**Supporting Information:**

**Table S1.** Result summary of genome analysis of C. coralloides DSM2259 genome (NCBI accession # CP003389) with antiSMASH. NP = natural product, bp = base pairs, DB = database

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cluster ID | NP class | bpstart | bpend | # bp | Predicted BGC | sequence similarity [%] | DB BGC | Origin of DB BGC |
| 1 | Terpene | 913,294 | 930,557 | 17,263 | carotenoid | 100 | BGC0000648 | *Myxococcus xanthus* |
| 2 | T1 PKS-NRPS | 1,032,294 | 1,080,211 | 47,917 | - | - | - | - |
| 3 | Terpene | 2,119,082 | 2,141,484 | 22,402 | - | - | - | - |
| 4 | T1 PKS-NRPS | 2,428,410 | 2,482,711 | 54,301 | chloromyxamide | 13 | BGC0001945 | *Myxococcus sp.* |
| 5 | T1 PKS | 2,606,636 | 2,651,986 | 45,350 | chloromyxamide | 27 | BGC0001945 | *Myxococcus sp.* |
| 6 | NRPS | 2,816,735 | 2,882,770 | 66,035 | - | - | - | - |
| 7 | RiPP-like | 3,013,876 | 3,022,723 | 8,847 | - | - | - | - |
| 8 | T1 PKS-NRPS | 3,103,725 | 3,257,110 | 153,385 | - | - | - | - |
| 9 | NRPS, T1PKS | 3,442,275 | 3,494,934 | 52,659 | BE-43547A1/ BE-43547A2… | 10 | BGC0001330 | *Micromonospora sp. RV43* |
| 10 | lanthipeptide | 4,030,200 | 4,051,486 | 21,286 | - | - | - | - |
| 11 | T1 PKS-NRPS | 4,186,913 | 4,241,185 | 54,272 | - | - | - | - |
| 12 | T1 PKS-NRPS | 4,412,963 | 4,485,151 | 72,188 | - | - | - | - |
| 13 | lanthipeptide | 4,529,903 | 4,551,241 | 21,338 | - | - | - | - |
| 14 | RiPP-like | 4,746,094 | 4,757,661 | 11,567 | - | - | - | - |
| 15 | NRPS | 4,857,415 | 4,924,895 | 67,480 | - | - | - | - |
| 16 | lanthipeptide | 5,052,309 | 5,073,083 | 20,774 | - | - | - | - |
| 17 | T1 PKS-NRPS | 5,209,355 | 5,345,413 | 136,058 | myxoprincomide | 66 | BGC0000393 | *Myxococcus xanthus* |
| 18 | T1 PKS-NRPS | 5,481,949 | 5,577,500 | 95,551 | myxochelin A/ B | 86 | BGC00001345 | *Stigmatella aurantiaca* |
| 19 | NRPS | 5,625,043 | 5,674,634 | 49,591 | - | - | - | - |
| 20 | RiPP-like | 5,680,374 | 5,690,671 | 10,297 | - | - | - | - |
| 21 | RiPP-like, LAP, thiopeptide | 5,825,525 | 5,852,242 | 26,717 | ficellomycin | 5 | BGC0001593 | *Streptomyces ficellus* |
| 22 | T1 PKS | 6,407,278 | 6,448,051 | 40,773 | puwainaphycin A/ B / C / D | 30 | BGC0001125 | *Cylindrospermum alatosporum* CCALA 988 |
| 23 | lanthipeptide | 6,566,995 | 6,592,859 | 25,864 | - | - | - | - |
| 24 | terpene | 6,928,334 | 6,945,580 | 17,246 | - | - | - | - |
| 25 | thiopeptide | 7,099,821 | 7,138,262 | 38,441 | - | - | - | - |
| 26 | T1 PKS-NRPS | 7,184,802 | 7,246,797 | 61,995 | rakicidin A / B | 22 | BGC0001327 | *Micromonospora purpureochromogenes* |
| 27 | NRPS, arylpolyene | 7,341,187 | 7,422,939 | 81,752 | APE-Ec | 36 | BGC0000836 | *Escherichia coli* CFT073 |
| 28 | lanthipeptide | 7,528,620 | 7,551,841 | 23,221 | - | - | - | - |
| 29 | butyrolactone | 8,181,142 | 8,191,966 | 10,824 | - | - | - | - |
| 30 | phenazine | 8,386,250 | 8,406,681 | 20,431 | streptobactin | 11 | BGC0000368 | *Streptomyces sp.* ATCC 700974 |
| 31 | T3 PKS | 9,028,261 | 9,069,358 | 41,097 | alkylpyrone-407/ alkylpyrone-393 | 34 | BGC0001964 | *Cystobacterineae bacterium* |
| 32 | terpene | 9,239,314 | 9,261,572 | 22,258 | geosmin | 100 | BGC0000661 | *Nostoc punctiforme* PCC 73102 |
| 33 | RiPP-like, RRE-containing | 9,512,033 | 9,533,635 | 21,602 | - |  |  |  |

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**Figure S1.** Inoculation plan for SD plate with added cell pellets. White = control and blank, grey = univariate experiments, black = bivariate experiments.

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**Figure S2.** Inoculation plan for SD plate with added supernatants. White = control and blank, grey = univariate experiments, black = bivariate experiments.

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**Figure S3.** Inoculation plan for SD plate with added organic solvents. White = control and blank, grey = univariate experiments, black = bivariate experiments.

**Table S2.** List of chemicals, chemical formulae, and supplier. Chemicals were used in the purest form available.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Chemical** | **Chemical formula** | **Supplier** | **Chemical** | **Chemical formula** | **Supplier** |
| BactoPeptone | - | Beckto Dickinson | magnesium sulfate heptahydrate | MgSO4 x 7 H2O | Carl Roth |
| meat extract | - | Fluka | dipotassium-phosphate | K2HPO4 | Carl Roth |
| raffinose D(+) pentahydrate | C18H32O16 x 5 H2O | Sigma Aldrich | calcium chloride dihydrate | CaCl2 x 2 H2O | Carl Roth |
| sucrose D(+) | C12H22O11 | Carl Roth | vitamin B12 | C63H88CoN14O14P | Carl Roth |
| galactose D(+) | C6H12O6 | Carl Roth | EDTA | C10H16N2O8 | Carl Roth |
| soluble starch | (C6H10O5)n | Carl Roth | iron (II) sulfate heptahydrate | FeSO4 x 7 H2O | Carl Roth |
| BactoCasitone | - | Beckto Dickinson | zinc sulfate heptahydrate | ZnSO4 x 7 H2O | AppliChem |
| boric Acid | H3BO3 | Carl Roth | manganese (II) cloride tetrahydrate | MnCl2 x 4 H2O | Carl Roth |
| cobalt (II) chloride hexahydrate | CoCl2 x 6 H2O | Carl Roth | copper (II) chloride dihydrate | CuCl2 x 2 H2O | Carl Roth |
| nickel (II) chloride dihydrate | NiCl2 x 6 H2O | Alfa Aesar | sodium molybdate dihydrate | MoNa2O4 x 2 H2O | Carl Roth |
| sodium chloride | NaCl | Carl Roth | D (+) glucose | C6H12O6 | Carl Roth |
| malt extract | - | Carl Roth | Bacto yeast extract | - | Beckto Dickinson |
| potassium dihydrogen phosphate | KH2PO4 | Carl Roth | sodium nitrate | NaNO3 | Carl Roth |
| manganese (II) sulfate hydrate | MnSO4 x H2O | Carl Roth | thiamine-HCl | C12H17ClN4OS x HCl | Carl Roth |
| ethyl acetate | C4H8O2 | VWR | L-proline | C5H9NO2 | Carl Roth |
| acetonitrile | C2H3N | Carl Roth | disodium hydrogen phosphate | Na2HPO4 x 2 H2O | AppliChem |
| toluene | C7H8 | Fisher Scientific | ammonium chloride | NH4Cl | Carl Roth |
| methanol | CH4O | Carl Roth |  |  |  |

**Table S3.** Steps and settings used for raw data processing in MZmine 2.35.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input** | **Step** | **Settings** | **Output** |
| raw data, mzXML-format | Peak Detection -> Mass Detection | MS level: 1Mass Detector: CentroidNoise level: 1.0E4  | mass list |
| mass list | Peak Detection -> Chromatogram Builder | MS level: 1Min time span: 0.01 minMin height: 3.0E4m/z tolerance: 0.0 m/z or 20 ppm | peak lists, suffix:chromatograms |

**Table S4.** Steps and settings used for peak list processing in MZmine 2.35.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input** | **Step** | **Settings** | **Output** |
| peak lists, suffix:chromatograms | Peak Detection -> Chromatogram Deconvolution | Algorithm: Baseline cut-off | peak lists, suffix:chromatograms deconvoluted |
| peak lists, suffix:chromatograms deconvoluted | Isotopes -> Isotopic peaks grouper | m/z tolerance: 0.0 m/z or 20 ppmRT tolerance: 0.1 minMaximum charge: 3Representative isotope: lowest m/z | peak lists, suffix:chromatograms deconvoluted deisotoped |
| peak lists, suffix:chromatograms deconvoluted deisotoped | Alignment -> Join Aligner | m/z tolerance: 0.0 m/z or 20 ppmWeight for m/z: 75RT tolerance: 0.1 minWeight for RT: 25 | aligned peak list |
| aligned peak list | Filtering -> Peak list rows filter | Minimum peaks in a row: 2remove rows that match all criteria | aligned peak list, suffix:filtered |
| aligned peak list, suffix:filtered | Filtering -> Peak list rows filter | RT: 1.0-11.0 minkeep rows that match all criteria | aligned peak list, suffix:filtered filtered |

**Table S5.** List of control groups and background samples for each univariate experiment with C. coralloides. The control group for all univariate experiments was C. coralloides grown on SP medium without any additives.

|  |  |
| --- | --- |
| **Univariate Experiments** | **Background samples to be subtracted** |
| SP medium + PBa | SP medium and extracted PBa |
| SP medium + PSg | SP medium and extracted PSg |
| SP medium + SupBa | SP medium and extracted SupBa |
| SP medium + SupSg | SP medium and extracted SupSg |
| SP medium + 1% v/v Tol | SP medium with 1% v/v toluene |
| SP medium + 3% v/v ACN | SP medium with 3% v/v acetonitrile |
| M9 medium | M9 medium |
| MD1 medium | MD1 medium |
| GMS medium | GMS medium |
| GMS FeX medium | GMS FeX medium |

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|  |  |  |  |
| --- | --- | --- | --- |
| **Bivariate Experiments** | **Background samples to be subtracted** | **Univariate condition 1: additive (to be subtracted)** | **Univariate condition 2: medium (to be subtracted)** |
| M9 medium + PSg | M9 medium andextracted PSg | Cc on SP medium + PSg | Cc on M9 medium |
| M9 medium + PBa | M9 medium andextracted PBa | Cc on SP medium + PBa | Cc on M9 medium |
| GMS FeX medium + PSg | GMS FeX medium and extracted PSg | Cc on SP medium + PSg | Cc on GMS FeX medium |
| GMS FeX medium + PBa | GMS FeX mediumand extracted PBa | Cc on SP medium + PBa | Cc on GMS FeX medium |
| M9 medium + SupSg | M9 mediumand extracted SupSg | Cc on SP medium + SupSg | Cc on M9 medium |
| M9 medium + SupBa | M9 medium andextracted SupBa | Cc on SP medium + SupBa | Cc on M9 medium |
| GMS medium + SupSg | GMS medium andextracted SupSg | Cc on SP medium + SupSg | Cc on GMS medium |
| GMS medium + SupBa | GMS medium andextracted SupBa | Cc on SP medium + SupBa | Cc on GMS medium |
| M9 medium + 1% v/v Tol | M9 medium with 1% v/v Tol | Cc on SP medium + 1% v/v Tol | Cc on M9 medium |
| M9 medium + 3% v/v ACN | M9 medium with 3% v/v ACN | Cc on SP medium + 3% v/v ACN | Cc on M9 medium |
| MD1 medium + 1% v/v Tol | MD1 medium with 1% v/v Tol | Cc on SP medium + 1% v/v Tol | Cc on MD1 medium |
| MD1 medium + 3% v/v ACN | MD1 medium with 3% v/v ACN | Cc on SP medium + 3% v/v ACN | Cc on MD1 medium |

**Table S6.** List of background samples and univariate samples for each bivariate experiment with C. coralloides (Cc). The control group for all bivariate experiments was C. coralloides grown on SP medium without any additives. A combined background sample was used for the experiments with organic solvents, i.e., the solvent (acetonitrile (ACN) or toluene (Tol)) was directly added to the respective medium which was then extracted.

**Table S7.** New mass features from univariate OSMAC experiments and culture conditions under which they were produced. # p.c. = number of producing conditions. PBa = B. amyloliquefaciens pellet, SupBa = B. amyloliquefaciens supernatant, PSg = S. griseochromogenes pellet, SupSg = S. griseochromogenes supernatant, ACN = acetonitrile, Tol = toluene. If adduct forms are not indicated, they could not be determined based on the obtained mass spectra.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Mass feature ID | m/z [-] | tR [min] | # p.c. | univariate producing conditions |
| MF1 | 470.22 [M+H]+ | 6.23 | 1 | M9 medium |
| MF2 | 875.57 [M+H]+ | 11.04 | 2 | M9 medium, GMS medium |
| MF4 | 306.26 [M+H]+ | 5.51 | 2 | M9 medium, GMS medium |
| MF6 | 449.20 [M+H]+ | 6.64 | 1 | SupSg |
| MF8 | 272.16 [M+H]+ | 4.65 | 1 | SupSg |
| MF39 | 170.06 [M+H-H2O]+ | 8.39 | 2 | GMS medium, SupBa |
| MF54 | 295.15 [M+H]+ | 7.99 | 2 | PBa, SupBa |
| MF107 | 290.27 [M+H]+ | 5.39 | 1 | M9 medium |
| MF120 | 164.11 [M+H]+ | 5.31 | 2 | SupBa, SupSg |
| MF127 | 269.16 [M+H]+ | 5.04 | 1 | SupBa |
| MF128 | 227.16 [M+H]+ | 5.64 | 1 | SupBa |
| MF129 | 422.22 | 7.84 | 1 | SupBa |
| MF133 | 288.25 [M+H]+ | 5.42 | 1 | SupBa |
| MF153 | 396.46 | 10.35 | 1 | M9 medium |
| MF197 | 227.16 [M+H]+ | 5.56 | 1 | MD1 medium |
| MF198 | 252.16 [M+H]+ | 5.95 | 1 | ACN |
| MF199 | 359.27 [M+H]+ | 8.43 | 1 | MD1 medium |
| MF202 | 313.14 [M+Na]+ | 8.02 | 1 | Tol |

**Table S8.** New mass features from bivariate OSMAC experiments and culture condition sets under which they were produced. # p.c. = number of producing conditions. PBa = B. amyloliquefaciens pellet, SupBa = B. amyloliquefaciens supernatant, PSg = S. griseochromogenes pellet, SupSg = S. griseochromogenes supernatant, ACN = acetonitrile, Tol = toluene. If adduct forms are not indicated, they could not be determined based on the obtained mass spectra.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Mass feature ID | m/z [-] | tR [min] | # p.c. | Producing conditions |
| CcSD10 | 366.29 | 7.75 | 1 | GMS FeX + PBa |
| CcSD56 | 292.22 | 7.55 | 2 | M9 + PBa, M9 + SupBa |
| CcSD57 | 230.21[M+H]+ | 6.5 | 2 | M9 + PBa, M9 + SupBa |
| CcSD59 | 293.21 [M+H]+ | 8.46 | 1 | M9 + PBa |
| CcSD60 | 323.22 [M+H]+ | 7.06 | 2 | M9 + PBa, M9 + SupBa |
| CcSD61 | 216.1921 [M+H]+ | 6.03 | 2 | M9 + PBa, M9 + SupBa |
| CcSD62 | 252.23 [M+Na]+ | 7.55 | 1 | M9 + PBa |
| CcSD65 | 268.2248 [M+H]+ | 7.45 | 2 | M9 + PBa, M9 + SupBa |
| CcSD66 | 322.2323 [M+H]+ | 6.37 | 2 | M9 + PBa, M9 + SupBa |
| CcSD69 | 288.2379 [M+H]+ | 7.67 | 1 | M9 + SupBa |
| CcSD73 | 257.13 [M+H]+ | 7.62 | 3 | GMS FeX + PBa, M9 + PSg, M9 + SupSg |
| CcSD79 | 310.06 [M+H]+ | 6.79 | 1 | M9 + PSg |
| CcSD80 | 263.22 [M+H]+ | 6.01 | 1 | M9 + PSg |
| CcSD82 | 303.252 [M+H]+ | 10.37 | 1 | M9 + PSg |
| CcSD83 | 255.15 [M+H]+ | 7.92 | 1 | M9 + PSg |
| CcSD101 | 264.23 [M+Na]+ | 6.35 | 1 | M9 + SupBa |
| CcSD102 | 317.2681 [M+H]+ | 10.89 | 2 | GMS FeX + PSg, M9 + SupSg |
| CcSD134 | 318.3 [M+H]+ | 7.92 | 1 | M9 + SupSg |
| CcSD136 | 230.2075 | 6.51 | 1 | GMS + SupSg |
| CcSD139 | 330.2583 [M+H]+ | 6.14 | 1 | M9 + SupBa |
| CcSD142 | 281.1 [M+H]+ | 3.86 | 1 | M9 + SupBa |
| CcSD143 | 286.2328 | 5.95 | 1 | M9 + SupBa |
| CcSD145 | 283.22 | 7.06 | 1 | M9+ SupBa |
| CcSD151 | 279.13 [M+H]+ | 3.42 | 1 | GMS + SupBa |
| CcSD205 | 265.14 [M+H]+ | 4.87 | 1 | MD1 + Tol |
| CcSD206 | 180.1038 [M+H]+ | 3.38 | 1 | MD1 + Tol |