Arch Toxicol (2011) 85:861–862
DOI 10.1007/s00204-011-0738-6

EDITORIAL

A comprehensive review about micronuclei: mechanisms of formation and practical aspects in genotoxicity testing

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Published online: 26 July 2011

The micronucleus test is one of the most frequently applied assays in genotoxicity testing and is also one of the most popular assays used by our authors (Hothorn and Gerhard 2009; Serpeloni et al. 2010; Lima et al. 2010; Westphal et al. 2009; Angeli et al. 2009; Dorn et al. 2008; Krishnamurthi et al. 2008; Bolt et al. 2004; Hengstler et al. 2003). The increasing relevance and distribution of the micronucleus test can easily be demonstrated by entering the terms "micronucleus or micronuclei" into ISI Web of Knowledge: In 1992, there were less than 2,000 hits. This number increased over 6,000 in 2004 to more than 13,000 in 2010, which is remarkably high compared to other toxicity tests. Considering the outstanding relevance of micronuclei in genotoxicity testing, the editors are happy that Micheline Kirsch-Volders and colleagues from Brussels University accepted our invitation to contribute a comprehensive review on the subject (Kirsch-Volders et al. 2011; this issue). The authors have significantly contributed to the micronuclei test development and successfully proposed the currently accepted internationally harmonized protocol.

It is well known that the micronucleus assay allows detection of both clastogenic and aneugenic events and in combination with centromeric probes the mechanistic origin can be easily determined. However, the complexity of the possible mechanisms leading to micronuclei, a specific focus of the current article, may be new even for well-informed toxicologists. They include chromosome fragments, whole chromosomes or chromatids, that lag behind in anaphase, whereby misattachment of tubulin may play an important role. Also defects in Kinetochore proteins or in Kinetochore assembly, late replication, epigenetic modifications of histones, nucleoplasmic bridge formation, and gene amplification. Furthermore, the authors address the survival and fate of micronuclei in the micronucleated cell and its association with cancer predictivity. A large prospective study has been performed where micronuclei were quantified in lymphocytes of 6,718 subjects. High micronucleus frequency was significantly associated with increased prospective cancer risk in this study.

Finally, the authors give an overview of updated protocols and address the practical aspects of assay performance including the relevance of modifying factors such as: age and gender, genotype, smoking, micronutrients, and diet.

The review of Kirsch-Volders is a must read for everybody interested in genotoxicity testing.

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