Editorial:

CURRENT DEVELOPMENTS IN TOXICOLOGY

Stewart JD, Marchan R

Leibniz-Institut für Arbeitsforschung an der TU Dortmund, Leibniz Research Centre for Working Environment and Human Factors (IfADo), Ardeystrasse 67, 44139 Dortmund, Germany

marchan@ifado.de

As already previously reported the EXCLI Journal closely cooperates with the Archives of Toxicology as a partner for articles focussing on basic and clinical research (Bolt, 2011; Bolt and Stewart, 2011). To give our readers an overview over current cutting-edge topics in toxicology we publish a compilation of brief ‘key messages’ from the most cited articles (Table 1). The citation ranking illustrates that research on nanoparticles has evolved to the currently most studied field in toxicology (Xie et al., 2010; Foldbjerg et al., 2011). As in the previous years oxidative stress research remains a cutting-edge topic (Kell, 2010). Clearly, alternative methods of toxicity testing represent an emerging field of research. This development was further intensified by the 7th amendment to the EU Cosmetics Directive that prohibits to put animal-tested cosmetics on the market after 2013 (Adler et al., 2011). Although this directive has been controversially discussed it has nevertheless initiated intensive research activities to establish novel in vitro tests. The review of Adler and colleagues gives a comprehensive analysis of the current status of alternative methods and of the time necessary to achieve full replacement of animal testing.

Table 1: Key messages of the most cited articles in Archives of Toxicology (2010-2011)
(from: Bolt et al., 2012)

| Key message                                                                                                                                                                                                 | Reference |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Many degenerative diseases and toxicological insults converge on iron dysregulation. This review summarises concepts of autocatalytic production of hydroxyl radicals a process which is intensified by positive feedback loops. Systems biology approaches predict that interventions, such as iron chelators and antioxidants may prove most effective in diseases such as Parkinson’s, Huntington’s, Alzheimer’s, prions as well as any intoxications. The comprehensive review is the most cited article of the current evaluation period (2010, 2011). | Kell, 2010 |
| The trichothecene mycotoxin deoxynivalenol (DON) is produced by the fungus Fusarium in wheat and corn. This review summarises the molecular mechanisms of DON; which are ribotoxic stress, disturbed protein synthesis, compromised cell signalling, differentiation and proliferation. Proinflammatory gene induction, disruption of the growth hormone axis and altered gut integrity finally lead to gastroenteritis ("vomitoxin"), anorexia, immunotoxicity and impaired reproduction in experimental animals. This review is the second most cited article of this evaluation period. | Pestka, 2010 |
Table 1 (cont.):  Key messages of the most cited articles in Archives of Toxicology (2010-2011)  
(from: Bolt et al., 2012)

| Key message                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Reference                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| This review summarises the state of the art of in vitro toxicity tests in five critical fields of toxicity: toxicokinetics, repeated close toxicity, carcinogenicity, skin sensitisation, and reproductive toxicity. The background of this review is the prohibition to put animal-tested cosmetics on the market in Europe after 2013. The status and perspectives of each field are carefully analysed. For example, for skin sensitisation, in vitro techniques may already be able to identify sensitisers ahead of 2017. However, in other fields, particularly carcinogenesis, repeated dose toxicity and reproductive toxicity a time horizon cannot yet be estimated. This comprehensive review ranked third in the current evaluation period. | Adler et al., 2011                |
| Silica nanoparticles (SiNPs) are widely developed for biomedical applications. This study quantitatively analysed the time-dependent tissue and subcellular distribution of SiNPs in mice, including radioactive counting, transmission electron microscopy and histology. SiNPs accumulate in lungs, liver and spleen, are retained for more than 30 days, are endozytosed by macrophages and could cause liver toxicity. This is the most cited original article of the current evaluation period. It underlines that nanotoxicology emerged as one of the most popular fields in toxicology. | Xie et al., 2010                   |
| Metabolism of inorganic arsenic (iAs) is critical for its toxicity. This study analysed the relevance of arsenic transporters on human hepatocytes for generation of methylated metabolites from iAs. A major finding is that MRP2 expression inversely correlates with cellular retention of iAs as well as methylated metabolites in hepatocytes. This suggests that MRP2 plays an important role in the efflux of iAs and its metabolites. This study is the second most cited original article from the evaluation period. | Drobná et al., 2010               |
| The comprehensive review article gives an overview over the mutagenicity and carcinogenicity studies on selenium and discusses its molecular mechanisms. At low concentrations selenium shows anti-carcinogenic effects. However, at concentrations higher than needed for nutrition it can be genotoxic and carcinogenic. This study may help to regulate the use of selenium in nutrition. | Valdiglesias et al., 2010          |
| Silver nanoparticles (AgNPs) concentration dependently induced reactive oxygen species (ROS), mitochondrial damage DNA adducts and apoptosis in a human alveolar cell line. Pretreatment with antioxidants reduced ROS as well as DNA adducts underlining the relevance of ROS in toxicity of AgNPs. This study ranks third among the most cited original articles. | Foldbjerg et al., 2011            |
| Metabolomics have successfully identified novel biomarkers of disease prognosis and drug efficacy as well as toxicity. This review recommends how novel biomarkers discovered by metabolomics should be verified and introduced into clinical practice. | Mamas et al., 2011                |
| This review focusses on the following aspects of selenium toxicity: (i) The majority of epidemiological studies suggest a cancer-preventing activity. (ii) In cancer treatment selenium acts as a prooxidant inducing apoptosis. (iii) The use of saccharomyces cerevisiae is reviewed as a powerful tool for the study of the mode of action of selenium. | Brozmanová et al., 2010           |
| Ammonium perfluorooctanoate, used in the production of fluoropolymers, induces hepatocellular hypertrophy in rats by activation of the nuclear receptors PPAR alpha and CAR/PXR. | Elcombe et al., 2010              |
| Key message                                                                 | Reference                   |
|---------------------------------------------------------------------------|-----------------------------|
| Formaldehyde causes nasal cancer and lymphohematopoietic malignancies (LHM) in laboratory animals. Nasal cancer seems to be associated with cytotoxicity induced proliferation. LHM occurs at even higher doses than nasal cancer. This study discusses the guideline value of 0.08 ppm formaldehyde as preventive of carcinogenic effects. | Nielsen and Wolkoff, 2010   |
| (1,3)-beta-d glucan, which occurs on damp building materials, induces an inflammation-associated gene transcription profile in mouse lungs. | Rand et al., 2010           |
| This review discusses the future perspectives of organoselenium as pharmacological agents. It also focuses on epidemiological evidence that selenium overexposure leads to chronic degenerative diseases. | Nogueira and Rocha, 2011    |
| This is a comprehensive review about the protective network controlled by the Keap 1-Nrf2 axis, foocusing on proliferation, angiogenesis and apoptosis. | Baird and Dinkova-Kostava, 2011 |
| This review about Nrf2 foocuses on the relevance of Nrf2-disruption in colon, bladder, lung, stomach, breast, skin and liver cancer. | Slocum and Kensler, 2011    |
| This review gives an overview how arsenate and arsenite interfere with intracellular signal transduction networks. | Druwe and Vaillancourt, 2010 |
| High brain concentrations of the organoselenium compound diphenyl diselenide are associated with shorter time to seizure episodes in rats. | Prigol et al., 2010         |
| The development of Parkinson's disease following exposure to welding fumes is an area of emerging concern. This study demonstrates that repeated exposure of rats manganese containing welding fumes causes persistent alterations in dopaminergic targets. | Sriram et al., 2010         |
| Recent studies suggest that inhaled nanoparticles from diesel engine exhaust may also reach the brain. This study demonstrates that inhalation of diesel engine exhaust by rats causes region specific gene expression changes in brain to a comparable extent to that observed in the lung. | van Berlo et al., 2010      |
| Phosphorylated butyrylcholinesterase and phosphorylated albumin were compared as biomarkers of organophosphorus exposure. | Read et al., 2010           |
| This review gives a comprehensive update of the micronucleus assay: toxicological relevance, protocols, application as high-throughput and mechanisms of micronucleus formation. | Kirsch-Volders et al., 2011 |
| The comprehensive review gives an overview over the use of human pluripotent stem cells, embryonic stem cells and induced pluripotent stem cells in developmental, cardio and hepatotoxicity testing. | Wobus and Löser, 2011       |
| Furan is formed during thermal treatment of food and is consistently found in baby foods. It induces hepatocellular and bile duct tumors in rodents. This review gives a thorough risk assessment of furane in human diet. | Bakhiya and Appel, 2010     |
| The liver tumor promoter piperonyl butoxide generates reactive oxygen species which increase c-Myc- and E2F1-related pathways and thereby activate cell proliferation. | Kawai et al., 2010          |
| Oxidative stress alone is not sufficient to explain specific mechanisms induced by nanoparticles. This article addresses nanoparticle induced activation of MAP kinase cascades, p38, JNK, NF kappa B and Nrf-2 signalling pathways. | Marano et al., 2011         |
Table 1 (cont.): Key messages of the most cited articles in Archives of Toxicology (2010-2011)  
(from: Bolt et al., 2012)

| Key message                                                                 | Reference                      |
|-----------------------------------------------------------------------------|--------------------------------|
| Flavonoids have been reported to provide neuroprotection. However, this     | Wagner et al., 2010            |
| article gives evidence of a more complex situation: Quercetin and quercitrin |                                 |
| protected mitochondria of rat brain slices from MeHg induced lipid          |                                 |
| peroxidation. In contrast, rutin did not show a protective effect. Ca 2+     |                                 |
| plays a central role in MeHg induced toxicity.                               |                                 |
| Silica nanoparticles (SiO2-NPs) were found in the endosomes and the cytosol | Al-Rawi et al., 2011           |
| of HeLa cells. No accumulation in mitochondria or nuclei was seen. In       |                                 |
| contrast, the larger ‘submicron particles’ (SiO2-SMPs) accumulated in       |                                 |
| lysosomes.                                                                   |                                 |
| A single nucleotide polymorphism, rs710521[A] located near TP63, recently   | Lehmann et al., 2010            |
| discovered in genome wide association studies, was associated with human    |                                 |
| bladder cancer risk in a case-control series of 1,425 cases and 1,740        |                                 |
| controls.                                                                   |                                 |
| The pyrethroid insecticide cypermethrin disrupts testosterone synthesis    | Wang et al., 2010               |
| in testes of mice.                                                          |                                 |
| The capping material of nanocrystal quantum dots and not the material of    | Hoshino et al., 2011            |
| the care determines toxicity.                                               |                                 |
| The toxicokinetics of thiomersal is completely different from that of      | Rodrigues et al., 2010          |
| methylmercury. Therefore, toxicity data of methylmercury are not an        |                                 |
| appropriate reference for assessing the risk from mercury released from     |                                 |
| the ethylmercury releasing preservative thiomersal.                         |                                 |
| Perfluorooctane (PFOS) is a bio-accumulative pollutant. In rat brain tissue | Liu et al., 2010a               |
| PFOS activates calcium signalling and c-fos as well as c-jun.               |                                 |
| This study applied a genotoxicity assay based on the detection of histone   | Audebert et al., 2011           |
| H2AX phosphorylation to compare bisphenol A and bisphenol F. Bisphenol A   |                                 |
| was not found to be genotoxic whereas bisphenol F showed positive effects.  |                                 |
| Sodium fluoride suppresses proliferation and induces apoptosis in cultivated | Wang et al., 2011               |
| osteoblasts. This effect was caused by decreased insulin-like growth factor- |                                 |
| I expression.                                                               |                                 |
| The flavonoid quercetin protects against methylmercury induced DNA damage   | Barcelos et al., 2011           |
| and oxidative stress in rats.                                               |                                 |
| This review discussed the current possibilities and perspectives of in vitro| Clift et al., 2011              |
| test systems for nanotoxicology.                                            |                                 |
| The aspect ratio (defined as the ratio length: diameter) of carbon nanotubes| Kim et al., 2011                |
| has no influence on genotoxicity.                                           |                                 |
| Inorganic arsenic induces apoptosis in the cerebrum of mice.                 | Yen et al., 2011                |
| Increasing age leads to alterations of hepatic cytochrome P450 isoforms in | Yun et al., 2010                |
| rats. CYP1A1, CYP1A2, CYP2B1 and CYP2E1 were maximally expressed at three   |                                 |
| weeks and decreased late.                                                   |                                 |
| This review gives an update about the mechanisms of action and cellular     | Sinicropi et al., 2010          |
| targets of toxic metals as well as the use of chelating agents for          |                                 |
| pharmaceutical treatment.                                                   |                                 |
| This review summarises epidemiologic studies on maternal exposure to        | Bosetti et al., 2010            |
| particulate matters and adverse pregnancy outcomes. Overall, there is no    |                                 |
| convincing evidence of an association.                                       |                                 |
| Transition metal ions induce lipid peroxidation in artificial phospholipid | Repetto et al., 2010            |
| liposomes.                                                                   |                                 |
| The antioxidants isoquercitrin and melatonin reduce oxidative stress       | Nishimura et al., 2010          |
| mediated liver tumor promotion by the benzimidazole anthelmin oxfendasole   |                                 |
| in rats.                                                                    |                                 |

695
**Table 1 (cont.):** Key messages of the most cited articles in Archives of Toxicology (2010-2011)
(from: Bolt et al., 2012)

| Key message                                                                 | Reference                      |
|----------------------------------------------------------------------------|--------------------------------|
| Administration of silver nanoparticles to rats caused a dose-dependent accumulation of particles in the lamina propria of the small and large intestine, increased numbers of goblet cells and altered mucus composition. | Jeong et al., 2010             |
| The author critically discusses Hermann J. Muller’s well-known Nobel lecture where a linear dose-response for radiation-induced germ cell mutations was presented. In contrast to this concept Calabrese presents arguments speaking against the linear no-threshold model. | Calabrese, 2011                |
| Zinc oxide nanoparticles induce the release of pro-inflammatory cytokines in mouse and human cell systems. | Heng et al., 2011              |
| A single intratracheal instillation of carbon nanotubes may induce early lung fibrosis. | Park et al., 2011              |
| Indole-3-carbinol and flutamide increased expression of CYP1A1 and induced liver cell foci in rats. | Shimamoto et al., 2011         |
| Synephrine is added to dietary supplements for weight loss. The hydroxyl group in the p-position favours transporter mediated uptake into cardiomyocytes. Moreover, isomerisation of synephrine influences its toxicological profile. | Rossato et al., 2011           |
| DNA strand breaks induced by platinum nanoparticles are mediated by platinum ions released from the nanoparticles. | Gehrke et al., 2011            |
| This review deals with the description and comparison of cyclotron-based irradiation techniques for the generation of radiolabelled nanoparticles applicable in nanotoxicity tracing approaches. | Gibson et al., 2011            |
| In urinary bladder cancer all known validated individual SNPs are associated with only moderate risk that is too low to justify preventive measures. The authors review this issue and propose that these so-called wimp-SNPs may interact and therefore collectively result in much higher risk with preventive relevance. | Golka et al., 2011             |
| The genotoxic potential of dental composite components, such as BisGMA, TEGDMA, HEMA and MMA, was studied in gingival fibroblasts. It was found that DNA strand breaks comparable to those induced by irradiation are only achieved with concentrations that are unrealistic. | Durner et al., 2011            |
| Elevated expression of Th2 cytokines and signal molecules during the inflammation response in silica-induced pulmonary fibrosis in mice is mediated by IL-6R alpha. | Tripathi et al., 2010          |
| This study shows that beta-carboline alkaloids, such as rutaecarpine, annonontine and xestomanzamine A, are stimulators of AhR and lead to AhR-target gene expression. | Haarmann-Stemmann et al., 2010 |
| Possible estrogenic effects of cadmium were analysed in the rat intestine. Cadmium exposure was shown to modulate molecular and functional parameters of estrogenicity such as proliferation and expression of the estrogen-regulated gene ER beta. | Höfer et al., 2010             |
| Exposure to the commercial formulation of the herbicide glyphosate during the puberty period disrupts the reproductive development of rats by altering testosterone level and testicular morphology. | Romano et al., 2010            |
| Gene expression alterations in the brains of neonate mice exposed to methylmercury and polychlorinated biphenyls, alone or in combination, reveal not only toxicity effects but also a protective, detoxication response upon co-exposure. | Shimada et al., 2010           |
Table 1 (cont.): Key messages of the most cited articles in Archives of Toxicology (2010-2011) (from: Bolt et al., 2012)

| Key message                                                                 | Reference                        |
|----------------------------------------------------------------------------|----------------------------------|
| Perinatal exposure to perfluorooctane sulfonate during the critical period of brain development may have neurotoxic effects on the CNS by altering the expression of calcium-dependent signaling pathway molecules. | Liu et al., 2010b                 |
| An overview of currently available metabolic databases is given with the MetaCyc family being described in particular detail. | Karp and Caspi, 2011             |
| The mechanism by which fenvalerate negatively affects male reproduction and spermatogenesis was investigated. The results show that fenvalerate induces germ cell apoptosis in testes by upregulating expression of Fas and Fasl. | Zhao et al., 2011                |
| Only minor pulmonary irritation and inflammation potencies were found for TiO2 nanoparticles in standardised mouse bioassays. | Leppänen et al., 2011            |
| The importance of nanoparticle surface functionalization could be shown in an in vivo model of embryonic zebrafish, whereby two lead sulfide nanoparticles with identical core size but different surface functionality led to drastic differences in embryo mortality. | Truong et al., 2011              |
| This work uncovers a cell density-related resistance to cytotoxicity induced by zinc oxide nanoparticles in monolayer cultures of different cell lines and emphasizes the importance of standardization of cell culture protocols for toxicology screening. | Heng et al., 2011                |
| Prediction of relevant concentrations for in vitro studies of cytotoxicity can be successfully achieved by applying BPTK modelling. | Mielke et al., 2011              |
| The mechanism underlying perfluorooctane (PFOS)-mediated decrease in circulating thyroid hormone levels was studied. It was shown that PFOS increased hepatic expression of OATP2 and MRP2 leading to enhanced hepatic uptake and metabolism of T4. | Yu et al., 2011                   |
| The carotenoid lutein protects against cisplatin-induced DNA damage and chromosome instability in peripheral blood cells by improving antioxidant defense. | Serpeloni et al., 2010           |
| Standardisation of the cell response to sodium nitroprusside (SNP) revealed that long-term culturing-associated resistance to SNP-induced cell toxicity was accompanied by higher levels of the stress protein Hsp70. Suggested mechanism of action of Hsp70 include increase of CAT and GSH-Px activities as well as decrease in caspase-3 activation. | Romero et al., 2010              |
| The genotoxicity potential of beauvericin (BEA) and ochratoxin A (OTA) was evaluated in PK15 cells and human leukocytes using the alkaline comet assay. It was found that BEA is more toxic than OTA and that the combined genotoxic action is additive or both synergistic and additive depending on the cell line. | Klarić et al., 2010              |
| A comparison of the effects of curcumin and resveratrol on aflatoxin B-1-induced liver injury in rats revealed that only curcumin has an hepatoprotective effect against damage by aflatoxin B-1. | El-Agamy, 2010                   |

REFERENCES

Adler S, Basketter D, Creton S, Pelkonen O, van Benthem J, Zhuang V et al. Alternative (non-animal) methods for cosmetics testing: current status and future prospects-2010. Arch Toxicol 2011;85(5):367-485.

Al-Rawi M, Diabaté S, Weiss C. Uptake and intracellular localization of submicron and nano-sized SiO₂ particles in HeLa cells. Arch Toxicol 2011;85(7):813-26.
Audebert M, Dolo L, Perdu E, Cravedi JP, Zalko D. Use of the γH2AX assay for assessing the genotoxicity of bisphenol A and bisphenol F in human cell lines. Arch Toxicol 2011;85(11):1463-73.

Baird L, Dinkova-Kostova AT. The cytoprotective role of the Keap1-Nrf2 pathway. Arch Toxicol 2011;85(4):241-72.

Bakhiya N, Appel KE. Toxicity and carcinogenicity of furan in human diet. Arch Toxicol 2010;84(7):563-78.

Barcelos GR, Grotto D, Serpeloni JM, Angeli JP, Rocha BA, de Oliveira Souza VC et al. Protective properties of quercetin against DNA damage and oxidative stress induced by methylmercury in rats. Arch Toxicol 2011;85(9):1151-7.

Bolt HM. Publications in toxicology: the current situation. Arch Toxicol 2011;85(1):1-2.

Bolt HM, Stewart JD. The field of tension between toxicology and basic and clinical sciences. Arch Toxicol 2011;85(11):1311-2.

Bolt HM, Marchan R, Hengstler JG. Nanotoxicology and oxidative stress control; cutting edge topics in toxicology. Arch Toxicol 2012;86 (11):1629-35.

Bosetti C, Nieuwenhuijsen MJ, Gallus S, Cipriani S, La Vecchia C, Parazzini F. Ambient particulate matter and preterm birth or birth weight: a review of the literature. Arch Toxicol 2010;84(6):447-60.

Brozmanová J, Mániková D, Vlčková V, Chovanec M. Selenium: a double-edged sword for defense and offence in cancer. Arch Toxicol 2010;84(12):919-38.

Calabrese EJ. Muller's Nobel lecture on dose-response for ionizing radiation: ideology or science? Arch Toxicol 2011;85(12):1495-8.

Clift MJ, Gehr P, Rothen-Rutishauser B. Nanotoxicology: a perspective and discussion of whether or not in vitro testing is a valid alternative. Arch Toxicol 2011;85(7):723-31.

Drobná Z, Walton FS, Paul DS, Xing W, Thomas DJ, Stýblo M. Metabolism of arsenic in human liver: the role of membrane transporters. Arch Toxicol 2010;84(1):3-16.

Druwe IL, Vaillancourt RR. Influence of arsenate and arsenite on signal transduction pathways: an update. Arch Toxicol 2010;84 (8):585-96.

Durner J, Dębiak M, Bürkle A, Hickel R, Reichl FX. Induction of DNA strand breaks by dental composite components compared to X-ray exposure in human gingival fibroblasts. Arch Toxicol 2011;85(2):143-8.

El-Agamy DS. Comparative effects of curcumin and resveratrol on aflatoxin B(1)-induced liver injury in rats. Arch Toxicol 2010;84(5):389-96.

Elcombe CR, Elcombe BM, Foster JR, Farrar DG, Jung R, Chang SC et al. Hepatocellular hypertrophy and cell proliferation in Sprague-Dawley rats following dietary exposure to ammonium perfluorooctanoate occurs through increased activation of the xenosensor nuclear receptors PPARα and CAR/PXR. Arch Toxicol 2010;84(10):787-98.

Foldbjerg R, Dang DA, Autrup H. Cytotoxicity and genotoxicity of silver nanoparticles in the human lung cancer cell line, A549. Arch Toxicol 2011;85(7):743-50.

Gehrke H, Pelka J, Hartinger CG, Blank H, Bleimund F, Schneider R et al. Platinum nanoparticles and their cellular uptake and DNA platination at non-cytotoxic concentrations. Arch Toxicol 2011;85(7):799-812.
Gibson N, Holzwarth U, Abbas K, Simonelli F, Kozempel J, Cydzik I et al. Radio-labeling of engineered nanoparticles for in vitro and in vivo tracing applications using cyclotron accelerators. Arch Toxicol 2011; 85(7):751-73.

Golka K, Selinski S, Lehmann ML, Blaszkewicz M, Marchan R, Ickstadt K et al. Genetic variants in urinary bladder cancer: collective power of the "wimp SNPs". Arch Toxicol 2011;85(6):539-54.

Haarmann-Stemmann T, Sendker J, Götz C, Krug N, Bothe H, Fritsche E et al. Regulation of dioxin receptor function by different beta-carboline alkaloids. Arch Toxicol 2010;84(8):619-29.

Heng BC, Zhao X, Tan EC, Khamis N, Assodani A, Xiong S et al. Evaluation of the cytotoxic and inflammatory potential of differentially shaped zinc oxide nanoparticles. Arch Toxicol 2011;85(12):1517-28.

Höfer N, Diel P, Wittsiepe J, Wilhelm M, Kluxen FM, Degen GH. Investigations on the estrogenic activity of the metallohormone cadmium in the rat intestine. Arch Toxicol 2010;84(7):579-81.

Hoshino A, Hanada S, Yamamoto K. Toxicity of nanocrystal quantum dots: the relevance of surface modifications. Arch Toxicol 2011;85(7):707-20.

Jeong J, Han BS, Cho WS, Choi M, Ha CS, Lee BS et al. Carcinogenicity study of 3-monochloropropane-1, 2-diol (3-MCPD) administered by drinking water to B6C3F1 mice showed no carcinogenic potential. Arch Toxicol 2010;84(9):719-29.

Karp PD, Caspi R. A survey of metabolic databases emphasizing the MetaCyc family. Arch Toxicol 2011;85(9):1015-33.

Kawai M, Saegusa Y, Dewa Y, Nishimura J, Kemmochi S, Harada T et al. Elevation of cell proliferation via generation of reactive oxygen species by piperonyl butoxide contributes to its liver tumor-promoting effects in mice. Arch Toxicol 2010;84(2):155-64.

Kell DB. Towards a unifying, systems biology understanding of large-scale cellular death and destruction caused by poorly liganded iron: Parkinson's, Huntington's, Alzheimer's, prions, bactericides, chemical toxicology and others as examples. Arch Toxicol 2010;84(11):825-89.

Kim JS, Lee K, Lee YH, Cho HS, Kim KH, Choi KH et al. Aspect ratio has no effect on genotoxicity of multi-wall carbon nanotubes. Arch Toxicol 2011;85(7):775-86.

Klarić MS, Darabos D, Rozgaj R, Kasuba V, Pepeljnjak S. Beauvericin and ochratoxin A genotoxicity evaluated using the alkaline comet assay: single and combined genotoxic action. Arch Toxicol 2010;84(8):641-50.

Lehmann ML, Selinski S, Blaszkewicz M, Orlich M, Ovsianников D, Moormann O et al. Rs710521[A] on chromosome 3q28 close to TP63 is associated with increased urinary bladder cancer risk. Arch Toxicol 2010;84:967-78.

Leppänen M, Korpi A, Miettinen M, Leskinen J, Torvela T, Rossi EM et al. Nano-sized TiO₂ caused minor airflow limitation in the murine airways. Arch Toxicol 2011;85(7):827-39.
Liu X, Liu W, Jin Y, Yu W, Wang F, Liu L. Effect of gestational and lactational exposure to perfluorooctanesulfonate on calcium-dependent signaling molecules gene expression in rats’ hippocampus. Arch Toxicol 2010a;84(1):71-9.

Liu X, Liu W, Jin Y, Yu W, Liu L, Yu H. Effects of subchronic perfluorooctane sulfonate exposure of rats on calcium-dependent signaling molecules in the brain tissue. Arch Toxicol 2010b;84(6):471-9.

Mamas M, Dunn WB, Neyses L, Goodacre R. The role of metabolites and metabolomics in clinically applicable biomarkers of disease. Arch Toxicol 2011;85(1):5-17.

Marano F, Hussain S, Rodrigues-Lima F, Baeza-Squiban A, Boland S. Nanoparticles: molecular targets and cell signalling. Arch Toxicol 2011;85(7):733-41.

Mielke H, Anger LT, Schug M, Hengstler JG, Stahlmann R, Gundert-Remy U. A physiologically based toxicokinetic modelling approach to predict relevant concentrations for in vitro testing. Arch Toxicol 2011;85(6):555-63.

Nielsen GD, Wolkoff P. Cancer effects of formaldehyde: a proposal for an indoor air guideline value. Arch Toxicol 2010;84(6):423-46.

Nishimura J, Saegusa Y, Dewa Y, Jin M, Kawai M, Kemmochi S et al. Antioxidant enzymatically modified isoquercitrin or melatonin supplementation reduces oxidative stress-mediated hepatocellular tumor promotion of oxendazole in rats. Arch Toxicol 2010;84(2):143-53.

Nogueira CW, Rocha JB. Toxicology and pharmacology of selenium: emphasis on synthetic organoselenium compounds. Arch Toxicol 2011;85(11):1313-59.

Park EJ, Roh J, Kim SN, Kang MS, Han YA, Kim Y et al. A single intratracheal instillation of single-walled carbon nanotubes induced early lung fibrosis and subchronic tissue damage in mice. Arch Toxicol 2011;85(9):1121-31.

Pestka JJ. Deoxynivalenol: mechanisms of action, human exposure, and toxicological relevance. Arch Toxicol 2010;84(9):663-79.

Prigol M, Pinton S, Schumacher R, Nogueira CW, Zeni G. Convulsant action of diphenyl diselenide in rat pups: measurement and correlation with plasma, liver and brain levels of compound. Arch Toxicol 2010;84(5):373-8.

Rand TG, Sun M, Gilyan A, Downey J, Miller JD. Dectin-1 and inflammation-associated gene transcription and expression in mouse lungs by a toxic (1,3)-beta-D glucan. Arch Toxicol 2010;84(3):205-20.

Read RW, Riches JR, Stevens JA, Stubbs SJ, Black RM. Biomarkers of organophosphorus nerve agent exposure: comparison of phosphorylated butyrylcholinesterase and phosphorylated albumin after oxime therapy. Arch Toxicol 2010;84(1):25-36.

Repetto MG, Ferrarotti NF, Boveris A. The involvement of transition metal ions on iron-dependent lipid peroxidation. Arch Toxicol 2010;84(4):255-62.

Rodrigues JL, Serpeloni JM, Batista BL, Souza SS, Barbosa F Jr. Identification and distribution of mercury species in rat tissues following administration of thimerosal or methylmercury. Arch Toxicol 2010;84(11):891-6.

Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. Arch Toxicol 2010;84(4):309-17.
Romero C, Benedí J, Villar A, Martín-Aragón S. Involvement of Hsp70, a stress protein, in the resistance of long-term culture of PC12 cells against sodium nitroprusside (SNP)-induced cell death. Arch Toxicol 2010;84(9):699-708.

Rossato LG, Costa VM, de Pinho PG, Carvalho F, de Lourdes Bastos M, Remião F. Structural isomerization of synephrine influences its uptake and ensuing glutathione depletion in rat-isolated cardiomyocytes. Arch Toxicol 2011;85(8):929-39.

Serpeloni JM, Grotto D, Mercadante AZ, de Lourdes Pires Bianchi M, Antunes LM. Lutein improves antioxidant defense in vivo and protects against DNA damage and chromosome instability induced by cisplatin. Arch Toxicol 2010;84(10):811-22.

Sinicropi MS, Amantea D, Caruso A, Saturnino C. Chemical and biological properties of toxic metals and use of chelating agents for the pharmacological treatment of metal poisoning. Arch Toxicol 2010;84(7):501-20.

Shimada M, Kameo S, Sugawara N, Yaginuma-Sakurai K, Kurokawa N, Mizukami-Murata S et al. Gene expression profiles in the brain of the neonate mouse perinatally exposed to methylmercury and/or polychlorinated biphenyls. Arch Toxicol 2010;84(4):271-86.

Shimamoto K, Dewa Y, Kemmochi S, Taniai E, Hayashi H, Imaoka M et al. Relationship between CYP1A induction by indole-3-carbinol or flutamide and liver tumor-promoting potential in rats. Arch Toxicol 2011;85(9):1159-66.

Slocum SL, Kensler TW. Nrf2: control of sensitivity to carcinogens. Arch Toxicol 2011;85(4):273-84.

Sriram K, Lin GX, Jefferson AM, Roberts JR, Chapman RS, Chen BT et al. Dopaminergic neurotoxicity following pulmonary exposure to manganese-containing welding fumes. Arch Toxicol 2010;84(7):521-40.

Tripathi SS, Mishra V, Shukla M, Verma M, Chaudhury BP, Kumar P et al. IL-6 receptor-mediated lung Th2 cytokine networking in silica-induced pulmonary fibrosis. Arch Toxicol 2010;85(4):947-55.

Truong L, Moody IS, Stankus DP, Nason JA, Lonergan MC, Tanguay RL. Differential stability of lead sulfide nanoparticles influences biological responses in embryonic zebrafish. Arch Toxicol 2011;85(7):787-98.

Valdiglesias V, Pásaro E, Méndez J, Laffón B. In vitro evaluation of selenium genotoxic, cytotoxic, and protective effects: a review. Arch Toxicol 2010;84(5):337-51.

van Berlo D, Albrecht C, Knaapen AM, Cassee FR, Gerlofs-Nijland ME, Kooter IM et al. Comparative evaluation of the effects of short-term inhalation exposure to diesel engine exhaust on rat lung and brain. Arch Toxicol 2010;84(7):553-62.

Wagner C, Vargas AP, Roos DH, Morel AF, Farina M, Nogueira CW et al. Comparative study of quercetin and its two glycoside derivatives quercitrin and rutin against methylmercury (MeHg)-induced ROS production in rat brain slices. Arch Toxicol 2010;84(2):89-97.

Wang H, Wang Q, Zhao XF, Liu P, Meng XH, Yu T et al. Cypermethrin exposure during puberty disrupts testosterone synthesis via downregulating StAR in mouse testes. Arch Toxicol 2010;84(1):53-61.
Wang Z, Yang X, Yang S, Ren G, Ferreri M, Su Y et al. Sodium fluoride suppress proliferation and induce apoptosis through decreased insulin-like growth factor-I expression and oxidative stress in primary cultured mouse osteoblasts. Arch Toxicol 2011;85(11):1407-17.

Wobus AM, Löser P. Present state and future perspectives of using pluripotent stem cells in toxicology research. Arch Toxicol 2011;85(2):79-117.

Xie G, Sun J, Zhong G, Shi L, Zhang D. Biodistribution and toxicity of intravenously administrated silica nanoparticles in mice. Arch Toxicol 2010;84(3):183-90.

Yen CC, Ho TJ, Wu CC, Chang CF, Su CC, Chen YW et al. Inorganic arsenic causes cell apoptosis in mouse cerebrum through an oxidative stress-regulated signaling pathway. Arch Toxicol 2011;85(6):565-75.

Yu WG, Liu W, Liu L, Jin YH. Perfluorooctane sulfonate increased hepatic expression of OAPT2 and MRP2 in rats. Arch Toxicol 2011;85(6):613-21.

Yun KU, Oh SJ, Oh JM, Kang KW, Myung CS, Song GY et al. Age-related changes in hepatic expression and activity of cytochrome P450 in male rats. Arch Toxicol 2010;84(12):939-46.

Zhao XF, Wang Q, Ji YL, Wang H, Liu P, Zhang C et al. Fenvalerate induces germ cell apoptosis in mouse testes through the Fas/FasL signaling pathway. Arch Toxicol 2011;85(9):1101-8.