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Review On the Role of DNA Microarrays in Cancer Therapy

Mustapha G[1*]., Nafi'u A[1]., J. Ukomadu[2], Hizbullah M. U[1]., Fatima I. J[1]., H. M. Maiturare[1]
[1] Microbiology Department Sokoto State University, Along Airport road Sokoto State Nigeria.
[2] Plant Science and biotechnology Department, University of Port Harcourt, Nigeria.
*Corresponding author: Mustapha Gani, Email: mustaphagani1@gmail.com
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ABSTRACT:

Bioinformatics is an interdisciplinary science that provides an incorporated understanding of several sciences to explain a particular problem based on existing biological data. DNA microarrays have the potential to assess the expression of thousands of genes simultaneously and used in the identification of new targets and discovery of new drugs for cancer therapy. It offers the capability to develop personalized therapeutic treatments by supporting clinical decision and improve understanding of the molecular basis of cancer as well as provide massive source of data on gene expression. During the past 20 years, DNA microarray technology has been developed and combined as a mundane tool in research laboratories and is now transitioning to the clinic. Studies show that DNA microarrays are widely used for diagnosing of immunosuppression cholesterol biosynthesis which was discovered as a target of radio sensitization Through DNA microarrays. This review aimed at determining the role of DNA microarray in cancer therapy.

Keyword: *DNA microarrays, Review, cancer therapy, Bioinformatics*

INTRODUCTION

The complexity of living organisms makes it challenging to completely understand their biological activities. Systems biology studies the organisms as integrated systems made up of dynamic and interconnected genetic, metabolic, protein, and cellular mechanisms with the application of biology, computer science, technology and mathematics. [1] Bioinformatics has been applied to deal with the complex data generated by various interdisciplinary fields. Bioinformatics is an interdisciplinary science that provides an incorporated understanding of several sciences to explain a particular problem based on existing biological data. [2] It utilizes high throughput data analysis in order to elucidate various challenges faced in solving biological problems one of which is DNA microarray technology. [3]

DNA microarrays signify a high-throughput measurement technology that is extensively applied in biological research, especially gene expression experiments. It has been successful in the identification of new targets and discovery of new drugs for cancer therapy. In this article the importance of DNA microarray data analysis for cancer therapeutics will be reviewed. [4]

Applications of bioinformatics in drug discovery

Bioinformatics have enabled the discovery of drug targets which has led to the development of new drugs through identifying the biologically active candidates. [5] This is predicted to lead to an increase in the number of available drugs from pharmaceutical industries and subsequently providing useful drug targets (enzymes, proteins, receptors, RNA, DNA) data by the use of algorithms and master plan to develop novel targets, organize and save data of the targets. Algorithms such as Paradigm divides patients into appropriate groups and by using the genetic copy number and variation and incorporating different interactions obtained from NCBI thereby integrating patient's data with pathways which helps in selection of patients for clinical trials. [6] Bioinformatics has been used over the years to reduce the cost of production of drugs and also limit the number of non-successes during drug discovery. this is done to increase the number of available drugs in the market. [7] Bioinformatics has increased the chances of speedy drug discovery processes for target identification to high throughput screening with the aim of discovering novel prospective chemical entities thus enabling more successes in drug discovery through speedy approval phases and subsequently reducing cost. [8] Computational methods such as genetic algorithm or neural network based applications [9] are successfully applied to remove molecules which are likely not to get to the future phases of drug discovery. Methods such as molecular docking which envisage the intermolecular structure within two molecules is applied in drug discovery for similarity prediction of drug targets and the subsequent drug. Successes have been recorded with docking accounting for 70%-80% in some programs. [10] In lead optimization stage of drug discovery, tools such as Biskit is used for scrutinizing the 3D arrangement of genes or proteins and subsequently establishing the extensive source of origination and development of disease. [11]

Importance of DNA Microarray in Cancer Therapy

The completion of the Human Genome Project in 2001, gave rise to innovative fascinating challenges from biological exploration to medicine applications. During this period, astonishingly fast advances of high-throughput technologies have been observed. [12]

DNA microarrays is one of significant technologies for high-throughput genomic analysis during the past 20 years, DNA microarray technology has been developed and combined as a mundane tool in research laboratories and is now transitioning to the clinic.

The high-throughput analysis of DNA microarray permits parallelism through a direct comparison between thousands of probes spotted on the microarray and their complementary targets. This benefit has been attained thanks to miniaturization of the array surface, giving rise also to a substantial improvement in terms of decrease of reaction volumes, increase of sample concentration and acceleration of hybridization dynamic. Welfare comes from the practice of fluorochrome labelling techniques, which circumvent management by the operator of radioactive or poisonous compounds during the experimental procedure.

Through this procedure shown above successes has been registered in drug discovery and target Identification. Study by [13] showed the use of DNA microarray for the discovery of drugs s HSp90 inhibitor 17AAG and compounds such as RTA402 and Parthenolide this was achieved by a approach via microarray

data from both and human murine samples to select a clinically appropriate set of drugs to be possibly developed in human clinical trials of Metastatic pheochromocytoma or paraganglioma.

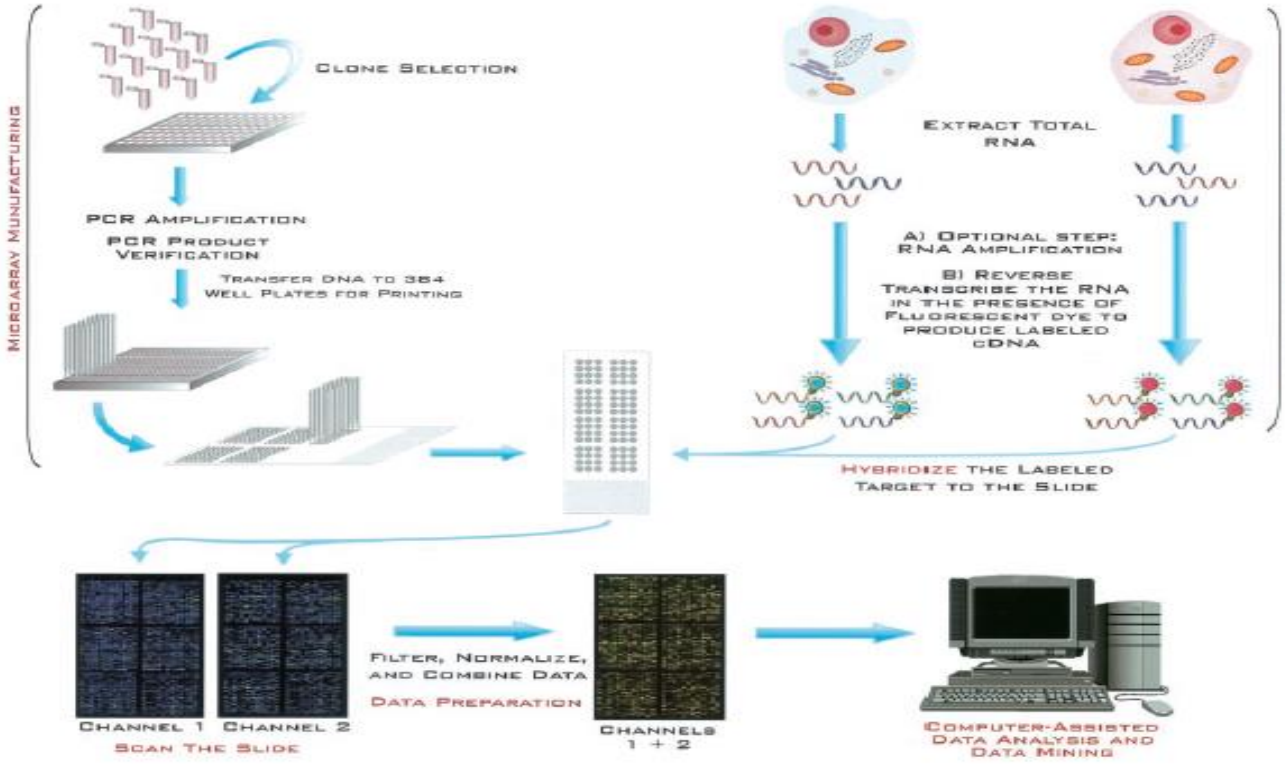

Figure. A schematic representation of the steps involved in Microarray Procedure. [12]

Similarly [14] demonstrated the immunosuppressive effect of cyclosporine on human lung fibroblast *in vitro* by countering the actions of TGF-β their study.

Also a novel radio sensitizer known as Zol as pancreatic cancer radiation was discovered by [15] in this study cholesterol biosynthesis was identified as a novel target for radio sensitisation. Another benefit of this method is that since the cell microarrays are produced with the similar robotic microarray device as used to produce conventional DNA microarrays, same amount of density can be attained which may be 6000–10,000 spots per slide. These resultant microarrays can be used to recognize a novel drug targets by characterising the massive amounts of gene products functionally the assays based-cells; to estimate the specificity of potential drugs; and to detect requisite proteins for drugs which mechanism-of-action is not yet identified or for candidates recognised in assay based on phenotype. [16]

However the application of DNA microarray data analysis is however not without short limitations or challenges

The use of DNA microarrays allows the potent interrogation of several genes for variations in RNA expression, DNA copy number, and the existence of polymorphisms and mutations. Dealing with the avalanche of data produced and specifically translating this data into clinically active therapeutics. This is a critical question because of the very high cost and very low proficiency of bringing a drug against a specific target through development and to the clinic. The drug development process is estimated to cost over $800 million for single drug and may take over 10 years to be accomplished. Prediction from the thousands of candidate targets those whose pharmaceutical operation will sway on cancer become a challenge [17].

Bose [17] noted that some of these limitations one of which is the failure of microarray to give panoramic view of the subject under examination as a result of complexity and dimensionality of the subject under investigation. Sometimes sources of samples become a challenge as most samples comprises of dead cells.

Successes AND breakthroughs

Clinically available data from patients have been used to develop a network, the phenotype disease network which reveals the correlation between diseases. [18] Drug design using computer simulations has demonstrated victory in the production of drugs against diseases such as Alzheimer's disease, [19] inhibitors for the growth of new blood vessels [20] among others. Another breakthrough in drug discovery is the development of Combinatorial Drug Assembler (CDA) which targets gene expression profiling and multiple signalling pathways for combinatorial drug design. It quantifies useful similitude between information quality sets and 6,100 particle treated expression profiles utilizing Kolmogorov-Smirnov insights.

At that point it records up best example coordinating single medications/combinatorial medication matches. This software is available free of charge at http://cda.i-pharm.org. [21] Also, it is very challenging or nearly impossible to design arrays in which numerous related RNA/DNA sequences not binding to the identical probe in an array for the mammalian genomes. A sequence on an array that was made to identify say "gene 1", has the potential of detecting "Genes 2, 3 and 4" if these genes have major sequence homology to gene 1. This can be particularly difficult for gene families and for genes with multiple splice variants. There is a possibility of designing arrays specifically to identify splice variants either [22] or to exon intersections. It is however, demanding to create arrays that will specifically identify the exons or in genes of genomes having multiple related genes.

Despite the challenges faced DNA microarray array has been successful and offers a lot of potentials in the nearest future of which is personalised medicine.

CONCLUSION

DNA microarray analysis bioinformatics tool has been applied in the identification of novel targets and discovery of cancer therapeutics. In other to successfully carry out this research the integration of other fields is involved such as computation and statistics to mention but view. The series of biological activities that goes on in humans are too numerous how they the gene mutate to give rise to certain disease has not been fully understood thereby making it a complex biological system. To successfully find a therapy for cancer a target has be discovered and eventually leading to a discovery of new drugs, these involves series of processes for which bioinformatics is not excluded.

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