Biosynthetic Pathway Elucidation through Chemistry-Guided Single-Cell Transcriptomics

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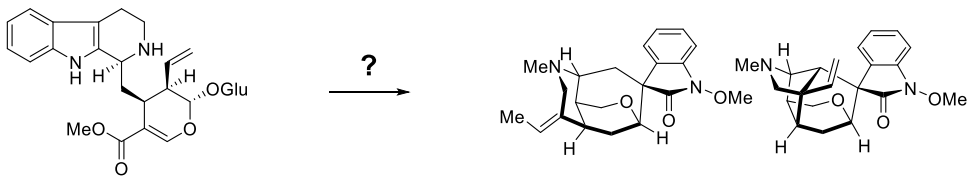
Nature has evolved specialized enzymes that produce structurally complex and diverse secondary metabolites. Identifying the corresponding biosynthetic genes offers opportunities to streamline chemical synthesis by enabling us to understand and harness their unique reactivities. Despite recent advances, plant biosynthetic pathways remain challenging to elucidate. Many intermediates are transient and often undetectable because biosynthetic pathways are highly efficient. Moreover, unlike in bacteria and fungi, the genes responsible for plant biosynthetic pathways are generally not clustered, making pathway elucidation even more challenging.

The recent emergence of single-cell transcriptomics has enabled gene expression to be analyzed at cellular resolution, facilitating correlation-based candidate selection. However, without the correct biosynthetic hypothesis, this information may not lead to gene discovery, because enzymatic reactivity cannot be properly evaluated without a bona fide substrate.

Gelsemium alkaloids, isolated from plants in the family Gelsemiaceae, feature unique carbon skeletons that differ from those of monoterpene indole alkaloids found in other Gentianales plants. Although the biosynthetic pathways of monoterpene indole alkaloids from Rubiaceae (quinine[1]), Loganiaceae (strychnine[2]), and Apocynaceae (vinblastine[3]) have been substantially elucidated, little is known about the biogenesis of *Gelsemium* alkaloids. This seminar will focus on the elucidation of *Gelsemium* alkaloid biosynthesis, highlighting how chemical logic, together with single-cell transcriptomic analysis, facilitated the discovery process[4].



strictosidine

***Gelsemium* alkaloids**

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