

A new triazolothiadiazine derivative inhibits stemness and induces cell death in HCC by oxidative stress dependent JNK pathway activation

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Supplementary Information

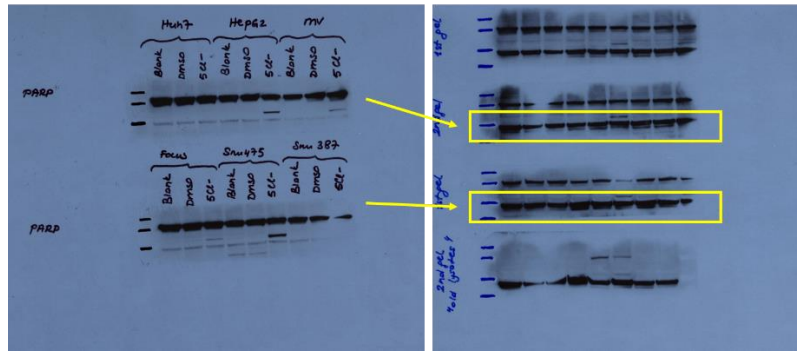
Supplementary Table S1. IC₅₀ values of selected compounds **7a**, **7b** and **7c** in μ M concentrations on Huh7, HepG2, Hep3B, PLC, SK-Hep1, Mahlavu, FOCUS, SNU182 and SNU475 cells determined by SRB assay after 72h of treatment.

Compounds	Huh7	HepG2	Hep3B	PLC	SK-Hep1	Mahlavu	FOCUS	SNU182	SNU475
7a	8.6	5.6	14.8	23.6	24.3	21.3	13.7	12.4	15.0
7b	0.3	0.2	0.8	1.6	6.0	1.0	0.6	0.9	0.5
7c	16.4	7.9	30.3	NI	NI	NI	NI	15.4	26.2

* NI: no inhibition

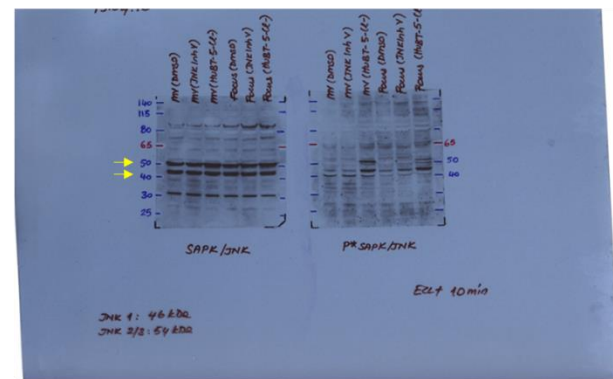
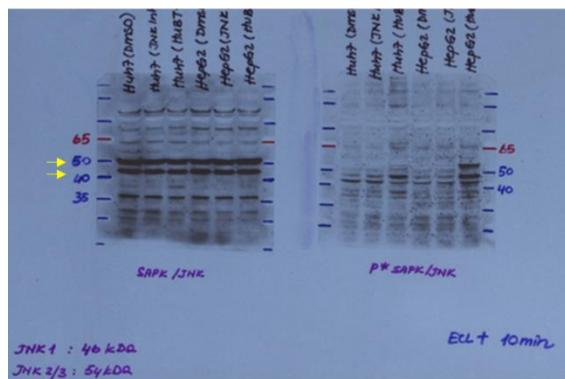
PARP

Calnexin of PARP

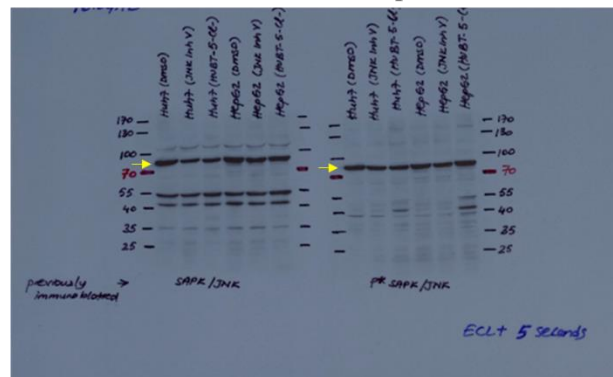


SAPK/JNK

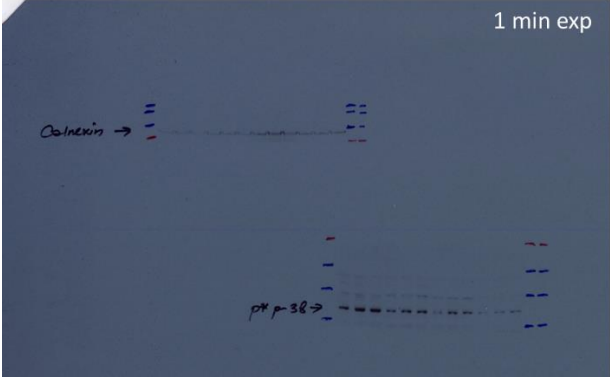
phospho-SAPK/JNK



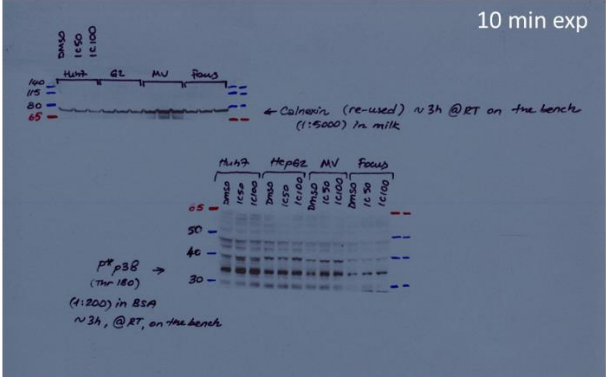
Calnexin of SAPK/JNK and p-SAPK/JNK



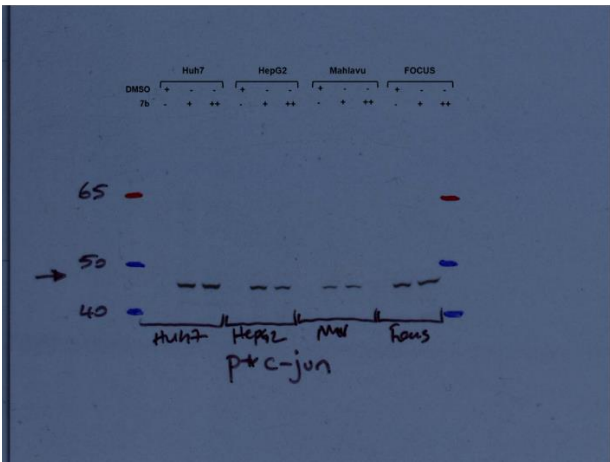
phospho-p38 and calnexin



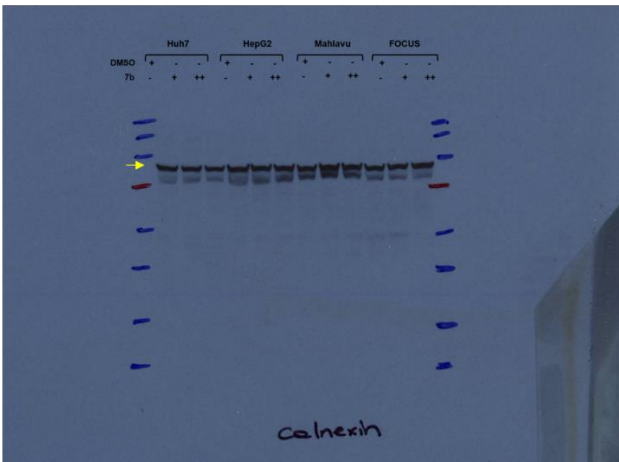
phospho-p38 and calnexin



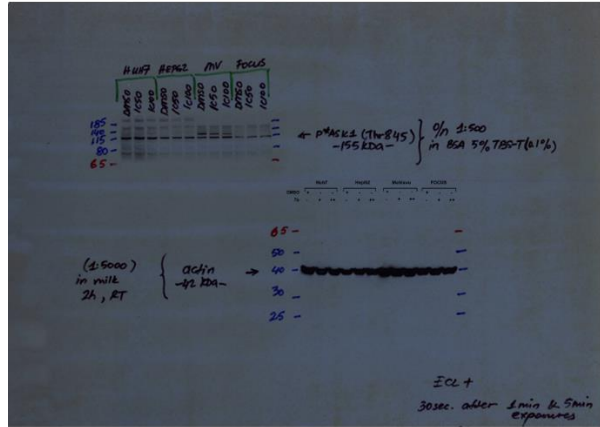
phospho-c-Jun



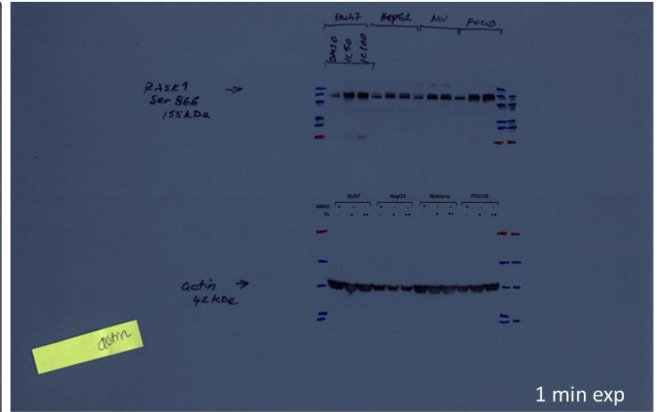
Calnexin of p-c-Jun



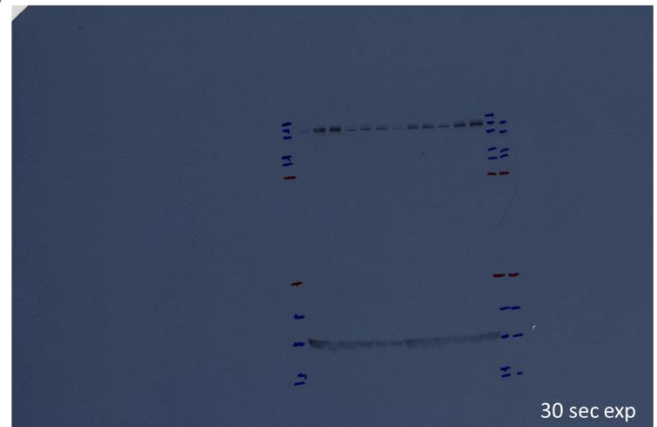
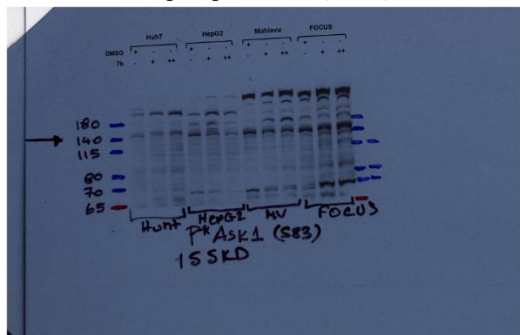
phospho-ASK (Thr845)

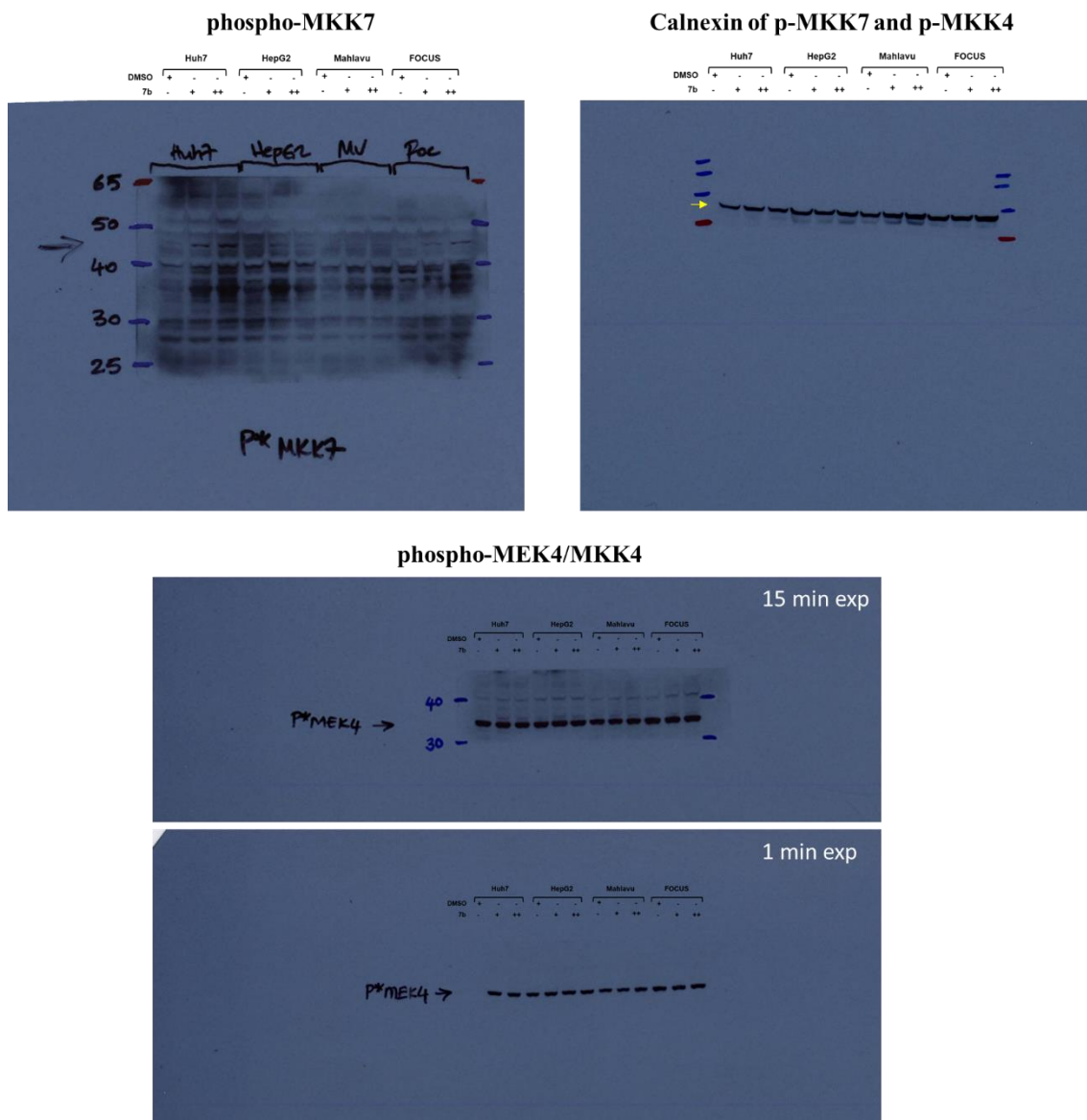


phospho-ASK1 (Ser966)

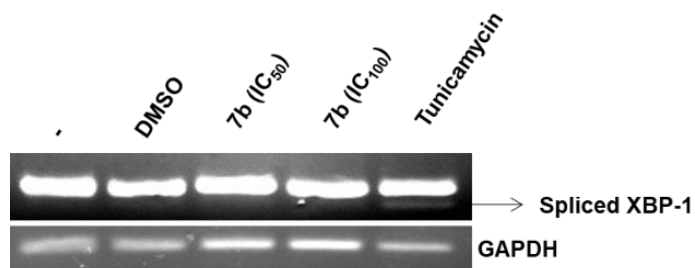


phospho-ASK1 (Ser83)

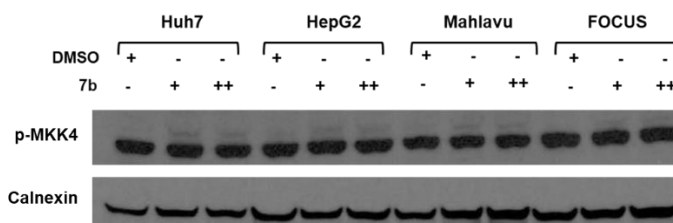




Supplementary Figure S1. Uncropped images of all western blots represented in the manuscript.



Supplementary Figure S2. PCR analysis of XBP-1 expression in Huh7 cells, treated with increasing concentrations of compound **7b** (-: untreated, DMSO: vehicle control, and 500 ng/mL Tunicamycin: positive control). Spliced XBP-1 is a marker for ER stress.



Supplementary Figure S3. The effect of compound **7b** on the protein expression of phospho-MKK4 in HCC cells treated with increasing concentrations of compound **7b** for 24 h determined by western blot analysis. Calnexin are used as equal loading control.