First selective small molecule inhibitor of FGFR4 for the treatment of hepatocellular carcinomas with an activated FGFR4 signaling pathway

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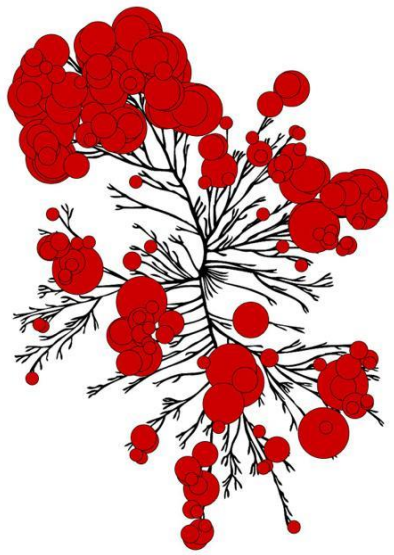
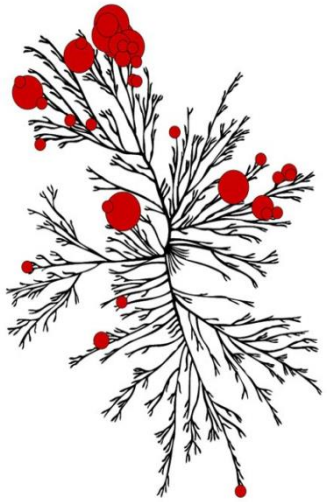
Supplementary Figures

Figure S1. Potency against FGFR family and kinome selectivity

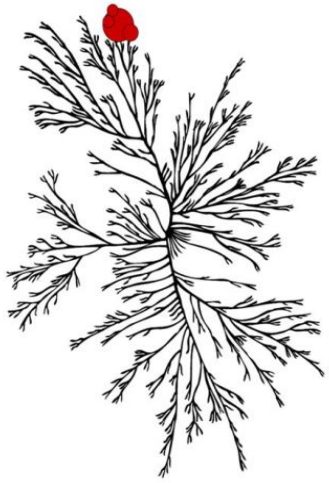
IC_{50} (nM)	FGFR4	FGFR1	FGFR2	FGFR3	S (10)
BLU9931	3	591	493	150	0.005 (3 μM)
BGJ398	26	0.4	0.2	0.1	0.033 (3 μM)
LY-2874455	1	0.2	0.2	0.1	0.347 (1 μM)



LY-2874455



BGJ398



BLU9931

Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

Figure S2. Kinases with a cysteine at the equivalent position to Cys552 in FGFR4

Kinase	% Sequence Identity	% Sequence Similarity	% Active site Identity	Gatekeeper
FGFR4	-	-	-	Val
MAPKAPK3	30	47	50	Met
MAPKAPK2	26	43	50	Met
p70S6Kb	25	44	44	Leu
TTK	21	42	44	Met
PI4K	NONE	NONE	17	Ile
ChaK1	NONE	NONE	N/A	Glu

Figure S3. MALDI Mass Spectrometry of FGFR4

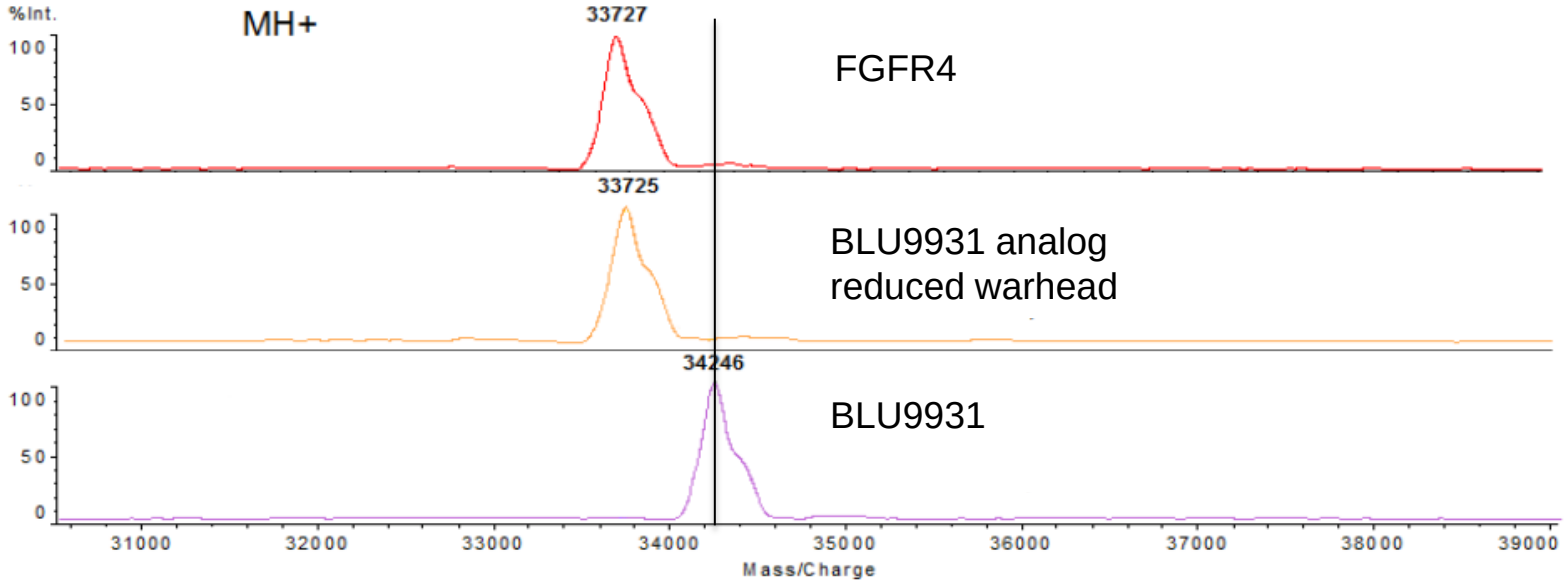


Figure S4. Induction of Caspase 3/7 activity in Hep 3B cells

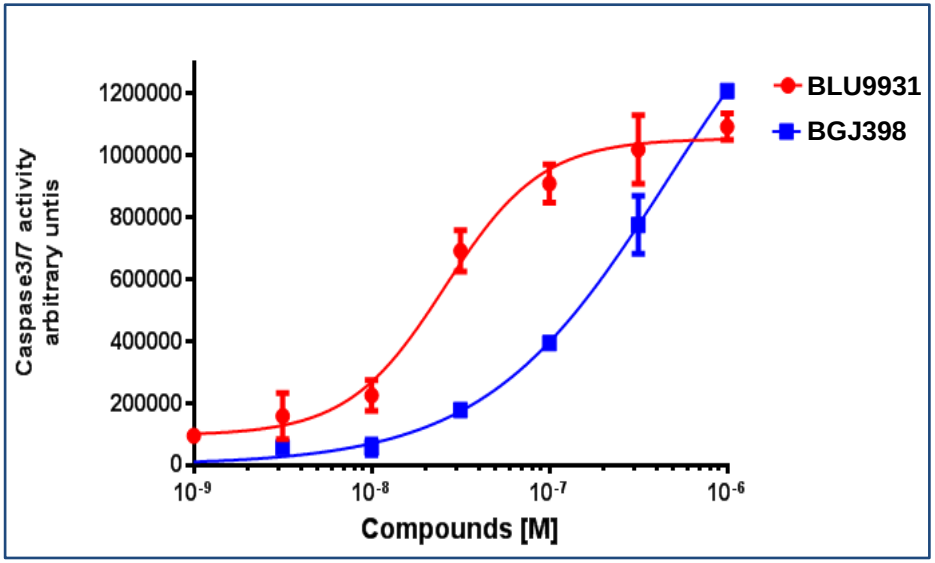


Figure S5. FGFR4 turnover rates in Hep 3B cells

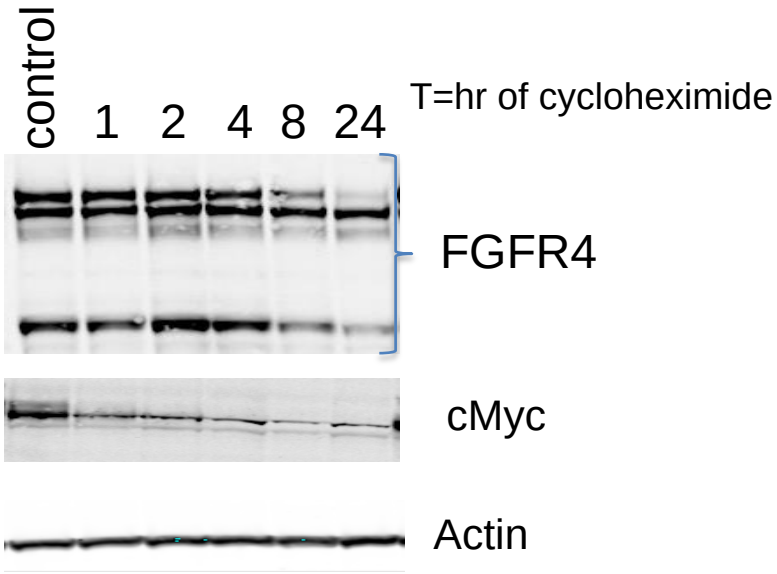


Figure S6. Analysis of TCGA HCC samples

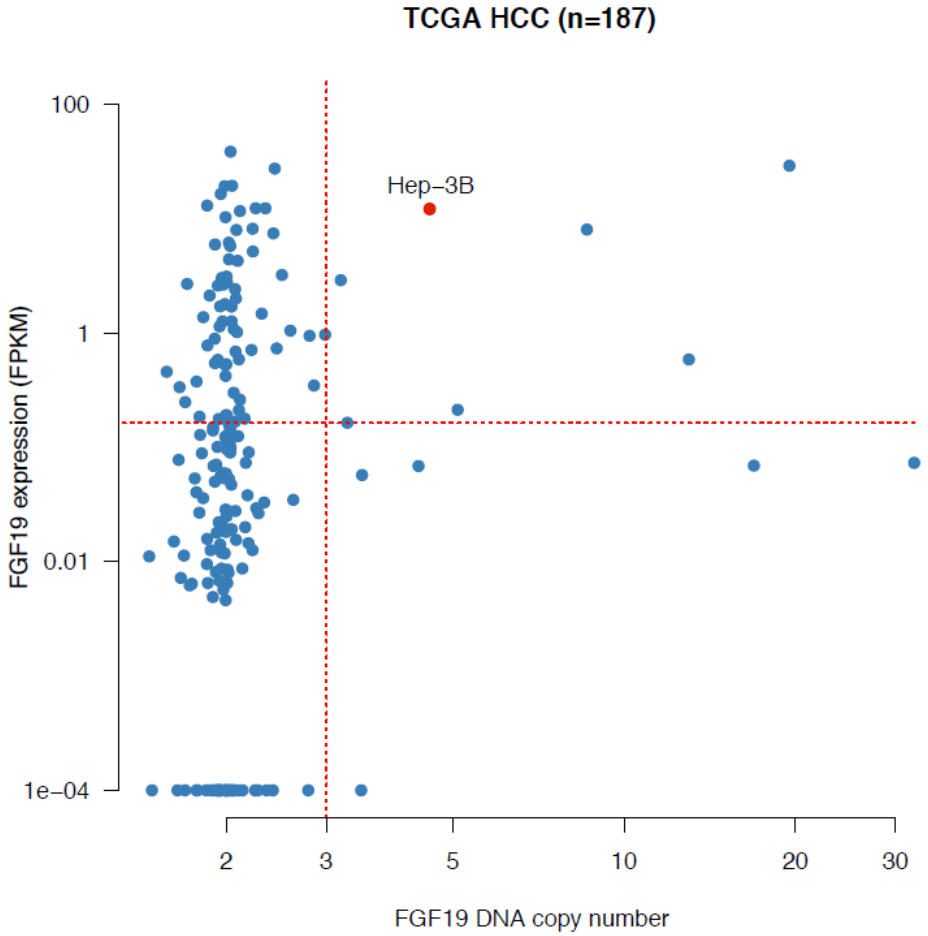


Table S1. Kinetic parameters of FGFR4 inhibition by BLU9931

K_I (nM)	27
k_{inact} (s^{-1})	0.002
k_{inact}/K_I ($M^{-1}s^{-1}$)	$0.6x10^5$

Table S2. Pharmacokinetic characteristics of BLU9931 in mouse

	Dose (mg/kg)	AUC (ng·hr/mL)	CL (mL/min/kg)	Vdss (L/kg)	F %	$T_{1/2}$ (h)
Mouse (IV)	1	815	20	1.3	-	1.1
Mouse (PO)	10	1362	-	-	18	2.3