

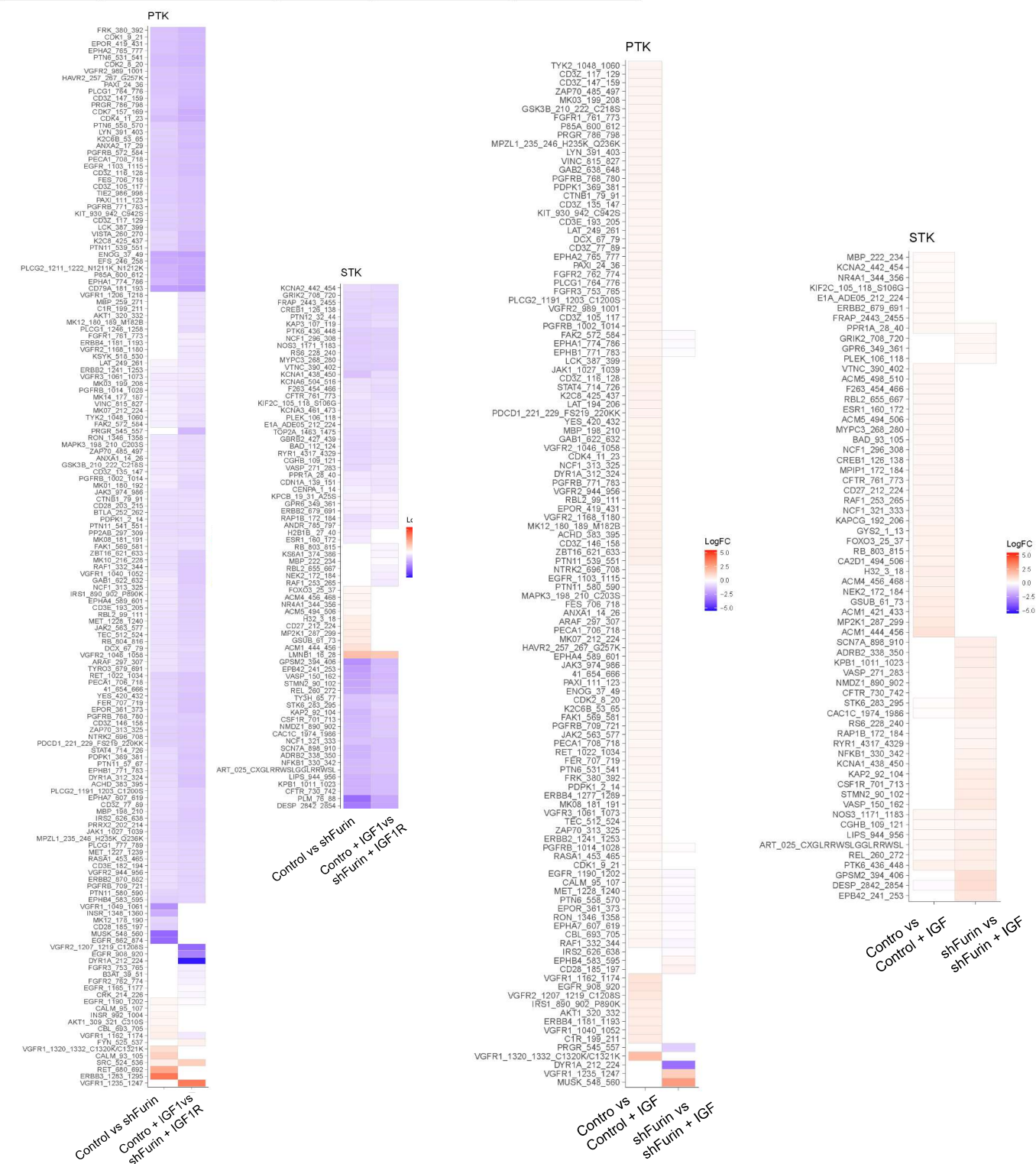
Supplementary Table S1. The mouse primers used for this study

Gene	Primer Direction	Sequence (5' -> 3')
mPTGS2	Forward	TTCAACACACTCTATCA CTGGC
mPTGS2	Reverse	AGAAGCGTTTGCGGTAC TCAT
mPTGER1	Forward	GGGCTTAACCTGAGCCT AGC
mPTGER1	Reverse	GTGATGTGCCATTATCG CCTG
mPTGER3	Forward	CCGGAGCACTCTGCTGA AG
mPTGER3	Reverse	CCCCACTAAGTCGGTGA GC
mPTGER4	Forward	ACCATTCCTAGATCGAA CCGT
mPTGER4	Reverse	CACCACCCCGAAGATGA ACAT
mPTGES	Forward	GGATGCGCTGAAACGT GGA
mPTGES	Reverse	CAGGAATGAGTACACGA AGCC
mTGF-beta1	Forward	CTCCCGTGGCTTCTAGT GC
mTGF-beta1	Reverse	GCCTTAGTTTGGACAGG ATCTG

Supplementary Table S2. Phosphosite analysis: Number and heatmap of up-regulated and downregulated Protein tyrosine kinases (PTKs) and Serine/threonine kinases (STKs) in control KPN cells and the same cells expressing shFurin in the absence and presence of IGF-1

Assay Type Comparisons	PTK		STK	
	Up	Down	Up	Down
control vs shFurin	11	114	10	63
control+IGF1 vs shFurin+IGF1	3	139	1	61
control vs control+IGF1	111	0	43	1
shFurin vs shFurin+IGF1	3	15	30	0

^aSignificance was obtained using a two-sided unpaired Student's T-test, $p < 0.05$.



Supplementary Table S3. Kinase analysis: The most PTKs and STKs up-regulated and downregulated in control KPN cells and the same cells expressing shFurin in the absence and presence of IGF-1

Assay Type Comparisons	PTK Up	PTK Down	STK Up	STK Down
Control vs shFurin		LYN, MST1R, LCK, TEC, MERTK, SRC, ABL1, BMX, FRK, CSF1R		CAMK4, PRKACA, PRKACB, PRKG2, RPS6KB2, PRKX, CHEK2, RPS6KA5, SGK2, STK38L
Control+IGF1 vs shFurin+IGF1		EPHA1, LYN, FYN, FRK, TEC, SYK, SRC, SRMS, ABL1, BLK		PRKACA, PRKACB, PRKX, RPS6KB2, PRKCA, SGK2, PRKG2, PSKH1, CAMK4, STK38L
Control+IGF1 vs Control	KDR, FYN, ROR1, FLT4, BLK, FES, FRK, TEC, BMX, GSK3B		MAPK11, CDKL2, DYRK1A, AKT2, AURKB, RPS6KA6, COQ8A, CDK18, CDK17, PRKAB1	
shFurin+IGF1 vs shFurin	FGFR1, FGFR3	SRMS, RYK, MERTK, NTRK2, MET, KIT, FRK, JAK2		PRKACA, PRKACB, PRKG2, RPS6KB2, PRKCA, STK38L, PRKG1, PRKCG, PRKCD, CAMK2D

Supplementary Table S4. Kinase Score of the top 10 PTKs and STKs up-regulated and downregulated in control KPN cells and the same cells expressing shFurin in the absence and presence of IGF-1

Rank	PTK			STK		
	Kinase Name	Kinase Score	Kinase Statistic	Kinase Name	Kinase Score	Kinase Statistic
1	LYN	3.67	-9.33	CAMK4	3.67	-11.69
2	MST1R	3.06	-11.84	PRKACA	3.67	-8.19
3	LCK	2.82	-8.54	PRKACB	3.67	-9.13
4	TEC	2.82	-7.43	PRKG2	3.67	-8.08
5	MERTK	2.71	-7.43	RPS6KB2	3.19	-8.75
6	SRC	2.55	-6.97	PRKX	2.97	-8.10
7	ABL1	2.49	-7.01	CHEK2	2.82	-9.20
8	BMX	2.29	-7.22	RPS6KA5	2.76	-6.98
9	FRK	2.29	-7.12	SGK2	2.59	-9.00
10	CSF1R	2.23	-9.32	STK38L	2.59	-11.19

Table S4a Control vs shFurin

Rank	PTK			STK		
	Kinase Name	Kinase Score	Kinase Statistic	Kinase Name	Kinase Score	Kinase Statistic
1	KDR	3.36	3.20	MAPK11	2.76	2.46
2	FYN	3.19	3.01	CDKL2	2.71	2.71
3	ROR1	2.80	5.88	DYRK1A	2.67	2.56
4	FLT4	2.76	4.91	AKT2	2.32	1.79
5	BLK	2.29	2.84	AURKB	2.30	2.27
6	FES	2.19	2.90	RPS6KA6	2.30	1.94
7	FRK	1.97	2.37	COQ8A	2.27	2.05
8	TEC	1.92	2.35	CDK18	2.25	2.33
9	BMX	1.82	2.31	CDK17	2.12	2.20
10	GSK3B	1.81	2.80	PRKAB1	2.06	2.17

Table S4b Control vs Control+ IGF1

Rank	PTK			STK		
	Kinase Name	Kinase Score	Kinase Statistic	Kinase Name	Kinase Score	Kinase Statistic
1	SRMS	2.68	-0.57	PRKACA	3.67	2.06
2	RYK	2.07	-1.07	PRKACB	3.06	2.35
3	MERTK	1.97	-0.43	PRKG2	3.06	2.13
4	NTRK2	1.84	-0.52	RPS6KB2	2.71	2.18
5	FGFR1	1.76	0.52	PRKCA	2.67	2.18
6	MET	1.72	-0.44	STK38L	2.46	2.82
7	FGFR3	1.70	0.54	PRKG1	2.44	1.93
8	KIT	1.69	-0.55	PRKCG	2.34	2.36
9	FRK	1.68	-0.40	PRKCD	2.27	2.10
10	JAK2	1.67	-0.49	CAMK2D	2.25	2.67

Table S4c shFurin vs shFurin + IGF1

Rank	PTK			STK		
	Kinase Name	Kinase Score	Kinase Statistic	Kinase Name	Kinase Score	Kinase Statistic
1	EPHA1	3.67	-20.65	PRKACA	3.67	-6.68
2	LYN	2.62	-9.26	PRKACB	3.67	-7.41
3	FYN	2.46	-9.18	PRKX	3.67	-6.93
4	FRK	2.30	-8.07	RPS6KB2	3.67	-7.25
5	TEC	2.29	-8.08	PRKCA	3.06	-6.67
6	SYK	2.19	-7.50	SGK2	2.97	-8.05
7	SRC	2.16	-7.90	PRKG2	2.89	-6.43
8	SRMS	2.06	-8.11	PSKH1	2.82	-10.61
9	ABL1	2.05	-7.82	CAMK4	2.71	-8.23
10	BLK	2.05	-8.56	STK38L	2.62	-8.33

Table S4d Control + IGF1 vs shFurin + IGF1