Engineered polyketides: Synergy between protein and host level engineering

Metabolic engineering efforts toward rewiring metabolism of cells to produce new compounds often require the utilization of non-native enzymatic machinery that is capable of producing a broad range of chemical functionalities. Polyketides encompass one of the largest classes of chemically diverse natural products. With thousands of known polyketides, modular polyketide synthases (PKSs) share a particularly attractive biosynthetic logic for generating chemical diversity. The engineering of modular PKSs could open access to the deliberate production of both existing and novel compounds. In this review, we discuss PKS engineering efforts applied at both the protein and cellular level for the generation of a diverse range of chemical structures, and we examine future applications of PKSs in the production of medicines, fuels and other industrially relevant chemicals.