

The application of Microarray in Medicine

Aplicarea Microarray in medicină

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Abstract

Today reliability, rapidity and accuracy in clinical diagnostics are the first choices. Combination of molecular techniques and Bioinformatics have upgraded diagnostic methods and treating managements. Among advanced clinical technologies, microarrays are effective diagnostics in medicine. Medical microbiology is consisted of medical bacteriology, medical mycology, and medical virology; clinical diagnostics of infectious and non-infectious diseases, gene expression profiling, genetic disorders, detection of pathogenic microbial agents and treatment are different pieces of medicine puzzles. The applications of microarrays in medicine are in progress. The most important problem for public use of microarrays is their expensive costs. Covering the costs of microarray technologies will change them into a gold standard method for diagnosing and treatment in public medical centers, laboratories and hospitals around the world.

Keywords: microarray, diagnosis, diseases, medicine

Rezumat

Astăzi, rapiditatea, acuratețea și fiabilitatea sunt primele cerințe ale diagnosticului clinic. Asocierea tehnicilor moleculare cu cele bioinformatică a perfecționat metodele de diagnostic, precum și protocoalele terapeutice. Printre tehnologiile clinice avansate, microarray s-a dovedit a fi o metodă eficientă de diagnostic în medicină. Microbiologia medicală este alcătuită din bacteriologia, micologia și virusologia medicală; diagnosticul clinic al bolilor infecțioase și non-infecțioase, profilul genetic, patologiile genetice și tratamentul sunt piese distincte ale puzzle-ului medical. Aplicarea microarray în medicină este într-un continuu progres. Problema cea mai importantă a utilizării acestei tehnici în populația generală este costul mare al metodei. Acoperirea acestor costuri va transforma această metodă de diagnostic în metoda standard de elecție pentru diagnostic și tratament în centrele medicale, laboratoarele și spitalele din întreaga lume.

Cuvinte-cheie: microarray, diagnostic, boală, medicină

Introduction

Microarray is the final outcome of progressive combination of molecular techniques and clinical Bioinformatics^(1,2). Microarrays are microminiaturized technologies originated from dot blotting techniques of Northern/Southern blots. The procedures of microarray involve a vast range of applications (Figure 1)⁽³⁻⁷⁾.

Target molecules in microarrays include DNA, RNA and proteins. Microarray is a powerful molecular diagnostic method which can manage an enormous volume of information and data. Thousands of RNA or DNA target sequences are detectable at the same time via microarray^(3,4,8).

DNA microarray comprises fabrication, process of target labeling, probe designing, hybridization and image scanning and data interpretation (Figure 2)^(1,3,7).

DNA microarray is an accurate, rapid, reliable, sensitive and specific diagnostic technology, which has influential and effective treating management^(1,6).

DNA microarrays are divided into PCR and Oligonucleotide arrays. Oligonucleotide DNA microarrays introduce a definite diagnostic tool for different diseases, including infectious diseases, autoimmune diseases, inflammatory diseases, metabolic and genetic disorders⁽⁶⁾.

In this review, we have a bald look at medical applications of Microarrays.

Gene Expression Profiling

Precise detection, identification and measurement of gene function and expression is possible via microarrays through the extraction of RNA molecules in clinical samples of cells and tissues. Gene expression profiling may

lead to more accurate prognosis, diagnosis, control, and definite treatment of various diseases^(1,4-6,8-10).

According to different studies, microarray techniques are known as appropriate and powerful screening procedures for identifying and detecting genes clusters associated with a determinant biological process. The advantage of microarray technology for profiling gene expressions is to measure the function and the pattern similarities of tens of thousands of genes in the form of a single assay^(6,8,11,12).

Data analyses relating to gene expressions show the functional and the pattern of gene clusters which may lead to categorize and mapping different classes of the genes. Each set of gene cluster will be identified via negative and positive labeling^(1,6,12).

The secret of gene expression profiling is to screen the biomarkers relating to an individual disease. Therefore, the use of DNA microarray is a prompt approach to diagnose a wide range of non-infectious diseases such as cancers, leukemia, lymphoma, melanoma, diabetes, arthritis, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and Crohn's disease via biomarker genes^(6,8,13).

So, mapping the appeared changes in gene coding regions related to gene regulation and expression via DNA microarray technology is a great revolution in molecular diagnostic methods^(1,6).

Diagnosis of Genetic Disorders

Chromosomal malformations and DNA mutations (including SNPs) are categorized as inherited genetic disorders. DNA mutations may lead to protein deformities, protein malfunctions, absence of protein products, and the

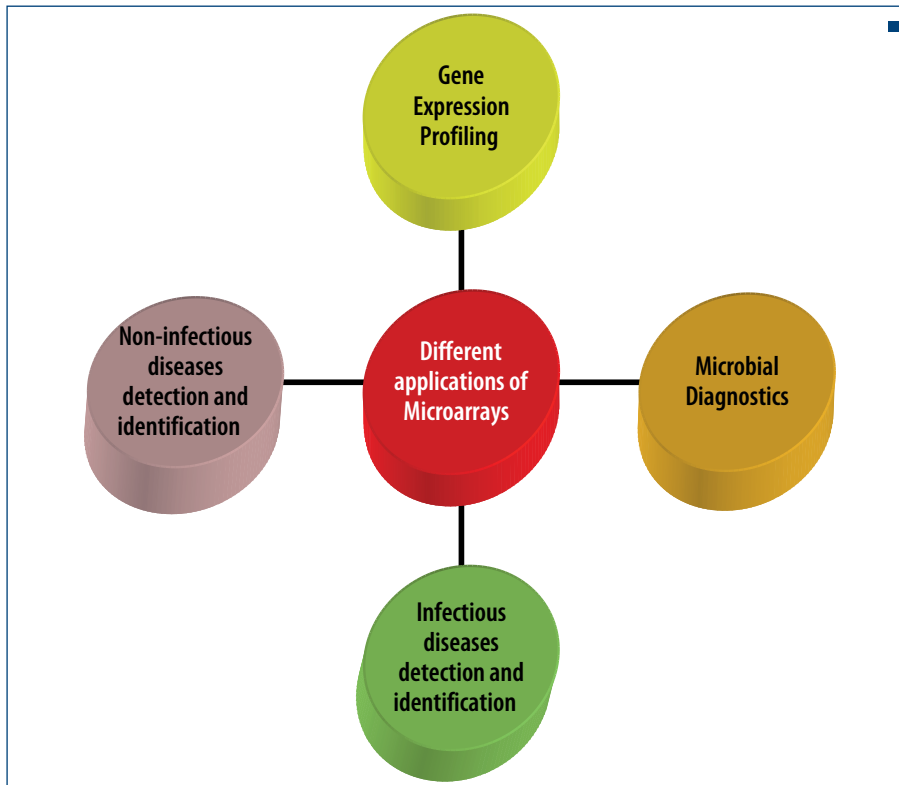


Figure 1. The most important medical applications of microarray tests

appearance of phenotypic genetic diseases. SNPs are helpful to detect genetic disorders in various life stages. DNA microarray technology is an advanced molecular-bioinformatics diagnostics for diagnosing genetic diseases and disorders. Also chromosomal diseases, including Down's syndrome, Edward syndrome, and Turner's syndrome are detectable via designed DNA microarray bacterial artificial chromosome (BAC) chips^(6,14,15).

Diagnosis of Infectious Diseases

One of the most important factors relating to human death is the appearance of infectious diseases. There are different clinical diagnostics which have their advantages and disadvantages. Traditional diagnostic methods, including culture media, biochemical, immunological and serological tests are time consuming and show a wide range of false positive or negative results. Thus, the use of traditional microbiological assays may lead to weak diagnoses and uncertain treating management of infectious diseases^(6,16).

On the other hand, molecular-bioinformatics approaches such as microarrays are accurate, rapid, and reliable diagnostics which have high levels of sensitivity and specificity. Therefore, clinical diagnostics based on nucleic acids are suitable and progressive tests which have bright promise in future^(6,8,16,17).

Detection of pathogenic microbial agents

Pathogenic microorganisms, including bacteria, fungi, and viruses are detectable in a variety of clinical samples like blood, cerebral spinal fluid, sputum, stool, and urine

via different microbiological tools. According to aforementioned part, traditional diagnostic techniques are not suitable methods for detecting pathogenic microorganisms. The traditional diagnostics are even weaker for detecting and identifying multidrug-resistant pathogenic microbial agents. For these reasons, the nucleic acid based technologies and in particular microarray techniques are the best choice for detecting pathogens; because they are reliable, rapid, accurate, sensitive and specific clinical tests^(1,3,6).

Also, the microarray tools are appropriate for determining bacterial agents comprising Methicillin-resistant *Staphylococcus aureus* (MRSA), *Mycobacterium tuberculosis*, *Escherichia coli* etc. in species level. Today, there is a wide range of bacteria that can be detected via microarrays^(1,6,8).

The range of fungal diseases has significantly increased. That is why, there are several pathogenic fungi, including *Aspergillus*, *Candida*, *Mucor*, *Penicillium* (particularly *Penicillium marneffeii*), and *Rhizopus* which are detectable in species levels via microarrays^(3,6,18).

And finally, the important pathogenic viruses like hepatitis viruses, and human papilloma viruses as obligate endoparasites are detected via microarrays^(1,6).

Conclusions

Microarray technologies are predominant and powerful clinical tests because of their high accuracy, rapidity, reliability, sensitivity, and specificity. These techniques are suitable to identify gene expressions, biomarkers, genetic disorders, infectious and non-infectious diseases and pathogenic microbial agents. The basis of microarrays is

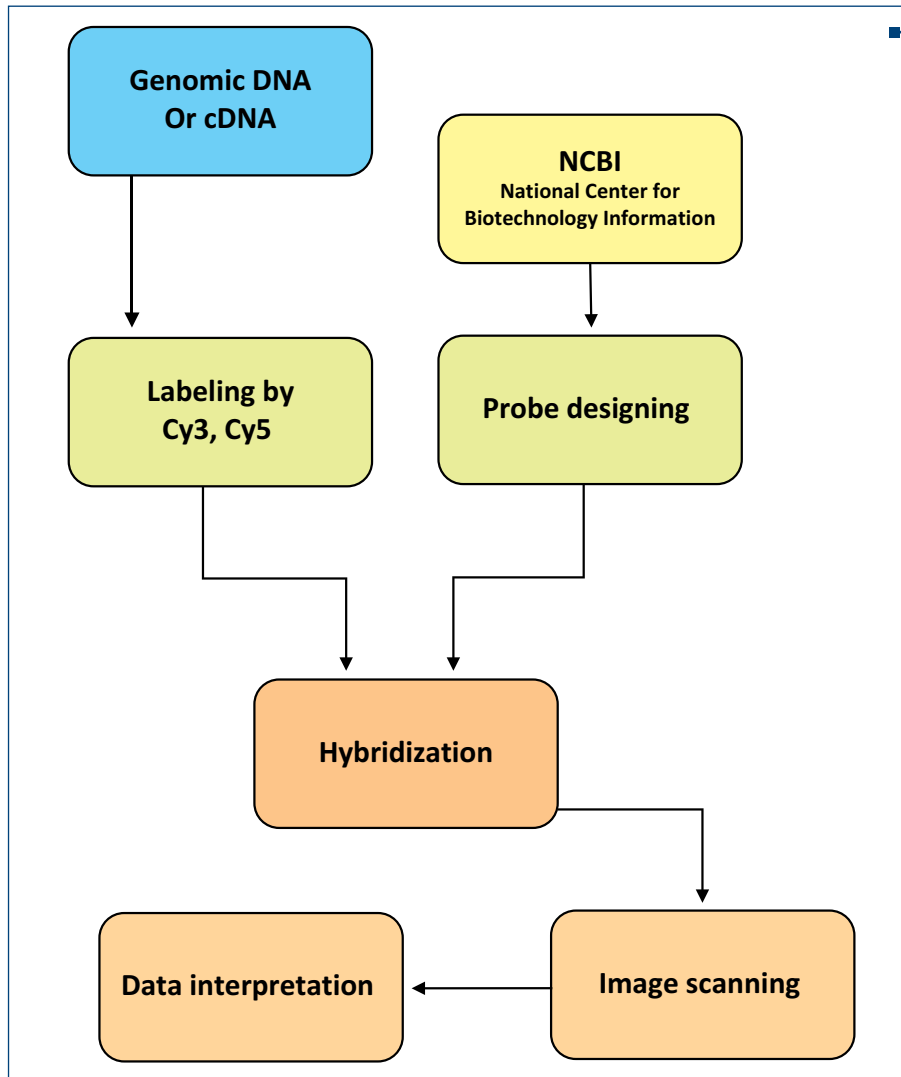


Figure 2. Oligonucleotide based Microarray procedures

funded on probes, nucleic acid labeling and hybridization. Although the microarray procedures are obvious and determined, but the interpretation of data analyses is the most important part of microarray tools. Currently, the cost of

technology, tools, data analyzers and specialists are too expensive to be used in every routine medical center. So, it takes time for using microarray technologies in public medical centers, clinical laboratories and hospitals. ■

References

- Najafi A, Ram M, Ranjbar R. Microarray Principles & Applications. 1st ed. Tehran: Persian Science & Research Publisher; 2012.
- Wang X, Liotta LA. Clinical bioinformatics: a new emerging science. J Clinical Bioinformatics. 2011;1:1.
- Behzadi P, Najafi A, Behzadi E., R. R. Detection and Identification of Clinical Pathogenic Fungi by DNA Microarray. Infectio. 2013;35(3):6-10.
- Campbell C, Ghazal P. Molecular signatures for diagnosis of infection: application of microarray technology. Journal of applied microbiology. 2004;96(1):18-23.
- Stoughton RB. Applications of DNA microarrays in biology. Annu Rev Biochem. 2005;74:53-82.
- Yoo SM, Choi JH, Lee SY, Yoo NC. Applications of DNA microarray in disease diagnostics. J Microbiol Biotechnol. 2009;19(7):635-46.
- Ye RW, Wang T, Bedzyk L, Croker KM. Applications of DNA microarrays in microbial systems. Journal of microbiological methods. 2001;47(3):257-72.
- Aitman TJ. Science, medicine, and the future: DNA microarrays in medical practice. BMJ: British Medical Journal. 2001;323(7313):611.
- Lovén J, Orlando DA, Sigova AA, Lin CY, Rahl PB, Burge CB, et al. Revisiting global gene expression analysis. Cell. 2012;151(3):476-82.
- Gracey AY, Cossins AR. Application of microarray technology in environmental and comparative physiology. Annual Review of Physiology. 2003;65(1):231-59.
- Tan PK, Downey TJ, Spitznagel Jr EL, Xu P, Fu D, Dimitrov DS, et al. Evaluation of gene expression measurements from commercial microarray platforms. Nucleic acids research. 2003;31(19):5676-84.
- Brown MP, Grundy WN, Lin D, Cristianini N, Sugnet CW, Furey TS, et al. Knowledge-based analysis of microarray gene expression data by using support vector machines. Proceedings of the National Academy of Sciences. 2000;97(1):262-7.
- Behzadi P, Behzadi E, Ranjbar R. Crohn's disease and anti-Saccharomyces cerevisiae autoantibodies. Pharmacist'ro. 2014;156(1):50-2.
- Wapner RJ, Martin CL, Levy B, Ballif BC, Eng CM, Zachary JM, et al. Chromosomal microarray versus karyotyping for prenatal diagnosis. New England Journal of Medicine. 2012;367(23):2175-84.
- Malone FD, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. New England Journal of Medicine. 2005;353(19):2001-11.
- Behzadi P, E. B. Study of microbial biochemical reactions in bacteriology laboratories. Tehran: Persian Science & Research Publisher; 2012.
- BEHZADI P BE, R. R. Basic Modern Molecular Biology. 1st ed. Tehran: Persian Science & Research Publisher; 2014.
- Behzadi P, E. B. Modern Medical Mycology and Opportunistic Pathogenic Yeasts. 1st ed. Tehran: Persian Science & Research Publisher; 2011.