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Genomics-guided discovery of peptide natural products in microbes and plants

One of the key steps in innovating new pharmaceutical solutions to human diseases is the discovery of new natural products. In the 20th century, natural product-based drug discovery was largely bioactivity-guided and was faced with limited source material and frequent rediscovery of bioactive lead structures. In the last two decades, whole genome sequencing revealed that fungal and microbial genomes harbor more biosynthetic pathways than characterized natural product structures. This untapped biosynthetic potential inspired gene-guided discovery of natural products – or 'genome mining' - by applied knowledge that certain biosynthetic genes in a genome are connected to certain natural product structures. Genome mining has led to the discovery of many new natural product classes from microbes and fungi, and synthetic biology approaches have subsequently enabled sustainable scaled production and diversification of these natural products for further drug development by source-independent expression of their biosynthetic genes in heterologous hosts.

Here, I'll present how genome mining in the microbial and plant kingdoms can enable discovery of new natural product chemistry and underlying biochemistry for potential pharmacological applications. Specifically, I will discuss genome mining approaches utilizing mass spectrometry for the characterization of peptide natural products, including how they translate from compact microbial genomes to complex plant genomes and what awaits to be discovered in light of a rapidly growing resource of plant genomes in the near future.

Bio

Roland Kersten is a postdoctoral associate of Prof. Jing-Ke Weng's lab at Whitehead Institute for Biomedical Research at MIT. He has a diploma in biochemistry from Free University of Berlin, Germany. He completed his PhD in 2013 from Scripps Institution of Oceanography, UC San Diego, under joint supervision of Prof. Pieter Dorrestein (Skaggs School of Pharmacy, UCSD) and Prof. Bradley Moore (Scripps Institution of Oceanography, UCSD) focusing on mass spectrometry-guided approaches for natural product discovery from microbes. In his postdoctoral research, Roland is developing gene-guided approaches for discovery and diversification of natural products from plants.