

Network Analysis of Genes Involved in the Biosynthesis of Medicinally Important Naphthodianthrone Derivatives of *Hypericum perforatum*

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Abstract : Hypericins (hypericin and pseudohypericin) are natural naphthodianthrone derivatives produced by *Hypericum perforatum* (St. John's Wort), which have many medicinal properties such as antitumor, antineoplastic, antiviral, and antidepressant activities. Production and accumulation of hypericin in the plant are influenced by both genetic and environmental conditions. Despite the existence of different high-throughput data on the plant, genetic dimensions of hypericin biosynthesis have not yet been completely understood. In this research, 21 high-quality RNA-seq data on different parts of the plant were integrated into metabolic data to reconstruct a coexpression network. Results showed that a cluster of 30 transcripts was correlated with total hypericin. The identified transcripts were divided into three main groups based on their functions, including hypericin biosynthesis genes, transporters, detoxification genes, and transcription factors (TFs). In the biosynthetic group, different isoforms of polyketide synthase (PKSs) and phenolic oxidative coupling proteins (POCPs) were identified. Phylogenetic analysis of protein sequences integrated into gene expression analysis showed that some of the POCPs seem to be very important in the biosynthetic pathway of hypericin. In the TFs group, six TFs were correlated with total hypericin. qPCR analysis of these six TFs confirmed that three of them were highly correlated. The identified genes in this research are a rich resource for further studies on the molecular breeding of *H. perforatum* in order to obtain varieties with high hypericin production.

Keywords : hypericin, St. John's Wort, data mining, transcription factors, secondary metabolites

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