# Supplementary Materials

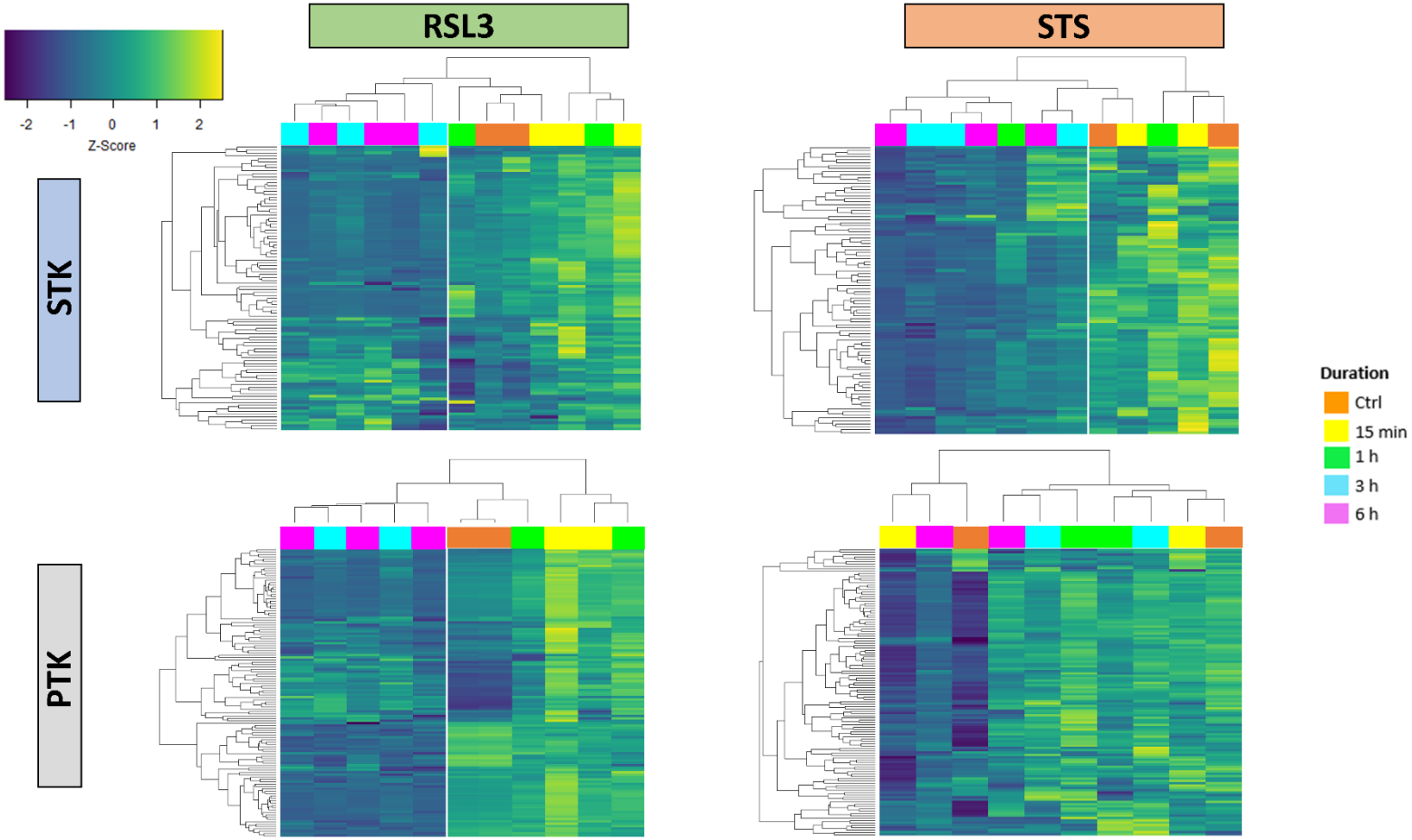



**Figure S1.** Heatmap visualization of individual phosphorylation intensities, represented as normalized z-scores, of peptides on serine/threonine kinase (STK) (upper panel) or tyrosine kinase (PTK) (lower panel) chips which serve as substrates for serine/threonine or tyrosine kinases, respectively. Higher z-scores (yellow) indicate kinase activation while lower z-scores (dark blue) indicate kinase inhibition. MM1R cells were treated with either 5 μM RSL3 (left panel) or 1 μM STS (right panel) for increasing timepoints, as indicated by the figure legend.

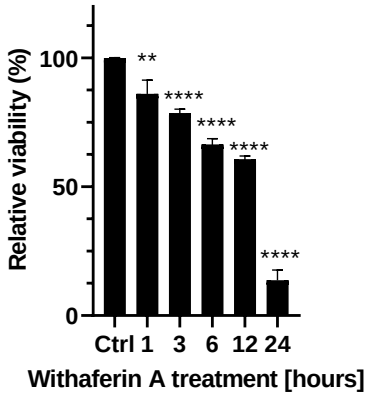



**Figure S2**. Relative cell viability (%) of MM1R cells treated with 1 μM WA. Data are presented as the mean ± s.d., n=3 biologically independent samples per treatment (**p < 0.01, ****p < 0.0001, ANOVA).

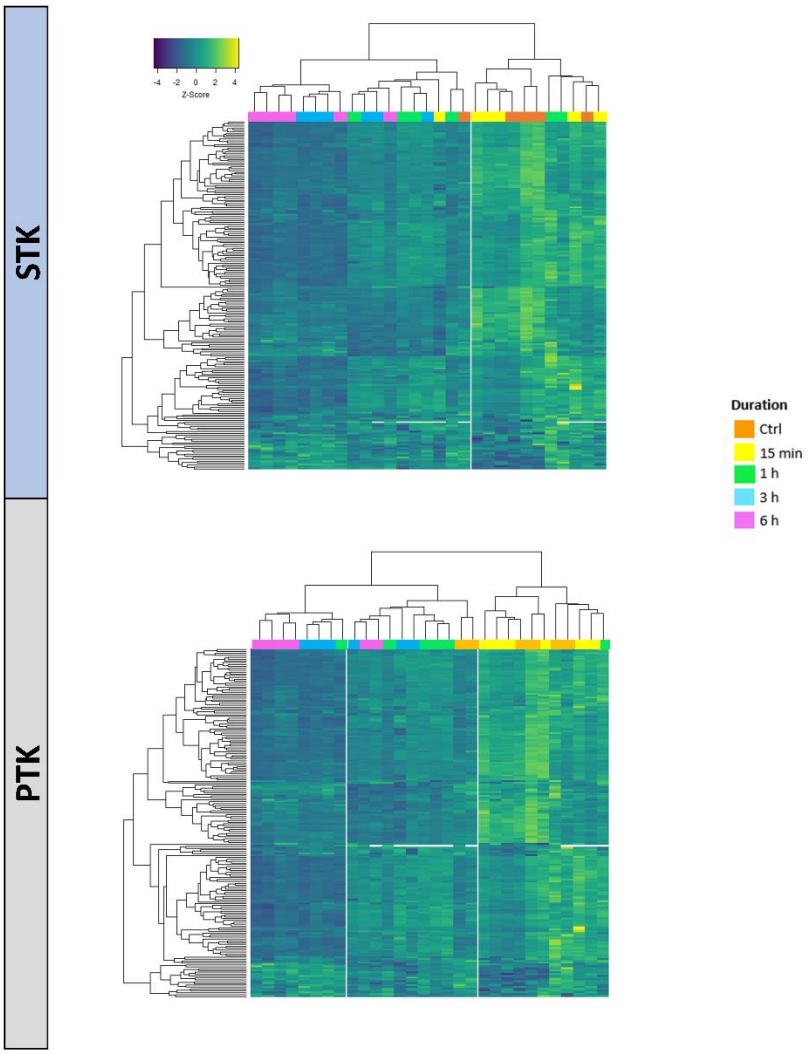



**Figure S3.** Heatmap visualization of individual phosphorylation intensities, represented as normalized z-scores, of peptides on serine/threonine kinase (STK) (upper panel) or tyrosine kinase (PTK) (lower panel) chips which serve as substrates for serine/threonine or tyrosine kinases, respectively. Higher z-scores (yellow) indicate kinase activation while lower z-scores (dark blue) indicate kinase inhibition. MM1R cells were treated with 1 μM Withaferin A for increasing timepoints, as indicated by the figure legend.

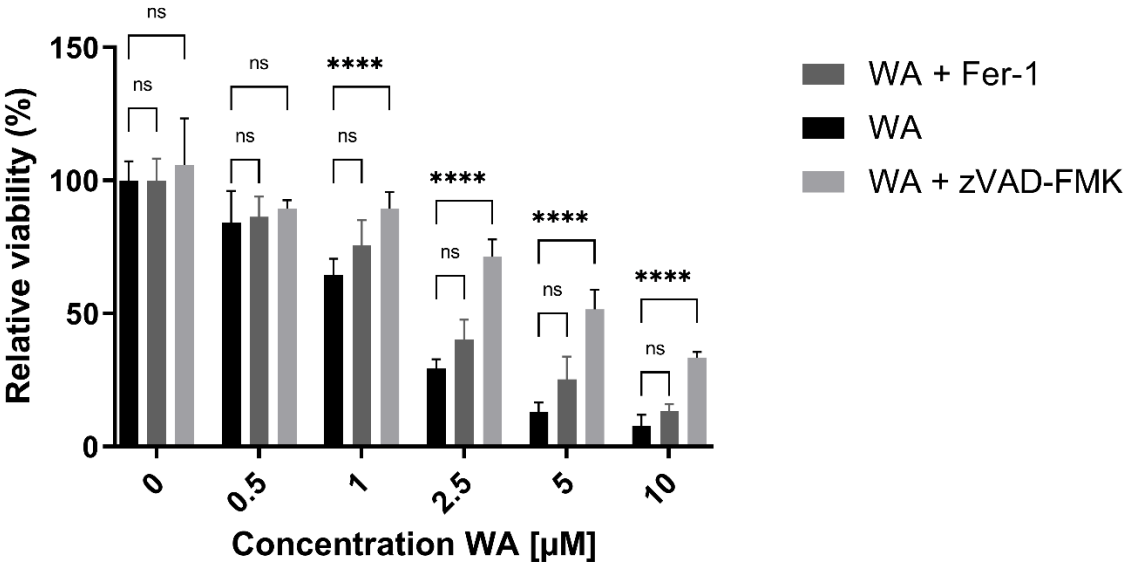



**Figure S4.** Relative cell viability (%) of MM1R cells treated with 1 μM WA for 24 hours with or without 2 hour pre-treatment with 2 μM ferrostatin-1 (Fer-1) or 50 μM zVAD-FMK. Data are presented as the mean ± s.d., n=3 biologically independent samples per treatment (ns $p > 0.05$, ****$p < 0.0001$, ANOVA).

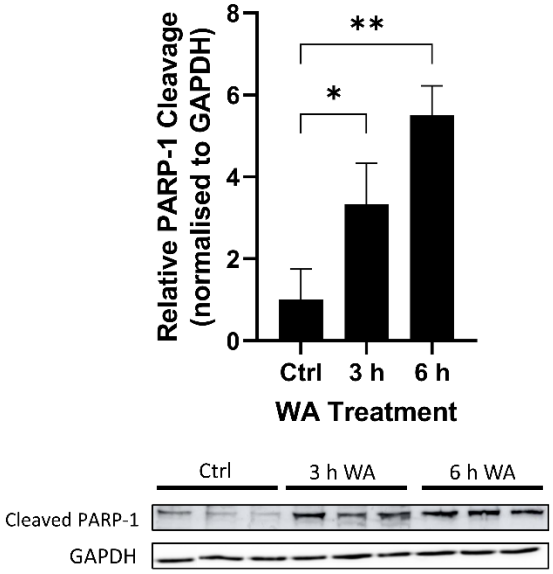



**Figure S5.** Western blot detection and quantification of PARP-1 cleavage and GAPDH expression levels in MM1R cells treated with 1 μM withaferin a (WA) for 3 and 6 hrs. All data are presented as the mean ± s.d., n=3 biologically independent samples per treatment (*$p < 0.05$, **$p < 0.01$, ANOVA).

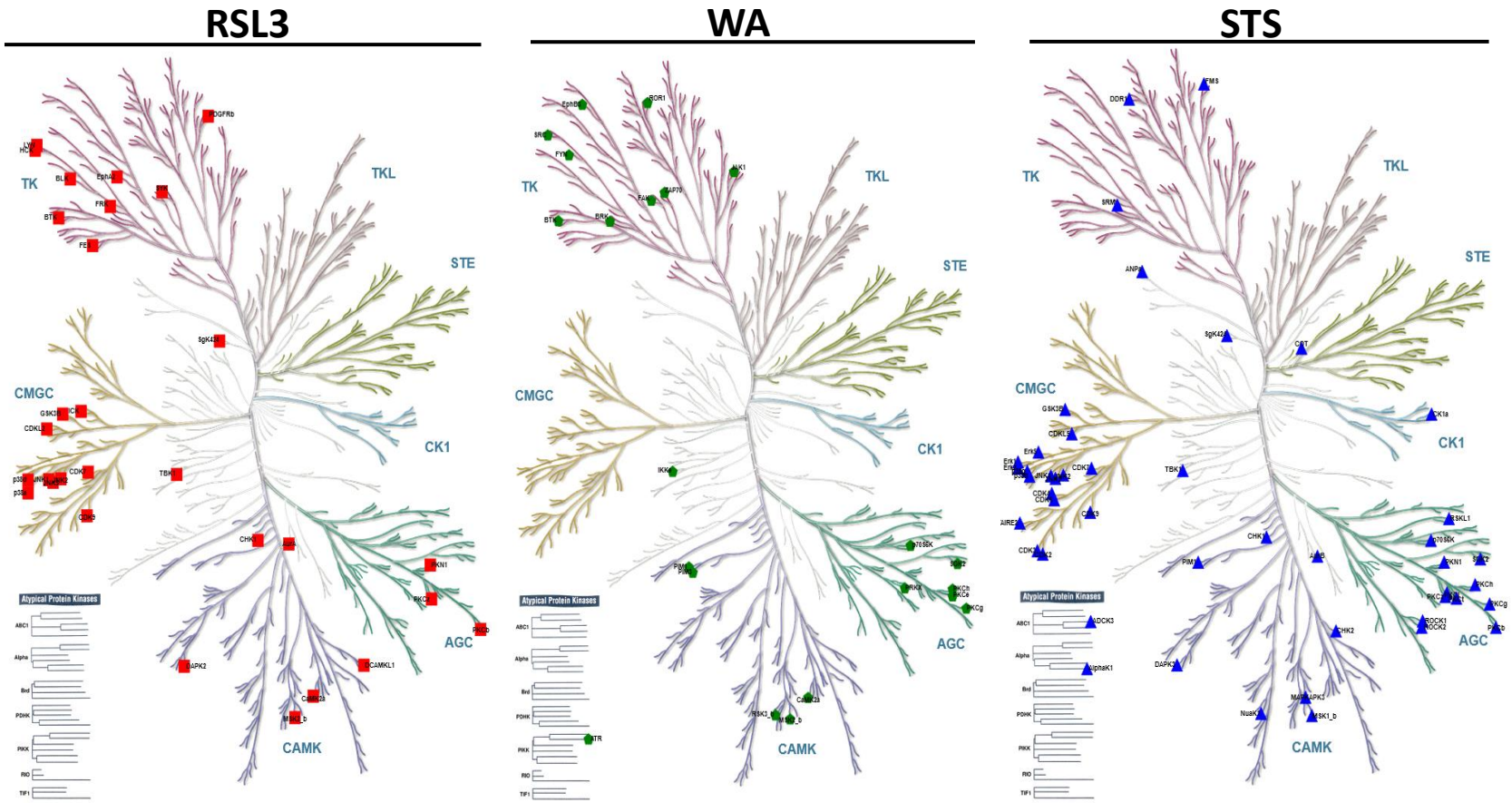
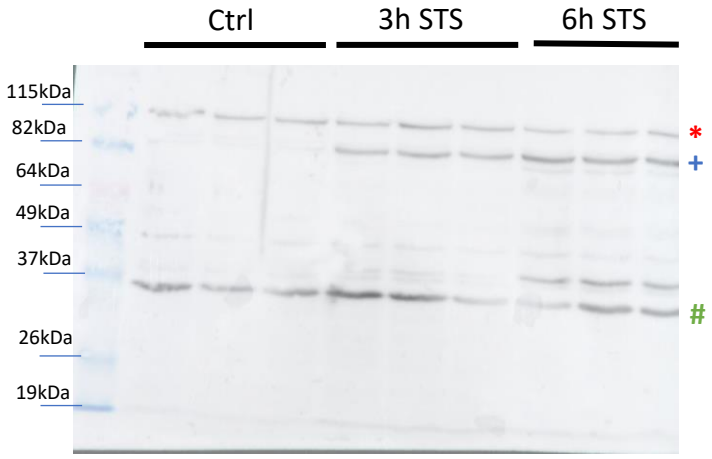
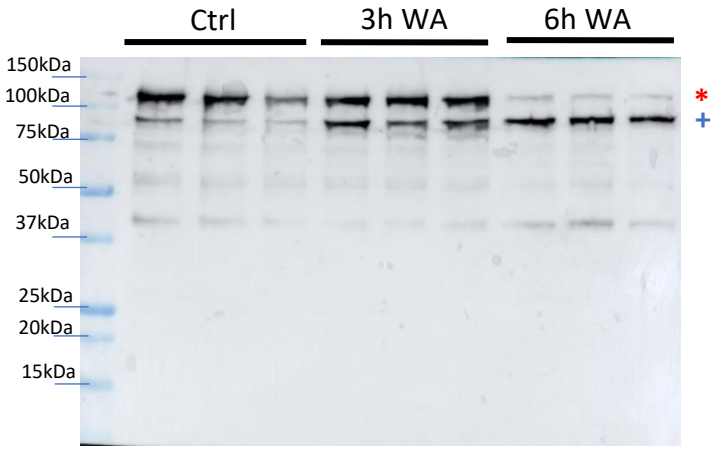
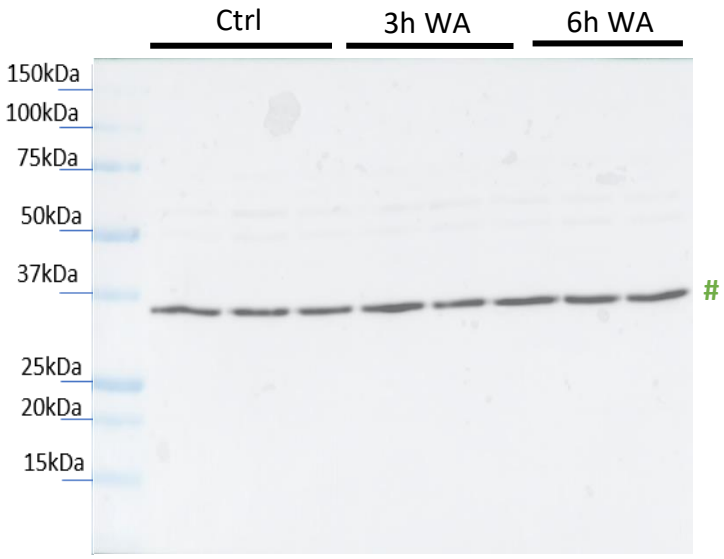
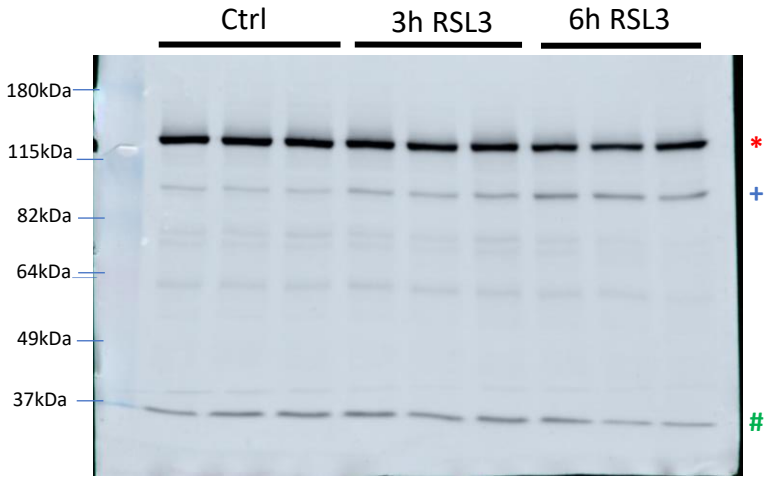



**Figure S6:** KinMap phylogenetic kinome tree. Kinases inhibited by RSL3 treatment are indicated by red squares (■) (left), kinases inhibited by STS treatment are marked as blue triangles (▲) (right), kinases inhibited by WA are indicated as green hexagons (⬢). Only kinases with a mean final score ≥ 1.3 are included in the graph. Abbreviations: TK, tyrosine kinase group ;TKL, tyrosine kinase-like group; STE, serine/threonine kinase group; CK1, casein kinase 1 group; AGC, protein kinase A, G, and C group; CAMK, $Ca^{2+}$/calmodulin-dependent kinase group; CMGC, cyclin-dependent kinase, mitogen-activated protein kinase, glycogen synthase kinase, and CDC-like kinase group.

**Table S1.** Original images western blot analysis

| **Figure** | **Blot(s) with molecular marker** |
|---|---|
| **1c**: Western blot detection and quantification of PARP-1 cleavage and GAPDH protein expression levels after STS treatment in MM1R cells | α-PARP-1 (full length 116 kDa*, cleaved 81 kDa+) and α-GAPDH (37 kDa#)<br>*marker:* Benchmark Pre-stained protein standard (Thermo, #10748-010)<br>  <br> |
| **S6:** Western blot detection and quantification of PARP-1 cleavage and GAPDH protein expression levels after WA treatment in MM1R cells | α-PARP-1 (full length 116 kDa*, cleaved 81 kDa+) and α-GAPDH (37 kDa#)<br>*marker:* Precision Plus Protein All Blue prestained protein standard (Bio-Rad, #1610373)<br><br>α-PARP-1<br>  <br> |

| | |
|---|---|
| | α-GAPDH<br>  <br> |
| **S1:** Western blot detection and quantification of PARP-1 cleavage and GAPDH protein expression levels after RSL3 treatment in MM1R cells | α-PARP-1 (full length 116 kDa*, cleaved 81 kDa+) and α-GAPDH (37 kDa#)<br>*marker:* Benchmark Pre-stained protein standard (Thermo, #10748-010)<br>  <br> |