CNIO - LILLY CELL SIGNALLING AND IMMUNOMETABOLISM SECTION

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OVERVIEW

Our laboratory, in collaboration with Loxo@Lilly Oncology, is working on the identification and validation of novel molecular targets engaged in the induction of chromosomal instability (CIN). Our goal is to find novel therapies that would make tumours bearing CIN more susceptible to destruction, either with the use of single agents, or acting synergistically with other anti-tumour therapies. Exploring how to better target these mechanisms would lead to better and more efficient therapeutic options, including more personalised therapies.

A combination of *in vitro* and *in vivo* approaches is being utilised to obtain a complete understanding of the role of CIN in tumour development and anti-tumour response. Each target goes through an *in vivo* validation process using xenografts, allografts, and mouse models developed at the CNIO that includes the use of non-invasive *in vivo* imaging technologies, and immune histochemical characterisation of tumours for different metabolic, immune, and tumour markers. The final step is the validation in human samples using tumour tissue arrays.

RESEARCH HIGHLIGHTS

Chromosomal instability (CIN) and whole genome duplication (WGD) are a hallmark of human cancer and are associated with poor prognosis, metastasis, and therapeutic resistance (FIGURE 1). CIN results from errors in chromosome segregation during mitosis, leading to structural and numerical chromosomal abnormalities, including loss or amplification of DNA segments, rearrangements, extrachromosomal DNA, and micronuclei formation. These abnormalities lead to the activation of oncogenes or the inactivation of tumour suppressor genes, as well as other genes aiding in the processes of metastasis, drug resistance, and immune scape. The causes of CIN are diverse, including mitotic errors, replication stress, homologous recombination deficiency (HRD), and telomere crisis. ■

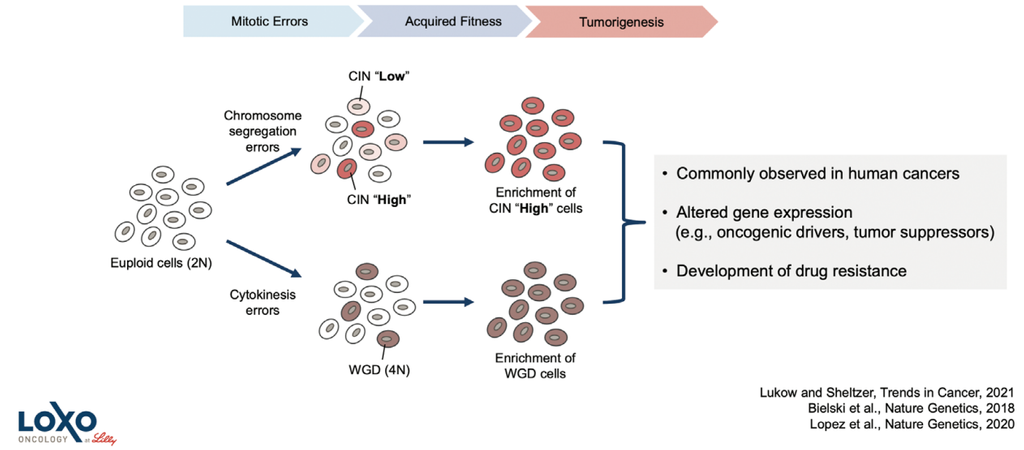

FIGURE 1 Chromosome instability (CIN) and/or whole genome duplication (WGD) promote tumorigenesis.