Recurrent chromosomal rearrangements are very common and well-known hallmarks of cancer. One of their main consequences is the creation of new chimeric genes as a result of the fusion of the coding sequences of 2 different genes. The research activity of the Molecular Cytogenetics and Genome Editing Unit (MC&GEU) is focused on increasing the knowledge about the genetics of tumours and the discovery of new therapeutic targets. With the combined use of CRISPR genome editing and cytogenetic techniques, we are creating human in vitro models that recapitulate chromosomal, genetic and epigenetic cancer alterations. The goal of the Unit is to provide the CNIO and external researchers with the latest technologies used in the field of molecular cytogenetics and genome editing. The Unit is constantly implementing and developing new technologies in the gene editing field. We also participate in collaborative projects with clinical and basic science investigators at the CNIO and other institutions.

"We have applied genome engineering approaches for cancer modelling, reproducing chromosome rearrangements and gene alterations. We provide access to the latest Cytogenetic and CRISPR Technologies."

OVERVIEW

RESEARCH HIGHLIGHTS

Modelling cancer using CRISPR/Cas9 genome editing technology

Efficient methodologies for recreating cancer-associated chromosome aberrations and gene mutations are in high demand as tools for investigating how such events initiate cancer. We have recently demonstrated the feasibility of utilising gRNA/Cas9 ribonuclease-protein (RNlp) complexes to model cancers driven by fusion genes generated by chromosomal rearrangements. We have optimised new strategies to enhance the efficiency of the CRISPR-mediated translocation induction in human stem cells, including mesenchymal and induced pluripotent stem cells. We found that the generation of targeted translocation is significantly increased by using a combination of ribonuclease protein complexes (Cas9 protein-sgRNA) and ssODNs. The CRISPR-Cas9 mediated generation of targeted translocations in human stem cells opens up new avenues to model cancer.

Technological and translational activities

We provide state-of-the-art Molecular Cytogenetic and Genome Editing services. The Unit supplies research groups with various techniques that may provide more sensitive and accurate tools to analyse cancer cells, such as chromosome stability studies based on a combined array CGH-FISH approach, or the use of CRISPR libraries to perform high-throughput functional analysis. For gene editing experiments, we have set up a specific PCR-based FISH analysis to detect genome integration sites of small constructs including LV particles. At the field of cancer cytogenomics moves forward with the identification and cataloguing of recurrent chromosomal aberrations and gene mutations in a variety of human cancers, our CRISPR-based cellular platforms offer a rapid, precise and affordable opportunity to functionally interrogate the cancer genome. In 2018, we carried out over 1,500 assays for experimental and clinically-oriented projects.