

Whole genome sequence of *Streptomyces humi* strain MUSC 119^T isolated from intertidal soil

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Abstract : Over the past few decades, microorganisms have made major contribution in natural product research, particularly those from the genus *Streptomyces*. *Streptomyces humi* MUSC 119^T was previously isolated as novel streptomycete from mangrove soil in Malaysia. During the screening programme for bioactive strains, this strain was discovered to possess antioxidant activity – scavenging and reducing accumulation of free radicals in biochemical assays. Consequently, whole genome sequencing was performed to evaluate genomic potential of the strain. Based on our analysis, the genome size of MUSC 119^T is described to be 10.01 Mbps with G + C content of 71.80%. Based on antiSMASH analysis, the strain possess great genomic potential, having nine biosynthetic gene clusters displaying high similarities to known gene clusters. These findings indicates that mangrove *Streptomyces* species like MUSC 119^T may potentially play an important role in drug development process, while the availability of its whole genome sequences allows further manipulation to isolate and identify compound of interest.

Keywords: *Streptomyces*; antioxidant; mangrove; genome; MUSC 119^T; actinobacteria

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Short Introduction

Owing to their ability in synthesizing bioactive compounds of various structures, members of *Streptomyces* have always been in the limelight for the search of pharmaceutically important compounds^[1-6]. Coupled with their ability to synthesize various bioactive compounds, their unique life cycle and spore formation has allowed these filamentous bacteria to survive and colonize various habitats, covering both terrestrial and marine region^[7-18]. *Streptomyces humi* MUSC 119^T was recovered from mangrove soil in east coast of Peninsular Malaysia^[19]. Using polyphasic approach^[20], strain MUSC 119^T was determined as a novel species belonging to the genus *Streptomyces*. The type strain of MUSC 119^T is available at two culture collection centres with accession of (=DSM 42174^(T)) =

MCCC 1K00505^(T)). Further investigation of the strain revealed that its fermentative extract possessed potent antioxidant activity (unpublished). Therefore, the strain was subjected whole genome sequencing to assist in the understanding of its genomic potential, particularly for the biosynthesis of pharmaceutically important compounds.

Data description

For DNA extraction, genomic DNA of MUSC 119^T was obtained using Masterpure™ DNA purification kit (Epicentre, Illumina Inc., Madison, WI, USA) before subjected to RNase (Qiagen, USA) treatment^[21-23]. Genomic DNA quality was evaluated with NanoDrop spec-

trophotometer (Thermo Scientific, Waltham, MA, USA) and a Qubit version 2.0 fluorometer (Life Technologies, Carlsbad, CA, USA). Subsequently, DNA library was prepared using Nextera™ DNA Sample Preparation kit (Nextera, USA) and the quality of DNA library was checked with Bioanalyzer 2100 high sensitivity DNA kit (Agilent Technologies, Palo Alto, CA)^[24]. Whole genome shotgun project of MUSC 119^T was performed using paired sequencing on an Illumina MiSeq platform with MiSeq Reagent Kit 2 (2 × 250 bp; Illumina Inc., Madison, WI, USA), which generated 4,376,924 paired-end reads. The assembly of trimmed sequence was carried out on CLC Genomic Workbench version 5.1 (CLC Bio, Denmark), resulted in 214 contigs and an N₅₀ contig size of approximately 126,586 bp. The assembled genome size comprised 10,014,215 bp, with an average coverage of 148.0-fold and G + C content of 71.80 %. The genome sequence of *Streptomyces humi* MUSC 119^T has been deposited at DDBJ/EMBL/GenBank under accession of LBMU00000000. The version described here is the second version.

<i>Streptomyces humi</i> MUSC 119 ^T	
Genome size (bp)	10,014,215
Contigs	214
Contigs N ₅₀ (bp)	126,586
G + C content %	71.80
Genome coverage	148.0x
Protein coding genes	8,338

Table 1. General genomic features of *Streptomyces humi* strain MUSC 119^T.

The assembled genome was annotated using Rapid Annotation using Subsystem Technology (RAST)^[25]. Gene prediction was performed using Prodigal version 2.6, while ribosomal RNA (rRNA) and transfer RNA (tRNA) were predicted using RNAmmer and tRNAscan SE ver-

sion 1.21, respectively^[26-28]. The analysis from RAST revealed 8,338 protein-coding genes, along with a total of 72 RNA genes (Figure 1). Based on RAST system, most of the protein-coding genes were involved in amino acids metabolism (8.8 %), followed by carbohydrate metabolism (8.7 %) and production of cofactors, vitamins, prosthetic groups, pigments (4.6 %). Further analysis on antibiotics & Secondary Metabolite Analysis SHell (antiSMASH)^[29] predicted more than 100 biosynthetic gene clusters in MUSC 119^T genome. A total of nine biosynthetic gene clusters showed similarity more than 70% to known gene clusters. Among these gene clusters, there were gene clusters associated with production of melanin, lantipeptides and non-ribosomal peptides. Furthermore, there was one gene cluster associated with biosynthesis of siderophores, desferrioxamine B. There have been several reports indicated potential of *Streptomyces* species to produce desferrioxamine^[30-31]. As an iron chelating molecule, desferrioxamine is often used to treat iron overload clinically^[31] and there have been reports indicating potential use of desferrioxamine for the diseases like antibacterial and anticancer.

The detection of these gene clusters highlight genomic potential of MUSC 119^T and prompt deeper investigation into their expression and function. With the availability of the whole genome sequence of MUSC 119^T, the current project opens a new window to hasten the drug discovery process, allowing genomic manipulations to exploit the strain for production of useful bioactive products.

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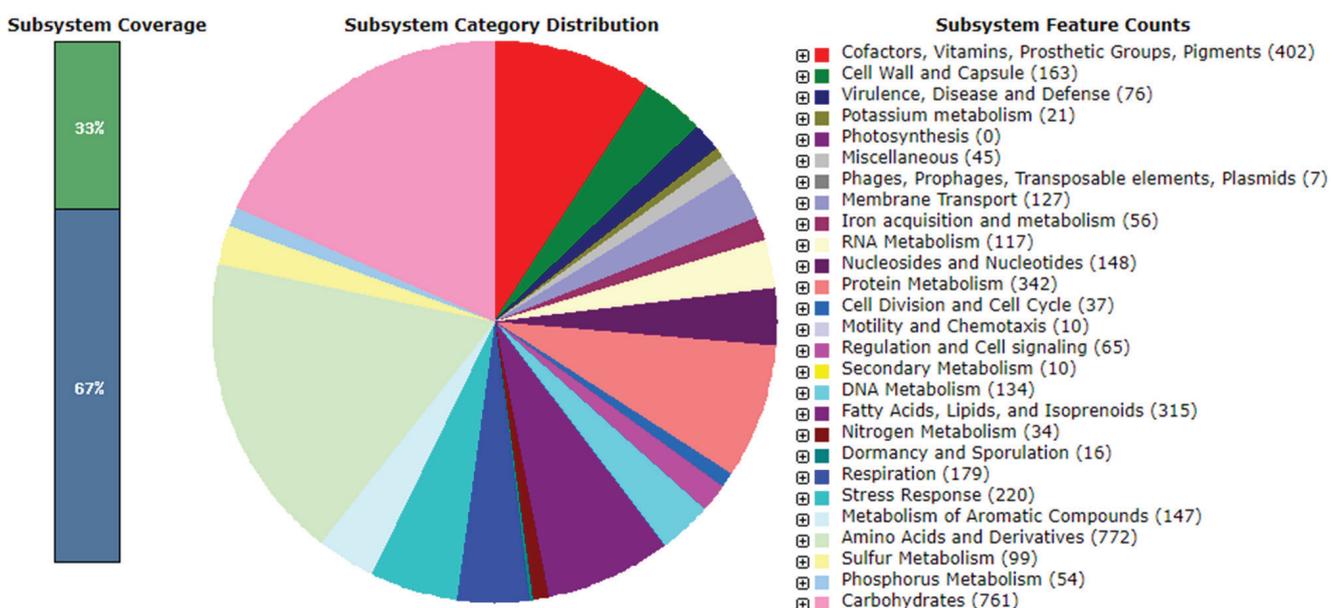


Figure 1. Subsystem category distribution of *Streptomyces humi* MUSC 119^T (based on RAST annotation server).

Conflict of Interest

The authors declared that there is no conflict of interest.

Reference

- Bérdy J. Thoughts and facts about antibiotics: Where we are now and where we are heading. *J Antibiotics* 2012; 65(8): 385.
- Subramani R, Aalbersberg W. Marine actinomycetes: An ongoing source of novel bioactive metabolites. *Microbiol Res* 2012; 167(10): 571-580.
- Ser HL, Tan WS, Ab Mutalib NS, *et al.* Genome sequence of *Streptomyces pluripotens* MUSC 135^T exhibiting antibacterial and antioxidant activity. *Mar Gen* 2015; 24: 281-283.
- Sangkanu S, Rukachaisirikul V, Suriyachadkun C, *et al.* Evaluation of antibacterial potential of mangrove sediment-derived actinomycetes. *Microbial Pathogen* 2017; 112: 303-312.
- Law JW, Ser HL, Khan TM, *et al.* The potential of *Streptomyces* as biocontrol agents against the rice blast fungus, *Magnaporthe oryzae* (*Pyricularia oryzae*). *Front Microbiol* 2017; 8: 3.
- Dhakal D, Pokhrel AR, Shrestha B, *et al.* Marine rare actinobacteria: Isolation, characterization, and strategies for harnessing bioactive compounds. *Front Microbiol* 2017; 8: 1106.
- Ser HL, Tan LT, Law JW, *et al.* Focused review: Cytotoxic and antioxidant potentials of mangrove-derived *Streptomyces*. *Front Microbiol* 2017; 8: 2065.
- Jose PA, Jha B. Intertidal marine sediment harbours Actinobacteria with promising bioactive and biosynthetic potential. *Sci Rep* 2017; 7(1): 10041.
- Qin S, Li WJ, Dastager SG, *et al.* Actinobacteria in special and extreme habitats: Diversity, function roles, and environmental adaptations. *Front Microbiol* 2016; 7: 1415.
- Ser HL, Law JW, Chaiyakunapruk N, *et al.* Fermentation conditions that affect clavulanic acid production in *Streptomyces clavuligerus*: A systematic review. *Front Microbiol* 2016; 7: 522.
- Sarmiento-Vizcaino A, Braña AF, González V, *et al.* Atmospheric dispersal of bioactive *Streptomyces albidoflavus* strains among terrestrial and marine environments. *Microbial Ecol* 2016; 71(2): 375-386.
- Tan LT, Chan KG, Chan CK, *et al.* Antioxidative potential of a *Streptomyces* sp. MUM292 isolated from mangrove soil. *BioMed Res Int* 2018; 2018.
- Tan LT, Chan KG, Pusparajah P, *et al.* Mangrove derived *Streptomyces* sp. MUM265 as a potential source of antioxidant and anticancer agents. *BMC Microbiol* 2019; 19(1): 38.
- Ser HL, Yin WF, Chan KG, *et al.* Antioxidant and cytotoxic potentials of *Streptomyces gilvigriseus* MUSC 26^T isolated from mangrove soil in Malaysia. *Prog Microbes Mol Biol* 2018; 1(1).
- Ghosh S, Kuisiene N, Cheeptham N. The cave microbiome as a source for drug discovery: Reality or pipe dream?. *Biochem Pharm* 2017; 134: 18-34.
- Law JW, Ser HL, Ab Mutalib NS, *et al.* *Streptomyces monashensis* sp. nov., a novel mangrove soil actinobacterium from East Malaysia with antioxidative potential. *Sci Rep* 2019; 9(1): 3056.
- Li K, Tang X, Zhao J, *et al.* *Streptomyces cadmiisoli* sp. nov., a novel actinomycete isolated from cadmium-contaminated soil. *Int J Syst Evol Microbiol* 2019.
- Adam D, Maciejewska M, Naômé A, *et al.* Isolation, characterization, and antibacterial activity of hard-to-culture actinobacteria from cave moonmilk deposits. *Antibiotics* 2018; 7(2): 28.
- Zainal N, Ser HL, Yin WF, *et al.* *Streptomyces humi* sp. nov., an actinobacterium isolated from soil of a mangrove forest. *Antonie van Leeuwenhoek* 2016; 109(3):467-74.
- Law JW, Tan KX, Wong SH, Ab Mutalib NS, Lee LH. Taxonomic and characterization methods of *Streptomyces*: a review. *Prog Microbes Mol Biol* 2018; 1(1).
- Ser HL, Tan WS, Cheng HJ, *et al.* Draft genome of amylolytic actinobacterium, *Sinomonas humi* MUSC 117^T isolated from intertidal soil. *Mar Gen* 2015; 24: 209-210.
- Ser HL, Ab Mutalib NS, Yin WF, *et al.* Genome sequence of *Streptomyces antioxidans* MUSC 164^T isolated from mangrove forest. *Prog Microbes Mol Biol* 2018. url: <http://www.journals.hh-publisher.com/index.php/pmb/article/view/1/14>.
- Ser HL, Tan WS, Cheng HJ, *et al.* Draft genome of starch-degrading actinobacterium, *Microbacterium mangrovi* MUSC 115^T isolated from intertidal sediments. *Prog Drug Dis Biomed Sci* 2018. url: <http://www.journals.hh-publisher.com/index.php/pddb/article/view/41>.
- Ser HL, Tan WS, Ab Mutalib NS, *et al.* Genome sequence of *Streptomyces mangrovisoli* MUSC 149^T isolated from intertidal sediments. *Braz J Microbiol* 2018; 49(1): 13-15.
- Aziz RK, Bartels D, Best AA, *et al.* The RAST Server: Rapid annotations using subsystems technology. *BMC Genomics* 2008; 9: 75.
- Lowe TM, Eddy SR. tRNAscan-SE: A program for improved detection of transfer RNA genes in genomic sequence. *Nuc Acids Res* 1997; 25: 955-964.
- Lagesen K, Hallin P, Rodland EA, *et al.* RNAmmer: Consistent and rapid annotation of ribosomal RNA genes. *Nuc Acids Res* 2007; 35: 3100-3108.
- Hyatt D, Chen GL, Locascio PF, *et al.* Prodigal: Prokaryotic gene recognition and translation initiation site identification. *BMC Bioinform* 2010; 11: 119.
- Blin K, Wolf T, Chevrette MG, *et al.* antiSMASH 4.0—improvements in chemistry prediction and gene cluster boundary identification. *Nuc Acids Res* 2017; 45(W1): W36-41.
- Ser HL, Palanisamy UD, Yin WF, *et al.* *Streptomyces malaysiense* sp. nov.: A novel Malaysian mangrove soil actinobacterium with antioxidative activity and cytotoxic potential against human cancer cell lines. *Sci Rep* 2016; 6: 24247.
- Gáll T, Lehoczki G, Gyémánt G, *et al.* Optimization of desferrioxamine E production by *Streptomyces parvulus*. *Acta microbiologica et immunologica Hungarica* 2016; 3(4): 475-489.
- Banin E, Lozinski A, Brady KM, *et al.* The potential of desferrioxamine-gallium as an anti-*Pseudomonas* therapeutic agent. *PNAS* 2008; 105(43): 16761-16766.
- Salis O, Bedir A, Kilinc V, *et al.* The anticancer effects of desferrioxamine on human breast adenocarcinoma and hepatocellular carcinoma cells. *Cancer Biomarkers* 2014; 14(6): 419-426.