

Under the Hood Seminar
September 26, 2024
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Lecture Hall (00.187) at BioZentrum I, Hanns-Dieter-Hüsch-Weg 15, 55128 Mainz

Dr. Laurence Ettwiller

New England Biolabs Inc., USA

Leveraging genotype-phenotype relationships in complex microbiomes

to generate new tools for biotechnology

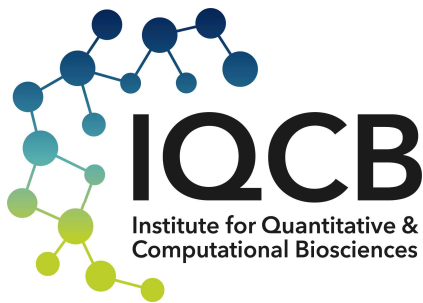
The study of phage-bacteria interactions has recently gained significant attention due to their similarities with eukaryotic immune-regulatory processes and their potential to yield novel enzymes for biotechnological applications and antimicrobial therapies. Components of bacterial defense mechanisms against phages—such as restriction endonucleases and CRISPR-Cas systems—have become fundamental tools in molecular biology. More recently, metagenomic sequencing has helped to accelerate the discovery of potential candidate genes for such tools. However, the true potential of such genes for biotechnological applications often remains hidden as they rarely can be directly linked to function.

To address this challenge, my lab at New England Biolabs developed the Metagenomics Genome-Phenome Association (MetaGPA) approach. MetaGPA is an analysis strategy resembling that genome-wide association studies which allows to associate findings from high-throughput sequencing of environmental metagenomes with any pre-specified phenotype in the respective sample. We applied an early iteration of MetaGPA by enzymatically modifying nucleic acids for phenotype selection. This led to the identification of several new enzyme families with roles in modifying or hypermodifying cytosine. Among others, we discovered a

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novel DNA O-carbamoyltransferase that can be used to detect 5-hydroxymethylcytosine (5hmC) in DNA. We have since expanded MetaGPA to uncover numerous genotype-phenotype associations in environmental metagenomes revealing novel enzymes and pathways that can help drive innovations in various fields of biotechnology.

The IQCB seminar series “Under the Hood” provides a forum for scientists at all career levels to present the technical side of their research. Talks are aimed at an audience interested in the methods, algorithms, and programs used to address a specific research question. “Under the Hood” talks stimulate lively discussions among researchers facing similar computational challenges in their research, lead to transfer of technical knowledge and ideas and promote collaboration.

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