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Combating ESKAPE Pathogens: Metabolomic Exploration of Marine Sponge-Derived Fungi Through OSMAC and Epigenetic Induction

Shivankar Agrawal[1*], Pauline Scanlan[1,2]

[1] APC Microbiome, Ireland

[2] School of Microbiology, University College Cork, Ireland

ABSTRACT

Antimicrobial resistance (AMR) in ESKAPE pathogens—*Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* spp.—continues to pose a major threat to global health, while the discovery of novel antibiotics lags behind. In this study, we explored a culture collection of marine sponge-associated fungi at University College Cork to unlock their untapped chemical diversity and identify potential antimicrobial leads. A total of 25 fungal strains exhibited antibacterial activity against at least one member of the ESKAPE panel, with 30% showing inhibition of methicillin-resistant *S. aureus* (MRSA). Media optimization using the OSMAC (One Strain–Many Compounds) approach revealed that Czapek Dox and Potato Dextrose Broth were the most effective in inducing secondary metabolite production, yielding the broadest antimicrobial profiles. Epigenetic modulation using histone deacetylase (HDAC) and DNA methyltransferase (DNMT) inhibitors had limited impact on inducing bioactive metabolite production under the tested conditions. However, treatment with suberoylanilide hydroxamic acid (SAHA), an HDAC inhibitor, resulted in visible changes in colony morphology and pigmentation in several fungal isolates, indicating latent epigenetic responsiveness. These observations suggest that higher concentrations or alternative epigenetic modulators may be required to elicit significant metabolic changes. Overall, this study underscores the effectiveness of the OSMAC strategy in expanding the chemical space of marine-derived fungi. Coupled with metabolomic profiling, this approach offers a powerful platform for tracing and categorizing bioactive metabolites, paving the way for downstream scale-up and structural elucidation of promising antibiotic candidates.

Keywords: antimicrobial resistance, antibiotic, marine natural product, epigenetic modulators, fungi secondary metabolites

References:

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[*]Corresponding Author:

Shivankar Agrawal, APC Microbiome, Ireland.
Email: sagrawal@ucc.ie