Herbert Auer

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 need an increasing number of tools to either interrogate or alter genes at a genome-wide scale.

The Functional Genomics Core Facility provides state-of-the-art genomic tools for researchers at IRB Barcelona and other organisations. These tools fall into two categories:

i) Genome-wide analysis of transcription, DNA polymorphisms, and chromatin immunoprecipitation (ChIP). These analyses are performed using microarrays and Next Generation Sequencing. For all these analysis methods, the facility provides a complete service, including initial consultation during the design of the project, quality control of starting material, sample and array processing, data analysis in collaboration with statisticians, and data interpretation and validation by real-time PCR.

ii) Alteration of gene expression. For knock-down of gene expression, the facility provides genome-wide human and mouse shRNA libraries (Sigma), each containing approximately 100,000 clones, covering the majority of all known transcripts. For over-expression, the facility provides a human open-reading-frame library (Open Biosystems) containing 15,000 clones, covering three quarters of all human genes.

During 2009, the facility performed projects with over 20 research groups from all five programmes at IRB Barcelona and from other institutions throughout Barcelona, Catalonia and Spain.

Using products provided by Affymetrix, the facility performs genome-wide expression analysis at gene and exon level, as well as comparative genome hybridisation analysis (CGH analysis). These technologies are provided for over 20 organisms, including all standard model organisms and humans. For CGH analysis, resolution is further increased by using tiling arrays. These provide probes tiled across the entire genome without prediction

Figure 1. ***SNP density analysis in*** **Drosophila** ***strains.*** *A chromosomal region of 1.2 million nucleotides was analysed in four DNA samples for their density of single nucleotide polymorphisms relative to the reference genome. Two regions of high SNP density are highlighted. SNP analysis was performed using Next Generation Sequencing.*

of genes; therefore, this type of array provides the most comprehensive picture of genomic alterations currently available in microarray technology.

Services based on NimbleGen microarray products are also offered. NimbleGen technology provides longer probes than Affymetrix and therefore higher specificity. In addition, NimbleGen microarray production is extremely flexible and consequently facilitates the design of customized microarrays, even for small projects. This technology is currently used for expression analysis and CGH analysis.

Next Generation Sequencing on Illumina's Genome Analyzer II is offered for the qualitative and quantitative analysis of nucleic acids. Services include ChIP-Seq, miRNA-Seq, mRNA-Seq and genomic sequencing.

The tools for altering gene expression, namely the shRNA libraries and the open-reading-frame library, contain over 200,000 clones. These clones are centrally stored and a database has been developed for their administration. It also provides information about knock-down efficiency and the accuracy of clone annotation.

Services for IRB Barcelona researchers

DNA/RNA quantification and quality control

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

Microarray services

- Expression profiling on gene arrays and 3' biased arrays containing one probe set per gene, and on Exon arrays, tiling arrays and miRNA arrays.
- DNA polymorphism analysis for copy number variation (CNV) and single nucleotide polymorphisms (SNPs).

Next generation sequencing service

- ChIP-Seq for chromatin immune precipitation and input material is usually performed by single-end reads of 40 nucleotides per molecule.

Research Group Members

Core Facility Manager:
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Senior Research Officers:
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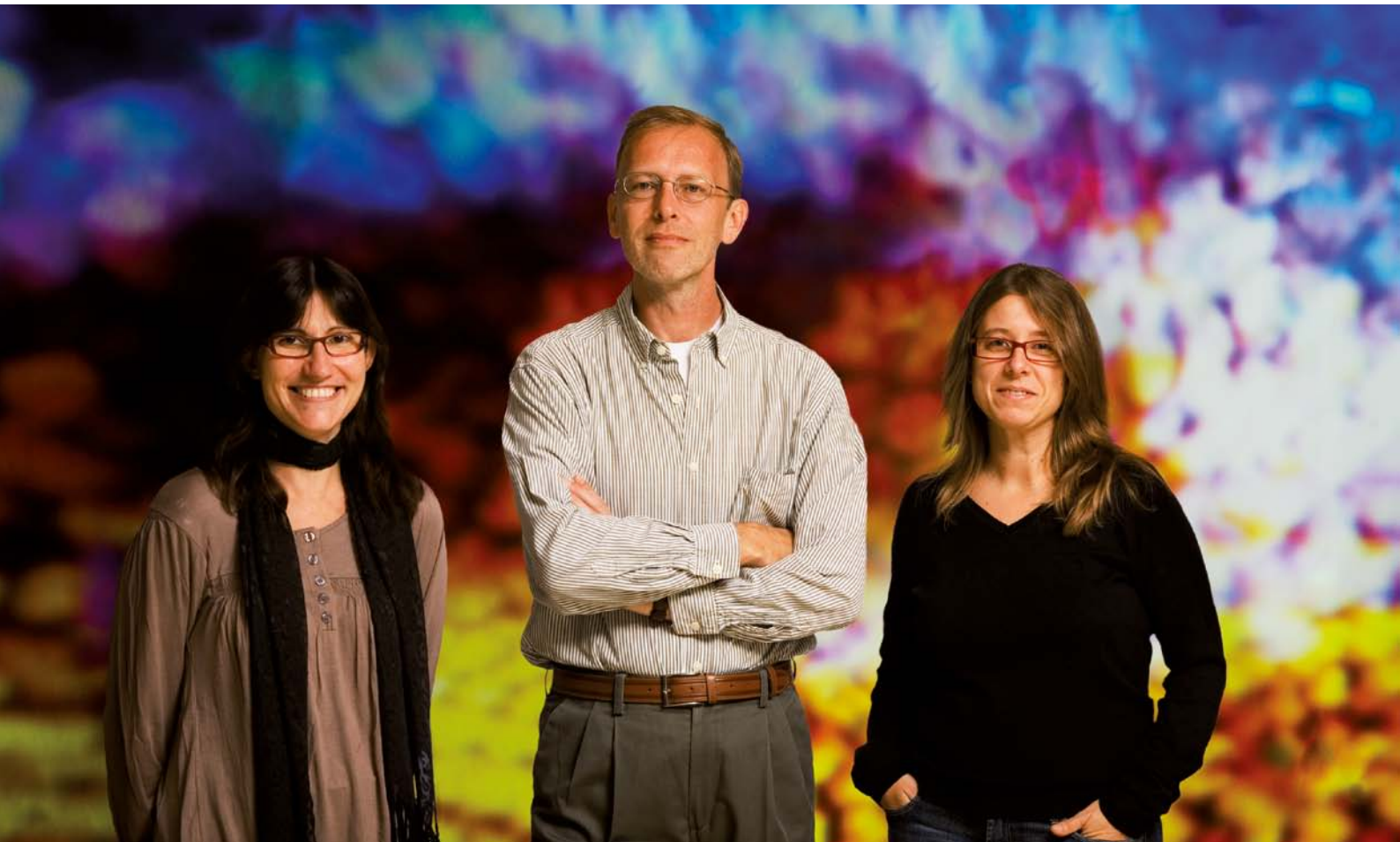

- mRNA-Seq for the discovery of unknown transcripts and splice variants is usually performed by paired-end reads of 40 or more nucleotides per molecule.
- miRNA-Seq for the quantification of known miRNAs and the discovery of unknown small RNAs are performed by single-end reads of 40 or fewer nucleotides.
- Genomic DNA sequencing is performed by single-end or paired-end sequencing, dependent on the underlying scientific question. Read lengths of up to 100 nucleotides are possible.

Validation of results by real-time PCR

For real-time PCR validation of microarray data, assays are designed, preformed and data are analysed for differential expression.

Alteration of gene expression

Bacterial clones are provided for the knock-down of almost all well characterised human and mouse transcripts. Multiple clones targeting the same transcript are available to assess off-target effects. For over-expression, one open-reading-frame clone is available per human gene. Clones are centrally administrated at the facility and are provided as bacterial stocks to IRB Barcelona researchers. The clone database provides information about knock-down efficiency and the accuracy of clone annotation.

Scientific output

Publications

Auer H. Expression divergence and copy number variation in the human genome. *Cytogenet Genome Res,* Epub Mar 11 (2009)

References

Auer H, Newsom DL and Kornacker K. Expression profiling using Affymetrix GeneChip microarrays. *Methods Mol Biol*, **509**, 35-46 (2009)

Cuscó I, Medrano A, Gener B, Vilardell M, Gallastegui F, Villa O, González E, Rodríguez-Santiago B, Vilella E, Del Campo M and Pérez-Jurado LA. Autism-specific copy number variants further implicate the phosphatidylinositol signaling pathway and the glutamatergic synapse in the etiology of the disorder. *Hum Mol Genet*, **18**(10), 1795-804 (2009)