Omics methods in regulatory toxicology: Experts discussed possibility of application

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Advances in *omics* techniques and molecular toxicology represent great challenges, new perspectives and possible solutions for regulatory toxicology. Consequently, a central question is if and how these methods can be used for regulatory purposes in a way that they enable regulators to address important open questions in toxicology. On the one hand, more information may be gained from toxicity studies and the number of animal experiments may be reduced. On the other hand, the relevance and applicability of data obtained by new methods need cautious expert judgement.

To discuss under what conditions and for which purposes *omics* methods might be applied and validated in regulatory toxicology, the German Federal Institute for Risk Assessment (BfR) organised an international expert workshop. The workshop took place in Berlin from October 9 to 10, 2014 . Among the more than 30 participants were experts from a total of 10 countries. Experts discussed requirements on data quality and validation, biological relevance of effects and areas of regulatory toxicology *omics* methods might be used for.

The term *omics* describes methods that aim to analyse complex biological samples by focussing on the whole genome, transcriptome, proteome or metabolome. *Omics* methods consist of a number of techniques sharing the ability to characterize and quantify biomolecules from pools of biological samples. They have been applied in experimental toxicology for more than a decade and are used for mechanistic analysis of toxic effects, inter-species or *in vivo* / *in vitro* comparison.

Advances in *omics* techniques and molecular toxicology represent both chances and challenges for regulatory authorities who consider implementing the use of *omics* methods for purposes such as the identification of adverse outcome pathways or mode of action analysis. *Omics* methods should mainly contribute to grouping of toxic substances, identification of sensitive subgroups and may also be used for prioritisation for further testing within an integrated testing strategy.

Prior to a general utilisation of *omics* data in regulatory toxicology several issues need to be clarified. Therefore, the following issues were discussed:

- requirements on validation, data quality and analysis
- biological relevance of effects detected by *omics* methods and
- identification of areas of regulatory toxicology in which these methods might be used.

From the perspective of the BfR, the symposium has produced the following main outcomes:

Adversity of effects

- The organism level is regarded the anchor point for definition of adversity. Impairment of functional capacity is essential.
- A case-by-case decision is needed, taking into consideration the magnitude of the effect. A link between *omics* findings and classical endpoints should be established.

- No single method is sufficient to reveal an adverse effect.

Application of *omics* methods

- The most advanced applications of *omics* for regulatory purposes are the analysis of mode of action (MoA), the prioritization of substances or their combinations for further toxicological testing, grouping of substances, building of trustable ”adverse outcome pathways” (AOP), and biomarker identification. In addition, *omics* might be helpful in classification and labelling.

Toxicological relevance of *omics* effects

- As a prerequisite, quality of studies and reliability of results must be confirmed. Therefore, validation of methods is essential.
- Results may be considered toxicologically relevant when obtained by different molecular methods and when relevant pathways are affected. The results must be consistent and reproducible and must undergo independent verification. If investigations were performed *in vitro*, effects should be observed in different cell lines.

Perspective

- For new or amended data requirements, *omics* approaches should be considered from the beginning
- The inclusion of *omics* methods might enable a more flexible approach in toxicological testing

The presentations of the symposium will be published soon at the BfR website: www.bfr.bund.de. A full workshop report will be prepared for publication in a scientific journal.