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Real time *in vitro* evaluation of the carcinogenic potential of contaminants

The Genotrace project, combining targeted research and technology transfer[1], aims to develop an innovative test to ensure that chemicals, drugs and food are safer for humans, animals and the environment. The project consortium is led by INRA (French National Institute for Agricultural Research) and includes the CNRS (French National Center for Scientific Research), the University Toulouse III – Paul Sabatier and the company Biopredic International. The Genotrace project has just received the support of the French National Research Agency (ANR) for three years.

Among the current short-term assays developed to assess DNA damage induced by a physical or chemical agent, the micronucleus assay (MN) represents a reliable and precise method that is already validated as a regulatory test in a battery of predictive tests for carcinogenesis. The Genotrace project aims at bringing major technological innovations to develop a new MN assay that will make it possible to monitor both dynamically and in real time the production of chromosome damages and the signal of a genotoxicity reporter on HepaRG® cells (HepaRG® cells are human hepatic cells that can metabolize chemical compounds, this metabolization step is required for many carcinogenic compounds).

What is the micronucleus assay?
As its name suggests, the MN test is based on the presence of DNA breaks visible as small pieces after coloring. Two mechanisms contribute to the formation of micronuclei: a chromosome break or a fault in chromosome distribution at the end of the cell division stage. This test is performed either on cells, generally lymphocytes from an animal or human exposed to genotoxic products or on cells cultured *in vitro*. While the assessment of disruptions *in vivo* cannot be foreseen, the MN test, in its *in vitro* version, does not enable a real time evaluation of the disruptions that will lead to the formation of micronuclei, and thus prevents the identification of the mechanism causing the chromosome fragments.

A new test for real time monitoring

The new test developed within the Genotrace project will rely on fluorescent biotracers recently developed by the academic partners (INRA, CNRS, University Toulouse III - Paul Sabatier). The first biotracer will make it possible to visualize the chromatin (the DNA filament associated with proteins, forming the chromosomes), without cellular toxic effect, thus allowing the cellular chromatin to be dynamically monitored in real time. In addition, the expression of a specific gene will enable the evaluation of any associated activation of the DNA damage pathway. The test will therefore provide information on the origin of the micronuclei, whether they are induced by mechanisms of DNA breaks (clastogenic) or produced through the abnormal distribution of chromosomes during mitosis (aneugenic). To take into account the metabolism of many chemical compounds, these biotracers will be stably expressed in the HepaRG® cells, human liver cells that are metabolically active, optimized for the MN test by the industrial partner (BIOPREDIC International).

The new *in vitro* MN assay will be adapted to a medium- to high throughput analysis and results will be easy to interpret thanks to image analysis and classification instruments. It will enhance the conventional MN assay and may lead to breakthroughs in the prevention and/or diagnosis of exposure to genotoxicants present in the environment, food or future drug candidates.

The innovative genotoxicity test developed by the Genotrace stakeholders will be able to meet today's requirements, while providing significant scientific, technical and economical improvements. More generally, the Genotrace project seeks to make all chemicals, drugs, and food safer for humans, pets and the environment.

[1] The public/ private Genotrace consortium includes the project initiator, INRA joint research unit « Food Toxicology » (Toxalim) , the "Institut des technologies avancées en sciences du Vivant" (ITAV) of the CNRS and Toulouse III - Paul Sabatier university, and the company Biopredic International, which markets the human hepatic cell line HepaRG®.

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About:

Toxalim is an INRA joint research unit in partnership with the University of Toulouse III - Paul Sabatier. Established in January 2011, it brings together more than 200 staff (including 130 permanent scientists and eleven research teams). Toxalim contributes to a better understanding of the long-term toxic effects of pesticides, mycotoxins and other chemical contaminants, at very low concentrations, alone or mixed with food and feed. Toxalim covers various research fields and disciplines, from digestive physiology to perturbations in the expression of genes involved in chronic metabolic diseases such as diabetes, obesity and cancer. Toxalim is widely used in agro-veterinary and toxicology lectures.
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to find out more: http://www.toulouse.inra.fr/toxalim/

Biopredic International. Since 1993, Biopredic International produces and distributes human and animal products (tissues, primary cells, cell lines, blood products, fluids) for academic and private pharmaceutical and cosmetic research, Biopredic International, which makes most of its sales overseas, is internationally recognized for its expertise in liver products (tissues, primary cells) and is the exclusive worldwide licensor of the HepaRG® cell line.
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ITAV, Institut des technologies avancées en sciences du Vivant, is a Service and Research Unit (USR3505) placed under the authority of the CNRS, INSA and Paul Sabatier University - Toulouse III and headed by Pr. Bernard Ducommun. This institute is located on the Toulouse Oncopole site in the Pierre Potier Center, where it shares the premises of and pools resources with a biotech incubator. ITAV is a project platform (*hôtel à projet*) set up to welcome teams working on interdisciplinary projects for a limited period of time. Its objective is to bring together biologists, chemists, physicists, mathematicians, computer scientists, and other researchers within an environment conducive to collaboration. The institute places particular emphasis on technology enhancement and transfer leading to mature entrepreneurial projects. The two main focus areas of the ITAV's scientific project include: "Innovation for the exploration of dynamic processes in the life sciences " and "Innovation for diagnosis and therapeutics". These projects are based on ITAV's technological resources in imaging, bionanotechnology and chemistry.
to find out more: www.itav.fr and www.oncopole-toulouse.com