Supplementary Figures

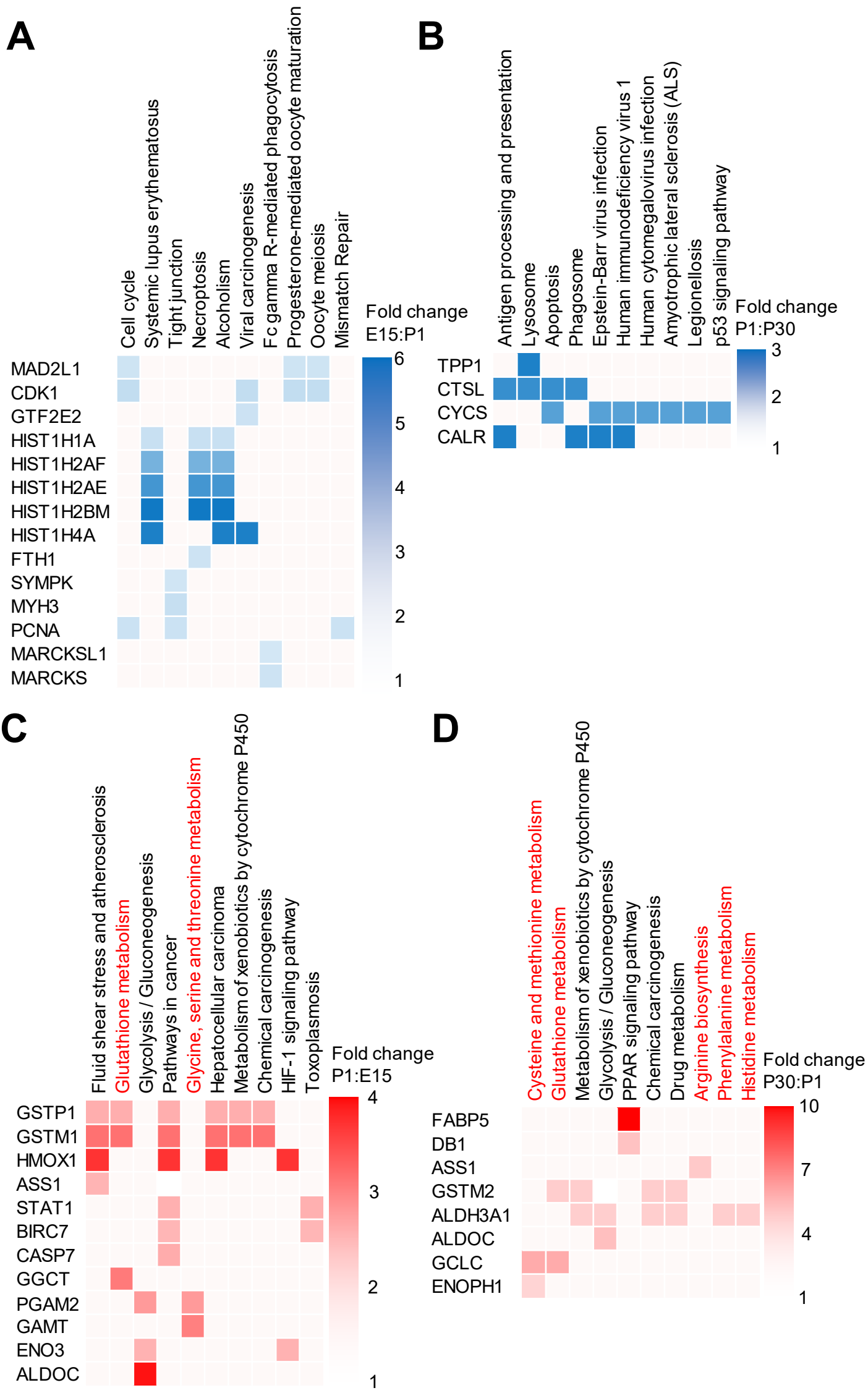
Fig. S1 Quantitative proteomics revealed upregulation in amino acid and glutathione metabolism pathways during WT lens development. **(A-B)** Developmentally downregulated DEPs in the lens at P1 compared to **(A)** E15 or **(B)** P1 compared to P30. **(C-D)** Developmentally upregulated DEPs in the lens at P1 compared to **(C)** E15 or **(D)** P1 compared to P30. The top ten (ranking by p-value) associated KEGG pathways are shown. Fold changes are indicated by color intensity according to key on right (blue is downregulated, red is upregulated developmentally). Pathways involved in glutathione and amino acid metabolism are highlighted in red.

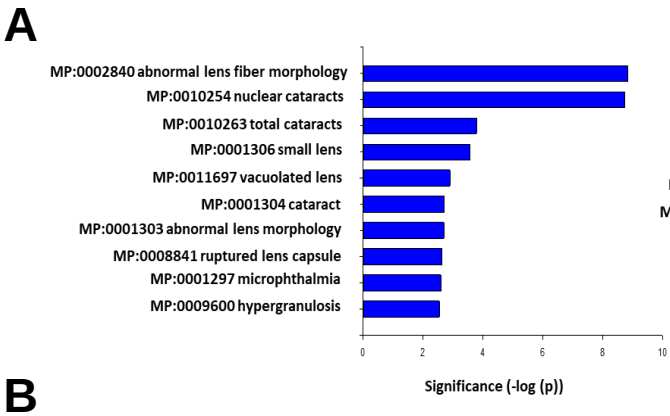
Fig. S2 Mammalian phenotypes ontology characteristics associated with DEPs in K6W-Ub lenses. **(A-C)** Bar chart based on the -log10(p-value) of top 10 enriched terms from the MGI Mammalian Phenotype library associated with downregulated proteins in K6W-Ub lenses at **(A)** E15**, (B)** P1**,** and **(C)** P30. **(D-F)** Bar chart based on the -log10(p-value) of top 10 enriched terms from the MGI Mammalian Phenotype library associated with upregulated DEPs in K6W-Ub lenses at **(D)** E15, **(E)** P1, and **(F)** P30.

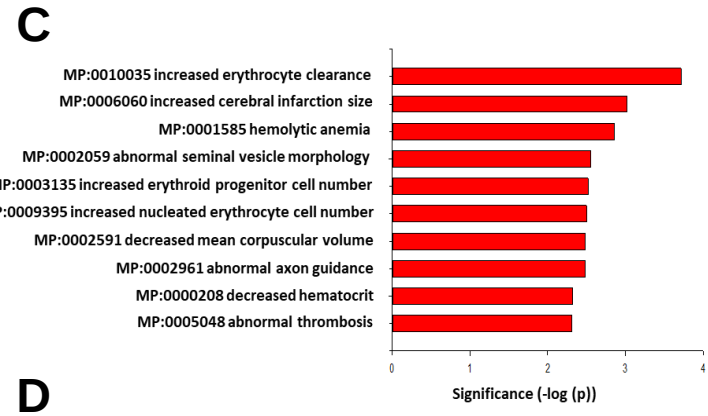
Fig. S3 Gene ontology biological processes associated with DEPs in K6W-Ub lenses. **(A-C)** Bar chart based on the -log10(p-value) of top 10 enriched terms from the GO Biological Process library associated with downregulated proteins in K6W-Ub lenses at **(A)** E15, **(B)** P1, and **(C)** P30. **(D-F)** Bar chart based on the -log10(p-value) of top 10 enriched terms from the GO Biological Process associated with upregulated DEPs in K6W-Ub lenses at **(D)** E15, **(E)** P1, and **(F)** P30.

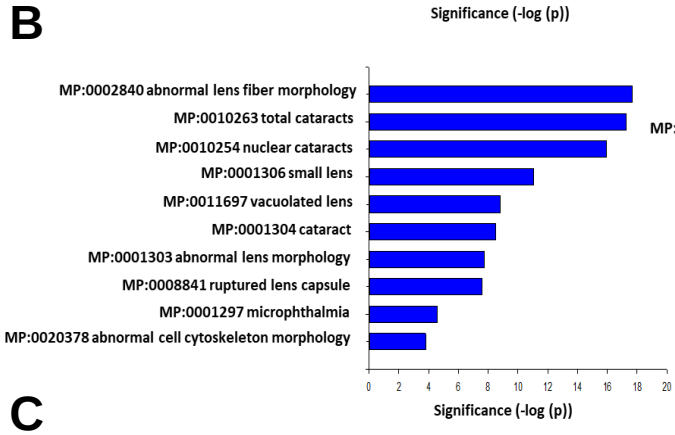
Fig. S4 CMP data quantification for different metabolites in lenses from WT and K6W-Ub collected at different developmental stages. **(A-N)** Average intensity for **(A)** alanine, **(B)** cysteine, **(C)** aspartate, **(D)** lysine, **(E)** glutamate, **(F)** glutamine, **(G)** glycine, **(H)** arginine, **(I)** valine, and **(J)** serine in wild types and K6W-Ub lenses collected at E15 (*left*), P1 (*middle*) and P30 (*right*) are shown. All values are mean ± SEM. and differences with WT were significant for (**) $p<0.01$; n.s., not significant; n.a., not applicable due to sample size.

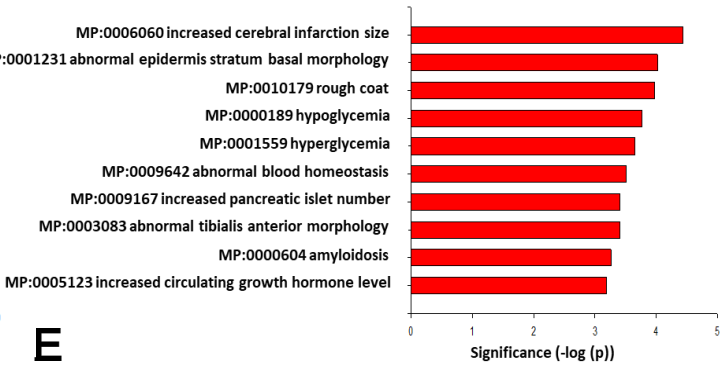
Fig. S5 HPLC data for different metabolites in lenses from WT and K6W-Ub collected at different developmental stages. **(A-N)** Lens content of **(A)** GSH, **(B)** GSSG, **(C)** serine, **(D)** glutamine, **(E)** histidine, **(F)** glycine, **(G)** threonine, **(H)** valine, **(I)** phenylalanine, **(J)** phenylalanine, **(K)** tyrosine, **(L)** lysine, **(M)** aspartic acid and **(N)** glutamic acid in wild types and K6W-Ub lenses collected at P1 (*left*) and P30 (*right*) are shown. All values are mean ± SEM. and differences with WT were significant for (**) $p<0.01$.

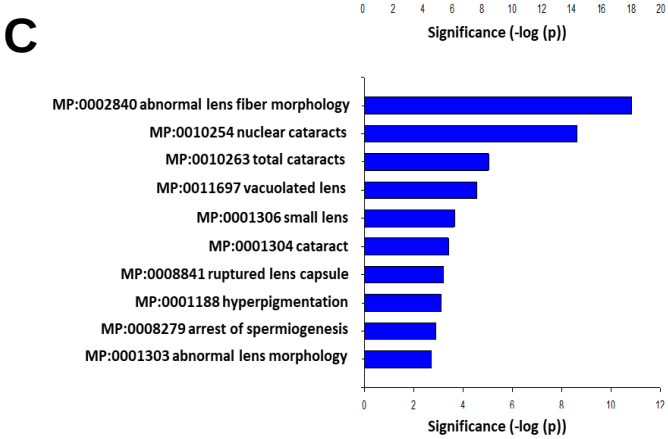

A
Cell cycle
Systemic lupus erythematosus
Tight junction
Necroptosis
Alcoholism
Viral carcinogenesis
Fc gamma R-mediated phagocytosis
Progesterone-mediated oocyte maturation
Oocyte meiosis
Mismatch Repair
MAD2L1
CDK1
GTF2E2
HIST1H1A
HIST1H2AF
HIST1H2AE
HIST1H2BM
HIST1H4A
FTH1
SYMPK
MYH3
PCNA
MARCKSL1
MARCKS
Fold change
E15:P1
6
5
4
3
2
1
B
Antigen processing and presentation
Lysosome
Apoptosis
Phagosome
Epstein-Barr virus infection
Human immunodeficiency virus 1
Human cytomegalovirus infection
Amyotrophic lateral sclerosis (ALS)
Legionellosis
p53 signaling pathway
TPP1
CTSL
CYCS
CALR
Fold change
P1:P30
3
2
1
C
Fluid shear stress and atherosclerosis
Glutathione metabolism
Glycolysis / Gluconeogenesis
Pathways in cancer
Glycine, serine and threonine metabolism
Hepatocellular carcinoma
Metabolism of xenobiotics by cytochrome P450
Chemical carcinogenesis
HIF-1 signaling pathway
Toxoplasmosis
GSTP1
GSTM1
HMOX1
ASS1
STAT1
BIRC7
CASP7
GGCT
PGAM2
GAMT
ENO3
ALDOC
Fold change
P1:E15
4
3
2
1
D
Cysteine and methionine metabolism
Glutathione metabolism
Metabolism of xenobiotics by cytochrome P450
Glycolysis / Gluconeogenesis
PPAR signaling pathway
Chemical carcinogenesis
Drug metabolism
Arginine biosynthesis
Phenylalanine metabolism
Histidine metabolism
FABP5
DB1
ASS1
GSTM2
ALDH3A1
ALDOC
GCLC
ENOPH1
Fold change
P30:P1
10
7
4
1

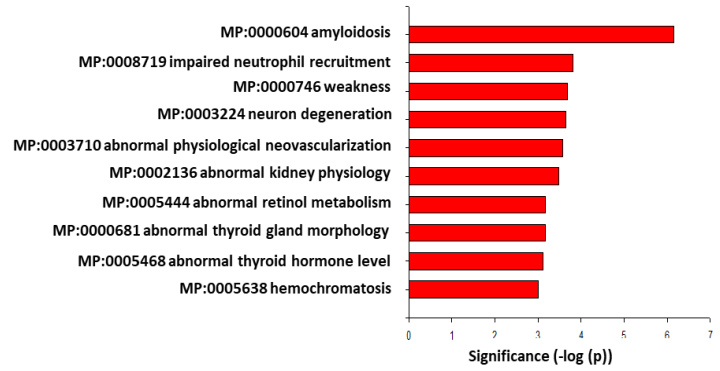




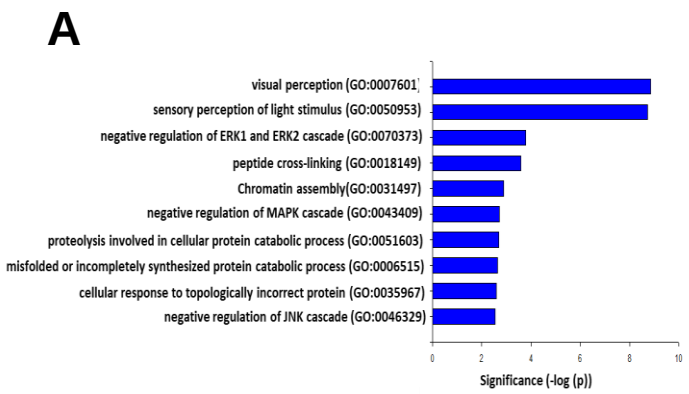


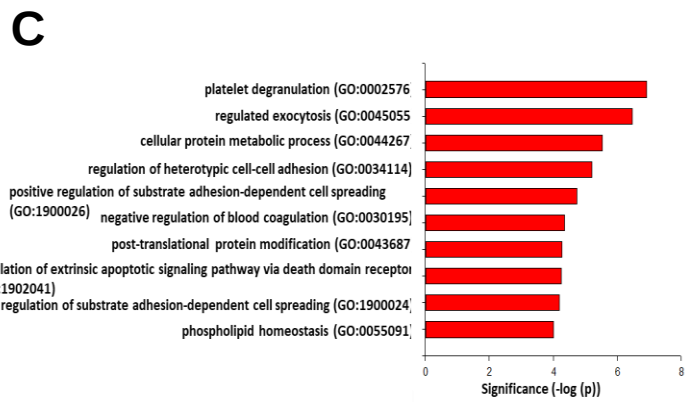


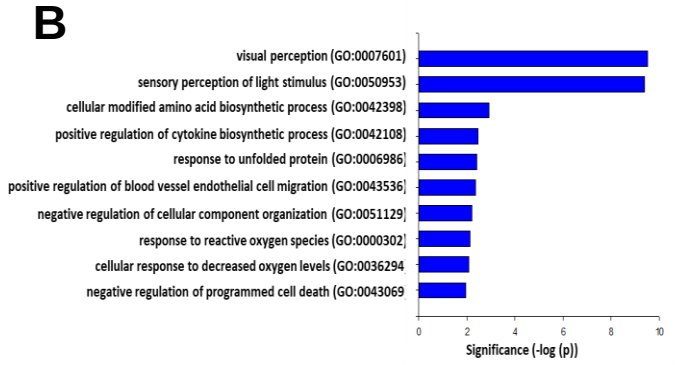


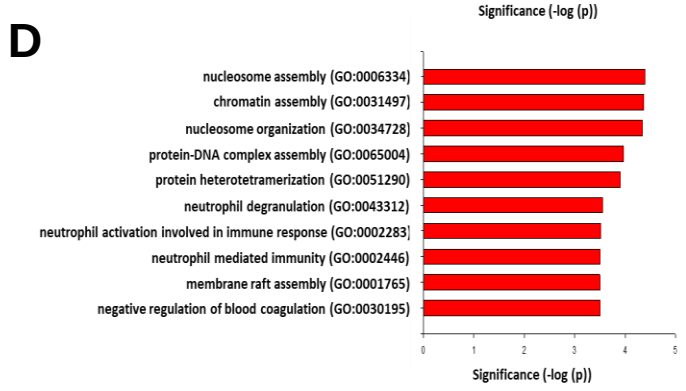


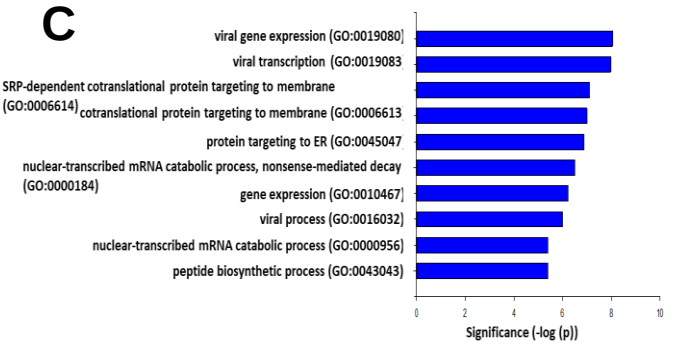
Congenital cataracts and unbalanced redox status.- Supp Figure 2


A
visual perception (GO:0007601)
sensory perception of light stimulus (GO:0050953)
negative regulation of ERK1 and ERK2 cascade (GO:0070373)
peptide cross-linking (GO:0018149)
Chromatin assembly(GO:0031497)
negative regulation of MAPK cascade (GO:0043409)
proteolysis involved in cellular protein catabolic process (GO:0051603)
misfolded or incompletely synthesized protein catabolic process (GO:0006515)
cellular response to topologically incorrect protein (GO:0035967)
negative regulation of JNK cascade (GO:0046329)
0 2 4 6 8 10
Significance (-log (p))


C
platelet degranulation (GO:0002576)
regulated exocytosis (GO:0045055)
cellular protein metabolic process (GO:0044267)
regulation of heterotypic cell-cell adhesion (GO:0034114)
positive regulation of substrate adhesion-dependent cell spreading (GO:1900026)
negative regulation of blood coagulation (GO:0030195)
post-translational protein modification (GO:0043687)
gulation of extrinsic apoptotic signaling pathway via death domain receptor
O:1902041)
regulation of substrate adhesion-dependent cell spreading (GO:1900024)
phospholipid homeostasis (GO:0055091)
0 2 4 6 8
Significance (-log (p))


B
visual perception (GO:0007601)
sensory perception of light stimulus (GO:0050953)
cellular modified amino acid biosynthetic process (GO:0042398)
positive regulation of cytokine biosynthetic process (GO:0042108)
response to unfolded protein (GO:0006986)
positive regulation of blood vessel endothelial cell migration (GO:0043536)
negative regulation of cellular component organization (GO:0051129)
response to reactive oxygen species (GO:0000302)
cellular response to decreased oxygen levels (GO:0036294)
negative regulation of programmed cell death (GO:0043069)
0 2 4 6 8 10
Significance (-log (p))


D
nucleosome assembly (GO:0006334)
chromatin assembly (GO:0031497)
nucleosome organization (GO:0034728)
protein-DNA complex assembly (GO:0065004)
protein heterotetramerization (GO:0051290)
neutrophil degranulation (GO:0043312)
neutrophil activation involved in immune response (GO:0002283)
neutrophil mediated immunity (GO:0002446)
membrane raft assembly (GO:0001765)
negative regulation of blood coagulation (GO:0030195)
0 1 2 3 4 5
Significance (-log (p))


C
viral gene expression (GO:0019080)
viral transcription (GO:0019083)
SRP-dependent cotranslational protein targeting to membrane (GO:0006614)
cotranslational protein targeting to membrane (GO:0006613)
protein targeting to ER (GO:0045047)
nuclear-transcribed mRNA catabolic process, nonsense-mediated decay (GO:0000184)
gene expression (GO:0010467)
viral process (GO:0016032)
nuclear-transcribed mRNA catabolic process (GO:0000956)
peptide biosynthetic process (GO:0043043)
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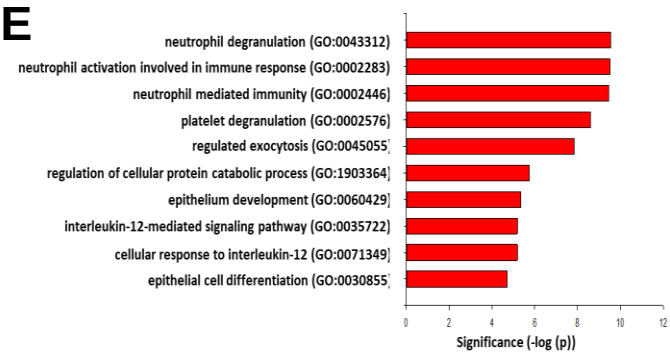
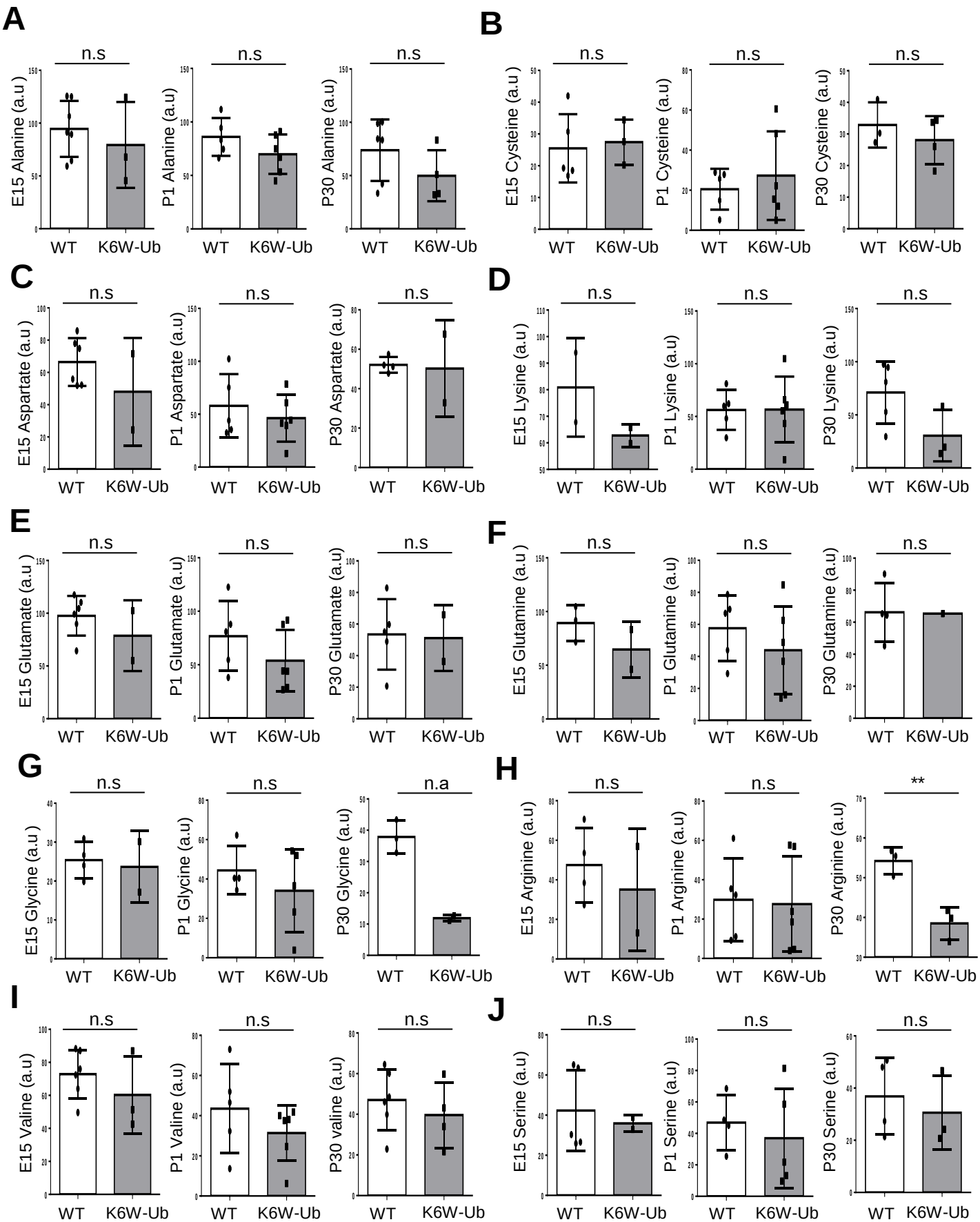
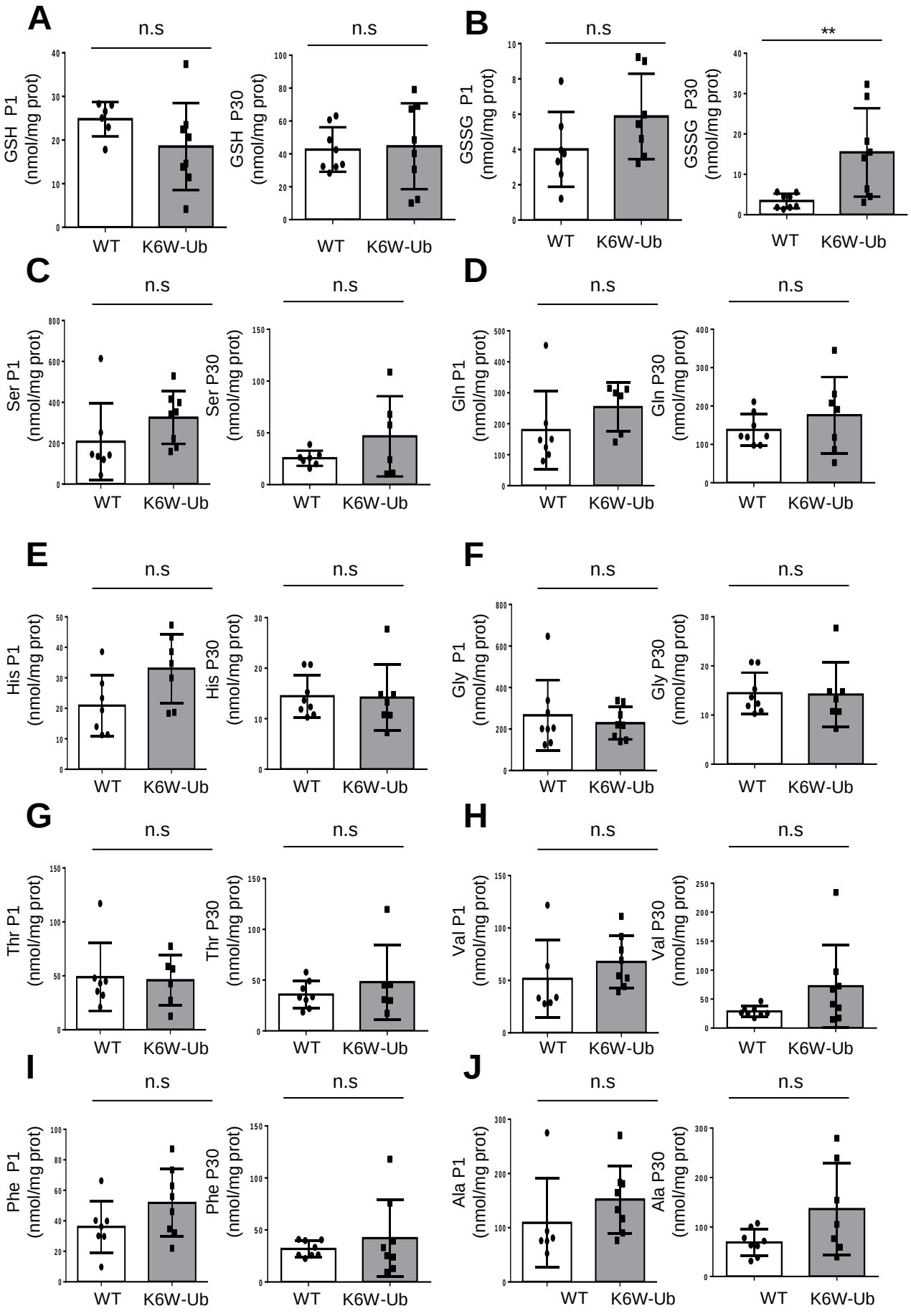
Significance (-log (p))

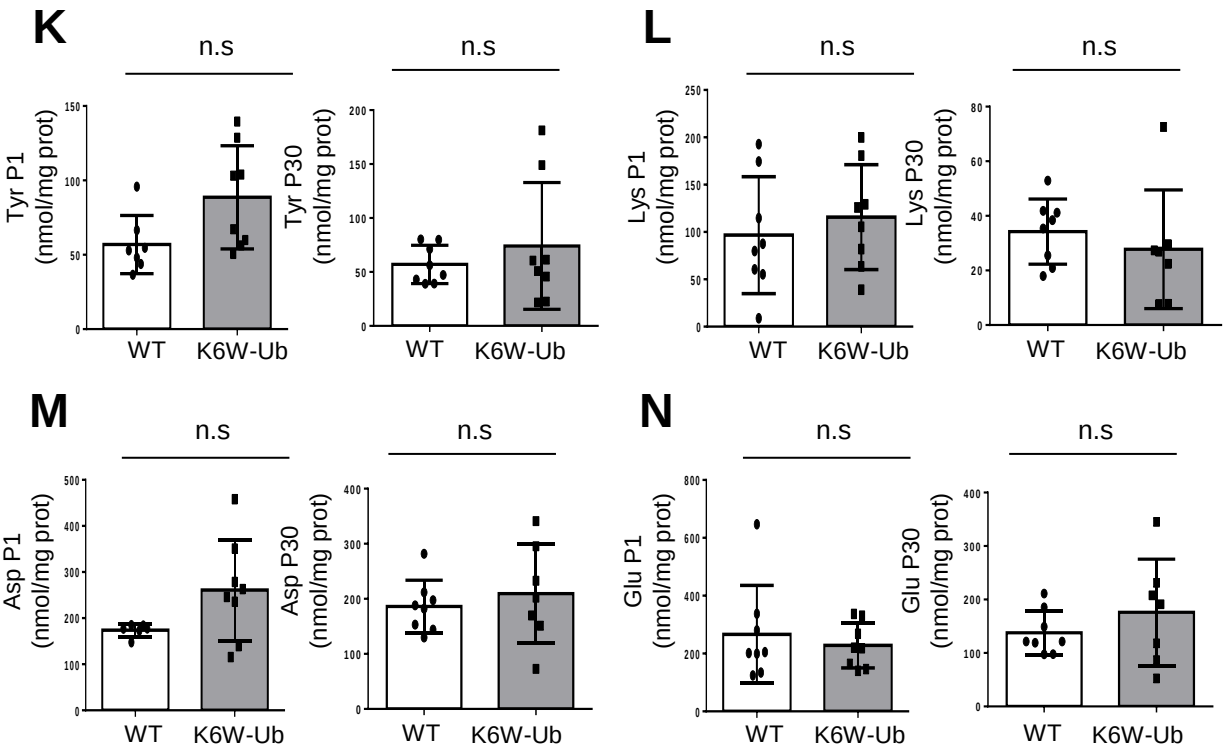

E
neutrophil degranulation (GO:0043312)
neutrophil activation involved in immune response (GO:0002283)
neutrophil mediated immunity (GO:0002446)
platelet degranulation (GO:0002576)
regulated exocytosis (GO:0045055)
regulation of cellular protein catabolic process (GO:1903364)
epithelium development (GO:0060429)
interleukin-12-mediated signaling pathway (GO:0035722)
cellular response to interleukin-12 (GO:0071349)
epithelial cell differentiation (GO:0030855)
0 2 4 6 8 10 12
Significance (-log (p))



Congenital cataracts and unbalanced redox status.- Suppl. Figure 4



Congenital cataracts and unbalanced redox status.- Supp Figure 5



Congenital cataracts and unbalanced redox status.- Supp Figure 5 (cont)