

WHEN EVOLUTION MEETS APPLICATION: AN EVOLUTION-INSPIRED STRATEGY FOR GRUG DISCOVERY IN ACTINOBACTERIA

Francisco (Paco) Barona-Gómez, Evolution of Metabolic Diversity Laboratory
National Laboratory of Genomics for Biodiversity (Langebio)
CINVESTAV-IPN, Irapuato, Mexico fbarona@langebio.cinvestav.mx

“Nothing in biology makes sense except in the light of evolution” is a famous statement of the evolutionary biologist Theodosius Dobzhansky almost four decades ago. Unquestionably, this statement has had a profound impact on generations of microbiologists and biochemists and continues to do so. However, the relevance of evolution as the theoretical foundation of biology to drive drug discovery has largely been neglected. In this presentation, it will be demonstrated that evolutionary principles can guide the discovery of novel natural products in Actinobacterial genomes. Due to the predictive nature of the theory of evolution, the novel biosynthetic pathways uncovered by this approach - termed EvoMining - include chemical conversions beyond known Non-ribosomal Peptide Synthetases and Polyketide Synthases, i.e. empirical knowledge. In addition to describing an ad hoc bioinformatics pipeline supporting the conceptual framework behind EvoMining, which includes automatically generated genome-scale metabolic models as a source for leveraging enzymatic expansions within metabolic sub-systems (Kbase), experimentally validated examples will be presented. This will include novel biosynthetic pathways in the well-studied laboratory strains *Streptomyces lividans* 66 and *Streptomyces coelicolor* M145 that could not be discovered after years of experimental investigation, including genome-mining approaches in vogue such as AntiSMASH.