

Requirements for Automation of the Human Micronucleus Cytome Assay for High Throughput Analysis

M. Kirsch-Volders (1), I. Decordier (1), A. Papine (2), F. Soussaline (2)

(1) Laboratorium voor Cellulaire Genetica, Vrije Universiteit Brussel, Brussels, Belgium; (2) IMSTAR, Paris, France

Analysis of micronuclei (MN) is widely used for human biomonitoring or *in vitro/in vivo* genotoxicity testing, and provides a sensitive and relatively easy method to assess genetic damage. The fact that baseline MN frequencies in cytokinesis-blocked (CB) lymphocytes have been shown to be a predictive biomarker for cancer risk strengthens the importance of the CBMN assay as a reliable method for human biomonitoring of early genetic effects. We showed (Kirsch-Volders and Fenech, *Mutagenesis* 2001, 16:51-8) that scoring MN frequencies in binucleated and mononucleated cells enhances the predictive capacity of the assay. Automation of MN analysis is needed for quicker, more reliable, detection while minimizing subjective judgement and scoring. Within the framework of NewGeneris, an EU project, we developed an automated image analysis system for scoring MN in human lymphocytes in collaboration with IMSTAR. The following requirements should be fulfilled for development of an automated MN analysis system: i) the system should be applicable to the CBMN methodology and accurately distinguish mono, bi- and polynucleated cells; ii) well defined scoring criteria for cell type and MN (e.g., Fenech et al., *Mutat Res* 2003, 534:65-75); iii) experienced cytologists to score MN according to the HUMN criteria; iv) a standardized slide preparation protocol to obtain uniformity in cell size, cell density, and reproducibility (Decordier et al., *Mutagenesis* 2009, 24:85-93); v) validation of the automated versus manual scoring. Further development of the software should allow detection of apoptosis, necrosis, nuclear buds and nucleoplasmic bridges.

Funded by the EU Integrated Project NewGeneris, (Contract no. FOOD-CT-2005-016320). NewGeneris is the acronym of "Newborns and Genotoxic exposure risks" and ECNIS (Environmental Cancer Risk, Nutrition and Individual Susceptibility) (FOOD-CT-2005-513943).