

## **“Shining light on the dark matter of natural products: Structure and function of colibactin”**



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**Abstract:** The classical paradigm of large-scale production, isolation, and structure analysis has given us our understanding of almost all known natural products. Yet, advances in metabolomics and genetics suggest the existence of ultra-low abundance or cryptic metabolites that lie outside the scope of the traditional isolation–analysis approach. Analogous to the role of difficult-to-detect dark matter in shaping the universe in unanticipated ways, these dark metabolites may play significant roles in shaping human physiology and disease states. New approaches are required to find the structures and functions encoded here.

Here I'll describe how a synergistic combination of chemical synthesis, genetics, and enzymology revealed the structure of colibactin, a dark bacterial metabolite implicated in gut microbiome-associated colorectal cancer (CRC). Colibactin's presence was first detected in 2006, but because it is unstable and produced in vanishingly small quantities, its structure and mechanism of action could not be elucidated by classical approaches. We used techniques from a range of fields to infer the structure of colibactin and to construct a mechanistic model that explains its tumorigenic effects. This work provides a foundation to better understand gut microbiome-associated CRC and may provide strategies that are extensible to the elucidation of other dark natural products.

**Date:** Friday, February 19, 2021    **Time:** 11:30 AM

Please email [syb26@newark.rutgers.edu](mailto:syb26@newark.rutgers.edu) for Webex meeting link.

**Host: Joel Freundlich, Ph.D.**

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