An Ontology to represent Knowledge on Animal Testing Alternatives

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EU Directive 86/609/EEC for the protection of laboratory animals obliges scientists to consider whether a planned animal experiment can be replaced, reduced or refined (3Rs principle). To meet this regulatory obligation, scientists must consult the relevant scientific literature prior to any experimental study using laboratory animals. More than 50 million potentially 3Rs relevant documents are spread over the World Wide Web, biomedical literature and patent databases. In April 2008, the beta version of Go3R (www.Go3R.org), the first knowledge-based semantic search engine for alternative methods to animal experiments, was released. Go3R is free of charge and enables scientists and regulatory authorities involved in the planning, authorisation and performance of animal experiments to determine the availability of alternative methods in a fast and comprehensive manner.

The technical basis of this search engine is specific 3Rs expert knowledge captured within the Go3R Ontology containing 87,218 labels and synonyms. A total of 16,620 concepts were structured in 28 branches, where 1,227 concepts were newly defined to specifically describe directly 3Rs relevant knowledge. Additionally relevant headings from MeSH where referenced to reflect the topics associated with the definition of Animal Testing Alternatives. Therefore it is distinguished between thematic-defining and directly 3Rs relevant branches. In addition to the assignment of direct parent-child relationships, further relationship types were introduced to allow to model 3Rs relevant domain knowledge. Examples for such knowledge are e.g. (1) the characteristics of cell culture tests methods, which usually utilize "specific cell types" or "cell lines" and are associated with a specific "endpoint" and "endpoint detection method" or (2) named test methods like "PREDISAFE TM", which replaces an animal test namely the "eye irritation test" in rabbits and uses specific cells namely "SIRC Cells" or (3) the "Haemagglutinin-Neuraminidase Protein Assay", which detects a protein of the "Newcastle disease virus".

Thereby, an article in which e.g. a specific 3Rs method is not explicitly mentioned could still be recognized as relevant for the specific topic searched for in an indirect manner, for example if it mentions specific cells, endpoints or endpoint detection methods, which are relevant for the respective application.
The search engine Go3R with its novel ontology is already well recognized by the 3Rs community and will be further maintained and developed.

Methods: A platinum nanoparticle aerosol was generated using a spark discharge generator in nitrogen as the carrier gas. The Pt NP aerosol was diluted by the factor of 10 with synthetic air directly after the generation process. The aerosol was directed to the Karlsruhe Exposure system (Paur et al., 2008; Diabaté et al., 2008) to analyze the toxicological potential of the freshly generated Pt NP aerosol.

For the bioassay we employed the human alveolar epithelial cells A549 and the bronchial epithelial cells BEAS-2B, which was co-cultured with differentiated THP-1 macrophages, growing on Transwell inserts. The responses of the cells were analyzed by measuring viability (AlamarBlue assay), release of lactate dehydrogenase (LDH) as an indicator of membrane integrity, induction of heme oxygenase-1 (HO-1) as an indicator of an anti-oxidative response and release of Interleukin-8 (IL-8) as an indicator of a pro-inflammatory response. Additionally, Pt NPs collected on polycarbonate filters (pore diameter 0.4 µm) were used