



OPEN ACCESS

EDITED AND REVIEWED BY
Biswarup Mukhopadhyay,
Virginia Tech, United States

*CORRESPONDENCE

Pinmei Wang
✉ wangpinmei@zju.edu.cn
Wen-Bing Yin
✉ yinwb@im.ac.cn

RECEIVED 18 July 2023
ACCEPTED 07 August 2023
PUBLISHED 15 August 2023

CITATION

Wang P, Park H-S, Wang W and Yin W-B (2023)
Editorial: Gene regulation of fungal secondary
metabolism. *Front. Microbiol.* 14:1260849.
doi: 10.3389/fmicb.2023.1260849

COPYRIGHT

© 2023 Wang, Park, Wang and Yin. This is an
open-access article distributed under the terms
of the [Creative Commons Attribution License
\(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction
in other forums is permitted, provided the
original author(s) and the copyright owner(s)
are credited and that the original publication in
this journal is cited, in accordance with
accepted academic practice. No use,
distribution or reproduction is permitted which
does not comply with these terms.

Editorial: Gene regulation of fungal secondary metabolism

Pinmei Wang^{1*}, Hee-Soo Park², Wenjie Wang³ and
Wen-Bing Yin^{4*}

¹Ocean College, Zhejiang University, Zhoushan, China, ²School of Food Science and Biotechnology, Kyungpook National University, Daegu, Republic of Korea, ³School of Food Science and Biotechnology, Zhejiang Gongshang University, Hangzhou, China, ⁴State Key Laboratory of Mycology, Institute of Microbiology, Chinese Academy of Sciences, Beijing, China

KEYWORDS

gene regulation, transcription factors, fungal secondary metabolism, biosynthesis, secondary metabolites

Editorial on the Research Topic

Gene regulation of fungal secondary metabolism

Fungi are prolific producers of secondary metabolites (SMs), which encompass a wide range of low-molecular-mass compounds. These SMs serve essential functions such as defense against pathogens, inhibition of competing microorganisms, and intercellular communication (Keller, 2019; Yu et al., 2023). Therefore, SMs usually possess dual roles, hazardous mycotoxins (e.g., aflatoxin and patulin), and valuable pharmaceuticals (e.g., penicillin and lovastatin) (Wang et al., 2021b). Surprisingly, genome mining studies have unveiled that the potential of fungi to synthesize SMs has been greatly underestimated, as numerous of biosynthetic gene clusters (BGCs) remain silent or cryptic under laboratory culture conditions (Brakhage, 2013; Wang et al., 2021b). Transcription factors (TFs) play an essential regulatory role in the expression of SM genes (Yin and Keller, 2011; Keller, 2019; Wang et al., 2021a). In recent years, researchers have actively explored the gene regulation mechanism of fungal secondary metabolism by using the methods of genetics, molecular biology and biochemistry (Wang et al., 2022; Zhang et al., 2022; Wei et al., 2023). The aim of this Research Topic is to gain a better understanding of the regulatory elements and network of fungal SMs, providing genetic approaches to manipulate fungal secondary metabolism to produce novel compounds with beneficial properties for medicine, agriculture, and other applications.

This Research Topic contains one review paper and eight original research articles. Deng et al. review article presents a comprehensive summary of perylenequinones (PQs) with literatures spanning from 1967 to 2022. As photosensitizers, PQs have been applied in various fields, including medical, food, agricultural and manufacturing fields. The authors not only collected information of the sources, structure diversity and biological activities of PQs, but also the biosynthetic pathways and regulation mechanism. Besides, strategies are given to enhance PQ production and quality, including modulating regulatory mechanisms, coordinating signal-response pathways, constructing heterologous production platforms, and applying physical and chemical methods to stimulate biosynthesis.

Three research articles investigate the gene regulation of ganoderma triterpenoids (GTs) biosynthesis in *Ganoderma lucidum* and *Ganoderma lingzhi*, both of which are traditional Chinese medicines. GTs exhibit a variety of biological activities, and their biosynthesis is regulated through a complex interplay between environmental and genetic factors. Meng et al. employed a comprehensive approach involving transcriptome and metabolome analyses to investigate the transcription factors (TFs) involved in ganoderic acid (GA) biosynthesis in different developmental stages of *G. lucidum*. By comparing gene expression patterns, they identified that homeobox transcription factor and velvet family protein were responsible for GA biosynthesis, and provided a model for the involvement of TFs in GA biosynthesis during fruiting body formation. The research article by Luo et al. describes an essential function of the well-known methyltransferase LaeA in the regulation of GA in basidiomycete fungus *G. lingzhi*. The results of *laeA* gene deletion and overexpression suggested that LaeA could regulate the expression of GA biosynthetic genes and asexual sporulation. The study by Xu et al. focused on understanding how *G. lucidum* responds to methyl jasmonate, an important elicitor in inducing the production of triterpenes and the biomass of mycelia. Transcriptomic analysis allowed researchers to identify positive and negative transcription factors of GTs that response to methyl jasmonate, and a negative regulator gene *Glmhr1* was found. The study provides new insights into the molecular mechanisms underlying the response of *G. lucidum* to fungal hormones and may facilitate the development of new strategies for enhancing the production of bioactive compounds.

Other two studies explored the role of BcLAE1 and Bcfrp1 in the regulation of abscisic acid (ABA) biosynthesis and growth of *Botrytis cinerea*. The study conducted by Wei et al. demonstrated the significant role of the methyltransferase BcLAE1 in epigenetic regulation of ABA biosynthesis in *B. cinerea*. Chen et al. elucidated the positive role and molecular mechanism of an F-box protein Bcfrp1 in regulating ABA biosynthesis and fungal growth. These studies provide valuable insights into the molecular mechanisms involving the regulation of ABA biosynthesis in *B. cinerea*.

Additionally, two separate investigations have provided knowledge about the mechanisms governing microbe-microbe interactions and plant-microbe interactions, respectively. Brault et al. conducted a study revealing the crucial role of Sib proteins (Sib1, Sib2, and Sib3) in facilitating iron acquisition and cross-feeding interaction between *Schizosaccharomyces pombe* and *Saccharomyces cerevisiae*. These proteins are responsible for the transport of ferrichrome, and their knockout disrupted the transport process and hindered cross-feeding. In another article by Wu et al., they investigated the production and distribution of flavonoids by the endophytic fungus *Aspergillus* sp. Gbtc 2, which was isolated from the root of *Ginkgo biloba*. Through LC-MS analysis, they identified flavonoid metabolites and discovered a unique distribution pattern of these compounds, both intracellularly and extracellularly, within the fungus Gbtc 2. This research expands our understanding of the potential application of endophytic fungi in the industrial flavonoid production. In the study conducted by Wang et al., genomic alterations in *Fusarium proliferatum* strains were examined to understand their role in

adaptation and fumonisin production. Through their analysis, a total of 121 distinct genomic loci were identified, implicating 85 potential genes involved in adaptation to diverse environments and fumonisin B1 (FB1) production. Notably, five candidate genes were identified as being closely associated with FB1 production.

The articles within this Research Topic collectively highlight the significance of gene regulation in the biosynthesis of secondary metabolites in fungi. By investigating the regulatory mechanisms governing these processes, researchers can attain a comprehensive comprehension of the molecular mechanisms underlying fungal secondary metabolism. Moreover, these studies enable the identification of potential targets for genetic engineering, aiming to augment the production of bioactive compounds by these organisms. Such findings carry significant implications across various fields including medicine, agriculture, and biotechnology, as they contribute to the exploration and development of novel bioactive compounds of interest.

Author contributions

PW: Writing—original draft. H-SP: Writing—review and editing. WW: Writing—review and editing. W-BY: Writing—review and editing.

Funding

This research was supported in part by National Natural Science Foundation of China (32170066), the Key Laboratory of Tropical Marine Ecosystem and Bioresource, MNR (2022QN02) and Hainan Provincial Joint Project of Sanya Yazhou Bay Science and Technology City (420LH004), Key Research Program of Frontier Sciences, Chinese Academy of Sciences (ZDBS-LY-SM016), Biological Resources Program, Chinese Academy of Sciences (KFJ-BRP-009-005), and National Research Foundation of Korea (NRF) grant (NRF-2020R1C1C1004473).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- Brakhage, A.A. (2013). Regulation of fungal secondary metabolism. *Nat. Rev. Microbiol.* 11, 21–32. doi: 10.1038/nrmicro2916
- Keller, N.P. (2019). Fungal secondary metabolism: regulation, function and drug discovery. *Nat. Rev. Microbiol.* 17, 167–180. doi: 10.1038/s41579-018-0121-1
- Wang, G., Ran, H., Fan, J., Keller, N.P., Liu, Z., Wu, F., et al. (2022). Fungal-fungal cocultivation leads to widespread secondary metabolite alteration requiring the partial loss-of-function VeA1 protein. *Sci. Adv.* 8, eabo6094. doi: 10.1126/sciadv.abo6094
- Wang, W., Yu, Y., Keller, N.P., and Wang, P. (2021a). Presence, mode of action, and application of pathway specific transcription factors in *Aspergillus* biosynthetic gene clusters. *Int. J. Mol. Sci.* 22, 8709. doi: 10.3390/ijms22168709
- Wang, W.J., Drott, M., Greco, C., Luciano-Rosario, D., Wang, P.M., and Keller, N.P. (2021b). Transcription factor repurposing offers insights into evolution of biosynthetic gene cluster regulation. *Mbio* 12, 10–1128. doi: 10.1128/mBio.01399-21
- Wei, P.L., Fan, J., Yu, J., Ma, Z., Guo, X., Keller, N.P., et al. (2023). Quantitative characterization of filamentous fungal promoters on a single-cell resolution to discover cryptic natural products. *Sci. China Life Sci.* 66, 848–860. doi: 10.1007/s11427-022-2175-0
- Yin, W., and Keller, N.P. (2011). Transcriptional regulatory elements in fungal secondary metabolism. *J. Microbiol.* 49, 329–339. doi: 10.1007/s12275-011-1009-1
- Yu, W., Pei, R., Zhou, J., Zeng, B., Tu, Y., and He, B. (2023). Molecular regulation of fungal secondary metabolism. *World J. Microbiol. Biotechnol.* 39, 204. doi: 10.1007/s11274-023-03649-6
- Zhang, H., Li, Z., Zhou, S., Li, S.M., Ran, H., Song, Z., et al. (2022). A fungal NRPS-PKS enzyme catalyses the formation of the flavonoid naringenin. *Nat. Commun.* 13, 6361. doi: 10.1038/s41467-022-34150-7