

Table S1. Core characteristics of representative sugar C-MTs

Enzyme	UniProt ID and PDB ID	NCBI accession number	Related natural product	Source strain	Substrate type	Methylation site	MT classification	Reference
LobD2	A0ABS7WH09	AGC09482.1	lobophorin	<i>Streptomyces</i> sp. FXJ7.023	TDP sugar	C3	Class I SAM MT	1
LobS5	M9T4G0	AGI99499.1	lobophorin	<i>Streptomyces</i> sp. SCSIO 01127	TDP sugar	C3	Class I SAM MT	1
KijD1	B3TMQ9 PDB: 5T67	WP_067826717.1	kijanimicin	<i>Actinomadura kijaniata</i>	TDP sugar	C3	Class I SAM MT	2,3
TcaB9	B5L6K6 PDB: 3NDJ	WP_353902404.1	tetrocarcin A	<i>Micromonospora chalcea</i>	TDP sugar	C3	Class I SAM MT	4–6
RubN5	Q2PC68	CAI94697.1	rubradirin	<i>Streptomyces rubradiris</i>	TDP sugar	C3	Class I SAM MT	7
DacS3	K4IK25	AFU65915.1	dactylocycline	<i>Dactylosporangium</i> sp. SC14051	TDP sugar	C3	Class I SAM MT	8,9
EvdM8	A0A7H8XFQ8	WP_178063249.1	everninomicin D	<i>Micromonospora carbonacea</i>	TDP sugar	C3	Class I SAM MT	10–12
MCAG_03666		WP_007074609.1	everninomicin 13-384-1 (ziracin)	<i>Micromonospora</i> sp. ATCC 39149	TDP sugar	C3	Class I SAM MT	13
DvaC (OrfX)	Q939Y7	CAC48364.1	balhimycin	<i>Amycolatopsis balhimycina</i> DSM 5908	TDP sugar	C3	Class I SAM MT	14,15
EvaC	A0A193C6T2	WP_044851280.1	chloroeremomycin	<i>Amycolatopsis orientalis</i>	TDP sugar	C3	Class I SAM MT	16
Kid4		WAS29226.1	kidamycin	<i>Streptomyces</i> sp. W2061	TDP sugar	C3	Class I SAM MT	17
MT in saccharomicin	K0K6L8	WP_015103263.1	saccharomicin	<i>Saccharothrix espanaensis</i>	TDP sugar	C3	Class I SAM MT	18,19
MT in orienticin C	P96561	CAA11777.1	orienticin C	<i>Amycolatopsis orientalis</i> ( <i>Nocardia orientalis</i> )		C3	Class I SAM MT	20
ChryMT	D1H0B9	CBH32106.1	chrysomycin	<i>Streptomyces albaduncus</i>	TDP sugar	C3	Class I SAM MT	21
CmmC	Q70J72	CAE17543.1	chromomycin A3	<i>Streptomyces griseus</i> subsp. <i>griseus</i>	TDP sugar	C3	Class I SAM MT	22,23
ApoM5	G4XIK2	AEP40909.1	apoptolidin	<i>Amycolatopsis</i> sp. FU40	TDP sugar	C3	Class I SAM MT	24
NocS3	E5DUG7	ADR01071.1	nocathiacin	<i>Nocardia</i> sp. ATCC 202099	TDP sugar	C3	Class I SAM MT	25,26
MdpA4	B0BLL8	ABY66027.1	maduropeptin	<i>Actinomadura madurae</i> ATCC 39144	TDP sugar	C3	Class I SAM MT	27–29
SibM	COLTM7	ACN39736.1	sibiromycin	<i>Streptosporangium sibiricum</i>	TDP sugar	C3	Class I SAM MT	30
SnogG2	Q9RN56	WP_344346064.1	nogalamycin	<i>Streptomyces nogalater</i>	TDP sugar	C3	Class I SAM MT	31

MmyC		QVQ68803.1	metathramycin	Metagenome	TDP sugar	C3	Class I SAM MT	32
MtmC	Q194Q4 PDB: 4RVG	WP_252552390.1	mithramycin	<i>Streptomyces argillaceus</i>	TDP sugar	C3	Class I SAM MT	33–35
EvdM3	A0A7H8XG84	QLD23468.1	everninomicin D	<i>Micromonospora carbonacea</i>	TDP sugar	C3	Class I SAM MT	11,12
MCAG_03641	C4RP78	WP_007074584.1	everninomicin 13-384-1 (ziracin)	<i>Micromonospora</i> sp. ATCC 39149	GDP sugar	C3	Class I SAM MT	13,36
CBU_0691	Q93N52	WP_010957740.1		<i>Coxiella burnetii</i>	GDP sugar	C3	Class I SAM MT	37
AviG1	Q93KW9	WP_003998238.1	avilamycin	<i>Streptomyces viridochromogenes</i> Tue57	TDP sugar	C3	Class I SAM MT	38–40
MT in curamycin A	A0A117P7L9	KUM74559.1	curamycin A	<i>Streptomyces curacoi</i>	TDP sugar	C3	Class I SAM MT	41
KedS4	K4PC53	AFV52186.1	kedarcidin	<i>Streptoalloteichus</i> sp. ATCC 53650	TDP sugar	C3	Class I SAM MT	42
AurS11	A0A2U9I6I7	AWR88420.1	auroramycin	<i>Streptomyces filamentosus</i>	TDP sugar	C3	Class I SAM MT	43
LkmIII	Q83X77	WP_011113108.1	lankamycin	<i>Streptomyces rochei</i> 7434AN4	TDP sugar	C3	Class I SAM MT	44
EryBIII	A4F7P8	CAM00072.1	Erythromycin A	<i>Saccharopolyspora erythraea</i> NRRL 2338	TDP sugar	C3	Class I SAM MT	45,46
TxnM1	A0A0K1H3F6	AKT74284.1	trioxacarcin	<i>Streptomyces bottropensis</i>	TDP sugar	C3	Class I SAM MT	47
TylC3	Q9XC68	AAD41823.1	tylosin	<i>Streptomyces fradiae</i>	TDP sugar	C3	Class I SAM MT	48,49
CyaA3	S4WCR4	AGO97195.1	cyanosporaside	<i>Salinispora pacifica</i>	TDP sugar	C4	Class I SAM MT	50
CloU	V6KTP3	WP_023545093.1	clorobiocin	<i>Streptomyces roseochromogenus</i>	TDP sugar	C5	Class I SAM MT	51,52
CouU	Q9F8S9	WP_109005055.1	coumermycin A1	<i>Streptomyces rishiriensis</i>	TDP sugar	C5	Class I SAM MT	51
NovU	Q9L9E7	WP_069626149.1	novobiocin	<i>Streptomyces spheroides</i>	TDP sugar	C5	Class I SAM MT	51,53
SgcA3	Q8GMH7	AAL06661.1	enediyne C-1027	<i>Streptomyces globisporus</i>	TDP sugar	C5	Class I SAM MT	54,55
TiaS2	E9LIM4	WP_360572049.1	tiracumicin B	<i>Dactylosporangium aurantiacum</i> subsp. hamdenensis	TDP sugar	C5	Class I SAM MT	56
GenK	A0A0K0K526	ARV75717.1	gentamicin	<i>Micromonospora echinospora</i>	gentamicins	C6	Class B radical SAM MT	57,58
GenD1	Q6QVU0	ARV75711.1	gentamicin	<i>Micromonospora echinospora</i>	gentamicins	C4	Class B radical SAM MT	57,58

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