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Schmid W. The micronucleus test. *Mutat. Res.* 31:9-15, 1975.
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For large-scale genotoxicity screening in mammals, metaphase analysis of bone marrow cells is impractical. Searching for other end points of chromosome damage in hematological preparations from rodents, we demonstrated that scoring micronuclei in young polychromatic erythrocytes in bone marrow smears of mice is a sensitive, simple, and reliable method. [The *SCI*® indicates that this paper has been cited in over 365 publications.]

Mutagenicity Testing Must Be Practical

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Mutation research in *Drosophila* had been my early field of research between 1957 and 1961. As an MD I then turned to cytogenetics and medical genetics. In 1967, when claims were raised about mutagenic side effects of pharmaceuticals, my help was sought, and for the next several years at the University of Zurich I devoted much of my time *not* to mutagenicity testing but first to working out useful *in vivo* test systems. Together with G.R. Staiger,[1] I began with chromosome analyses in the bone marrow of Chinese hamsters. Despite a favorable karyotype (2n = 22), such work was not acceptable for toxicological screening. Since we had observed that treatments with classical mutagens caused severe hematological effects, I told K. Boller,[2] a medical student, to analyse hematologically stained bone marrow smears.

The shift in proportions of different cell types proved to be inconsistent and difficult to quantitate. In contrast, a number of nuclear anomalies showed a high degree of correlation with the results of our previous cytogenetical studies. To simplify matters I decided to concentrate future studies on the appearance of micronuclei in polychromatic erythrocytes. Micronuclei as a consequence of mitotic irregularities were, of course, known to cytologists since the time of Boveri. New, however, was the subsequent demonstration that micronuclei in young erythrocytes, after expulsion of the main nucleus, were an extremely useful feature apt for practical toxicological screening. Whoever wants to promote a new method should demonstrate its usefulness; therefore numerous basic methodological studies were performed, of which I wish to mention only two: B. Matter and I[3] compared the test in six mammalian species and showed that the laboratory mouse was highly suitable. Ten model mutagens, not only clastogens, but spindle poisons as well, were evaluated by P. Maier and me.[4]

Before directing my research interests, in the mid-1970s, to other fields, I concentrated on explaining and meticulously describing the test. In the beginning, we met with much criticism and scepticism on the part of cytogeneticists and mutation specialists but were greeted with enthusiasm by toxicologists who finally saw a light in their difficult task. In other circles, scepticism gave way to innumerable modifications and applications of scoring micronuclei in all kinds of cell types and tissues, including human cells from precancerous and cancerous lesions. In toxicology the test was successfully automated.[5] An overview of over 33 kinds of applications of micronuclei scoring was published in 1989.[6]

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2. **Boller K & Schmid W.** Chemische Mutagenese beim Säuger. Das Knochenmark des Chinesischen Hamsters als in vivo-Testsystem. Hämatolologische Befunde nach Behandlung mit Trenimon (Chemical mutagenesis in mammals. The bone marrow of Chinese hamsters as an *in vivo* test system. Hematologic evidence after treatment with trenimon). *Hum. Genet.* 11:35-54, 1970. (Cited 60 times.)
3. **Matter B & Schmid W.** Trenimon-induced chromosomal damage in bone-marrow cells of six mammalian species, evaluated by the micronucleus test. *Mutat. Res.* 12:417-25, 1971. (Cited 110 times.)
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5. **Romagna F & Staniforth C D.** The automated bone marrow micronucleus test. *Mutat. Res.* 213:91-104, 1989.
6. **Arlett C F, Ashby J, Fielder R J & Scott D.** Micronuclei: origins, applications and methodologies—a workshop sponsored by the Health and Safety Executive held in Manchester, May 23-25, 1988. *Mutagenesis* 4:482-5, 1989.

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