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霊芝 *Ganoderma lucidum* の二次代謝産物合成の活性化

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[Objective] *Ganoderma lucidum*, one of the most widely cultivated medical mushrooms in East Asia, contains more than 400 compounds including various pharmaceutically active triterpenoids and polysaccharides. Interestingly, though its genome includes several genes encoding non-ribosomal peptide synthetase (NRPS) and polyketide synthase (PKS), polyketides and peptides have never been isolated from *G. lucidum*, suggesting that their syntheses might be tightly suppressed in the normal conditions. DNA methyltransferase (DNMT) and histone deacetylase (HDAC) inhibitors alter the epigenetic environment of fungi, resulting in chromatin remodeling which modulates the production of secondary metabolites. Therefore, epigenetic modifiers were utilized for the sake of mining novel secondary metabolites by arousing the silent genes in *G. lucidum*.

[Result] We supplied two HDAC inhibitors, nicotinamide and suberoylanilide hydroxamic acid (SBHA), one DNMT inhibitor, 5-azacytidine, to the cultures of *G. lucidum* incubated in potato-dextrose medium. As a result, a HDAC inhibitor, SBHA was found to increase the yield of two aromatic compounds significantly, whose structures are now being determined. It is the first time to produce novel secondary metabolites in basidiomycete by making use of epigenetic chemical modifiers, which also exemplified that it is an effective technique for promoting the transcription of silent biosynthetic pathways to produce unique secondary metabolites.

