The Systems Toxicology Challenge

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sbv IMPROVER
SYSTEMS BIOLOGY VERIFICATION

sbv IMPROVER Challenges

2014/2015 - Network Verification Challenge

- The NVC Challenge aims at verifying the biological network models to ensure their relevance to lung biology and COPD.

Symposium 2014, Montreux (Switzerland)
Symposium 2015, Barcelona (Spain)

2013 - Species Translation Challenge

- Changes in phosphorylation status and gene set activation induced by cellular response to 52 different perturbations in human cells can be predicted to a certain extent given responses generated in rat cells.
- The data generation was summarized in: Scientific Data 2014. The Species Translation Challenge. A Systems Biology Perspective on Human and Rat Bronchial Epithelial Cells Scientific Data.
- A special issue of Bioinformatics summarizes the findings and methodologies of the best performers.

2012 - Diagnostic Signature Challenge

- The goal of this challenge was to assess and verify computational approaches that classify clinical samples based on transcriptomics data.
- The high quality of predictions confirmed the value of the approaches used and concluded successfully in two publications [1], [2].

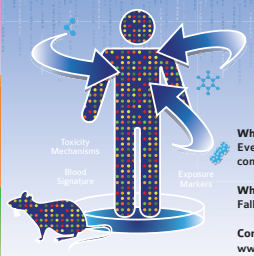
Benchmarking
Use our Diagnostic Signature Benchmarking tool to see how you compare with your peers
DOWNLOAD SUBMIT COMPARE

Use our free web-based Diagnostic Signature Benchmarking tool to self-asses how well your method is able to classify clinical samples based on transcriptomics data and compare your results with the ones of your peers.

Symposium 2012, Boston (USA)

2015-2016 Systems Toxicology Challenge

Designed to verify that a robust predictive gene signature can be extracted from gene expression data that differentiates exposed and non-exposed subjects.



Who can be part of the Challenge?
Everyone - Knowledge in computational science is an asset

When?
Fall 2015 - Srping 2016

Contact
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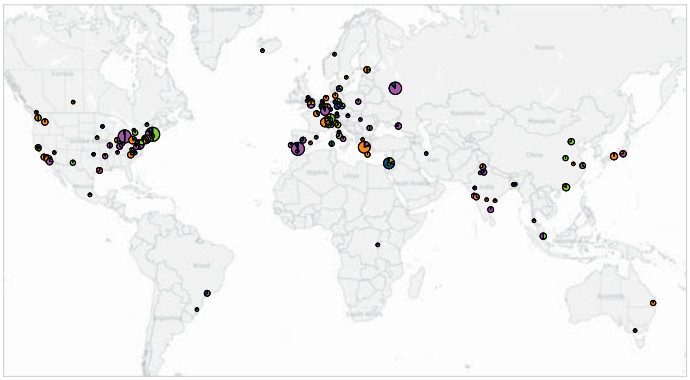
Benchmark your Methods !

Systems Response Profiles → Identify Perturbed Networks → Network Perturbation Amplitudes → Product Biological Impact Factor

Design of Experiment & Experimental Data Production

[1] Hoeng et al., 2013; Systems Biomedicine Sep 1;4: 1935
[2] Tarca et al., 2013; Bioinformatics Nov 15;29(22):2892-9

Worldwide Participation in sbv IMPROVER March 2012 - December 2014



Number of participants: 1, 10, 20, 40

Challenge: sbv IMPROVER, DSC, STC, NVC

5 Continents
38 Countries
>250 Institutions
>450 Participants

Systems Toxicology Challenge

The current scope of sbv IMPROVER (Industrial Methodology for Process Verification in Research; http://sbvimprover.com/) is the verification of methods and concepts in systems biology research via challenges opened to the scientific community.

Risk assessment in the context of 21st century toxicology relies on the elucidation and understanding of mechanisms of toxicity. For that purpose, datasets generated by high-throughput technologies (e.g., high-throughput/content screening) combined with various omics data types are now generated in vitro to test large and diverse set of chemicals (e.g. ToxCast). The development of relevant computational approaches for the analysis and integration of these big data remains challenging and requires qualitative and quantitative evaluation

The next question IMPROVER aims to address in the framework of the Systems Toxicology Challenge is: "are omics measurements sufficiently informative to predict/quantify the activity of cellular pathways involved in toxicity response?", which includes:

1. The Marker of Exposure Response Identification sub-challenge (Launch Fall 2015)
that aims at evaluating methodologies for the identification of specific markers of exposure response.

2. The In-vitro Toxicity Mechanisms prediction sub-challenge (Launch later 2016)
that aims at evaluating the predictability of toxicity mechanisms by omics data.

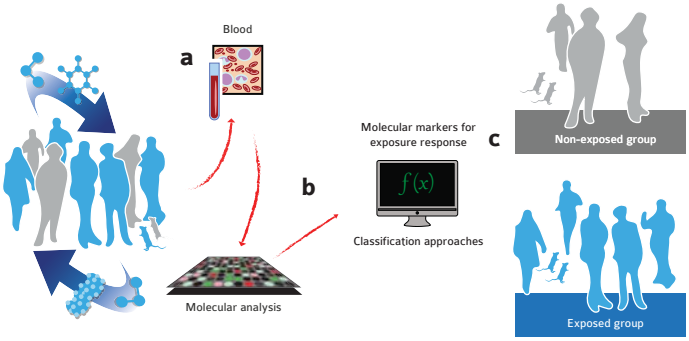
Participants will be provided with high quality data sets to develop predictive models/classifiers.

The integration of a priori biological knowledge in the development of computational approaches may be required to enable biological interpretability/understanding of the predictions.

The results and post-challenge analyses will be shared with the scientific community, and published in scientific journals.

Markers of Exposure Response Identification

Objective: to verify that robust gene signatures of exposure response can be extracted in whole blood gene expression data from human, or human and rodent to predict exposed and non-exposed group labels.



a. Blood samples are collected from human and mouse subjects belonging to exposed or non-exposed groups.
b. Gene expression profiles (GEX) are measured using microarray-based technology.
c. Participants are provided with GEX and asked to develop a classification approach that identifies a gene signature capable to associate subjects to the correct exposure group.

The Two Sub-Challenges (Fall 2015)

Sub-challenge1: Human blood signature as exposure response marker
Humans are constantly exposed to individual or mixtures of chemicals (e.g. cigarette smoke, polluants, pesticides, drugs) that may trigger molecular changes in their organism. The identification of specific response markers is important to assess the exposure status of an individual. The blood is an easily accessible matrix, however remains a complex biofluid to analyze.

Scientific Question
Are gene expression changes in blood sufficiently informative to extract a predictive gene signature for smoking exposure (Smoker vs Non-current smoker) or cessation (Former smoker vs Never smoker) in human?

Sub-challenge2: Species translatable blood signature as exposure response marker
Most of pre-clinical in vivo studies are conducted in rodents which raises the question of translatability and applicability of results to human.

Scientific Question
Are gene expression changes in blood of humans and rodents sufficiently informative to define a unique rule or classifier to extract a specific gene signature predictive of smoking exposure (Smoker vs Non-current smoker) or cessation (Former smoker vs Never smoker) in both species?

Key references

1. Hoeng et al. Where are we at regarding species translation? A review of the sbv IMPROVER challenge. Bioinformatics, 2015
2. Rhrissorrakrai et al. Understanding the limits of animal models as predictors of human biology: lessons learned from the sbv IMPROVER Species Translation Challenge. Bioinformatics, 2015
3. Bilal et al. A crowd-sourcing approach for the construction of species-specific cell signaling networks. Bioinformatics, 2015
4. Hormoz et al. Inter-species inference of gene set enrichment in lung epithelial cells from proteomic and large transcriptomic datasets. Bioinformatics, 2015
5. Dayarianet al. Predicting protein phosphorylation from gene expression: top methods from the IMPROVER Species Translation Challenge. Bioinformatics, 2015
6. Biehl et al, Inter-species prediction of protein phosphorylation in the sbv IMPROVER species translation challenge. Bioinformatics, 2015
7. Poussin et al, The species translation challenge—A systems biology perspective on human and rat bronchial epithelial cells. Scientific Data, 2014
8. Tarca et al. Strengths and limitations of microarray-based phenotype prediction: lessons learned from the IMPROVER Diagnostic Signature Challenge. Bioinformatics, 2013
9. sbv IMPROVER project team. Enhancement of COPD biological networks using a web-based collaboration interface. F1000Res, 2015
10. sbv IMPROVER project team. Reputation-based collaborative network biology. Pac Symp Biocomput, 2015
11. Boué et al. Causal biological network database: a comprehensive platform of causal biological network models focused on the pulmonary and vascular systems. Database (Oxford), 2015
12. sbv IMPROVER project team. On Crowd-verification of Biological Networks. Bioinform Biol Insights, 2013
13. Hoeng et al. A network-based approach to quantifying the impact of biologically active substances. Drug Discov Today, 2012
14 Meyer et al. Industrial methodology for process verification in research (IMPROVER): toward systems biology verification. Bioinformatics, 2012
15. Meyer et al. Verification of systems biology research in the age of collaborative competition. Nat Biotechnol, 2011

The sbv IMPROVER project, the website and the symposia are part of a collaborative project designed to enable scientists to learn about and contribute to the development of a new crowd sourcing method for verification of scientific data and results. The current challenges, website and biological network models were developed and are maintained as part of a collaboration among Philip Morris International, Selventa, OrangeBus, and ADS. The project is led and funded by Philip Morris International. For more information on the focus of Philip Morris International's research, please visit www.pmi.com.

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