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The Pan G-Quadruplex experimental drug QN-302 in PDAC: identification of potential biomarkers for clinical studies

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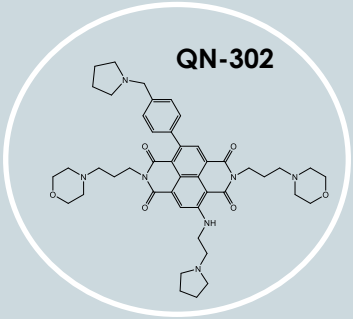
Abstract # A081

- QN-302: a potent tetra-substituted naphthalene diimide compound
- Designed for targeting quadruplex (G4) sequences in the promoter regions of cancer genes
- Orphan Drug Designation for pancreatic ductal adenocarcinoma (PDAC) was granted by the FDA in January 2023
- QN-302 was granted IND clearance by the FDA in July 2023
- Patient recruitment for multi-center Phase I trials starting in 4Q23
- Selected biomarkers will be monitored and evaluated
- Choice to be made from genes highly up-regulated in human PDAC and down-regulated in cells and *in vivo models* by QN-302
- Increased expression of S100P and CX3CL1 correlates with human PDAC disease progression - previously proposed as biomarkers
- We show here that both genes are highly down-regulated at the mRNA and protein levels by QN-302
- Since these genes contain many potential G4 sequences, they are possible direct targets of the drug

S100P and CX3CL1 are thus plausible mechanistic biomarkers of response to QN-302 in human PDAC

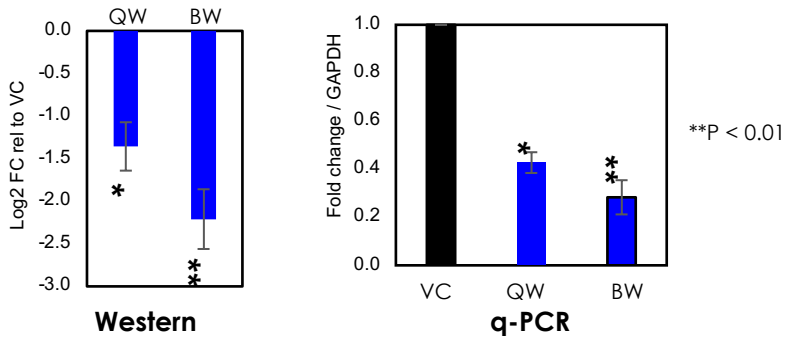


In MIA-PACA2 cells: Changes in log2 RNA expression, from RNA-seq + QN-302

Gene	log_2 FC change	Protein function	Elevated expression implicated in PDAC?
CX3CL1	-2.91	Chemokine, SRC activator	Y
S100P	-3.23	Ca-binding, cancer initiation	Y

From MIA-PACA2 xenograft (see below): Western and RT-PCR studies on tumor material at the end of 28-day dosing, with dosing 1 mg/kg BW or QW

S100P



CX3CL1

VC – Vehicle Control
Gem – Gemcitabine BW