

**Microarray Resource
Yale University**

The Keck Microarray Resource is a full service facility dedicated to providing RNA expression profiling, DNA genotyping, high throughput DNA sequencing, and microRNA analysis services using Affymetrix, Illumina, NimbleGen, Solexa, Sequenom, Applied Biosystems 7900 instrumentation, as well as in house spotted arrays. The Microarray Resource is devoted to enabling its users to rapidly and effectively utilize RNA and DNA analysis to answer important biological and biomedical questions and thereby better understand, diagnose, stage, treat, and prevent a wide range of human diseases.

The microarray Resource has 10 full time staff including one Ph.D. and two MS level staff appointments. Dr. Shrikant Mane is the director of this resource and he has over 20 years experience in molecular and cell biology. He received his doctoral degree in cancer biology and previously established and directed the Affymetrix core facility at the Moffitt Cancer Center in Florida. The Microarray Resource occupies 5,350 ft² of custom-designed space on the 2nd Floor of 300 George Street and contains a large Class 100 cleanroom for printing and a Class 1000 clean room for slide processing.

Microarray Resource is a full service facility and as indicated in table 1 below, offers wide variety of services using multiple platforms.

Table 1: Overview of the Available Technologies to Study Genetic Events

Genetic Events	Common Detection Methods	Applicable technology/platforms
Genetic Susceptibility	Linkage and Association	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
Somatic and germ line mutations	SNP identification and genotyping	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
Gene amplification and deletions	Comparative genome amplification analysis	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
	Gene and Exon-level amplification analysis	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
Epigenetic modifications	Methylation, PCR/bisulfite sequencing, ChIP	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
Differential gene expression	Gene and Exon-level analysis	Affymetrix, Illumina, Sequenom, Nimblegen and Solexa
Alternative splicing	Exon level analysis	Affymetrix
Gene regulation	ChIP	Affymetrix, Nimblegen, Solexa
SNP discovery	Direct sequencing	Solexa
miRNA discovery	Direct sequencing	Solexa
miRNA Analysis	Microarray and sequence analysis	Exiqon miRCURRY arrays, Illumina and Solexa
Sequencing and resequencing	Direct sequencing	Solexa

The Resource is well equipped with the multiple platforms and has kept pace with the rapidly evolving microarray field. The brief description of the technologies and services available through the Microarray Resource:

The resource provides services to both Yale and outside researchers. For FY05-07, the Microarray Resource has provided >18,000 services to 537 researchers from Yale and 313 from 160 other institutions including Washington U, Johns Hopkins U, Colorado State U., NIH, U. of Chicago, and Columbia U. The brief overview of the services offered by the Microarray Resource is as follows:

A. Affymetrix GeneChip platform:

1. Performs gene expression and SNP genotyping analysis at the whole genome as well as at custom levels.
2. Newly introduced GeneArrays interrogates **whole transcript** rather than standard 3' biased arrays and the cost for these arrays is significantly less.
3. Analysis of alternative splicing on a genome-wide scale using whole-transcript Exon arrays
4. Gene amplification/loss using SNP and tiling arrays.
5. Methylation and Epigenetic modifications can be analyzed at the whole genome level using tiling arrays
6. Gene regulation studies: Genome wide surveys of transcription binding sites can be performed.
7. Using a combination of chromatin immunoprecipitation along with tiling and promoter arrays, somatic and germ line mutation analysis can be performed using resequencing arrays.

B. Custom Spotted Glass Slide Microarrays:

1. Custom arrays of the highest quality are printed in the Class 100 clean rooms in our Resource.
2. Enables the in-house manufacturing of arrays not available commercially and that can be readily custom-tailored to meet the individual needs of researchers (e.g., economical custom arrays with relatively few features of interest/array can be made to enable screening of larger numbers of patient samples).

C. Illumina Bead Array Technology:

1. Uses fiber optics, microfabrication, and advanced information processing to create very high density arrays
2. Widely regarded platform of choice for SNP genotyping arrays: These arrays can be used to study disease association, genomic loss and amplification, copy number variation, and chromosomal rearrangements.
Clinical sample analysis: the Microarray Resource analyzed over 4,000 samples in a short period of 4 months for disease association and copy number analysis.
3. Biomarker Discovery: Gene expression arrays provide a cost effective approach for disease biomarker discovery and gene expression analyses at the whole genome level.

D. Sequenom MassArray:

1. This system is designed for medium to high-throughput, "fine-mapping" SNP Genotyping using the iPLEX MS-based technology. This MS system also supports Quantitative Gene Expression (QGE) and DNA methylation (EpiTYPER) analyses.
2. Precisely measures the relative amount of genetic material by MALDI-TOF mass spectrometer
3. Allows up to 40-plex assays per well for SNP genotyping.

E. NimbleGen

1. NimbleGen high-density arrays (up to 2.1million features) are suitable for multiple analyses including: CGH, DNA Methylation, Chip-chip (Chromatin Immunoprecipitation), Gene Expression, and Comparative Genome Sequencing.
2. Extremely flexible system capable of synthesizing custom arrays for any organism with known sequence.

F. miRNA Exiqon miRCURY LNA arrays

1. miRCURY LNA arrays allow miRNA expression analysis of all known miRNAs in 54 organisms which cover 92% of the SANGER mirBASE database.
2. 10 amol of sample miRNA can be detected on >90% array capture probes allowing the use of samples that contain as little as 250 ng of total RNA per hybridization.

G. Illumina Genome Analyzer (GA):

Highly economical and scalable "next generation" sequencing technology. It is anticipated that these advanced sequencing technologies will replace microarrays in the near future and may lead the way to "personalized" medicine. Currently, we are in possession of two GAs that are being used for the following applications:

1. Digital gene expression analysis: Direct sequencing of mRNA tags, miRNA and biomarker discovery.
2. Transcriptome Analysis
3. Sequencing and resequencing: Sequencing of entire genomes or a large candidate region
4. Immunoprecipitate sequencing: ChIP-Seq combines chromatin immunoprecipitation with massively parallel sequencing for genome wide identification of binding sites of DNA associated factors and epigenetic modifications.
5. miRNA analysis and discovery
6. Epigenetic Analysis

Yale/NIH Neuroscience Microarray Center

Keck Microarray Resource houses one of the four centers of the NIH Neuroscience Microarray Consortium that provides microarray and high-throughput DNA sequencing services at highly subsidized rate. The Yale Microarray Center for Research on the Nervous System was established in June 2006 through a 6.5 million dollar grant from the NIH (PI: Shrikant Mane).

Investigators who would like to take advantage of the subsidized services offered by the Consortium should follow directions provided at: <http://arrayconsortium.tgen.org/np2/public/theProcess.jsp> . Briefly, the investigator must first register themselves at the above mentioned Consortium website or by contacting Consortium coordinator at arrayconsortium@tgen.org or (602) 343-8732. Investigators are required to submit a two page proposal describing the significance, specific aims, experimental procedure, hypothesis, and sample information. The services are usually started once the project is approved by the appropriate center member.

Microarray Resource Publications

To our knowledge, >150 publications utilizing services or otherwise supported by the Microarray Resource have appeared since its inception. Twenty six of these publications include Resource authors and are focused on basic research, microarray technology and database tools.