LETTER TO THE EDITOR

RE: The evaluation of micronucleus frequency by acridine orange fluorescent staining in peripheral blood of rats treated with lead acetate.

(Mutagenesis, 20, 411–415, 2005)

Raymond J. Proudlock*

Charles River Laboratories Preclinical Services Montreal Inc., Senneville, Quebec, Canada

In their paper in the November 2005 edition of Mutagenesis, Çelik et al. (1) describe small increases in micronucleated cells following 7 weekly oral treatments with lead acetate and conclude that this is indcative of genotoxic effects. However, in the same paper, the authors describe the equivocal nature of earlier in vitro and in vivo experiments on lead salts as well as anaemia and increases in erythropoiesis in mammalian systems.

The authors do not discuss indirect mechanisms of micronucleus formation. In particular, micronucleated erythrocytes can be induced by administration of erythropoietins without any corresponding increase in bone marrow chromosome damage [e.g. (2)] presumably due to errors in enucleation or possibly decreased fidelity of DNA proof-reading in over stimulated erythroblasts. Earlier studies (3) demonstrated that bleeding and phenylhydrazine-induced haemolysis also cause increases in circulating micronucleated reticulocytes in the mouse, probably via the same mechanism. This is further discussed by Hamada et al. (4) in the context of six compounds, which gave exaggerated increases in micronucleated reticulocytes in the rat following multiple administration.

The results of the Çelik et al. study cannot yield any concrete conclusion regarding the genotoxicity of lead acetate, since the increases in micronuclei could be a consequence of chronic anaemia. Where anaemia is suspected, it may be appropriate to prepare bone marrow metaphase slides from the same animals for potential examination of chromosome aberrations as described by Albanese (5) so that genotoxicity can be confirmed by a second related endpoint.

Finally, Figure 1 of the Çelik et al. paper implies that the quality of smears, with adherent and overlapping cells, was not of an adequate quality for quantitative analysis. The supravital staining technique used by the international collaborative group (4) and described in detail elsewhere (6) allows identification of the stage of maturity of the reticulocytes and produces a uniform monolayer of cells.

References


*To whom correspondence should be addressed: Tel: +514 630 8254; Fax: +514 630 8230; E-mail raymond.proudlock@ca.crl.com

© The Author 2006. Published by Oxford University Press on behalf of the UK Environmental Mutagen Society. All rights reserved. For permissions, please email: journals.permissions@oxfordjournals.org