

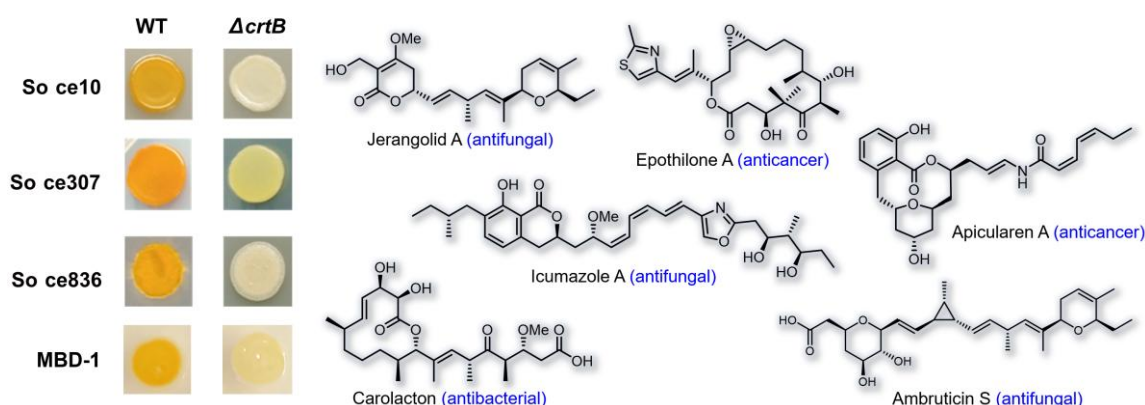
PLENARY PRESENTATIONS

GENETIC ENGINEERING OF *Sorangium cellulosum*: A PLATFORM FOR DECODING MYXOBACTERIAL SECONDARY METABOLISM

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Sorangium cellulosum is a cellulolytic myxobacterium renowned for producing a vast array of complex natural products with diverse chemical scaffolds and biological activities, including the anticancer drug epothilones. Despite its remarkable biosynthetic potential, progress in understanding and harnessing these metabolites has been hampered by the lack of effective genetic manipulation tools. To address this challenge, we have developed a versatile genetic engineering method applicable across multiple *Sorangium cellulosum* strains, effectively overcoming their genetic intractability. This facilitated delineation of the biosynthetic pathways to several biologically important natural products including ambruticin, jerangolid and carolacton. Our findings reveal a series of biosynthetic steps characterised by remarkable enzymology, offering significant insights into the molecular machinery governing myxobacterial natural product biosynthesis. Our work establishes a robust platform for further pathway engineering of *Sorangium* strains, opening new avenues for expanding the chemical and biological diversity accessible from myxobacteria.



References:

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2. Bowen JI, Zhong X, Gao K, Reed B, Crump MP, Wang L, Willis CL. Combining total synthesis and genetic engineering to probe dihydropyran formation in ambruticin biosynthesis. *Chemical Science*, **2024**, 15(14):5319-5326.