MOLECULAR CYTOGENETICS UNIT

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OVERVIEW

Recurrent chromosomal rearrangements — changes in the structure of native chromosomes — are very common and well-known hallmarks of cancer. A better understanding of these cancer-causing mechanisms will lead to novel therapeutic regimens to fight cancer. The research activity of the Molecular Cytogenetics Unit focuses on increasing the knowledge about the role of chromosomal rearrangements in cancer development and progression and the discovery of new therapeutic targets. With the combined use of CRISPR genome editing and cytogenetic technologies, we are creating models that recapitulate chromosomal and genetic cancer alterations. The goal of the Unit is to provide CNIO and external researchers with the latest technologies used in the fields of molecular cytogenetics and genome editing. The Unit is continuously implementing and developing new technologies in those fields. We also participate in collaborative projects with clinical and basic science investigators across the CNIO and other institutions.

"We apply genome engineering approaches to reproduce and eliminate chromosome rearrangements and gene alterations. We provide access to the latest cytogenetic and CRISPR technologies."

Technicians
M. Carmen Martín, Marta Martínez-Lage (TS)*, Francisco José Moya (TS)* (PEJ) **

Visiting Scientist
Doron Tolomeo (until March) (*Università degli Studi di Bari Aldo Moro*, Bari, Italy)

**Titulado Superior* (Advanced Degree)
***Plan de Empleo Joven* (Youth Employment Plan)

RESEARCH HIGHLIGHTS

In vivo CRISPR/Cas9 targeting of fusion oncogenes for selective elimination of cancer cells

Fusion oncogenes (FOs) are common alterations found in around 20% of cancer types and are powerful drivers of tumour development. Because their expression is exclusive to cancer cells and their elimination induces apoptosis in FO-driven cancer cells, FOs are attractive therapeutic targets. However, specifically targeting the resulting chimeric products is challenging. Based on CRISPR/Cas9 technology, we devised a gene-editing strategy targeting 2 introns of the genes involved in the rearrangement, allowing for robust disruption of the FO specifically in cancer cells. As a proof-of-concept of its potential, we demonstrated the efficacy of intron-based targeting of FOs in reducing tumour burden/mortality in *in vivo* Ewing sarcoma and chronic myeloid leukaemia models. The FO targeting approach might open new horizons for the selective elimination of cancer cells.

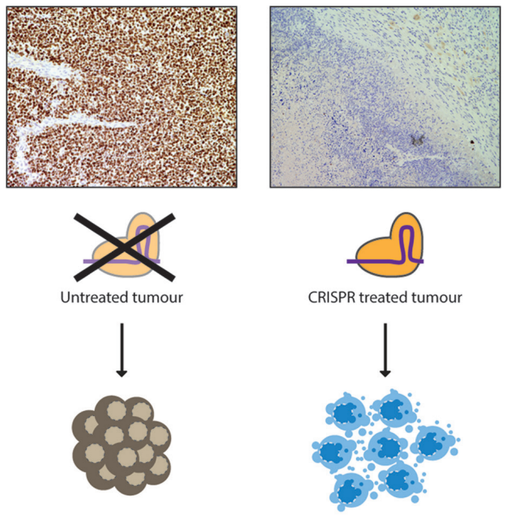

FIGURE Representative images of non-edited (left) and CRISPR edited tumours for the elimination of fusion genes (right). Cells are stained with the Ki67 proliferation marker. Brown staining indicates a high proliferation rate, while the absence of staining (cells in blue) indicates no proliferation.

Technological and translational activities

We provide state-of-the-art Molecular Cytogenetic and Genome Editing services. The Unit makes available a complete suite of tools for cellular and genetic manipulation to research groups; these tools can be used interchangeably with an array of delivery vehicles, offering a flexible, modular platform for precision genome manipulation. The Unit offers molecular cytogenetics technology analysis of human and mouse chromosomes, including conventional karyotyping, FISH, SKY and CGH array.

Our Unit offers rapid, precise, and affordable technologies to analyse cancer cells at the chromosome level and to functionally interrogate the cancer genome. In 2020, we carried out over 2,700 assays for experimental and clinically oriented projects. ■

PUBLICATIONS

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