Report of the NJDEP Science Advisory Board

Prepared by the Science Advisory Board
Public Health Standing Committee

The Role of "Omics" in Environmental Health Research and Its Use by NJDEP

Approved by the
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The following report has been issued by the Science Advisory Board to the Commissioner of the New Jersey Department of Environmental Protection

Response to the Charge Questions regarding:

The Role of "Omics" in Environmental Health Research and Its Use by NJDEP

This report was prepared by the Public Health Standing Committee and sent to the Science Advisory Board for review and approval. The Science Advisory Board based this final report on those recommendations from the Public Health Standing Committee.

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The Role of "Omics" in Environmental Health Research and Its Use by NJDEP

Introduction

In 2017, the Public Health Standing Committee (PHSC) of the NJDEP-Science Advisory Board was tasked with investigating "omics" technologies for potential use by NJDEP. The PHSC subsequently formed a three-member Subcommittee to specifically address this topic. The "omics" are research fields that utilize a diverse set of information-dense technologies (e.g., gene arrays, mass spectrometry) aimed at assessing biological processes at the subcellular level. A goal of "omics" research is to identify and quantify the cellular components within a class of biological molecules (e.g., nucleic acids). With the potential to identify molecular events associated with chemical exposures, "omics" have the potential to inform human health risk assessments of environmental contaminants. Additionally, as "omics" may help elucidate fundamental biological processes and be less invasive than traditional toxicity testing methods, "omics" have the potential to contribute to the more humane use of animals in biomedical research (i.e., the "3Rs" principles of reduce, refine, replace; Hendriksen, 2006). The PHSC was asked to deliberate on four charge questions pertaining to "omics" technologies. This report contains the PHSC's response to these charge questions.

Response of PHSC to charge questions

Charge Question #1 – *Describe and summarize the current uses of "omics" (e.g., metabolomics, genomics) in terms of human health.*

The 2017 NRC report, *Using 21st Century Science to Improve Risk-Related Evaluations*, defines seven -omics or omics-related terms.

Adductomics: The comprehensive identification of chemicals that bind to DNA or selected proteins, such as albumin.

Epigenomics: The analysis of epigenetic changes in DNA, histones, and chromatin that regulate gene expression. Epigenetic changes are changes other than changes in DNA sequence that are involved in gene silencing.

Exposome: A term first coined by Wild (2005) to represent the totality of a person's exposure from conception to death; exposome research involves the measurement of multiple exposure indicators by using -omics approaches.

Genomics: The analysis of the structure and function of genomes.

Metabolomics: The scientific study of small molecules (metabolites) that are created from chemicals that originate inside the body (endogenously) or outside the body (exogenously) (National Academies of Sciences, Engineering, and Medicine 2016). For purposes of the present report, metabolomics is assumed to include exogenous chemicals found in biological systems in their unmetabolized forms.

Proteomics: The analysis of the proteins produced by cells, tissues, or organisms. Analysis is conducted to understand the location, abundance, and post-translational modification of proteins in a biological sample.

Transcriptomics: Qualitative and quantitative analysis of the transcriptome, that is, the set of transcripts (mRNAs, noncoding RNAs, and miRNAs) that is present in a biological sample.

The following is a specific description for one of these omics technologies. A thoughtful summary of Metabolomics can be found in a white paper by Beger et al. *Metabolomics*, 2016, 12:149. Metabolomics is the comprehensive study of the metabolome, the repertoire of biochemicals (or small molecules) present in cells, tissues, and body fluids. The study of metabolism at the global or ''-omics'' level is a rapidly growing field that has the potential to have a profound impact upon medical practice. At the center of metabolomics, is the concept that a person's metabolic state provides a close representation of that individual's overall health status. This metabolic state reflects what has been encoded by the genome, and modified by diet, environmental factors, and the gut microbiome. The metabolic profile provides a quantifiable readout of biochemical state from normal physiology to diverse pathophysiologies in a manner that is often not obvious from gene expression analyses.

As pointed out in an article by Khymenets, et al, 2016 "Metabolomic Approaches in the Study of Wine Benefits in Human Health", nutrition is an area where –omics has been employed extensively and is likely an area where it can be used broadly to study human health and nutrition interactions. Specifically, with the molecular profiles that have been developed for DNA, RNA, proteins, lipids, etc.

Charge Question #2 – *Which of these "omics" methods could be used to support and supplement NJDEP's existing tools for risk assessment?*

A paper by Ankley et al (2016) provides insight into how these omics tools (such as those described in charge question 1) can be used, the paper *Pathway-Based Approach for Environmental Monitoring and Risk Assessment* provides four categories of risk assessment applications:

- understanding of adverse outcome pathways (AOP),
- having a mechanistic understanding of environmental assessment,
- using environmental monitoring data and assessment of mixtures, and
- linking exposure to effect.

For NJDEP and similar agencies charged with protecting human health, the –omics databases provide a universal type of data reservoir that allows scientists at NJDEP and their academic partners to look at existing data and apply the conditions of concern, in this case in New Jersey, to make informed decisions about a kind of risk either to human or environmental health.

It is recommended that NJDEP continues to follow the proceedings of authoritative efforts (e.g., review articles, workshops, etc.) to monitor the developments in the use of omics for risk assessment. For example, in a workshop sponsored by the NIEHS (Birnbaum et al. 2015) they described omics as being the tool that allows for multiple information sources across a wide range of conditions with multiple chemicals (mixtures) to be considered in performing risk assessments.

Charge Question #3 – *Provide recommendations for their use.*

Omics techniques incorporate various approaches for analyzing different large groups of data, such as genes (genomics), mRNA (transcriptomics), proteins (proteomics) and metabolites (metabolomics), to evaluate biological samples have been used successfully in biomedical research but not yet in risk assessment for regulatory purposes. A major concern in attempting to use these omics techniques in

regulatory settings is that no standardized approach for applying them when processing data sets have been developed. Therefore, different outcomes can result from different investigators evaluating the same data set. Further, reference materials on chemicals have not been developed for the techniques that can be applied to compare different studies and datasets.

The promise of omics applications is that complex systems can be better understood if they are considered as a whole system through a system biology approach. Additionally, incorporating different data groups that consider genetic, environmental and metabolic factors can better address risk to environmental contaminants across different populations. However, the current state of knowledge is still insufficient to apply these techniques to derive risk estimates for regulatory purposes.

The following are the recommendations relative to using omics techniques for Risk Assessment:

- Omics can be used as a screening tool to identify potential risks that link mixtures of environmental contaminants and diseases across different populations with different genetic variations;

- Results from Omics techniques can be one component of supporting a risk assessment but should not be relied upon as the definitive result for assigning a risk; and

- DEP should work with others or keep appraised on progress in developing a standardized approach for using omics techniques to identify future opportunities for incorporating them into risk assessments.

Charge Question #4 – *Are there opportunities for the development of chemical-specific case studies, preferably based on existing risk assessments, demonstrating the application of "omics" research to public health issues with relevance to NJ?*

Pre-existing case studies prepared by authoritative bodies serve as examples for how NJDEP may apply "omics" research to public health issues. Specifically, examples exist for how data from "omics" research (e.g., *in vitro* data) can generally be applied to risk assessment and for chemical-specific scenarios.

As was stated earlier in Questions 1, 2, and 3 "omics" are a tool in risk assessment, combined with other tools and methodologies for assessing risk from chemical exposures. With the Using 21st Century Science to Improve Risk-Related Evaluations Report, from the National Research Council (2017) as the key reference for this charge question, we feel that *in vitro* data are useful for risk assessment; however, these tools and data are specific and often not easy to apply to a real-world risk. As a suggested resource for NJDEP, Appendix D in the NRC report outlines very carefully the application of these tools. Quoting directly from the NRC report: "It is important to note that the assays used in the ToxCast program do not represent the entire spectrum of biological processes that might be relevant to human health (that is, all possible adverse effects of exposure to chemicals); therefore, there are likely to be gaps in knowledge of how the three chemicals would interact in a biological system."

Risk situations from specific environmental contaminants range from chemicals that are data rich to data poor. Appendix B in the NRC report provides case studies for both circumstances. It is likely that NJDEP will encounter both scenarios and should look to the case studies in this NRC report as a guide for how to approach similar situations.

Overall Summary

- "Omics" are an informative line of mechanistic evidence that can be used to support human health risk assessment
- "Omics" may or may not predict toxicity and cannot be used as the sole piece of evidence for human health risk assessment
- NJDEP should monitor the activities of other authoritative entities for how to best apply "omics" data to human health risk assessment

References

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