Genedata Phylosopher®
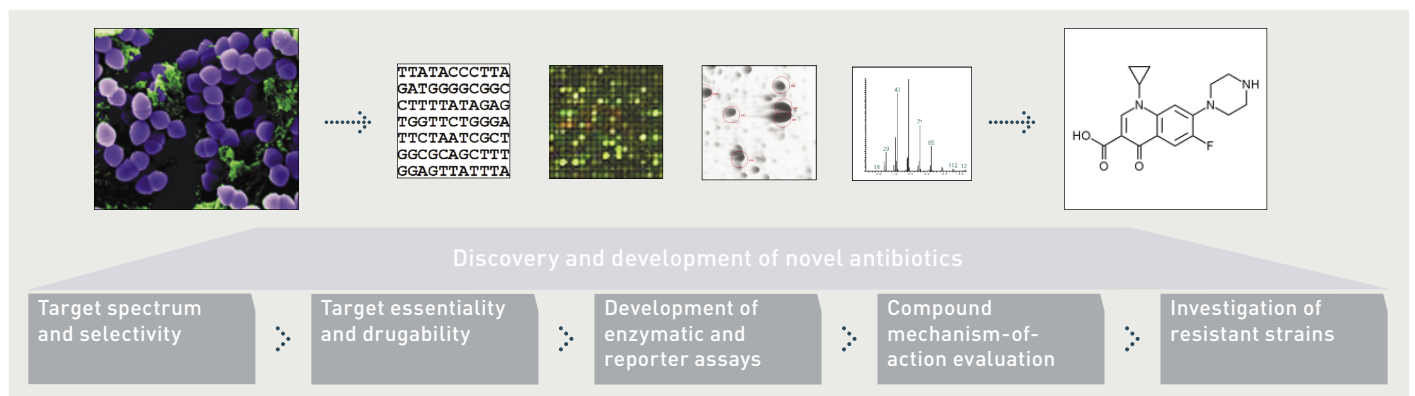## PathoLead Edition

Genedata
solutions in-silico

The enterprise system for *in silico* anti-infectives research

The exponentially increasing number of complete microbial genomes permits for the first time ever a systematic approach to the discovery of novel structural classes of antibiotics. Transcriptomics, proteomics and metabolomics technologies allow for the molecular monitoring of virtually all fundamental processes relevant for infectious diseases. Key processes for infection include the pathogen's ability to invade the host, its ability to survive as well as its drug resistance mechanisms preventing it from being eradicated by antibiotics. Currently, the utilization of the '-omics' data in drug discovery projects is hampered by the complexity and the sheer volume of the automatically generated experimental data.

Genedata Phylosopher® PathoLead Edition Overview

Discovery and development of novel antibiotics

| Target spectrum and selectivity | Target essentiality and drugability | Development of enzymatic and reporter assays | Compound mechanism-of-action evaluation | Investigation of resistant strains |

The Genedata Phylosopher® PathoLead edition is a unique computational system for target, assay and compound information that enables the interpretation and exploitation of '-omics' data in the context of the modern antibiotics discovery process. Phylosopher PathoLead contains a relational database that harbors comprehensive information on all critical themes of pathogen biology. This information ranges from complete pathogen genomes, proteomes and metabolomes to high quality functional information; from the metabolic, regulatory and signaling pathway context to structural characteristics of proteins; from experimental data such as knockout or microarray data to information on known small-molecule inhibitors. Phylosopher PathoLead contains specialized tools for testing hypotheses about newly discovered pathways, algorithms for identifying, validating and ranking target candidates as well as modules to prioritize the development of novel potent drug classes to cure infectious diseases.

Streamlining the Anti-microbial Discovery Process

Phylosopher PathoLead represents a unique enterprise-wide research platform that addresses all the needs of modern anti-bacterial, anti-fungal and anti-viral drug discovery and development. Its integrated relational database serves as a reference system for storing, analyzing and interpreting genomics, transcriptomics, proteomics and metabolomics data. As an enterprise solution Phylosopher PathoLead comes with modules for streamlining department- and company-wide research projects.

Identifying Antibiotic Targets

Phylosopher PathoLead comes with tools to identify and prioritize novel antibiotic target candidates. The system supports the target selection process of a pharmaceutical company by applying rule-based target prioritization criteria. Algorithms to automatically rank broad-spectrum as well as lineage-specific target candidates facilitate the target selection process. A multitude of target selection criteria are taken into account, ranging from the target's pathogen spectrum, its host selectivity, target related phenotypes to drugability criteria such as specific structural properties that make the target amenable to chemical inhibition.
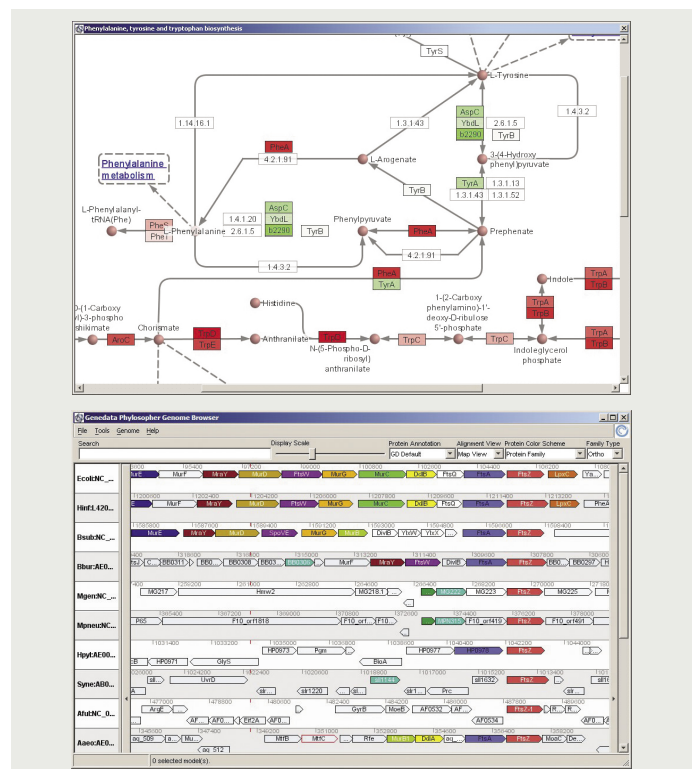
Validating Target Candidates

By integrating experimental data such as phenotype screens, Phylosopher PathoLead further qualifies and ranks target candidates as being suitable for assay development and compound screening. Protein and mRNA expression activity, together with the evidence of a target's essential role in the pathogen provide support for deliberate go or no-go decisions. Scientifically validated tools elucidate the functional context of the target proteins which is critical for downstream assay development. Research groups benefit from a shared and structured repository of information and work performed by colleagues on common target-, assay and compound projects.

Supporting Assay Development

In order to successfully develop enzymatic antibiotic screening assays it is essential to have a thorough understanding of the target protein's molecular function. Phylosopher PathoLead's cutting-edge algorithms shed light onto functionally uncharacterized targets, making many of them tractable candidates for successful assay projects. Tools to pinpoint suitable promoters for reporter assay development enable the identification of promoters whose activation is indicative of a specific pathway or a compound's mode-of-action. Phylosopher PathoLead thus efficiently supports the construction of enzymatic as well as promoter-inducible assay systems of high sensitivity and specificity.

Prioritizing Bioactive Compounds as Drug Candidates

Phylosopher PathoLead reveals the molecular mechanism-of-action of uncharacterized bioactive molecules. Proprietary algorithms automatically rank and evaluate compounds according to their underlying efficacy mechanisms. These methods are particularly helpful for evaluating and characterizing libraries of natural products or HTS hits. Complementary tools for guiding chemical development help in efficient mode-of-action tracking of lead compounds.

Understanding Pathogenicity and Drug Resistance

Phylosopher PathoLead compares a wide range of pathogens in parallel and thereby identifies and characterizes the shared genes as well as differences of phylogenetically diverse microbes and closely related strains. The automated comparison of genome sequences and whole-genome expression patterns of resistant and non-resistant strains helps to unravel drug resistance mechanisms, including drug efflux mechanisms and drug metabolism. Tools for analyzing strain genotypes correlate pathogenicity of strains with clinical outcome and thereby facilitate the identification of robust diagnostic markers.

For further information about Phylosopher PathoLead and other focused Phylosopher editions, please visit our website at www.genedata.com or contact us at phylosopher@genedata.com