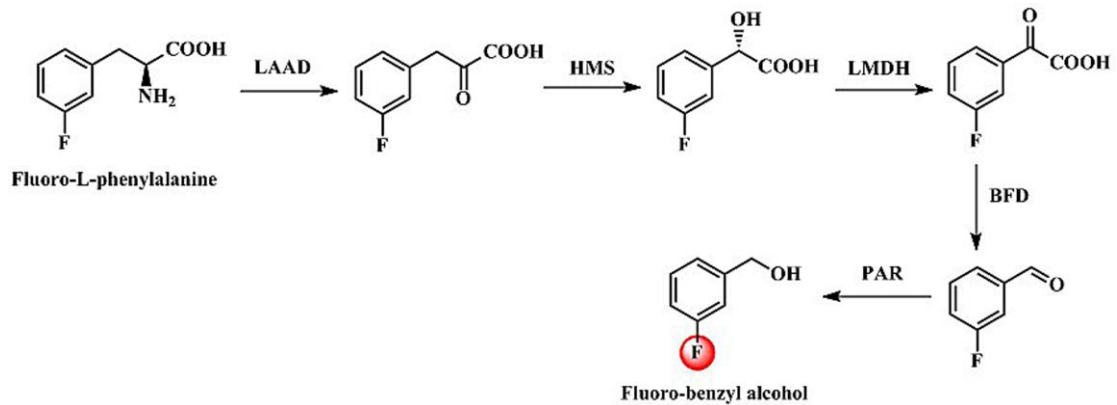
67



68

69 **Figure S10.** Biosynthesis fluoro-L-mandelic acid catalyzed by aromatic
 70 amino acid transaminase and HMS.

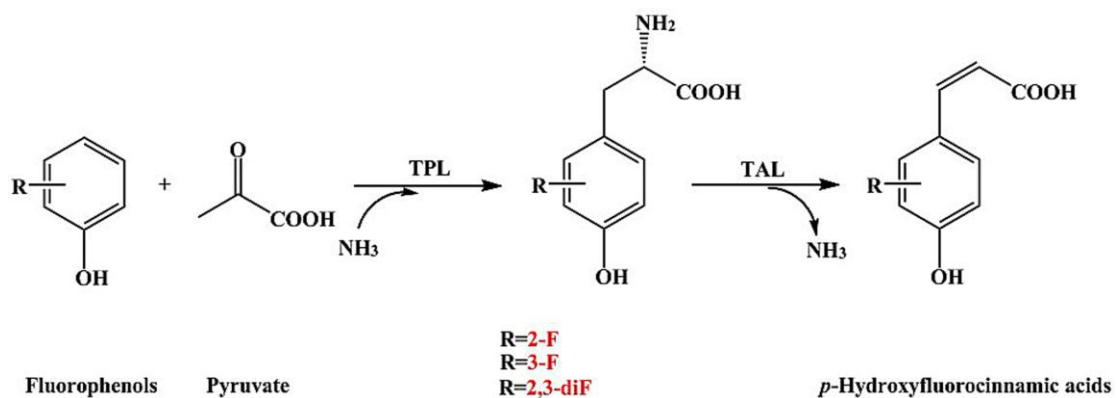
71



72

73 **Figure S11.** Biosynthesis fluoro-benzyl alcohol catalyzed by LAAD, HMS,
 74 LMDH, BFD and PAR.

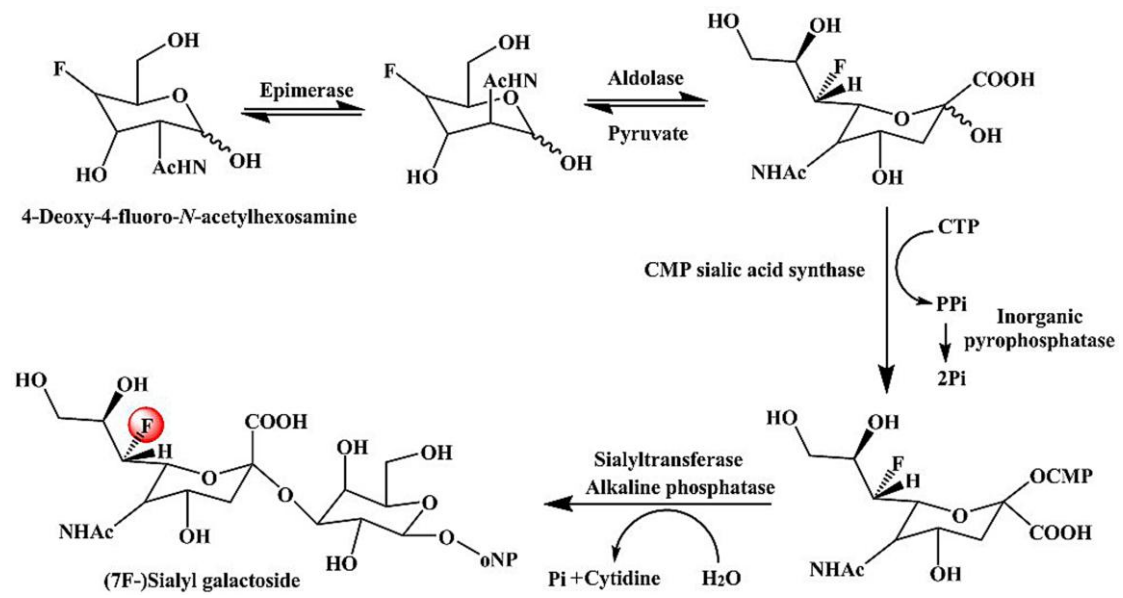
75



76

77 **Figure S12.** *p*-Hydroxyfluorocinnamic acids were obtained by TPL and
 78 TAL.

79



80

81 **Figure S13.** Multi-enzyme synthesis route of (7F-)sialyl galactoside.

82 *o*-Nitrophenol=oNP.

83

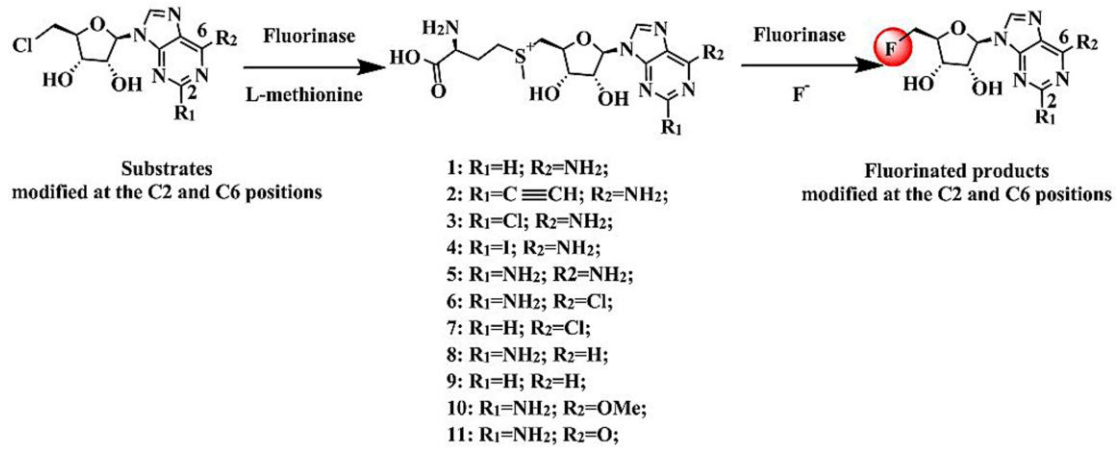
Streptomyces_xinghaiensis	MSADPTQRPIIGFMSDLGTTDDSV AQCRGLMHSICPGVTIV	40
Actinopolyspora_mzabensisMSDLGTTDDSV AQCRGLMMSICQDVTIV	27
Streptomyces_sp.MA37	MAANGSQRPIIAFMSDLGTTDDSV AQCRGLMHSICPGVTIV	40
Actinoplanes_sp.N902-109	..MPANGNPPIIAFMSDLGTTDDSV AQCRGLMMSICPGVTIV	38
Nocardia_brasiliensisMSDLGITDDSV AQCRGLMMSVCGEDVTIV	27
Streptomyces_cattleya	MAANSTRRPIIAFMSDLGTTDDSV AQCRGLMYSICPGDVTIV	40
Consensus	msdlg tddsvaqckglm s c vt	
Streptomyces_xinghaiensis	IDVCHSMTPWDVEEGARYIVDLPRFFPEGTVFATTYPAT	80
Actinopolyspora_mzabensis	VDVCHSMEPNWVEEGARYIVDLPRFFPEGTVFATTYPAT	67
Streptomyces_sp.MA37	VDVCHSMTPWDVEEGARYIVDLPRFFPEGTVFATTYPAT	80
Actinoplanes_sp.N902-109	VDVNSMTPWDVEEGARYIVDLPRFFPEGTVFATTYPAT	78
Nocardia_brasiliensis	VDICHTMQFPWVEEGARYIVDLPRFFPEGTVFATTYPAT	67
Streptomyces_cattleya	VDVCHSMTPWDVEEGARYIVDLPRFFPEGTVFATTYPAT	80
Consensus	d h m pw veegaryivdlpr fpegtvfattypat	
Streptomyces_xinghaiensis	GTETRSVAVRIKQAAKGGARGQWAGSAGGFERAEGSYIIV	120
Actinopolyspora_mzabensis	GTTARSAVARIKYPAGKGGARGQWAGSGEGFERSEGSYIIV	107
Streptomyces_sp.MA37	GTTTRSAVARIKQAAKGGARGQWAGSGDGFERADGSYIIV	120
Actinoplanes_sp.N902-109	GTATRSVALRIKQAAKGGARGQWAGSAGGFERAEGSYIIV	118
Nocardia_brasiliensis	GTTARSAVALRIAHASKGGARGQWAGSAGGFERKEGSYIIV	107
Streptomyces_cattleya	GTTTRSAVARIKQAAKGGARGQWAGSAGGFERAEGSYIIV	120
Consensus	gt rsva ri qgaargqwags gfer gsyiy	
Streptomyces_xinghaiensis	APNNGLLTTVLEEHGYIEAYEVSSSTKVIIPERPEPTFYSRE	160
Actinopolyspora_mzabensis	APNNGLLTTVLEEHGYIEAYEVSSSTDVVFARPEPTFYSRE	147
Streptomyces_sp.MA37	APNNGLLTTVLEEHGYIEAYEVSTTKVIIPANPEPTFYSRE	160
Actinoplanes_sp.N902-109	APNNGLLTTVIEEHGYIEAYEVSNTKVIIPAEPEPTFYSRE	158
Nocardia_brasiliensis	APNNGLLTTVIEEHGYIEAYEVSSPEVIEPEPEPTFYSRE	147
Streptomyces_cattleya	APNNGLLTTVLEEHGYIEAYEVTSPEKVIIEPEPEPTFYSRE	160
Consensus	apnngllttv ehgy eayev v p peptfysre	
Streptomyces_xinghaiensis	MVAIPSAHLAAGFPLEVGRRLDSEIVRFHRAVEISGD	200
Actinopolyspora_mzabensis	MVAIPSAHLAAGYPLEKVRKQLDSEIVRFPTPQATVSPE	187
Streptomyces_sp.MA37	MVAIPSAHLAAGFPLAEVGRRLDSEIVRFHRAVEISGD	200
Actinoplanes_sp.N902-109	MVAIPSAHLAAGFPLNEVGRRLDSEIVRFHRAVEISGD	198
Nocardia_brasiliensis	MVAIPSAHLAAGFPLEKVRRLADSEIVRFERKDFELVAD	187
Streptomyces_cattleya	MVAIPSAHLAAGFPLEVGRPLEDSEIVRFHRAVEIQDGE	200
Consensus	mva p ahlag pl vgr l d eivr	
Streptomyces_xinghaiensis	.TLTGVVSAIDHPFGNVWNTNIHRTDLEKAGIGYGRRIKII	239
Actinopolyspora_mzabensis	GDLSCVVTAIDHPFGNIWTSIHHDNLESAAGVGYGTNLKIV	227
Streptomyces_sp.MA37	.ALSCVVTAIDHPFGNIWNTNIHRTDLEKAGIGYGRKHLKII	239
Actinoplanes_sp.N902-109	GVLSCVITNIDHPFGNLWNTNIHRTDLEKAGIGYQTQLRLL	238
Nocardia_brasiliensis	HDLVGYVTNIDHPFGNVWNTNIHRTDLEKLGVGYGTLKIRIT	227
Streptomyces_cattleya	.ALVGVVSAIDHPFGNVWNTNIHRTDLEKAGIGYGARLRLT	239
Consensus	l g idhpfgn wt ihr le g g	
Streptomyces_xinghaiensis	LDDVLFPEELIPTTFADAGEIGVAAVYVNSRGYLSIARNA	279
Actinopolyspora_mzabensis	LDDVLFPEELIPTTFADAGEVGDVYVYVNSRGYLSIARNA	267
Streptomyces_sp.MA37	LDDVLFPEELIPTTFADAGAIQNIATVYVNSRGYLSIARNA	279
Actinoplanes_sp.N902-109	LDGVITFDLIVPTTFADAGQIGDVIYVNSRGYLSIARNA	278
Nocardia_brasiliensis	LDGVLFPEELIPTTFADAGEIGAAVYVLSRGYLSIARNA	267
Streptomyces_cattleya	LDGVLFPEELIPTTFADAGEIGNIATVYVNSRGYLSIARNA	279
Consensus	ld v f l ptfadag g y srgyl arna	
Streptomyces_xinghaiensis	ASLAYFYNLRAGLKVRETV	298
Actinopolyspora_mzabensis	ASLAYFYNLRKEGMSVTR	286
Streptomyces_sp.MA37	ASLAYFYNLRAGLKVREVA	298
Actinoplanes_sp.N902-109	APLAYFYNLRAGLTVIVTK	297
Nocardia_brasiliensis	ASLAYFYNLRAGISVQKV	286
Streptomyces_cattleya	ASLAYFYNLRKEGMSARVEA	298
Consensus	a layp lk g v	

84

85 **Figure S14.** Multiple sequence alignment of fluorinases from different

86 microorganisms. Green: 100% homology level; Pink: $\geq 75\%$ homology
87 level; Light green: $\geq 50\%$ homology level.

88



89

90 **Figure S15.** C2 and C6 modified substrates catalyzed by fluorinase.