



GENOMARK CHIP
- AN EASY-TO-USE RTqPCR ARRAY -
PROVIDING HUMAN-BASED MECHANISTIC INFORMATION FOR
DE-RISKING POTENTIAL GENOTOXIC COMPOUNDS

BACKGROUND

Genotoxicity is a key endpoint in the hazard assessment of any sort of chemical, as damage to the genetic material might lead to detrimental effects on human health. To assess the potential of chemicals to induce genotoxicity, several *in vitro* and *in vivo* tests have been developed. Regulatory bodies worldwide recommend a battery of *in vitro* tests to cover the three important genotoxicity endpoints i.e. mutagenicity, clastogenicity and aneugenicity. A positive outcome in this battery is usually followed up by *in vivo* genotoxicity studies. To avoid the use of experimental animals, or in case legislation (cosmetics in Europe) does not permit animal usage, new technologies can be introduced to de-risk the positive outcome. In this way a compound can be saved, in an ethical way, through molecular information.

THE GENOMARK INNOVATION

In close collaboration, VUB and WIV-ISP have generated an easy-to-use 96-well qPCR array for genotoxicity detection, providing an additional *in vitro* tool to de-risk false positives emerging from the very sensitive standard genotoxicity battery of Ames and micronucleus tests. The GENOMARK chip translates a genotoxic-specific transcriptomics signature into a qPCR array of 84 biomarker genes. The assay is based on the well-established human HepaRG™ cell line and can be run in any lab with basic PCR equipment. Using IC₁₀ concentrations, the GENOMARK chip has shown 100% specificity and sensitivity for the non-equivocal compounds tested so far. Furthermore, the chip provides mechanistic information on compounds under debate, allowing for exploration of the mechanisms of genotoxicity at the gene level and assessment of human relevance.

GENOMARK POTENTIAL

Though recently developed, the GENOMARK chip has already generated promising results indicating its potential value in strategies for *in vitro* genotoxicity testing. It allows the incorporation of gene expression profiling in routine genotoxicity testing. Compounds that show positive results in a regulatory *in vitro* battery - known to generate a high proportion of false positive results – might still be saved by using this tool in a weight-of-evidence approach. The GENOMARK chip is valuable in all sectors, where compound development is hampered by excessive, expensive and time-consuming *in vivo* testing.

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