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A literature review on Toxicogenomics

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ABSTRACT

Toxicogenomics is a field of science that studies toxicology with genomics and other high-throughput molecular technologies and bioinformatics. Typically, it applies transcript, protein and metabolite profiling technologies to investigate the interaction between genes/proteins/ metabolites and environmental stress in disease causation and toxicity. The concept of toxicogenomics was first introduced in 1999, inspired by the rapid advancement of microarray technologies. The field has quickly expanded by including proteomics, metabolomics and other new high-throughput technologies. In *Ayurvedic* perspective, toxicogenomics can be correlated with the *Beeja Dosha Dushti*.

Key words: *Toxicogenomics, Bioinformatics, technology, Gene, Beeja Dosha*

INTRODUCTION

Toxicogenomics is derived from two word ‘toxicology’ and ‘genomics’. Toxicology mean is the study of the adverse effects of chemicals or substances on living organisms. It involves understanding how toxicants, which are substances that can cause toxicity, interact with biological systems and how they can lead to harmful effects. Genomics mean takes a broader perspective by analyzing and interpreting the entire genome, including all genes and non-coding regions, to gain a comprehensive understanding of how genes work together, regulate each other, and contribute to the phenotype and diseases of an organism. Toxicogenomics is a multidisciplinary field that brings together toxicology and genomics to investigate how genes and toxic chemicals interact. Understanding how exposure to diverse environmental agents, such as chemicals, medications, or pollutants, impacts an organism's gene expression and general cellular function includes the application of genomic technology and molecular biology techniques.[1]

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‘Toxicogenomics’ main tenet is that due to genetic variances, different people may react to harmful substances in different ways. It focuses on comprehending how biological processes and gene expression patterns might be affected by exposure to diverse environmental factors, such as chemicals, medications, or pollution.[2] Advances in genomics technology, like as microarray analysis and next-generation sequencing, which enable researchers to thoroughly and methodically investigate the complete genome and its expression patterns, gave rise to the area of toxicogenomics.[3] Toxicogenomics tries to pinpoint certain genes, pathways, and molecular mechanisms that are impacted by hazardous compounds by examining the changes in gene expression profiles.[4]

AIM AND OBJECTIVES

The aim of toxicogenomics is to understand how genes and gene expression patterns are influenced by exposure to toxic substances. It integrates the sciences of toxicology and genetics to look into the biological processes that underlie hazardous responses and to find potential toxicity biomarkers.

1. Identifying toxicological pathways: Toxicogenomics aims to uncover the biological pathways and networks that are affected by exposure to toxic substances.
2. Characterizing toxicological responses: It seeks to characterize the molecular responses of cells, tissues, and organisms to toxicants. This involves examining changes in gene expression, protein levels, and metabolites in order to understand how toxic substances interact with biological systems.
3. Discovering biomarkers of toxicity: It aims to identify biomarkers that can serve as early indicators of toxic responses.
4. Enhancing toxicological risk assessment: It can aid in the discovery of more pertinent toxicological endpoints and enhance our capacity to forecast the consequences of chemical exposures on human health by offering molecular-level insights into toxic responses.
5. Advancing drug safety assessment: It can help in the early detection of drug-induced toxicities, adverse effects and help prioritize drug candidates based on their safety profiles.

1. Principle of Toxicogenomics

Gene Expression Profiling:

Toxicogenomics involves the analysis of gene expression patterns in response to toxic agents. It compares the expression levels of thousands of genes simultaneously to identify genes that are up regulated or down regulated upon exposure to a toxic substance. This information can provide insights into the biological pathways and molecular mechanisms affected by the toxic agent.**[5]**

Biomarkers of Toxicity:

Toxicogenomics aims to identify specific genes or gene expression patterns that can serve as biomarkers of toxicity. These biomarkers can be used to assess an individual's susceptibility to toxic substances or to monitor the effects of exposure. Biomarkers help in early detection, diagnosis, and personalized treatment of toxicological disorders.**[6]**

Molecular pathways and networks:

It plays a crucial role in toxicogenomics by providing a systems-level understanding of the interactions between genes, proteins, and other molecules involved in toxicological responses. They help to identify key biological processes and signaling cascades that are perturbed by toxicants, unravel the mechanisms of toxicity, and identify potential therapeutic targets.**[7]**

2. Applications of Toxicogenomics

Toxicogenomics involves the use of high-throughput technologies such as microarrays or next-generation sequencing to analyze the expression levels of thousands of genes simultaneously.[8]

This allows comparing gene expression profiles between exposed and unexposed individuals or between different dose levels to identify genes that are specifically affected by the toxic substance.**[9]**

Environmental Toxicology:

Toxicogenomics plays a crucial role in environmental toxicology by providing insights into the effects of environmental contaminants on organisms and ecosystems. It helps in identifying genes and pathways affected by environmental pollutants, understanding the impact on biodiversity, and assessing the potential risks to human and ecological health. Toxicogenomics also aids in the identification of novel targets for environmental monitoring and the development of more effective remediation strategies.**[10]**

Drug Development and Safety Assessment:

Toxicogenomics has applications in drug development and safety assessment. By analyzing gene expression patterns and genetic variations, researchers can gain insights into the safety and efficacy of drugs. Toxicogenomics data can be used to predict drug responses, identify potential adverse drug reactions, understand mechanisms of drug-induced toxicity, and optimize drug development pipelines.**[11]**

3. Advantages of Toxicogenomics

The large quantity and comprehensiveness of information that a single experiment can generate is much greater than that which traditional experiments generate.

4. Branches of Toxicogenomics

1. Phenotypic toxicogenomics
2. Metabolomics toxicogenomics

Phenotypic toxicogenomics

- Phenotypic toxicogenomics involves studying the observable characteristics or traits (phenotypes) of organisms in response to toxicants.[12]
- It aims to understand how exposure to toxic substances affects the overall phenotype of an organism, including physiological, morphological, and behavioral changes.[13]
- Phenotypic toxicogenomics may include assessments of growth, development, reproductive capacity, behavior, and other observable traits.

Metabolomics toxicogenomics

- Study of small molecules, known as metabolites that are involved in cellular metabolism.
- It involves the analysis of changes in metabolite profiles in response to toxic substances.[14]

MATERIALS AND METHODS

Materials and methods in toxicogenomics research can vary depending on the specific experimental design and objectives. Here is a general overview of commonly used materials and methods in toxicogenomics:

Materials:

- **Biological samples:** It includes cells, tissues, organs, or biological fluids (blood, urine, etc.
- **Toxicants:** These can include environmental pollutants, chemicals, drugs, or any other agents that have the potential to induce toxic responses.
- **RNA/DNA extraction kits:** To analyze gene expression patterns, the extraction of RNA or DNA from biological samples is necessary. Commercially available extraction kits specific for RNA or DNA isolation are commonly used to isolate and purify the nucleic acids for subsequent analysis.
- **Microarrays or next-generation sequencing (NGS) platforms:** These technologies are utilized to measure gene expression levels on a global scale. Microarrays consist of solid supports (glass slides or chips) containing thousands of immobilized DNA or RNA probes, while NGS platforms enable high-throughput sequencing of the entire transcriptome or genome.
- **Bioinformatics tools:** Bioinformatics software and databases are essential for analyzing and interpreting large-scale genomic data. These tools facilitate gene expression analysis, identification of differentially expressed genes, pathway analysis, and integration of various data types.

Methods:

- **Experimental design:** Toxicogenomics studies require careful experimental design, including the selection of appropriate sample sizes, controls, and treatment groups. Factors such as dose and duration of exposure, time points for sample collection, and replication should be considered to ensure statistical reliability.
- **RNA/DNA analysis:** The extracted RNA or DNA is typically subjected to quality control measures to assess integrity and purity. Methods such as spectrophotometry, agarose gel electrophoresis, or automated electrophoretic systems can be employed. Reverse transcription of RNA to complementary DNA (cDNA) may also be performed for subsequent gene expression analysis.
- **Gene expression analysis:** Microarrays or NGS platforms are used to measure gene expression levels. Microarrays involve hybridizing labeled cDNA or RNA samples to the immobilized probes, while NGS platforms sequence the cDNA or RNA

libraries. The resulting data can be analyzed using various statistical and bioinformatics approaches.

- **Data analysis and interpretation:** Bioinformatics tools are employed to analyze gene expression data, identify differentially expressed genes, and perform functional enrichment analyses. This involves comparing expression levels between different experimental conditions or time points and assessing the significance of gene expression changes.
- **Validation techniques:** Selected genes of interest identified through gene expression analysis can be further validated using quantitative real-time PCR (qPCR), which provides a more targeted and quantitative measurement of gene expression. Other validation techniques may include Western blotting, immunohistochemistry, or functional assays to confirm the functional relevance of the identified genes or pathways.
- **Integration of data:** Integration of toxicogenomics data with other omics datasets (such as proteomics or metabolomics) can provide a more comprehensive understanding of toxic responses and the underlying mechanisms.

It is important to note that the specific materials and methods employed in toxicogenomics can vary based on the research objectives, target organisms, and available resources. Researchers often tailor the approach to suit their specific research questions and experimental constraints.

Ayurvedic perspective of Toxicogenomics

Beeja Dosha described in *Ayurveda Shastra* can be correlated with toxicogenomics. Genetic illness is caused by *Beeja Dosha*. Its transmission occurs from one generation to another generation in either dominant or recessive form. Numerous ailments have been listed in *Ayurveda Shastra* as being caused by *Beeja Dosha*. Primarily *Beeja* is of two types i.e., *Shukra* and *Artava*. *Beeja Dosha Dushti* is caused by environmental poisoning, including (*Vayu, Jala, Desha,* and *Kala*), known in the scriptures as *Janapadodhvansa*, as well as man-made and chemical poisons etc. When there is exposure of this poison to our body, it causes *Beeja Dosha Dushti* and further congenital diseases and some hereditary diseases (*Kulaja Vikara*). The *Kulaja Vikaras* mentioned in *Charak Samhita* are *Prameha, Kushtha, Arsha*. According to *Acharya Charaka*, the congenital diseases named *Bandhya, Putipraja* and *Trinputrika* are caused by *Shukra Beeja Dosha Dushti* and the diseases named *Bandhyaa, Putiprajaa* and *Varta* are caused by *Artava Beeja Dosha Dushti*.[15] *Acharya Sushruta* has termed it as *Janmabala Pravritta Vikara* due to intake of incompatible food during the duration of pregnancy.[16] He has also mentioned about *Kalyanaka Ghrita* for the *Shamana* of *Beeja Dosha Dushti Vikaras.*[17]

DISCUSSION

Toxicogenomics offers a potent method for comprehending the intricate relationships between genes and toxins. It has the potential to revolutionize personalized medicine, toxicological research, risk assessment, and toxicology, improving public health and safety. The research and discovery of new drugs can benefit from toxicogenomics. Researchers can learn more about a medicine's potential toxicities or pinpoint particular patient populations who may be more vulnerable to negative drug reactions by looking at how it affects gene expression profiles. The creation of safer and more specialized therapies may be guided by this information. In *Ayurveda, Beeja Dosha Dushti* have been described briefly by different *Acharyas.* Also, the treatment *Yoga* of these *Vikaras* has been mentioned.

CONCLUSION

Overall, toxicogenomics offers valuable insights into the molecular mechanisms of toxicity and can contribute to the development of safer drugs, environmental risk assessment, and personalized approaches to healthcare. It provides a powerful approach to understand the complex interactions between genes and environmental factors in relation to toxic substances. Ultimately, it contributes to a better understanding of toxicity mechanisms and the development of more precise strategies for prevention and treatment. *Ayurveda* tries to provide a universal perspective to the life, health and even to cell and molecular biology, thus covers all aspects of life including genetic and phenotypic. *Ayurveda* also considers holistic approach in management of *Beeja Dosha Vikaras* by *Shamana Yogas*.

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