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Headline: Systems Toxicology Computational Challenge Impacts Diagnostics, Personalized Medicine, Toxicological Risk Assessment

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Results of the Systems Toxicology Computational Challenge have demonstrated how transcriptomics information present in the blood can be used to predict whether people have been exposed to specific toxicants (Computational Challenge Symposium 2016; Intelligent Systems for Molecular Biology Conference, July 11, 2016, Orlando, Fl.). Challenge participants used their own computational techniques to make predictions, with best performers achieving accuracy of up to 95%.

“The real-world application of models based on blood gene expression markers for predictive classification in toxicology is uniquely challenging,” said Dr. Carine Poussin, Computational Biology, Philip Morris International. “The difficulty resides in the identification of relevant markers in blood after chemical exposure and the low success of correct classification when predictive models are applied on new individual blood samples. Furthermore, most preclinical toxicological in vivo studies are conducted in rodents, adding a degree of complexity when applying the results to humans. The Systems Toxicology Computational Challenge has explored these questions and helped to increase our understanding of what is necessary to reach higher levels of predictability and robustness in both humans and across species.”

The Systems Toxicology Computational Challenge aimed to verify that robust markers could be extracted from blood gene expression data that would distinguish current tobacco smokers from nonsmokers, and then discriminate nonsmokers as former smokers and never-smokers. This question was addressed in two subchallenges, the first looking at human data only, and the second one investigating human and mouse data together. Anonymized participants’ submissions were scored against a gold-standard data set. Final results and team rankings were reviewed and approved by an independent expert scoring review panel.

Participants were successful in developing models with a high level of predictive performance in distinguishing current tobacco smokers from nonsmokers. Predicting whether nonsmokers were former smokers or never-smokers was more challenging, suggesting that these two groups are likely to have similar gene expression profiles.

“While the Systems Toxicology Computational Challenge asked participants to make predictions on smoking status, the techniques that participants put forward could in theory be applied to make predictions on exposure to any toxicant or external stimuli,” said Dr. Julia Hoeng, director of Systems Toxicology, Biological Systems Research, Philip Morris International. “Importantly, the challenge rules stipulated that models had to be applicable to new individual blood samples without the need for adjustments, making them potentially suitable for ready-to-use diagnostic tools.”

Dr. Vincenzo Belcastro, Systems Biology, Philip Morris International, commented: “The best-performers in the Systems Toxicology Computational Challenge have achieved near perfect prediction to discriminate smokers from nonsmokers. Different methods were used and it is worth considering how these methods could be combined to improve predictability even further, and to add to the confidence we can have in using them. Many of the techniques that have been tested in this challenge should be highly interesting for scientists working in a number of different fields, as well as for industries such as pharmaceuticals and biotech.”

The Systems Toxicology Computational Challenge is the latest to be run under the sbv IMPROVER umbrella, a crowd-sourcing initiative led and funded by Philip Morris International, which is designed to test and verify scientific methods and results. More information on the sbv IMPROVER project is available at http://www.sbvimprover.com.

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