

メタボローム解析による新規代謝産物同定

近年、糸状菌のゲノム解析が急速に進められる中、糸状菌ゲノム中には予想以上に膨大な数の二次代謝関連遺伝子群が存在することが明らかになった。しかし、そのほとんどは一般的な実験室培養条件下では休眠状態であることも明らかになっている。この休眠二次代謝関連遺伝子群の活性化のために様々な方法が試されている。その中でもエピジェネティック制御による糸状菌の休眠二次代謝活性化は成果を挙げている方法の一つである。今回、紹介する論文はエピジェネティック制御により起きる糸状菌(*Aspergillus nidulans*)の全代謝産物の変化をMSにより解析し、新しい代謝産物の同定に応用したので紹介する。

紹介論文

Large-Scale Metabolomics Reveals a Complex Response of *Aspergillus nidulans* to Epigenetic Perturbation

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Abstract

The microbial world offers a rich source of bioactive compounds for those able to sift through it. Technologies capable of quantitatively detecting natural products while simultaneously identifying known compounds would expedite the search for new pharmaceutical leads. Prior efforts have targeted histone deacetylases in fungi to globally activate the production of new secondary metabolites, yet no study has directly assessed its effects with minimal bias at the metabolomic level. Using untargeted metabolomics, we monitored changes in >1000 small molecules secreted from the model fungus, *Aspergillus nidulans*, following genetic or chemical reductions in histone deacetylase activity (HDACi). Through quantitative, differential analyses, we found that nearly equal numbers of compounds were up- and down-regulated by >100 fold. We detected products from both known and unknown biosynthetic pathways and discovered that *A. nidulans* is capable of producing fellutamides, proteasome inhibitors whose expression was induced by ~100 fold or greater upon HDACi. This work adds momentum to an “omics”-driven resurgence in natural products research, where direct detection replaces bioactivity as the primary screen for new pharmacophores.