ISOLATION AND CHARACTERIZATION OF METHYL VIOLOGEN-RESISTANT *Synechocystis* sp. PCC 6803 MUTANTS

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A Thesis Submitted in Partial Fulfillment of the Requirements
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การแยกและการศึกษาลักษณะสมบัติของ *Synechocystis* sp. PCC 6803 สายพันธุ์กลายที่ทนต่อเมทิลไวโอโลเจน

น.ส.จิดาภา เล็กสิงห์โต

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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Thesis Title	ISOLATION AND CHARACTERIZATION OF METHYL VIOLOGEN-RESISTANT *Synechocystis* sp. PCC 6803 MUTANTS
By	Miss Jidapa Leksingto
Field of Study	Biochemistry and Molecular Biology
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จิดาภา เล็กสิงห์โต : การแยกและการศึกษาลักษณะสมบัติของ *Synechocystis* sp. PCC 6803 สายพันธุ์กลายที่ทนต่อเมทิลไวโอโลเจน. (ISOLATION AND CHARACTERIZATION OF METHYL VIOLOGEN-RESISTANT *Synechocystis* sp. PCC 6803 MUTANTS) อ.ที่ปรึกษาหลัก : รศ. ดร.ธนะกาญจน์ มัญชุพาณี

เมทิลไวโอโลเจน (Methyl viologen) เป็นสารกำจัดวัชพืชที่ใช้กันอย่างแพร่หลาย สามารถรับอิเล็กตรอนจากระบบแสง และกระตุ้นการก่อตัวของอนุมูลอิสระที่ก่อให้เกิดความเครียดจากปฏิกิริยาออกซิเดชันของเซลล์พืช ในไซยาโนแบคทีเรียที่สังเคราะห์ด้วยแสง อย่างไรก็ตามยังไม่สามารถระบุโมเลกุลเป้าหมายที่แน่นอนของเมทิลไวโอโลเจนในเซลล์ได้ การศึกษานี้มีวัตถุประสงค์เพื่อหาการกลายพันธุ์ที่นำไปสู่การต้านทานต่อเมทิลไวโอโลเจนในไซยาโนแบคทีเรียสายพันธุ์ *Synechocystis* sp. PCC 6803 โดยมีการเพาะเลี้ยงเป็นเวลา 30 วัน เพื่อให้ถึงระยะการเจริญเติบโตแบบคงที่ (stationary-growth phase) และเกิดการกลายพันธุ์ที่เกิดขึ้นเองตามธรรมชาติ (spontaneous mutation) ในเซลล์ที่มีอายุมาก จากนั้นเซลล์ประมาณ 10^9 เซลล์ ถูกกระจายบนอาหารเลี้ยงเชื้อที่มีความเข้มข้นของเมทิลไวโอโลเจน 10 ถึง 40 ไมโครโมลาร์ ซึ่งสามารถยับยั้งการเจริญเติบโตของเซลล์ได้อย่างสมบูรณ์ หลังจากเพาะเลี้ยงผ่านไป 30 ถึง 40 วัน พบเซลล์กลายพันธุ์ที่ต้านทานต่อเมทิลไวโอโลเจนเกิดขึ้นถึง 23 176 และ 2,936 โคโลนี จากอาหารเลี้ยงเชื้อที่มีความเข้มข้นของเมทิลไวโอโลเจน 40 20 และ 10 ไมโครโมลาร์ตามลำดับ จากนั้นได้เลือกสายพันธุ์ที่กลายพันธุ์มาทั้งหมด 7 ตัว เพื่อวิเคราะห์ลำดับจีโนมในการระบุตำแหน่งการกลายพันธุ์ที่ต้านทานต่อเมทิลไวโอโลเจนในสายพันธุ์กลายพันธุ์ พบว่าในสายพันธุ์ A9 มีการกลายพันธุ์ที่ได้รหัสหยุดการสังเคราะห์โปรตีนก่อนกำหนด (stop codon gained mutation) และรบกวนการทำงานของยีน *cntO_1* ที่ถอดรหัสให้ตัวรับสัญญาณ TonB ซึ่งมีหน้าที่เกี่ยวข้องกับกระบวนการขนส่งสารที่มีประจุบวกข้ามผ่านเยื่อหุ้มเซลล์ ดังนั้นการกลายพันธุ์ที่ตำแหน่งตัวรับสัญญาณนี้จึงถูกรบกวน และส่งผลให้เกิดการต้านทานต่อเมทิลไวโอโลเจน ในสายพันธุ์กลายพันธุ์ C14 และ C21 พบการกลายพันธุ์แบบเฟรมชิพท์ (frameshift mutation) ส่งผลให้ระงับการทำงานของยีน *menH_2* ที่ถอดรหัสให้เอนไซม์ไตรเอซิลกลีเซอรอล ไลเปส (triacylglycerol lipase) ซึ่งเป็นองค์ประกอบหลักของเยื่อหุ้มเซลล์ เมื่อยีนนี้ถูกรบกวนจึงส่งผลต่อการขนส่งเมทิลไวโอโลเจนเข้าสู่เซลล์ ยิ่งไปกว่านั้นในทุกสายพันธุ์กลายพันธุ์พบการเปลี่ยนกรดอะมิโนหนึ่งตัวในโปรตีนไม่ทราบหน้าที่ (hypothetical protein) ที่ถอดรหัสจากยีน *FMAMFGPO_01147* ที่มีกรดอะมิโนทั้งหมด 92 ตัว จากการทำนายโครงสร้างโปรตีนแสดงให้เห็นว่าโครงสร้างของโปรตีนที่ไม่ทราบหน้าที่นี้เกิดการเปลี่ยนแปลงอย่างมีนัยสำคัญเมื่อแทนที่กรดอะมิโนเมไทโอนีนตำแหน่งที่ 53 ด้วยกรดอะมิโนไลซีน ยิ่งไปกว่านั้นยังพบการกลายพันธุ์ในยีนที่เกี่ยวข้องกับกระบวนการสังเคราะห์องค์ประกอบเยื่อหุ้มเซลล์ การสังเคราะห์เปบทิโดไกลแคนในผนังเซลล์ การสร้างไบโอฟิล์ม และกระบวนการป้องกันสารต้านอนุมูลอิสระในสายพันธุ์กลาย A9 C14 และ C21 จากการศึกษานี้สรุปได้ว่ากลไกการต้านทานต่อเมทิลไวโอโลเจนเกี่ยวข้องกับการเปลี่ยนแปลงของการขนส่งเมทิลไวโอโลเจนในเซลล์กลายพันธุ์ องค์ประกอบที่เปลี่ยนแปลงของเยื่อหุ้มเซลล์และผนังเซลล์ และการเปลี่ยนแปลงกลไกการต้านอนุมูลอิสระ ซึ่งข้อมูลที่ได้นี้เป็นข้อมูลพื้นฐานเกี่ยวกับการกลายพันธุ์ที่เกิดขึ้นเองตามธรรมชาติในการต้านทานต่อเมทิลไวโอโลเจนของจุลชีพที่อาศัยอยู่ในแหล่งน้ำ และมีความสามารถในการสังเคราะห์ด้วยแสงได้

สาขาวิชา	ชีวเคมีและชีววิทยาโมเลกุล	ลายมือชื่อนิสิต .....
ปีการศึกษา	2565	ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

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KEYWORD: Methyl viologen, Synechocystis sp. PCC 6803, Spontaneous mutation, Resistance

Jidapa Leksingto : ISOLATION AND CHARACTERIZATION OF METHYL VIOLOGEN-RESISTANT *Synechocystis* sp. PCC 6803 MUTANTS. Advisor: Assoc. Prof. TANAKARN MONSHUPANEE, Ph.D.

Methyl viologen (MV) is a widely used herbicide that competes electrons from photosystem I and induces the formation of active radical species causing cellular oxidative stress in plants and photosynthetic cyanobacteria. However, the exact target molecule of methyl viologen in the cells has yet to be identified. This study aimed to identify the mutation(s) that lead to MV resistance in cyanobacterium *Synechocystis* sp. PCC 6803. *Synechocystis* wild type was cultured for 30 days to reach the stationary-growth phase to allow the occurrence of spontaneous mutations in aged cells. Approximately 10^9 cells were spread on an agar medium containing high MV concentrations (10-40 µM), which could completely inhibit cell growth. After 30-40 days, spontaneous MV-resistant mutants up to 23, 176 and 2,936 colonies were obtained from agar plates containing 40, 20 and 10 µM of MV, respectively. MV-resistant mutations were subsequently identified in seven selected MV-resistant mutants using genome sequencing. Mutant A9 contained the stop codon gained mutation that disrupted the function of *the cntO_1* gene encoding the TonB-dependent receptor involved in the transport of positively charged ions across the cell membrane. Thus, this TonB-dependent receptor might transport MV to the cell, and the disrupted function leads to MV resistance. Mutant C14 and C21 contained the frameshift mutation that abolished the function of *the menH_2* gene encoding triacylglycerol lipase (enzyme generating diacylglycerol, the main component of cell membrane), suggesting that this gene disruption may affect MV import to the cells. Moreover, mutant A9, A11, B1, B14, C10, C14 and C21 contained one amino acid alteration (53Met-->Lys) in a small hypothetical protein (a 92-amino-acid protein product of the gene *FMAMFGPO_01147*) with an unknown function. Protein structure prediction showed that the structure of this hypothetical protein was significantly changed upon 53Met-->Lys substitution. Additionally, the mutations in genes associated with the biosynthesis of cell-membrane component, the biosynthesis of cell-wall peptidoglycan, the biofilm formation, and the antioxidant defense were found in the MV-resistant mutants A9, C14 and C21. In conclusion, the mechanisms of MV resistance found in this study is related to the alteration of MV transport and the modified composition of the cell membrane. This data provides basic information on spontaneous MV resistance in an aquatic photosynthetic microbe.

Field of Study:	Biochemistry and Molecular Biology	Student's Signature .....
Academic Year:	2022	Advisor's Signature .....

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Jidapa Leksingto

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CHAPTER I
INTRODUCTION

1.1 Background, rationales, and theories

Herbicides has been used to kill unwanted weeds, but these chemicals have accumulated and are toxic for other plants, animals and human beings. Some herbicides have been known to be mutagenic or carcinogenic agents (Nguyen-Ngoc et al., 2009). Accumulation of herbicide waste in aquatic systems is one of a great concern due to its negative impact on aquatic ecosystems such as aquatic plant, and microalgal cyanobacteria.

MV (N,N′-dimethyl-4,4′-bipyridinium dichloride) is typical in the form of salt with chloride or other anions (Fig. 1). MV is one of the most widely used herbicides in the world for the control of broadleaf weeds. MV is adsorbed very quickly by weed leaves and blocks photosynthesis by acting as electron acceptor at photosystem I complex of weeds (Fuerst & Vaughn, 1990). This action disrupts photosynthetic electron transfer systems and prevents the generation of NADPH (Fig. 2). As a result, the excess electron is transferred to molecular oxygen and generate the toxic reactive oxygen species (Ananieva et al., 2004), such as superoxide anions, singlet oxygen, hydroxyl and peroxyl radicals which are accumulated in chloroplasts of weeds (Autor, 1974). These toxic compounds subsequently result in the productions of harmful hydroxyl radicals and hydrogen peroxide that cause DNA damage, protein degradation and lipid peroxidation which are the important cellular metabolisms (Casano et al., 1994; Szigeti & Lehoczki, 2003). Nevertheless, the cellular mechanism in photosystem I complex that is the target of MV inhibition is still unclear.

Cyanobacteria have also been found to be highly sensitive to MV(Li et al., 2013). Previous study determined the localization of membrane proteins in *Synechococcus* sp. PCC7942 (Sherman et al., 1994). These authors speculated that MV could interact with photosystem I (PSI) and inhibit PSI function.

However, MV may not be able to bind PSII because PSII locates at inner thylakoid membrane where MV may not be able to get in (Sherman et al., 1994). For this reason, the MV competes for the electrons only in the PSI. It has been hypothesized that MV blocks electron transport by interacting membrane-bound nonheme iron-sulfur proteins (Fa/Fb) in PSI because Fa/Fb is the reduction site of PSI. (Fuerst & Norman, 1991). However, this hypothesis has not been verified. In addition, eukaryotic algal *Chlorella vulgaris*, the expression of *psaB* gene encoding PSI protein was down regulated upon exposing to MV (Qian et al., 2009). Therefore, this result supported the hypothesis that MV inhibits PSI from above.

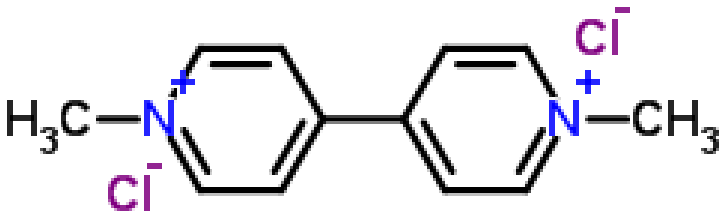


Figure 1 Chemical structure of MV dichloride salt (N,N-dimethyl-4,4-bipyridinium dichloride).
It has the chemical formula $[(C_6H_7N)_2]Cl_2$. It belongs to the family of redox-active heterocycles (Michaelis, 1932). The structure is obtained from www.chemsrc.com/en/cas/.

Since cellular mechanism that is a target of MV inhibition has not been identified. This research aims to identify mutation conferring MV resistance. We speculated that the product of gene(s) that is mutated is likely the target of MV inhibition. Therefore, the product of wild type gene is sensitive to MV, while the

product of the mutated gene(s) is resistant to MV. Thus, the isolation of MV resistant mutation is one way to suggest the cellular target of MV.

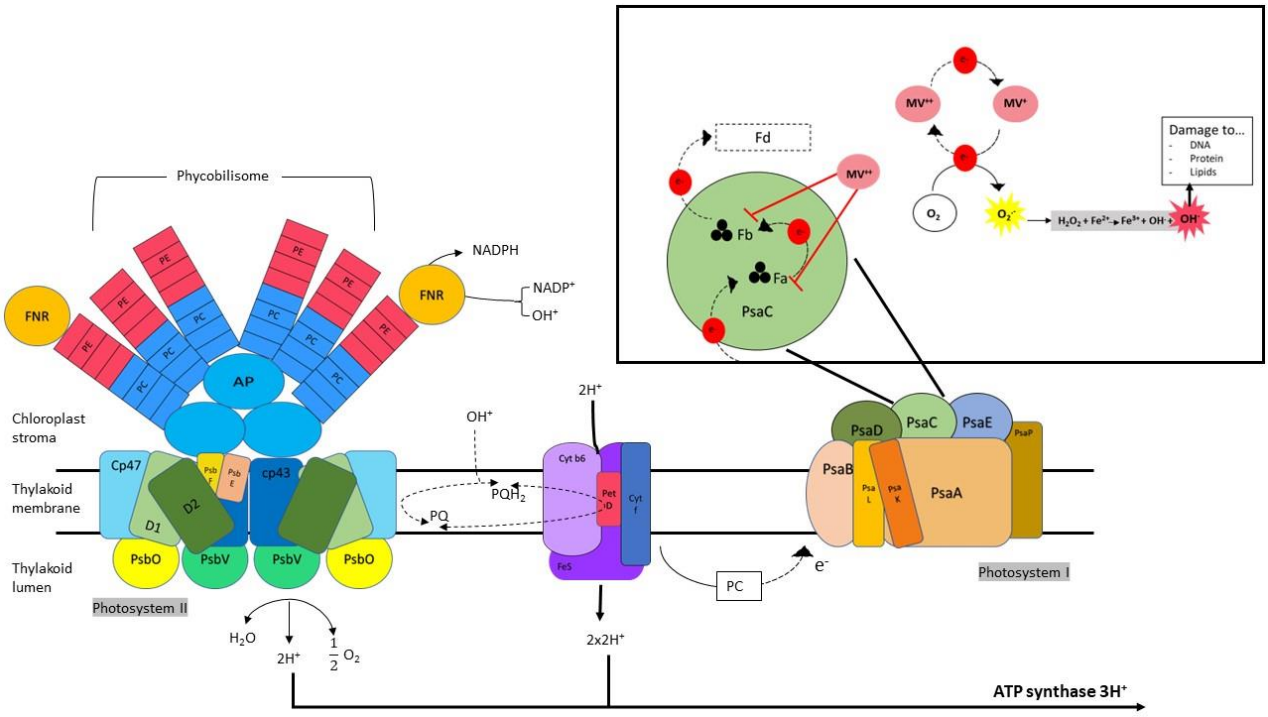


Figure 2 MV inhibits photosynthesis by blocking photosystem I electron transport.

Photosynthetic system and electron transport of *Synechocystis* sp. PCC 6803 (Vermaas, 2001) Photosystem I (PSI) and photosystem II (PSII) containing pigments (such as chlorophyll *a* and carotenoid) absorbs light and transfers electron to the electron accepter protein complex. The electron transport chain moves from PSII to PSI via the cytochrome b6f complex which used for the reduction of $NADP^+$ to NADPH. During electron transport a H^+ gradient was used to generate ATP via ATPase. MV in the form of MV^{++} acts as an electron acceptor and competes electron flow in PSI transport. Hence, it is speculated that MV^{++} probably inhibits PSI electron transport by interacting membrane-bound nonheme iron-sulfur proteins (Fa/Fb). Then, MV^+ is generated and was reacted to molecular oxygen (O_2) and generated super oxides (O_2^-). Next, O_2^- induces lipid peroxidation and other oxidative stress responses. The information above was obtained and the figure was redrawn from Fuerst and Norman, 1991.

To isolate MV resistant mutants, spontaneous mutation was used. The spontaneous mutations are the infrequent and random mutation that occur in cells via the error of DNA replication and repair system. Probability that a mutation will be observed each time from the cells divided themselves generally between 1 in 10,000 and 1 in a trillion (Engelkirk et al., 2020). In cyanobacteria (*Prochlorococcus* sp.) has the mutation rate about 1 in a ten billion mutations per base pairs per generation (Kashtan et al., 2014).

Isolation of spontaneous mutation has been done in the well-studied cyanobacterium *Synechocystis* sp. PCC 6803 resistant to acetazolamide (Bedu et al., 1990) and cadmium (Xu et al., 2018). MV resistant mutations have been reported (Table 1). In the plant *Arabidopsis thaliana*, the mutation in *pqr2* gene encoding a polyamine uptake transporter is associated with the MV resistant phenotype, suggested that this transporter may involve in MV transport (Dong et al., 2016). In bacteria, the mutation in *sodA1* gene encoding superoxide dismutase (Passalacqua et al., 2007) and the mutation in *ubiG* gene encoding a methyltransferase required for the ubiquinone biosynthesis (involving in cellular antioxidant response) were found in MV-resistant mutants (Gonidakis et al., 2011). These data suggested that these mutated enzymes may help the cells by destroying antioxidants occurred from MV exposure in these bacteria. In addition, the mutation in *zwf* gene encoding glucose-6-phosphate dehydrogenase (G6PDH), an enzyme generation NADPH (the cofactor of enzymes in defense against MV toxicity) was report in *Pseudomonas aeruginosa* mutant that is resistant to MV (Ma et al., 1998). In *Synechocystis*, a single mutation in the gene involving in MvrA membrane transporter (Kreslavski et al., 2007), a single mutation in SodB superoxide dismutase (enzyme for antioxidant removal) (Nefedova et al., 2003) and the triple mutations potentially lead to MV secretion including that in Slr1901 ATPase, Slr1174 transporter protein and Slr0610 membrane transporter permease, lead to MV resistance (Prosecka et al., 2009). However, no report of a

mutation in PSI where is the target of MV inhibition. Thus, a mutation in PSII conferring MV resistance has yet to be isolated.

Synechocystis sp. PCC 6803 is one of cyanobacterial models with well known for genome data, and with well-studied biochemistry, physiology and photosynthesis (Shevela et al., 2013). Thus, *Synechocystis* is suitable to be used as a strain for the isolation of spontaneous MV resistant mutants. Therefore, this study isolated spontaneous MV resistant mutants. Genomic mutations conferring MV resistance was identified using next generation sequencing. The mutated proteins were investigated for structural changes. The mutants were analyzed for cell growth under other osmotic and oxidative stresses and examined for the photosynthetic and antioxidant activity. The possible mechanism of MV resistant in cyanobacteria along with the cyanobacterial strategy of MV tolerance are discussed.

Table 1 MV-resistant mutations, previously reported in plant, bacteria and cyanobacteria.
NA: data not available

Organism of MV resistant mutants	Concen-tration of MV	Mutation site	Effect of cellular process	Reference
Arabidopsis thaliana	2 μM	***pqr2* gene:** encoding a polyamine uptake transporter	Under MV treatment, the *pqr2* mutation might significantly lessen superoxide buildup and cell death in the *pqr2* plants.	Dong et al., 2016
Bacillus anthracis Sterne (34F2)	100 μM – 800 μM	***sodA1* gene:** encoding superoxide dismutase.	The mutants were found to alter expression of gene implicated in the glyoxalase pathway, metal/ion transport, bacillibactin siderophore production, and oxidoreductase activity.	Passalacqua et al., 2007
Escherichia coli	300 μM	***ubiG* gene:** encoding a methyltransferase required for the ubiquinone biosynthesis	The increasing of lifespan and enhance oxidative stress resistance in the *ubiG* mutant.	Gonidakis et al., 2011
Pseudomonas aeruginosa	5 μM	***zwf* gene:** encoding glucose-6-phosphate dehydrogenase (G6PDH) an enzyme that convert NAD^+ or $NADP^+$ and glucose-6-phosphate to 6-phosphogluconate	The mutant was more reactive to the superoxide-producing substance methyl viologen. The latter studies indicate that this cofactor is necessary for the activity of enzymes crucial in the defense against MV toxicity because NADPH is one of the by-products of G6PDH activity.	Ma et al., 1998

Organism of MV resistant mutants	**Concen-tration of MV**	**Mutation site**	**Effect of cellular process**	**Reference**
Synechocystis sp. PCC 6803	4 μM	***mvrA*:** encoding the transmembrane protein	The MvrA protein is thought to be necessary for the effective removal from cells of harmful chemicals produced during oxidative stress or to take part in the repair of membranes damaged by oxidants.	Nefedova et al., 2004
	6 μM	***sodB*:** encoding iron-containing superoxide dismutase	The *sodB* gene encodes the unique SOD (Fe-SOD) that neutralizes superoxide radical in *Synechocystis* 6803 cells. Therefore, it is unlikely that an increased resistance to MV by changes in the activity of any other antioxidant enzyme	Babykin et al., 2003
	10 μM	***Slr1901*:** encoding ATPase, ***Slr1174*:** encoding transporter protein and ***Slr0610*:** encoding membrane transporter permease	Each component of the MV transporter (an ATP-binding protein), which is made up of the products of the genes *slr1901, slr1174,* and *slr0610,* is essential for MV excretion.	Prosecka et al., 2009

1.2 Hypotheses

When the mutation occurred, will provide the mechanism of PQ resistance in cyanobacteria *Synechocystis* sp. PCC 6803 which is the model system for the study of photosynthetic organisms and higher plants and will provide basic information for further development of other compound that can inhibit photosynthesis for further use in weed control.

1.3 Objective

1.3.1. To isolate mutant strain(s) that being resistant to MV

1.3.2. To identify DNA mutation(s) in the mutant strain(s) by genome sequencing

1.3.3. To determine cell growth and photosynthetic efficiency in the mutant

1.3.4. To characterize mutated protein by bioinformatics computational analysis

CHAPTER II
LITERATURE REVIEWS

2.1 Implications of methyl viologen to wildlife and the environmental.

Methyl viologen, an extremely hazardous herbicide has been used more than 50 years and has highest acute toxicity compared to all other pesticides. Due to its extremely high acute toxicity and lack of an antidote, paraquat is currently the most lethal pesticide on the market. The first use of methyl viologen (MV) occurred in Malaysian rubber plantations in 1961. (Calderbank & Farrington, 1995). Since then, it has been widely used. China is presently the country with the highest production. MV kills both grasses and weeds with broad leaves as a nonselective herbicide. It is used on field crops (maize), in direct planting (or conservation tillage), in forestry, and as a defoliant or desiccant to dry crop plants (cotton, pineapple, soybean, sugar cane, for example). It is also used on fruit and plantation crops (banana, cocoa, coffee, oil palm) (Tomlin, 2003) Additionally, MV has been utilized to manage aquatic weeds (Vismara et al., 2000).

2.1.1 Soil

In clay particles, MV is thought to be substantially adsorbed. In Thailand, sandy loam soils showed 5.83% desorption, while clay soils showed only 0.17% (Amondham et al., 2006). The 79% of the MV was adsorbed in a Spanish vineyard soil experiment, but 11% of it was desorbed later (Pateiro-Moure et al., 2010). Adsorption increases with increasing pH, and decreases with increasing acidity (Muhamad et al., 2011). Because of the strong adherence to the soil, MV is not readily available to plants or other creatures; as a result, it biodegrades very slowly. It is resistant to microbial destruction in both aerobic and anaerobic circumstances. According to the US EPA (2009) no microbial degradation was observed after 180 days of aerobic incubation or after 60 days of anaerobic incubation following a 30 day aerobic incubation. While employing paraquat as a nitrogen source, some authors claim that bacteria, fungi, actinomyces, and yeast can significantly break down MV

(Amondham et al., 2006). Moreover, MV does not photodegrade, even when exposed to natural sunlight for 85 weeks, according to the US EPA (1997).

2.1.2 Water

MV is adsorbed onto the suspended matter in water. It moves from the water itself onto aquatic weeds, sediment, and suspended solids. According to Eisler 1990, in freshwater habitats, MV is rapidly lost from the water phase, about 50% in 36 hours and 100% in 4 weeks. In marine ecosystems, paraquat is typically lost from seawater between 50% and 70% within 24 hours(Eisler, 1990). MV is likely to enter surface waters attached to soil particles and then be redeposited into the bottoms of surface water bodies or lowland regions that receive eroded sediments from uplands (for example, riparian zones and wetlands) (US EPA 2009). Moreover, the reports from many countries showed the contamination of methyl viologen (MV) in the water. In Spain, MV was found in 6.6% of samples from a lagoon (maximum level 3.95 µg/L), and in 9.35% of samples from a marsh (maximum level 1.45 µg/L), (Fernández et al., 1998). MV was found 5.3 µg/L in drinking water in the EU in 1995, also found in a number of rivers and dams at a maximum concentration of 1 µg. In Thailand, MV has been found in groundwater at levels up to 18.9 µg/L (Amondham et al., 2006).

2.1.3 Wildlife

Weed plants that are resistant to MV has been recorded since 1980 in Japan, Canada, USA, Belgium, Taiwan, Malaysia, and Sri Lanka. By June 2010, 22 species of weeds in 13 countries had developed resistance to MV (Heap, 2010) as showed in Table 2. However, as referred to earlier, aquatic plants can concentrate high levels of paraquat, sufficient to cause toxic, behavioral, and teratogenic effects in tadpoles (Calderbank & Farrington, 1995).

Table 2 Weed resistance to paraquat.
Twenty-two species of weeds that are resistant to MV has been recorded since 1980 in thirteen countries.

Weeds	Countries
Amaranthus lividus (Livid amaranth)	Malaysia
Bidens Pilosa (Hairy beggarticks)	Kenya
Conzya bonariensis (Hairy fleabane)	Egypt, Japan, South Africa, USA
Conyza canadensis (Horseweed)	Japan, Canada, USA,
Conyza sumatrensis (Sumatran fleabane)	Japan, Canada, USA, Belgium
Crassocephalum crepidiodes (Redflower ragleaf)	Malaysia
Cuphea carthagenenis (Tarweed cuphea)	Fiji
Eleusine indica (Goosegrass)	Malaysia, USA
Epilobium adenocaulon (American willowherb)	Belgium, UK
Erigeron philadelphicus (Philadelphia fleabane)	Japan
Hordeum glaucum (Wall barley)	Australia
Hordeum leporinum (Barley grass)	Australia
Ischaemum rugosum (Saramollagrass)	Malaysia
Landoltia punctata (Dotted duckweed)	USA
Lepidium virginicum (Virginia pepperweed)	Canada
Lolium rigidum (Rigid ryegrass)	South Africa, Australia
Mitracarpus hirtus (Small square weed)	Australia
Poa annua (Annual bluegrass)	UK, Belgium
Solanum americanum (American black nightshade)	USA
Solanum nigrum (Black nightshade)	Malaysia
Vulpia bromoides (Silvergrass)	Australia
Youngia japonica (Asiatic hawkbeard)	Japan

2.2 Spontaneous mutation

During an organism's life cycle, changes in DNA chemistry can result in spontaneous mutations, which are the overall effect (Glickman et al., 1986). Therefore, all mutagenic and antimutagenic biological mechanisms produce the types and quantities of spontaneous mutations. The fact that modest changes in experimental settings significantly alter the types and rates of spontaneous mutations is not commonly found.

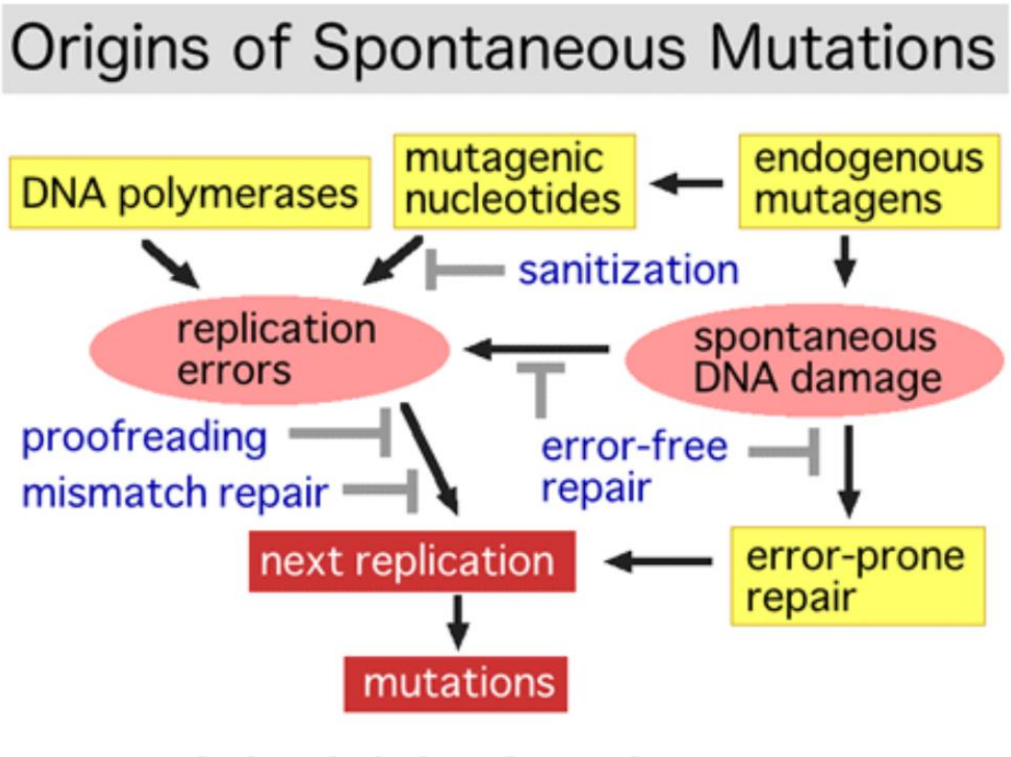


Figure 3 The origin of spontaneous mutations.
The mapping is obtained from https://quizlet.com/79824919/chapter-14-how-life-works-barrera-flash-cards/

The spontaneous mutations occur in cells via the error of DNA replication and repair system. A mutation will be observed each time from the cells divided themselves, generally between 1 in 10,000 and 1 in a trillion (Engelkirk et al., 2020). In cyanobacteria (*Prochlorococcus* sp.), the mutation rate is about 1 in a ten billion mutations per base pairs per generation (Kashtan et al., 2014). Moreover, spontaneous

mutation has been done in the well-studied cyanobacterium *Synechocystis* sp. PCC 6803 resistant to acetazolamide (Bedu et al., 1990) and cadmium (Xu et al., 2018).

2.3 Methyl viologen resistance mediated by the enhanced ability of antioxidant in others organism.

2.3.1 *Arabidopsis thaliana*

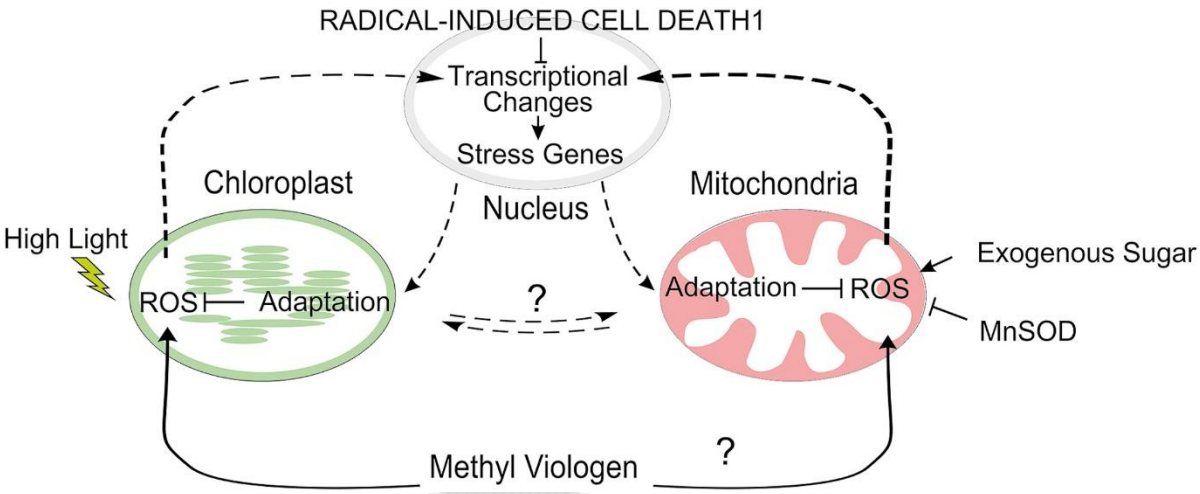


Figure 4 Effect of MV in plant *Arabidopsis thaliana*

Methyl viologen (MV), a herbicide and research tool, stimulates ROS formation in the chloroplast when illuminated, although it is also hazardous to non-photosynthetic organisms. MV was utilized to examine plant ROS signaling in locations other than the chloroplast. This study used natural variation, QTL mapping, and mutant experiments with MV when the chloroplast electron transport is inactive in the model plant Arabidopsis (*Arabidopsis thaliana*). Researchers investigated the relationships between organelles using the radical-induced cell death mutant, which is resistant to MV-induced ROS and has altered mitochondrial signaling. The outcome demonstrated a light-independent ROS-signaling mechanism triggered by MV, pointing to mitochondrial participation. Further support for the function of mitochondria is provided by the finding that mitochondrial Mn superoxide dismutase

was necessary for ROS tolerance and that the effect of MV was improved by exogenous sucrose. This study suggests that mitochondria are involved in response to ROS induced by MV in plants (Cui et al., 2019).

Moreover, the study of mechanism paraquat (same meaning as MV) tolerance in plant that switches off activated oxidative response by targeting histone-modifying protein methyltransferase4b.

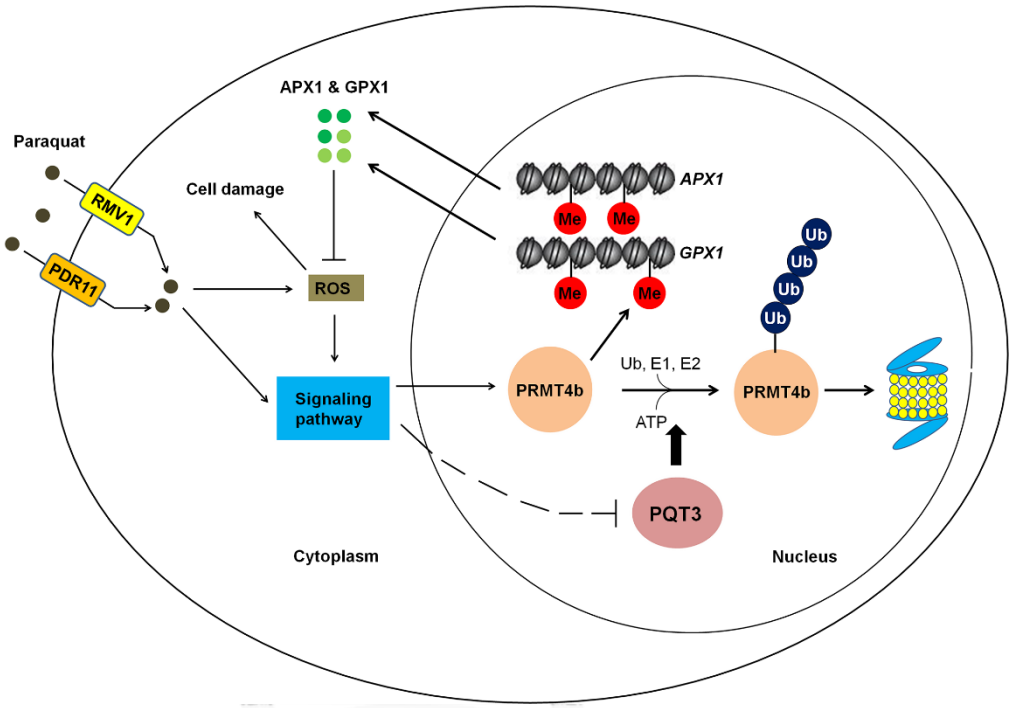


Figure 5 A working model for PQT3 acting as a negative regulator of oxidative stress response in the higher plants.

From Fig. 5, stress signaling increases PRMT4b expression while decreasing PQT3 expression in response to oxidative stress. This increased PRMT4b activity will activate APX1 and GPX1 and increase their antioxidation capacity. PRMT4b expression decreases, and PQT3 expression increases when oxidative stress is reduced. As a result, PQT3 activity increases, which causes the 26S proteasome to remove PRMT4b more rapidly. APX1 and GPX1 expression will decrease along with a rapid decline in PRMT4b activity and PRMT4b expression. Then, oxidative stress that activates the reaction is turned off (Luo et al., 2016).

2.3.2 *Paraburkholderia xenovorans* LB400

Paraburkholderia xenovorans (strain LB400), has one of the largest known prokaryotic genomes (9.7 Mb) and is one of the best aerobic PCB degrading strains (Consortium, 2010). The physiological and molecular reaction of *Paraburkholderia xenovorans* (strain LB400) to Paraquat (same meaning as MV) and H_2O_2. In contrast to Paraquat, which showed adverse effects on growth and increased cytoplasmic ROS formation only after more prolonged exposure, H_2O_2 showed growth inhibition. It increased cytoplasmic ROS accumulation after a shorter incubation period, likely because of its oxidizing nature. This is likely because H_2O_2 first needs to produce radicals. Due to its ongoing production of superoxide in the cytoplasm and membrane diffusion limitation for H_2O_2, Paraquat demonstrated a greater loss in cell density than H_2O_2 (Méndez et al., 2022)

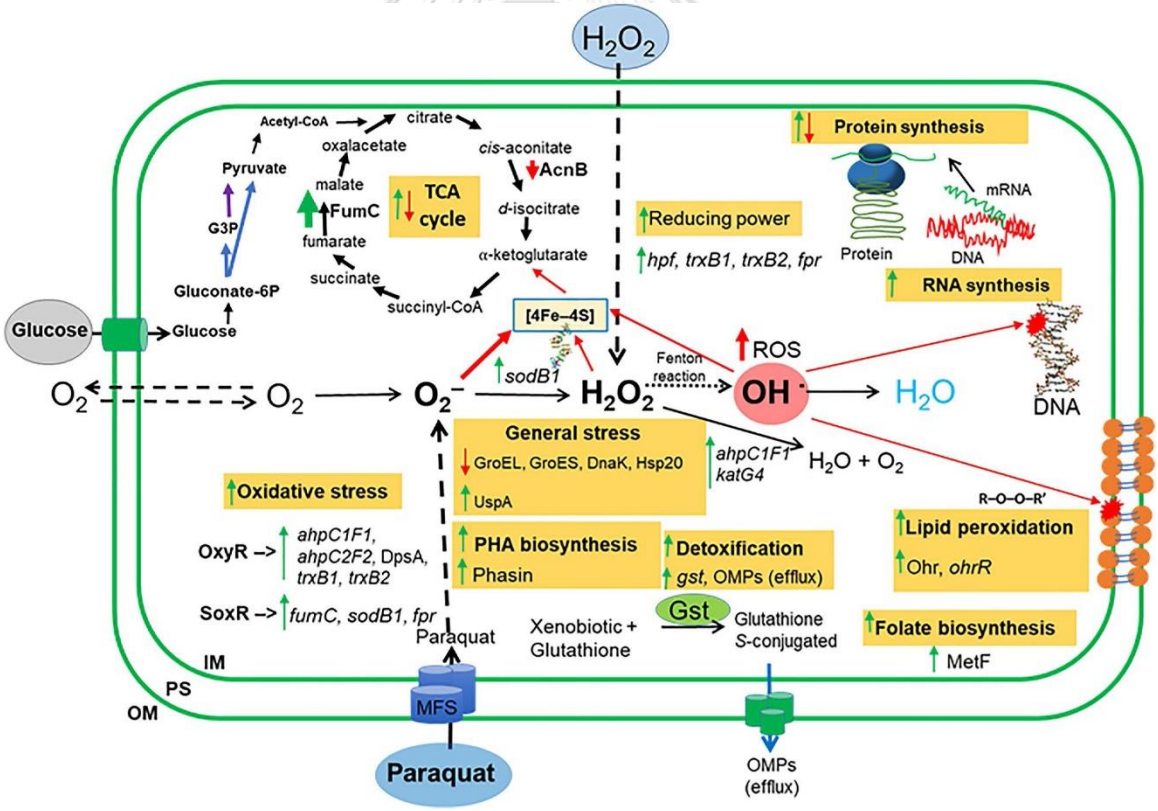


Figure 6 Molecular oxidative stress response of *P. xenovorans* LB400 during exposure to paraquat and H_2O_2

P. xenovorans LB400 had a report of genes for the antioxidant defense, including the *oxyR, ahpC, ahpF, kat, trxB, dpsA* and *gorA* genes, whose orthologous genes are regulated by the transcriptional regulator OxyR in *E. coli.* Additionally, the LB400 genome contains the genes *soxR, fumC, acnA, sodB, fpr,* and *fldX*, whose orthologous genes in *E. coli.* are controlled by the transcriptional regulator SoxR. The complementation of a null mutant *P. aeruginosa*, *soxR* gene demonstrated the functioning of the LB400 *soxR* gene. LB400 cells were more sensitive to paraquat than H_2O_2 in growth, susceptibility, and ROS production tests. Following exposure to H_2O_2, transcriptional studies in LB400 cells showed an increase of the *oxyR, ahpC1*, *katE*, and *ohrB* genes, whereas the *oxyR, fumC, ahpC1*, *sodB1*, and *ohrB* genes were increased in the presence of paraquat. The oxidative stress response proteins AhpCF and DpsA, the universal stress protein UspA, and the RNA chaperone CspA were all increased by paraquat, according to a proteome study. The Ohr protein, implicated in resistance to organic peroxide, was stimulated by both oxidizing agents. Thus, *P. xenovorans* LB400 has a wide range oxidative stress response, which accounts for its strong resistance to the oxidizing substances paraquat and H_2O_2 (Méndez et al., 2022)

2.4 Methyl viologen resistance mediated by the alterations in cellular transport system.

2.4.1 *Synechocystis* sp. PCC 6803

Genes that responded to MV stress have been identified in *Synechcocystis* wild type. *sll1621* encoding peroxidase with the greatest fold change in the induced expression which has reported to be the core component in the antioxidant defense system and the dithiol-disulfide redox regulatory network of cyanobacteria (Dietz et al., 2011). Moreover, the expression of *slr1516* encoding the SOD enzyme and the level of the SOD activity were upregulated after treat with MV at 6 and 12 hours. (Hu, Zhang et al. 2021). Importantly MV induced the oxidative stress resulting to reduce the rate of PSII photoinhibition repair and inhibits the synthesis of the D1 protein as well as the synthesis of other proteins (Allakhverdiev & Murata, 2004; Nishiyama et al., 2004; Nishiyama et al., 2001). However, ABC transporters play an important role in the tolerance of toxic compounds by mediating active transport on the cell membrane. Therefore, the ABC transporters participate in the entire process of MV outflow and response (Dubey et al., 2016). In addition, the oxidative stress caused by

MV was the strongest when it was treated for 6 h, and the proportion of the upregulated genes and metabolites involved in the metabolic pathways were the most effected (Hu et al., 2021).

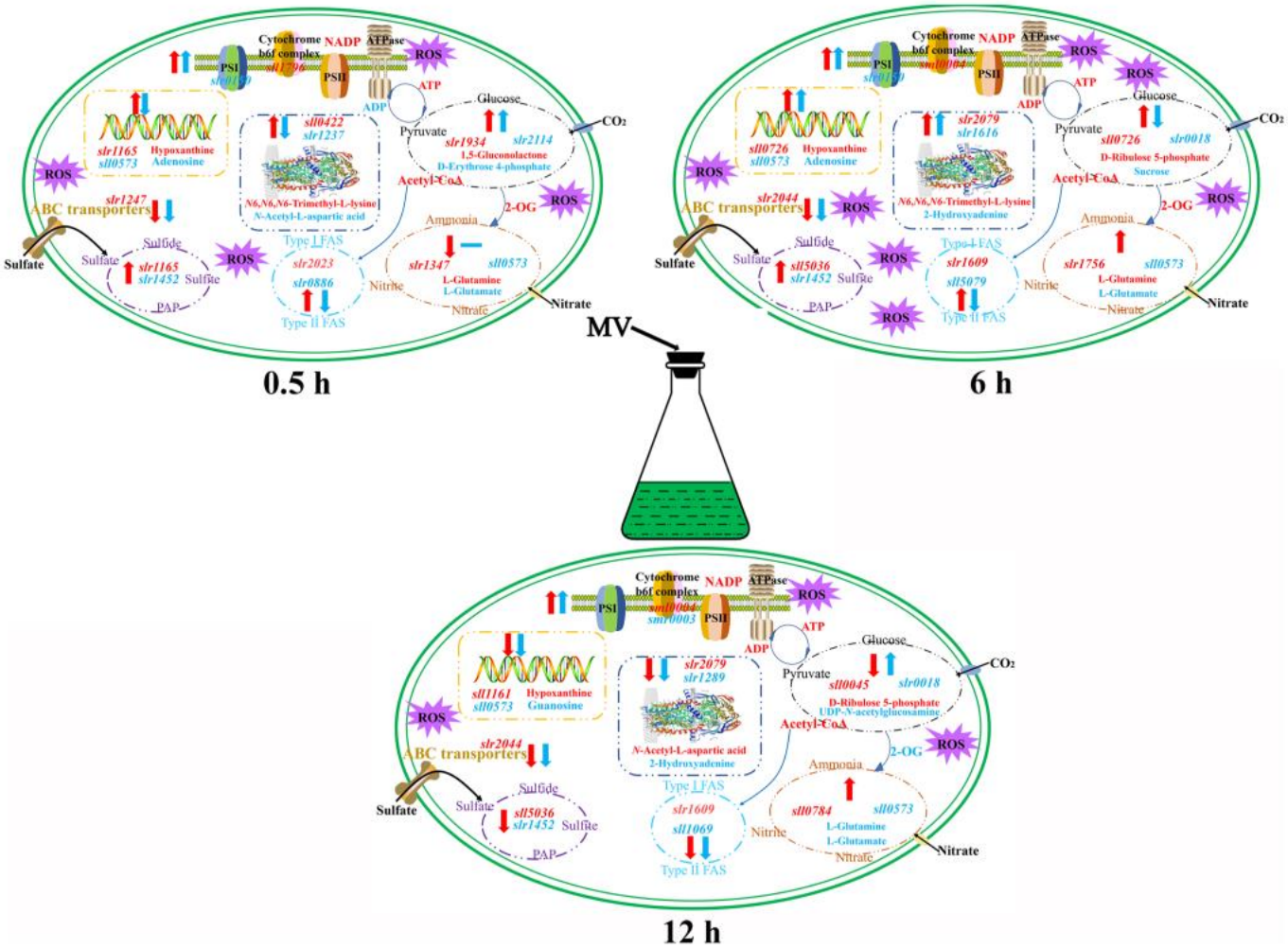


Figure 7 Response of *Synechocystis* sp. PCC 6803 to MV

CHAPTER III
MATERIALS AND METHODS

3.1 Materials

3.1.1 Instrument

Autoclave HV-100: Hirayama, Japan

Autopipette PIPETMAN Classic: Gilson, Paris, France

Bio clean bench MCV-B161F: Sanyo, Japan

BioPhotometer D30: Eppendorf, Thailand

Gel documentation: Syngene, USA

GENESYSUV-Vis spectrophotometer: Thermo Fisher Scientific, USA

Geno ElectroPhore electrophoresis system: G-Biosciences, USA

Innova 4000 digital incubator shaker: New brunswick scientific, USA

Light shaker: Sac Science, Thailand

Microwave: Sharp, Thailand

MIKRO 120 microliter centrifuge: Hettich, Germany

SevenEasy pH meter: Mettler-Toledo, Switzerland

Sonopuls GM2200: Bandelin, Germany

Sorvall Legend XTR refrigerated centrifuge: Thermo Fisher Scientific, Germany

StableTemp ceramic stirring hot plate: Cole-Parmer, USA

Synergy™ H1 microplate reader: BioTek, USA

Vacuum Filter: Pyrex, USA

Vortex-Genie 2: Scientific Industries, USA

Weighing PB303-S balances: Mettler-Toledo, Switzerland

3.1.2 Chemicals

Agar powder biological grade: HIMEDIA, India

Agarose: Invitrogen, USA

Boric acid: Scharlau, Spain

Calcium chloride: Sigma, USA

Cethyl trimethyl ammonium bromide (CTAB): Kemaus, Australia

Chloroform: Merck, Germany

Citric acid: VWR International, UK

Cobalt nitrate: Univer, Canada

Copper sulphate: Fisher Scientific, UK

Crotonic acid: Sigma, USA

Ethanol: Merck, Germany

Ethylene diamine tetra acetic acid: Sigma, USA

Ferric sulphate: Merck, Germany

Folin & Ciocalteu's phenol reagent: Sigma, USA

Glycerol: Univer, Canada

HEPES-NaOH: Sigma, USA

Hydrochloric acid: Merck, Germany

Isoamyl alcohol: Sigma, USA

Isocitric acid: Spectrum Chemical, USA

Lysozyme: Sigma, USA

Magnesium sulphate: Sigma, USA

Manganese chloride: Univer, Canada

Methanol: Merck, Germany

Oxaloacetic acid: Sigma, USA

Phenol: Thermo Fisher Scientific, Germany

Potassium chloride: Fisher Scientific, UK

Potassium dihydrogen phosphate: RANKEM, India

Potassium sodium tartrate: CARLO ERBA Reagents, France

RNase: Sigma, USA

Sarkosyl: Sigma, USA

Sodium acetate: VWR International, UK

Sodium carbonate: Sigma, USA

Sodium chloride: CARLO ERBA Reagents, France

Sodium hydroxide: Merck, Germany

Sodium hypochlorite: Clorox, USA

Sodium molybdate: VWR International, UK

Sodium nitrate: VWR International, UK

Sodium thiosulphate: Sigma, USA

Sulfuric acid: Merck, Germany

Taq polymerase kit: Volantis Technologies, Malaysia

Tris(hydroxymethyl) aminomethane: Sigma, USA

Zinc sulphate: Univer, Canada

3.2 Methods

3.2.1. Cyanobacteria strains, cell cultivation and cell growth measurement

Wild type *Synechocystis* sp. PCC 6803 (hereafter *Synechocystis*) was obtained from the Pasteur culture collection (PCC), France. Cells were grown in BG-11 (Rippka et al., 1979) liquid medium or agar medium supplemented with 20 mM HEPES-NaOH (pH 7.5). Cells were cultured at 30°C with the supply by the constant white light (50 µmol photons m^{-2} s^{-1}). The growth of cyanobacterial cultures was determined by measuring the optical density at 730 nm (OD_{730nm}) using spectrophotometer. Methyl viologen (MV) was added to the medium when it was required.

3.2.2. Generation of MV resistant mutants

To generate MV resistant mutant, wild type *Synechocystis* sp. was grown in liquid media for 30 days to reach stationary-growth phase to allow the occurrence of spontaneous mutation(s) in aged cells. The cells (about 2 OD_{730nm} in one mL of the cell culture) were harvested and spread on agar medium (35 mL of agar medium in 0.7 cm diameter petri dish) containing 10, 20, or 40 µM of MV. Cells were cultured under the continuous illumination for 30-40 days to obtain survival colonies of MV-resistant mutants. About 20-34 colonies of MV-resistant mutants obtained from each MV concentration (10, 20, or 40 µM) were selected and were restreaked two times into a single colony to obtain a pure genetic clone on a new agar medium plate containing the respective MV concentration. Wild type cells (as a negative control) were also streaked on agar plate containing MV as wild type cells were unable to grow in this agar plate containing MV to ensure the MV inhibition of the growth of wild type cells.

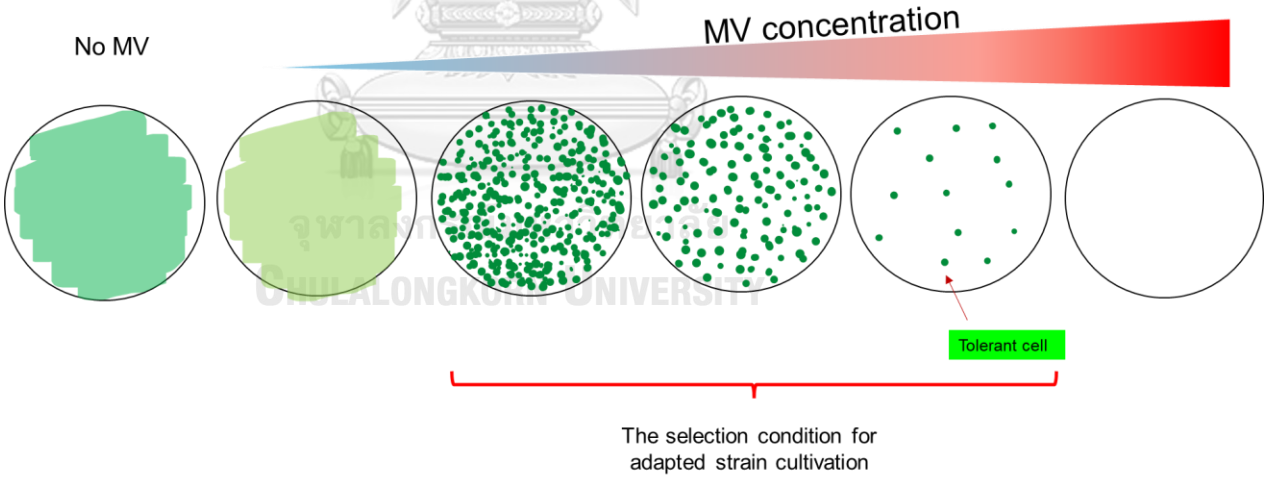


Figure 8 Diagram showing the generation of spontaneous MV resistant mutants. The 30-day old cells (about 2 OD_{730nm}) were spread on agar medium containing MV. Cells were cultured for 30-40 days to obtain survival colonies of MV-resistant mutants.

3.2.3. Genomic DNA isolation and genome sequence

Genomic DNA of *Synechocystis* sp. PCC 6803 were extracted using a modified protocol (Draper and Scott, 1998). Cells were harvest from the culture on BG11 Agar. Cells were suspended in 400 µL of Tris-EDTA solution (10 mM Tris-HCl and 1 mM EDTA at pH 8) and vortexed at maximum speed for 3 minutes. The cell suspension was added with 100 µL of 50 mg/mL lysozyme and incubated at 37°C for 5 minutes with shaking. The mixture was added with 50 µL of 10% w/v sarkosyl and 600 µL of saturated phenol and mixed by shaking for 15 minutes. After centrifugation for 10 minutes, the aqueous phase was collected, added with 10 µL of (2 µg/µL) RNase and incubated at 37°C for at least 15 minutes. The mixture was added with 100 µL of 5 M NaCl, 100 µL of CTAB-NaCl (10% w/v CTAB and 0.7 M NaCl) and 600 µL of chloroform:isoamyl alcohol (24:1, v:v). After centrifugation, the aqueous phase was added with 600 µL of isopropanol and centrifuged to precipitate genomic DNA. Genomic DNA was purified to remove RNA and other contaminants using Genomic DNA Clean & Concentrator Kit (Cat. No: D4010, Zymo research, USA). Genome sequences of wild type and mutants were determined using next-generation pair-read whole-genome sequencing which was operated by lllumina Sequencing-MiSeq machine and conducted by Omics Science and Bioinformatics Center, Faculty of Science, Chulalongkorn University, Thailand.

3.2.4. Identification of mutation conferring methyl viologen resistance

The obtained FASTQ formatted raw read sequences were aligned against the reference genome sequence of *Synechocystis* sp. PCC 6803 (NCBI accession number: PRJNA224116) using map command and BWA-MEM Galaxy software which has higher sensitivity and specificity for long read sequence (>100 nucleotide). The detection of mutation and the annotation of the mutated genes were conducted using the Galaxy softwares: FreeBayes and SnpEff eff. FreeBayes is a haplotype-based Bayesian genetic variant detector designed to detect single nucleotide polymorphisms (SNPs), insertions,

deletions, multi-nucleotide polymorphisms (MNPs) and complex events (composite insertion and substitution events) (Garrison & Marth, 2012). SnpEff eff is a flexible open source tool designed for annotating alterations in genes and proteins and for the prediction of effects of changes such as synonymous or non-synonymous replacement, and frameshift etc. (Cingolani et al., 2012).

3.2.5. Determination of minimum inhibitory concentrations (MIC) of MV resistance mutant

The colony of each mutant was streaked on agar medium containing 0 to 160 µM of MV. The MIC was recorded on the minimum concentration that the mutant cells could grow.

3.2.6. Determination of oxygen evolution

The method is according to Towijit et al., 2018 (Towijit et al., 2018). The living cell culture of wild type and mutants (10 mL) was harvested by centrifugation 6,000 rpm for 10 minutes. The cell pellets were resuspended in 2 mL of fresh BG-11 medium. Cells were incubated under darkness for 30 min and were determined for oxygen evolution using Oxygraph plus oxygen electrode (Hansatech Instruments, U.K.). The oxygen evolution measurement was conducted at 25 °C using fluorescent white light (50 µmol/m^2/s) as a saturated light source. The unit of oxygen evolution rate was presented as µmol O_2 /mgDW/h.

3.2.7. Determination of growth under osmotic and oxidative stresses

3.2.7.1. Under the osmotic stress, cells at an initial concentration of 0.1 OD_{730nm} were cultivated in the absence or the presence of osmotic stress inducing agent: sorbitol at 1M and sodium chloride at 1 M. These concentrations of sorbitol (Marin et al., 2006) and sodium

chloride (บุญบูรพงศ์ et al., 2014) have been shown to induce osmotic stress and remarkably affect cell growth. The growth of cell cultures was determined by measuring optical density at 730 nm (OD_{730nm}) using spectrophotometer.

3.2.7.2. Under the oxidative stress, cells at an initial concentration of 0.1 OD_{730nm} were cultivated in the absence or the presence of oxidative-stress inducing agent: copper sulphate at 1µM and hydrogen peroxide at 7 mM. These concentrations of copper sulphate (Giner-Lamia et al., 2014) and hydrogen peroxide (Leksingto, 2018) have been shown to induce osmotic stress and remarkably affect cell growth. The growth of cultivation was determined by measuring optical density at 730 nm (OD_{730nm}) using spectrophotometer.

3.2.8. Measurement of the scavenging capacity of antioxidants by 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay.

The method was modified from the method of Abe et al., 1998. The living cell culture of wild type and the MV-resistant mutants (1 OD_{730nm} in one mL) was harvested by centrifugation at 6,000 rpm for 10 minutes. The cell pellets were resuspended in 1 mL of 50 mM potassium phosphate buffer (29 mM $Na_2HPO_4 \cdot 7H_2O$ and 21mM $NaH_2PO_4 \cdot H_2O$) . Cells in the suspension was lysed using ultrasonic homogenizers (Sonopuls GM2200, Bandelin, Germany) at 15 hertz, for 50 cycles and 4 minutes. The supernatant was used for the next step. The supernatant of 0.04 mL was mixed with 0.5 mM DPPH ethanol solution (1 mL) and 10 mM acetate buffer (pH 5.5, 2 mL) and incubated at room temperature for 10 minutes. Then, the samples were measured for the absorbance at 517 nm using spectrophotometer (Thermo Fisher Scientific, USA). The percentage of radical scavenging activity: $(A_0-A_t)/A_0 \times 100\%$ was calculated. A_0 is the initial absorbance (immediately after mixing all reagents) and A_t is the absorbance after mixing all reagents at 10 minutes.

CHAPTER IV
RESULTS

4.1 Determination of Minimum inhibitory concentration (MIC) of MV for wild type *Synechocystis*

Firstly, approximately the thousand colonies were obtained from 10 µM after treat with various of methyl viologen (MV) concentration. The colonies were survival after restreaking again in the agar plate that contained 10 of MV, but wild type *Synechocystis* sp. PCC 6803 (hereafter wild type) do not grow. Under the 20 µM and 40 µM of MV found the number of colonies in the hundreds and the tens respectively (Table. 3).

Table 3 The numbers of methyl viologen (MV)-resistant colonies of *Synechocystis* sp. PCC6803 obtained from a normal BG11 agar plate containing MV.

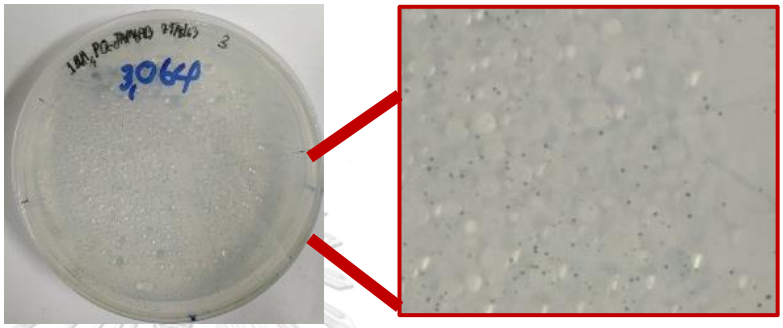
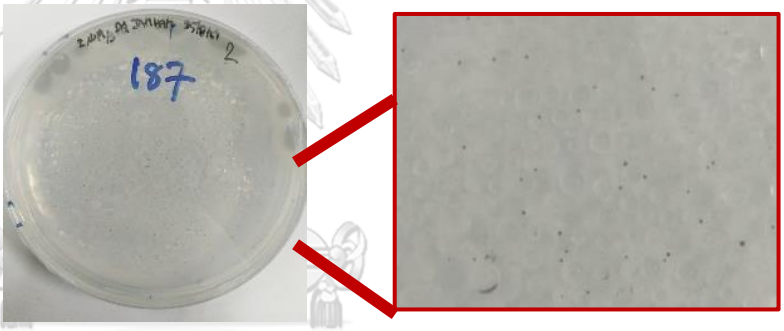
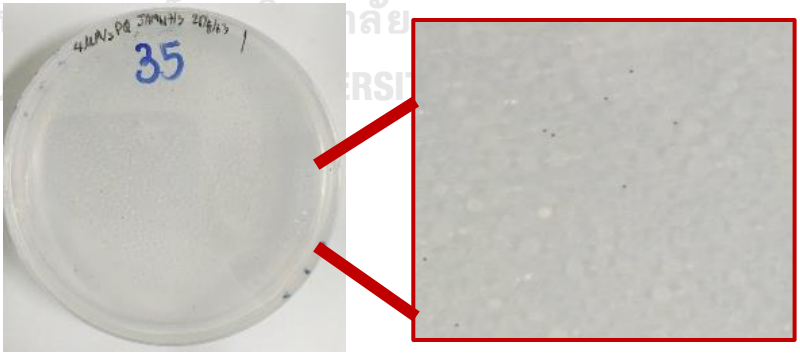
Minimum inhibitory concentration of MV for wild type *Synechocystis* is 10 µM. The average number of MV-resistant colonies were derived from three independent agar plates.

MV concentration on agar plate (µM)	Average number of MV-resistant colonies on an agar plate
10	2,936 ± 188
20	176 ± 13
40	23 ± 11

4.2 Generation of MV resistant mutants

Spontaneous mutants of *Synechocystis* showing MV resistance were derived from agar plate containing 10, 20 and 40 µM of MV (Table 3), after 30-40 days. The lower MV concentration (10 and 20 µM) yielded the higher mutant colonies on agar plate than those of the higher concentration (40 µM) (Table 4). Some of MV-resistant colonies were selected as a mutant that were the subject for genomic DNA isolation and genome sequencing in the next section.

Table 4 The MV-resistant colonies of *Synechocystis* sp. PCC6803 obtained from on a normal BG11 agar plate containing MV at 10, 20 or 40 µM.
The picture was derived of one agar plate selected from three independent agar plates.

MV concentration on agar plate (µM)	MV resistant colonies derived from agar plate
10	
20	
40	

4.3 Determination of MIC of MV of MV-resistant mutants

Results in Table 5, the 31, 17 and 16 colonies from 40, 20 and 10 µM of MV respectively were tested for cell growth effect under the contained of higher MV concentration. The most effective growth of MV with a minimum inhibitory concentration (MIC) at 60 µM. At 80 µM of MIC test were found 90.3%, 41.2% and 50% of survival colonies from 40, 20 and 10 µM of MV respectively.

4.4 Isolation and quality determination of genomic DNA of the MV-resistant mutants

The good quality of genomics DNA of wild type and mutants were obtained, and the purification of genomic DNA was successful in Fig. 9B and Fig. 10 (After purification). The amount and purity of the extracted genomic DNA samples was measuring at 230 nm, 260 nm and 280 nm. The ratio of absorbance 260 nm to 280 nm (A_{260}/A_{280}) represents a good indicator of protein contamination: when $\geqslant$ 1.8, it indicates a pure DNA sample. After cleanup with purification kit, most of extracted genomic DNA samples had higher ratio of A_{260}/A_{280} (Table 4). As a A_{260}/A_{230} is commonly in the range of 2.0-2.2. If the ratio is appreciably lower than expected, it may indicate the presence of contaminants which absorb at 230 nm. The result in Table 6 showed that most of extracted genomic DNA samples had higher ratio after cleanup with the kit.

4.5 Mutations found in the genome of MV-resistant mutants.

Wild type and the selected seven MV-resistant mutant (Table 8) were subjected for genome sequencing. Results in table 8 showed the mutation(s) found in each mutant.

The mutant A9 harbors six-point mutations in six genes resulting in the disrupted function of five putative proteins (caused by either frameshift or stop-gained mutation) or and the single-amino acid change in one protein. Of particular relating to chemical transport is the disrupted function of *cntO_1* gene encoding the ortholog of TonB-dependent receptor involving in the transport of Fe^{+++} across cytoplasmic membrane of *Synechocystis* (Katoh et al., 2000).

Table 5 MV minimum concentration of MV-resistant mutants.
Each mutant clone was streak on the normal BG11 agar plate containing MV at 0–160 µM. Cell growth was shown in (+) plus sign, while no cell growth was indicated by minus sign (-).

MV concentration (µM) used to generate the mutant	Mutant clone	MV concentration (µM)					MV minimum concentration (µM)
		20	40	60	80	160	
WT		-	-	-	-	-	
10	A1 - A5	+	+	+	+	-	80
	A6 - A8	+	+	+	-	-	60
	A9 - A10	+	+	+	+	-	80
	A11 - A12	+	+	+	-	-	60
	A13	+	+	+	+	-	80
	A14 - A16	+	+	+	-	-	60
20	B1 - B3	+	+	+	+	-	80
	B4 - B5	+	+	+	-	-	60
	B6	+	+	+	+	-	80
	B7 - B8	+	+	+	-	-	60
	B9 - B10	+	+	+	+	-	80
	B11 - B12	+	+	+	-	-	60
	B13	+	+	+	+	-	80
	B14 - B17	+	+	+	-	-	60
40	C1	+	+	+	-	-	60
	C2 - C5	+	+	+	+	-	80
	C6	+	+	+	-	-	60
	C7 - C12, C14 - C20	+	+	+	+	-	80
	C21	+	+	+	-	-	60
	C22 - C23, C25, C27 - C34	+	+	+	+	-	80

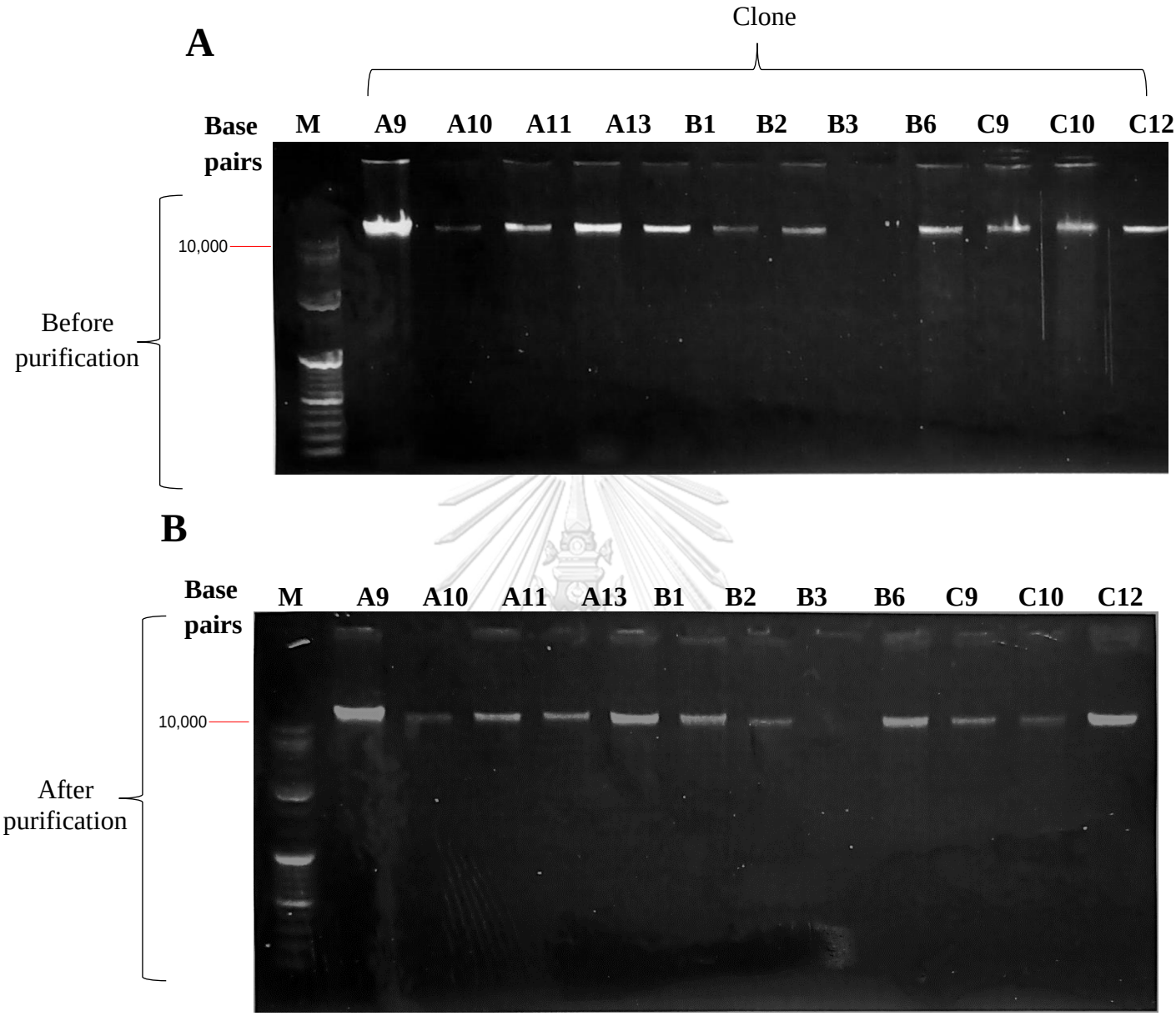


Figure 9 Genomic DNA of MV-resistant mutants clone number A9-C14, analyzed on 0.8 % agarose gel electrophoresis.
M: 1-kb DNA marker. The photos showed the results of genomic DNA before the purification (A), and after the purification using the kit: Genomic DNA Clean Kit, Zymo research, USA (B).

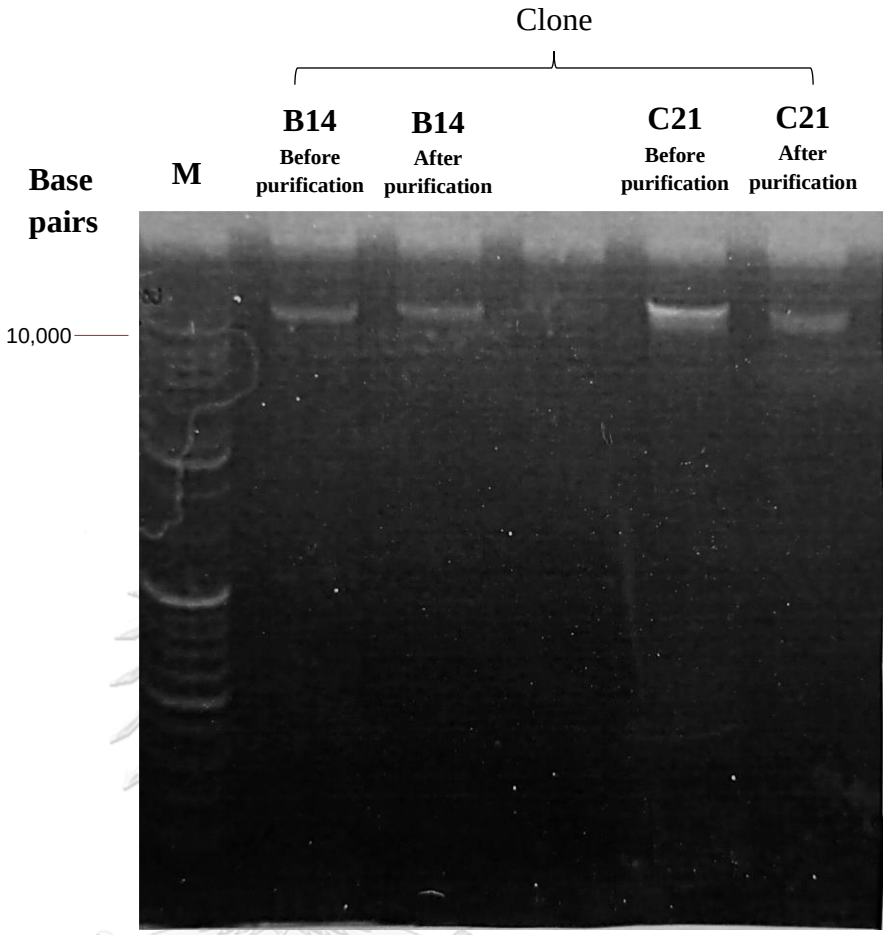


Figure 10 Genomic DNA of MV-resistant mutants clone number B14 and C21, analyzed on 0.8 % agarose gel electrophoresis.
M: 1-kb DNA marker. The photos showed the results of genomic DNA before the purification and after the purification using the kit: Genomic DNA Clean Kit, Zymo research, USA.

The mutants A11, B1, B14 and C10 contained the same point mutation which resulting the change of amino acid residue 93 (from Met to Lys) of a hypothetical protein with unknown function (Table 8-10 and Fig 14.). Results from the predicted 3D protein structure (Fig. 14) shown that the alteration of Met→Lys lead to the obvious change of the protein structure of this hypothetical protein, particularly the reduction of helical structure.

Beside the change to Lys led to the presence of negatively charged residue, comparing to the Met with has no charge. Thus, this Met→Lys mutation may potentially affect the function of this protein.

Table 6 Determination of purity of genomic DNA extracted from MV-resistant mutants.

The extracted genomic DNA before the purification and after the purification (using the kit: Genomic DNA Clean Kit, Zymo research, USA) were determined for the ratio of absorbance (A) at A_{260nm}/A_{280} nmand A_{260nm}/A_{230nm} of. A_{260nm}/A_{280nm} was used to assess the purity of DNA and the leftover protein. A_{260nm}/A_{230nm} was used to assess the purity of DNA and the leftovers caused by organic compounds.

MV -resistant mutants clone	Absorbance (A) ratio of genomic DNA			
	Before cleanup		After cleanup	
	A_{260nm}/A_{28nm0}	A_{260nm}/A_{230nm}	A_{260nm}/A_{280nm}	A_{260nm}/A_{230nm}
A 9	1.55	1.35	1.94	2.15
A10	1.40	0.94	1.83	1.80
A11	1.27	0.94	1.70	1.48
A13	1.61	1.43	1.98	2.22
B 1	1.64	1.39	1.87	1.87
B 2	1.44	1.12	1.96	2.07
B 3	1.37	1.13	1.84	1.72
B 6	1.12	0.68	1.87	1.90
B14	1.80	1.63	1.20	0.66
C 9	1.46	1.15	1.80	1.62
C10	1.45	1.07	1.94	2.10
C12	1.27	1.09	1.92	1.99
C14	1.55	1.35	1.76	1.52
C21	1.86	1.48	2.03	0.87

The mutant C14 contains two-point mutation resulting in the disrupted function of one protein (triacylglycerol lipase, Table 10 and Fig. 12) and the change of amino acid residue 93 (from Met to Lys) of a hypothetical protein with unknown function (Table 10 and Fig 12.) Of particular relating to cell membrane function is the disrupted function of *menH_2* gene encoding the ortholog of triacylglycerol lipase that converts triacylglycerol to diacylglycerol which is the main composition of the cell membrane.

The mutant C21 harbors several point mutations in 21 genes. Of particular relation to cellular transport, the mutations in: (i) *cpcF* gene encoding heat repeat domain-containing protein (involved in intracellular transport (Andrade & Bork, 1995), (ii) *lpxD_1* encoding UDP-3-o-acylglucosamine N-acyltransferase (involved in the biosynthesis of lipid A, a phosphorylated glycolipid that anchors the lipopolysaccharide to the outer membrane of the cell (Consortium, 2010), *mshA_4* encoding glycosyltransferase family 4 protein (involved in Biosynthesis of cell-wall peptidoglycan, (Consortium, 2010)), and the *arnC_4* encoding glycosyltransferase (involved in biofilm formation (Suban et al., 2022)) (Table 10).

Table 7 Mutation(s) identified in genomes of the seven MV-resistant mutants.
Mutants A9 and A11 were obtained under 10 µM, Mutants B1 and B14 were obtained under 20 µM, Mutants C10, C14 and C21 were obtained under 40 µM of treatment. + is the presence of a mutation in the genome. - is the absence of a mutation in the genome.

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
285389	c.550A>G	p.Thr184Ala	missense	*FMAMFGPO_00273*	+	+	+	+	+	+	+
1211597	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu	missense	*FMAMFGPO_01144*	+	+	+	+	+	+	+
1211656	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg	missense	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1211751	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del	missense& disruptive inframe deletion	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1211860	c.558_561delGCTGinsCATT	p.GluLeu186AspIle	missense	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1211869	c.550_552delGCCinsTCG	p.Ala184Ser	missense	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1212064	c.356_357delCGinsTC	p.Ala119Val	missense	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1212090	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg	missense	*FMAMFGPO_01145*	+	+	+	+	+	+	+
1213678	c.T>A	p.Met	missense	*FMAMFGPO_01147*	+	+	+	+	+	+	+
1213701	c.25_26delCAinsTG	p.Gln9Trp	missense	*FMAMFGPO_01147*	+	+	+	+	+	+	+
1213707	c.34_36delGTGinsATA	p.Val12Ile	missense	*FMAMFGPO_01147*	+	+	+	+	+	+	+
1455459	c.559_561delCTGinsATT	p.Leu187Ile	missense	*FMAMFGPO_01386*	+	+	+	+	+	+	+
1455523	c.622_623delCGinsGA	p.Arg208Glu	missense	*FMAMFGPO_01386*	+	+	+	+	+	+	+
1455543	c.642_643delTTinsCA	p.Leu215Ile	missense	*FMAMFGPO_01386*	+	+	+	+	+	+	+

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
1455555	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAAACinsGGGGAAAT	p.Glu225_Leu232del	disruptive inframe deletion	*FMAMFGPO_01386*	+	+	+	+	+	+	+
1972493	c.340A>G	p.Arg114Gly	missense	*FMAMFGPO_01896*	+	+	+	+	+	+	+
1972708	c.100G>A	p.Gly34Arg	missense	*FMAMFGPO_01897*	+	+	+	+	+	+	+
1972727	c.119T>C	p.Val40Ala	missense	*FMAMFGPO_01897*	+	+	+	+	+	+	+
1972813	c.205C>T	p.Pro69Ser	missense	*FMAMFGPO_01897*	+	+	+	+	+	+	+
2558293	c.1480C>T	p.Arg494Trp	missense	*FMAMFGPO_02422*	+	+	+	+	+	+	+
2817680	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile	missense	*FMAMFGPO_02674*	+	+	+	+	+	+	+
2817746	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal	missense	*FMAMFGPO_02674*	+	+	+	+	+	+	+
2922421	c.762G>C	p.Met254Ile	missense	*FMAMFGPO_02765*	+	+	+	+	+	+	+
2997876	c.205C>T	p.Pro69Ser	missense	*FMAMFGPO_02833*	+	+	+	+	+	+	+
2998688	c.238G>A	p.Glu80Lys	missense	*FMAMFGPO_02834*	+	+	+	+	+	+	+
2998753	c.173A>G	p.Glu58Gly	missense	*FMAMFGPO_02834*	+	+	+	+	+	+	+
2998822	c.104G>A	p.Arg35Lys	missense	*FMAMFGPO_02834*	+	+	+	+	+	+	+
3096187	c.140T>C	p.Ile47Thr	missense	*FMAMFGPO_02926*	+	+	+	+	+	+	+
1213755	c.79G>A	p.Asp27Asn	missense	*FMAMFGPO_01147*	-	+	+	+	+	+	+
1944928	c.343C>A	p.Arg115Ser	missense	*FMAMFGPO_01873*	-	+	+	+	+	+	+
1455225	c.324_328delTCAGGinsCCAGT	p.Val110Leu	missense	*FMAMFGPO_01386*	-	-	-	+	+	-	-

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
1763123	c.123A>G	p.Ile41Met	missense	*FMAMFGPO_01697*	-	+	-	-	-	-	+
2998658	c.268G>A	p.Val90Ile	missense	*FMAMFGPO_02834*	-	+	-	+	+	-	+
1455444	c.543_550delCCTGCTG GinsTCTGCTAT	p.Ala184Ser	missense	*FMAMFGPO_01386*	-	+	+	-	+	+	+
2808916	c.17T>C	p.Leu6Pro	missense	*dfa1*	-	+	+	-	+	-	-
1212076	c.340_345delTTACACins GTGCAT	p.Leu114Val	missense	*FMAMFGPO_01145*	-	+	+	-	+	+	-
1213743	c.67_68delAAinsGG	p.Lys23Gly	missense	*FMAMFGPO_01147*	-	+	+	-	+	+	-
2284284	c.428T>G	p.Val143Gly	missense	*glcK*	-	+	+	+	-	+	-
2998367	c.559A>G	p.Ile187Val	missense	*FMAMFGPO_02834*	+	-	-	-	+	-	-
2998493	c.433C>A	p.Pro145Thr	missense	*FMAMFGPO_02834*	+	-	-	-	+	-	-
1200306	c.599C>A	p.Pro200Gln	missense	*FMAMFGPO_01135*	+	-	-	-	-	-	+
2714818	c.1799C>G	p.Ser600Cys	missense	*carB_2*	+	-	-	+	-	-	+
1455441	c.543_550delCCTGCTG GinsTCTGCTAT	p.Ala184Ser	missense	*FMAMFGPO_01386*	+	-	-	+	-	-	-
2998711	c.215C>T	p.Ser72Phe	missense	*FMAMFGPO_02834*	+	-	+		+	-	+
1972196	c.43C>A	p.Pro15Thr	missense	*FMAMFGPO_01896*	+	-	+	+	+	-	+
2997948	c.133G>C	p.Glu45Gln	missense	*FMAMFGPO_02833*	+	+	-	-	-	-	-
3096875	c.488_489delCTinsGC	p.Ala163Gly	missense	*FMAMFGPO_02927*	+	+	+	-	+	+	-
1970818	c.238G>A	p.Glu80Lys	missense	*FMAMFGPO_01894*	+	+	+	-	+	+	-
1763238	c.238G>A	p.Glu80Lys	missense	*FMAMFGPO_01697*	+	+	+	+	+	+	-

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
2998803	c.123A>G	p.Ile41Met	missense	*FMAMFGPO_02834*	+	+	+	+	+	+	-
389757	c.588delG	p.Gly199fs	frameshift	*dadA_1*	+	-	-	-	-	-	-
1637579	c.104C>A	p.Ser35*	nonsense	*FMAMFGPO_01563*	+	-	-	-	-	-	-
1763318	c.325delA	p.Arg109fs	frameshift	*FMAMFGPO_01697*	+	-	-	-	-	-	-
2763615	c.446C>A	p.Thr149Lys	missense	*betI*	+	-	-	-	-	-	-
2997953	c.128G>A	p.Cys43Tyr	missense	*FMAMFGPO_02833*	+	-	-	-	-	-	-
2998281	c.641_642insA	p.Ser215fs	frameshift	*FMAMFGPO_02834*	+	-	-	-	-	-	-
1211773	c.639_640insGGCAAATTGGAGGGTCGGTTGGAAGGAAAATTAGAG	p.Ala213_Gly214insGlyLysLeuGluGlyArgLeuGluGlyLysLeuGlu	conservative_inframe_insertion	*FMAMFGPO_01145*	-	+	-	-	-	-	-
1443027	c.1014_1020delCATCATCinsAGTGATT	p.Ile339Val	missense	*rcsC_12*	-	+	-	-	-	-	-
1416421	c.2296A>G	p.Ile766Val	missense	*topA*	-	-	+	-	-	-	-
2998425	c.499_501delCCAinsACG	p.Pro167Thr	missense	*FMAMFGPO_02834*	-	-	-	-	+	-	-
42461	c.64delT	p.Ser22fs	frameshift	*yfiY_2*	-	-	-	-	-	-	+
88483	c.177delG	p.Ala60fs	frameshift	*cpcF*	-	-	-	-	-	-	+
103106	c.2002delA	p.Lys668fs	frameshift	*FMAMFGPO_00092*	-	-	-	-	-	-	+
118510	c.1023T>A	p.Tyr341*	nonsense	*lpd*	-	-	-	-	-	-	+
125774	c.670C>T	p.Gln224*	nonsense	*sasA_1*	-	-	-	-	-	-	+
216028	c.202C>T	p.Gln68*	nonsense	*lpxD_1*	-	-	-	-	-	-	+

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
223375	c.262C>A	p.Leu88Met	missense	*FMAMFGPO_00210*	-	-	-	-	-	-	+
240005	c.142_143insG	p.Val49fs	frameshift	*FMAMFGPO_00224*	-	-	-	-	-	-	+
285649	c.290G>A	p.Arg97His	missense	*FMAMFGPO_00273*	-	-	-	-	-	-	+
398734	c.481A>G	p.Lys161Glu	missense	*gloB*	-	-	-	-	-	-	+
434912	c.1247C>T	p.Ala416Val	missense	*FMAMFGPO_00416*	-	-	-	-	-	-	+
561226	c.433A>G	p.Ser145Gly	missense	*FMAMFGPO_00531*	-	-	-	-	-	-	+
908675	c.276delG	p.Glu96fs	frameshift	*menH_2*	-	-	-	-	-	-	+
950522	c.15C>A	p.Tyr5*	nonsense	*mshA_4*	-	-	-	-	-	-	+
1022471	c.2174_2175insA	p.Thr728fs	frameshift	*pcrA*	-	-	-	-	-	-	+
1100481	c.1669G>T	p.Gly557Cys	missense	*FMAMFGPO_01046*	-	-	-	-	-	-	+
1119469	c.2329dupC	p.Gln777fs	frameshift	*malP_2*	-	-	-	-	-	-	+
1158558	c.352A>G	p.Ile118Val	missense	*uvrC_1*	-	-	-	-	-	-	+
1249094	c.811C>T	p.Gln271*	nonsense	*FMAMFGPO_01189*	-	-	-	-	-	-	+
1266755	c.804T>G	p.Asp268Glu	missense	*gyrB*	-	-	-	-	-	-	+
1267537	c.22G>A	p.Ala8Thr	missense	*gyrB*	-	-	-	-	-	-	+
1319856	c.686A>G	p.Asp229Gly	missense	*FMAMFGPO_01254*	-	-	-	-	-	-	+
1373455	c.1637G>A	p.Arg546Gln	missense	*mutS*	-	-	-	-	-	-	+
1441801	c.2246T>C	p.Leu749Pro	missense	*rcsC_12*	-	-	-	-	-	-	+
1574393	c.1545T>A	p.Asp515Glu	missense	*rcsC_14*	-	-	-	-	-	-	+

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
1667441	c.510_512delAATinsCAA	p.Ile171Asn	missense	*atpD*	-	-	-	-	-	-	+
1708644	c.1328A>T	p.Asp443Val	missense	*lnt*	-	-	-	-	-	-	+
1712857	c.396_397insC	p.Val134fs	frameshift	*rpe*	-	-	-	-	-	-	+
1744011	c.569T>A	p.Val190Glu	missense	*cysE*	-	-	-	-	-	-	+
1799197	c.396delT	p.Thr133fs	frameshift	*mqnB*	-	-	-	-	-	-	+
1827608	c.352G>A	p.Ala118Thr	missense	*FMAMFGPO_01757*	-	-	-	-	-	-	+
1847690	c.552T>A	p.Phe184Leu	missense	*FMAMFGPO_01779*	-	-	-	-	-	-	+
1873634	c.979T>C	p.Tyr327His	missense	*tilS*	-	-	-	-	-	-	+
2025305	c.313A>G	p.Lys105Glu	missense	*rlmB_2*	-	-	-	-	-	-	+
2033278	c.842_846delTCACGinsTCGACT	p.Thr282fs	frameshift &missense	*arnC_4*	-	-	-	-	-	-	+
2052148	c.1149delC	p.Pro386fs	frameshift	*FMAMFGPO_01976*	-	-	-	-	-	-	+
2116886	c.427G>T	p.Ala143Ser	missense	*FMAMFGPO_02031*	-	-	-	-	-	-	+
2127133	c.457A>T	p.Thr153Ser	missense	*FMAMFGPO_02040*	-	-	-	-	-	-	+
2154245	c.45dupC	p.Glu16fs	frameshift	*FMAMFGPO_02070*	-	-	-	-	-	-	+
2233442	c.423A>T	p.Leu141Phe	missense	*exoA*	-	-	-	-	-	-	+
2264058	c.232G>A	p.Gly78Arg	missense	*lipB*	-	-	-	-	-	-	+
2284348	c.492G>T	p.Leu164Phe	missense	*glcK*	-	-	-	-	-	-	+
2285540	c.458A>G	p.Gln153Arg	missense	*FMAMFGPO_02182*	-	-	-	-	-	-	+

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
2309220	c.152C>T	p.Ala51Val	missense	*FMAMFGPO_02206*	-	-	-	-	-	-	+
2338219	c.232A>G	p.Ile78Val	missense	*FMAMFGPO_02228*	-	-	-	-	-	-	+
2361471	c.1015G>A	p.Gly339Arg	missense	*FMAMFGPO_02238*	-	-	-	-	-	-	+
2380931	c.1951G>A	p.Asp651Asn	missense	*FMAMFGPO_02248*	-	-	-	-	-	-	+
2431282	c.191C>G	p.Pro64Arg	missense	*FMAMFGPO_02304*	-	-	-	-	-	-	+
2467726	c.1147T>A	p.Ser383Thr	missense	*clpC*	-	-	-	-	-	-	+
2552500	c.463T>C	p.Tyr155His	missense	*FMAMFGPO_02416*	-	-	-	-	-	-	+
2562188	c.137delT	p.Leu46fs	frameshift	*rsbQ*	-	-	-	-	-	-	+
2564021	c.1069G>C	p.Gly357Arg	missense	*FMAMFGPO_02427*	-	-	-	-	-	-	+
2575721	c.142A>G	p.Met48Val	missense	*ilvH*	-	-	-	-	-	-	+
2660259	c.355_363delTCCCCAACCinsAACCCGACG	p.Ser119Asn	missense	*glyQ*	-	-	-	-	-	-	+
2727596	c.550C>A	p.Leu184Ile	missense	*clsB*	-	-	-	-	-	-	+
2749723	c.494G>T	p.Trp165Leu	missense	*FMAMFGPO_02610*	-	-	-	-	-	-	+
2841541	c.1585G>T	p.Ala529Ser	missense	*dnaB*	-	-	-	-	-	-	+
2882897	c.1520_1521delTGinsGT	p.Leu507Arg	missense	*FMAMFGPO_02730*	-	-	-	-	-	-	+
2990852	c.1047T>A	p.Phe349Leu	missense	*sasA_14*	-	-	-	-	-	-	+
3062783	c.1427A>G	p.Gln476Arg	missense	*ziaA*	-	-	-	-	-	-	+
3151457	c.521A>T	p.Asp174Val	missense	*FMAMFGPO_02972*	-	-	-	-	-	-	+
3159498	c.1154T>C	p.Val385Ala	missense	*mgsA*	-	-	-	-	-	-	+

Position in genome	Mutations	Putative Consequence	Mutation Type	Location	Mutant clones						
					A9	A11	B1	B14	C10	C14	C21
3257297	c.2699C>T	p.Ala900Val	missense	*FMAMFGPO_03064*	-	-	-	-	-	-	+
3268649	c.319T>C	p.Phe107Leu	missense	*ndhI*	-	-	-	-	-	-	+
3277803	c.121A>T	p.Lys41*	nonsense	*FMAMFGPO_03083*	-	-	-	-	-	-	+
3486734	c.3178T>C	p.Cys1060Arg	missense	*ftsA_2*	-	-	-	-	-	-	+
3520794	c.901C>T	p.Gln301*	nonsense	*prfA*	-	-	-	-	-	-	+

Table 8 Point mutation(s) identified in the genome of MV-resistant mutants.
Mutants A9 and A11 were obtained under 10 µM treatment. (*) indicates stop-codon gained mutation. (fs) marks frameshift mutations

Mutant	Mutation in Genome (number is nucleotide number in coding sequence)	Amino acid change (number is amino acid residue in protein sequence)	Gene name	Predicted gene function	Type of mutation
A9	1522A→T	Lys508 →*	*cntO_1*	**TonB-dependent siderophore receptor:** involved in chemiosmotic potential transport of the cytoplasmic membrane with siderophore uptake across the outer membrane (Ferguson & Deisenhofer, 2002)	stop-codon gained
	588G→deleted	Gly199 →fs	*dadA_1*	**FAD-binding oxidoreductase:** Enzyme that catalyzes the transfer of electrons from the electron donor to the electron acceptor. This group of enzymes usually utilizes NADP+ or NAD+ as cofactors.(Karplus & Bruns, 1994)	frameshift
	A is deleted at 325	Arg109→fs	*FMAMFGPO_01697*	**Pseudo, Partial stop / frameshifted; incomplete; partial in the middle of a contig; missing C-terminus:** An enzyme that binds to the end of a transposon and catalyses its movement to another part of the genome by a cut and paste mechanism or a replicative transposition mechanism. (Watabe et al., 2014)	frameshift
	104C→A	Ser35→*	*FMAMFGPO_01563*	**DUF115 domain-containing protein:** Protein of unknown function DUF115	stop-codon gained
	2T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense
	A is inserted between 641 and 642	Ser215→fs	*FMAMFGPO_02834*	**IS701 family transposase:** IS707 and IS702 share a structural particularity. In the IR sequence located upstream from their putative transposase. The role of these sequences is still unknown. (Mazel et al., 1991)	frameshift
A11	161T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense

Table 9 Point mutation(s) identified in the genome of MV-resistant mutants.
Mutants B1 and B14 were obtained under 20 µM treatment. (*) indicates stop-codon gained mutation. (fs) marks frameshift mutations

Mutant	**Mutation in Genome** (number is nucleotide number in coding sequence)	**Amino acid change** (number is amino acid residue in protein sequence)	**Gene name**	**Predicted gene function**	**Type of mutation**
B1	161T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense
B14	161T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense

Table 10 Point mutation(s) identified in the genome of MV-resistant mutants.
Mutants C10, C14 and C21 were obtained under 40 µM treatment. (*) indicates stop-codon gained mutation. (fs) marks frameshift mutations

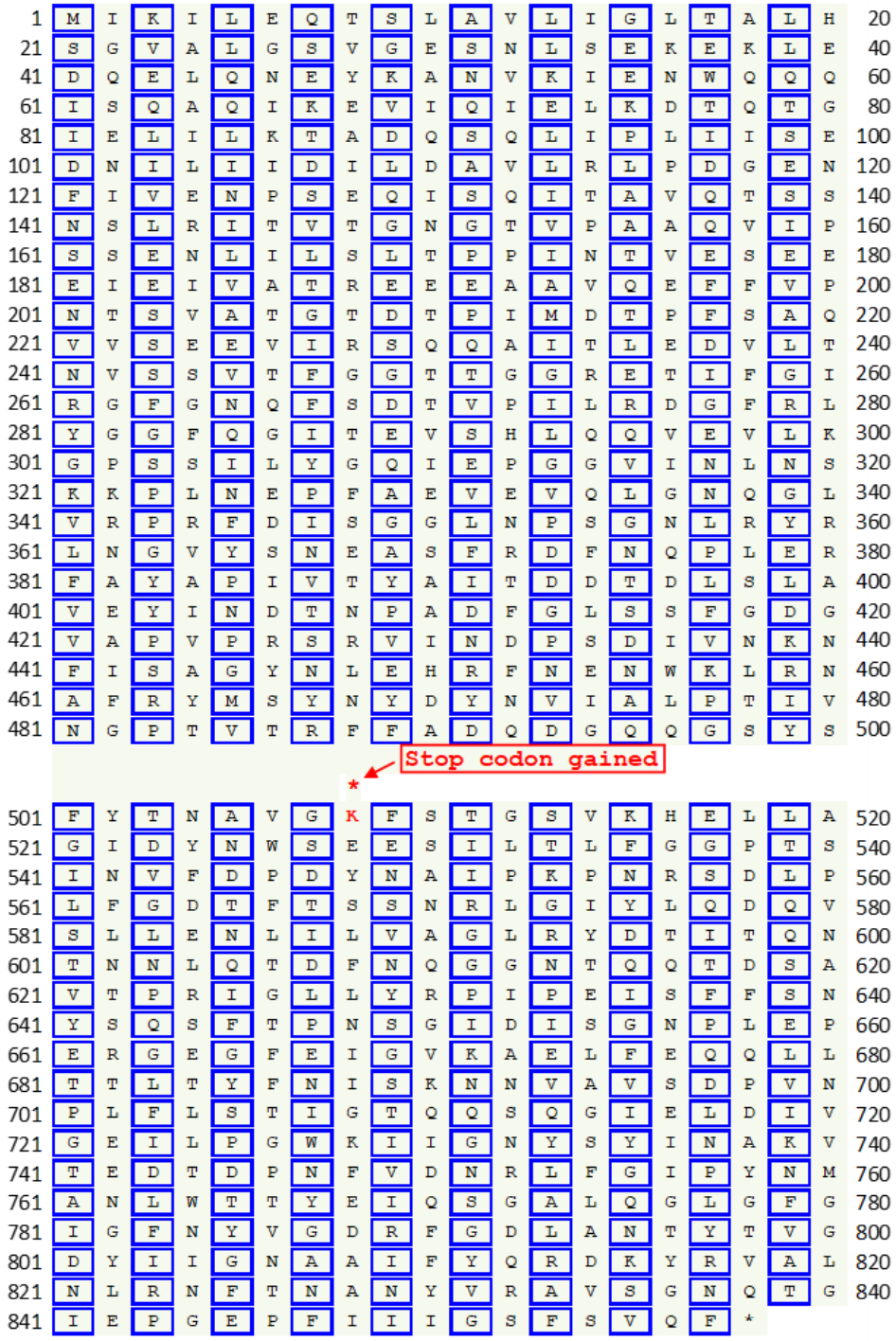
Mutant	**Mutation in Genome** (number is nucleotide number in coding sequence)	**Amino acid change** (number is amino acid residue in protein sequence)	**Gene name**	**Predicted gene function**	**Type of mutation**
C10	161T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense
C14	G is deleted at 276	Glu96→fs	*menH_2*	**Triacylglycerol lipase:** involved in the conversion of triacylglycerol to diacylglycerol by releasing one carboxylate (Sneha et al., 2018).	frameshift
	161T→A	Met54→Lys	*FMAMFGPO_01147*	Unknown function	missense

Mutant	Mutation in Genome (number is nucleotide number in coding sequence)	Amino acid change (number is amino acid residue in protein sequence)	Gene name	Predicted gene function	Type of mutation
C21	T is deleted at 64	Ser22→fs	*yfiY_2*	Unknown function	frameshift
	G is deleted at 177	Ala60→fs	*cpcF*	**HEAT repeat domain-containing protein:** Involved in intracellular transport (Andrade & Bork, 1995).	frameshift
	A is deleted at 2002	Lys668→fs	*FMAMFGPO_00092*	Hypothetical protein	frameshift
	1023T→A	Tyr341→*	*Lpd*	**NAD(P)/FAD-dependentoxidoreductase:** This protein are considered in microbiology a crucial target of antibiotics or chemotherapeutics (Trisolini et al., 2019).	stop-codon gained
	670C→T	Gln224→*	*sasA_1*	**ATP-binding protein:** ATP binding proteins (ABPs) have a binding site that allows ATP molecule to interact.by changing the shape of the protein and/or making the enzyme catalytically active (Chauhan et al., 2009).	stop-codon gained
	202C→T	Gln68→*	*lpxD_1*	**UDP-3-O-acylglucosamine N-acyltransferase:** Catalyzes the N-acylation of UDP-3-O-acylglucosamine using 3-hydroxyacyl-ACP as the acyl donor. Is involved in the biosynthesis of lipid A, a phosphorylated glycolipid that anchors the lipopolysaccharide to the outer membrane of the cell (Consortium, 2010).	stop-codon gained
	G is inserted between 142 and 143	Val49→fs	*FMAMFGPO_00224*	Hypothetical protein	frameshift

Mutant	Mutation in Genome (number is nucleotide number in coding sequence)	Amino acid change (number is amino acid residue in protein sequence)	Gene name	Predicted gene function	Type of mutation
C21 (Continue)	G is deleted at 276	Glu96→fs	*menH_2*	**Triacylglycerol lipase:** Involved in the conversion of triacylglycerol to diacylglycerol by releasing one carboxylate (Sneha et al., 2018).	frameshift
	15C→A	Tyr5→*	*mshA_4*	**Glycosyltransferase family 4 protein:** Biosynthesis of cell-wall peptidoglycan (Consortium, 2010).	stop-codon gained
	A is inserted between 2174 and 2174	Thr728→fs	*pcrA*	**DNA helicase PcrA:** DNA helicase. Has a broad nucleotide specificity, even being able to hydrolyze ethenonucleotides, and is able to couple the hydrolysis to unwinding of DNA substrates (Consortium, 2010).	frameshift
	C is duplicated at 2329	Gln777→fs	*malP_2*	**Glycogen/Starch/alpha-Glucan phosphorylase:** Using inorganic phosphate to cleave an alpha 1,4 linkage between the terminal glucose residue (Consortium, 2010).	frameshift
	161T→A	Met54→Lys	*FMAMFGPO_01147*	Hypothetical protein	missense
	811C→T	Gln271→*	*FMAMFGPO_01189*	**GNAT family N-acetyltransferase:** Aminoglycoside antibiotic resistance, transcription regulation, protein acetylation and stress reaction (Shirmast et al., 2021).	stop-codon gained
	C is inserted between 396 and 397	Val134→fs	*rpe*	**Ribulose-phosphate 3-epimerase:** Catalyzes the reversible epimerization of D-ribulose 5-phosphate to D-xylulose 5-phosphate (Consortium, 2010).	frameshift
	T is deleted at 396	Thr133→fs	*mqnB*	Hypothetical protein	frameshift

Mutant	Mutation in Genome (number is nucleotide number in coding sequence)	Amino acid change (number is amino acid residue in protein sequence)	Gene name	Predicted gene function	Type of mutation
C21 (Continue)	c.842_846del TCACGinsTCGACT	Thr282→fs	*arnC_4*	**Glycosyltransferase:** Inactivation of glycosyltransferase homolog results in robust biofilm formation (Suban et al., 2022).	frameshift &missense
	C is deleted at 1149	Pro386→fs	*FMAMFGPO_01976*	Hypothetical protein	frameshift
	C is duplicated at 45	Glu16→fs	*FMAMFGPO_02070*	**DUF6439 family protein:** This family of proteins is functionally uncharacterized (Lu et al., 2020).	frameshift
	T is deleted at 137	Leu46→fs	*rsbQ*	**Alpha/Beta Hydrolase:** Catalyzes the hydrolysis of peptides, esters, lactones, haloalkanes, and epoxides (ARMSTRONG, 1999).	frameshift
	121A→T	Lys41→*	*FMAMFGPO_03083*	**M1 family metallopeptidase:** Important in the cell cycle and normal growth and development (Peer, 2011).	stop-codon gained
	901C→T	Gln301→*	*prfA*	**Peptide chain release factor 1:** Facilitate the release of the growing polypeptide chain at stop codons (Consortium, 2010).	stop-codon gained

A



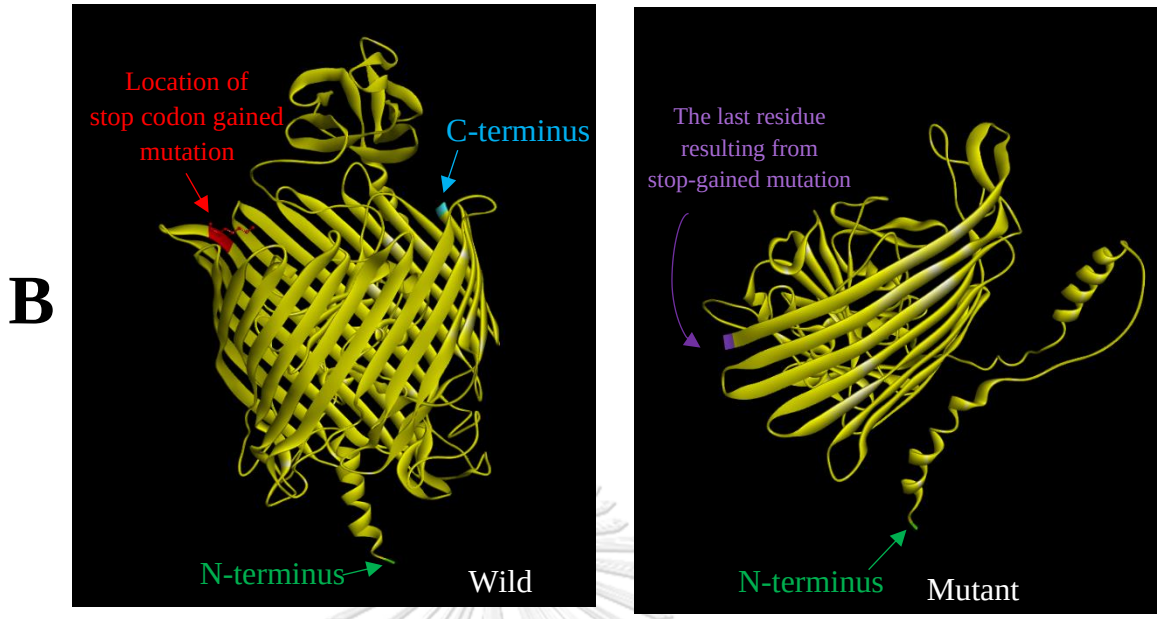


Figure 11 The protein sequence of *cntO_1* gene which obtained the stop-gained mutation in the genome of the MV-resistant mutant clone A9.
(A) The gene *cntO_1* is an ortholog of TonB-dependent siderophore receptor: chemiosmotic potential of the cytoplasmic membrane with siderophore uptake across the outer membrane (Ferguson & Deisenhofer, 2002). The protein sequence was obtained from *Synechocytis* genome NCBI accession number: PRJNA224116 (protein ID: WP_020861331). (B) the predicted 3D structure of the wild type protein. The structures were generated computationally using BIOVIA Discovery Studio Visualizer software (http://www.accelrys.com).

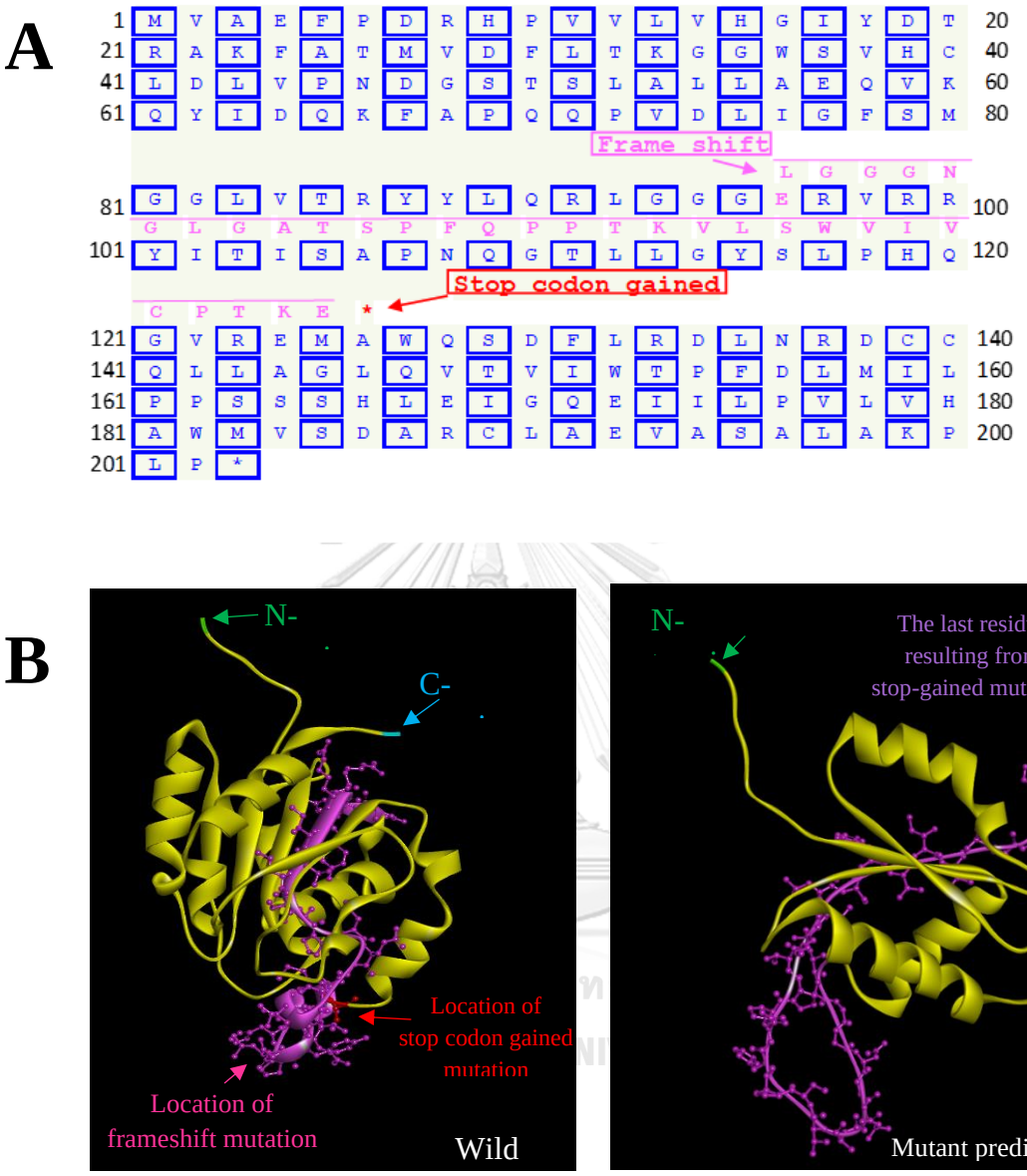
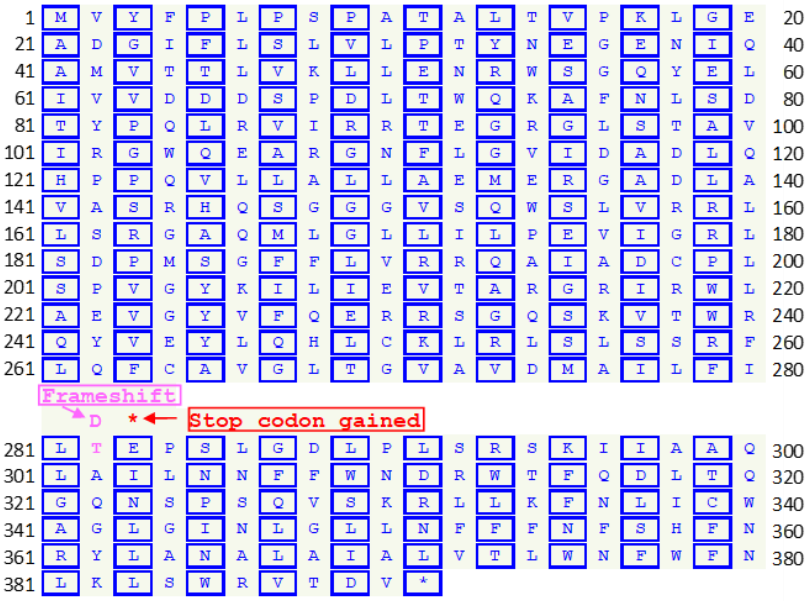


Figure 12 The protein sequence of *menH_2* gene which obtained the frameshift mutation in the genome of the MV-resistant mutant clone C14.
(A) The gene *menH_2* is a triacylglycerol lipase: involved in the conversion of triacylglycerol to diacylglycerol by releasing one carboxylate (Sneha et al., 2018). The protein sequence was obtained from *Synechocytis* genome NCBI accession number: PRJNA224116 (protein ID: WP_010872033). (B) the predicted 3D structure of the wild type protein. The structures were generated computationally using BIOVIA Discovery Studio Visualizer software (http://www.accelrys.com).

A



B

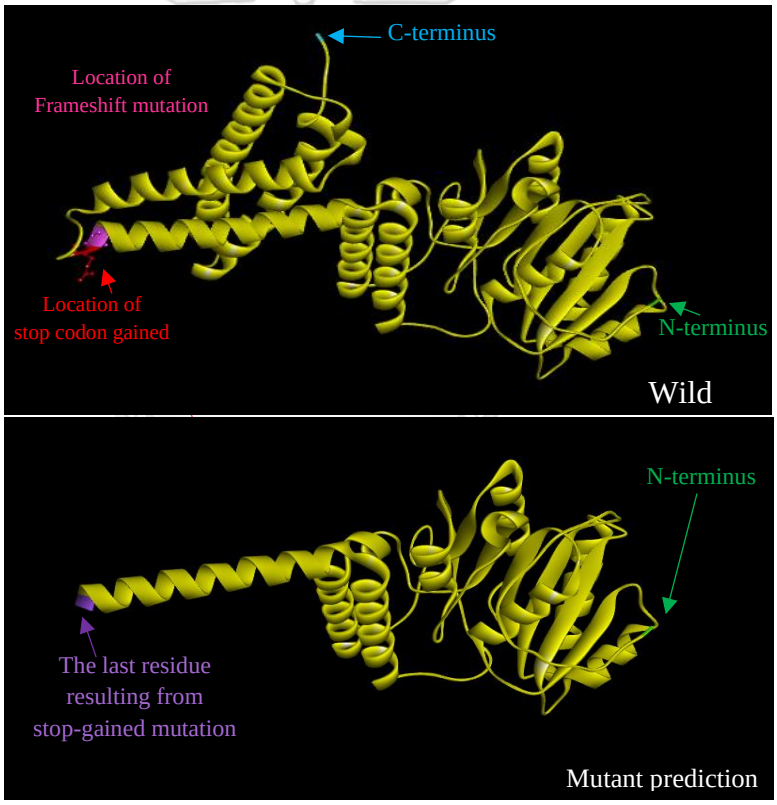


Figure 13 The protein sequence of *arnC_4* gene which obtained the frameshift mutation in the genome of the MV-resistant mutant clone C21.

(A) The gene *arnC_4* is a glycosyltransferase: Inactivation of glycosyltransferase homolog results in robust biofilm formation (Suban et al., 2022). The protein sequence was obtained from *Synechocytis* genome NCBI accession number: PRJNA224116 (protein ID: WP_010873051). (B) the predicted 3D structure of the wild type protein. The structures were generated computationally using BIOVIA Discovery Studio Visualizer software (http://www.accelrys.com).

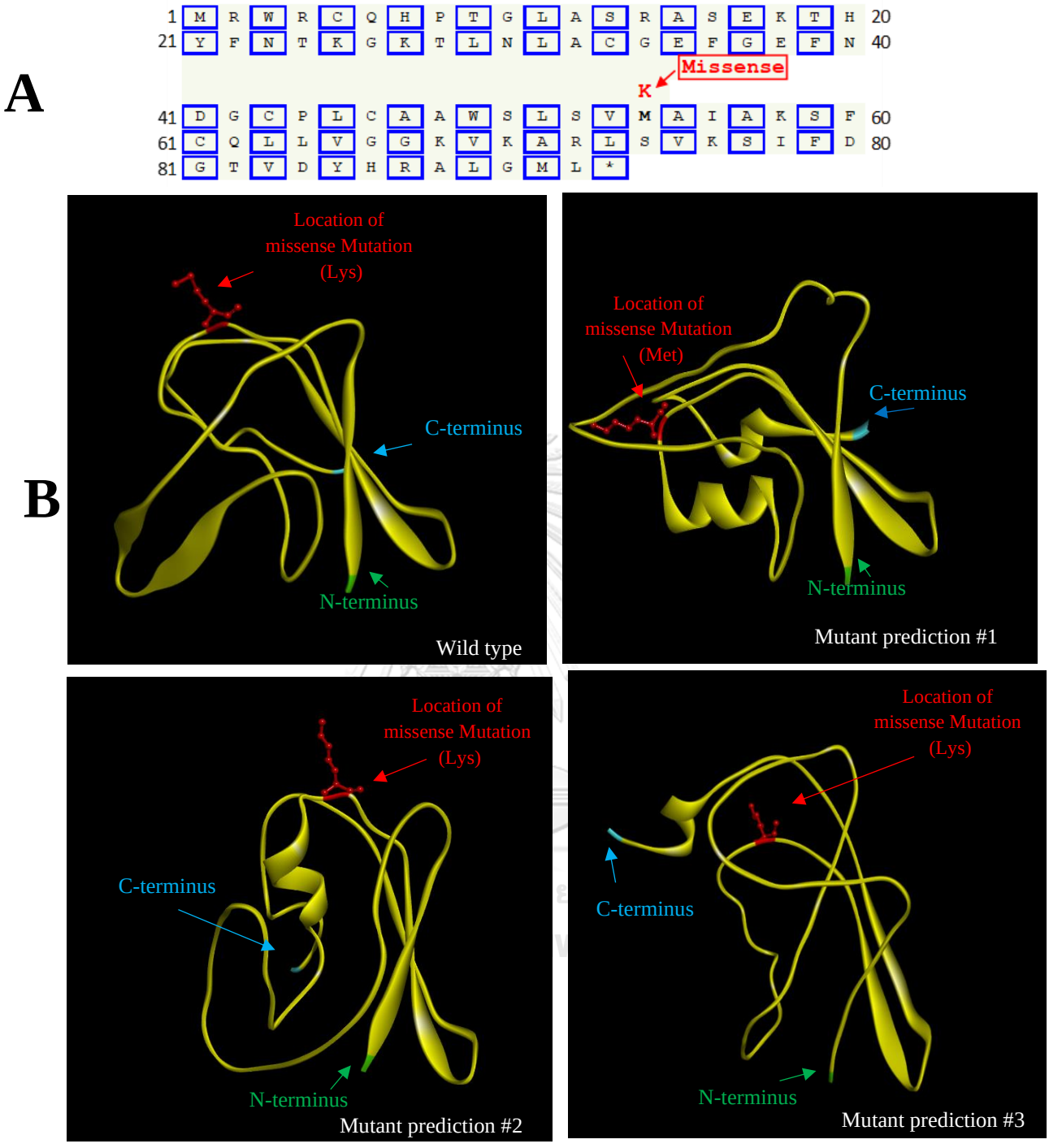


Figure 14 The protein sequence of *FMAMFGPO_01147* gene which obtained the missense mutation in the genome of the MV-resistant mutant all clone.
(A) The gene *FMAMFGPO_01147* is an unknown function. The protein sequence was obtained from *Synechocytis* genome NCBI accession number: PRJNA224116 (protein ID: WP_020861648). (B) the predicted 3D structure of the wild type protein. The three possibilities of the mutated protein structures #1, #2 and #3 were predicted. The structures were generated computationally using BIOVIA Discovery Studio Visualizer software (http://www.accelrys.com)

4.6 Cell growth of the seven selected MV-resistant mutants under the absence and presence of MV

Under normal growth condition with the absence of MV, all seven MV-resistant mutants grew at the comparable rate to wild type strain during 15-day period, but with the exception that at day 11 the growth of C21 mutant was slightly higher than that of wild type (Fig. 15).

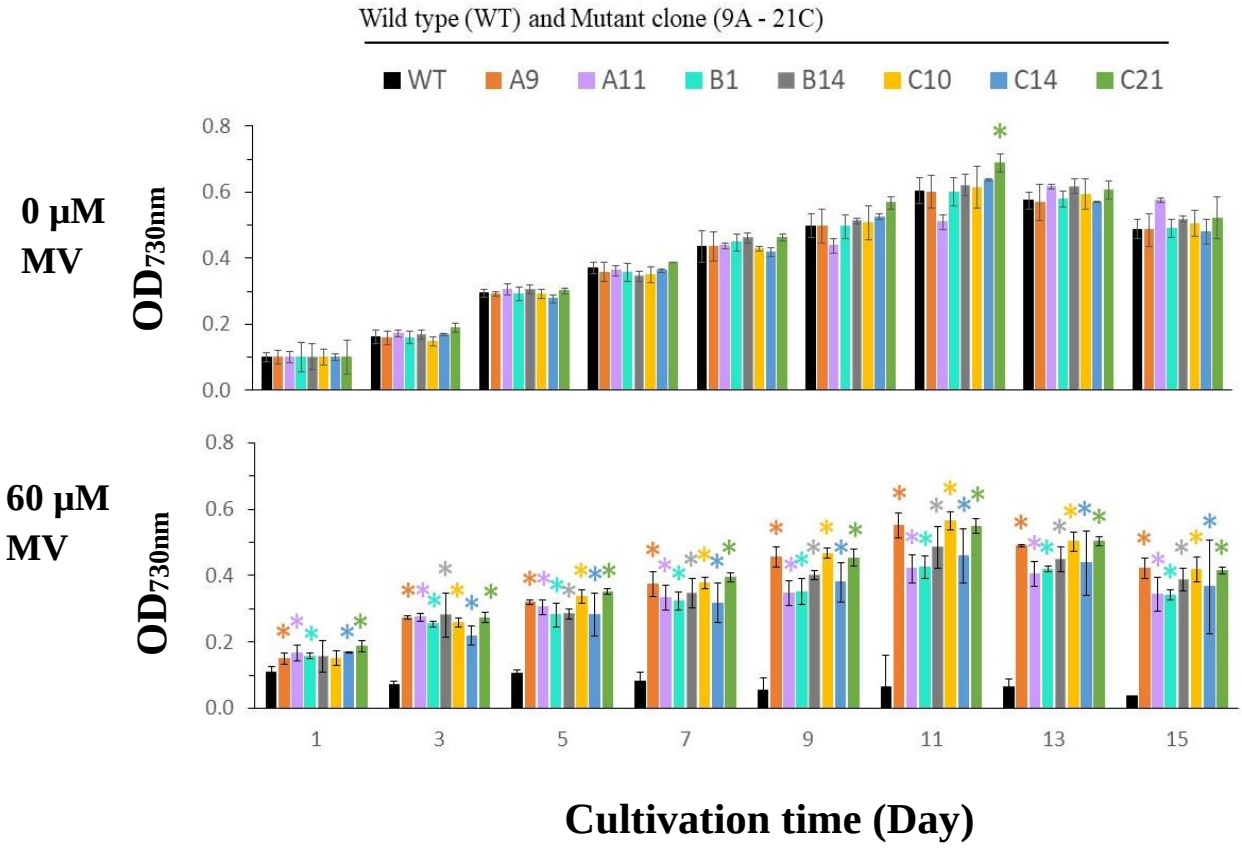


Figure 15 Growth profiles for *Synechocystis* sp. PCC 6803 wild type and the MV-resistant mutants.
Cell cultures at an initial concentration of 0.2 OD_{730nm} were cultivated with the indicated under 0 and 60 µM of MV concentration. Cell growth was defined as a significantly increased OD_{730nm} level. The data shows the mean ± SD derived from three independent biological cultures. Significantly different levels (*, $P < 0.05$: two-tailed student's t-test).

Under the presence of 60 µM MV, wild type was not able to grow, while mutant can grow as the evidence in the significant increase of cell density during 15-day period (Fig. 15). Thus, these results confirmed the MV-resistant phenotype of the mutants.

4.7 Oxygen-gas evolution of MV-resistant mutants under the absence and presence of MV

Oxygen-gas evolution that represents the photosynthetic ability of the cells were determined. Under the absence of MV, wild type and MV-resistant mutants had comparable oxygen-gas evolution rate, but with the exceptions that B14 mutant (cultured for 1 day) and A9 mutant (cultured for 7 days) had the higher oxygen-gas evolution rate and C10 mutant (cultured for 1 day) had the lower oxygen-gas evolution rate than wild type (Fig. 16).

The treatment by 60 µM MV completely inhibited oxygen-gas evolution rate of wild type. However, the MV exposure did not significantly affected oxygen-gas evolution rate of the mutants A9, C10, C14 and C21, or slightly reduced oxygen-gas evolution rate of the mutant B14 (Fig. 16). The results suggesting that the 60 µM MV exposure did not severely affect photosynthesis of the MV-resistant mutants.

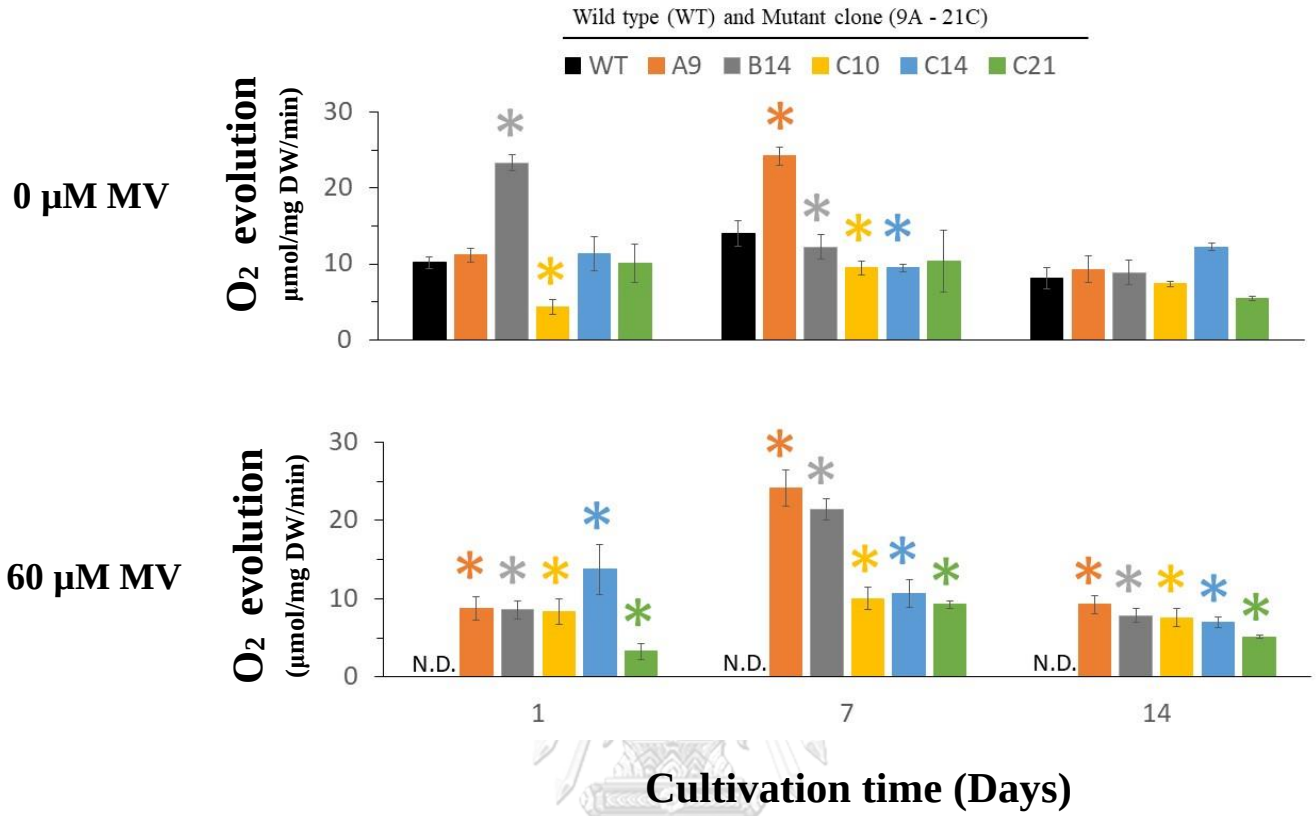


Figure 16 Oxygen-gas evolution of wild type (WT) and the MV-resistant mutants (clones A9-C21) under the absence of presence of MV.
Cell cultures at an initial cell density at 0.2 OD_{730nm} were cultivated for 14 days. The data shows the mean ± SD derived from three independent biological cultures. Significantly different levels from that of wild type (*, $P < 0.05$: two-tailed student's t-test).

4.8 Cell growth of MV-resistant mutants under osmotic stress

Under normal growth condition (without external stress), the MV-resistant mutants and wild type grew at the comparable rate (Fig. 17). The osmotic stress by the treatment using 1M sorbitol (Marin et al., 2006) and 1M sodium chloride (บุญบูรพงศ์ et al., 2011) for 15 days which has been previously used for osmotic stress generation in *Synechocytis*, was induced in the cultures of wild type and the mutants. Results in Fig. 17 showed that the growth of A9 and C10 mutants were remarkably negatively

affected, while the growth of wild type and other mutants were not significantly affected (Fig. 17). The severe growth inhibition caused by these osmatic stresses was clearly seen in A9 mutant. Thus, the mutations occurred in A9 and B10 mutants may be related to the defected ability of cellular export of such osmotic stress agents (sodium chloride or sorbitol) or the defective activity of cellular osmotic homeostasis.

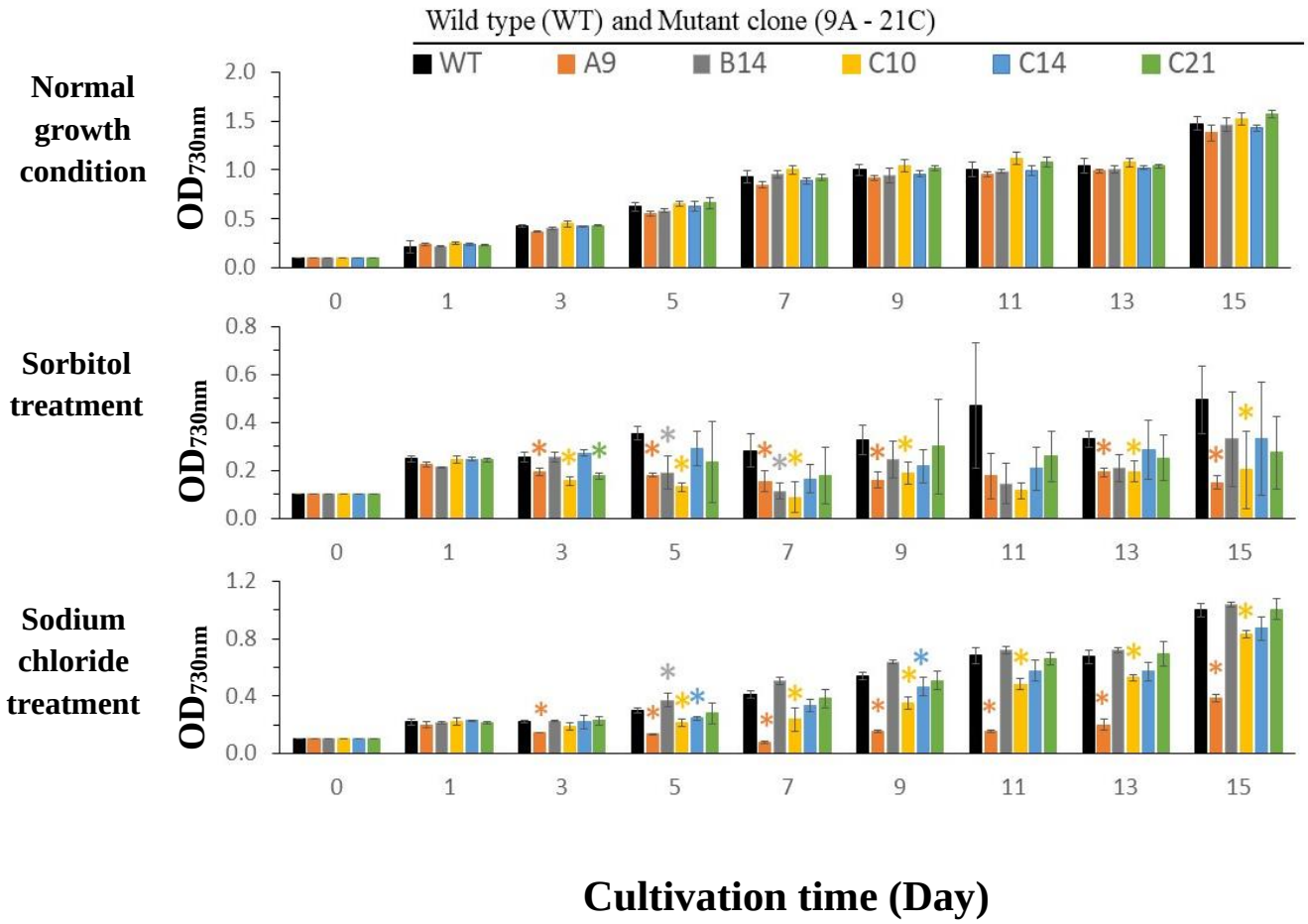


Figure 17 Growth profiles under osmotic stress of *Synechocystis* sp. PCC 6803 wild type and the MV-resistant mutants.
Cell were cultures at an initial concentration of 0.1 OD_{730nm} under the absence or presence of sorbitol at 1 M (Marin et al., 2006) or sodium chloride at 1 M (บุญบูรพงศ์ et al., 2014) which have previously been used to generate osmotic stress in *Synechocystis*. Data are shown as the mean ±SD derived from three independent cultures. Significantly different levels from that of wild type (*, $P < 0.05$: two-tailed student's t-test).

4.9 Cell growth of MV-resistant mutants under oxidative stress

The oxidative stress induced by the treatment with copper sulphate had no or little effect on cell growth of wild type and the mutants (Fig. 18). However, the stronger oxidative stress induced by the treatment by H_2O_2 did not affect growth of wild type, but remarkably reduced cells growth of the mutants A9, B14, and C10 (Fig. 18). Thus, the mutations occurred in A9, B14 and C10 mutants may be related to the defected ability of cellular export of H_2O_2 agent or the defective activity of cellular antioxidant. In addition, H_2O_2 agent slightly affects growth of D14 and C21 mutants (Fig. 18).

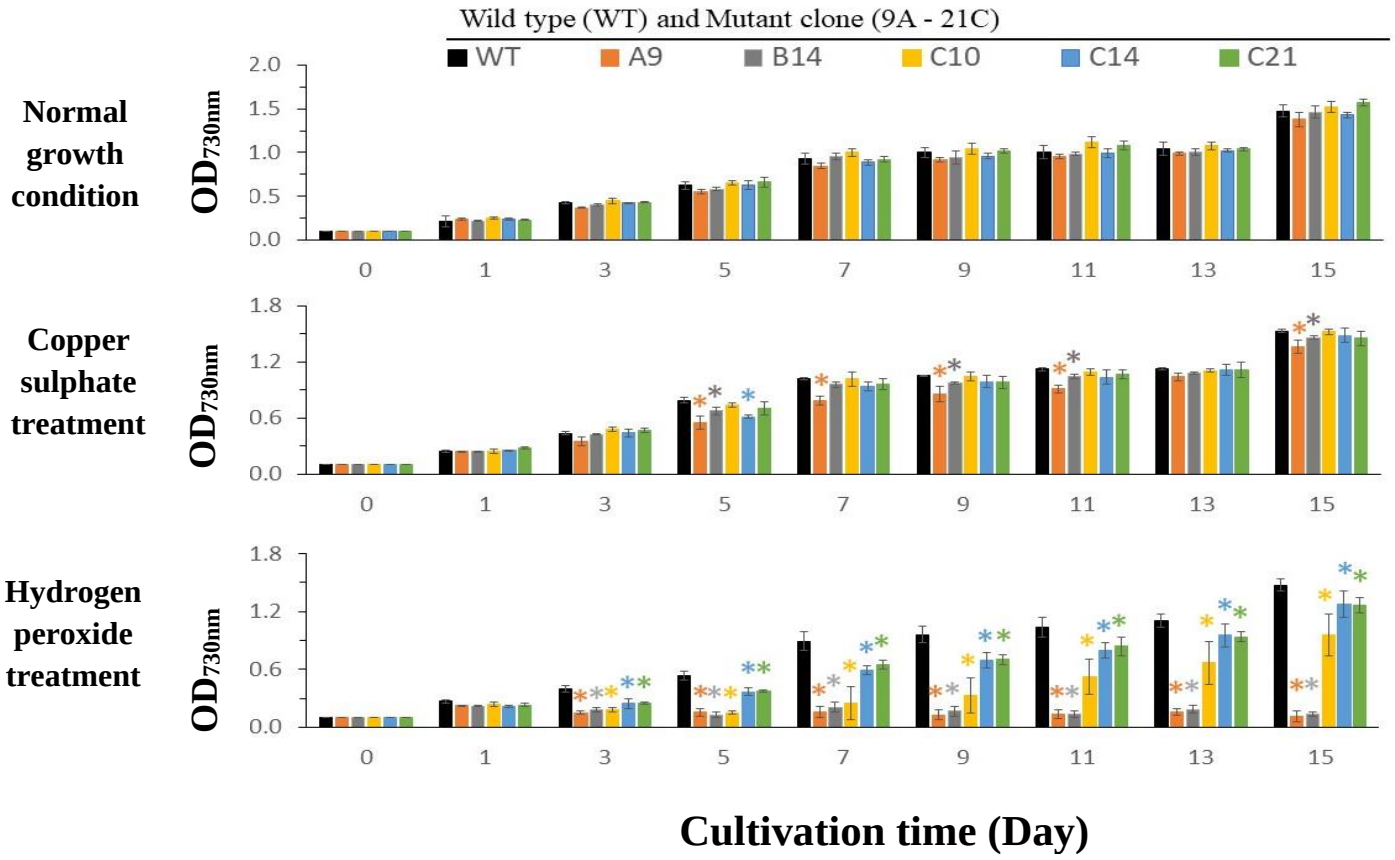


Figure 18 Growth profiles under oxidative stress of *Synechocystis* sp. PCC 6803 wild type and the MV-resistant mutants.
Cell were cultures at an initial concentration of 0.1 OD_{730nm} under the absence or presence of copper sulphate at 2 µM (Giner-Lamia et al., 2014) or hydrogen peroxide at 7 mM (From my Bachelor research, 2018) which have previously been used to generate oxidative stress in *Synechocystis*. Data are shown as the mean ±SD derived from three independent cultures. Significantly different levels from that of wild type (*, $P < 0.05$: two-tailed student's t-test)

4.10 Cellular antioxidant activity of MV resistant mutants under the absence and presence of MV

DPPH assay was used to determine cellular antioxidant activity (Koleva et al., 2003). Under normal condition, wild type and the mutants had comparable cellular antioxidant activities at 7, but at day 14, all mutants had significantly higher antioxidant activities than that of wild type (Table 11).

Table 11 Quantitative analysis and in vitro free radical scavenging activity of wildtype and MV-resistant mutant under absence of MV.
The supernatant of living cell culture from wild type and mutants (1 OD730nm in one mL of the cell culture) with the indicated under absence of MV concentration. The data shows the mean ± SD derived from three independent biological cultures. Significantly different levels between wildtype and MV-resistant mutant (*P < 0.05, **P < 0.01: two-tailed student's t-test).

	% Radical scavenging without MV		
Ascorbic acid	88 ± 4		
	Day 0	**Day 7**	**Day 14**
WT	61 ± 1	41 ± 1	31 ± 1
A 9	54 ± 1**	40 ± 1	52 ± 0.5**
B14	53 ± 1**	36 ± 4**	43 ± 1**
C10	55 ± 3**	45 ± 1*	37 ± 1**
C14	65 ± 0.4**	43 ± 1	43 ± 0.2**
C21	57 ± 1**	43 ± 1	40 ± 0.4**

Under 60 µM MV exposure, wild type and the mutants had comparable cellular antioxidant activities at day 7, but at day 14, A9, C10 and C21 mutants significantly exhibited higher antioxidant activities than that of wild type (Table 12). Thus, the mutations occurred in A9, C10 and C21 mutants may involve to the increased cellular antioxidant activity.

Table 12 Quantitative analysis and in vitro free radical scavenging activity of wildtype and MV-resistant mutant under presence of MV.

The supernatant of living cell culture from wild type and mutants (1 OD730nm in one mL of the cell culture) with the indicated under presence of MV concentration. The data shows the mean ± SD derived from three independent biological cultures. Significantly different levels between wildtype and MV-resistant mutant ($P < 0.05$, $^{**}P < 0.01$: two-tailed student's t-test).

	% Radical scavenging with the MV treatment		
Ascorbic acid	88 ± 4		
	Day 0	**Day 7**	**Day 14**
WT	61 ± 1	45 ± 1	33 ± 2
A 9	54 ± 1**	44 ± 1	41 ± 3**
B14	54 ± 1**	41 ± 2**	36 ± 3
C10	55 ± 3**	41 ± 1**	44 ± 1**
C14	65 ± 0.4**	45 ± 0.4	28 ± 1
C21	57 ± 1**	41 ± 1**	50 ± 1**

CHAPTER V
DISCUSSION

MV can act as an electron acceptor at photosystem I in plant weeds (Fuerst & Vaughn, 1990). However, This action disrupts photosynthetic generation of NADPH (Fig. 2), and the excess electron is further transferred to O_2 and generate toxic reactive oxygen species (Ananieva et al., 2004). These toxic compounds cause DNA damage, protein degradation and lipid peroxidation which severely affect the cellular metabolism (Casano et al., 1994; Szigeti & Lehoczki, 2003). Nevertheless, the cellular mechanism in photosystem I complex that is the target of MV inhibition is still unclear. In *Synechocystis*, wild-type cells grew poorly in the presence of 0.6 μm MV (Prosecka et al., 2009). Previous study determined the localization of membrane proteins in *Synechococcus* sp. PCC7942 and it was speculated that MV could also interact with cyanobacterial photosystem I and inhibit PSI function by interacting membrane-bound nonheme iron-sulfur proteins. For *Synechocystis*, treatment with 1 μM methyl viologen drastically reduced the cell density, biomass production, total protein contents, phycobiliprotein contents and oxygen evolution (Sukkasam et al., 2022). By improving the effectiveness of MV excretion from the cell, cyanobacteria can lower the levels of intracellular MV and oxidative stress. According to a recent study, the PrqA protein, which is a homolog of the multi-drug transporter (drug efflux protein), can remove intracellular MV in *Synechocystis* sp. PCC 6803, and the PrqR protein can control gene expression to influence how *Synechocystis* cells respond to ROS caused by MV. (Babykin et al., 2003).

Spontaneous MV-resistant mutant has been reported in plant, bacteria and cyanobacteria (Table 2). In *Arabidopsis thaliana*, the mutation in Pqr2 uptake transporter of positively-charged polyamine (and also potentially uptake MV) is associated with the MV resistance (Dong et al., 2016). In bacteria, the mutation in *Bacillus anthracis* Soda1 superoxide dismutase (Passalacqua et al., 2007) and the mutation in *E. coli* UbiG methyltransferase required for ubiquinone biosynthesis (involving in cellular antioxidant response) were found in MV-resistant mutants (Gonidakis et al., 2011). In addition, the mutation in Zwf glucose-6-phosphate

dehydrogenase (an enzyme generating NADPH required as the cofactor of enzymes in defense against paraquat toxicity) was report in MV-resistant mutant of *Pseudomonas aeruginosa* (Ma et al., 1998).

In *Synechocystis*, a mutation in MvrA membrane transporter (Nefedova et al., 2003), a mutation in SodB superoxide dismutase (enzyme for antioxidant removal) (Babykin et al., 2003) and the triple mutations potentially lead to MV secretion including that in Slr1901 ATPase, Slr1174 transporter protein and Slr0610 membrane transporter permease, lead to a low level of MV resistance (up to 4-6 µM MV) in this cyanobacterium (Prosecka et al., 2009). Thus, the mechanisms of MV resistance found so far are related to the alteration of MV transport/excretion, and the increased cellular antioxidant activity. However, no report of a mutation in photosystem I (PSI) where is the molecular target of MV inhibition.

This study has isolated six spontaneous mutants that exhibited a high level of MV resistance up to 60-80 µM MV (Table. 5) and identified mutations associated to this high-level MV-resistant phenotype. The mutant A9 harbors the disrupted function of TonB-dependent receptor involving in the transport of Fe^{+++} across cell membranes of *Synechocystis* and the altered FAD-binding oxidoreductase involving in the generation NADH (required as the cofactor of enzymes in defense against methyl viologen toxicity (Fig. 10 Table 8).

For TonB-dependent receptor, it plays roles in TonB-dependent uptake systems that permit bacterial growth in a wide range of iron-limited environments (Guerinot, 1994). These systems are also considered as targets of the antibiotics because they contribute to the specific permeability of the gram-negative cell envelope (Ghosh et al., 1996). Advances in understanding iron carrying by gram-negative bacteria have centered around two strategies: (i) uptalking small (< 1000 Dalton) microbially produced ferric iron chelators called siderophores; and (ii) utilizing host iron-binding proteins (Moeck & Coulton, 1998). TonB-dependent receptor is possibly used to uptake MV by these siderophores because MV has molecular weight only 186.26 Daltons (Caspi R, SRI International: MetaCyc

Database) and also has positive charge like iron. It might possible that this TonB-dependent receptor also transport MV to the cells and disrupted its function leads to MV resistance.

The mutant C14 contains the disrupted function of triacylglycerol lipase (enzyme generating diacylglycerol, the main composition of cell membrane, Table 9 and Fig. 11), suggesting this mutation may potentially affect cell membrane and MV transport. The mutant C21 harbors several point mutations in 21 genes including those relating intracellular transport, the biosynthesis of lipid A, the biosynthesis of cell-wall peptidoglycan, and biofilm formation, Table 7). Thus, the mechanisms of MV resistance found in this study are related to the alteration of MV transport and excretion, the altered composition of cell membrane and cell wall, and the increased cellular antioxidant activity.

Moreover, this study found that the mutants A11, B1, B14 and C10 contained the Met53→Lys alteration in 92-amino-acid hypothetical protein with unknown function (Table 10 and Fig. 11). This Met→Lys alteration possibly altered the overall 3D structure of the protein, particularly the reduction of helical structure (Fig. 13). How this mutation leads to MV resistant is still unknown. Further investigation would highlight whether this 97-amino-acid hypothetical protein involves in the process of photosynthesis and PSI which are the molecular targets of MV interaction, remained to be studied.

The six MV-resistant mutants and wild type grew at the comparable rate (Fig. 16), indicating that the mutation in these mutants did not affect cell growth. However, the osmotic stress induced by sorbitol and sodium chloride significantly affected cells growth of A9 mutant when compared with wildtype, but not wild type (Fig. 16). Thus, the mutations occurred in A9 and B10 mutants might be related to the defected cellular excretion of sodium chloride or sorbitol or the defective activity of cellular osmotic homeostasis. In agreement with this contention, A9 mutants has the disrupted function of TonB-dependent receptor involving in the transport of Fe^{+++}. In addition, A9 also contains the disrupted function of FAD-binding oxidoreductase involving in

the generation NADH (required as the cofactor of enzymes for defense against abiotic stress (Fig. 10 Table 8). Thus, the disrupted FAD-binding oxidoreductase function may contribute to the cell sensitivity to osmotic stress of A9 mutant.

For oxidative stress effect, A9, B14 and C10 showed the significantly reduced growth under H_2O_2 oxidative stress, while wild type did not. Since A9 contained the disrupted TonB-dependent receptor (Fig. 16), and the disrupted FAD-binding oxidoreductase (Fig. 16), these two proteins may involve in cellular export or detoxification of H_2O_2. B14 and C10 contains the Met53→Lys alteration in 92-amino-acid hypothetical protein with remarkably altered the overall 3D structure of the protein (Table 10 and Fig. 11). Thus, this hypothetical protein may involve with the cellular response to H_2O_2 stress.

MV treatment affected photosynthesis by inhibiting PSI electron transport and resulting in the reduced or terminated photosynthetic O_2 evolution in wild type *Synechocystis* (Kreslavski et al., 2007). In this study MV treatment at 60 µM completely terminated O_2 evolution in wild type, but not in those five mutants. Thus, MV did not inhibit photosynthesis in the mutants. This may be resulted from that MV cannot get into the cells due to a loss of MV transport ability or cellular strong antioxidant activity. These contentions were supported by the presence of the disrupted function of proteins related to ion transports in the mutants A9, and the increased antioxidant activity in the mutants A9, C10 and C21. It has been also found that a spontaneous MV-resistant mutant of *Nostoc punctiforme* exhibited the increased catalase activity in the presence of MV (Moirangthem et al., 2014).

Genes that responded to MV stress have been identified in *Synechcocystis* wild type (Hu et al., 2021). The significantly up-regulated genes (Hu et al., 2021) include: (i) *sll1621* encoding peroxidase playing roles in antioxidant defense system in cyanobacteria (Dietz, 2011); (ii) *slr1516* encoding the SOD (Superoxide dismutases) enzyme responsible for degrading superoxide ; ABC transporters playing an important role in MV transport (Dubey et al., 2016). In addition, MV reduced the rate of PSII photoinhibition repair and inhibited the synthesis of the D1 protein (the

major component of the PSII reaction center) as well as the synthesis of other photosynthetic proteins (Allakhverdiev and Murata 2004; Nishiyama et al., 2001, 2004). Overall wild type *Synechocystis* enhanced expression of genes responsible in oxidative stress defense and inhibited genes encoding photosynthetic components to respond to MV stress. These data are in agreement with the characteristics of the MV-resistant mutations found in this study (Table 8-10, Fig. 11-14) that these mutations involve in the increased cellular antioxidant activity found in the mutant A9, and the MV detoxification by mediating MV excretion found in the
mutants A9, C14 and C21.

CHAPTER VI
CONCLUSION

Seven MV-resistant mutants were obtained. The genome of seven mutants was fully sequenced. They contain the mutations in genes associated with the biosynthesis of cell-membrane components, the biosynthesis of cell-wall peptidoglycan, the biofilm formation, and the antioxidant defense found in the MV-resistant mutants A9, C14 and C21. The mechanisms of MV resistance found in this study may be related to the alteration of MV transport, the modified composition of the cell membrane and cell wall and the change in antioxidant mechanism that may lead to the inability to import MV to the cells. Further specific gene knockout of these mutation sites would help confirm whether these mutations cause MV resistance. Characterization of other MV-resistant mutants may lead to the understanding of MV transport, as well as the mechanism of MV resistance in cyanobacteria. This knowledge provides basic information for the further development of other compounds that can inhibit photosynthesis for further use in weed control. Additionally, the MV-resistant mechanism found in this study might be applied to generate economic and agricultural plants or algae that can tolerate MV and related herbicides.

APPENDICE

APPENDIX A
MEDIA AND SOLUTION

BG11 medium (Rippka et al., 1979)

Stock	**per 1 liter**
1.Dipotassium phosphate	4.00 g
2.Sodium nitrate	150.00 g
3.Calcium chloride dihydrate	3.60 g
4.Magnesium sulfate heptahydrate	7.50 g
5.Ammonium ferric citrate, green	0.60 g
6.Citric acid	0.60 g
7.Sodium carbonate	2.00 g
8.Disodium ethylenediaminetetraacetate dihydrate	0.10 g
	per 1 liter
9.Trace metal solution	
Boric acid	2.86 g
Manganese II chloride tetrahydrate	1.81 g
Zinc sulphate heptahydrate	0.22 g
Sodium molybdate dihydrate	0.39 g
Copper sulfate pentahydrate	0.08 g
Cobalt II nitrate hexahydrate	0.05 g

BG11 agar medium

	per 1 liter
Stock solution number 1-8	10 mL/1solution
Stock solution number 9	1 mL
Bacteriological agar	15 g

Adjust pH to 7.1 with 1M sodium hydroxide or 1 M hydrochloric acid

Adjust the volume to 1 liter with distilled water

Autoclave under a pressure of approximately 15 psi and achieve a chamber temperature of a least 121°C for 15 minutes

BG11 broth medium

	per 1 liter
Stock solution number 1-8	10 mL/1solution
Stock solution number 9	1 mL

Adjust pH to 7.1 with 1M sodium hydroxide or 1 M hydrochloric acid

Adjust the volume to 1 liter with distilled water

Autoclave under a pressure of approximately 15 psi and achieve a chamber temperature of a least 121°C for 15 minutes

Tris-acetate-EDTA buffer (TAE) (Green & Sambrook, 2012)

50X stock solution TAE buffer (1 liter)

242.0 g Tris-base

57.1 mL of 99.85% acetic acid

100 mL of 800 mM ethylene diamine tetra-acetic acid sodium salt dihydrate pH8

Adjust the volume to 1 liter with distilled water

Potassium Phosphate buffer (AAT Bioquest, 2022)

4.7 g Potassium phosphate dibasic

3.2 g Potassium phosphate monobasic

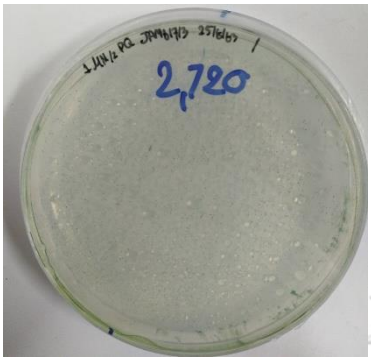
Adjust pH to 7 with 1M sodium hydroxide or 1 M hydrochloric acid

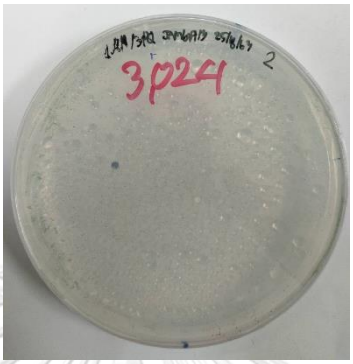
Adjust the volume to 1 liter with distilled water

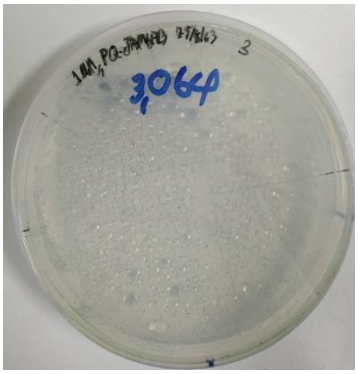
APPENDIX B
PICTURE AND DATA

Colonies of *Synchocystis* sp PCC 6803 on BG11 agar plate

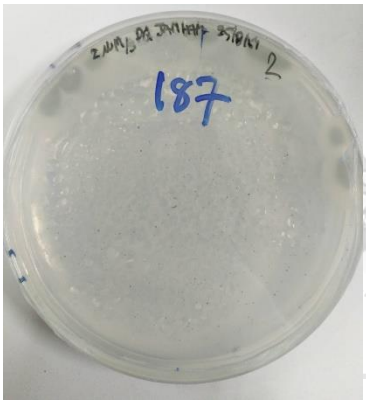
10 µM of MV

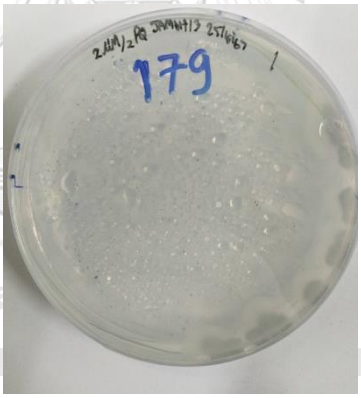


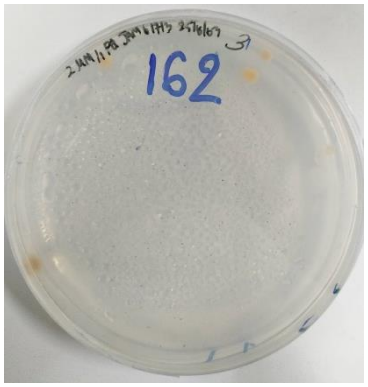




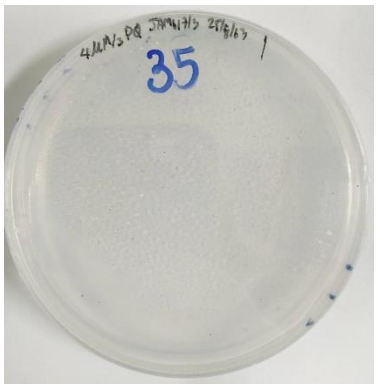
20 µM of MV

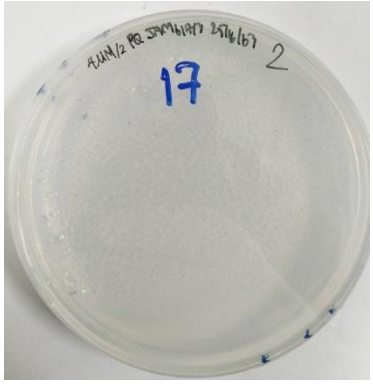


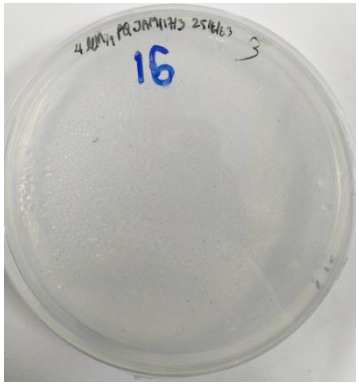




40 µM of MV







Mutation(s) identified in genomes of the MV-resistant mutants (A9 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
26318	T	A	22.9657	stop_gained	HIGH	cntO_1	c.1522A>T	p.Lys508*
285153	T	C	203.137	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCT	63.891	synonymous_variant	LOW	FMAMFGPO_00273	c.738_741delGGAGinsAGAA	p.248
285389	T	C	290.947	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285420	C	T	699.327	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285672	G	A	212.059	synonymous_variant	LOW	FMAMFGPO_00273	c.267C>T	p.His89His
285726	C	G	197.296	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
285777	C	T	34.4399	synonymous_variant	LOW	FMAMFGPO_00273	c.162G>A	p.Leu54Leu
389757	ACCCCCCCCCGCCAGA	ACCCCCCCCGCCAGA	35.0908	frameshift_variant	HIGH	dadA_1	c.588delG	p.Gly199fs
512893	G	A	735.564	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
967981	G	A	38.4768	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly
1080438	G	A	51.7679	synonymous_variant	LOW	FMAMFGPO_01027	c.1782G>A	p.Ala594Ala
1152737	C	A	1043.59	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1211597	GATC	TAGA	282.908	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	223.359	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211656	AACGAATTT	AACAAACCG	1710.45	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	5259.09	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	1137.48	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211794	C	T	806.443	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	858.12	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser
1211860	CAGC	AATG	253.433	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	27.9999	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1211893	A	T	390.104	synonymous_variant	LOW	FMAMFGPO_01145	c.528T>A	p.Ser176Ser
1211896	G	A	351.083	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	712.57	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	3676.79	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	1168.43	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	463.608	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212090	CCACCTGA	TTAACTGA	269.804	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1212103	ATCC	GTCT	126.042	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	225.419	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212148	A	G	131.174	synonymous_variant	LOW	FMAMFGPO_01145	c.273T>C	p.Phe91Phe
1212160	A	C	40.6831	synonymous_variant	LOW	FMAMFGPO_01145	c.261T>G	p.Thr87Thr
1212172	GAAACGA	GAAACGG	1076.65	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	128.13	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	112.501	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	312.416	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	3833.37	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA	2441.84	missense_variant	MODERATE	FMAMFGPO_01147	c.34_36delGTGinsATA	p.Val12Ile
1454925	TCTGGCC	TCTAGCT	1256.4	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1455087	G	C	858.266	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455108	T	C	151.116	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly
1455159	AACG	GACA,GACG	4296.6	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	2238.27	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455225	TCAGGTGG	TCAAGTGG	697.254	synonymous_variant	LOW	FMAMFGPO_01386	c.327G>A	p.Gln109Gln
1455405	A	G	766.041	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	969.767	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455441	AATCCTGCTGGCC	AATTCTGTTGTCG, AATTCTGCTATCC	1029.17	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1455459	GCTG	GATT	1241.73	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1455489	T	C	1376.49	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455523	CG	GA	1202.19	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA	1083.93	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	283.023	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAACinsGGGGAAAT	p.Glu225_Leu232del
1455609	TCTGTTGAAA	CCTGTTGAAA	367.039	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455627	TCTTACGATCG	TCTTACAATTG	436.563	synonymous_variant	LOW	FMAMFGPO_01386	c.732_735delGATCinsAATT	p.246
1455651	GGAG	AGAA	308.041	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	268.791	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	164.96	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	171.001	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1637579	C	A	36.7879	stop_gained	HIGH	FMAMFGPO_01563	c.104C>A	p.Ser35*
1763204	T	C	65.9231	synonymous_variant	LOW	FMAMFGPO_01697	c.204T>C	p.Phe68Phe
1763238	G	A	79.6226	missense_variant	MODERATE	FMAMFGPO_01697	c.238G>A	p.Glu80Lys
1763318	CAAAAAAAGGGAAAAC	CAAAAAAGGGAAAAC	36.5738	frameshift_variant	HIGH	FMAMFGPO_01697	c.325delA	p.Arg109fs
1970784	T	C	324.697	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1970818	G	A	246.589	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1972168	C	T	159.353	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala
1972196	C	A	390.95	missense_variant	MODERATE	FMAMFGPO_01896	c.43C>A	p.Pro15Thr
1972493	A	G	520.575	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1972516	C	T	399.192	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	431.993	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	858.819	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972708	G	A	721.78	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1972727	T	C	718.426	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972813	C	T	319.862	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2558293	C	T	1048.17	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2660261	CCCAACC	GCCGACG	1341.11	synonymous_variant	LOW	glyQ	c.357_363delCCCAACCinsGCCGACG	p.122
2660273	GGCC	CGCG	1355.86	synonymous_variant	LOW	glyQ	c.369_372delGGCCinsCGCG	p.125
2558286	A	G	1048.32	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2714818	G	C	2137.15	missense_variant	MODERATE	carB_2	c.1799C>G	p.Ser600Cys
2763615	C	A	535.068	missense_variant	MODERATE	betI	c.446C>A	p.Thr149Lys
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	1273.71	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2817746	GGCGGC	CGAAGT,GGAGGT	1816.07	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2922421	G	C	184.924	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2997876	G	A	334.289	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2997948	C	G	45.8428	missense_variant	MODERATE	FMAMFGPO_02833	c.133G>C	p.Glu45Gln
2997953	C	T	40.3717	missense_variant	MODERATE	FMAMFGPO_02833	c.128G>A	p.Cys43Tyr
2998281	GGATC	GGATTC	420.229	frameshift_variant	HIGH	FMAMFGPO_02834	c.641_642insA	p.Ser215fs
2998367	T	C	67.6621	missense_variant	MODERATE	FMAMFGPO_02834	c.559A>G	p.Ile187Val
2998493	G	T	26.0809	missense_variant	MODERATE	FMAMFGPO_02834	c.433C>A	p.Pro145Thr
2998688	C	T	772.073	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998711	G	A	54.9236	missense_variant	MODERATE	FMAMFGPO_02834	c.215C>T	p.Ser72Phe
2998753	T	C	214.056	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	46.4156	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met
2998822	C	T	62.2226	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
2817698	TCAA	CCAG	931.253	synonymous_variant	LOW	FMAMFGPO_02674	c.33_36delTCAAinsCCAG	p.13
2817704	A	G	1902.59	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	1607.74	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817732	TTGTCC	TTATCC	208.04	synonymous_variant	LOW	FMAMFGPO_02674	c.69G>A	p.Leu23Leu
3096187	T	C	317.175	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
2817764	G	A	1662.51	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	1011.38	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2817776	T	A	53.858	synonymous_variant	LOW	FMAMFGPO_02674	c.111T>A	p.Ala37Ala
2922391	A	C	233.928	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
3096875	CT	GC	45.9124	missense_variant	MODERATE	FMAMFGPO_02927	c.488_489delCTinsGC	p.Ala163Gly
2294959	GTTTTTTGTTGTGGA	GTTTTTTTGTTGTGGA	36.1022	upstream_gene_variant	MODIFIER	FMAMFGPO_02190	c.-3087_-3086insA	
2383786	A	C	838.693	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2383794	T	C	675.799	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	977.081	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	849.197	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817492	T	C,G	1765.86	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817498	GT	AC,GC	1620.62	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817509	AATCCGATAGG	GATCTGTTAGA,AATTTGTTAGG	870.784	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	TG	CT,CG	829.881	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817542	TGGGCAAAC	GGGGCAAAC	722.905	upstream_gene_variant	MODIFIER	yciH	c.-4822A>C	
2817558	CTTTCATCTGTATT	GTCCCATCTTCATC	718.496	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGATGGGAC	
2817597	GGCCA	GGCCG	2114.18	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
2817644	TCGCCGGACTACGTTAACCATA	CCGCCGCACTGCGTTAACGATG,TCGCCGCACTGCGTTAACGATG	1251.37	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4924delTATGGTTAACGTAGTCCGGCGAinsCATCGTTAACGCAGTGCGGCGG	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
3043888	AAAG	AAAT	282.274	synonymous_variant	LOW	FMAMFGPO_02877	c.36C>A	p.Ser12Ser
3043897	GGCGAGG	GGCCAGA	520.294	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10
3043912	C	G	36.0438	synonymous_variant	LOW	FMAMFGPO_02877	c.15G>C	p.Leu5Leu
2984931	ATCG	GTCT	311.608	upstream_gene_variant	MODIFIER	FMAMFGPO_02817	c.-3967_-3964delCGATinsAGAC	
3065431	T	C	1735.31	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
2984939	A	T	179.937	upstream_gene_variant	MODIFIER	FMAMFGPO_02817	c.-3972T>A	
3043936	CTAAG	CTACC	332.362	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	1078.73	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	932.727	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr
3350510	G	A	67.7542	synonymous_variant	LOW	acnB	c.1821G>A	p.Ala607Ala

Mutation(s) identified in genomes of the MV-resistant mutants (A11 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285153	T	C	1500.26	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCC	389.94	synonymous_variant	LOW	FMAMFGPO_00273	c.741G>A	p.Glu247Glu
285389	T	C	2670.24	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285417	TGCC	TGCT	3631.98	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285672	G	A	1032.43	synonymous_variant	LOW	FMAMFGPO_00273	c.267C>T	p.His89His
285726	C	G	1237.67	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
285777	C	T	1001.17	synonymous_variant	LOW	FMAMFGPO_00273	c.162G>A	p.Leu54Leu
285827	AA	AG	427.73	synonymous_variant	LOW	FMAMFGPO_00273	c.111T>C	p.Ser37Ser
285833	GTTCCGTC	ATTCCGTT	84.1894	synonymous_variant	LOW	FMAMFGPO_00273	c.99_106delGACGGAACinsAACGGAAT	p.37
285846	C	G	180.272	synonymous_variant	LOW	FMAMFGPO_00273	c.93G>C	p.Leu31Leu
285852	A	G	121.683	synonymous_variant	LOW	FMAMFGPO_00273	c.87T>C	p.Thr29Thr
512893	G	A	3349.94	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
967900	G	T	177.791	synonymous_variant	LOW	FMAMFGPO_00916	c.453C>A	p.Ala151Ala
967981	G	A	574.588	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly
968002	G	C	544.15	synonymous_variant	LOW	FMAMFGPO_00916	c.351C>G	p.Gly117Gly
1152737	C	A	6567.52	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1211597	GATC	TAGA	2796.56	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	850.989	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	20917.3	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211656	AACGAATTT	AACAAACCG	17272.7	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	45213.8	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	13754.9	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211773	TAGTTTGCCG	TAGTTTCCCA,TAGTTTGCCCTCTAATTTTCCTTCCAACCGACCCTCCAA	19451.6	conservative_inframe_insertion	MODERATE	FMAMFGPO_01145	c.639_640insGGCAAATTGGAGGGTCGGTTGGAAGGAAAATTAGAG	p.Ala213_Gly214insGlyLysLeuGluGlyArgLeuGluGly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
		TTTGCCG						LysLeuGlu
1211794	C	T	4225.55	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	4850.49	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser
1211860	CAGC	AATG	8653.02	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	7269.16	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser
1211874	ACAGAATC	ACAGAATT	9900.59	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211893	A	T	1882.17	synonymous_variant	LOW	FMAMFGPO_01145	c.528T>A	p.Ser176Ser
1211896	G	A	7632.77	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	9581.21	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	27426.7	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	10258	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	3994.26	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212076	GTGTAA	ATGCAC,ATGCAA	16203.2	missense_variant	MODERATE	FMAMFGPO_01145	c.340_345delTTACACinsGTGCAT	p.Leu114Val
1212090	CCACCTGA	TTAACTGA	2360.01	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1212103	ATCC	GTCT	1323.95	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	1531.21	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212145	GACA	AACA	11416.8	synonymous_variant	LOW	FMAMFGPO_01145	c.276C>T	p.Val92Val
1212172	GAAACGA	GAAACGG	10522.1	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	2013.98	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	1523.05	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	2886.58	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	32757.6	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	22161.7	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213743	AAGTCTAT	GGGTTTAA,GGGTCTAT	62845	missense_variant	MODERATE	FMAMFGPO_01147	c.67_68delAAinsGG	p.Lys23Gly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1213755	GA	AA	1689.42	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1443027	GATGATG	AATCACT	94.5212	missense_variant	MODERATE	rcsC_12	c.1014_1020delCATCATCinsAGTGATT	p.Ile339Val
1455444	CCTGCTGGCC	TCTGTTGTCG,TCTGCTATCC	9439.83	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1213793	G	A	741.264	synonymous_variant	LOW	FMAMFGPO_01147	c.117G>A	p.Leu39Leu
1443015	T	C	88.1949	synonymous_variant	LOW	rcsC_12	c.1032A>G	p.Gly344Gly
1455459	GCTG	GATT	8828.42	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1454925	TCTGGCC	TCTAGCT	8700.91	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1454940	T	C	1310.85	synonymous_variant	LOW	FMAMFGPO_01386	c.39T>C	p.Phe13Phe
1455003	G	A	307.36	synonymous_variant	LOW	FMAMFGPO_01386	c.102G>A	p.Thr34Thr
1455087	G	C	12814.2	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	3239	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455108	T	C	3710.28	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly
1455147	TTTC	TTTT	3703.95	synonymous_variant	LOW	FMAMFGPO_01386	c.249C>T	p.Phe83Phe
1455159	AACG	GACA,GACG	36991.8	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	18448.9	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455183	CCTGAAA	TCTAAAA	2644	synonymous_variant	LOW	FMAMFGPO_01386	c.282_285delCCTGinsTCTA	p.96
1455225	TCAGGTGG	TCAAGTGG	2461.14	synonymous_variant	LOW	FMAMFGPO_01386	c.327G>A	p.Gln109Gln
1455405	A	G	3897.21	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	5463.9	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455523	CG	GA	8049	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA,CT	8652.26	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455489	T	C	9046.09	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	3104.53	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAAACinsGGGGAAAT	p.Glu225_Leu232del
1763123	A	G	227.201	missense_variant	MODERATE	FMAMFGPO_01697	c.123A>G	p.Ile41Met

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1763238	G	A	474.434	missense_variant	MODERATE	FMAMFGPO_01697	c.238G>A	p.Glu80Lys
1455609	TCTGTTGAAA	CCTGTTGAAA	3812.63	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	3606.01	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	2709.48	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	1857.95	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	1688.35	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1944928	C	A	2371.53	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>A	p.Arg115Ser
1763148	C	T	181.332	synonymous_variant	LOW	FMAMFGPO_01697	c.148C>T	p.Leu50Leu
1763204	T	C	381.731	synonymous_variant	LOW	FMAMFGPO_01697	c.204T>C	p.Phe68Phe
1970818	G	A	1664.91	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1972493	A	G	2948.51	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1970784	T	C	3383.78	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1972708	G	A	2839.1	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972727	T	C	2467.19	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972516	C	T	1906.82	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	2413.41	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	3141.04	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972813	C	T	907.588	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2284284	T	G	58.777	missense_variant	MODERATE	glcK	c.428T>G	p.Val143Gly
2558293	C	T	2700.05	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2808916	A	G	60.0659	missense_variant	MODERATE	dfa1	c.17T>C	p.Leu6Pro
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	16335.5	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2817746	GGCGGC	CGAAGT,GGAGGT	19534.4	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2558286	A	G	2628.5	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2922421	G	C	1364.76	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2997876	G	A	1020.37	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2997948	C	G	25.0552	missense_variant	MODERATE	FMAMFGPO_02833	c.133G>C	p.Glu45Gln
2998658	C	T	74.2325	missense_variant	MODERATE	FMAMFGPO_02834	c.268G>A	p.Val90Ile
2998688	C	T	6042.03	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998753	T	C	2106	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	930.328	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met
2998822	C	T	656.442	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3096187	T	C	2834.34	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
3096875	CT	GC	1106.69	missense_variant	MODERATE	FMAMFGPO_02927	c.488_489delCTinsGC	p.Ala163Gly
1213597	A	C	405.081	upstream_gene_variant	MODIFIER	deoC1	c.-4900T>G	
1213604	C	A	146.847	upstream_gene_variant	MODIFIER	deoC1	c.-4907G>T	
2383786	A	C	4111.9	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2383794	T	C	3792.6	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	2646.37	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2817704	A	G	12199.3	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	11181.3	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2558332	A	G	2417.49	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817764	G	A	9722.74	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	7013.38	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2817776	T	A	417.733	synonymous_variant	LOW	FMAMFGPO_02674	c.111T>A	p.Ala37Ala
2922391	A	C	1670.17	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2817492	T	C	9065.76	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817498	GT	AC	8335.89	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817509	AATCCGATAGG	GATCTGTTAGA	7258.84	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	TG	CG	7165.94	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817535	ACA	GTA	3891.45	upstream_gene_variant	MODIFIER	yciH	c.-4816_-4815delGTinsAC	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817542	TGGGCAAAC	GGGGGAAAA	3918.33	upstream_gene_variant	MODIFIER	yciH	c.-4830_-4822delGTTTGCCCAinsTTTTCCCCC	
2817558	CTTTCATCTGTATT	GTCACACCTTCATC	3782.81	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGGTGTGAC	
2817597	GGCCA	GGCCG	12819.7	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
2998905	C	T	20.1727	synonymous_variant	LOW	FMAMFGPO_02834	c.21G>A	p.Ala7Ala
3043888	AAAG	AAAT	451.393	synonymous_variant	LOW	FMAMFGPO_02877	c.36C>A	p.Ser12Ser
3043897	GGCGAGG	GGCCAGA	2944.72	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10
3043912	C	G	147.756	synonymous_variant	LOW	FMAMFGPO_02877	c.15G>C	p.Leu5Leu
2817612	GATTGGTGTTGGGGGGCA	GATTGGAGTGAGGGGGGTA	8892.76	upstream_gene_variant	MODIFIER	yciH	c.-4909_-4898delTGCCCCCCAACAinsTACCCCCCTCACT	
3065431	T	C	11403.7	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
2817644	TCGCCGGACTACGTTAACCATA	TCGCCGCACTGCGTTAACGATG	10351.7	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4930delTATGGTTAACGTAGTCinsCATCGTTAACGCAGTG	
3043936	CTAAG	CTACC	1537.06	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	6467.4	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	2955.21	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr

Mutation(s) identified in genomes of the MV-resistant mutants (B1 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285153	T	C	1919.83	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCC	506.761	synonymous_variant	LOW	FMAMFGPO_00273	c.741G>A	p.Glu247Glu
285389	T	C	2445.12	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285417	TGCC	TGCT	3615.2	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285672	G	A	1673.86	synonymous_variant	LOW	FMAMFGPO_00273	c.267C>T	p.His89His
285726	C	G	1868.52	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
285777	C	T	702.314	synonymous_variant	LOW	FMAMFGPO_00273	c.162G>A	p.Leu54Leu
512893	G	A	4693.11	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
517243	G	A	4944.11	synonymous_variant	LOW	FMAMFGPO_00491	c.969C>T	p.Thr323Thr
967981	G	A	45.1085	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly
968002	G	C	67.3985	synonymous_variant	LOW	FMAMFGPO_00916	c.351C>G	p.Gly117Gly
1152737	C	A	5120.91	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1200306	C	A	109.047	missense_variant	MODERATE	FMAMFGPO_01135	c.599C>A	p.Pro200Gln
1211597	GATC	TAGA	3672.78	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	698.96	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	21207.2	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211656	AACGAATTT	AACAAACCG	18230.7	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	45060.4	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	12055	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211794	C	T	4450.98	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	4805.29	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser
1211860	CAGC	AATG	6267.85	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	5063.16	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser
1211874	ACAGAATC	ACAGAATT	7440.18	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211893	A	T	480.342	synonymous_variant	LOW	FMAMFGPO_01145	c.528T>A	p.Ser176Ser

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1211896	G	A	5035.87	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	6835.62	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	24075.9	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	9204.94	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	3829.82	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212076	GTGTAA	ATGCAC,ATGCAA	13388.7	missense_variant	MODERATE	FMAMFGPO_01145	c.340_345delTTACACinsGTGCAT	p.Leu114Val
1212090	CCACCTGA	TTAACTGA	2429.63	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1212103	ATCC	GTCT	1645.97	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	1721.34	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212145	GACA	AACA	8722.67	synonymous_variant	LOW	FMAMFGPO_01145	c.276C>T	p.Val92Val
1212160	A	C	198.552	synonymous_variant	LOW	FMAMFGPO_01145	c.261T>G	p.Thr87Thr
1212172	GAAACGA	GAAACGG	8294.37	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	2227.47	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	2034.39	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	3500.48	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	31754.7	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	21463.9	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213743	AAGTCTAT	GGGTTTAA,GGGTCTAT	58892.7	missense_variant	MODERATE	FMAMFGPO_01147	c.67_68delAAinsGG	p.Lys23Gly
1213755	GA	AA	1425.75	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1213793	G	A	1813.78	synonymous_variant	LOW	FMAMFGPO_01147	c.117G>A	p.Leu39Leu
1416421	A	G	68.0775	missense_variant	MODERATE	topA	c.2296A>G	p.Ile766Val
1454925	TCTGGCC	TCTAGCT	7213.9	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1454940	T	C	467.305	synonymous_variant	LOW	FMAMFGPO_01386	c.39T>C	p.Phe13Phe
1455003	G	A	754.59	synonymous_variant	LOW	FMAMFGPO_01386	c.102G>A	p.Thr34Thr
1455087	G	C	9317.53	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	1862.13	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455108	T	C	2564.91	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1455147	TTTC	TTTT	3686.44	synonymous_variant	LOW	FMAMFGPO_01386	c.249C>T	p.Phe83Phe
1455159	AACG	GACA,GACG	33302	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	18615	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455183	CCTGAAA	TCTAAAA	2311.61	synonymous_variant	LOW	FMAMFGPO_01386	c.282_285delCCTGinsTCTA	p.96
1455204	TTTA	CTTG	26597.6	synonymous_variant	LOW	FMAMFGPO_01386	c.303_306delTTTAinsCTTG	p.103
1455225	TCAGGTGG	TCAAGTGG	2268.63	synonymous_variant	LOW	FMAMFGPO_01386	c.327G>A	p.Gln109Gln
1455405	A	G	5496.45	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	7486.2	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455444	CCTGCTGGCC	TCTGTTGTCG,TCTGCTATCC	9614.32	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1455459	GCTG	GATT	10218.3	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1455489	T	C	10148.3	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455523	CG	GA	8875.86	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA	7810.72	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	3355.42	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAAACinsGGGGAAAT	p.Glu225_Leu232del
1455609	TCTGTTGAAA	CCTGTTGAAA	3993.28	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	3635.69	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	2653.59	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	1637.3	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	1446.43	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1763204	T	C	51.2958	synonymous_variant	LOW	FMAMFGPO_01697	c.204T>C	p.Phe68Phe
1763238	G	A	34.9905	missense_variant	MODERATE	FMAMFGPO_01697	c.238G>A	p.Glu80Lys
1944928	C	T	4553.18	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>T	p.Arg115Cys
1970784	T	C	2901.94	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1970818	G	A	1458.96	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1972168	C	T	597.208	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1972196	C	A	1077.58	missense_variant	MODERATE	FMAMFGPO_01896	c.43C>A	p.Pro15Thr
1972493	A	G	3064.76	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1972516	C	T	1580.42	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	1959.56	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	2220.07	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972708	G	A	1962.89	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972727	T	C	1852.81	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972813	C	T	256.429	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2284284	T	G	141.509	missense_variant	MODERATE	glcK	c.428T>G	p.Val143Gly
2558293	C	T	2546.6	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2808916	A	G	136.25	missense_variant	MODERATE	dfa1	c.17T>C	p.Leu6Pro
2558286	A	G	2508.88	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	12631	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2817746	GGCGGC	CGAAGT,GGAGGT	14517	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2922421	G	C	597.17	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2997876	G	A	969.62	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2998688	C	T	6158.94	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998753	T	C	2385.93	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	837.18	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met
2998822	C	T	535.233	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3096187	T	C	3865.7	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
3096875	CT	GC	432.85	missense_variant	MODERATE	FMAMFGPO_02927	c.488_489delCTinsGC	p.Ala163Gly
2383786	A	C	4118.93	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2383794	T	C	3671.77	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	2156.9	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	2006.92	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817492	T	C	7607.13	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817698	TCAA	CCAG	10034.9	synonymous_variant	LOW	FMAMFGPO_02674	c.33_36delTCAAinsCCAG	p.13
2817704	A	G	11237.5	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	10800	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2817498	GT	AC	6887.85	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817764	G	A	8926.59	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	6525.32	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2922391	A	C	1085.95	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2817509	AATCCGATAGG	GATCTGTTAGA	6308.68	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	TG	CG	6314.53	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817535	ACA	GTA	2707.8	upstream_gene_variant	MODIFIER	yciH	c.-4816_-4815delGTinsAC	
2817542	TGGGCAAAC	GGGGGAAAA	2866.61	upstream_gene_variant	MODIFIER	yciH	c.-4830_-4822delGTTTGCCCAinsTTTTCCCCC	
2817558	CTTTCATCTGTATT	GTCACACCTTCATC	2823.08	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGGTGTGAC	
2817597	GGCCA	GGCCG	11303.9	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
3043897	GGCGAGG	GGCCAGA	3194.53	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10
2817612	GATTGGTGTTGGGGGGCA	GATTGGAGTGAGGGGGGTA	7804.99	upstream_gene_variant	MODIFIER	yciH	c.-4909_-4898delTGCCCCCCAACAinsTACCCCCCTCACT	
3065431	T	C	11050.7	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
2817644	TCGCCGGACTACGTTAACCATA	TCGCCGCACTGCGTTAACGATG	9146.74	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4930delTATGGTTAACGTAGTCinsCATCGTTAACGCAGTG	
3043936	CTAAG	CTACC	1834.74	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	5386.73	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	2387.28	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr

Mutation(s) identified in genomes of the MV-resistant mutants (B14 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285153	T	C	892.572	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCT	264.135	synonymous_variant	LOW	FMAMFGPO_00273	c.738_741delGGAGinsAGAA	p.248
285389	T	C	1154.7	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285420	C	T	1744.39	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285726	C	G	266.124	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
512893	G	A	3026.55	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
1152737	C	A	3399.19	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1211597	GATC	TAGA	951.576	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	716.023	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	8616.64	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211656	AACGAATTT	AACAAACCG	9356.75	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	23518	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	7676.15	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211794	C	T	1889.75	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	2547.13	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser
1211860	CAGC	AATG	3912.45	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	3421.89	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser
1211874	ACAGAATC	ACAGAATT	4471.08	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211896	G	A	3843.84	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	4615.07	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	12822.9	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	4450.37	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	1570.49	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212090	CCACCTGA	TTAACTGA	1165.94	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuA

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
								rg
1212103	ATCC	GTCT	707.522	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	747.141	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212145	GACA	AACA	5195.84	synonymous_variant	LOW	FMAMFGPO_01145	c.276C>T	p.Val92Val
1212172	GAAACGA	GAAACGG	4667.57	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	1076.11	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	950.185	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	1336.93	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	15797.3	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	10841.4	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213755	GA	AA	106.84	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1455225	TCAGGTGG	CCAGTTGG	1906.95	missense_variant	MODERATE	FMAMFGPO_01386	c.324_328delTCAGGinsCCAGT	p.Val110Leu
1454925	TCTGGCC	TCTAGCT	4454.56	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1454940	T	C	408.03	synonymous_variant	LOW	FMAMFGPO_01386	c.39T>C	p.Phe13Phe
1455003	G	A	345.641	synonymous_variant	LOW	FMAMFGPO_01386	c.102G>A	p.Thr34Thr
1455087	G	C	5611.33	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	617.987	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455108	T	C	963.389	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly
1455147	TTTC	TTTT	1938.43	synonymous_variant	LOW	FMAMFGPO_01386	c.249C>T	p.Phe83Phe
1455159	AACG	GACA,GACG	20146.5	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	10980.2	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455183	CCTGAAA	TCTAAAA	1959.86	synonymous_variant	LOW	FMAMFGPO_01386	c.282_285delCCTGinsTCTA	p.96
1455441	AATCCTGCTGGCC	AATTCTGCTATCC	5103.1	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1455405	A	G	3303.97	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	4054.98	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455459	GCTG	GATT	5947.46	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1455523	CG	GA	4872.04	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1455489	T	C	5954.52	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455543	TT	CA	4679.84	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	2260.51	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAACinsGGGGAAAT	p.Glu225_Leu232del
1944928	C	A	3285.26	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>A	p.Arg115Ser
1455609	TCTGTTGAAA	CCTGTTGAAA	2691.67	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	2537.92	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	1814.58	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	762.426	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	630.41	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1970818	G	A	673.895	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1970784	T	C	1171.37	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1972196	C	A	1060	missense_variant	MODERATE	FMAMFGPO_01896	c.43C>A	p.Pro15Thr
1972168	C	T	597.413	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala
1972493	A	G	2134.53	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1972708	G	A	1707.26	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972516	C	T	1372.93	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	1427.85	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	1673.59	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972727	T	C	1820.4	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972813	C	T	590.875	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2284284	T	G	60.094	missense_variant	MODERATE	glcK	c.428T>G	p.Val143Gly
2558293	C	T	1853.16	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2714818	G	C	49.1368	missense_variant	MODERATE	carB_2	c.1799C>G	p.Ser600Cys
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	6801.11	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2558286	A	G	1954.99	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817746	GGCGGC	CGAAGT,GGAGGT	8471.7	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2922421	G	C	645.34	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2997876	G	A	852.394	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2998658	C	T	538.443	missense_variant	MODERATE	FMAMFGPO_02834	c.268G>A	p.Val90Ile
2998688	C	T	2857.96	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998711	G	A	307.922	missense_variant	MODERATE	FMAMFGPO_02834	c.215C>T	p.Ser72Phe
2998753	T	C	1708.12	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	674.891	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met
2998822	C	T	405.472	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3096187	T	C	2762.49	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
1213597	A	C	70.8751	upstream_gene_variant	MODIFIER	deoC1	c.-4900T>G	
2383786	A	C	1903.5	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2383794	T	C	1818.72	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	1699.82	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	1447.48	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817698	TCAA	CCAG	5200.69	synonymous_variant	LOW	FMAMFGPO_02674	c.33_36delTCAAinsCCAG	p.13
2817704	A	G	7832.96	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	7167.57	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2817734	G	A	100.131	synonymous_variant	LOW	FMAMFGPO_02674	c.69G>A	p.Leu23Leu
2817492	T	C	3979.9	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817764	G	A	6278.05	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	4133.73	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2817776	T	A	360.507	synonymous_variant	LOW	FMAMFGPO_02674	c.111T>A	p.Ala37Ala
2922391	A	C	838.182	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2817498	GT	AC	3727.51	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817509	AATCCGATAGG	GATCTGTTAGA	3476.41	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817527	TG	CG	3494.62	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817535	ACA	GTA	1639.4	upstream_gene_variant	MODIFIER	yciH	c.-4816_-4815delGTinsAC	
2817542	TGGGCAAAC	GGGGGAAAA	1692.1	upstream_gene_variant	MODIFIER	yciH	c.-4830_-4822delGTTTGCCCAinsTTTTCCCCC	
2817558	CTTTCATCTGTATT	GTCACACCTTCATC	1654.26	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGGTGTGAC	
2817597	GGCCA	GGCCG	6448.8	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
2817612	GATTGGTGTTGGGGGGCA	GATTGGAGTGAGGGGGGTA	4400.81	upstream_gene_variant	MODIFIER	yciH	c.-4909_-4898delTGCCCCCCAACAinsTACCCCCCTCACT	
3043888	AAAG	AAAT	149.148	synonymous_variant	LOW	FMAMFGPO_02877	c.36C>A	p.Ser12Ser
3043897	GGCGAGG	GGCCAGA	1061.68	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10
2817644	TCGCCGGACTACGTTAACCATA	TCGCCGCACTGCGTTAACGATG	4553.1	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4930delTATGGTTAACGTAGTCinsCATCGTTAACGCAGTG	
3065431	T	C	4969.55	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
3043936	CTAAG	CTACC	275.341	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	2699.85	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	2921.46	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr

Mutation(s) identified in genomes of the MV-resistant mutants (C10 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285153	T	C	1179.46	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCT	315.052	synonymous_variant	LOW	FMAMFGPO_00273	c.738_741delGGAGinsAGAA	p.248
285389	T	C	1465.96	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285417	TGCC	TGCT	2154.37	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285672	G	A	926.682	synonymous_variant	LOW	FMAMFGPO_00273	c.267C>T	p.His89His
285726	C	G	1504.95	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
285750	CTCC	TTCG,TTCC	3286.91	synonymous_variant	LOW	FMAMFGPO_00273	c.189G>A	p.Glu63Glu
285777	C	T	1072.42	synonymous_variant	LOW	FMAMFGPO_00273	c.162G>A	p.Leu54Leu
285827	AA	AG	169.676	synonymous_variant	LOW	FMAMFGPO_00273	c.111T>C	p.Ser37Ser
285846	C	G	57.9811	synonymous_variant	LOW	FMAMFGPO_00273	c.93G>C	p.Leu31Leu
512893	G	A	2373.53	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
967900	G	T	118.545	synonymous_variant	LOW	FMAMFGPO_00916	c.453C>A	p.Ala151Ala
967981	G	A	501.321	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly
968002	G	C	493.527	synonymous_variant	LOW	FMAMFGPO_00916	c.351C>G	p.Gly117Gly
1152737	C	A	4247.41	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1200306	C	A	44	missense_variant	MODERATE	FMAMFGPO_01135	c.599C>A	p.Pro200Gln
1211597	GATC	TAGA	2133.07	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	871.946	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	16325.2	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211656	AACGAATTT	AACAAACCG	12212.5	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	31215.4	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	7938.83	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211794	C	T	3879.63	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	3455.9	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1211860	CAGC	AATG	4711.63	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	3875.54	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser
1211874	ACAGAATC	ACAGAATT	5524.24	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211893	A	T	46.4323	synonymous_variant	LOW	FMAMFGPO_01145	c.528T>A	p.Ser176Ser
1211896	G	A	3844.87	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	4505.35	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	16799.4	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	7907.52	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	1319.08	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212076	GTGTAA	ATGCAC,ATGCAA	10333.1	missense_variant	MODERATE	FMAMFGPO_01145	c.340_345delTTACACinsGTGCAT	p.Leu114Val
1212090	CCACCTGA	TTAACTGA	463.046	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1212115	TAAA	CAAA	228.852	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212145	GACA	AACA	7783.7	synonymous_variant	LOW	FMAMFGPO_01145	c.276C>T	p.Val92Val
1212176	CGA	CGG	7423.37	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	1037.75	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	936.769	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	1756.14	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	19862.8	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	13273.7	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213743	AAGTCTAT	GGGTTTAA,GGGTCTAT	39979.1	missense_variant	MODERATE	FMAMFGPO_01147	c.67_68delAAinsGG	p.Lys23Gly
1213755	GA	AA	1373.42	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1455225	TCAGGTGG	CCAGTTGG	1587.41	missense_variant	MODERATE	FMAMFGPO_01386	c.324_328delTCAGGinsCCAGT	p.Val110Leu
1455444	CCTGCTGGCC	TCTGTTGTCG,TCTGCTATCC	7931.6	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1213793	G	A	1387.26	synonymous_variant	LOW	FMAMFGPO_01147	c.117G>A	p.Leu39Leu
1454925	TCTGGCC	TCTAGCT	6002.6	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1454940	T	C	373.45	synonymous_variant	LOW	FMAMFGPO_01386	c.39T>C	p.Phe13Phe
1455003	G	A	508.222	synonymous_variant	LOW	FMAMFGPO_01386	c.102G>A	p.Thr34Thr
1455087	G	C	7856.48	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	2735.19	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455108	T	C	3344.24	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly
1455147	TTTC	TTTT	3331.38	synonymous_variant	LOW	FMAMFGPO_01386	c.249C>T	p.Phe83Phe
1455159	AACG	GACA,GACG	24033.7	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	11659.3	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455183	CCTGAAA	TCTAAAA	2389.43	synonymous_variant	LOW	FMAMFGPO_01386	c.282_285delCCTGinsTCTA	p.96
1455459	GCTG	GATT	7964.88	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1455405	A	G	4414.35	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	5339.74	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455523	CG	GA	6989.41	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA,CT	6657.73	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455489	T	C	8378.15	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	2458.48	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAAACinsGGGGAAAT	p.Glu225_Leu232del
1763238	G	A	100.04	missense_variant	MODERATE	FMAMFGPO_01697	c.238G>A	p.Glu80Lys
1944928	C	T	2353.05	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>T	p.Arg115Cys
1455609	TCTGTTGAAA	CCTGTTGAAA	2925.37	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	2916.25	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	1891.39	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	1276.45	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	1074.36	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1763204	T	C	75.6735	synonymous_variant	LOW	FMAMFGPO_01697	c.204T>C	p.Phe68Phe
1970818	G	A	871.083	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1972196	C	A	1113.59	missense_variant	MODERATE	FMAMFGPO_01896	c.43C>A	p.Pro15Thr

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1970784	T	C	1643.69	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1972493	A	G	2657.06	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1972168	C	T	932.593	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala
1972708	G	A	1747.67	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972727	T	C	1641.97	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972516	C	T	1299.53	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	1753.16	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	1966.71	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972813	C	T	414.934	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2558293	C	T	2014.37	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2808916	A	G	122.56	missense_variant	MODERATE	dfa1	c.17T>C	p.Leu6Pro
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	11258	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2817746	GGCGGC	CGAAGT,GGAGGT	12463.9	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2558286	A	G	1965.53	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2922421	G	C	955.691	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2997876	G	A	745.49	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2998367	T	C	53.4564	missense_variant	MODERATE	FMAMFGPO_02834	c.559A>G	p.Ile187Val
2998425	TGG	CGT	198.208	missense_variant	MODERATE	FMAMFGPO_02834	c.499_501delCCAinsACG	p.Pro167Thr
2998658	C	T	779.02	missense_variant	MODERATE	FMAMFGPO_02834	c.268G>A	p.Val90Ile
2998688	C	T	3401.79	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998711	G	A	566.233	missense_variant	MODERATE	FMAMFGPO_02834	c.215C>T	p.Ser72Phe
2998753	T	C	1595.1	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	730.774	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met
2998822	C	T	473.452	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3096187	T	C	2200.44	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
3096875	CT	GC	717.813	missense_variant	MODERATE	FMAMFGPO_02927	c.488_489delCTinsGC	p.Ala163Gly
1213597	A	C	187.796	upstream_gene_variant	MODIFIER	deoC1	c.-4900T>G	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1213604	C	A	116.647	upstream_gene_variant	MODIFIER	deoC1	c.-4907G>T	
2383786	A	C	2671.64	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2817704	A	G	9341.14	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	8913.59	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2383794	T	C	2548.97	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2817764	G	A	7578.24	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	5794.41	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2817776	T	A	343.881	synonymous_variant	LOW	FMAMFGPO_02674	c.111T>A	p.Ala37Ala
2922391	A	C	1205.69	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2558324	C	T	1657.97	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	1529.78	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817492	T	C	5111.83	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817498	GT	AC	4351.87	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2998521	G	A	285.018	synonymous_variant	LOW	FMAMFGPO_02834	c.405C>T	p.Ala135Ala
2817509	AATCCGATAGG	GATCTGTTAGA	4280.65	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	TG	CG	4297.03	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817535	ACA	GTA	2486.59	upstream_gene_variant	MODIFIER	yciH	c.-4816_-4815delGTinsAC	
2817542	TGGGCAAAC	GGGGGAAAA	2514.41	upstream_gene_variant	MODIFIER	yciH	c.-4830_-4822delGTTTGCCCAinsTTTTCCCCC	
2817558	CTTTCATCTGTATT	GTCACACCTTCATC	2498.94	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGGTGTGAC	
2817597	GGCCA	GGCCG	8725.27	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
3043888	AAAG	AAAT	227.257	synonymous_variant	LOW	FMAMFGPO_02877	c.36C>A	p.Ser12Ser
3043897	GGCGAGG	GGCCAGA	2675.06	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10
2817612	GATTGGTGTTGGGGGGCA	GATTGGAGTGAGGGGGGTA	6445.7	upstream_gene_variant	MODIFIER	yciH	c.-4909_-4898delTGCCCCCCAACAinsTACCCCCCTCACT	

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
3065431	T	C	7204.19	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
2817644	TCGCCGGACTACGTTAACCATA	CCGTCGTACTGCTTTGACAATG,TCGCCGCACTGCGTTAACGATG	7235.88	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4924delTATGGTTAACGTAGTCCGGCGAinsCATTGTCAAAGCAGTACGACGG	
3043936	CTAAG	CTACC	1418.06	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	3901.22	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	1818.5	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr

Mutation(s) identified in genomes of the MV-resistant mutants (C14 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285153	T	C	2127.58	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285198	CTCC	TTCC	930.161	synonymous_variant	LOW	FMAMFGPO_00273	c.741G>A	p.Glu247Glu
285327	C	T	158.768	synonymous_variant	LOW	FMAMFGPO_00273	c.612G>A	p.Gln204Gln
285389	T	C	2482.27	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala
285417	TGCC	TGCT	3595.05	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285672	G	A	1125.74	synonymous_variant	LOW	FMAMFGPO_00273	c.267C>T	p.His89His
285726	C	G	999.071	synonymous_variant	LOW	FMAMFGPO_00273	c.213G>C	p.Arg71Arg
285777	C	T	987.019	synonymous_variant	LOW	FMAMFGPO_00273	c.162G>A	p.Leu54Leu
512893	G	A	3524.71	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
908675	TCCCCCCCCCCCAGT	TCCCCCCCCCCAGT	73.8294	frameshift_variant	HIGH	menH_2	c.276delG	p.Glu96fs
967981	G	A	329.187	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
968002	G	C	367.115	synonymous_variant	LOW	FMAMFGPO_00916	c.351C>G	p.Gly117Gly
1152737	C	A	5726.42	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1211597	GATC	TAGA	1977.94	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211601	A	G	783.236	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	18013.1	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211656	AACGAATTT	AACAAACCG	14899.8	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
1211692	CTCC	TTCC	39252.1	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	10831.8	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211794	C	T	5214.98	synonymous_variant	LOW	FMAMFGPO_01145	c.627G>A	p.Glu209Glu
1211821	G	A	6068.61	synonymous_variant	LOW	FMAMFGPO_01145	c.600C>T	p.Ser200Ser
1211860	CAGC	AATG	6929.89	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1211869	GGC	CGA	5940.82	missense_variant	MODERATE	FMAMFGPO_01145	c.550_552delGCCinsTCG	p.Ala184Ser
1211874	ACAGAATC	ACAGAATT	7781.85	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211896	G	A	6281.89	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	6180.08	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	22019	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	8579.97	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212064	CG	GA	3041.94	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212076	GTGTAA	ATGCAC,ATGCAA	11919.3	missense_variant	MODERATE	FMAMFGPO_01145	c.340_345delTTACACinsGTGCAT	p.Leu114Val
1212090	CCACCTGA	TTAACTGA	1653.98	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1212103	ATCC	GTCT	1044.79	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	1096.41	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212148	A	G	452.97	synonymous_variant	LOW	FMAMFGPO_01145	c.273T>C	p.Phe91Phe
1212172	GAAACGA	GAAACGG	7128.01	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	1082.74	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1212358	T	C	804.161	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1213678	T	A	2387.96	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	24950.1	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	16472.5	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213743	AAGTCTAT	GGGTTTAA,GGGTCTAT	46951.1	missense_variant	MODERATE	FMAMFGPO_01147	c.67_68delAAinsGG	p.Lys23Gly
1213755	GA	AA	746.566	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1455444	CCTGCTGGCC	TCTGTTGTCG,TCTGCTATCC	9633.01	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1455459	GCTG	GATT	9965.26	missense_variant	MODERATE	FMAMFGPO_01386	c.559_561delCTGinsATT	p.Leu187Ile
1213793	G	A	1694.33	synonymous_variant	LOW	FMAMFGPO_01147	c.117G>A	p.Leu39Leu
1454925	TCTGGCC	TCTAGCT	7245.13	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1455087	G	C	9990.44	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	2964.59	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455108	T	C	3442.31	synonymous_variant	LOW	FMAMFGPO_01386	c.207T>C	p.Gly69Gly
1455147	TTTC	TTTT	2904.41	synonymous_variant	LOW	FMAMFGPO_01386	c.249C>T	p.Phe83Phe
1455159	AACG	GACA,GACG	29725.6	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455174	CGTT	CGTG	14850.1	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>G	p.Val92Val
1455183	CCTGAAA	TCTAAAA	1997.75	synonymous_variant	LOW	FMAMFGPO_01386	c.282_285delCCTGinsTCTA	p.96
1455225	TCAGGTGG	TCAAGTGG	3735.49	synonymous_variant	LOW	FMAMFGPO_01386	c.327G>A	p.Gln109Gln
1455405	A	G	5834.12	synonymous_variant	LOW	FMAMFGPO_01386	c.504A>G	p.Lys168Lys
1455423	AACTTCT	AACTTCA	7211.88	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455489	T	C	10427.3	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455523	CG	GA	9003.27	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA,CT	9069.13	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	3101.86	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAACinsGGGGAAAT	p.Glu225_Leu232del
1763238	G	A	377.614	missense_variant	MODERATE	FMAMFGPO_01697	c.238G>A	p.Glu80Lys

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1944928	C	T	2361.72	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>T	p.Arg115Cys
1455609	TCTGTTGAAA	CCTGTTGAAA	3561.7	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	3379.46	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	2482.47	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	1705.75	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1455699	AAAT	GAAC	1167.89	synonymous_variant	LOW	FMAMFGPO_01386	c.798_801delAAATinsGAAC	p.268
1763204	T	C	189.195	synonymous_variant	LOW	FMAMFGPO_01697	c.204T>C	p.Phe68Phe
1970818	G	A	1490.24	missense_variant	MODERATE	FMAMFGPO_01894	c.238G>A	p.Glu80Lys
1972493	A	G	1642.27	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1970784	T	C	2910.58	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1972708	G	A	1138.34	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972168	C	T	22.3975	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala
1972727	T	C	970.97	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972516	C	T	654.898	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972533	GC	GT	1184.29	synonymous_variant	LOW	FMAMFGPO_01896	c.381C>T	p.Gly127Gly
1972665	G	A	1353.36	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
1972813	C	T	378.719	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser
2284284	T	G	28.0662	missense_variant	MODERATE	glcK	c.428T>G	p.Val143Gly
2558293	C	T	1258.74	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2817680	AATGAATCTCC	AATTAACCTAA,AATTAATCTGC	15159.4	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile
2817746	GGCGGC	CGAAGT,GGAGGT	16828.1	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2922421	G	C	1287.49	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2558286	A	G	1287.11	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2997876	G	A	377.924	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2998688	C	T	3859.9	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998753	T	C	1466.76	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998803	T	C	662.611	missense_variant	MODERATE	FMAMFGPO_02834	c.123A>G	p.Ile41Met

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2998822	C	T	332.463	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3096187	T	C	2747.7	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
3096875	CT	GC	1402.55	missense_variant	MODERATE	FMAMFGPO_02927	c.488_489delCTinsGC	p.Ala163Gly
1213597	A	C	377.007	upstream_gene_variant	MODIFIER	deoC1	c.-4900T>G	
1213604	C	A	218.751	upstream_gene_variant	MODIFIER	deoC1	c.-4907G>T	
2383786	A	C	3433.66	upstream_gene_variant	MODIFIER	rsmD	c.-1565A>C	
2383794	T	C	3166.71	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	1143.89	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	1050.51	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2817492	T	C	8543.46	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817704	A	G	11602.6	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	10624.9	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2817498	GT	AC	7680.34	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817764	G	A	9867.95	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	7967.28	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2922391	A	C	1594.64	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2817509	AATCCGATAGG	GATCTGTTAGA	7475.06	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	T	C	7923.11	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817535	ACA	GTA	3510.63	upstream_gene_variant	MODIFIER	yciH	c.-4816_-4815delGTinsAC	
2817542	TGGGCAAAC	GGGGGAAAA	3553.66	upstream_gene_variant	MODIFIER	yciH	c.-4830_-4822delGTTTGCCCAinsTTTTCCCCC	
2817558	CTTTCATCTGTATT	GTCACACCTTCATC	3515.38	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGGTGTGAC	
2817597	GGCCA	GGCCG	10581.8	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
3043888	AAAG	AAAT	616.82	synonymous_variant	LOW	FMAMFGPO_02877	c.36C>A	p.Ser12Ser
3043897	GGCGAGG	GGCCAGA	3085.96	synonymous_variant	LOW	FMAMFGPO_02877	c.24_27delCCTCinsTCTG	p.10

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
2817612	GATTGGTGTTGGGGGGCA	GATTGGAGTGAGGGGGGTA	8076.64	upstream_gene_variant	MODIFIER	yciH	c.-4909_-4898delTGCCCCCCAACAinsTACCCCCCTCACT	
3065431	T	C	10460.3	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
2817644	TCGCCGGACTACGTTAACCATA	CCGTCGTACTGCTTTGACAATG,TCGCCGCACTGCGTTAACGATG	9273.3	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4924delTATGGTTAACGTAGTCCGGCGAinsCATTGTCAAAGCAGTACGACGG	
3043936	CTAAG	CTACC	1364.51	upstream_gene_variant	MODIFIER	FMAMFGPO_02875	c.-1268_-1267delCTinsGG	
3095730	TAAGCCATCAATC	GAAACTATCCATG	5841.68	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348773	T	C	962.196	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr

Mutation(s) identified in genomes of the MV-resistant mutants (C21 strain).

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
42461	ATTTTTTTCTGC	ATTTTTTCTGC	21.4863	frameshift_variant	HIGH	yfiY_2	c.64delT	p.Ser22fs
88483	GCCACCG	GCACCG	21.0566	frameshift_variant	HIGH	cpcF	c.177delG	p.Ala60fs
103106	ATTTAAC	ATTAAC	46.8346	frameshift_variant	HIGH	FMAMFGPO_00092	c.2002delA	p.Lys668fs
118510	A	T	23.842	stop_gained	HIGH	lpd	c.1023T>A	p.Tyr341*
125774	G	A	22.9369	stop_gained	HIGH	sasA_1	c.670C>T	p.Gln224*
216028	G	A	22.9017	stop_gained	HIGH	lpxD_1	c.202C>T	p.Gln68*
223375	C	A	20.0472	missense_variant	MODERATE	FMAMFGPO_00210	c.262C>A	p.Leu88Met
240005	ACCCGT	ACCCCGT	20.0471	frameshift_variant	HIGH	FMAMFGPO_00224	c.142_143insG	p.Val49fs
285389	T	C	122.021	missense_variant	MODERATE	FMAMFGPO_00273	c.550A>G	p.Thr184Ala

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
285649	C	T	81.9412	missense_variant	MODERATE	FMAMFGPO_00273	c.290G>A	p.Arg97His
398734	T	C	21.0398	missense_variant	MODERATE	gloB	c.481A>G	p.Lys161Glu
434912	G	A	136.22	missense_variant	MODERATE	FMAMFGPO_00416	c.1247C>T	p.Ala416Val
561226	T	C	21.9614	missense_variant	MODERATE	FMAMFGPO_00531	c.433A>G	p.Ser145Gly
908675	TCCCCCCCCCCCAGT	TCCCCCCCCCCAGT	48.8858	frameshift_variant	HIGH	menH_2	c.276delG	p.Glu96fs
950522	G	T	23.842	stop_gained	HIGH	mshA_4	c.15C>A	p.Tyr5*
1022471	GTTTTTTTTCGG	GTTTTTTTTTCGG	24.218	frameshift_variant	HIGH	pcrA	c.2174_2175insA	p.Thr728fs
1100481	C	A	38.4526	missense_variant	MODERATE	FMAMFGPO_01046	c.1669G>T	p.Gly557Cys
1119469	ACCAA	ACCCAA	23.9503	frameshift_variant	HIGH	malP_2	c.2329dupC	p.Gln777fs
1158558	T	C	23.7224	missense_variant	MODERATE	uvrC_1	c.352A>G	p.Ile118Val
1211597	GATC	TAGA	47.5903	missense_variant	MODERATE	FMAMFGPO_01144	c.197_200delGATCinsTAGA	p.ArgSer66IleGlu
1211656	AACGAATTT	AACAAACCG	1666	missense_variant	MODERATE	FMAMFGPO_01145	c.757_762delAAATTCinsCGGTTT	p.Lys253Arg
154583	A	T	59.165	synonymous_variant	LOW	lptD_1	c.441A>T	p.Leu147Leu
285153	T	C	55.5224	synonymous_variant	LOW	FMAMFGPO_00273	c.786A>G	p.Gln262Gln
285420	C	T	325.969	synonymous_variant	LOW	FMAMFGPO_00273	c.519G>A	p.Ala173Ala
285606	T	C	21.0261	synonymous_variant	LOW	FMAMFGPO_00273	c.333A>G	p.Gly111Gly
285642	G	A	494.065	synonymous_variant	LOW	FMAMFGPO_00273	c.297C>T	p.Asn99Asn
285663	GACA	CACG	21.7862	synonymous_variant	LOW	FMAMFGPO_00273	c.273_276delTGTCinsCGTG	p.93
285747	AGGCTCC	AGGTTCC	144.921	synonymous_variant	LOW	FMAMFGPO_00273	c.189G>A	p.Glu63Glu
512893	G	A	312.958	synonymous_variant	LOW	recF_1	c.279G>A	p.Val93Val
835536	T	C	32.5265	synonymous_variant	LOW	rplF	c.264A>G	p.Glu88Glu
857909	C	A	538.912	synonymous_variant	LOW	rpoB	c.2958G>T	p.Arg986Arg
954942	A	G	58.2192	synonymous_variant	LOW	bfmBAB	c.486T>C	p.Ile162Ile
967891	G	A	23.5567	synonymous_variant	LOW	FMAMFGPO_00916	c.462C>T	p.Ser154Ser
967900	G	T	43.7508	synonymous_variant	LOW	FMAMFGPO_00916	c.453C>A	p.Ala151Ala
967981	G	A	58.9189	synonymous_variant	LOW	FMAMFGPO_00916	c.372C>T	p.Gly124Gly
968002	G	C	63.1786	synonymous_variant	LOW	FMAMFGPO_00916	c.351C>G	p.Gly117Gly

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1039597	T	C	20.0471	synonymous_variant	LOW	FMAMFGPO_00986	c.402T>C	p.Asn134Asn
1150008	G	T	32.5265	synonymous_variant	LOW	aat	c.60C>A	p.Ala20Ala
1152737	C	A	458.758	synonymous_variant	LOW	fabG	c.189C>A	p.Ala63Ala
1211601	A	G	31.7462	synonymous_variant	LOW	FMAMFGPO_01144	c.201A>G	p.Ser67Ser
1211644	ATTT	GTTC,ATTC	1741.22	synonymous_variant	LOW	FMAMFGPO_01145	c.774A>G	p.Gln258Gln
1211692	CTCC	TTCC	3167.35	synonymous_variant	LOW	FMAMFGPO_01145	c.729G>A	p.Glu243Glu
1211874	ACAGAATC	ACAGAATT	745.623	synonymous_variant	LOW	FMAMFGPO_01145	c.540G>A	p.Gly180Gly
1211893	A	T	130.801	synonymous_variant	LOW	FMAMFGPO_01145	c.528T>A	p.Ser176Ser
1211895	AG	AA	722.647	synonymous_variant	LOW	FMAMFGPO_01145	c.525C>T	p.Thr175Thr
1211917	C	T	736.644	synonymous_variant	LOW	FMAMFGPO_01145	c.504G>A	p.Lys168Lys
1212010	T	C	1996.46	synonymous_variant	LOW	FMAMFGPO_01145	c.411A>G	p.Leu137Leu
1212034	T	C	577.149	synonymous_variant	LOW	FMAMFGPO_01145	c.387A>G	p.Thr129Thr
1212103	ATCC	GTCT	26.0682	synonymous_variant	LOW	FMAMFGPO_01145	c.315_318delGGATinsAGAC	p.107
1212115	TAAA	CAAA	67.1459	synonymous_variant	LOW	FMAMFGPO_01145	c.306A>G	p.Leu102Leu
1212148	A	G	108.767	synonymous_variant	LOW	FMAMFGPO_01145	c.273T>C	p.Phe91Phe
1212160	A	C	73.7488	synonymous_variant	LOW	FMAMFGPO_01145	c.261T>G	p.Thr87Thr
1212172	GAAACGA	GAAACGG	472.467	synonymous_variant	LOW	FMAMFGPO_01145	c.243T>C	p.Arg81Arg
1212343	AATG	GATT	77.484	synonymous_variant	LOW	FMAMFGPO_01145	c.75_78delCATTinsAATC	p.27
1212358	T	C	134.834	synonymous_variant	LOW	FMAMFGPO_01145	c.63A>G	p.Leu21Leu
1421482	C	T	20.0472	synonymous_variant	LOW	FMAMFGPO_01359	c.543C>T	p.Ser181Ser
1454925	TCTGGCC	TCTAGCT	786.674	synonymous_variant	LOW	FMAMFGPO_01386	c.27_30delGGCCinsAGCT	p.11
1454940	T	C	68.4347	synonymous_variant	LOW	FMAMFGPO_01386	c.39T>C	p.Phe13Phe
1455066	TTTACATT	TTTACATC	2819.84	synonymous_variant	LOW	FMAMFGPO_01386	c.172T>C	p.Leu58Leu
1455087	G	C	355.783	synonymous_variant	LOW	FMAMFGPO_01386	c.186G>C	p.Thr62Thr
1455093	T	C	60.2729	synonymous_variant	LOW	FMAMFGPO_01386	c.192T>C	p.Pro64Pro
1455159	AACG	GACA,GACG	3515.92	synonymous_variant	LOW	FMAMFGPO_01386	c.258A>G	p.Lys86Lys
1455177	T	C,G	2687.54	synonymous_variant	LOW	FMAMFGPO_01386	c.276T>C	p.Val92Val

POSITION IN GENOME	REFERENCE	ALTERNATE	QUAL	TYPE OF MUTANT	LEVEL	GENE	BASE CHANGE	PROTEIN CHANGE
1455204	TTTA	CTTG	3034.59	synonymous_variant	LOW	FMAMFGPO_01386	c.303_306delTTTAinsCTTG	p.103
1455423	AACTTCT	AACTTCA	73.8161	synonymous_variant	LOW	FMAMFGPO_01386	c.528T>A	p.Ser176Ser
1455489	T	C	292.94	synonymous_variant	LOW	FMAMFGPO_01386	c.588T>C	p.Ile196Ile
1455609	TCTGTTGAAA	CCTGTTGAAA	163.186	synonymous_variant	LOW	FMAMFGPO_01386	c.708T>C	p.Pro236Pro
1455651	GGAG	AGAA	143.32	synonymous_variant	LOW	FMAMFGPO_01386	c.750_753delGGAGinsAGAA	p.252
1455675	A	G	134.626	synonymous_variant	LOW	FMAMFGPO_01386	c.774A>G	p.Leu258Leu
1455690	C	T	32.5347	synonymous_variant	LOW	FMAMFGPO_01386	c.789C>T	p.Val263Val
1561740	C	T	20.0471	synonymous_variant	LOW	FMAMFGPO_01484	c.48C>T	p.Val16Val
1650311	A	G	23.842	synonymous_variant	LOW	FMAMFGPO_01577	c.79T>C	p.Leu27Leu
1667435	A	G	29.1127	synonymous_variant	LOW	atpD	c.504A>G	p.Lys168Lys
1667454	T	C	27.904	synonymous_variant	LOW	atpD	c.523T>C	p.Leu175Leu
1667459	T	C	31.5409	synonymous_variant	LOW	atpD	c.528T>C	p.Ile176Ile
1682981	A	T	21.0767	synonymous_variant	LOW	yhfK	c.549T>A	p.Ala183Ala
1797984	A	G	472.627	synonymous_variant	LOW	potA	c.675T>C	p.Asp225Asp
1952144	A	G	20.24	synonymous_variant	LOW	FMAMFGPO_01876	c.2532A>G	p.Glu844Glu
1970600	CG	CA	278.149	synonymous_variant	LOW	FMAMFGPO_01894	c.21G>A	p.Ala7Ala
1970784	T	C	59.1019	synonymous_variant	LOW	FMAMFGPO_01894	c.204T>C	p.Phe68Phe
1972168	C	T	139.344	synonymous_variant	LOW	FMAMFGPO_01896	c.15C>T	p.Ala5Ala
1972516	C	T	565.174	synonymous_variant	LOW	FMAMFGPO_01896	c.363C>T	p.Ile121Ile
1972665	G	A	776.657	synonymous_variant	LOW	FMAMFGPO_01897	c.57G>A	p.Arg19Arg
2322984	C	T	52.5315	synonymous_variant	LOW	tolB_1	c.1644G>A	p.Ala548Ala
2374477	C	T	20.0536	synonymous_variant	LOW	FMAMFGPO_02243	c.312G>A	p.Leu104Leu
2385479	C	T	51.59	synonymous_variant	LOW	rsmD	c.129C>T	p.Asp43Asp
2467706	A	G	671.877	synonymous_variant	LOW	clpC	c.1167T>C	p.Asp389Asp
2502997	G	T	22.0794	synonymous_variant	LOW	mtgA_2	c.882C>A	p.Gly294Gly
2558286	A	G	957.362	synonymous_variant	LOW	FMAMFGPO_02422	c.1473A>G	p.Pro491Pro
2660273	GGCC	CGCG,CGCC	857.599	synonymous_variant	LOW	glyQ	c.369G>C	p.Gly123Gly

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2678376	A	T	21.9614	synonymous_variant	LOW	metG	c.237A>T	p.Val79Val
2715492	G	A	23.842	synonymous_variant	LOW	carB_2	c.1125C>T	p.Asn375Asn
2817698	TCAA	CCAG	591.229	synonymous_variant	LOW	FMAMFGPO_02674	c.33_36delTCAAinsCCAG	p.13
2817704	A	G	1284.51	synonymous_variant	LOW	FMAMFGPO_02674	c.39A>G	p.Lys13Lys
2817713	T	C	827.158	synonymous_variant	LOW	FMAMFGPO_02674	c.48T>C	p.Gly16Gly
2817732	TTGTCC	TTATCC	277.719	synonymous_variant	LOW	FMAMFGPO_02674	c.69G>A	p.Leu23Leu
2817764	G	A	1272.77	synonymous_variant	LOW	FMAMFGPO_02674	c.99G>A	p.Glu33Glu
2817773	A	G	409.686	synonymous_variant	LOW	FMAMFGPO_02674	c.108A>G	p.Gln36Gln
2817776	T	A	226.644	synonymous_variant	LOW	FMAMFGPO_02674	c.111T>A	p.Ala37Ala
2922391	A	C	66.5832	synonymous_variant	LOW	FMAMFGPO_02765	c.732A>C	p.Thr244Thr
2998521	G	A	147.166	synonymous_variant	LOW	FMAMFGPO_02834	c.405C>T	p.Ala135Ala
3065431	T	C	527.145	synonymous_variant	LOW	tcrA_2	c.180A>G	p.Ser60Ser
3348773	T	C	514.727	synonymous_variant	LOW	acnB	c.84T>C	p.Thr28Thr
3348816	GAG	GAA	473.218	synonymous_variant	LOW	acnB	c.129G>A	p.Glu43Glu
3348861	GAC	GAT	420.5	synonymous_variant	LOW	acnB	c.174C>T	p.Asp58Asp
1211751	GTTTCGCCTCCAGCCTACCT	ATTTTCCC	1590.15	missense_variant&disruptive inframe deletion	MODERATE	FMAMFGPO_01145	c.651_670delAGGTAGGCTGGAGGCGAAACinsGGGAAAAT	p.Arg219_Ala222del
1211860	CAGC	AATG	707.435	missense_variant	MODERATE	FMAMFGPO_01145	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1212064	CG	GA	215.969	missense_variant	MODERATE	FMAMFGPO_01145	c.356_357delCGinsTC	p.Ala119Val
1212090	CCACCTGA	TTAACTGA	81.2886	missense_variant	MODERATE	FMAMFGPO_01145	c.328_331delGTGGinsTTAA	p.ValGly110LeuArg
1213678	T	A	237.672	start_lost	HIGH	FMAMFGPO_01147	c.2T>A	p.Met1?
1213701	CAGT	TGGC,TGGT	2120.17	missense_variant	MODERATE	FMAMFGPO_01147	c.25_26delCAinsTG	p.Gln9Trp
1213707	CTGGTG	CTGATA,CTGATG	1283.57	missense_variant	MODERATE	FMAMFGPO_01147	c.34G>A	p.Val12Met
1213755	GA	AA	216.312	missense_variant	MODERATE	FMAMFGPO_01147	c.79G>A	p.Asp27Asn
1249094	C	T	32.5265	stop_gained	HIGH	FMAMFGPO_01189	c.811C>T	p.Gln271*
1266755	A	C	20.0471	missense_variant	MODERATE	gyrB	c.804T>G	p.Asp268Glu

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1267537	C	T	60.1096	missense_variant	MODERATE	gyrB	c.22G>A	p.Ala8Thr
1319856	T	C	60.1096	missense_variant	MODERATE	FMAMFGPO_01254	c.686A>G	p.Asp229Gly
1373455	C	T	31.5824	missense_variant	MODERATE	mutS	c.1637G>A	p.Arg546Gln
1441801	A	G	39.3945	missense_variant	MODERATE	rcsC_12	c.2246T>C	p.Leu749Pro
1455444	CCTGCTGGCC	TCTGTTGTCG,TCTGCTATCC	521.062	missense_variant	MODERATE	FMAMFGPO_01386	c.543_550delCCTGCTGGinsTCTGCTAT	p.Ala184Ser
1455459	GCTG	GATT,CATT	402.083	missense_variant	MODERATE	FMAMFGPO_01386	c.558_561delGCTGinsCATT	p.GluLeu186AspIle
1455523	CG	GA	305.129	missense_variant	MODERATE	FMAMFGPO_01386	c.622_623delCGinsGA	p.Arg208Glu
1455543	TT	CA,CT	511.32	missense_variant	MODERATE	FMAMFGPO_01386	c.642_643delTTinsCA	p.Leu215Ile
1455555	CAAACTGGAAGGGAAACTAGAGGGTCGGCTCGAGGGAAAAC	CAAACTGGAGGGGAAAT	121.085	disruptive inframe deletion&synonymous_variant	MODERATE	FMAMFGPO_01386	c.663_694delAGGGAAACTAGAGGGTCGGCTCGAGGGAAACinsGGGGAAAT	p.Glu225_Leu232del
1574393	T	A	60.1096	missense_variant	MODERATE	rcsC_14	c.1545T>A	p.Asp515Glu
1667441	AAT	CAA	20.6918	missense_variant	MODERATE	atpD	c.510_512delAATinsCAA	p.Ile171Asn
1708644	A	T	20.0472	missense_variant	MODERATE	lnt	c.1328A>T	p.Asp443Val
1712857	CGGGCA	CGGGGCA	20.0472	frameshift_variant	HIGH	rpe	c.396_397insC	p.Val134fs
1744011	T	A	20.0471	missense_variant	MODERATE	cysE	c.569T>A	p.Val190Glu
1763123	A	G	81.4211	missense_variant	MODERATE	FMAMFGPO_01697	c.123A>G	p.Ile41Met
1799197	ATTAC	ATAC	32.5265	frameshift_variant	HIGH	mqnB	c.396delT	p.Thr133fs
1827608	G	A	30.6373	missense_variant	MODERATE	FMAMFGPO_01757	c.352G>A	p.Ala118Thr
1847690	A	T	20.0471	missense_variant	MODERATE	FMAMFGPO_01779	c.552T>A	p.Phe184Leu
1873634	T	C	32.5265	missense_variant	MODERATE	tilS	c.979T>C	p.Tyr327His
1944928	C	T	426.809	missense_variant	MODERATE	FMAMFGPO_01873	c.343C>T	p.Arg115Cys
1972196	C	A	280.116	missense_variant	MODERATE	FMAMFGPO_01896	c.43C>A	p.Pro15Thr
1972493	A	G	447.384	missense_variant	MODERATE	FMAMFGPO_01896	c.340A>G	p.Arg114Gly
1972708	G	A	569.484	missense_variant	MODERATE	FMAMFGPO_01897	c.100G>A	p.Gly34Arg
1972727	T	C	524.326	missense_variant	MODERATE	FMAMFGPO_01897	c.119T>C	p.Val40Ala
1972813	C	T	138.144	missense_variant	MODERATE	FMAMFGPO_01897	c.205C>T	p.Pro69Ser

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2025305	A	G	23.8955	missense_variant	MODERATE	rlmB_2	c.313A>G	p.Lys105Glu
2033278	CGTGA	AGTCGA	36.586	frameshift_variant&missense_variant	HIGH	arnC_4	c.842_846delTCACGinsTCGACT	p.Thr282fs
2052148	TGGGGGGGGGAGCCGGC	TGGGGGGGGAGCCGGC	20.1047	frameshift_variant	HIGH	FMAMFGPO_01976	c.1149delC	p.Pro386fs
2116886	C	A	20.0471	missense_variant	MODERATE	FMAMFGPO_02031	c.427G>T	p.Ala143Ser
2127133	T	A	45.8849	missense_variant	MODERATE	FMAMFGPO_02040	c.457A>T	p.Thr153Ser
2154245	ACCCCGA	ACCCCCGA	20.2229	frameshift_variant	HIGH	FMAMFGPO_02070	c.45dupC	p.Glu16fs
2233442	T	A	20.0825	missense_variant	MODERATE	exoA	c.423A>T	p.Leu141Phe
2264058	G	A	23.8669	missense_variant	MODERATE	lipB	c.232G>A	p.Gly78Arg
2284348	G	T	20.0474	missense_variant	MODERATE	glcK	c.492G>T	p.Leu164Phe
2285540	T	C	20.0493	missense_variant	MODERATE	FMAMFGPO_02182	c.458A>G	p.Gln153Arg
2309220	G	A	22.9017	missense_variant	MODERATE	FMAMFGPO_02206	c.152C>T	p.Ala51Val
2338219	T	C	24.9691	missense_variant	MODERATE	FMAMFGPO_02228	c.232A>G	p.Ile78Val
2361471	G	A	20.0825	missense_variant	MODERATE	FMAMFGPO_02238	c.1015G>A	p.Gly339Arg
2380931	G	A	23.9061	missense_variant	MODERATE	FMAMFGPO_02248	c.1951G>A	p.Asp651Asn
2431282	C	G	23.8464	missense_variant	MODERATE	FMAMFGPO_02304	c.191C>G	p.Pro64Arg
2467726	A	T	555.75	missense_variant	MODERATE	clpC	c.1147T>A	p.Ser383Thr
2552500	A	G	20.0472	missense_variant	MODERATE	FMAMFGPO_02416	c.463T>C	p.Tyr155His
2558293	C	T	1002.77	missense_variant	MODERATE	FMAMFGPO_02422	c.1480C>T	p.Arg494Trp
2562188	GTTTTATTTGA	GTTTATTTGA	20.0472	frameshift_variant	HIGH	rsbQ	c.137delT	p.Leu46fs
2564021	G	C	23.8518	missense_variant	MODERATE	FMAMFGPO_02427	c.1069G>C	p.Gly357Arg
2575721	T	C	20.1742	missense_variant	MODERATE	ilvH	c.142A>G	p.Met48Val
2660259	TCCCCAACC	TCGCCGACG,AACCCGACG	566.811	missense_variant	MODERATE	glyQ	c.355_363delTCCCCAACCinsAACCCGACG	p.Ser119Asn
2714818	G	C	662.808	missense_variant	MODERATE	carB_2	c.1799C>G	p.Ser600Cys
2727596	C	A	23.842	missense_variant	MODERATE	clsB	c.550C>A	p.Leu184Ile
2749723	G	T	23.01	missense_variant	MODERATE	FMAMFGPO_02610	c.494G>T	p.Trp165Leu
2817680	AATGAATCTCC	AATTAATCTGC	756.936	missense_variant	MODERATE	FMAMFGPO_02674	c.18_24delGAATCTCinsTAATCTG	p.Met6Ile

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2817746	GGCGGC	CGAAGT,GGAGGT	1809.9	missense_variant	MODERATE	FMAMFGPO_02674	c.81_86delGGCGGCinsCGAAGT	p.AlaAla28GluVal
2841541	G	T	22.9017	missense_variant	MODERATE	dnaB	c.1585G>T	p.Ala529Ser
2882897	TG	GT	24.8372	missense_variant	MODERATE	FMAMFGPO_02730	c.1520_1521delTGinsGT	p.Leu507Arg
2922421	G	C	45.0374	missense_variant	MODERATE	FMAMFGPO_02765	c.762G>C	p.Met254Ile
2990852	A	T	60.1096	missense_variant	MODERATE	sasA_14	c.1047T>A	p.Phe349Leu
2997876	G	A	308.019	missense_variant	MODERATE	FMAMFGPO_02833	c.205C>T	p.Pro69Ser
2998493	G	T	90.5913	missense_variant	MODERATE	FMAMFGPO_02834	c.433C>A	p.Pro145Thr
2998658	C	T	229.109	missense_variant	MODERATE	FMAMFGPO_02834	c.268G>A	p.Val90Ile
2998688	C	T	248.706	missense_variant	MODERATE	FMAMFGPO_02834	c.238G>A	p.Glu80Lys
2998711	G	A	144.828	missense_variant	MODERATE	FMAMFGPO_02834	c.215C>T	p.Ser72Phe
2998753	T	C	94.9943	missense_variant	MODERATE	FMAMFGPO_02834	c.173A>G	p.Glu58Gly
2998822	C	T	25.1508	missense_variant	MODERATE	FMAMFGPO_02834	c.104G>A	p.Arg35Lys
3062783	A	G	20.0471	missense_variant	MODERATE	ziaA	c.1427A>G	p.Gln476Arg
3096187	T	C	211.616	missense_variant	MODERATE	FMAMFGPO_02926	c.140T>C	p.Ile47Thr
3151457	T	A	33.855	missense_variant	MODERATE	FMAMFGPO_02972	c.521A>T	p.Asp174Val
3159498	A	G	54.4348	missense_variant	MODERATE	mgsA	c.1154T>C	p.Val385Ala
3257297	C	T	29.067	missense_variant	MODERATE	FMAMFGPO_03064	c.2699C>T	p.Ala900Val
3268649	A	G	23.842	missense_variant	MODERATE	ndhI	c.319T>C	p.Phe107Leu
3277803	T	A	32.5265	stop_gained	HIGH	FMAMFGPO_03083	c.121A>T	p.Lys41*
3486734	A	G	20.1527	missense_variant	MODERATE	ftsA_2	c.3178T>C	p.Cys1060Arg
3520794	G	A	20.0485	stop_gained	HIGH	prfA	c.901C>T	p.Gln301*
462732	C	T	20.0471	upstream_gene_variant	MODIFIER	FMAMFGPO_00436	c.-3875G>A	
810781	C	T	23.842	upstream_gene_variant	MODIFIER	pacL_1	c.-4397G>A	
1022056	C	G	21.6629	upstream_gene_variant	MODIFIER	rsmH	c.-3554G>C	
1046839	C	T	20.0471	upstream_gene_variant	MODIFIER	bfd	c.-2146G>A	
1412176	TGGGCT	TGGCT	36.6744	upstream_gene_variant	MODIFIER	FMAMFGPO_01346	c.-2665delC	
1454889	TTAGAATT	TTAGTAAAATT	419.555	upstream_gene_variant	MODIFIER	FMAMFGPO_01382	c.-2375_-2374insTTA	

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1596723	A	T	20.0477	upstream_gene_variant	MODIFIER	plsX	c.-72A>T	
1619767	G	C	588.247	upstream_gene_variant	MODIFIER	FMAMFGPO_01535	c.-1954C>G	
1619789	TGGAC	CGGAT,GGGAT	2529.08	upstream_gene_variant	MODIFIER	FMAMFGPO_01535	c.-1980_-1976delGTCCAinsATCCG	
1619803	T	C,G	2431.55	upstream_gene_variant	MODIFIER	FMAMFGPO_01535	c.-1990A>G	
1619812	C	T	264.539	upstream_gene_variant	MODIFIER	FMAMFGPO_01535	c.-1999G>A	
2325741	T	G	20.0476	upstream_gene_variant	MODIFIER	tolB_1	c.-1114A>C	
2383794	T	C	21.9948	upstream_gene_variant	MODIFIER	rsmD	c.-1557T>C	
2558324	C	T	825.396	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4536G>A	
2558332	A	G	785.493	upstream_gene_variant	MODIFIER	FMAMFGPO_02418	c.-4544T>C	
2604781	T	A	28.365	upstream_gene_variant	MODIFIER	guaD	c.-4290A>T	
2817492	T	C,G	559.229	upstream_gene_variant	MODIFIER	yciH	c.-4772A>G	
2817498	GT	AC,GC	517.623	upstream_gene_variant	MODIFIER	yciH	c.-4779_-4778delACinsGT	
2817509	AATCCGATAGG	GATCTGTTAGA	219.403	upstream_gene_variant	MODIFIER	yciH	c.-4799_-4789delCCTATCGGATTinsTCTAACAGATC	
2817527	TG	CG	193.48	upstream_gene_variant	MODIFIER	yciH	c.-4807A>G	
2817542	TGGGCAAAC	GGGGCAAAC	108.236	upstream_gene_variant	MODIFIER	yciH	c.-4822A>C	
2817558	CTTTCATCTGTATT	GTCCCATCTTCATC	110.082	upstream_gene_variant	MODIFIER	yciH	c.-4851_-4838delAATACAGATGAAAGinsGATGAAGATGGGAC	
2817597	GGCCA	GGCCG	843.701	upstream_gene_variant	MODIFIER	yciH	c.-4881T>C	
2817644	TCGCCGGACTACGTTAACCATA	TCGCCGCACTGCGTTAACGATG	624.809	upstream_gene_variant	MODIFIER	yciH	c.-4945_-4930delTATGGTTAACGTAGTCinsCATCGTTAACGCAGTG	
2984931	ATCG	GTCT	109.612	upstream_gene_variant	MODIFIER	FMAMFGPO_02817	c.-3967_-3964delCGATinsAGAC	
2984939	A	T	21.3151	upstream_gene_variant	MODIFIER	FMAMFGPO_02817	c.-3972T>A	
3095730	TAAGCCATCAATC	GAAACTATCCATG	535.788	upstream_gene_variant	MODIFIER	FMAMFGPO_02923	c.-1897_-1885delGATTGATGGCTTAinsCATGGATAGTTTC	
3348682	ACCATCCC	ACCGTCCT	559.305	upstream_gene_variant	MODIFIER	FMAMFGPO_03142	c.-2910_-	

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							2906delGGGATinsAGGAC	
3369655	C	T	60.1096	upstream_gene_variant	MODIFIER	cugP_3	c.-3858G>A	
3404308	G	T	21.1946	upstream_gene_variant	MODIFIER	walK	c.-3958C>A	

Growth of 7 selected MV-resistant mutant and wild type under absence and presence of MV

	Day1		Day3		Day5		Day7		Day9		Day11		Day13		Day15	
Strain	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD
WT	0.1618	0.0206	0.2937	0.0159	0.3699	0.0362	0.4353	0.0261	0.4977	0.0301	0.6032	0.0366	0.5741	0.0377	0.488235	0.0325
WT PQ	0.1099	0.0163	0.0707	0.0072	0.1067	0.0365	0.0830	0.0263	0.0543	0.0011	0.0637	0.0013	0.0636	0.0102	0.036477	0.0038
9A	0.1586	0.0198	0.2899	0.0287	0.3575	0.0514	0.4353	0.0551	0.4960	0.0504	0.6012	0.0613	0.5678	0.0479	0.485454	0.0482
9A PQ	0.1510	0.0168	0.2731	0.0068	0.3208	0.0304	0.3744	0.0037	0.4553	0.0313	0.5516	0.0381	0.4903	0.0193	0.422418	0.0142
11A	0.1717	0.0100	0.3049	0.0164	0.3624	0.0208	0.4372	0.0066	0.5093	0.0073	0.6173	0.0089	0.5760	0.0064	0.490398	0.0042
11A PQ	0.1653	0.0239	0.2739	0.0221	0.3057	0.0366	0.3336	0.0377	0.3474	0.0510	0.4203	0.0621	0.4047	0.0632	0.342233	0.0459
1B	0.1596	0.0187	0.2911	0.0263	0.3564	0.0368	0.4477	0.0244	0.4953	0.0271	0.6003	0.0330	0.5797	0.0355	0.488699	0.0397
1B PQ	0.1574	0.0091	0.2536	0.0352	0.2817	0.0384	0.3229	0.0078	0.3518	0.0164	0.4257	0.0200	0.4199	0.0312	0.341769	0.0207
14B	0.1685	0.0130	0.3049	0.0152	0.3448	0.0084	0.4614	0.0220	0.5126	0.0088	0.6213	0.0107	0.6180	0.0480	0.518672	0.0385
14B PQ	0.1564	0.0472	0.2821	0.0147	0.2850	0.0144	0.3471	0.0381	0.4007	0.0341	0.4852	0.0415	0.4496	0.0450	0.387038	0.0294
10C	0.1478	0.0149	0.2922	0.0243	0.3510	0.0522	0.4292	0.0463	0.5063	0.0388	0.6136	0.0472	0.5929	0.0381	0.50523	0.0241
10C PQ	0.1513	0.0227	0.2585	0.0215	0.3365	0.0161	0.3777	0.0300	0.4669	0.0377	0.5657	0.0458	0.5023	0.0215	0.418092	0.0148
14C	0.1685	0.0049	0.2765	0.0059	0.3624	0.0082	0.4171	0.0019	0.5259	0.0368	0.6375	0.0448	0.5700	0.0126	0.480356	0.0028
14C PQ	0.1698	0.0019	0.2177	0.0659	0.2820	0.0584	0.3172	0.0974	0.3795	0.1411	0.4594	0.1717	0.4379	0.1086	0.367262	0.0740
21C	0.1876	0.0136	0.3012	0.0000	0.3877	0.0182	0.4636	0.0276	0.5680	0.0630	0.6888	0.0767	0.6058	0.0273	0.522071	0.0184
21C PQ	0.1863	0.0161	0.2735	0.0084	0.3518	0.0259	0.3952	0.0146	0.4532	0.0103	0.5490	0.0125	0.5033	0.0184	0.416084	0.0017

Oxygen-gas evolution of wild type (WT) and the MV-resistant mutants (clones 9A-21C) under the absence of presence of MV.

Day	No	Strain	Average	Error bar
Day1	1	10C1		
	2	10C2		
	3	10C3	4.26	0.99
	4	10C PQ1		
	5	10C PQ2		
	6	10C PQ3	8.31	1.63
	7	14C1		
	8	14C2		
	9	14C3	11.34	2.28
	10	14C1 PQ1		
	11	14C2 PQ2		
	12	14C3 PQ3	13.75	3.18
	13	21C1		
	14	21C2		
	15	21C3	10.12	2.54
	16	21C1 PQ1		
	17	21C2 PQ2		
	18	21C3 PQ3	3.29	1.03
	19	WT1		
	20	WT2		
	21	WT3	10.19	0.77
	22	WT1 PQ1		
	23	WT2 PQ2		
	24	WT3 PQ3	0	0
	25	9A1		
	26	9A2		
	27	9A3	11.13	0.88
	28	9A1 PQ1		
	29	9A2 PQ2		
	30	9A3 PQ3	8.75	1.51
	31	14B1		
	32	14B2		
	33	14B3	23.31	1.06
	34	14B1 PQ1		
	35	14B2 PQ2		
	36	14B3 PQ3	8.59	1.14

Day	No	Strain	Average	Error bar
Day7	37	10C1		
	38	10C2		
	39	10C3	9.46	0.97
	40	10C PQ1		
	41	10C PQ2		
	42	10C PQ3	10.03	1.47
	43	14C1		
	44	14C2		
	45	14C3	9.50	0.49
	46	14C1 PQ1		
	47	14C2 PQ2		
	48	14C3 PQ3	10.63	1.79
	49	21C1		
	50	21C2		
	51	21C3	10.36	4.04
	52	21C1 PQ1		
	53	21C2 PQ2		
	54	21C3 PQ3	9.27	0.45
	55	WT1		
	56	WT2		
	57	WT3	13.99	1.69
	58	WT1 PQ1		
	59	WT2 PQ2		
	60	WT3 PQ3	0.00	0
	61	9A1		
	62	9A2		
	63	9A3	24.20	1.21
	64	9A1 PQ1		
	65	9A2 PQ2		
	66	9A3 PQ3	24.12	2.29
	67	14B1		
	68	14B2		
	69	14B3	12.24	1.57
	70	14B1 PQ1		
	71	14B2 PQ2		
	72	14B3 PQ3	21.37	1.36

Day	No	Strain	Average	Error bar
Day 14	73	10C1		
	74	10C2		
	75	10C3	7.38	0.35
	76	10C PQ1		
	77	10C PQ2		
	78	10C PQ3	7.59	1.19
	79	14C1		
	80	14C2		
	81	14C3	5.97	0.47
	82	14C1 PQ1		
	83	14C2 PQ2		
	84	14C3 PQ3	6.95	0.66
	85	21C1		
	86	21C2		
	87	21C3	5.48	0.31
	88	21C1 PQ1		
	89	21C2 PQ2		
	90	21C3 PQ3	5.09	0.20
	91	WT1		
	92	WT2		
	93	WT3	8.13	1.39
	94	WT1 PQ1		
	95	WT2 PQ2		
	96	WT3 PQ3	0.00	0.00
	97	9A1		
	98	9A2		
	99	9A3	9.24	1.76
	100	9A1 PQ1		
	101	9A2 PQ2		
	102	9A3 PQ3	9.23	1.14
	103	14B1		
	104	14B2		
	105	14B3	8.85	1.61
	106	14B1 PQ1		
	107	14B2 PQ2		
	108	14B3 PQ3	7.86	0.90

Growth under osmotic stress of *Synechocystis* sp. PCC 6803 wild type and the MV-resistant mutants

		Day1		Day3		Day5		Day7		Day9		Day11		Day13		Day15	
	Strain	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD
BG-11	WT	0.210	0.063	0.427	0.015	0.624	0.044	0.932	0.066	1.004	0.056	1.004	0.075877	1.045	0.070713	1.473	0.068
	9A	0.242	0.014	0.371	0.003	0.552	0.025	0.848	0.034	0.919	0.028	0.951	0.026438	0.989	0.023106	1.380	0.081
	14B	0.216	0.007	0.400	0.014	0.586	0.021	0.955	0.037	0.945	0.077	0.987	0.014297	1.002	0.035888	1.461	0.068
	10C	0.253	0.013	0.449	0.028	0.653	0.029	1.003	0.044	1.039	0.062	1.121	0.062176	1.078	0.041892	1.525	0.061
	14C	0.243	0.003	0.424	0.014	0.631	0.012	0.887	0.099	0.961	0.056	0.998	0.14051	1.024	0.127999	1.431	0.133
	21C	0.234	0.009	0.434	0.008	0.662	0.052	0.922	0.035	1.019	0.029	1.086	0.050518	1.039	0.015789	1.570	0.033
Sorb	WT	0.248	0.011	0.255	0.019	0.354	0.028	0.284	0.070	0.327	0.060	0.471	0.26194	0.330	0.032633	0.495	0.140
	9A	0.226	0.010	0.195	0.014	0.180	0.009	0.155	0.044	0.160	0.034	0.177	0.095123	0.193	0.017841	0.150	0.029
	14B	0.212	0.004	0.256	0.022	0.191	0.067	0.115	0.035	0.245	0.078	0.145	0.084499	0.209	0.05588	0.330	0.199
	10C	0.244	0.014	0.157	0.017	0.131	0.018	0.088	0.064	0.189	0.046	0.116	0.032538	0.195	0.044024	0.202	0.164
	14C	0.248	0.006	0.272	0.012	0.289	0.071	0.166	0.059	0.217	0.070	0.207	0.088758	0.287	0.121032	0.332	0.234
	21C	0.244	0.008	0.178	0.013	0.235	0.168	0.179	0.120	0.300	0.197	0.259	0.103027	0.253	0.093326	0.274	0.153
NaCl	WT	0.219	0.018	0.222	0.007	0.299	0.017	0.411	0.022	0.539	0.022	0.684	0.055968	0.675	0.047837	0.998	0.050
	9A	0.199	0.020	0.148	0.000	0.134	0.004	0.078	0.009	0.151	0.008	0.153	0.01036	0.200	0.040211	0.388	0.027
	14B	0.217	0.004	0.227	0.005	0.371	0.014	0.503	0.049	0.638	0.045	0.720	0.023558	0.720	0.044984	1.039	0.054
	10C	0.222	0.011	0.193	0.002	0.213	0.004	0.239	0.045	0.351	0.034	0.483	0.034727	0.528	0.052843	0.831	0.052
	14C	0.229	0.011	0.219	0.003	0.246	0.007	0.333	0.030	0.464	0.014	0.577	0.048375	0.571	0.101747	0.869	0.121
	21C	0.216	0.020	0.228	0.009	0.282	0.016	0.381	0.029	0.507	0.053	0.659	0.017176	0.694	0.038595	1.005	0.014

Growth under oxidative stress of *Synechocystis* sp. PCC 6803 wild type and the MV-resistant mutants

		Day1		Day3		Day5		Day7		Day9		Day11		Day13		Day15	
	Strain	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD	Av OD	STD OD
CuSO4	WT	0.247	0.012	0.437	0.013	0.789	0.027	1.023	0.009	1.052	0.010	1.122	0.015475	1.126	0.014172	1.534	0.016
	9A	0.243	0.005	0.351	0.045	0.551	0.075	0.785	0.042	0.855	0.081	0.909	0.038936	1.040	0.041389	1.363	0.068
	14B	0.238	0.009	0.422	0.007	0.675	0.045	0.959	0.027	0.975	0.012	1.043	0.027761	1.082	0.015944	1.459	0.018
	10C	0.242	0.023	0.476	0.026	0.737	0.028	1.016	0.081	1.044	0.045	1.093	0.038631	1.109	0.01999	1.526	0.027
	14C	0.252	0.004	0.438	0.045	0.613	0.014	0.941	0.046	0.990	0.062	1.036	0.075524	1.115	0.063429	1.487	0.082
	21C	0.275	0.009	0.467	0.028	0.702	0.074	0.963	0.063	0.981	0.065	1.068	0.042232	1.117	0.083235	1.454	0.075
H2O2	WT	0.268	0.018	0.402	0.034	0.533	0.049	0.893	0.094	0.959	0.084	1.038	0.10158	1.107	0.071095	1.477	0.063
	9A	0.228	0.004	0.152	0.014	0.154	0.042	0.163	0.057	0.130	0.049	0.134	0.047888	0.159	0.03619	0.109	0.058
	14B	0.220	0.005	0.182	0.027	0.128	0.029	0.209	0.050	0.167	0.051	0.134	0.031579	0.186	0.042009	0.138	0.024
	10C	0.238	0.026	0.180	0.026	0.149	0.015	0.247	0.169	0.330	0.187	0.524	0.179322	0.668	0.221547	0.960	0.214
	14C	0.216	0.010	0.246	0.048	0.368	0.039	0.592	0.048	0.693	0.078	0.798	0.082005	0.953	0.117927	1.277	0.142
	21C	0.231	0.015	0.250	0.012	0.377	0.009	0.647	0.044	0.702	0.047	0.840	0.093942	0.939	0.054496	1.267	0.078

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