Genomic and Epigenomic Profiling of the Brain Tumor in a Pharmacogenomic Approach in Indian Population

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Abstract

Cancer is one of the deadliest diseases which is proven lethal. It is one of the major reasons for the millions of fatalities all across the world. Out of this, the Brain Tumor study is very sensitive and challenging. The main challenge is diagnosing the disease at the early level and finding the personalised treatment based on the genomic sequence of a person. With this research, we decided to find an individual level treatment among the Indian population by the Genomics and Epigenomics and Pharmacogenomics approach.

***Keywords:-** Genomics, Epigenomics, Pharmacogenomics, Single nucleotide polymorphism, DNA methylation, Brain tumor.*

INTRODUCTION

Genomic profiling is a technique used to understand the genome sequence of an individual or a gene sequence of a specific cell type [1]. Hence the profiling technique can be applied to understand the genomic variations on a time scale and to discover new technologies for identifying the optimum treatment for various disorders. Because of the development of new and automated technologies such as Artificial Intelligence [2] and availability of the online data tools (like ICGC, NCBI) [3] [4], profiling of the human genome has become faster and much more economical and efficient, resulting in the more effective and timely diagnosis of the disease. With the pharmacogenomics approach, genomic profiling provides an efficient way for researchers and scientists to invalidate the genomic profile [5] among the Indian population [6]. They could study the effects of drugs on an individual. The study suggests a game-changer in genomic research as it explores an individual's genomic and epigenomic character with the responses to drugs.

A brain tumour is an uncontrolled cell division affecting the intracranial region in the brain. The tumour progression occurs mainly through the primary and secondary pathways. The primary generation is the in-situ development of the tumour, and secondary tumour progression is caused through metastasis. Identification of genes and variants associated with tumour progression helps us study the proneness of individuals towards the disease.

The study also allowed us to verify the cause and effect of the SNP variations by crosschecking the multiple affected persons and finding their gene co-relation [7]. Also, the other cancer types proliferations besides the brain tumour can now possibly be detected. A relationship can be set up to the gene of interest within the human body. Over the search tool NCBI (National Centre for Biotechnology Information), we came across other types of cancer types such as liver cancer, skin cancer, leukaemia, bladder cancer, prostate cancer and others whose occurrences also depend on the presence of taken genes. Quantifying the functionality of the gene can be done by measuring the expression value in TPM (Transcript Per Million), which gives us the replication potential of the gene, so defining its mutation capability shown with the blue colour, the darker the colour intensity refer greater is the expression value of that specific gene. With the procurement of the expression data, one can easily decipher the cancer-causing capability and its comparison with the other genes.

MATERIALS AND METHODOLOGY

Visualised responses illuminated by the genomic profile when the drug is administered to the

system. These responses are recorded by using the various characteristics. Mendelian disorder and the genetics involved here are studied in correlation with the gene expression or SNPs by Pharmacodynamics and Pharmacokinetics [8].

A. Genomics

Through the various bioinformatic tools, we selected the genes IDH1, IDH2, GSTT1, GSTM1, PTCH1, CTNNB1, PGDRFA, which are primarily responsible for causing a Brain tumour. Additionally, the proteomic data set was also created through which the nucleotide sequence of the genes was carefully studied, and Genomic profiling [9] of each gene was noted down. Hence we created a primary bioinformatics database for further (epigenomic) research [10].

B. Epigenomic Data Set

Using the database NCBI (National Centre for Biotechnology Information), we collected the clinical variations of each gene, presenting the data about their cytogenetic locations, clinical significance, variant type and the SNPs (showing the various missense mutations occurrences in the nucleotide sequences).

The cross-correlation between the SNPs acquired was made with IGVdb (Indian Genome Variation Database). Using the gene expression atlas, the expression analysis of each gene was performed, and the data was correlated to TPM values which is the quantifying unit for the gene expression analysis.

The experimental data were collected from HDBR (Human Developmental Biology Research), an ongoing collection of human embryonic and foetal material ranging from 3 to 20 weeks of development and the Fantom Project (Functional Annotation of Mammalian Genome) project charts an atlas of gene activity over the human body. Within the pharmacogenomics [11], the studies relating to gene methylation were performed. Few pre-tested blood sample data were affected with the gene of interest (available over the I-Methyl online bioinformatics tool) taken, and the relevant information was extracted. The methylation [12] affects the gene transcription capacity and suppresses the mutation effects.

RESULTS

Expression values with respect to each gene were obtained and tabulated (showing the expression value in TPM). Mutated genes, namely GSTT1 and GSTM [13], were found among the Indian population (mentioned over the IGVdb-Indian Genome Variation Database).

Gene Expression Analysis is the method of finding the appropriate gene here, which plays a more significant role in causing Neurodegenerative diseases (tumours, cancers etc.). Hence, the dark blocks with the figure represent the positive expression with respect to the shown diseases. The darker block is regarded as the greater expression of that particular gene towards any specific type of disease.

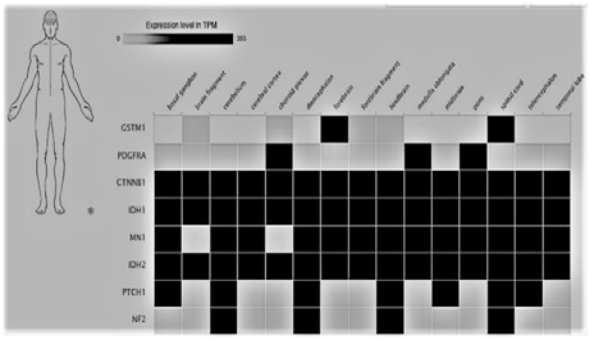

Fig. 1: Gene Expression Analysis

Relative box plot representing the gene vs TPM values has also been plot.

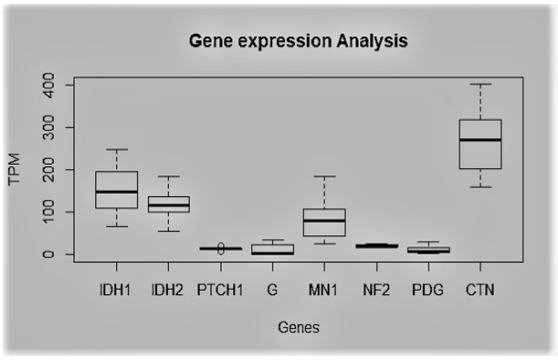

Fig. 2: Expression Box Plot

Methylation analysis

The methylation [14] values and age and the gender-wise onset of the disease is shown with graphical representation for the IDH1 gene, which is highly responsible for the brain tumour and causing the onset of the disease at the very late years of the life span (later than 70 years on an average).

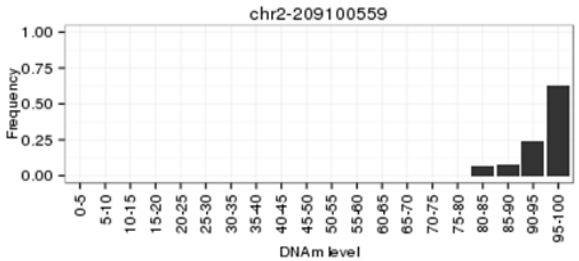

Fig. 3: Methylation Analysis

GSTT1 and GSTM1 both are significantly less expressed in the Indian population. But the presence among the Indian population itself cannot

be neglected. There is a possibility that these genes may be one of the causes of the onset of brain tumours among the Indian population.

CONCLUSION

The research could be beneficial specifically for the early detection of the onset of the brain tumour. It could help the researchers to develop the personalised treatment (individual base, gender base, age base) based on the genome analysis. With the development of new and advanced scientific methods like machine learning and Artificial Intelligence, a discriminator and other machine learning tools can also be employed for faster diagnoses and early-stage treatments.

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