Supplementary Table 1. Comparison of live cell imaging kinetic data using the GLIMMIX procedure

Treatment comparison	Genotype comparison	Estimate	Pr > |t|	Adj P	OR 1	OR 2
Birinapant v. DMSO	*Ripk1*$^{\Delta PMN}$ v wild-type	0.0943	<.0001	<.0001	1.0514	0.9569
	Ripk1^{D138N} v wild-type	0.0917	<.0001	<.0001	1.0768	0.9825
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v wild-type	0.1103	<.0001	<.0001	1.0726	0.9606
	Ripk1^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0026	0.6749	0.9988	1.0242	1.0268
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*$^{\Delta PMN}$	0.0160	0.0200	0.1142	1.0201	1.0039
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*^{D138N}	0.0186	0.0025	0.0148	0.9960	0.9777
Birinapant/zVAD-fmk v. DMSO	*Ripk1*$^{\Delta PMN}$ v wild-type	0.1529	<.0001	<.0001	1.1150	0.9569
	Ripk1^{D138N} v wild-type	0.1403	<.0001	<.0001	1.1305	0.9825
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v wild-type	0.1474	<.0001	<.0001	1.1132	0.9606
	Ripk1^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0126	0.0399	0.2165	1.0139	1.0268
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0055	0.4065	0.9563	0.9984	1.0039
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*^{D138N}	0.0072	0.2870	0.8686	0.9847	0.9777
zVAD-fmk/TNF v. TNF	*Ripk1*$^{\Delta PMN}$ v wild-type	0.0742	<.0001	<.0001	1.0172	0.9445
	Ripk1^{D138N} v wild-type	-0.0024	0.7467	0.9997	0.9997	1.0021
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v wild-type	0.0046	0.5728	0.9939	0.9909	0.9863
	Ripk1^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0766	<.0001	<.0001	0.9828	1.0610
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0696	<.0001	<.0001	0.9741	1.0443
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*^{D138N}	0.0070	0.3810	0.9437	0.9912	0.9842
Birinapant/zVAD-fmk/TNF v. TNF	*Ripk1*$^{\Delta PMN}$ v wild-type	0.2591	<.0001	<.0001	1.2239	0.9445
	Ripk1^{D138N} v wild-type	0.1759	<.0001	<.0001	1.1948	1.0021
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v wild-type	0.1699	<.0001	<.0001	1.1690	0.9863
	Ripk1^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0833	<.0001	<.0001	0.9763	1.0610
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0892	<.0001	<.0001	0.9551	1.0443
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*^{D138N}	-0.0060	0.4916	0.9827	0.9784	0.9842
Birinapant/TNF v. TNF	*Ripk1*$^{\Delta PMN}$ v wild-type	0.1258	<.0001	<.0001	1.0710	0.9445
	Ripk1^{D138N} v wild-type	0.1011	<.0001	<.0001	1.1087	1.0021
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v wild-type	0.0927	<.0001	<.0001	1.0821	0.9863
	Ripk1^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0247	0.0878	0.4238	1.0352	1.0610
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*$^{\Delta PMN}$	-0.0330	0.0300	0.1673	1.0103	1.0443
	Ptpn6$^{\Delta PMN}$*Ripk1*^{D138N} v *Ripk1*^{D138N}	-0.0084	0.4106	0.9581	0.9760	0.9842

Contrast estimate tables from log-binomial linear mixed models of CTG+ proportion. Each row specifies a genotype comparison and treatment comparison of interest. "Estimate" gives the unlinked estimate of the difference, between the two treatments of interest, of the differences between the two genotypes of interest. "Pr > |t|" gives the *p*-value of a *t* test against a null hypothesis that the unlinked difference of differences is equal to 0. "Adj P" gives the Sidak-corrected *p*-value. "OR 1" gives the hourly odds ratio for remaining in the CTG+ state between the specified genotypes in the first of the two compared treatments (e.g. BPT in the first comparison). "OR 2" gives the hourly odds ratio of the same genotypes in the second of two compared treatments (e.g. DMSO in the first comparison).

Supplementary Table 2. MS/MS analysis of proteins interacting with a wild-type Ptpn6 peptide from the C-SH2 domain of Ptpn6.

Proteins identified	Species	Number of peptides identified	Accession number
Band A (upper)			
Myosin-9	*Mus musculus*	106 (52 % coverage)	Q8VDD5
Actin, cytoplasmic 1	*Mus musculus*	4 (18 % coverage)	P60710
Band B (lower)			
Actin, cytoplasmic 2	*Mus musculus*	29 (81 % coverage)	P63260
Actin, cytoplasmic 1	*Mus musculus*	30 (81 % coverage)	P60710
Lamin-B receptor	*Mus musculus*	1 (2 % coverage)	Q3U9G9
Serine/threonine-protein kinase N1	*Mus musculus*	1 (1 % coverage)	P70268

Interacting proteins were isolated by incubation of biotinylated wild-type (Y208) peptides with mouse bone marrow neutrophil lysates and streptavidin beads. Protein complexes were analyzed by SDS-PAGE, and 2 bands were excised and subjected to LS-MS/MS analysis.