



PROYECTOS SINÉRGICOS 2018 EN I+D

ACRONIMO: Y2018/BIO-4747

TÍTULO PROYECTO: Nanobiología Estructural y Molecular de
Procesos de Reparación de ADN relacionados con Cáncer

PRESUPUESTO CONCEDIDO: 812.900 €
(413.200 € -- CNB, 381.700 € – CNIO)



www.nanobiocancer.com

Madrid, 1 de febrero de 2023

Y2018/BIO-4747 - ¿Quiénes participamos?

Coordinator



Fernando MORENO-HERRERO
CNB-CSIC, Madrid, Spain

Single molecule Biophysics
Atomic Force Microscopy
Optical / Magnetic tweezers

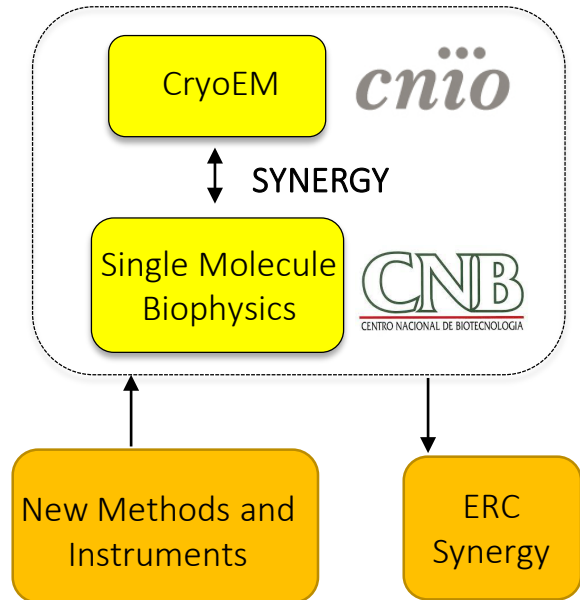


Resolve complex biological questions in Cancer involving protein complexes and nucleic acids (DNA / RNA)



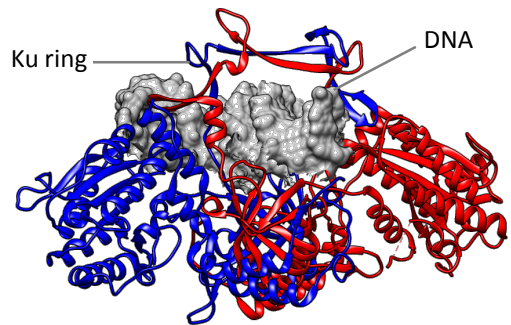
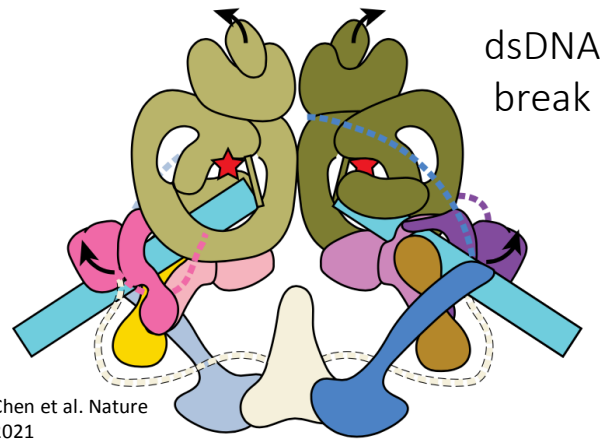
Oscar LLORCA
CNIO, Madrid, Spain

Cryo-Electron Microscopy
Structural Biology

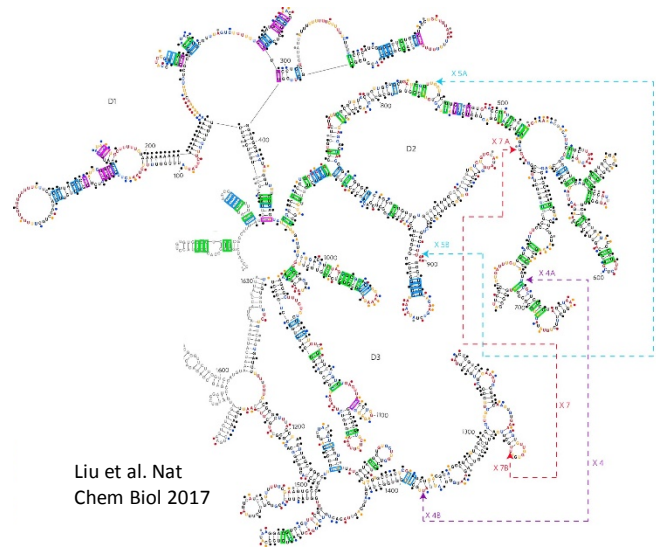


Y2018/BIO-4747 - ¿Qué objetivos planteamos?

Non-homologous End-Joining (NHEJ)

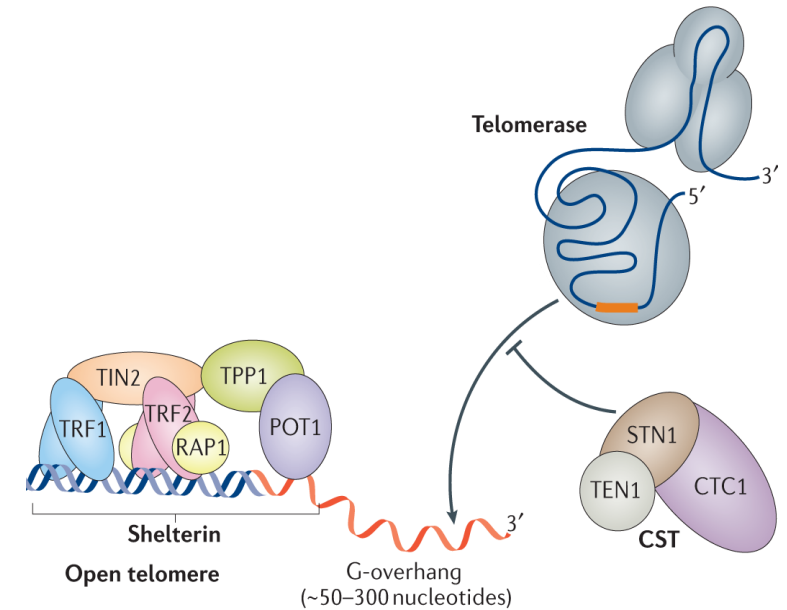


Ku70-Ku80 (Ku heterodimer)



Long non-coding RNAs (lncRNAs)

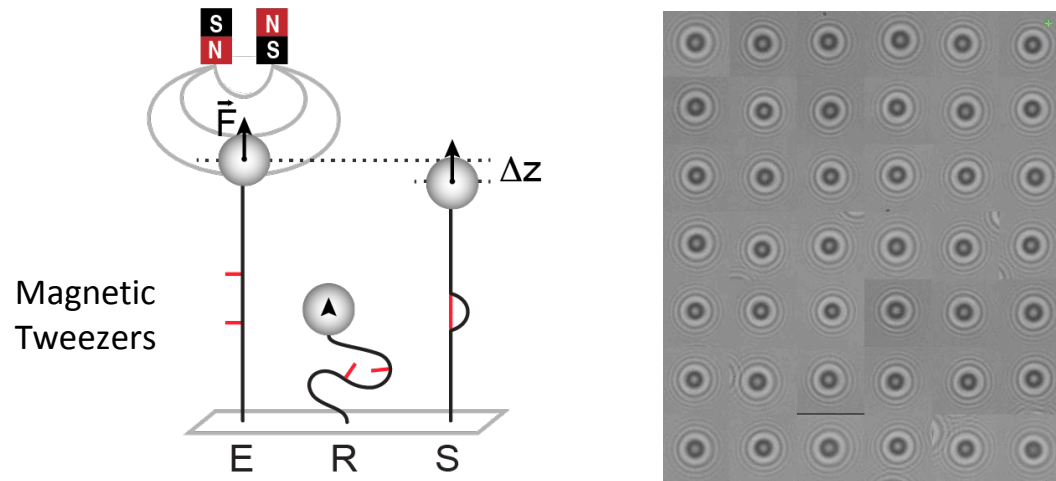
Telomere maintenance / CST complex



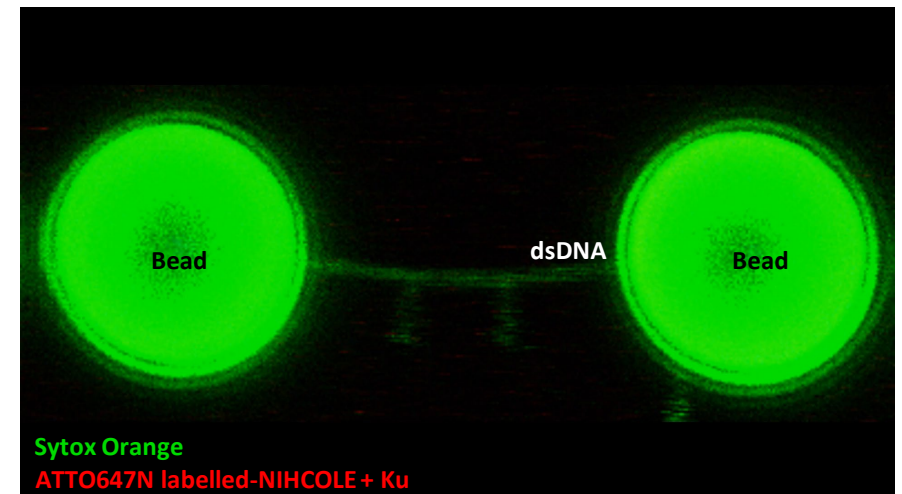
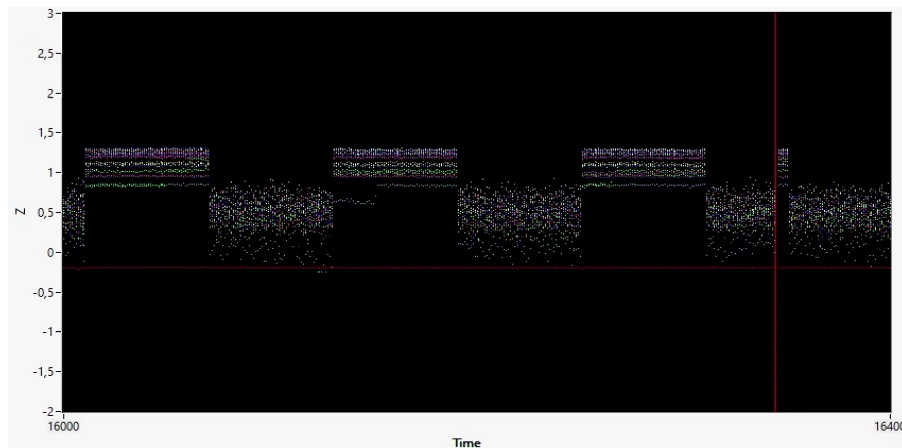
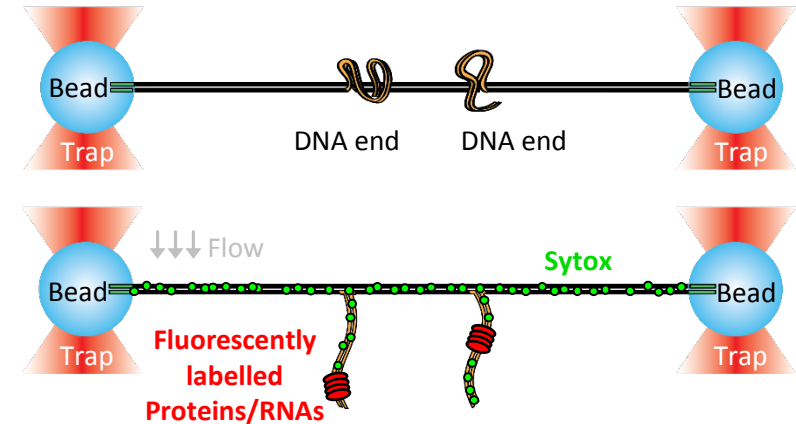
Y2018/BIO-4747 - ¿Qué resultados hemos obtenido?

METHODS DEVELOPMENT

Mimicking a double-strand DNA break to study the DNA repair pathways



Direct visualization of the interaction of proteins and RNAs with dsDNA ends



Unpublished data

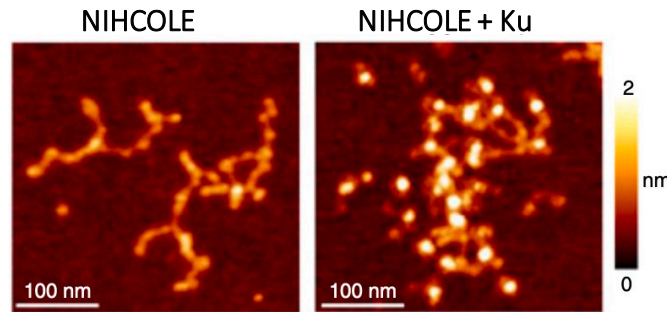


Y2018/BIO-4747 - ¿Qué resultados hemos obtenido?

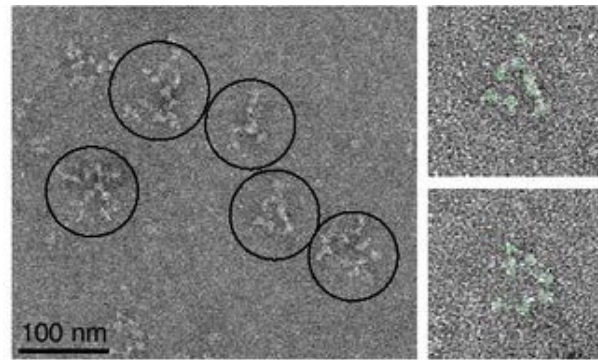
lncRNA NIHCOLE

- Upregulated in Hepatocellular carcinoma
- Decreased survival, aggressive tumors
- Confers advantage to HCC cells.

ATOMIC FORCE MICROSCOPY (AFM)

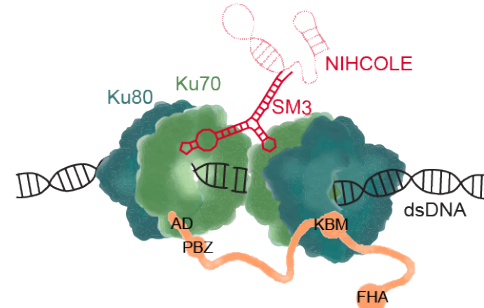
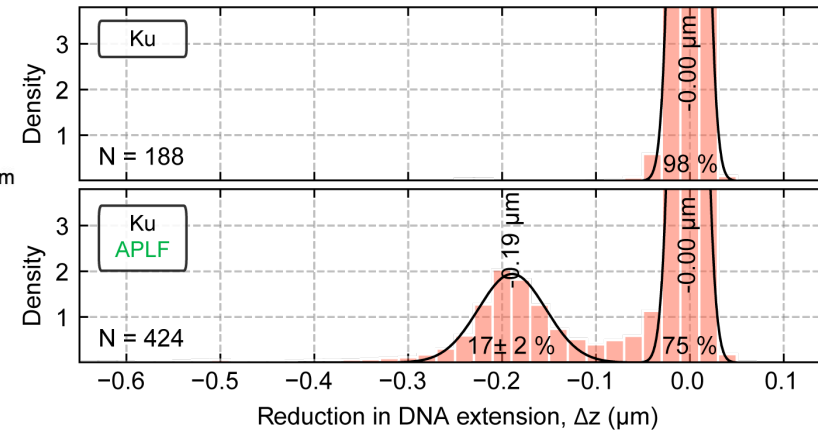


ELECTRON MICROSCOPY



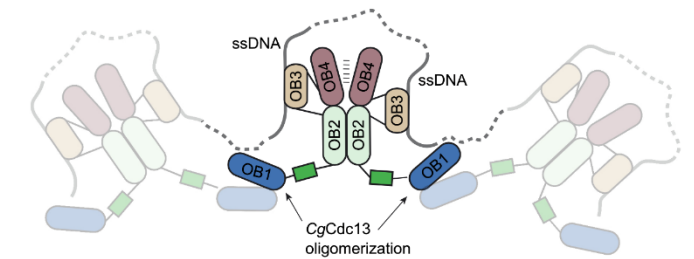
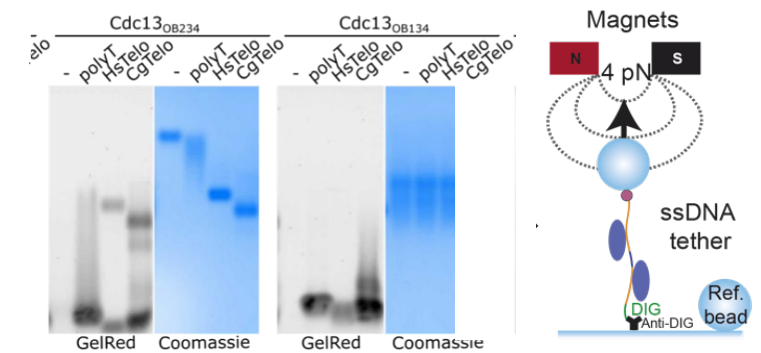
APLF, Ku and NIHCOLE in NHEJ

- In NHEJ, the Ku-APLF complex supports DNA end synapsis for several minutes under piconewton forces
- lncRNA NIHCOLE fortifies the DNA synapsis



Cdc13 in telomere maintenance

- Cdc13 interaction with ssDNA
- Molecular structure and function of Cdc13



Unfried et al. Cancer Research 2021
De Bragança et al Cell reports 2023
Coloma et al Nucleic Acids. Res. 2023



"la Caixa" Foundation

Health Research Call 2021

lncRNAs in DNA replication and colon cancer
995.200 € Maite Huarte (CIMA – U. Navarra)



Synergy Antonin MORILLON (Curie-CNRS)
Grants Janusz BUJNICKI (IIMCB)

Calls 2019, 2021 – Step 3 Interview

New call 2022 - pending

Y2018/BIO-4747– ¿Cómo hemos continuado?



This was a new consortium in 2019
Now – consolidated and great future ahead!!

LncRNA
rules



LncRNAs in
colon cancer

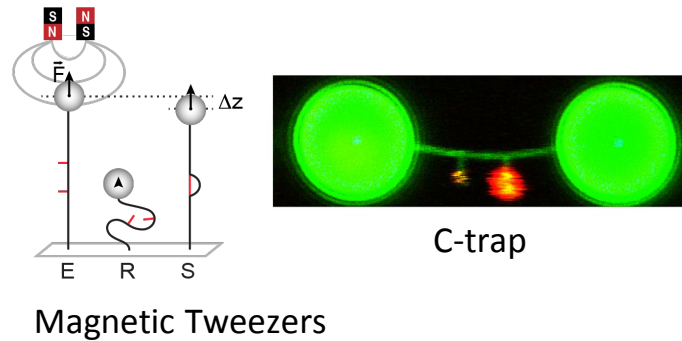


Maite Huarte
CIMA – Univ de Navarra

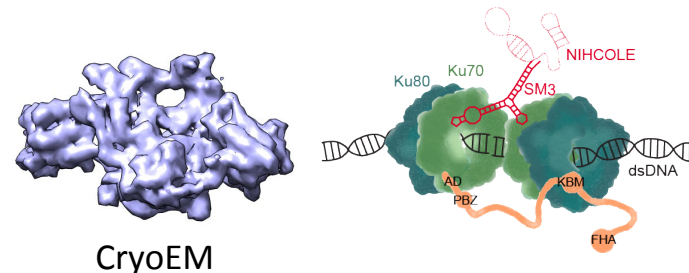
LncRNAs in
hepatocellular
carcinoma

Puri Fortes
CIMA – Univ de Navarra

Non Homologous End-Joining (NHEJ)



Magnetic Tweezers



CryoEM

Human CST and telomeres

