science summary

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# Endocrine disruption horizon scanning: Molecular and genomic contributions

Summary SC030276/SS2

The growing use of genomics will improve our understanding of the effects of chemicals on wildlife, according to a new report by the Environment Agency. The report, *Endocrine disruption horizon scanning: molecular and genomic contributions*, is part of a series on endocrine disrupting chemicals, which are thought to cause hormonal and sex changes in aquatic organisms such as dogwhelks and fish.

Most studies of endocrine disrupting chemicals (EDCs) have focused on high doses or very polluted environments. The advent of genomics means we can measure effects at much lower doses, to establish whether important changes are occurring at the level of gene expression (gene activation or suppression).

Genomics encompasses several disciplines including transcriptomics, the study of gene expression at the transcript level. DNA chips and microarrays now enable the study of thousands of genes simultaneously, although publication guidelines require microarray results to be confirmed by independent gene expression methods and real-time PCR (RT-PCR), also known as quantitative (real-time) PCR (Q-PCR), is often the method of choice.

Proteomics is the study of a protein's specific function, how it interacts with other proteins, and protein differences between healthy and diseased cells. Metabolomics is the newest genomic technology, but because of its vast potential is moving at a very fast pace. The technique can identify biochemical differences between a biological control sample such as blood plasma, urine or tissues and a test sample (at a specific disease state or stress response), where an organism's phenotype may have become altered.

Probably the greatest advantage of these techniques is that they can reveal the mechanism of action of a toxicant. Understanding the mechanisms of action of EDCs is critical, as this is central to determining whether the chemical is an endocrine disrupter and is causing an adverse response in an individual or population.

Genomic tools have already been used to study the effects of EDCs on model organisms, mainly to assess gene expression responses to exposure to EDCs (especially in fish). These transcript studies have enabled researchers to identify and functionally characterise genes involved in endocrine disruption, and work towards developing biomarkers. They have also been used to clone steroid and non-steroid receptors in wildlife, to study the function of hormone receptors and gain insights into underlying mechanisms. Proteomic and metabolomic approaches have been less forthcoming, although they are on the increase.

While these tools are available for studying changes in gene transcripts, proteins and metabolites, the techniques are at different stages of development and as a result, their potential integration into regulation will occur at different points in time. In terms of applying genomic tools in ecotoxicological testing, at present they are not in a state to replace traditional methods, but can nevertheless enhance the type of information derived from an experiment.

This report concludes that further research is needed to establish and validate the use of genomics for environmental monitoring, before these tools can be considered for regulatory application.

Research is needed to:

- validate the tools being developed;
- develop datasets for various species and environments, documenting normal gene expression profiles and fingerprints of exposure;
- further develop resources for analysing the datasets generated, and maintain publicly available databases to support work in this area of research;

- develop scientific partnerships of experts in ecotoxicology and genomics, in order to fully make use of the tools that these technologies are able to provide.

Among the most promising emerging technologies, microarrays and real-time PCR are likely to be especially useful for the detection, monitoring and mechanistic understanding of the risks posed by environmental chemicals. Microarrays can help elucidate the mechanisms of action of individual chemicals and identify new biomarkers for environmental monitoring, but their complexity and cost restricts their use to large specialised laboratories. Once molecular biomarkers are identified, real-time PCR can be applied to large numbers of samples at a relatively low cost, making this technique particularly suited for environmental monitoring.

The genome sequencing efforts of the last decade have opened new avenues for biologists in all areas of research. However, progress in the application of these resources to ecotoxicology will depend on progress in our understanding of the relationships between gene expression alterations and phenotypic changes as a result of chemical exposure, and this area requires further research.

This report is one of four reports produced under the *Endocrine disruption horizon scanning project* (SC030276), which is part of Environment Agency's project (P6-020/U), *Development of methods for detection of endocrine disruption and application to environmental samples.* The aim of the *Horizon scanning project* is to review new and emerging aspects of endocrine disruption. The full list of reports is:

*Endocrine disruption horizon scanning: Aquatic invertebrates review*
- *Endocrine disruption horizon scanning: Molecular and genomic contributions*
- *Endocrine disruption horizon scanning: Priority and new endocrine disrupting chemicals*
- *Endocrine disruption horizon scanning: Current status of endocrine disruptor research and policy*

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