GENOMICS CORE UNIT

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**Plan de Empleo Joven* (Youth Employment Plan)

"The Genomics Unit, with its toolbox for DNA and RNA analyses, helps CNIO scientists to understand the molecular processes underlying cancer in a large number of basic and applied research projects."

OVERVIEW

Genomics is the discipline that studies the structure and dynamics of the genome, its features, its regulation and expression. The genome is the core of life, the ensemble of the genetic material that conserves the assembly instructions of the species. Each cell in an individual keeps a copy of it deep in its nucleus. Chemically made of linear DNA macromolecules and distributed into chromosomes, it is packed with and interpreted by a myriad of protein cohorts acting in concert. It is expressed into RNA transcripts; some are functional in and of themselves, and others, constitute an intermediate step leading to the functional proteins that govern the cell. While less than a 2% fraction of a mammalian genome codes for protein, a vast majority of it (80%) has been found to participate in biochemical events. The genome is not immutable, it can suffer alterations. A chance for biological evolution or for damage. In fact, cancer derives from the accumulation of such alterations. Cells with a damaged genome can transform and develop into a tumour. The field of Genomics sheds light on this world of complexity.

RESEARCH HIGHLIGHTS

All tumours, even those of the same type and sharing a similar fate, are molecularly different and heterogeneous at the molecular level. By employing a distinct set of powerful methodologies, Genomics reveals the genetic diversity of cancer and helps to dissect molecular mechanisms. These methodologies have the capacity to interrogate a wide number of genetic loci, or even a whole genome in a single assay. Some tools detect modifications at a structural level: mutations, binding of protein factors, variations in chromatin folding. Others are suitable for observing functional choreographies, transcriptomic changes – for example, in response to treatments – that may uncover therapeutic targets and prognostic biomarkers.

The Genomics Unit provides services at two levels of complexity. The genomic wide level is addressed by both deep-sequencing and microarray technologies. Deep-sequencing permits a variety of applications, such as whole-genome or whole-exome tumour sequencing, transcriptome analyses by RNAseq, or location of interacting protein factors on chromosomal DNA by ChIPseq. As a novel sample type, the Unit successfully participated in the exome sequencing of *cell free* DNA obtained from cancer patients' blood. This year has seen a 40% increase in the overall demand and in the number of samples processed.

On the other hand, the DNA microarray platform can be efficiently used for transcriptome determinations or for the detection of chromosomal copy number abnormalities. At the single locus level other offers are available. A traditional DNA capillary sequencing service, based on a 3730xl DNA Analyzer from Applied Biosystems, is being used to find and confirm mutations in candidate genes as well as for the verification of cloned genes or inserts. The Unit also provides a transgenic mouse genotyping service, based on allele-specific quantitative PCR for a quick and efficient turnaround time. With a current, but continuously growing, catalogue of over 30 genetic modifications, the demand for genotyping services this year has almost doubled in comparison to former years. ■

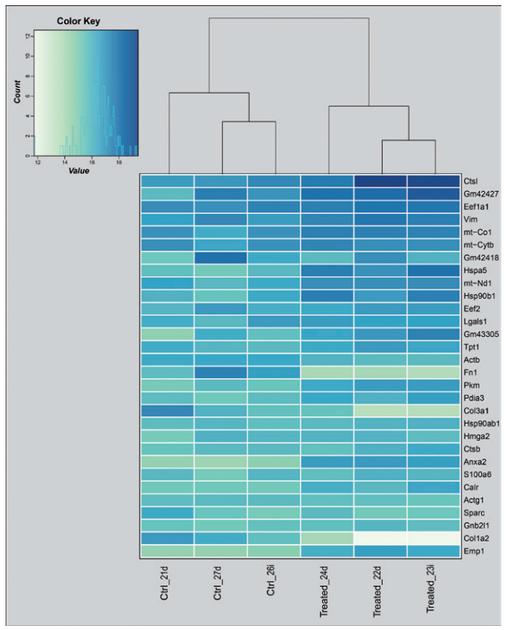

Figure An RNAseq experiment reveals the effects of a treatment at the RNA level. A blind analysis properly clusters samples of the same type together in columns. Genes whose transcription is significantly affected by treatment are shown in rows. Colour intensity reflects the transcriptional level. Some gene expression variability is apparent among replicates from the same condition.