Functional and mechanistic role of lncRNA-A1 in cholangiocarcinoma

Tinahones-Ruano A, *Blázquez-Vicens J, Aparicio-Rey A, Esquinas-Román EM, Maseda I, Riobello C, Capelo-Diz A, Cañas-Martín J, Larraona E, Perdikari S, García C, García-Fernandez de Barrena M, Porteiro B, Lozano J, Gonzalez-Sanchez E, Bañales JM, Milkiewicz P, Milkiewicz M, Bujanda-Fernández L, Avila MA, Aransay A, Nogueiras R, Pelacho B, Amengual J, Fabregat I, Vaquero J, Entrialgo-Cadiero R, Vicent S, Sancho-Bru P, Affo S, Guicciardi ME, Arana A, Sanchez-Piñon LE, Fildalgo M, Gores GJ, Woodhoo A, Varela-Rey M.*

CCF 13th Annual Conference | Salt Lake City May 1-3 2026

Background

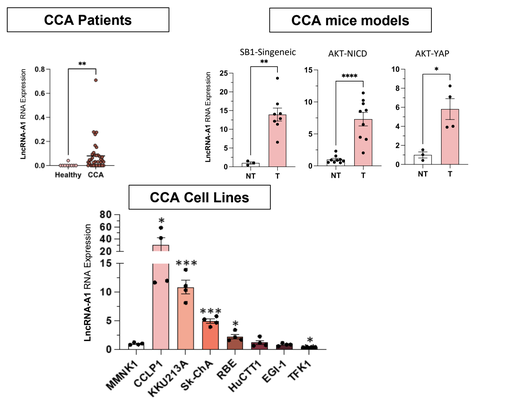
- **Cholangiocarcinoma** (CCA) is a highly heterogeneous biliary malignancy with **limited therapeutic options**, characterized by poor clinical outcomes and a high degree of chemoresistance.
- Despite their lack of coding potential, recent studies suggest that long non-coding RNAs **(lncRNAs) regulate** gene expression, influencing processes such as **proliferation, migration, invasion, and apoptosis in CCA**.
- Using RNA-sequencing of liver tissue from two cholestasis mouse models *we identified a clinically relevant signature of 52 lncRNAs associated with cholestasis-induced liver injury*. **LncRNA-A1 was selected to investigate its functional role CCA development.**

Methods

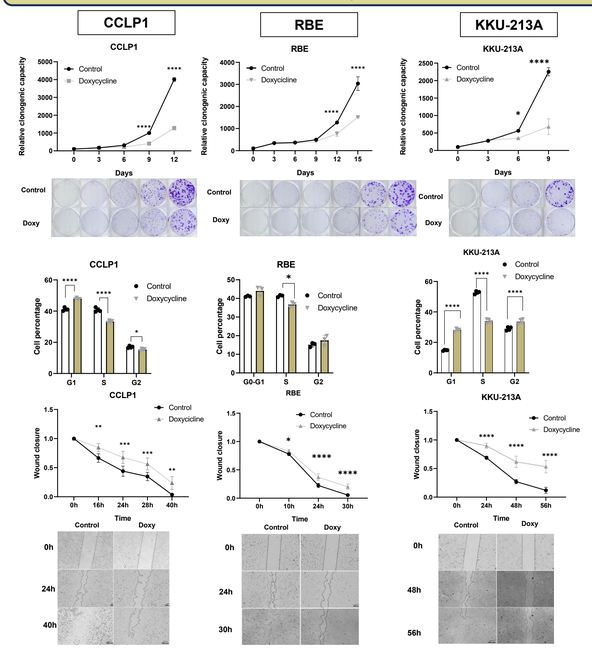
Cultures: CCA cell lines (CCLP-1, RBE, KKU-213A), cholangiocyte cell line (MMNK-1), Cholangiocyte organoids
Mice models: Mouse CCA (SB1, AKT-NICD, AKT-YAP), Xenografth (NMRI nude mice)
Plasmids: Inducible Tet-On ShRNA-A1
Assays: qPCR, WB, Cell proliferation MTT, Colony forming ability, Cell cycle analysis and migration assay, RNAseq (DEG).

Results

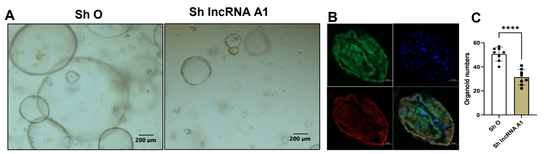
1. LncRNA-A1 is upregulated in human and mice CCA



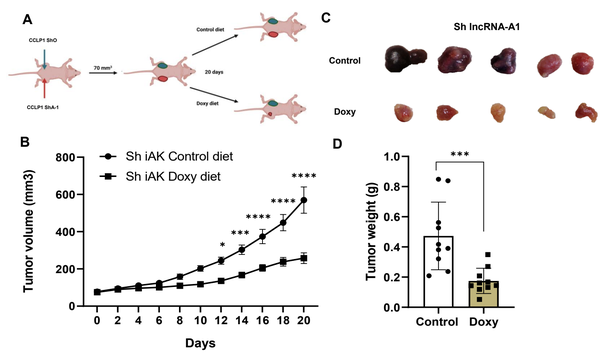
2. LncRNA-A1 promotes cell viability, migration, colony formation and cell cycle *in vitro*.



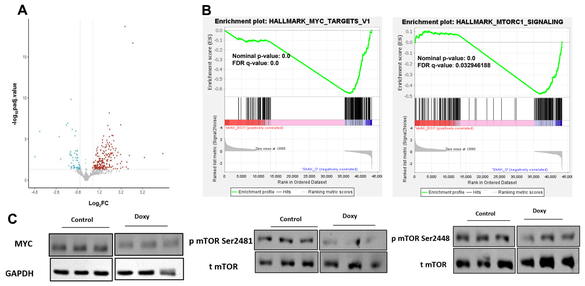
3. LncRNA-A1 promotes cholangiocyte organoid survival



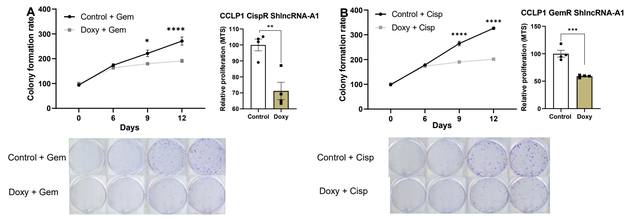
4. LncRNA-A1 promotes cell growth *in vivo*



5. LncRNA-A1 regulates c-myc and mTOR pathways



6. lncRNA-A1 silencing synergizes with chemotherapy and targets chemoresistant CCA cells



Conclusion

LncRNA-A1 acts as a **key oncogenic regulator** in cholangiocarcinoma, **promoting tumor progression by** enhancing proliferation and survival through modulation of **c-MYC and mTOR** signaling pathways. **Its inhibition impairs tumor growth, synergizes with chemotherapy and reduces chemoresistance**, highlighting lncRNA-A1 as a promising therapeutic target in CCA.

Future Directions for Research

In future studies, we aim to **deliver ASOs targeting lncRNA-A1 using nanoparticle-based systems** for intravenous treatment of cholangiocarcinoma.

albertotruano@gmail.com. PhD Student CiMUS (USC)

Background/Objective

Cholangiocarcinoma is a hard-to-treat cancer with few effective therapies.
Long non-coding RNAs (lncRNAs) can control cancer cells growth and survival.

Methods

We blocked lncRNA-A1 in lab models and mice, including chemotherapy-resistant cells.

Results

A molecule called **lncRNA-A1** helps cancer cells grow and resist chemotherapy.

Conclusion

Blocking **lncRNA-A1** slows tumor growth and also reduces resistance to treatment.