Universidad Autónoma de Madrid

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

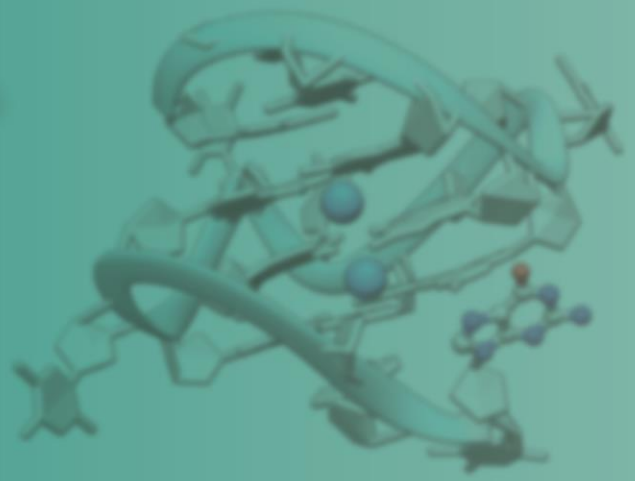
CiQUS Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares

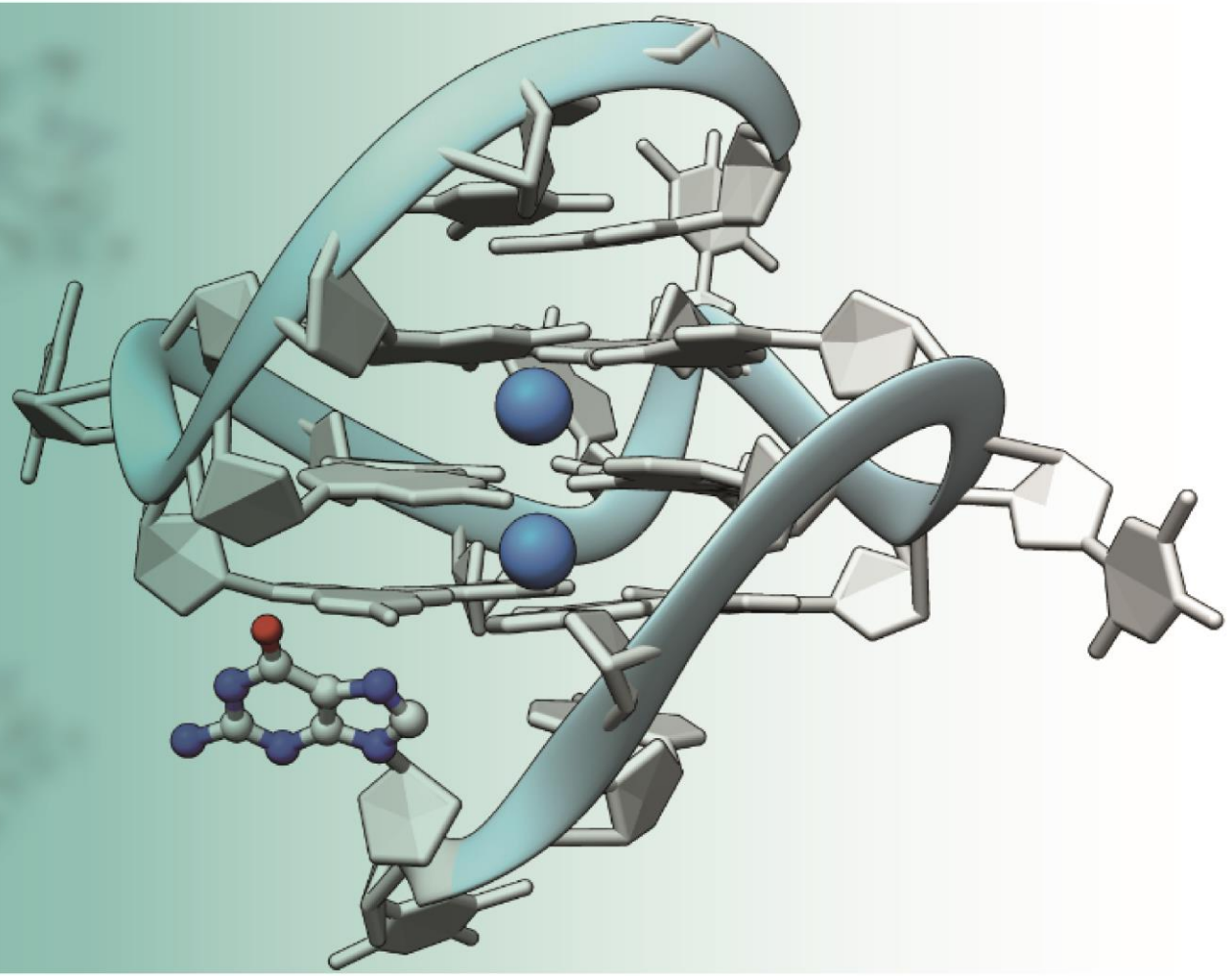
XUNTA DE GALICIA

AXENCIA GALEGA DE INNOVACIÓN

IGN 116

Targets And Eliminates Cancer Stem Cells (CSC)





Problem

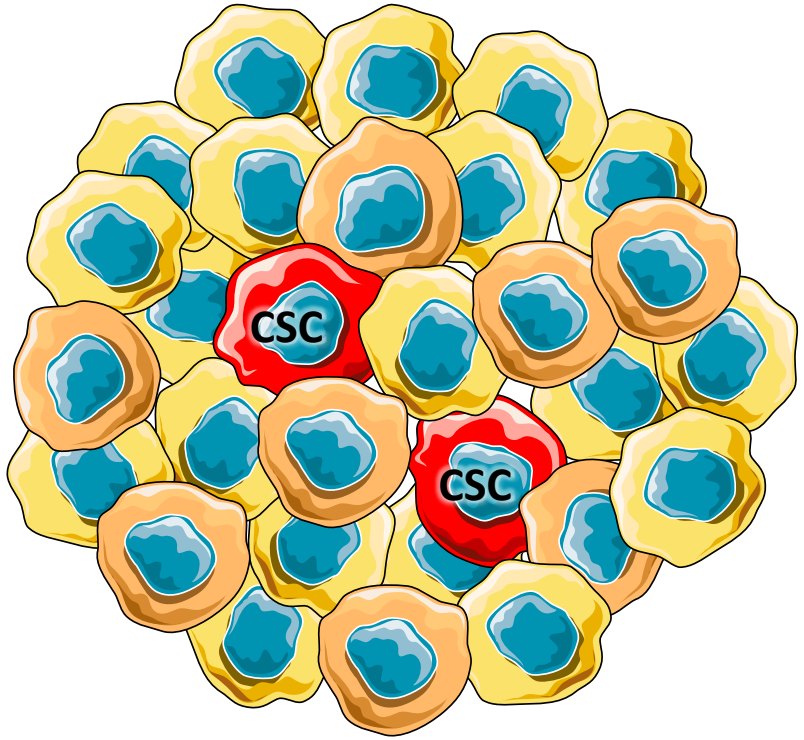
While the cancer market is growing, survival rates are still **low**.

Why?

Conventional chemotherapy does not cure all cancers

Problem

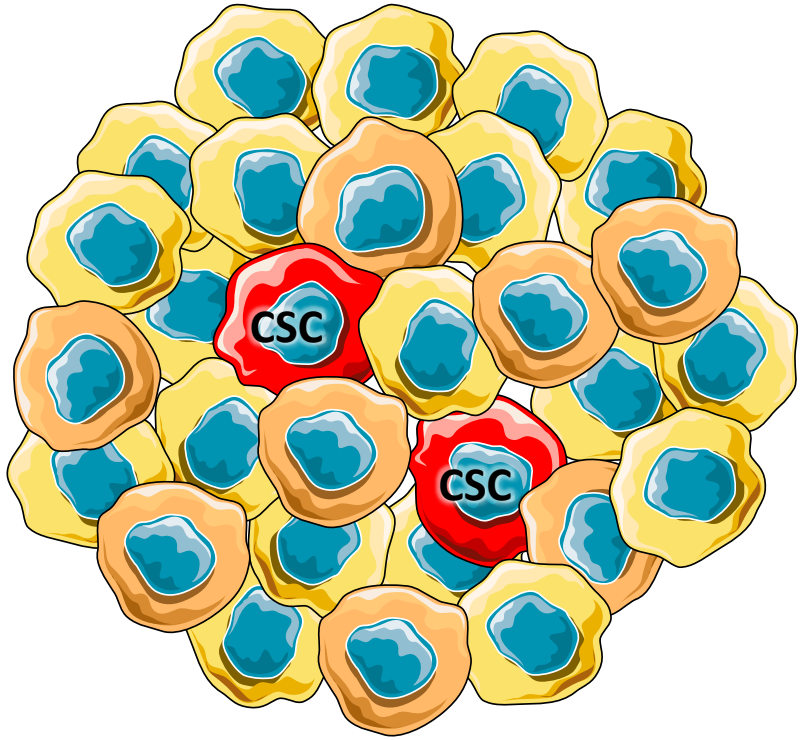
This is because not all cancer cells are the same



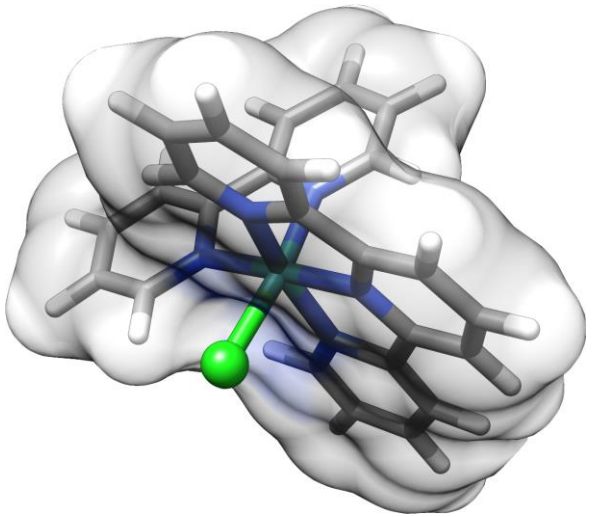
Cancer Stem Cells (CSCs) give rise to all of the other tumor cells, establishing the hierarchy and heterogeneity of the tumor. **CSC possess exclusive tumorigenic and metastatic potential, and are the drivers of tumorigenesis, chemoresistance and relapse.**

OUR Therapeutic Solution

Therefore, we need to target the CSCs within the tumor



IGN116 is our therapeutic **lead**



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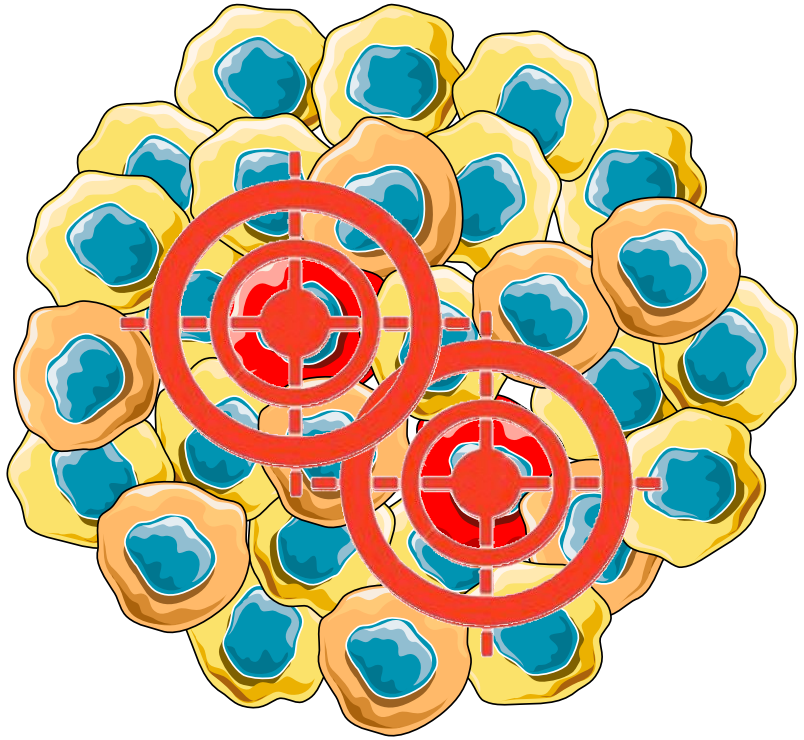


IGN116 exhibits **a different mode of action** compared to conventional anti-cancer drugs, by targeting **CSCs**

Target population

Our **target population** are patients with **CSC-driven** tumors, as the maintenance of these cancers **depend on CSCs.** We has focused on Pancreatic cancer as a model tumor, but this technology could be extended to many other cancers. For example (but not limited to):

Pancreatic cancer

Colorectal cancer

Lung cancer

Breast cancer

Current state of IGN116

2018 - 2022 → 2022-2024 (CaixaResearch Fundación "la Caixa") →

Discovery

Drug discovery phase:

Target discovery
- ✓ Identification of tumors amenable to therapy
- ✓ Identification of cell type to be targeted (i.e., CSC)
- ✓ Identification of targets that can be targeted

Drug Discovery
- ✓ Hit discovery
- ✓ Lead compound (IGN111/116)
- ✓ Pre-formulation
- ✓ Synthesis (IGN111 & IGN116)
- ✓ Stability and degradation studies

Preclinical testing (in vitro & in vivo)

Preclinical phase:

Mechanism of action
- ✓ Identification of MOA (inhibition of mtDNA transcription)

In vitro toxicity
- ✓ CRO led: Toxicity, Cardiotoxicity, Cytochrome interactions, Permeability, Plasma protein binding, metabolic stability

In vivo efficacy and safety
- ✓ Efficacy in 6 PDAC PDX models (subcutaneous & orthotopic)
- ✓ Efficacy in 2 CRC and 1 Osteosarcoma PDX models
- ✓ CRO led in vitro toxicity studies and preliminary PK studies
- ✓ Maximum tolerated dose (MTD) determined
- ✓ **Dosing interval** and **admin route** studies

Chemistry
- ✓ Scale up, protocols for detection by MS, and synthesis

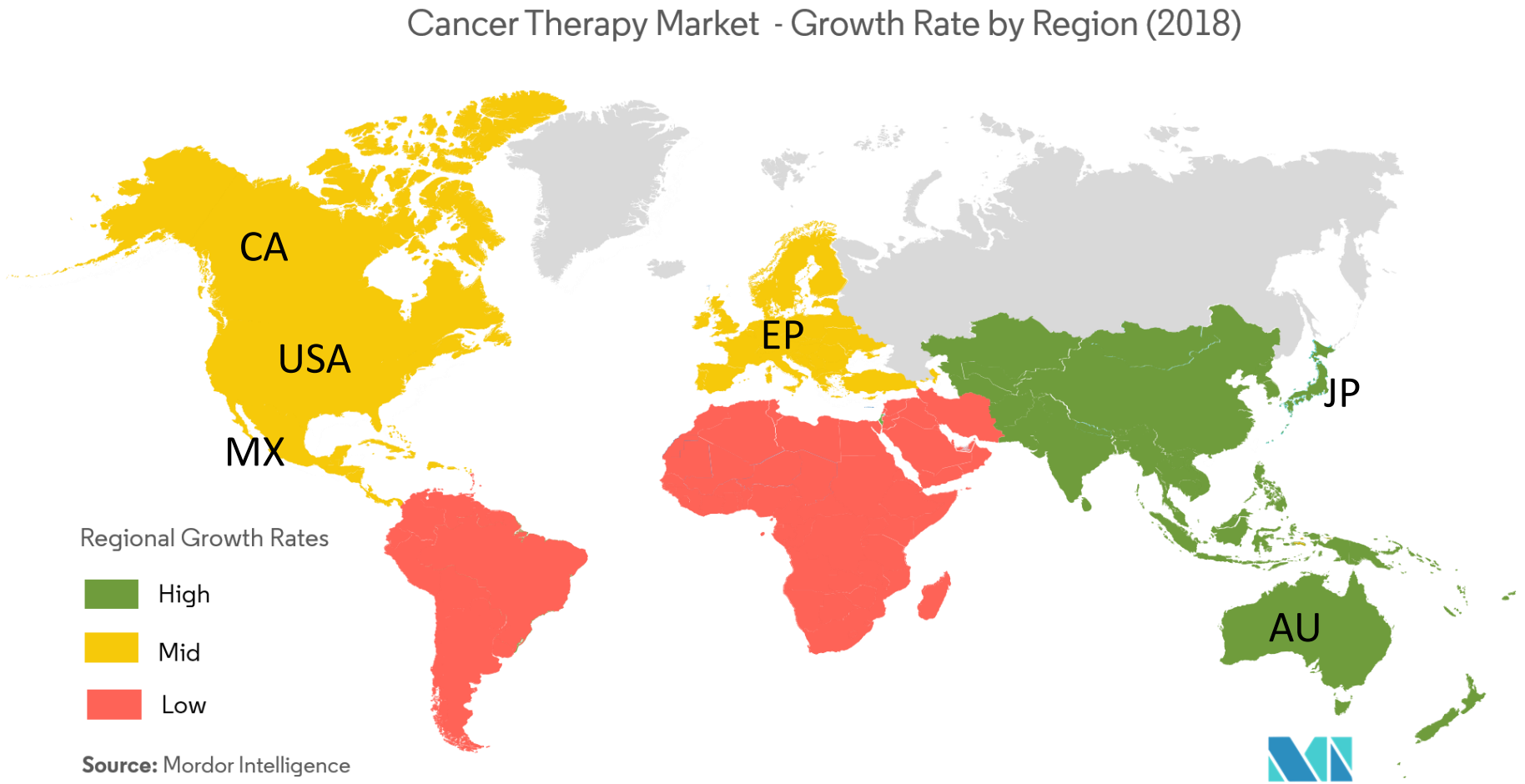
CRO led, non-regulatory in vivo studies (SAI & AMSlab)
- ✓ Analytical protocol for Ru detection (ICP-MS)
- ✓ Initial PK study
- ✓ MTD study (i.v. bolus)
- ✓ PK & PD studies, Therapeutic index determination
- ✓ Single and repeat dose & safety studies in 2 species

CDMO led, Manufacturing (Galquimia)
- ✓ Protocol for GMP-amenable scale-up and production

Other
- ✓ **Lower doses** and **alternative admin route** studies
- ✓ Test in other tumors (NSCLC, NECs, Breast, CRC)
- ✓ Test **analogues** in vitro & **in vivo**
- ✓ PK efficacy study with PDAC PDX

TO DO
- ✓ Regulatory & Pre-clinical roadmap
- ✓ Business plan

Patent Family – IGN116



Multidisciplinary team

IGN116 has developed from a multidisciplinary collaboration:

Principal inventor
Dr. José L. Mascareñas
Professor, Dept Organic Chemistry

Synthetic chemistry

Interface

CSC expert
Dr. Bruno Sainz
Dept of Biochemistry

Cancer biology