



DISCOVERY OF NOVEL METABOLIC PATHWAYS BY EVOLUTION-INSPIRED GENOME MINING STRATEGIES

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Introduction. In recent years, the ease of microbial genome sequencing and the development of powerful genome mining tools specialized on Natural Products (1) has prompted the identification of novel chemicals. A plethora of novel putative NP biosynthetic pathways has been predicted and several of their final products have been identified. Most frequently these new compounds belong to known chemical classes.

Methods. We have developed an evolution-inspired NP genome mining strategy that led to the identification of putative novel classes of molecules and biosynthetic systems. This approach is based on the identification of expansions on central metabolic enzyme families (2) and their recruitment by NP biosynthetic pathways. After reconstructing the evolutionary history of these enzyme families, we predicted novel biosynthetic pathways on microbial genomes using phylogenetic profiles, divergence, gene context and tree topology (Figure 1).

Results. Using our databases, we were able to identify thirty three enzyme families from central metabolism recruited in 60 known Natural Product biosynthetic pathways. We used this enzyme recruitment database to mine for Natural Product biosynthetic pathways on publically available and private genome sequences. We identified several putative novel and previously known NP biosynthetic gene clusters.

Conclusions. According to our results, the recruitment of a central metabolic enzyme for the biosynthesis of NPs is not exclusive of a single class of NP. We postulate that this approach can be applied systematically to identify novel biosynthetic gene clusters of NPs in an unbiased fashion (i.e. using NRPS or PKS domains as queries for genome mining), and provide the possibility for the prediction of biosynthetic pathways for unknown classes of compounds(3).

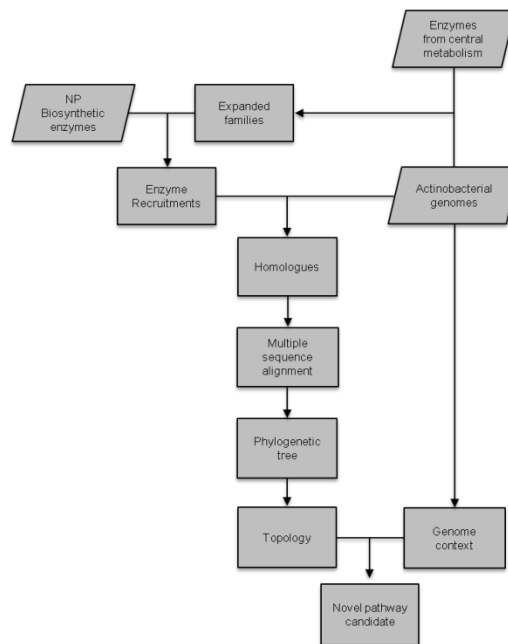


Figure 1. Pipeline for Evolution-inspired genome mining of NPs

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