**IJCRR**
Vol 05 issue 22
Section: General Sciences
Category: Review
Received on: 21/09/13
Revised on: 18/10/13
Accepted on: 19/11/13

# A REVIEW ON DNA MICROARRAY TECHNOLOGY

Amandeep Singh[1], Naresh Kumar[2]

[1]Department of Biosciences, Central University of Punjab, Bathinda, Punjab, India.
[2]Department of Biotechnology, Chaudhary Devi Lal University, Sirsa, Haryana, India.

## ABSTRACT

Microarray analysis allows scientists to understand the molecular mechanisms underlying normal and dysfunctional biological processes. It has provided scientists with a tool to investigate the structure and activity of genes on a wide scale. Microarray technology could speed up the screening of thousands of DNA and protein samples simultaneously.

DNA microarrays have been used for clinical diagnosis and for studying complex phenomena of gene expression patterns. Present review article focus on history, technique and future applications of DNA microarray technology.

**Key Words**: Microarray, DNA, Technology

## INTRODUCTION

DNA microarray technology emerged in the early 1990s by convergence of two advances. DNA sequencing efforts and focused on the expressed component of the genome, provided DNA sequence information and physical clones for thousands of human genes. Technical advances provided methods to manufacture slides or chips containing thousands of DNA probes arrayed within a small surface area by Dr. Patrick Brown and colleagues at Stanford University[1]. A DNA microarray is composed of pieces of DNA ranging from 20-5000 base pairs concentrated into specific areas on a solid support such as a glass chip.[2] DNA microarrays are used for the investigation of prokaryotic biology because they allow the simultaneous monitoring of the expression of all genes in any bacterium. They offer a more holistic approach to study cellular physiology and therefore complement the traditional "gene-by-gene" approaches.[3] The location of a specific probe on the array is termed spot or feature. Whereas the probes are immobilized on a solid support, the targets are applied as a solution onto the array for hybridization after fluorescent labeling.[4] Microarray analysis allows scientists to understand the molecular mechanisms underlying normal and dysfunctional biological processes. It has provided scientists with a tool to investigate the structure and activity of genes on a wide scale. Microarray technology could speed up the screening of thousands of DNA and protein samples simultaneously.[5]

## HISTORY

The idea of performing chemical or biological reactions with one reagent spatially immobilized is not new. Southern's 1975 paper described a technique that needs no introduction, and forever altered molecular biology.[6] DNA arrays are logical extension of the method described by Gillespie and Spiegelman in 1965, in which DNA immobilized on a membrane can bind a complementary RNA or DNA strand through specific hybridization and the methods described for applying DNA to a treated cellulose surface [7] and DNA blotting hybridization.[6] Several publications from the 1980s describe the use of such arrays in DNA mapping and sequencing.[8,9] Scientists at the California-based biotech company

Affymax produce the first DNA chips.[10] Miniaturized microarrays for gene expression profiling was used in 1995.[1] A complete eukaryotic genome (*Saccharomyces cerevisiae*) on a microarray was published in 1997.[11] A DNA microarray which is used to follow changes in gene expression as *Deinococcus radiodurans* recovers from a sub-lethal dose (3000Gy) of ionizing radiation was constructed in 2002.[12]

**DNA Microarray Technique**

In DNA Microarray collection of DNA probes that are arrayed on a solid support and are used to assay, through hybridization in the presence of complementary DNA that is present in a sample.[13] DNA Microarray is a chip of size of fingernail having 96 or more tiny wells and each well has thousands of DNA probes or oligonucleotides arranged in a grid pattern on the chip.[14, 15] Thousands of different genes are immobilized at fixed locations on chip and it means that a single DNA chip can provide information about thousands of genes simultaneously by base pairing and hybridization. There are two types of DNA microarray: cDNA microarrays and oligonucleotide arrays.[16,17, 18] cDNA arrays are produced by printing a double stranded cDNA on a solid support (glass or nylon) using robotic pins.[19] Oligonucleotide arrays are made by synthesizing specific oligonucleotides in a specific alignment on a solid surface using photolithography.[19] The labeled cDNAs are applied to the microarray and allowed to hybridize under conditions analogous to those established for Southern blotting. After the slide is washed to remove nonspecific hybridization, it is read in a laser scanner that can differentiate between Cy3- and Cy5-signals, collecting fluorescence intensities to produce a separate 16-bit TIFF image for each channel.[20, 21] Cy3 and Cy5 fluorescent dyes are used to distinguish cDNA pools which is reverse transcribed from different mRNA samples which have been isolated from cells or tissues.[19] Quantification of results is done by measuring the intensity of fluorescence, which corresponds to the amount of gene expressed in the sample.[22, 23] The three major steps of a microarray technology are preparation of microarray, preparation of labeled probes and hybridization and finally, scanning, imaging and data analysis.[24, 25] Using this technique, a comprehensive understanding of the cell can be achieved.[26,27]

**Applications of DNA Microarray Technology**

DNA microarray technology has been used to study many bacterial species which include *Escherichia coli* [28, 29], *Mycobacterium tuberculosis* [30,31], *Streptococcus pneumonia* [32, 33] and *Bacillus subtilis*[34,35, 36] With DNA microarray entire microbial genome can be easily represented in a single array and it is feasible to perform genome-wide analysis [37]. Microarray technique is used in medicine development by providing microarray data of a patient which could be used for identifying diseases.[38] DNA microarray technology has been used for analyses of natural and anthropogenic factors in yeast and analyzed how the whole genome of yeast is respond to environmental stressors such as temperature, pH, oxidation, and nutrients.[39,40,41]. Microarray analysis has been applied to identify molecular markers of pathogen infection in salmon.[42] DNA microarray has been used for studying gene expression analysis in neurological disorders.[43] DNA microarray experiments are carried out to find genes which are differentially expressed between two or more samples of cells. [44,45,46,47] cDNA microarrays provide a powerful tool for studying complex phenomena of gene expression patterns in human cancer.[1,48,49] DNA microarrays has been used for clinical diagnosis such as histopathology and molecular pathology e.g. Microarray technique has been identified for analysis of *AMACR* (α-methylacyl-CoA racemase in prostate cancer compared with normal prostate. [50, 51,52]

## CONCLUSION

DNA Microarray analysis has provided scientists with a tool to screen thousands of DNA and protein samples. After the completion of Human Genome Project, DNA Microarrays have been used for clinical diagnosis of gene expression patterns. DNA Microarray technology has proved boon to industrial fields serving in clinical diagnosis.

## REFERENCES


1. Schena M, Shalon D, Davis RW, Brown PO. Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Science 1995; 270: 467−470.
2. Schena M. Microarrays: Biotechnology's Discovery Platform for Functional Genomics. TIBTech 1998; 16(7): 301-6.
3. Wildsmith SE, Elcock FJ. Microarrays under the microscope. Molecular Pathology 2001; 54(1): 8–16.
4. Brown PO, Botstein D. Exploring the new world of the genome with DNA microarrays. Nature Genetics 1999; 21 Suppl 1: 33–37.
5. Mattick J, The Human Genome as an RNA Machine. Febit Science LoungeWebinar, June 12, 2008.
6. Southern EM. Detection of specific sequences among DNA fragments separated by gel electrophoresis. Journal of Molecular Biology 1975; 98: 503–517.
7. Southern EM, Mitchell AR. Chromatography of nucleic acid digests on thin layers of cellulose impregnated with polyethyleneamine. Biochemical Journal 1971; 123: 613-617.
8. Bains W, Smith GC. A novel method for nucleic acid sequence determination. Journal of Theoretical Biology 1988; 135:303–307.
9. Khrapko KR, Lysov Y, Khorlyn AA, Shick VV, Florentiev VL and Mirzabekov AD. FEBS Lett. 1989; 256: 118–122.
10. Fodor SP, Read JL, Pirrung MC, Stryer L, Lu AT and Solas D. Light-directed, spatially addressable parallel chemical synthesis. Science 1991; 251: 767–773.
11. Lashkari DA, DeRisi JL, McCusker JH, Namath AF, Gentile C, Hwang SY, Brown PO and Davis RW. Yeast microarrays for genome wide parallel genetic and gene expression analysis. PNAS USA 1997; 94 (24): 13057–13062.
12. Battista JR, Howell, HA, Park, MJ, Earl, AM and Peterson SN. The *Deinococcus radiodurans* Microarray: Changes in Gene Expression Following Exposure to Ionizing Radiation 2002 Microbial Cell Project 125, DOE Genome Contractor-Grantee Workshop IX.
13. Marmur J and Doty P. Thermal renaturation of deoxyribonucleic acids. Journal of Molecular Biology 1961; 3: 585–594.
14. Sundberg SA, Chow A, Nikiforov T, Wada G, Microchip-based systems for biomedical and pharmaceutical analysis. European Journal of Pharmaceutical Sciences 2001; 14(1): 1-12.
15. Afshari CA. Perspective: Microarray Technology, Seeing More Than Spots. Endocrinology 2002; 143(6): 1983-1989.
16. Ponder BA, Cancer genetics. Nature 2001; 411: 336-341.
17. Rowley JD. A new consistent chromosomal abnormality in chronic myelogenous leukemia identified by quina-crine fluorescence and Giemsa staining, Nature 1973; 243: 290-293.
18. Druker BJ, Talpaz M, Resta DJ, Peng B, Buchdunger E, Ford J, et al.., Sawyers C. L Efficacy and safety of a specific inhibitor of the BCR-ABL tyrosine kinase in chronic myeloid leukemia. The New England Journal of Medicine 2001; 344: 1084-1086.
19. Gray JW, Collins C. Genome changes and gene expression in human solid tumors. Carcinogenesis 2000; 21: 443-452.
20. Venter JC, Adams MD, Myers EW, Li PW, Mural RJ, Sutton GG, et al. The sequence of the human genome. Science, 2001, 291: 1304-1351.

21. Young RA. Biomedical discovery with DNA arrays. Cell 2000; 102: 9-15.
22. Pandey G, Paul D, Jain K. Branching of *o*-nitrobenzoate degradation pathway in *Arthrobacter protophormiae* RKJ100: identification of new intermediates. FEMS Mi-crobiol Lett 2003; 229:231-6.
23. Labana S, Singh OV, Basu A, Pandey G, Jain RK. A microcosm study on bioremediation of p-nitrophenol-contaminated soil using *Arthrobacter protophormiae* RKJ100. Applied Microbiology and Biotechnology 2005; 68: 417-24.
24. Labana S, Pandey G, Paul D, Sharma NK, Basu A, Jain RK. Plot and field studies on bioremediation of *p*-nitrophenol contaminated soil using *Arthrobacter protophormiae* RKJ100. Environmental Science and Technology 2005; 39: 3330-7.
25. Esteve-Nunez A, Caballero A, Ramos JL. Biological degradation of 2, 4, 6-trinitrotoluene. Microbiology and Molecular Biology Reviews 2001; 65: 335-52.
26. Schut GJ, Zhou J, Adams MW. DNA microarray analysis of the hyperthermophilic archaeon *Pyrococcus furi-osus*: evidence for a new type of sulfur-reducing enzyme complex. Journal of Bacteriology 2001; 183: 7027-36.
27. Krivobok S, Kuony S, Meyer C, Louwagie M, Wilson JC, Jouanneau Y. Identification of pyrene-induced proteins in *Mycobacterium* spp. strain 6PY1: evidence for two ring-hydroxylating dioxygenas-es. Journal of Bacteriology 2003 185: 3828-41.
28. Richmond CS, Glasner JD, Mau R, Jin H, Blattner FR. Genome-wide expression profiling in *Escherichia coli* K-12. Nucleic Acids Research 1999; 27, 3821–3835.
29. Tao H, Bausch C, Richmond C, Blattner FR., Conway T. Functional genomics: expression analysis of *Escherichia coli* growing on minimal and rich media. Journal of Bacteriology 1999 181: 6425–6440.
30. Wilson M, DeRisi J, Kristensen, HH, Imboden P, Rane S, Brown PO, Schoolnik GK. Exploring drug-induced alterations in gene expression in *Mycobacterium tuberculosis* by microarray hybridization. PNAS USA 1999; 96: 12833–12838.
31. Behr MA, Wilson MA, Gill WP, Salamon H, Schoolnik GK, Rane S, et al. Comparative genomics of BCG vaccines by whole-genome DNA microarray. Science 1999; 284: 1520–1523.
32. de Saizieu A, Gardes C, Flint N, Wagner C, Kamber M, Mitchell TJ, et al. Microarray-based identification of a novel *Streptococcus pneumoniae* regulon controlled by an autoinduced peptide. Journal of Bacteriology 2000; 182: 4696–4703.
33. Hakenbeck R, Balmelle N, Weber B, Gardes C, Keck W, de Saizieu A. Mosaic genes and mosaic chromosomes: intra- and interspecies genomic variation of *Streptococcus pneumoniae*. Infection and Immunity 2001; 69: 2477–2486.
34. Fawcett P, Eichenberger P, Losick R., Youngman. The transcriptional profile of early to middle sporulation in *Bacillus subtilis*. PNAS USA 2000; 97: 8063–8068.
35. Ye RW, Tao W, Bedzyk L, Young T, Chen M, Li L.Global gene expression profiles of *Bacillus subtilis* grown under anaerobic conditions. Journal of Bacteriology 2000; 182: 4458–4465.
36. Yoshida K, Kobayashi K, Miwa Y, Kang CM, Matsunaga M, Yamaguchi H, et al. Combined transcriptome and proteome analysis as a powerful approach to study genes under glucose repression in *Bacillus subtilis*. Nucleic Acids Research 2001; 29: 683–692.
37. DeRisi JL, Iyer V, Brown PO. Exploring the metabolic and genetic control of gene expression on a genomic scale. Science 1997; 278: 680–686.

38. Lovley DR. Cleaning up with genomic: applying molecular biology to bioremediation. Nature Reviews Microbiology 2003; 1: 35-44.
39. Causton HC, Ren B, Koh SS, Harbison CT, Kanin E, Jennings EG, et al. Remodeling of yeast genome expression in response to environmental changes. Molecular Biology of the Cell 2001; 12: 323–337.
40. Gasch AP, Spellman PT, Kao CM, Carmel-Harel O, Eisen MB, Storz G, et al. Genomic expression programs in the response of yeast cells to environmental changes. Molecular Biology of Cell 2000; 1: 4241–4257.
**41.** Momose Y, Iwahashi H. Bioassay of cadmium using a DNA microarray: genome-wide expression patterns of *Saccharomyces cerevisiae* response to cadmium. Environmental Toxicology & Chemistry 2001; 20: 2353–2360.
**42.** Rise ML, Jones SR, Brown GD, Von Schalburg KR, Davidson WS, Koop BF. Microarray analyses identify molecular biomarkers of Atlantic salmon macrophage and hematopoietic kidney response to *Piscirickettsia salmonis* infection. Physiological Genomics 2004; 20: 21–35.
**43.** Greenberg, SA. DNA microarray gene expression analysis technology and its application to neurological disorders. Neurology 2001; 57(5): 755-761.
44. Abiko Y, Hiratsuka K, Kiyama-Kishikawa M, Tsushima K, Ohta M, Sasahara H. Profiling of Differentially Expressed Genes in Human Gingival Epithelial Cells and Fibroblasts by DNA Microarray. Journal of Oral Science 2004; 46(1): 19-24.
45. Acin S, Navarro MA, Perona JS, Surra JC, Guillen N, Arnal C et al. Microarray Analysis of Hepatic Genes Differentially Expressed in the Presence of the Unsaponifiable
46. Fraction of Olive Oil in Apolipoprotein E-Deficient Mice. British Journal of Nutrition, 2007; 97(4): 628-638.
47. Caetano AR, Johnson RK, Ford JJ and Pomp D. Microarray Profiling for Differential Gene Expression in Ovaries and Ovarian Follicles of Pigs Selected for Increased Ovulation Rate. Genetics 2004; 168(3): 1529-1537.
48. De K, Ghosh G, Datta M, Konar A, Bandyopadhyay J, Bandyopadhyay D, et al. Analysis of Differentially Expressed Genes in Hyperthyroid-Induced Hypertrophied
49. Heart by CDNA Microarray. Journal of Endocrinology 2004; 182(2): 303-314.
50. Shalon D, Smith SJ, Brown PO. A DNA microarray system for analyzing complex DNA samples using two-color fluorescent probe hybridization. Genome Research 1996; 6: 639−645.
51. Schena M, Shalon D, Heller R, Chai A, Brown PO. Parallel human genome analysis: microarray-based expression of 1000 genes. PNAS USA 1996; 93: 10539−11286.
52. Xu J, Stolk JA, Zhang X, Silva SJ, Houghton RL, Matsumura M, et al. Identification of differentially expressed genes in human prostate cancer using subtraction and microarray. Cancer Research 2000; 60: 1677–1682.
53. Luo J, Zha S, Gage WR, Dunn TA, Hicks JL, Bennett CJ, et al. α-Methylacyl-CoA racemase: a new molecular marker for prostate cancer. Cancer Research 2002; 62: 2220–2226.
54. Rubin MA, Zhou M, Dhanasekaran SM, Varambally S, Barrette TR, Sanda MG, et al. α-Methylacyl coenzyme A racemase as a tissue biomarker for prostate cancer. JAMA. 2002; 287: 1662–1670.