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Exploiting toxicity networks as the basis for reliable prediction without animal testing

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Abstract

Toxicogenomics provides a library of generic expression profiles for different classes of toxicity that allows the characterization of an unknown compound based upon the profiles with which it fits.

Carcinogenicity testing is in this respect an interesting case study. The use of toxicogenomics for identifying the mechanisms of action of genotoxic and non-genotoxic carcinogens has resulted in useful training sets (Johnson et al., 2004); van Delft et al., 2004). Recently, Magkoufopoulou et al. (2011) developed a toxicogenomics-based test using the HepG2 human hepatocyte cell line providing a higher specificity (90-100%) than the currently used testing strategy for genotoxicity assessment (53%) when tested on the same chemicals.

Similar models for sensitization have been developed and refined. The assay consists of analysis of a cellular *in vitro* assay utilizing mRNA profiling, monitored by DNA microarrays, in combination with advanced computational analysis and prediction models for identification of potential sensitizers. The test system is based on a human dendritic cell line (MUTZ-3), mimicking relevant features of *in vivo* immune-regulatory cells. The cells are stimulated with low molecular weight chemicals in non-toxic concentrations in optimal growing conditions, and the readout is the regulated expression profile of a biomarker signature that can be used both to distinguish sensitizers from irritants and non-sensitizers and most importantly to assess potency of sensitizers (Johansson et al., 2011).

These examples demonstrate the usefulness of toxicogenomics as tool for identifying hazardous compounds useful as a brick in testing strategies for safety assessment.

Biography

Erwin Roggen holds a Ph.D. in Biochemistry (1984). Through fellowships he expanded his expertise to include protein chemistry, molecular biology, immunology, cell biology and management. He joined Novozymes AS (1996) where he developed and implemented tools and strategies for *in vitro* safety assessment. He started 3Rs Management and Consultancy (2009) to drive the implementation of these novel approaches by industry. He is president of IVTIP, member of EPAA, and the Scientific Boards of ECVAM, Ecopa, the Dutch Center for Toxicogenomics, the editorial board of Toxicology *In Vitro* and Frontiers. He is expert-evaluator for the European industry-academia partnership Biotech projects.