



PRESS RELEASE – SEPTEMBER 9TH, 2014

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

The Genotrace project, combining targeted research and technology transfer, aims at delivering an innovative test to improve the safety of chemical products, drugs, human and animal food and the environment. The project consortium is led by INRA (French National Institute for Agricultural Research) and includes 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 allow to monitor both dynamically and in real time the production of chromosome damages and the signal of a genotoxic reporter on HepaRG<sup>®</sup> cells (HepaRG<sup>®</sup> 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 the 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 break of chromosome or a defect in the chromosome distribution, at the end of the cell division stage. This test is performed either on cells, generally lymphocytes from an animal or a human exposed to genotoxic products or on cells cultured *in vitro*. Whilst 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 generated by the academic partners (INRA, CNRS, University Toulouse III - Paul Sabatier). The first biotracer will allow visualizing the chromatin (the DNA filament associated to proteins, forming the chromosomes), without cellular toxic effect, thus allowing the dynamic monitoring of the cellular chromatin in real time. Second, the expression of a specific gene will allow the evaluation of any associated activation of the DNA damage pathway. Therefore the test will provide information on the micronuclei origin, whether induced by mechanisms of DNA breaks (clastogenic) or produced through the abnormal chromosomes distribution during mitosis (aneugenic). To take into account the metabolism of many chemical compounds, these biotracers will be stably expressed in the HepaRG<sup>®</sup> cells, human liver cells that are metabolically active, optimized for the MN test by the industrial partner (BIOPREDIC International).

The developed *in vitro* MN assay will be adapted to a medium- to high throughput straightforward readable assay, thanks to the implementation of high content screening imaging protocols and the development of an image analysis and classification-based pipeline. The assay will bring new capacities to the classic MN assay and may lead to breakthroughs in the prevention and/or the 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 answer today's recommendations, with significant improvements in the scientific, technical and economical fields. Overall, the Genotrace project aims to a better safety of all chemicals, drugs, and foods exposure of human, farm animals/pets and environment.

<sup>1</sup> 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, that markets the human hepatic cell line HepaRG®.

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**About:**

**Toxalim**, joint research unit of INRA in partnership with the University of Toulouse III - Paul Sabatier, established in January 2011, gathers more than 200 people together (with 130 permanent scientists and eleven research teams). Toxalim contributes to a better understanding of long-term toxic effects of pesticides, mycotoxins and other chemical contaminants, at very low concentrations, alone or mixed in the food and feed. Toxalim covers different research fields and disciplines, from the digestive physiology to the perturbation of genes expression involved in chronic metabolic diseases such as diabetes, obesity and cancer. Toxalim is highly involved in agro-veterinary and university education in toxicology.

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**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 research in drug discovery, drug development and cosmetics. With most of the sales made overseas, Biopredic International is recognized worldwide 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, a Unit of Service and Research (USR3505) placed under the authority of CNRS, INSA and Paul Sabatier University - Toulouse III directed by Pr. Bernard Ducommun. This institute is located on the site of the Toulouse Oncopole in the Pierre Potier Centre, where it shares accommodation and pools resources with a biotech incubator. ITAV is a «hôtel à projet» set up to host teams working on interdisciplinary projects for a limited period of time. Its objective is to bring together in a unique environment conducive to collaboration, biologists, chemists, physicists, mathematicians, computer scientists along with researchers in other disciplines. It strives to give utmost significance to development and transfer leading to mature entrepreneurial projects. The two major thematic axes of the ITAV's scientific project are resolutely oriented towards the concept of innovation: "Innovation for exploration of dynamic processes in life sciences" and "Innovation for diagnosis and therapeutics".

to know more: [www.itav.fr](http://www.itav.fr) and [www.oncopole-toulouse.com](http://www.oncopole-toulouse.com)