SUPPLEMENTARY FIGURES AND TABLES

Supplementary Tables

Table S1.

GO-terms (biological process: BP-FAT, cellular component: CC-FAT, molecular function: MF-FAT) and KEGG pathways enriched in POS-stimulated phosphoproteome over POS-stimulated proteome. Table shows the percent of enrichment (%) and significance of each particular observation (Fisher's exact test, $P<0.05$).

Gene Ontology	Enriched term	%	significance
BP-FAT	single-organism organelle organization	3.275	2.61E-05
BP-FAT	cytoskeleton organization	2.924	1.08E-04
BP-FAT	cell-cell adhesion	3.509	3.35E-04
BP-FAT	microtubule cytoskeleton organization	0.936	3.45E-03
BP-FAT	actin cytoskeleton organization	2.105	6.30E-03
CC-FAT	cell-cell junction	3.392	2.44E-05
CC-FAT	actin cytoskeleton	2.690	3.29E-05
CC-FAT	cell-cell adherens junction	3.158	3.97E-05
CC-FAT	cell junction	4.795	4.81E-05
CC-FAT	adherens junction	4.561	5.10E-05
MF-FAT	cytoskeletal protein binding	2.924	1.65E-05
MF-FAT	cadherin binding	3.041	4.46E-05
MF-FAT	protein binding involved in cell-cell adhesion	3.041	4.46E-05
MF-FAT	protein binding involved in cell adhesion	3.041	4.46E-05
MF-FAT	cadherin binding involved in cell-cell adhesion	3.041	4.46E-05
KEGG PATHWAY	MAPK signalling pathway	0.702	5.86E-03
KEGG PATHWAY	Focal adhesion	1.053	2.04E-02

Table S2.

List of proteins and phosphorylation sites which exhibited significantly altered abundance/phosphorylation level in response to phagocytosis in both ARPE-19 and native RPE analysis.

Proteomic analysis	**Phosphoproteomic analysis**	
Protein	**Protein**	**Phosphorylation site**
ACTC1	ABI1	Ser184
ACTN4	AHNAK	Ser135
DECR1	AHNAK	Ser216
HNRNPA2B1	AHNAK	Ser1452
HNRNPH1	HNRNPU	Ser271
LIMA1	MAP1B	Ser1501
LMNA	MAPK1 (ERK2)	Tyr187
MYH14	MYLK	Ser365
NAMPT	NUFIP2	Ser629
PLEC	PDLIM4	Ser112
RPL30	PGM5	Ser122
SRI	PRKAR1A	Ser83
TPM1	RANBP2	Ser1160
VCL	RPTOR	Ser863
YWHAG	THRAP3	Ser682
	TRA2B	Thr201

Supplementary Figures

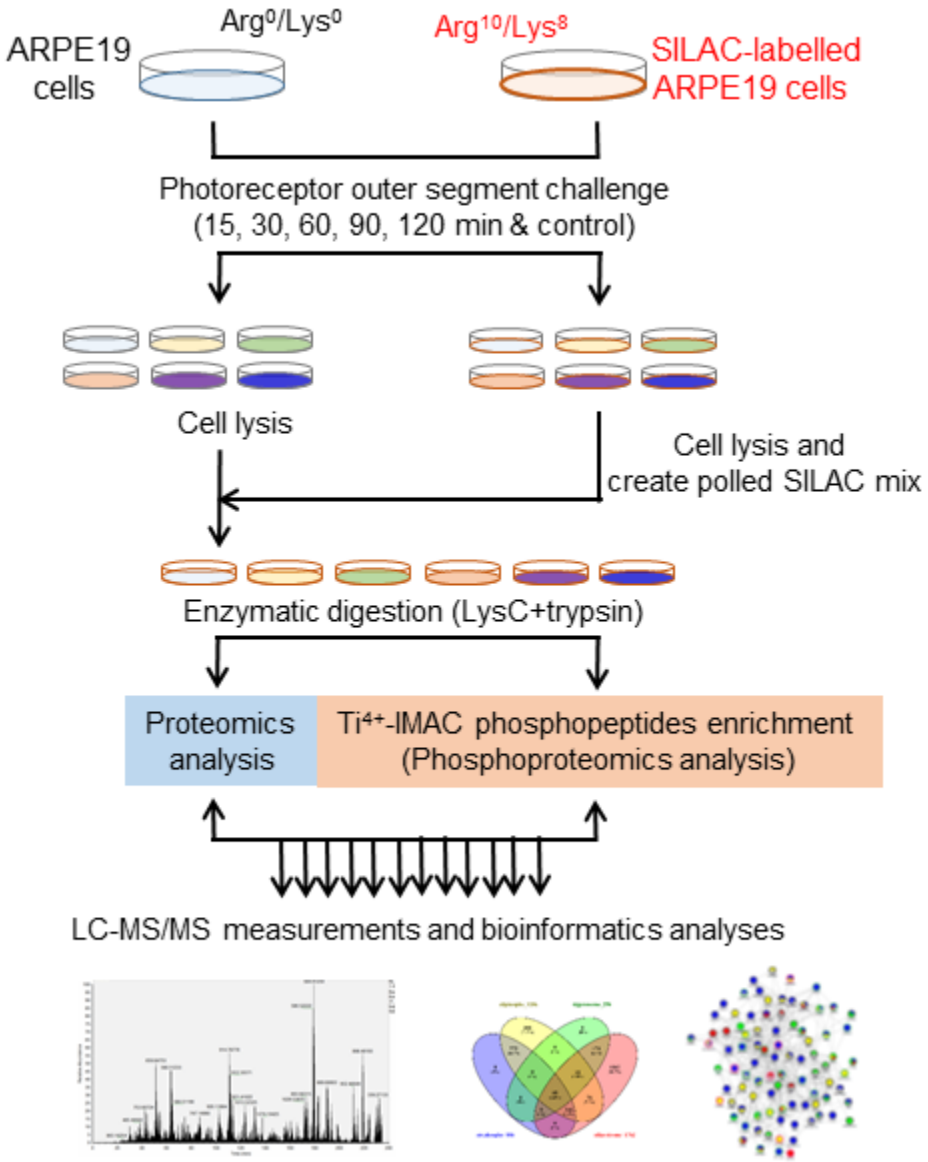

Figure S1. Schematic overview of the SILAC-based quantification of the ARPE-19 proteome and phosphoproteome under POS challenge for different time periods.

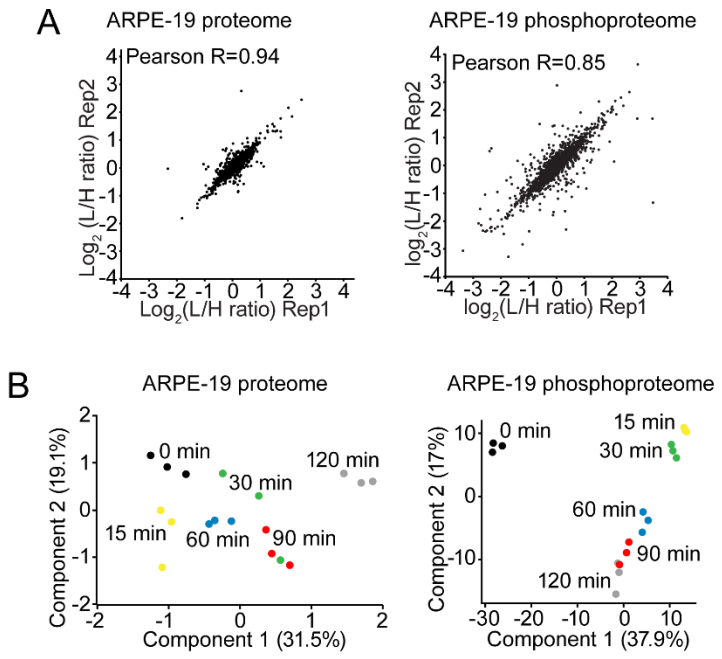

Figure S2. (A) Representative scatter plots showing the correlation between proteomic/phosphoproteomic measurements of biological replicates. (B) Principal component analysis (PCA) of significantly altered proteome (265 proteins) and phosphoproteome (1597 phosphosites).

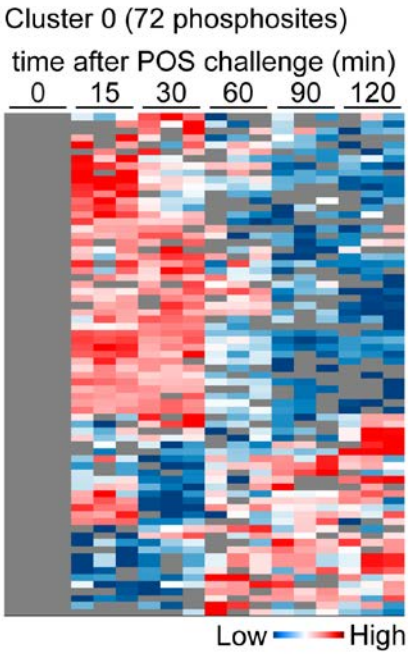

Figure S3. Heatmap showing relative phosphorylation levels of 72 sites with undetectable phosphorylation under control conditions (0 min). Phosphorylation levels are represented with color-coded boxes (blue: low, red: high, gray: not detected). Quantification for 3 biological replicates is presented for each time point.

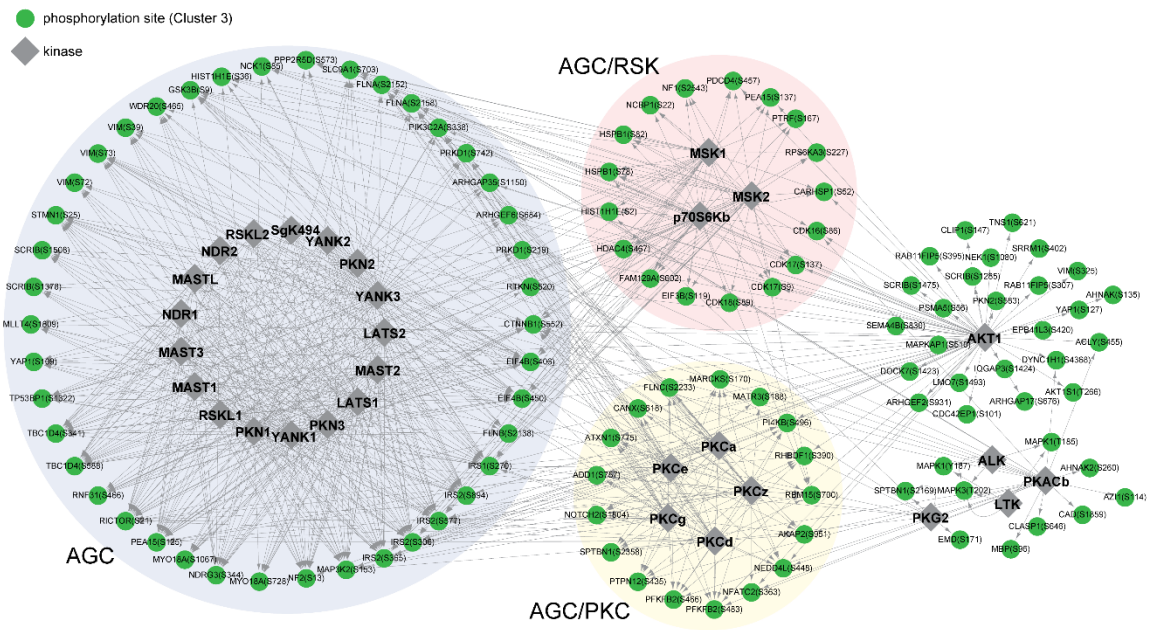

Figure S4. Protein interaction networks of potential site-specific kinase-substrate relations (ssKSRs) between the POS-stimulated phosphoproteome and enriched putative protein kinases. Information of each POS-stimulated dependent phosphorylation event was denoted by a different color code from each hierarchical cluster in Figure 2F.

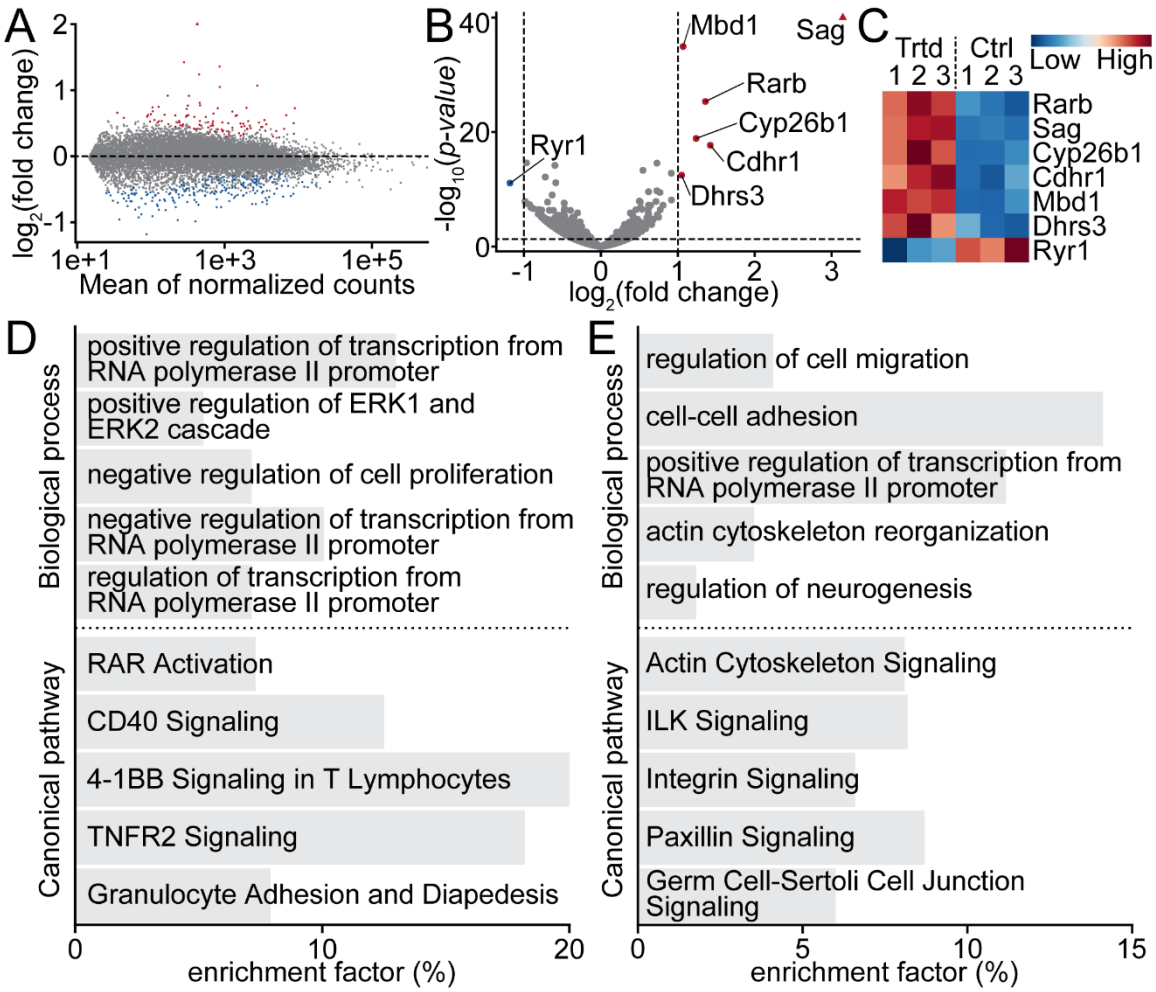

Figure S5. Transcriptomic and phosphoproteomic analysis of cultured primary RPE cells under POS stimulation

(A) RNA-seq libraries were generated for both POS-challenged and control primary RPE cells grown in culture (n=3). MA plot showing fold changes of individual genes in response to POS challenge. A total of 309 significantly altered genes (adjusted *P*-value <0.05) are marked in red (upregulated) or blue (downregulated). Significantly altered genes constituted less than 2.5% of the 12556 genes provided for the analysis after our initial pre-filtration steps. (B) Volcano plot showing rare genes with markedly (over 2-fold) increased or decreased expression under POS stimulation. (C) Heat map revealing normalized expression levels of seven markedly altered genes in three biological replicates of each condition. (D) Top five biological process GO-terms and enriched

canonical pathways characterizing the significantly altered transcriptome from cultured RPE cells. (E) Top five biological process GO-terms and enriched canonical pathways characterizing the subset of cultured RPE phosphoproteome homologous to the significantly altered phosphoproteome of ARPE-19.