

can be performed directly from cell lysates without RNA extraction or cDNA conversion. The 96-well plate format combined with multiplexing capacity of 30 targets per sample enables the detection of up to 2880 transcript levels for each run. The assay can be completed in 3–4 h with little hands-on time. The cost advantage of TRAC compared to qPCR is ca. 50–80%, in addition to time savings of 60–80%. Plexpress offers TRAC assays for both early-stage cell culture-based tox screening and for later stage toxicology assessment in animal studies. **Results:** The relevant toxicology related genes and normalization genes can be efficiently analyzed from the same sample to evaluate the drug induced reactions in liver or hepatocyte samples. The researcher may choose the desired genes for each run from Plexpress' target library or request customized targets. Plexpress has a growing library of marker genes for rat and human targets that has been successfully used in the evaluation of toxicity.

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Does microsampling of blood influence hematology parameters in mice?

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In mouse toxicity studies, blood samples for toxicokinetics (TK) and clinical pathology (plasma chemistry and hematology) are needed to evaluate exposure to the compound and adverse effects. Traditionally, due to the large volumes needed for bioanalysis, blood sampling for TK has not been collected from the main study animals, but from separate satellite animals.

New methods using micro volumes ($\leq 40 \mu\text{l}$ blood) for bioanalysis in blood/plasma give opportunities to take blood samples both for TK and clinical pathology in the same individuals. Since the total blood volume in mice is small, even the effect of TK microsampling needs to be investigated from a hematology perspective. A series of blood samples ($4 \times 40 \mu\text{l}$) was taken during 8 h followed by clinical pathology evaluation after 1, 2, 3, 5 and 7 days.

No alterations in clinical pathology variables were noted apart from decreased levels (8–9%) of red blood cell parameters (red blood cell count, hematocrit, hemoglobin concentration) on days 1 to 3 and an elevation of reticulocyte count by 29–34% on day 2 and 59–67% on day 3. All affected parameters returned to pretest levels on days 5–7.

We propose that microsampling for TK can be performed on main study animals 5 days before sampling for clinical pathology without any critical influence on hematology variables in mouse studies.

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Zebrafish (*Danio rerio*) behavioral analysis: A new tool in toxicological assays

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Pollution is a major critical problem for the preservation of aquatic ecosystems that will require the analysis of numerous molecules, alone, in combination and in their original and metabolized form. While most toxicological assays focus on lethality, teratogenicity, analysis of adverse effects of chemicals at sublethal or subteratogenic doses may improve our possibilities for best risk assessment. The zebrafish was recently used to test off target drug effects in particular by following behaviour for example for schizophrenia treatments; therefore we implemented a biological effect test at sublethal doses in this species.

A zebrafish behaviour analysis test was developed to allow aquatic pollutant effect screening, based on the larvae's response to light and dark stimuli, and its performance was tested using various important aquatic pollutants such as metals, insecticides, pesticides and psychotropic molecules. Measurement of activity (%) and active or mean velocity (mm/s) and calculation of various data provide a complete overview of pollutant effects on aquatic fauna behaviour, thus improving the toxicological description of aquatic pollutants which could be further extended to large scale screening of compounds.

Principal component analysis (PCA) was performed on calculated values and profiles associated to various compounds were compared to uncover correlations between pollutant groups. Zebrafish locomotion assays using this method offer a sensitive, rapid and powerful tool not only for pharmacological screening, but also during toxicological assays.

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Hematopoietic characterization of a non-rodent model for acute radiation syndrome

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Current regulations require evaluation of radiomitigation drug efficacy and safety in a rodent and a non-rodent model prior to approval under the FDA Animal Rule. Cell blood counts were obtained from 120 Rhesus monkeys for 12–60 days after whole body radiation using a Cobalt-60 at radiation dose levels ranging from 400 to 1210 Gy. White blood cell counts showed a progressive decrease with radiation dose-dependent nadirs. Neutrophil counts also showed a progressive decrease after irradiation and reached earlier and lower nadirs with higher irradiation doses. Severe neutropenia ($\leq 0.5 \times 10^9/\text{L}$) was first observed on Day 8 at 400 cGy and on Day 5 at 600 cGy and higher. Lymphocyte counts on Day 2 post-TBI were significantly decreased from baseline with a severity that was irradiation dose-dependent. Severe thrombocytopenia was first observed on Days 16, 11 and 10 at radiation doses of 400, 600 and 634 cGy, respectively. Platelet nadirs were observed earlier at higher irradiation doses and the recovery was comparable at irradiation doses of 400, 600 and 634 cGy. At 634 cGy, mean platelet volume reached a minimum (–12% from baseline) on Day 12 post-TBI. The hematology profiles obtained in this non rodent acute radiation syndrome model were comparable to radiation exposed humans and confirm the value of this non-rodent model for drug development.

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