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 cytogenetic and CRISPR tools for cellular and genetic manipulation to research groups; these tools can be used interchangeably with an array of delivery tools for cellular and genetic manipulation to research groups.

We provide state-of-the-art Molecular Cytogenetic and Genome Editing services. The Unit makes available a complete suite of technologies for the selective elimination of 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 vivo. Ewing sarcoma and chronic myeloid leukemia cells. The FO targeting approach might open new horizons for the selective elimination of cancer cells.

**Technological and translational activities**

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 vivo. Ewing sarcoma and chronic myeloid leukemia models. The FO targeting approach might open new horizons for the selective elimination of cancer cells.

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**Teaching Programme**

Human Cancer Genomics Programme: MOLECULAR CYTOGENETICS UNIT

**Research Highlights**

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