**TRANSCRIPTOME PROFILING IN A LICHEN-FORMING FUNGUS**

**DURING INDUCTION OF DEPSIDONE BIOSYNTHESIS**

**SHEDS LIGHT ON THE GENE NETWORKS INVOLVED**

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In lichen symbiotic fungi, a large and versatile group of natural product biosynthesizers, we know virtually nothing about the functional and regulatory gene networks involved in the biosynthesis of secondary compounds. Here, we examined global time-series gene expression profiles during induction of secondary metabolism in the cultured lichen fungus *Cladonia grayi*. For induction, we perfected a method to uniformly transition mycelial growth of the mycobiont from liquid to solid media, a switch that triggers production of the depsidone grayanic acid (GRA), the main natural product in this lichen. Gene expression was compared in two *C. grayi* strains, a high and a null GRA producer under identical induction conditions. Using functional and network analysis, we identified 1343 differentially expressed genes between the two strains, out of a total of 11293. A major biochemical dichotomy between the null and the high GRA producer was represented by the activation of the squalene pathway in the null producer *vs.* the activation of the GRA pathway in the high producer. In addition, the high producer downregulated mitochondrial ATPase and upregulated genes related to oxidoreductase activity and transmembrane transport. This suggests a significant diversion of Acetyl-CoA from mitochondrial ATP synthesis towards the GRA pathway in the high GRA producer. Our results also suggest that compartmentalization via peroxisomes and cytoplasmic vesicles, as seen in aflatoxin production in *Aspergillus*, may also characterize biosynthesis and secretion of GRA in *Cladonia*. We also identified a likely GRA-specific regulatory gene, CLAGR\_00823-RA, encoding a putative Zn(II)2Cys6 transcription factor.