EXCLI Journal 2011;10:130-132 – ISSN 1611-2156
Received: August 17, 2011, published: August 18, 2011

# Editorial:

# CARCINOGENESIS IN TOXICOLOGICAL RESEARCH

C. Cadenas

Leibniz Research Centre for Working Environment and Human Factors (***IfADo***), Ardeystrasse 67, 44139 Dortmund, Germany

E-mail: cadenas@ifado.de, Telephone: +49 231-1084-392, Fax: +49 231-1084-403

Current research in carcinogenesis is focussed on enzymes controlling reactive compounds and the maintenance of DNA integrity. An outstanding example is a review on epoxide hydrolases. known to be key enzymes in detoxification of carcinogenic epoxides (Decker et al., 2009). However, it has recently become clear that besides their function in xenobiotic metabolism, epoxide hydrolases also play a role in signal transduction and inflammatory control. A further highlight is a review on telomeres and the mechanisms that avoid the misinterpretation of chromosome ends as sites of DNA breaks. The table gives a brief overview of the key messages of recent studies in the field of carcinogenesis.

**Table 1:** Recent studies in carcinogenesis and human exposure to carcinogens

| Key message | Reference |
|---|---|
| A c-myc reporter cell line was established that allowed flow-sorting of cells with weak (10 %) and strong (70 %) c-myc overexpression. This technique allows differentiation of biological consequences in relation to the intensity of c-myc levels. | Knudsen et al., 2009 |
| Occupational exposure of workers to polycyclic aromatic hydrocarbons is associated with increased levels of 8-oxo-dGuo DNA adducts and DNA strand breaks in lymphocytes. | Marczynski et al., 2009 |
| Urinary 3-hydroxybenzo[a]pyrene can be used as a biomarker of dermal exposure to benzo[a]pyrene. However, it should be considered that the ratio of excretion may be overestimated. | Payan et al., 2009 |
| Epoxide hydrolases are key enzymes in xenobiotic metabolism catalyzing the hydrolysis of potentially carcinogenic epoxides. However, besides xenobiotic metabolism evidence accumulates that epoxide hydrolases are also involved in the metabolism of lipid derived epoxides playing a role in signal transduction, blood pressure control and inflammatory processes. | Decker et al., 2009 (review); Hengstler et al., 2009a (editorial) |
| Telomeres serve to prevent the mis-identification of chromosome ends as sites of DNA damage. This review focuses on the mechanisms eukaryotic cells have evolved to overcome this problem. | Liew and Norbury, 2009 (review); Hengstler et al., 2009b (editorial) |
| This review summarizes the anti-carcinogenic activities of polyphenolic compounds in tea. | Yang et al., 2009a (review) Hengstler et al., 2009c (editorial) |
| Exposure of male volunteers to 50 ppm toluene in an exposure chamber for 270 min does not reduce the nOGG1 repair activity. | Finkenwirth et al., 2009 |
| $SnCl_2$ interferes with DNA repair systems shifting the balance from error-free to error-prone repair processes. | Viau et al., 2009 |

**Table 1 (cont.):** Recent studies in carcinogenesis and human exposure to carcinogens

| Key message | Reference |
|---|---|
| A novel dual-label fluoroimmunoassay allows simple and fast simultaneous screening of the carcinogens aflatoxin $B_1$ and ochratoxin A. | Huang et al., 2009 |
| The heterocyclic aromatic amine PhIP induces preneoplastic lesions in rat colon without preceding or accompanying inflammation. | Kühnel et al., 2009 |
| Iso-GAMA was identified as a further human metabolite of acrylamide. This study presents the kinetics of iso-GAMA and other oxidative metabolites of acrylamide in human urine. | Hartmann et al., 2009 |
| Bisphenol A has been suspected as a risk factor of breast cancer. However, no significant difference of bisphenol A blood levels between breast cancer cases and controls could be found in Korean women. | Yang et al., 2009b |
| A variant of intron 6 of GSTM3 is associated with prostate cancer risk. | Kesarwani et al., 2009 |
| Piperonyl butoxide acts as a liver carcinogen by a threshold mechanism. The threshold dose is approximately 0.25 % piperonyl butoxide in the diet of rats. | Muguruma et al., 2009 |
| Human urinary bladder epithelial cells seem to consist of two subtypes with inducible as well as non-inducible CYP1A1. | Plöttner et al., 2009 |
| RasH2 mice are not susceptible to troglitazone in a two-stage hepatocarcinogenesis model. | Jin et al., 2009 |

## REFERENCES

Decker M, Arand M, Cronin A. Mammalian epoxide hydrolases in xenobiotic metabolism and signalling. Arch Toxicol 2009;83:297-318.

Finkenwirth P, Spelmeyer U, Hommel G, Rose DM, Jung D, Rossbach B et al. Effects of an acute exposure to toluene on the DNA repair activity of the human 8-oxoguanine DNA glycosylase 1 (hOGG1) in healthy subjects. Arch Toxicol 2009;83: 777-84.

Hartmann EC, Boettcher MI, Bolt HM, Drexler H, Angerer J. N-Acetyl-S-(1-carbamoyl-2-hydroxy-ethyl)-L-cysteine (iso-GAMA) a further product of human metabolism of acrylamide: comparison with the simultaneously excreted other mercaptuic acids. Arch Toxicol 2009;83:731-4.

Hengstler JG, Stewart JD, Bolt HM. Epoxide hydrolases are not only a molecular sponge sucking up genotoxic epoxides: new roles in control of blood pressure, inflammation as well as nociception and cell proliferation. Arch Toxicol 2009a;83:289-91.

Hengstler JG, Marchan R, Bolt HM. Mechanisms of telomere maintenance and attrition: linking cancer and ageing. Arch Toxicol 2009b;83:405-6.

Hengstler JG, Marchan R, Bolt HM. Can drinking tea prevent cancer? A controversy revisited. Arch Toxicol 2009c;83:1-2.

Huang B, Xiao H, Zhang J, Zhang L, Yang H, Zhang Y et al. Dual-label time-resolved fluoroimmunoassay for simultaneous detection of aflatoxin B1 and ochratoxin A. Arch Toxicol 2009;83:619-24.

Jin M, Saekusa Y, Dewa Y, Nishimura J, Matsumoto S, Shibutani M et al. Hepatocarcinogenic susceptibility of rasH2 mice to troglitazone in a two-stage hepatocarcinogenesis model. Arch Toxicol 2009;83:173-81.

Kesarwani P, Singh R, Mittal RD. Association of GSTM3 intron 6 variant with cigarette smoking, tobacco chewing and alcohol as modifier factors for prostate cancer risk. Arch Toxicol 2009;83:351-6.

Knudsen KJ, Nelander Holm GM, Krabbe JS, Listov-Saabye N, Kiehr B, Dufva M et al. Driving gradual endogenous c-myc overexpression by flow-sorting: intracellular signaling and tumor cell phenotype correlate with oncogene expression. Arch Toxicol 2009;83:1061-74.

Kühnel D, Taugner F, Scholtka B, Steinberg P. Inflammation does not precede or accompany the induction of preneoplastic lesions in the colon of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine-fed rats. Arch Toxicol 2009;83:763-8.

Liew LP, Norbury CJ. Telomere maintenance: all's well that ends well. Arch Toxicol 2009;83:407-16.

Marczynski B, Pesch B, Wilhelm M, Rossbach B, Preuss R, Hahn JU et al. Occupational exposure to polycyclic aromatic hydrocarbons and DNA damage by industry: a nationwide study in Germany. Arch Toxicol 2009;83:947-57.

Muguruma M, Kawai M, Dewa Y, Nishimura J, Saegusa Y, Yasuno H et al. Threshold dose of piperonyl butoxide that induces reactive oxygen species-mediated hepatocarcinogenesis in rats. Arch Toxicol 2009; 83:183-93.

Payan JP, Lafontaine M, Simon P, Marquet F, Champmartin-Gendre C, Beydon D et al. 3-Hydroxybenzo(a)pyrene as a biomarker of dermal exposure to benzo(a)pyrene. Arch Toxicol 2009;83:873-83.

Plöttner S, Selinski S, Bolt HM, Degen GH, Hengstler JG, Roos PH et al. Distinct subtypes of urinary bladder epithelial cells with inducible and non-inducible cytochrome P450 1A1. Arch Toxicol 2009;83:131-8.

Viau CM, Guecheva TN, Sousa FG, Pungartnik C, Brendel M, Saffi J et al. SnCl(2)-induced DNA damage and repair inhibition of MMS-caused lesions in V79 Chinese hamster fibroblasts. Arch Toxicol 2009;83: 769-75.

Yang CS, Lambert JD, Sang S. Antioxidative and anti-carcinogenic activities of tea polyphenols. Arch Toxicol 2009;83:11-21.

Yang M, Ryu JH, Jeon R, Kang D, Yoo KY. Effects of bisphenol A on breast cancer and its risk factors. Arch Toxicol 2009;83: 281-5.