KDDF
Korea Drug Development Fund

Asset #32
Boston University

TFCP2 Transcription Factor Inhibitors

Therapeutic Area	Oncology	**Indications**	Colorectal Cancer and Pancreatic Cancer
Modality	Small Molecule	**Development Stage**	Target Identification/Validation

Overview

Background

- Novel FQIs targeting LSF (TFCP2) show potential as cancer chemotherapeutics. The lead compound FQI1 induces concentration-dependent mitotic delay, rapidly causing reversible arrest by unexpectedly affecting microtubules and γ-tubulin localization.
- LSF, recognized for DNA interaction, interacts with α-tubulin, boosting polymerization. FQI1 hampers this, indicating its mitotic disruption role. Mass spectrometry connects FQI1-sensitive LSF interactions to microtubules, centrosomes, and spindle regulation, highlighting its non-transcriptional role in mitosis.

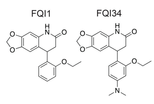
Technology Advantages

- Targeted Cancer Treatment: FQIs target LSF (TFCP2), implicated in cancer, for more effective therapies
- Mitotic Disruption: FQIs hinder mitosis by affecting microtubules and γ-tubulin
- Dual Mode: FQIs inhibit LSF and alter microtubules, enhancing anti-cancer effects
- Proteomics Insight: FQIs disrupt mitotic LSF-protein interactions, guiding interventions
- Reduced Side Effects: Focused microtubule disruption via LSF may minimize side effects

Key Data

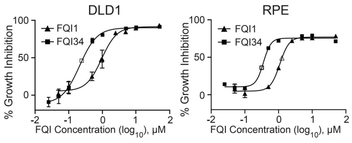
FQI34, a more potent LSF inhibitor, disrupts mitosis with spindle defects at 10-fold lower concentrations than FQI1

A



Comparison of structures of FQI1 and FQI34

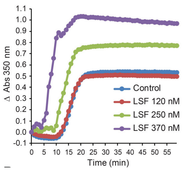
B



MTS assays measuring the number of viable cells upon treatment of parental DLD-1 cells (left) and RPE cells (right) with increasing concentrations of FQI1 versus FQI34. Calculated GI50's are: DLD-1 FQI1, 0.95 µM; DLD-1 FQI34, 0.24 µM; RPE FQI1, 1.25 µM; RPE FQI34, 0.32 µM. Data indicate averages +/- SEM from 6 replicates.

LSF facilitates tubulin polymerization

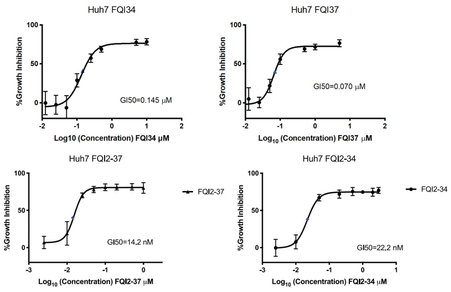
C



The tubulin polymerization assay was performed under standard conditions (Millipore kit) in the presence of 52 µMtubulin and 0 nM (blue), 120 nM (red), 250 nM (green) and 370 nM (purple) LSF

FQIs Inhibit Liver Cancer Cell Growth at nMConcentrations

D



(A) (Huh7 FQI34), the GI50 for FQI34 is 0.145 µM (B) (Huh7 FQI37), the GI50 for FQI37 is 0.070 µM (C) (Huh7 FQI2-37), the GI50 for FQI2-37 is 14.2 nM (D) (Huh7 FQI2-34), the GI50 for FQI2-34 is 22.2 nM

IP Status & Publication(s)

Intellectual Property

Patent Number	Patent Family
US 9802948 B2 (2017.10.31)	PCT, US, CN
US 11420977 B2 (2022.08.23)	PCT, US, EP, CN, CA, AU
US 11458132 B2 (2022.10.04)	PCT, US

Publication(s)

- Yunes at al. (2022). Factor quinolinone inhibitors disrupt spindles and multiple LSF (TFCP2)-protein interactions in mitosis, including with microtubule-associated proteins. PLOS ONE