Date: November 2015

Headline: A New Look into Toxicology Risk Assessment and Environmental Safety

Byline: n/a

Article online at: http://www.asiabiotech.com/19/1911/19110017x.html

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Julia Hoeng is Manager of Systems Toxicology at PMI Research & Development where she leads the Systems Biology Program, covering a portfolio of projects in vitro, in vivo and in silico research for product testing.

Julia has established her team with systems biology excellence at PMI Research & Development over the last seven years and she is the PMI project leader of the SBV IMPROVER project.

She holds a PhD and Post-doc from Cambridge University and a MS in Bioinformatics from Georgia Institute of Technology, Atlanta, Georgia, USA as well as an MBA from Business School Lausanne. Julia has published numerous articles and book chapters highlighting the use of systems biology approaches for toxicology.

1. A quick warm-up on what the *Network Verification Challenge* is about?

The purpose of the *Network Verification Challenge* is to engage the scientific community in the review of biological network models that are suitable for toxicological risk assessment among other applications. There are two main stages to the challenge:

- First, previously published network models are made available for communal verification by the global scientific community via a bespoke online platform.

- Second, the online stage closes, networks are assessed to identify controversial edges (i.e., those that did not obtain consensus from the community) which are then discussed at an in-person Jamboree meeting which further refines and verifies the networks. The top active performers from the online phase are invited to participate in the Jamboree.

There have been two *Network Verification Challenges* to date. The first culminated in a Jamboree in Montreux, Switzerland (18-20 March 2014). The second culminated in a Jamboree in Barcelona, Spain (15-18 June 2015). 150 participants from 18 countries took

part in the first challenge, while 173 participants from 26 countries took part in the second. The resulting models will be available for download on the challenge website in due course.

Systems Biology Verification— The Toxicology Risk Assessment — *Network Verification Challenge*

sbv IMPROVER stands for Systems Biology Verification combined with Industrial Methodology for Process Verification in Research. This approach aims to provide a measure of quality control of industrial research and development by verifying the methods used. The sbv IMPROVER project is a collaborative effort led and funded by PMI Research and Development.

It is different from other scientific crowdsourcing approaches as it focuses on the verification of processes in an industrial context, and not just on basic questions regarding science. The sbv IMPROVER approach allows an organization to benchmark its methods and industrial processes.

In this featured interview, Dr Julia Hoeng will be sharing with us about the *Network Verification Challenge*, and on how the verification network helps in risk assessments.
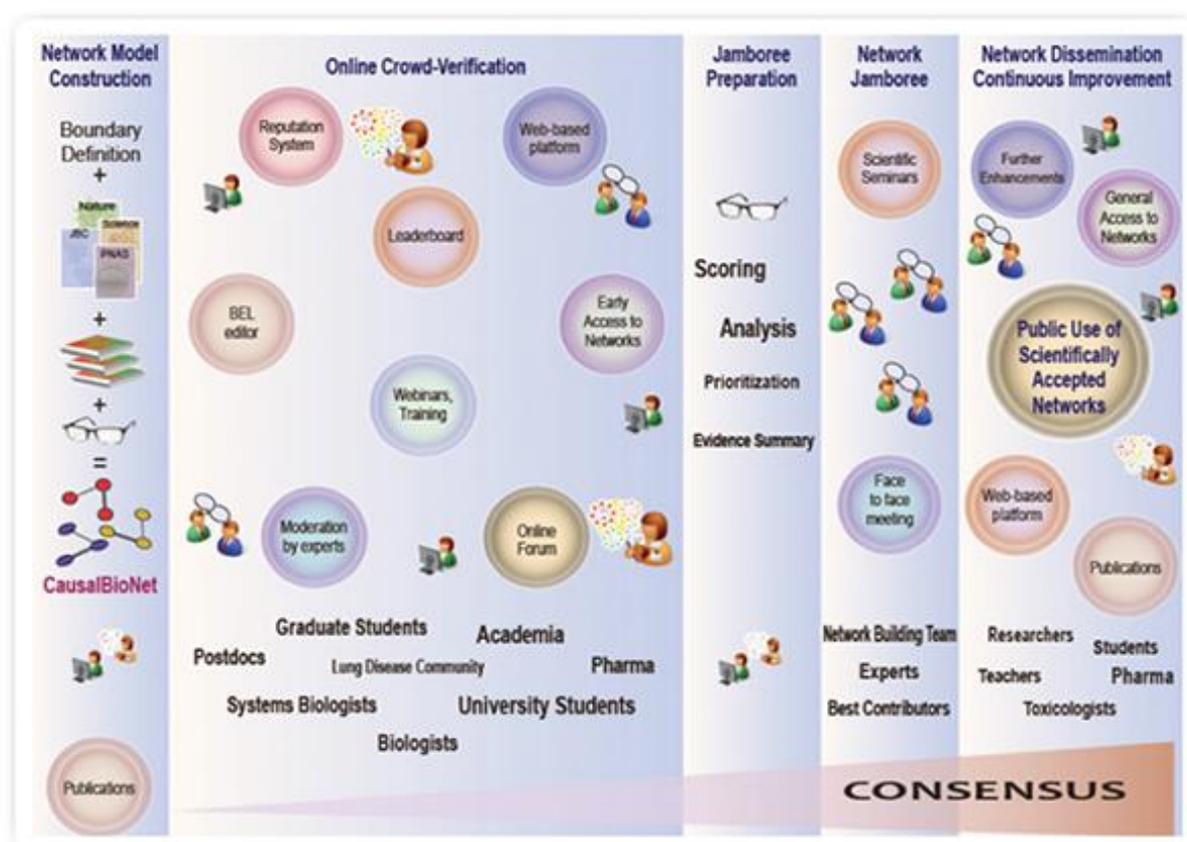

Figure 1. Illustrative chart involved in NVC

2. How is the *Network Verification Challenge* different from the traditional peer-review process?

The *Network Verification Challenge* is part of the SBV IMPROVER project (Systems Biology Verification: Industrial Methodology for PROcess VErification in Research) a collaborative effort led and funded by Philip Morris International Research and Development (PMI R&D)1-2. The overall aim of the project is to develop a robust methodology for verifying systems biology methods and results based on the principles of crowd-sourcing and collaborative competition.

SBV IMPROVER fills a gap in research quality assessment that is not addressed by traditional peer review. Although considered to be one of the most important mechanisms for quality control of scientific papers, it is also acknowledged that traditional peer-review has certain weaknesses. It is open to error / bias and reviewers can only assess whether a paper's conclusions are supported by the data and results that are shown in the paper (there is likely to be a great deal of data that the paper's authors have excluded). SBV IMPROVER is able to address these issues since:

- Each member of the crowd is identifiable and their contributions are made publically.

- All data is available at all times.

- Conclusions are verified based on full datasets, not by results presented by authors.

The scientific conclusions obtained through SBV IMPROVER are fully reproducible and thus can be applied with a high degree of confidence.

3. What are the criteria to participate in the NVC? And the benefits to join the challenge?

Like all SBV IMPROVER challenges, the *Network Verification Challenge* has been freely open to individuals of 18 years or over, excluding only those who have conflicts of interest (e.g., the organizers and related companies) and others who need to be excluded for legal purposes (e.g., those from sanctioned countries). Participants come from academic or research institutions as well as commercial entities.

The incentives for participation in the *Network Verification Challenge* are many, but include peer-recognition and the opportunity to engage with systems biology experts from around the world. Gamification principles are employed to encourage engagement, with users able to move up a leaderboard based on their contributions. Primarily, to take part in an SBV IMPROVER challenge is to be part of a pioneering community that is driving innovation and working together to improve how scientific research is conducted and verified.

4. Is the NVC working closely with publishing companies that may help to publish the research findings?

PMI R&D has published a range of scientific papers on SBV IMPROVER and the *Network Verification Challenge*. We are currently working on a manuscript for the second *Network Verification Challenge* which will be submitted in the comings weeks to a journal and go through the usual peer review process.

5. The NVC seems to place a strong emphasis on toxicology risk assessment. Are there are other risk assessments that may be of interests (e.g. exercise, obesity, occupational)?

As well as toxicological risk assessment, the biological network models being produced in the *Network Verification Challenge* are suitable for drug discovery and mechanistic research in respiratory disease. Furthermore, the *Network Verification Challenge* methodology could in theory be extended to support risk assessments in any biological domain. Indeed, the use of crowdsourcing is growing in popularity as a way to ensure credibility, impartiality and reproducibility of conclusions in a range of scientific contexts. CASP (Critical Assessment of Protein Structure Prediction), DREAM (Dialogue for Reverse Engineering Assessments and Methods) and BioCreAtIvE (Critical Assessment of Information Extraction Systems in Biology) are just three examples of other projects that are using crowdsourcing to address scientific issues in prediction and verification[3-5].

The overall SBV IMPROVER methodology could be applied in an academic context to any area that requires a more meaningful analysis of scientific data and has the potential to be useful for a variety of industries – biotechnology, pharmaceuticals, nutrition and environmental safety to name a few. The potential impact of SBV IMPROVER is thus far reaching and highly significant.

6. A brief illustration on what the BEL (Biological Expression Language) is? What are the advantages of BEL, and what are the changes that BEL will bring to the scientific community?

The Biological Expression Language (BEL) is a structured language that represents scientific findings by capturing causal and correlative relationships between biological entities in computable statements. It has been used in the *Network Verification Challenge* as the syntactical structure of the network models6.

The main advantage of BEL is that it is easily human-readable and machine-computable, making it an ideal language to capture literature evidences from manual curation as well as text mining processes. The language is being increasingly adopted by the scientific community given its simplicity of use and its descriptive power in the representation of biological relationships.

7. Will there be a third NVC? What is next for SBV IMPROVER?

There are no confirmed plans for a third *Network Verification Challenge* at this time. However, the network models we have will remain open for the crowd to further review. The SBV IMPROVER project continues and later this year we will be at the International Conference on Systems Biology in Singapore (23-26 November). We will have a booth promoting the next SBV IMPROVER challenge and we are looking forward to meeting more scientists, from Asia and around the world, that may be interested in taking part.

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