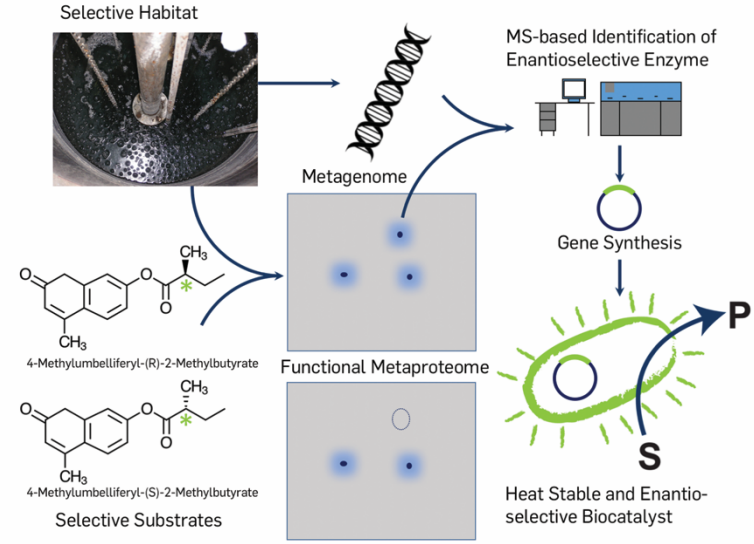
Project Lars Leichert

Discovery of tailor-made enzymes through functional metaproteomics

Background and preliminary work: Metagenomic approaches are widely used for biocatalyst discovery. Our group has developed a new methodology that goes beyond the current "DNA-only" metagenomics approaches in enzyme discovery. Combining the immediacy of traditional activity-based screening with the independence from lab-cultivability inherent in "meta-omic" approaches, our approach is substantially faster than current state-of-the-art methodology. We could already identify several novel lipolytic enzymes from environmental samples using metaproteomics. Through gene synthesis and heterologous expression we could obtain these new biocatalysts in quantity for biochemical characterization.



Exemplary functional meta-proteomics pipeline: Proteins and DNA from a promising habitat (e.g. a hot spring) will be isolated. Proteins will be separated on 2 D gels and screened for activity using tailor-made fluorogenic substrates. Enantio-specific biocatalysts will then be excised from the gel and identified by mass spectrometry. Through synthetic biology the biocatalyst will be obtained in quantity for characterization.

Work planned: We are looking for a candidate with a strong background in protein biochemistry or a related field. Experience in enzymology, 2D gels and/or biocatalyst research is a plus. The successful candidate will screen promising habitats such as hot springs and human microbiomes for new biocatalysts with desirable properties and develop new in-gel activity assays. Proteins and DNA will be isolated from environmental samples and 2D-zymography-based activity data linked to the environmental DNA encoding these biocatalysts. In addition to screening for enantioselectivity, one of the most desirable properties of enzymes over standard catalysts, the candidate will establish in-gel assays for new enzyme classes used in industry and potentially medicine. Selected genes encoding biocatalysts with promising substrate specificity will then be synthesized and biochemically characterized, providing new microbial biocatalysts for hydrolytic substrate conversion.

Selected references:

Sukul P, Schäkermann S, **Bandow JE**, Kusnezowa A, Nowrousian M, **Leichert LI.** 2017. Simple discovery of bacterial biocatalysts from environmental samples through functional metaproteomics. Microbiome. 5(1):28

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