GENOMICS CORE UNIT

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Plan de Empleo Joven (Youth Employment Plan)

OVERVIEW

The aim of the Genomics Unit is to provide technological services in the fields of genomics and genetics. Technologies with the capacity to interrogate genomes and their activities in a single assay are available. Methodologies able to dissect active molecular hierarchies and pathways (transcriptomic RNA profiling) or structural variations (mutation landscapes, chromatin structure) for the study of cancer or other biological processes. Our services cover a broad range of applications. Next-generation sequencing (NGS) is a staple among them. It is being used for chromatin structure studies, chromosomal protein location analysis, and for transcriptome determinations - even at the single-cell level. More traditional methodologies like Sanger capillary DNA sequencing are also provided. As a side activity, the Unit supports a genetically engineered mouse genotyping service.

"The Genomics Unit offers services in the genetics and genomics fields, which contribute to the understanding of disease and homeostasis at different levels of molecular complexity."

RESEARCH HIGHLIGHTS

The Genomics Unit, with its portfolio of services that survey different aspects of biological complexity, contributes to the research projects of CNIO Groups. The activities most in-demand are related to applications based on deep-sequencing technologies (NGS). NGS permits a variety of different explorations, such as whole genome and whole exome tumour characterisation, transcriptomic analysis, and the determination of genome structure and of chromatin functional states through the location of interacting factors or epigenomic modifications.

Some of our contributions in 2020 led to the publications referenced below, with some of the Unit's members as authors:

To better characterise colorectal cancer, Costales-Carrera *et al.* examined gene expression profiles in organoids generated from endoscopic biopsies. Rectal tumour organoids differ in gene expression with respect to colon tumour organoids. Interestingly, calcitriol (vitamin D) upregulates stemness genes in rectum and colon organoids, which is consistent with homeostatic action on the large intestine crypt stem cell compartment. Moreover, differences in biosynthetic processes between rectal tumour and colon tumour organoids suggest that the malignant transformation of stem cells differs even between neighbouring intestinal locations.

In the second reference, a pilot biomarker and efficacy study in advanced HER2-negative breast cancer patients, Quintela-Fandiño *et al.* discuss the potential priming role of a prior antiangiogenic therapy on subsequent immunotherapy. Vascular normalisation was seen after the antiangiogenic bevacizumab treatment in non-progressors' tumours, which also showed gene expression profiles with both increased T-effector and T-memory features and decreased Treg signatures. In summary, the antiangiogenic activity was found to immuno-prime at least a fraction of patients who will more likely benefit from subsequent immunotherapy. ■

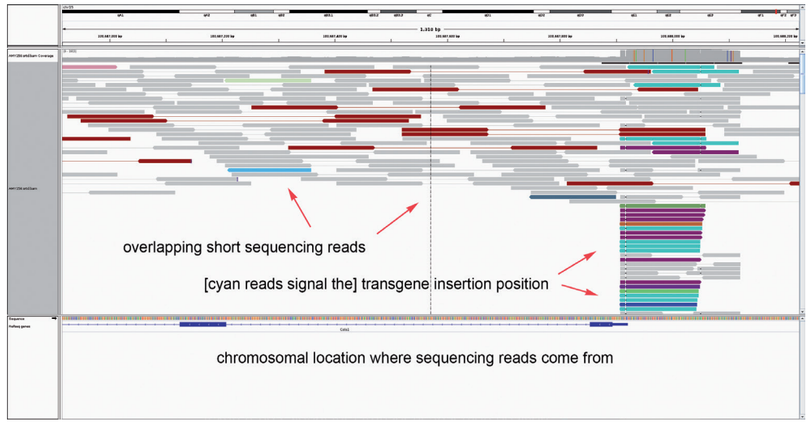

FIGURE Among its multiple applications, next-generation sequencing can be used to ascertain the position of the chromosomal insertion of transgenes. This figure highlights fragments whose sequencing reads map both in an endogenous locus and in the transgene (not shown).

PUBLICATIONS

- Costales-Carrera A, Fernández-Barral A, Bustamante-Madrid P, Domínguez O, Guerra-Pastrián L, Cantero R, Del Peso L, Burgos A, Barbáchano A, Muñoz A (2020). Comparative study of organoids from patient-derived normal and tumor colon and rectal tissue. *Cancers (Basel)* 12, 2302.
- Quintela-Fandino M, Holgado E, Manso L, Morales S, Bermejo B, Colomer R, Apala JV, Blanco R, Muñoz M, Caleiras E, Iranzo V, Martinez M, Dominguez O, Hornedo J, Gonzalez-Cortijo L, Cortes J, Gasol Cudos A, Malon D, Lopez-Alonso A, Moreno-Ortíz MC, Mouron S, Mañes S (2020). Immuno-priming durvalumab with bevacizumab in HER2-negative advanced breast cancer: a pilot clinical trial. *Breast Cancer Res* 22, 124.