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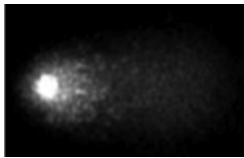


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## A new compact comet assay for versatile genotoxicity testing and environmental monitoring

The ComPack project is a French-Norwegian<sup>1</sup> collaborative research and innovation project that addresses the need for reliable and validated testing for industry and academia to assess the effect of chemicals on human health and the environment. The public-private consortium plans to develop by the end of 2016 a high throughput, automated, versatile, validated and user-friendly DNA testing facility based on the innovative modified comet assay.

The comet assay is the most widely used method for measuring DNA damage in eukaryotic cells. This test system is used for environmental agents as well as in human biomonitoring, for endogenous damage and antioxidant resistance analysis and DNA repair. The comet assay is employed by the pharmaceutical, cosmetic and chemical industries for screening novel drugs and chemicals for genotoxicity. The genotoxicity testing market is rapidly growing and is expected to reach €3,210 million in 2018<sup>2</sup>, 50% of which is currently represented by the cosmetics and personal-care industry and 32% by the pharmaceutical segment.



### What is the Comet assay?

The comet assay is a sensitive and versatile method for detecting DNA damage in eukaryotic cells. Alkaline electrophoresis of agarose-embedded, lysed cells (nucleoids) produces comet-like images, with broken DNA loops comprising the tail; the relative intensity of the tail indicates the frequency of DNA breaks.

Standard procedures for genotoxicity testing have been laid down by, among other organisations, the European Food Safety Authority (EFSA) and the International Committee for Harmonisation (ICH).

OECD guidelines are in preparation for the comet assay in *in vivo* genotoxicity testing, with the advantage that it can be applied to virtually all tissues. JACVAM (Japanese Committee for the Validation of Alternative Methods), in association with the corresponding European committee, ECVAM, is carrying out validation trials for the *in vitro* assay. REACH regulations (Registration, Evaluation, Authorisation and Restriction of Chemical substances) stipulate that chemicals whose usage per annum exceeds a certain level must be registered with details of toxicity for humans and possible environmental impact. As such, the comet assay is mentioned by REACH as a suitable assay for *in vitro* tests.

### A new plant-based comet assay to complement and strengthen conventional techniques

The comet assay is also a potentially powerful ecological research tool for assessing DNA damage and repair in sentinel animals such as mussels, earthworms or mice and plants in the environment. However, despite their fundamental roles in every ecosystem, plants have not been much used in these studies. There is therefore a need to develop an alternative, fast, cost-efficient, reliable and more informative plant-based assay. The project aims to increase several-fold the capacity and versatility of the comet assay, by adapting high throughput approaches for different cell types and for plants, incorporating enzymes that specifically convert altered bases to breaks, thus increasing the range of applications of the assay.

### The Human Hepatic cell line HepaRG™ used for the new comet assay

Many chemicals are genotoxic only after activation. HepaRG™ is a well-known human hepatic cell line commercially available through Biopredict International, which, uniquely, can differentiate into fully functional hepatocytes. These are particularly useful in genotoxicity testing, as they retain xenobiotic metabolizing (phase

I and phase II) enzymes and so can activate many potential carcinogens, unlike other permanent cell lines. Adapting the cells for use in the new comet assay will require the advanced cell culture skills of the French CRO Eurosafe, together with comet assay experience.

All partners in the project have proven expertise in relevant technological development to cover together the whole range of project needs. Overall, the Compack project will help chemical, nanomaterials, cosmetic, pharmaceutical and food industries and CROs by delivering to them all components for a more versatile, high throughput and fully automated comet assay for better safety-assurance of all chemicals, drugs, cosmetics and foods to which humans and the environment are exposed.

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<sup>1</sup> The public/ private ComPack consortium includes 5 organisations:

- the project initiator, NorGenoTech AS (NGT) lead by Pr. Andrew Collins, Dr Gunnar Brunborg and Dr Sergey Shaposhnikov whose facilities are based at the Department of Nutrition, University of Oslo
- The Department of Nutrition, part of the Medical Faculty of the University of Oslo
- LGCgE – Equipe Sols et Environnement – Laboratoire Génie Civil et géo Environnement
- Eurosafe, a CRO based in France, Brittany (that has recently acquired Xenoblis)
- IMSTAR SA, a French private SME

<sup>2</sup> According to Transparency Market Research.

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### **About**

**NorGenoTech AS (NGT)** was founded as a direct consequence of the success of the EC-funded STREP, COMICS (LSHB-CT-2006-037575). The core facilities of the company are based at the Department of Nutrition, Oslo University, which provides a productive research environment and modern laboratory facilities. The founders of NGT have extensive experience in running and participating in national and EU projects. The company was involved in carrying out R&D for industrial and academic customers, e.g. Kraft Foods Europe, Statoil, and Norwegian Institutes for Air Research and Water Research.

**University of Oslo.** Andrew Collins' group is responsible for various comet assay innovations, most recently through the EC-funded STREP, COMICS (LSHB-CT-2006-037575) and NewGeneris (FOOD-CT-2005-016320).

**LGCgE** (Equipe Sols et Environnement – Laboratoire Génie Civil et géo Environnement) is a French semi-public laboratory working for more than 30 years on soil contamination and the impacts of pollutants on human health and environment. It has developed several plant biomarkers to assess toxic effect of pollutants on the environment. LGCgE aims at advising national and local authorities on the management of polluted sites and pollution management. [www.lgcge.fr](http://www.lgcge.fr)

**Xenoblis, now part of Eurosafe,** was created more than 25 years ago by experts in hepatocyte isolation, Professors André Guillouzo and Christiane Guguen-Guillouzo, INSERM researchers. It has recently joined the French CRO EUROSAFE. Research on the liver remains the main focus in Eurosafe's *in vitro* team. The HepaRG® cell line, commonly used by Eurosafe, provides a new tool based on inducible hepatocyte differentiation. Learn more on [www.heparg.com](http://www.heparg.com)

**IMSTAR S.A.,** a private SME company founded by Dr Françoise Soussaline, focuses on developing innovative instruments for automated biomedical imaging and high throughput analysis in genetic toxicology, cytogenetics and cytopathology. Based on the Pathfinder™ range of High-Content Image Analysis systems, IMSTAR has patented an extensive set of technologies including software, hardware and content. The company was also a partner in the EU project COMICS. [www.imstarsa.com](http://www.imstarsa.com)