Supplemental information

Bacterial natural product discovery by heterologous expression

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SI Table S1. Summary of reviewed studies.

Biosynthetic class	Rationale for BGC prioritization	Cloning method	BGC Source	Host choice	Source taxa (class)	Host taxa (class)	Natural Products	Ref.
PKS, NRPS, hybrid thereof	Biosynthetic class	Library	100 *Streptomyces strains*	*S. albus* J1074, *S. lividans* RedStrep 1.7	Actinomycetia	Actinomycetia	Prolinolexin, Cinnamexin, Conkatamycin	(Libis et al. 2022)
Multiple classes	Structural novelty	Assembly	14 *Streptomyces* and 3 *Bacillus*	*S. avermitilis* SUKA17, S. *lividans* TK24, *B. subtilis* JH642	Actinomycetia	Actinomycetia	Bipentaromycins, Allenomycins, Angucyclines, Anthraquinones	(Enghiad et al. 2021)
RiPP	Structural novelty	Synthesis & Assembly	*Marinicella sediminis* F2T	*E. coli* BL21 (DE3)	Gamma-proteobacteria	Gamma-proteobacteria	Marinsedin	(Han et al. 2022)
PKS, NRPS, hybrid thereof	Structural novelty	Library	*S. versipellis* 4083-SVS6	*S. lividans* TK23	Actinomycetia	Actinomycetia	Polyene compound JBIR-159	(Hashimoto et al. 2021)
Multiple classes	Structural novelty	Assembly	*Streptococcus* strains, *Staphylococcus* strain, *Clostridium* strain	*Streptococcus mutans* UA159	Bacilli	Bacilli	Lipopeptide SNC1-465	(Hao et al. 2019)
RiPP	Structural novelty	Synthesis & Assembly	*Bacillus amyloliquefaciens*	*E. coli* BL21 (DE3)	Bacilli	Gamma-proteobacteria	Amylopeptins	(Zang et al 2021)
PKS, NRPS, hybrid thereof	Structural novelty	Library & Assembly	*S. albus ssp. chlorinus* NRRL B-24108	*S. albus* Del14	Actinomycetia	Actinomycetia	Bosecamin	(Lasch et al. 2021)

PKS, NRPS, hybrid thereof	Structural novelty	Library	*S. sp*. NA03103	*S. lividans* SBT18	Actinomycetia	Actinomycetia	Ashimides	(Shi et al. 2019)
PKS, NRPS, hybrid thereof	Structural novelty	Synthesis & Assembly	*Nocardia* strains associated with nocardiosis	*E. coli*	Actinomycetia	Gamma-proteobacteria	NOCAP (nocardis associated polyketide)	(Yuet et al. 2020)
Other	Structural novelty	Synthesis & Assembly	*Pseudoalteromonas rubra, Rheinheimera pacifica, Colwellia chukchiensis, Skermanella aerolata, Undibacterium pigrum*	*E. coli*	Many	Gamma-proteobacteria	Tyrazolones, Phenazolones	(De Rond, Asay, and Moore 2021)
RiPP	Structural novelty	Synthesis & Assembly	*Pseudoalteromonas flavipulchra* S16	*E. coli* BL21 (DE3)	Gamma-proteobacteria	Gamma-proteobacteria	Pseudorosins	(Wang et al. 2023)
PKS, NRPS, hybrid thereof	Structural novelty	Library	*S. sp*. B59	*S. albus* J1074	Actinomycetia	Actinomycetia	Shuangdaolides	(Y. Liu et al. 2021)
PKS, NRPS, hybrid thereof	Structural novelty	Library & Assembly	*S. albus ssp. Chlorinus* NRRL B-24108	*S. albus* Del14, *S. lividans* Del8	Actinomycetia	Actinomycetia	Dudomycins	(Lasch, Stierhof, et al. 2020)

Other	Structural novelty	Synthesis & Assembly	*S. venezuelae* ATCC 15439	*S. venezuelae, S. coelicolor*	Actinomycetia	Actinomycetia	Venezuelaenes	(Li et al. 2020)
PKS, NRPS, hybrid thereof	Structural novelty	Library	*Frankia alni* strain ACN14a	*S. albus* Del14	Actinomycetia	Actinomycetia	Fralnimycin	(Myronovskyi et al. 2018)
PKS, NRPS, hybrid thereof	Structural novelty	Library & Assembly	*Sorangiineae* strain MSr11367	*Myxococcus xanthus* DK1622	Myxococcia	Myxococcia	Sorangibactin	(Gao et al. 2023)
Other	Structural novelty	Library	*Micromonospora sp*. SCSIO 07395 (actinomycete)	*S. albus* J1074, *S. albus* del14	Actinomycetia	Actinomycetia	Microechmycins	(Cheng et al. 2023)
RiPP	Structural novelty	Synthesis & Assembly	*Thermobifida fusca*	*E. coli* BL21	Actinomycetia	Gamma-proteobacteria	Fuscanodin	(Koos and Link 2019)
RiPP	Structural novelty	Synthesis & Assembly	*Marinomonas fungiae* strain JCM 18476 T	*E. coli* BL21 (DE3)	Gamma-proteobacteria	Gamma-proteobacteria	Marinomonasin	(Kaweewan, Nakagawa, and Kodani 2021)
PKS, NRPS, hybrid thereof	Structural novelty	Library	*S. seoulensis* A01	*S. lividans* SBT18, *S. coelicolor* M1146, *S. albus* J1074	Actinomycetia	Actinomycetia	Ansaseomycin	(S. H. Liu et al. 2019)
Other	Structural novelty	Library & Assembly	*Kutzneria albida* DSM 43870	*S. albus* Del14	Actinomycetia	Actinomycetia	Huimycin	(Shuai et al. 2020)

PKS, NRPS, hybrid thereof	Structural novelty	Library & Assembly	*Micromonospora endolithica*	*S. albus* Del14	Actinomycetia	Actinomycetia	Loseolamycins	(Lasch, Gummerlich, et al. 2020)
PKS, NRPS, hybrid thereof	Structural novelty	Library & Assembly	*S. mirabilis* Lu17588	*S. albus* Del14	Actinomycetia	Actinomycetia	Miramides	(Paulus et al. 2022)
RiPP	Structural novelty	Synthesis & Assembly	*Pedobacter lusitanus* NL19	*E. coli*	Sphingobacteriia	Gamma-proteobacteria	PedAs	(Bothwell et al. 2021)
Multiple classes	Structural novelty	Library & Assembly	*Saccharothrix espanaensis*	S. lividans DYA6, *S. albus* J1074	Actinomycetia	Actinomycetia	Pentangumycin, SEK90	(Gummerlich et al. 2020)
PKS, NRPS, hybrid thereof	Structural novelty	Assembly	*S. sclerotialus* NRRL ISP-5269	*S. albus* J1074, *S. coelicolor* M1152	Actinomycetia	Actinomycetia	Scleric acid	(Alberti et al. 2019)
RiPP	Structural novelty	Synthesis & Assembly	*Thalassomonas viridans* XOM25T	*E. coli*	Gamma-proteobacteria	Gamma-proteobacteria	VsdsAs	(Vermeulen et al. 2022)
Other	Structural novelty	Assembly	*S. leeuwenhoekii* NRRL B-24963	*S. coelicolor* M1146, *S. albus* J1074	Actinomycetia	Actinomycetia	Streptoazines	(Zhang et al. 2021)
RiPP	Structural novelty	Synthesis & Assembly	*Grimontia marina*	*E. coli* BL21 (DE3)	Gamma-proteobacteria	Gamma-proteobacteria	Grimoviridin	(Unno et al. 2020)
PKS, NRPS, hybrid thereof	Biosynthetic class	Assembly	*S. chrestomyceticus*	*S. lividans* TK24	Actinomycetia	Actinomycetia	Guanipiperazines	(Shi et al. 2021)

Other	Biosynthetic class	Synthesis & Assembly	*S. monomycini*	*S. coelicolor* M1146	Actinomycetia	Actinomycetia	Guanitrypmycins	(Liu et al. 2019)
RiPP	Biosynthetic class	Synthesis & Assembly	Bacteroidota, Pseudomonadota, Cyanobacteriota, Actinomycetota and Bacillota	*E. coli* BL21 (DE3)	Many	Gamma-proteobacteria	LanII, LanII-2A, LanII-2B	(Ayikpoe et al. 2022)
RiPP	Biosynthetic class	Assembly	*Microbacterium paraoxydans* DSM 15019	*S. lividans* TK24, *S. albus* J1074.	Actinomycetia	Actinomycetia	Daptides	(Ren et al. 2023)
RiPP	Biosynthetic class	Synthesis & Assembly	*Methylovulum psychrotolerans*	*E. coli*	Gamma-proteobacteria	Gamma-proteobacteria	Mpr RiPPs	(Nguyen et al. 2022)
RiPP	Biosynthetic class	Synthesis & Assembly	*Cyanobacterium Kamptonema* sp. PCC 6506	*E. coli* BL21 (DE3)	Cyanophyceae	Gamma-proteobacteria	Landornamides	(Bösch et al. 2020)
RiPP	Biosynthetic class	Synthesis & Assembly	*Actinoalloteichus fjordicus* ADI127-1, *S. sp.* ADI94-01, *S. sp*. ADI98-10, *S. noursei* ATCC 11455, *S. venezuelae* ATCC 10712	*S. albus* J1074, *S. lividans* TK24	Actinomycetia	Actinomycetia	9401_LP1, 9810_LP, Snou_LP	(Mevaere et al. 2018)
RiPP	Biosynthetic class	Synthesis & Assembly	*Enterobacter cloacae* complex	*E. coli*	Gamma-proteobacteria	Gamma-proteobacteria	Cloacaenodin	(Carson et al. 2023)
RiPP	Biosynthetic class	Synthesis & Assembly	*Burkholderia ubonensis* MSMB2207	*E. coli* BL21	Beta proteobacteria	Gamma-proteobacteria	Ubonodin	(Cheung-Lee et al. 2020)

RiPP	Biosynthetic class	Synthesis & Assembly	*Pandoraea norimbergensis*	*E. coli* BL21	Beta proteobacteria	Gamma-proteobacteria	Pandonodin	(Cheung-Lee, Cao, and Link 2019)
RiPP	Biosynthetic class	Synthesis & Assembly	*S. leeuwenhoekii* C34T	*S. coelicolor* M1152, *S. coelicolor* M1154	Actinomycetia	Actinomycetia	Leepeptin	(Gomez-Escribano et al. 2019)
RiPP	Biosynthetic class	Synthesis & Assembly	*Thermobifida cellulosilytica, Lihuaxuella thermophila*	*E. coli* BL21 (DE3)	Many	Gamma-proteobacteria	Cellulonodin-2, Lihuanodin	(Cao et al. 2021)
RiPP	Biosynthetic class	Synthesis & Assembly	*Synechococcus* MITS9509	*Lactococcus lactis* NZ9000	Cyanophyceae	Bacilli	SyncAs	(Arias-Orozco et al. 2021)
RiPP	Biosynthetic class	Synthesis & Assembly	*Thermosporothrix hazakensis*	*E. coli* BL21 (DE3)	Ktedonobacteria	Gamma-proteobacteria	Hazakensins	(Kaweewan et al. 2023)
RiPP	Biosynthetic class	Synthesis & Assembly	*S. roseosprus* NRRL 11379	*E. coli* BL21 (DE3)	Actinomycetia	Gamma-proteobacteria	Roseocins	(Singh et al. 2019)
RiPP	Biosynthetic class	Synthesis & Assembly	*Thalassomonas actiniarum*	*E. coli* BL21 (DE3)	Gamma-proteobacteria	Gamma-proteobacteria	Thalassomonasins	(Thetsana et al. 2022)
RiPP	Biosynthetic class	Assembly	*S. varsoviensis*	*S. lividans* TK24, *S. coelicolor* M1146, *S. coelicolor* M1152	Actinomycetia	Actinomycetia	Thiovarsolins	(Santos-Aberturas et al. 2019)
PKS, NRPS, hybrid thereof	Structural similarity to known NP	Library & Assembly	Soil metagenome	*S. albus* J1074	Unknown	Actinomycetia	Cadasides	(Wu et al. 2019)

PKS, NRPS, hybrid thereof	Structural similarity to known NP	Library & Assembly	Soil metagenome	*S. albus* J1074	Unknown	Actinomycetia	Malacidins	(Hover et al. 2018)
PKS, NRPS, hybrid thereof	Structural similarity to known NP	Assembly	*Amycolatopsis sp*. WAC01416 and 7 *Streptomyces* strain	*S. coelicolor*	Actinomycetia	Actinomycetia	GP6738, GP6738	(Xu et al. 2020)
RiPP	Activity	Library	*S. rochei* Sal35	*S. lividans* GX28	Actinomycetia	Actinomycetia	Lexapeptide	(Xu et al. 2020)

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