

**Relationship between the in vitro effect of chemicals on human myeloid progenitors and the human peak plasma levels inducing toxicity.**

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The European Integrated Project A-Cute-Tox (LSHB-CT-2004-512051) was started up in January 2005. Our group is responsible for the characterization of the effect of xenobiotics on the hematopoietic tissue. Hematopoietic system displays a wide spectrum of cell populations whose constant proliferation and differentiation give rise to the different lineages of blood cells. CFU-GM assay based on the culture of human mononuclear cord blood cells have been used to characterize the effects of the selected compounds on the myeloid progenitors. Among the compounds included in the study there were pharmaceutical (22), environmental pollutants (16) industrial chemicals (12) and 5-Fluorouracile (as a positive control). Eleven out of 51 chemicals tested did not show any cytotoxic effect at the maximum concentration tested. For the rest of the compounds, the survival curves of CFU-GMs were obtained and IC values were calculated. Intralaboratory reproducibility of experimental data obtained was very good (85% of data showed CV values below 25%). CFU-GMs IC values and human peak plasma levels (data from the literature) were fitted to a linear regression model. The correlations of CFU-GM IC<sub>50</sub> values and sublethal and lethal plasma levels were of 0.82 and 0.77, respectively. Previous results have shown the relevance of the CFU-GM assay for the prediction of human acute neutropenia after treatment of antitumoral compounds, and have been recently approved by ECVAM's Scientific Advisory Committee. The results shown in the present study indicate that the CFU-GM assay could be also very helpful to characterize the toxicity of a wide variety of non-antitumoral xenobiotics.