

# Improved Early Identification of Cancer Causing Chemicals in Cell Cultures Could Reduce Animal Testing



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## The Basic Problem:

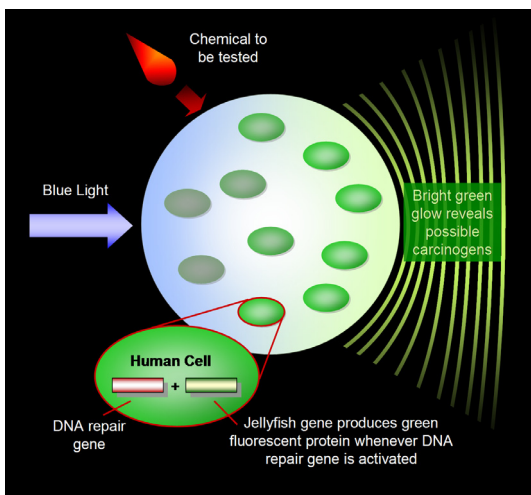
Cancer can arise as a consequence of DNA and chromosome damage caused by ultra violet radiation in sunlight, atomic radioactivity or chemicals known as 'genotoxins' or 'genotoxic carcinogens'. For this reason, all chemicals have to be tested for genotoxicity.

The current mammalian cell culture methods for the identification of genotoxic carcinogens are **over sensitive**, misclassifying many **safe** chemicals as potential human carcinogens.

To ensure patient safety, all new drugs that appear to damage DNA and/or chromosomes in mammalian cell cultures **currently have to be tested further using animals** for human risk assessment purposes.

## A New Test "GreenScreen HC"

- A new test "GreenScreen HC" (Human Cell) has been designed to improve the accuracy of the current mammalian cell culture methodologies in identifying chemical genotoxic carcinogens.
- An engineered human cell line has been created that **glows green** when its DNA or chromosomes are damaged as a result of exposure to genotoxins.



## The Challenge:

If we could improve the accuracy of cell cultures in identifying carcinogens that damage DNA and/or chromosomes prior to animal testing, then **we could reduce and replace animal testing.**

## Routine GreenScreen Use Could Reduce Animal Testing

- Studies with over 150 compounds look very good:
  - **Safe** compounds give **negative** results.
  - **Genotoxic carcinogens** give **positive** results.
  - **Safe** compounds **misclassified** by existing mammalian cell culture tests give the **correct negative result with GreenScreen.**
- By using GreenScreen to help correctly classify compounds with potential genotoxicity (as observed in mammalian cell culture tests) prior to animal testing **the number of animals tested for genotoxicity safety assessment could potentially be reduced by over 30% per company per year.**
- Investment in new technologies** such as GreenScreen, through **collaborations** with innovative **biotechnology companies** such as **Gentronix** enable the **pharmaceutical industry** to **reduce the cost of drug discovery** in terms of **time, money and animals**, and thereby allow **drugs to be brought to patients quicker** while **supporting the aims of the 3Rs without diminishing safety.**
- The benefits of GreenScreen may be extended beyond the Pharmaceutical industry; e.g. REACH Legislation will require over 30,000 compounds to be tested – and will impact cosmetic, household and chemical industrial sectors in the UK and beyond. If widely adopted **GreenScreen could potentially reduce the number of animals used by over half a million!**

## Abstract

Cancer can arise as a consequence of the chromosome damage caused by UV in sunlight, by radioactivity, and by chemicals known as 'genotoxins'. For this reason, all chemicals have to be tested for genotoxicity. However, the current 'test tube' genotoxicity test methods using mammalian cells are **seriously inaccurate**: they mis-classify over 50% of safe chemicals as potential carcinogens. As a result additional animal studies have to be carried out to determine the likely cancer risk - typically using over 200 for a new pharmaceutical. A simple new test ('GreenScreen HC') has been developed by the University of Manchester spinout company 'Gentronix Ltd' to tackle the accuracy problem. Exploiting recent advances in our understanding of the human genome and cutting edge genomic technologies, an engineered human cell line has been produced that glows green when exposed to genotoxins. Testing of over 150 compounds by Gentronix and GSK has shown that the **new test is highly predictive** of the regulatory animal tests, with over **95% accuracy in the identification of genotoxic carcinogens**. More importantly however, it very effectively discriminates between those chemicals that are truly genotoxic and the safe chemicals that regulatory test tube methods have misclassified as hazardous. In a collection of 26 such misclassified chemicals, 26 (over 90%) gave the correct negative result with GreenScreen. Use of this new test on these chemicals could have prevented 52 animal studies. The inaccuracy of existing cancer hazard assessment methods can contribute to the loss of potentially valuable new pharmaceuticals, industrial chemicals and household products. **The accuracy of the new test could save money and many animal lives** - imminent REACH legislation will require over 30,000 compounds to be tested

## Reference

High-specificity and high-sensitivity genotoxicity assessment in a human cell line: Validation of the GreenScreen HC GADD45a-GFP genotoxicity assay. Hastwell P.W., Chai L., Roberts K.J., Webster T.W., Harvey J.S., Rees R.W. and Walmsley R.M. (2006), Mutation Research 607: 160-175.

## Acknowledgments:



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