

Exploring the Diversity of Unusual Sugar Biosynthesis

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Many natural products derive their biological activities from their sugar components. Changing the structures of these sugar moieties can profoundly impact the biological properties of the glycosylated parent compounds. This has led to the modification of natural products with alternative sugar moieties by exploiting the sugar biosynthetic machinery. Realizing the potential of this approach requires both an understanding of the biosynthetic pathway of each target sugar and a detailed mechanistic knowledge of the key enzymes. Scientists have thus begun to unravel the biochemical principles underlying the assembly of glycosylated natural products wherein a core set of enzyme activities mix and match to synthesize structurally diverse carbohydrates. Mechanistic investigation of the responsible biosynthetic enzymes has also revealed several cases involving unique and interesting chemistry to accomplish the specific biosynthetic transformations. Carbohydrate biosynthesis in secondary metabolism has thus been found to include instances of radical mediated chemical transformations, some of which are catalysed by radical SAM enzymes. The biosynthetic roles of selected enzymes in this group, their mechanisms of catalysis, and the insights they can offer for understanding natural product biosynthesis and radical SAM enzymology will be discussed.