The Genome Enhancer

Based on the BioUML technology, a tool has been developed that analyzes genomics, transcriptomics, epigenomics, proteomics and metabolomics patient data and identifies key drug targets. The tool generates a comprehensive report, which includes detailed information about the genes found to characterize the studied clinical case, the transcription factors that regulate those genes, and the reconstructed intracellular signaling network with identified master regulators. Since they are potential drug targets for treating the studied pathology, the report also provides information about known drugs and further chemical compounds that may affect the identified targets.

Services

Making use of the expertise acquired during the past 20 years of development and applying own tools onto a range of biological problems, geneXplain also offers tailor-made data analysis services and collaborations on joint projects. These projects may refer to biomarker discovery, drug target identification and search for new drugs or new drug applications.

Recent publications

Kel A et al. (2019) Walking pathways with positive feedback loops reveal DNA methylation biomarkers of colorectal cancer. BMC Bioinformatics. 20 (Suppl 4), 119.

Kolpakov F et al. (2019) BioUML: an integrated environment for systems biology and collaborative analysis of biomedical data. Nucleic Acids Res. May 27. pii: [Epub ahead of print]

Boyarskikh U et al. (2017) Master-regulators driving resistance of non-small cell lung cancer cells to p53 reactivator Nutlin-3. Virtual Biology 4, 1-31.

More publications can be found on our web page.

Genome Enhancer

About geneXplain

GeneXplain's mission is to provide a comprehensive platform for bioinformatic, systems biological and cheminformatic tools. The raison d'être of this platform is to assist translational research in the life sciences, mainly in the context of cancer research, personalized medicine and pharmacogenomics. We intend to make our expertise available to academic and commercial partners in collaborative research projects.

To achieve this, geneXplain offers:

- TRANSFAC®, the most comprehensive database on eukaryotic transcription regulation. TRANSFAC® is now also available under the geneXplain platform, providing the most comprehensive collection of TF DNA-binding profiles.
- TRANSPATH®, one of the largest pathway/network databases presently available, particularly well suited for geneXplain's proprietary *Upstream Analysis*.
- HumanPSD™, a rich information resource connecting pathways with targets, drugs and clinical trials.
- PASS and PharmaExpert for predicting biological activities of compounds qualitatively.
- GUSAR for QSAR model building and quantitative activity prediction.

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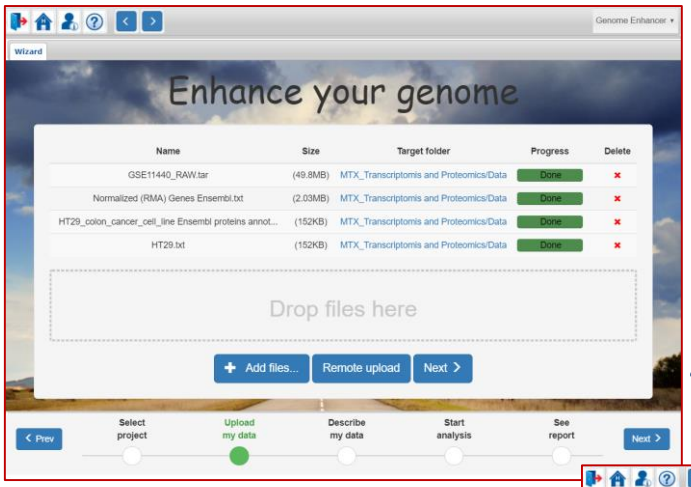
Genome Enhancer

The fully automated tool for multi-omics data analysis in precision medicine

geneXplain

Genome Enhancer:
a fully automated pipeline for precision medicine

Genome Enhancer is a fully automated pipeline for the analysis of patients' multi-omics data and identification of personalized drug targets. Genome Enhancer also predicts prospective therapies which can be used against the identified targets and gives a detailed insight into the identified molecular mechanism of the studied pathology. The tool integrates all omics data types inside one analysis pipeline, including genomics, proteomics, transcriptomics, epigenomics and metabolomics data.



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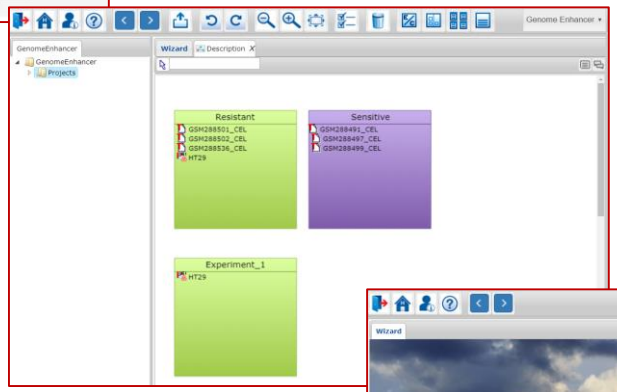
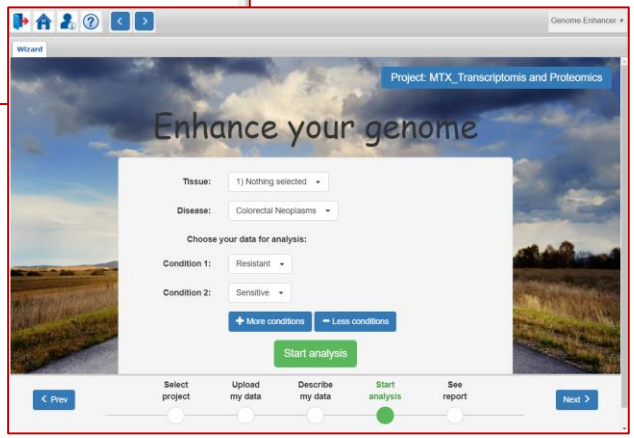


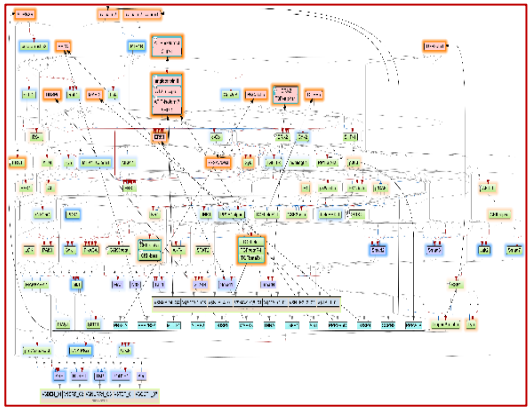


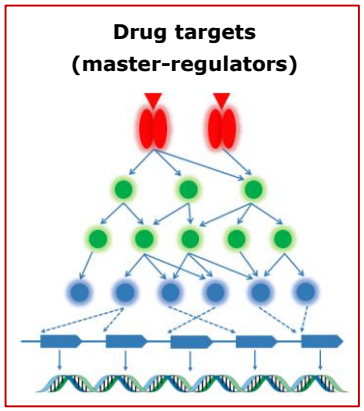
Key features

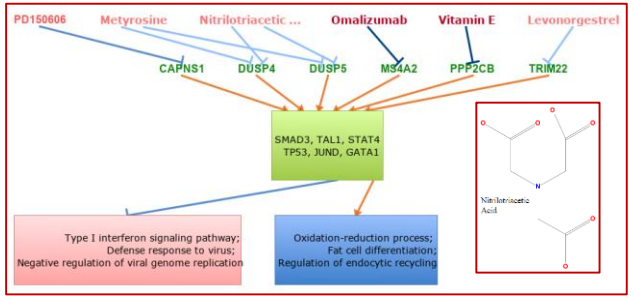
- Identifies activated targets in the examined patient data and selects the best fit therapy for every studied case
- Issues a clear result in the form of a scientific paper
- Suites for use by medical doctors and biologists
- Does not require special skills
- Processes all types of omics data
- Easy data upload and annotation
- One-click run
- Generates a comprehensive report on identified drug targets and prospective therapies

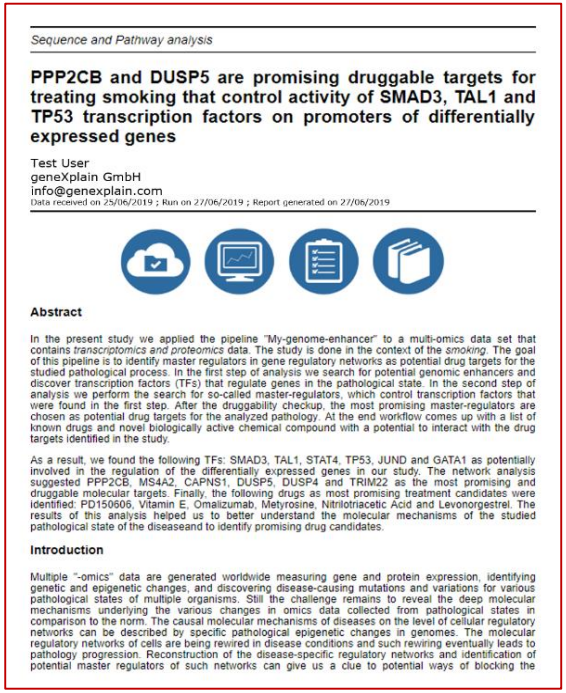
The workflow

Genome Enhancer uses geneXplain's proprietary *Upstream Analysis*, an integrated promoter and pathway analysis, to identify potential drug targets for the studied pathology. In the first step of this analysis the transcription factors that regulate differentially expressed or mutated genes are identified with the use of the TRANSFAC® database. The second step searches for common master-regulators of the identified transcription factors by building a personalized signal transduction network of the studied pathology using the TRANSPATH® database. The identified master regulators are prospective drug targets candidates and they are used for further selection of chemical compounds that can bring therapeutic benefit for the studied clinical case. In this step the HumanPSD™ database is employed to identify drugs that have been tested in clinical trials. Using the tool PASS, a cheminformatic analysis is performed to predict small molecules that can affect the identified targets. As the result of analysis a comprehensive report is generated. It includes the description of all methods used and results obtained.









Sequence and Pathway analysis

PPP2CB and DUSP5 are promising druggable targets for treating smoking that control activity of SMAD3, TAL1 and TP53 transcription factors on promoters of differentially expressed genes

Test User
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Data received on 25/06/2019 ; Run on 27/06/2019 ; Report generated on 27/06/2019

Abstract

In the present study we applied the pipeline "My-genome-enhancer" to a multi-omics data set that contains *transcriptomics and proteomics* data. The study is done in the context of the *smoking*. The goal of this pipeline is to identify master regulators in gene regulatory networks as potential drug targets for the studied pathological process. In the first step of analysis we search for potential genomic enhancers and discover transcription factors (TFs) that regulate genes in the pathological state. In the second step of analysis we perform the search for so-called master-regulators, which control transcription factors that were found in the first step. After the druggability checkup, the most promising master-regulators are chosen as potential drug targets for the analyzed pathology. At the end workflow comes up with a list of known drugs and novel biologically active chemical compound with a potential to interact with the drug targets identified in the study.

As a result, we found the following TFs: SMAD3, TAL1, STAT4, TP53, JUND and GATA1 as potentially involved in the regulation of the differentially expressed genes in our study. The network analysis suggested PPP2CB, MS4A2, CAPNS1, DUSP5, DUSP4 and TRIM22 as the most promising and druggable molecular targets. Finally, the following drugs as most promising treatment candidates were identified: PD150606, Vitamin E, Omalizumab, Metyrosine, Nitrilotriacetic Acid and Levonorgestrel. The results of this analysis helped us to better understand the molecular mechanisms of the studied pathological state of the diseaseand to identify promising drug candidates.

Introduction

Multiple "-omics" data are generated worldwide measuring gene and protein expression, identifying genetic and epigenetic changes, and discovering disease-causing mutations and variations for various pathological states of multiple organisms. Still the challenge remains to reveal the deep molecular mechanisms underlying the various changes in omics data collected from pathological states in comparison to the norm. The causal molecular mechanisms of diseases on the level of cellular regulatory networks can be described by specific pathological epigenetic changes in genomes. The molecular regulatory networks of cells are being rewired in disease conditions and such rewiring eventually leads to pathology progression. Reconstruction of the disease-specific regulatory networks and identification of potential master regulators of such networks can give us a clue to potential ways of blocking the