

Article

# Modulation of the MEP Pathway for Overproduction of 13-R-manoxyl Oxide in Cyanobacteria

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## Supplementary Information

**1 - 80**

ScGGPPS -----MEAKI

SjGGPPS -----MVAQTFNLDTYLSQRQQQV

PbGGPPS MRSMLVDAWVQNLPIFKQPHPSKFIHHPRFEPAFLKSRRPISSFAVSAVLTGEARIFTRGDEAPFNAYVVEKATHV

**81- 160**

ScGGPPS DELINNDPVWSSQNESLISKPYNHILLKPGKNFRLNLIVQINRVMNLPKDQLAIVSQIVELLHNSSLIDDI--EDNAPL

SjGGPPS EEALS--AALVPAYPERIYEAMRYSLLAGGKRLRPLCLAAACELAGGSVEQAMPTACALEEMIHTMSLIHDDLPAMDNDDF

PbGGPPS NKALD--DAVAVKNNPPMIHEAMRYSLLAGGKRVRPMLCIAACEVVGGPQAAAIPACAVEMIHTMSLIHDDLPCMDNDL

**161 - 240**

ScGGPPS RRGQTTSHLIEGVPSINTANYMYFRAMQLVSQITTKPEPLYHNLTIF--NE--ELINLHRGQQLDIYWRDLEPEDIPTQ

SjGGPPS RRGKPTNHKVFGEDIAILAGDALLAYAFEHIASQTRGVPPQLVLQVIARIGHAVAATGLVGGQVVDLESEGK--AISL--

PbGGPPS RRGKPTNHKVFGENVAVLAGDALLAFAFEFIATAATTGVAPERILA AAVAEELAKAIGTEGLVAGQVVDLHCTGN-PNVGL--

**241 - 320**

ScGGPPS EMYLNMVNMKTGGLFRTLRLMEALS PSSHGHSLVPFINLLGTYQ RDDYLNLKDFQMSSEKGFAEDITEGKLSFPI

SjGGPPS ETLEYIHSHKTGALLEASVVSGGILAGADEELLARLSHYARDIGLAFTQVDDILDVVTATSEQLGKTAGKDQAAAKATYP

PbGGPPS DTLEFIHHKTAALLEASVVLGAIDGGGSSDQVEKLRTFARKIGLLFQVVDDILDVTKSSEELGKTAGKD LAVDKTTYPK

**321 - 400**

ScGGPPS VHALNFTTKCQTEQHNEILRILLIRTSOKDKIKLKLQILEFDTN--SLAYTKNFINQLVNMIKNDNENKYLPDLASHS

SjGGPPS LLGLEASRQKAEE--LIQSAK-----EALRPYG-SQAEPPLLALADFITRRQH-----

PbGGPPS LLGLEKAMEFAER--LNEEAK-----QQLLDFPRKAAPLVALADYIAHRQN-----

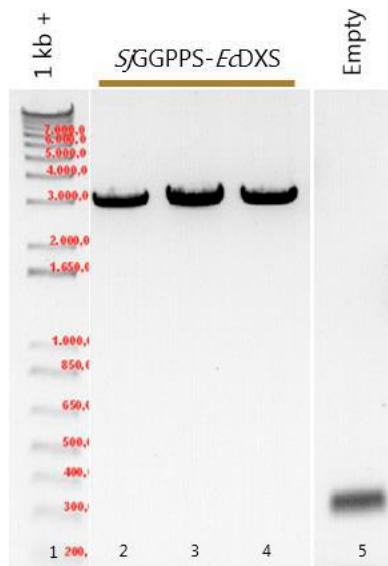
**401 - 420**

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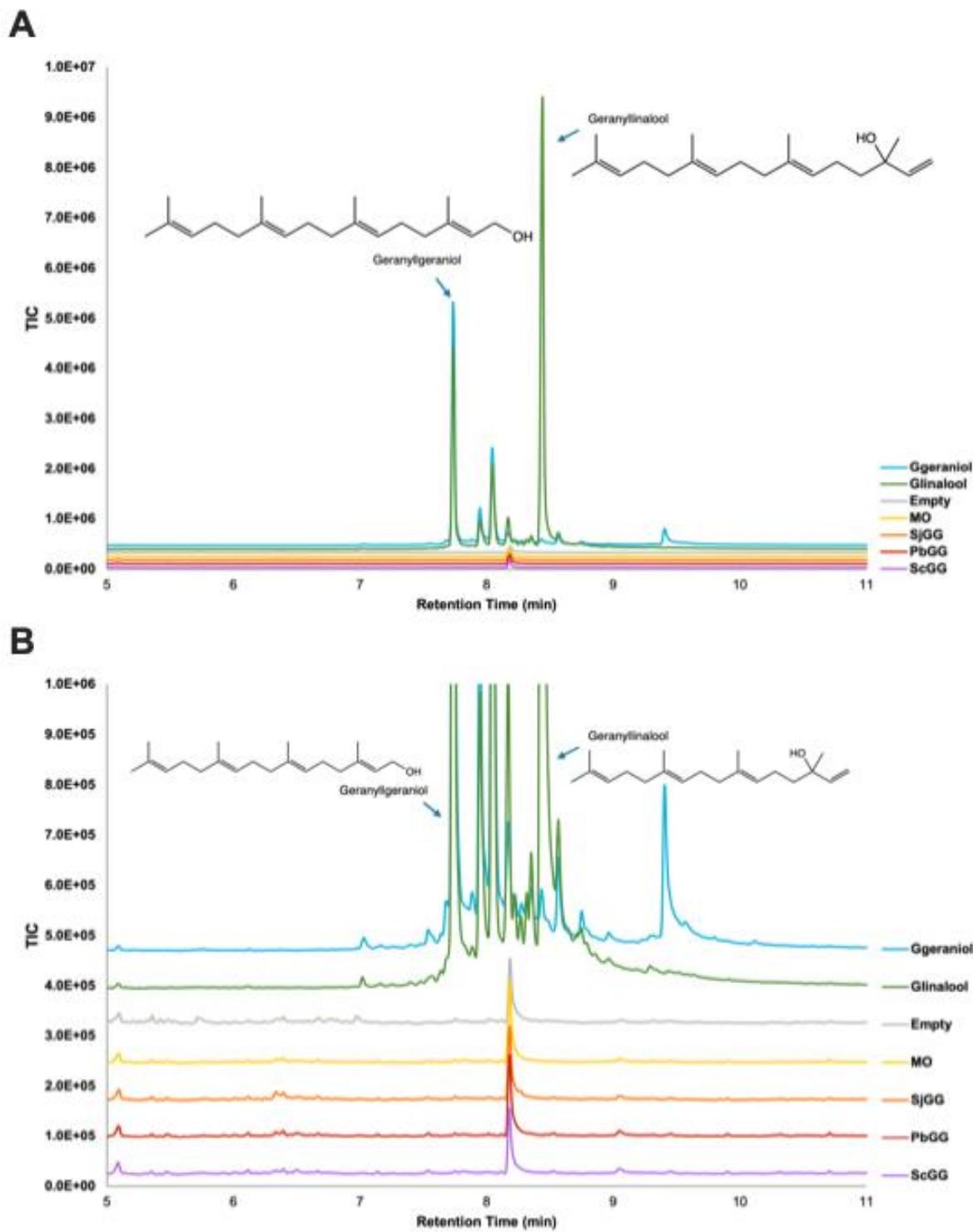
SjGGPPS -----

PbGGPPS -----

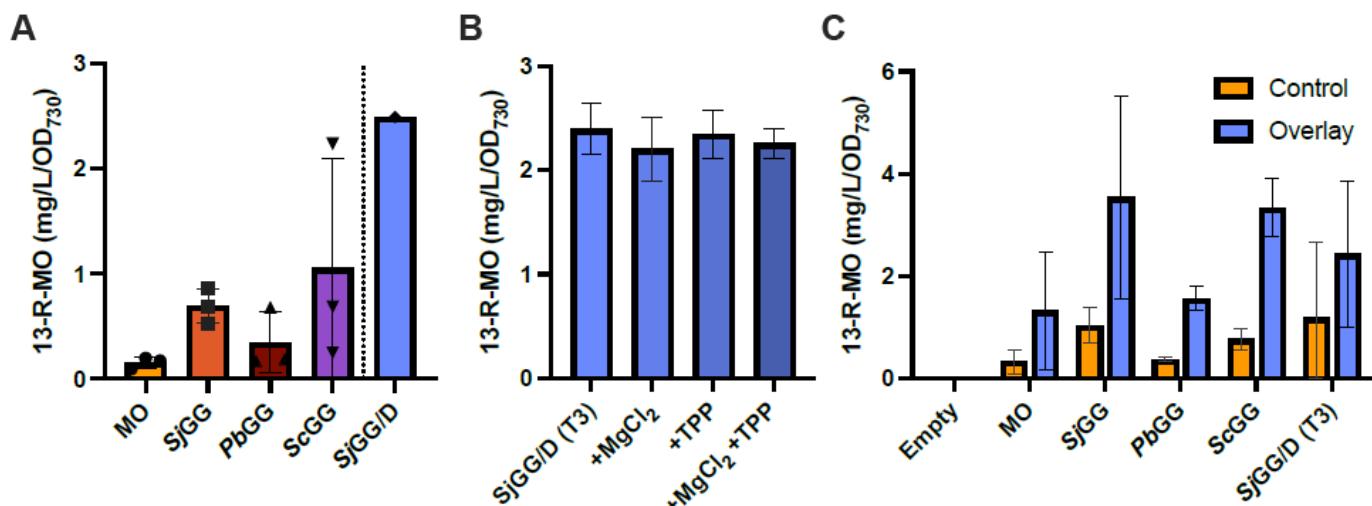
**Figure S1.** Alignment of GGDPSS used in this study.



**Figure S2. Colony PCR of SjGG/D transformants (T1-T3). A)** Colony PCR of the *SjGGPPS-EcDXS* operon and flanking regions. Lane 1: 1kb+ ladder, lane 2-4: Amplicon of *SjGGPPS-EcDXS* and flanking regions on pDF-trc (T1-T3) (expected band size: 2950 bp), land 5: amplicon of flanking regions on empty pDF-trc vector (expected band size: 215 bp).



**Figure S3. Side product analysis.** **A)** Supernatant extractions of cell cultures, Empty (with no TPSs or GGPPs), MO, *SjGG*, *PbGG* and *ScGG*, compared to authentic geranylgeraniol (Ggeraniol) and geranylinalool (Glinalool) standards. The constituent eluting at approximately 8.3 min is 1-eicosene, the internal standard. **B)** Enhanced view of the same chromatograms for better visualization of the cell supernatants.



**Figure S4. Titters of 13-R-MO normalized to OD<sub>730</sub>.** (A) Corresponding to Fig. 3A; (B) Corresponding to Fig. 3B and C) Corresponding to Fig 4A.

**Table S1.** Constructs used in this study. Homology to the genome and the plasmid backbone are truncated for brevity.

### Homology or Backbone

Promoter

CDS

Terminator

Antibiotic Cassette

## 1. TPS Integrative Construct

1160 bp homology – promoter – TPS2- TPS3 – terminator – kanamycinR – 1115 bp homology

**CCCGTCTGGTCAATATCCCTGGCAAAGTTAAATAATCTCGCATCAGCAATGGCTAGGGACTCTGACTAATCCCATGGCTAAACTCCTGTCAACGTAATGCATGCCGCTTCGCGCACCTGTAGAGAAAGAGTCCCTGAATATCAAAATGGTGGGATAAAAAGCTCAAAAAGGAAAGTAGGCTGTGGTCCCTAGGCAACAGTCTCCCTACCCCCACTGGAAACTAAAAAAACGAGAAAAGTTCGCACCGAACATCAATTGCATAATTTAGCCCTAAAACATAAGCTGAACGAAACTGGTTGTCTCCCTTCCAATCCAGGACAATCTGAGAATCCCTGCAACATTACTTAACAAAAAGCAGGAATAAAATAACAAAGATGTAACAGACATAAGTCCCACCGTTGTATAAAAGTTAACTGTGGGATTGCAAAAGCATTCAAGCCTAGGCGCTGAGCTGTTGAGCATCCCGTGGCCCTGTCGCTGCCTCCGTGTTCTCCCTGGATTATTAGGTAAATATCTCTCATAAATCCCCGGTAGTTAACGAAAGTTAATGGAGATCAGTAACAATAACTCTAGGGTCATTACTTGACTCCCTCAGTTATCCGGGGAAATTGTTTAAGAAAATCCCAACTCATAAAGTCAGTAGGAGATTAAATCAATGGAATTCCCTCGAGCTAGAAATGAGCCGTGTGGCCTCTCTGGATGCCCTAAATGGGATTCAAAAAGTGGGACCCGCTACTATTGGGACCCCCGAAGAAGAAAACAAGAAGATTGAAGATAGTATTGAATACGTGAAAGAAATTGTTAAAACATGGGGATGGACGTATTCCGTGAGTCCCTACGACACCGCTATTGTTGCCTTGATTAAAGATTAGAAGGGCGGTGACCTGAAAGAAAACGTTCATAAATTGAAAGACGGAAAATTGAACACATGCCGCTGGTTGAATTGTGGTCCCGCACCTTAGAACCGGCTAAAGCCCTGGGATTAAAGGATTGCCCTATGATGACCCCTTATTCGCGAAATTACAGTGCCAAACAAACCCGTTGACTAAAATTCCAAAGGGATGATTATGAATCCCCCACCAGTCTGTTACTCCTAGATGCCCTGGAAAGGTTGGAATGGACAAAATTGAAATTACAAAGCGCTGATGGCTCTTTATTACCTCCGTGTCAGTACTGCCCTTGTGGACAGCTGGGGAGTGCCCATACCTATCCCCTGATATTGCTCGTTATGGCCGTTGACCGGTTACAACGCCCTGGGGATTCCCGGTTTTCGAACCCGAAATTAAACTTGTGATGGCATATTAAACAACGTGTGGCGTAAAAAGGAGTTTAGCTCTCGGCACAGTCAGTTGCCGATATTGATGACACCAGCATGGGATTCGCTTACTGAAAATGCATGGATATAATGTGAACCCCCAATGCCCTGGAACACTTAAACAAAAAGATGGTAAATTACCTGTTACGCCGACCAGCATATTGAAAGCCCCTCTCCCATGTATAATTGTACCGGGCGCTCAATTACGCTTCCCGGGAAAGAAATTCTGCAACAGGCTTGCAGTTGCCATAATTCTGCATGAAAACCTGCCCTCTAATCACTTCAAGAAAAATGGGTGATTCCGATCTTGATTGACGAAGTTCGGATTGGCTTAAAATGCCCTGTTATGCTACAGTCAACACTACGGCGGTTCCAGTGATGTTGGATTGGTAAAACCTTGTATCGTATGCCGAAATTCCAACGATAACCTACAAAATTGGCTCAACTGGACTTTAACAAATGCCAACGCCAGCATCAATTAGAATGGATGTCTATGAAAGAATGGTACGTCCAACACGTGAAAGAATTGGCATTAGTAAAAAGAATTGCTGCTGCCACTTTGGCCGCTGCCACCATGTTGAACCCGAACGTACTCAAGAACGGATTATGTGGGCCAAAACCCAGGTTGTTAGTCGGATGATTACTAGCTTTAAACAAAGAAAACCCATGTCTTTGATCTGAAATTGCCCTGTTAACACTCAGCCCCAACATCAGATTAACGGGAGCGAAATGAAAAATGGATTGCCCAAACCTTACCCGCTGCCCTTCGCCAGCTGTTGAAAGAATTGATAAAATACCCGCCATCAATTACGTAACACTTGGAAATAATGGCTGATGAAATTGAAACAGGGCGATGACAATGGGGAGCTGATGCCGAATTACTGGCTAACACCTTAAATATTGTGCCGTCATAACGAAGACATTG**

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GTGAAATGTTCCCTGACCACCCCCACCGACTGATGGCAAAATTAAAGAAGTGTAAACCGG  
GAAGTGGATAACCTCCCCGCCGTATGACCACTCATCCACTGATATTCCCAGTAACCTGTGTA  
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## 2. pDF-trc-SjGGPPS

Backbone-SjGGDPS- Backbone

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CTTGTAGGTTGGAAAGCCAGTCGGAAAAAGCCGAAGAATTGATTCAATCCGCAAAGAAGC  
CTTACCCCCCTATGGGAGTCAAGCCGAACCTTGTAGCCTTAGCCGATTATTACCCGTCGG  
CAACATTATCCCTATGATGTGCCGATTATGCCTAA**TGGCTTTGGCGGATGAGAGAAGATT**  
**TTCAGCCTGATACAGATTAAATCAGAACGCAGAACCGG**

## 3. pDF-trc-PbGGDPS

Backbone-PbGGDPS- Backbone

**TTGACAATTAATCATCCGGCTCGTATAATGTGTGGAATTGTGAGCGGATAACAATTACACAGG**  
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TTATCCCTATGATGTGCCGATTATGCCTAA**TGGCTTTGGCGGATGAGAGAAGATTTCAGC**  
**CTGATACAGATTAAATCAGAACGCAGAACCGG**

## 4. pDF-trc-ScGGPPS

Backbone-ScGGDPS- Backbone

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### 5. pDF-trc-SjGGPPS-DXS\*

Backbone-SjGGDPS-EcDXS\*-Backbone

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CA GATCAAATCAGAACGCAGAACGCGG

