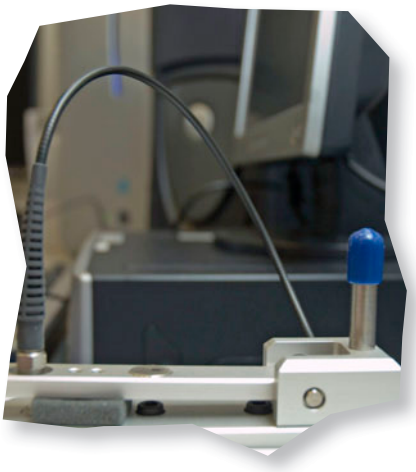
Functional Genomics Core Facility



During the last decade, molecular biology has developed from a gene-by-gene analysis into a more comprehensive approach to study regulatory networks involving dozens to hundreds of interacting partners. For successful performance in this field, researchers require an increasing number of tools to either analyse or alter genes on a genome-wide level. The Functional Genomics Core Facility provides state-of-the-art genomic tools for researchers at IRB Barcelona and other centres. These tools fall into two categories:

- Genome-wide analysis of transcription, DNA polymorphisms, and chromatin immunoprecipitation (ChIP-chip). These analyses are performed using microarrays produced by Affymetrix. For all of these analytical methods, the Functional Genomics Core Facility provides a complete service, including initial consultation during the design of a project, quality control of starting material, sample and array processing, initial data analysis, and data interpretation and validation by real-time-PCR.
- Knock-down of gene expression by shRNAs. For knock-down of gene expression, the Functional Genomics Core Facility provides a genome-wide human shRNA library (Sigma), containing approximately 75,000 clones covering the majority of all known transcripts.

The Functional Genomics Core Facility was established in April 2007 and by end of the year it was performing projects for over 15 research groups from three programmes at IRB Barcelona and from external institutions. The first service offered was expression profiling on a gene-by-gene level. Soon after, expression profiling was also established at higher resolution by measuring the exons of genes individually. For the detection of unknown transcripts, tiling array analysis is also now available. Alternative chemistries are available to perform expression analysis of a few hundred cells. Arrays are available for over 20 organisms, including all of the frequently used model organisms and humans. Validation of microarray expression profiling by real-time PCR has been performed since October 2007.

For the analysis of DNA polymorphisms, genome-wide interrogation of DNA copy number variation (amplifications and deletions) has been performed since July 2007 on a gene-resolution level. Measurement of amplifications and deletions is especially useful to identify oncogenes and tumour suppressor genes.

In December 2007, the complete human shRNA library became available. It contains on average four distinct constructs targeting each transcript. Bacterial stocks of these clones are provided by the Facility to researchers at IRB Barcelona. A database is available to collect information about bacterial growth, sequences of inserts and knock-down efficiency.

Services for IRB Barcelona researchers

DNA/RNA quantification and quality control

Various analyses are provided for assessment of purity, integrity and concentration of nucleic acids.

Expression profiling

Genome-wide analysis of transcripts is provided at three levels of resolution:

- 3' biased arrays containing one probeset per gene; these arrays are available for more than 20 organisms.
- Exon arrays containing one probeset per exon; these arrays are currently available for human, mouse and rat.
- Tiling arrays interrogating the entire genome at a 35-bp resolution; these arrays are currently available for human, mouse, *Drosophila* and yeast.

DNA polymorphism analysis

Genome-wide analysis of DNA polymorphisms comes in two forms:

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- For over twenty organisms, DNA copy number variation (CNV) is measured at the resolution of individual genes. For organisms where exon or tiling arrays are available (see above), even higher resolution can be provided.
- For human DNA, up to one million single nucleotide polymorphisms (SNPs) can be measured in parallel with the same number of CNVs across the genome.

Validation of microarray results by real-time PCR
For real-time PCR validation of microarray data, assays are designed and performed, and data are analysed for differential expression.

Knock-down of gene expression
Bacterial clones are provided for almost all well characterised human transcripts. Multiple clones targeting the same transcripts are available to assess off-target effects.

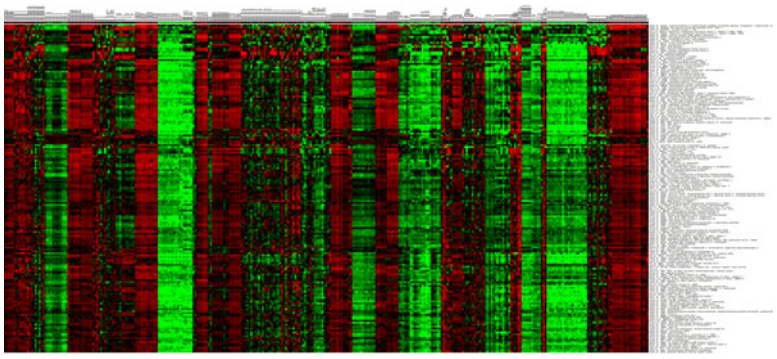

Figure 1. *A cluster of co-regulated genes in 336 samples including purified cord blood, B cell subpopulations, large B cell lymphomas, Burkitt-, follicular-, primary effusion-, and mantle cell-lymphoma, B cell chronic lymphocytic leukemia, hairy cell leukemia, Hodgkin disease, B cell lymphoma cell lines and lymphoblastic cell lines (Collaboration with K Kornacker, Nationwide Children's Research Institute).*

Collaborations

Comparison of comparative genomic hybridization technologies across microarray platforms
Susan Hester, Environmental Protection Agency (Durham, USA), Laura Reid, Expression Analysis Inc (Durham, USA), Agnes Viale, Memorial Sloan Kettering Cancer Center (New York, USA), Norma Nowak, Roswell Park Cancer Institute (Buffalo, USA), Kevin Knudtson, University of Iowa (Iowa, USA), William Ward, Environmental Protection Agency (Durham, USA), Jay Tiesman, Procter & Gamble (Cincinnati, USA), Caprice Rosato, Center for Genome Research and Biocomputing, Oregon State University (Corvallis, USA), Aldo Massimi, Albert Einstein College of Medicine (New York, USA), Greg Khitrov, Mount Sinai School of Medicine (New York, USA) and Nancy Denslow, University of Florida (Gainesville, USA)

Development of microarray quality control metrics
Karl Kornacker, Nationwide Children's Research Institute (Columbus, USA)

The ABRF MARG microarray survey 2008: Sensing the state of microarray technology
Chris Harrington, Oregon Health and Science University (Portland, USA), Susan Hester, US EPA (Durham, USA), Nadereh Jafari, Northwestern University (Chicago, USA), Steve Potter, Children's Hospital Medical Center (Cincinnati, USA), Jay Tiesman, Procter & Gamble (Cincinnati, USA), Richard Jensen, Virginia Bioinformatics Institute (Blacksburg, USA), Laura Reid, Expression Analysis (Durham, USA), Aldo Massimi, Albert Einstein College of Medicine (New York, USA), Agnes Viale, Memorial Sloan Kettering Cancer Center (New York, USA), Nancy Denslow, University of Florida (Gainesville, USA)