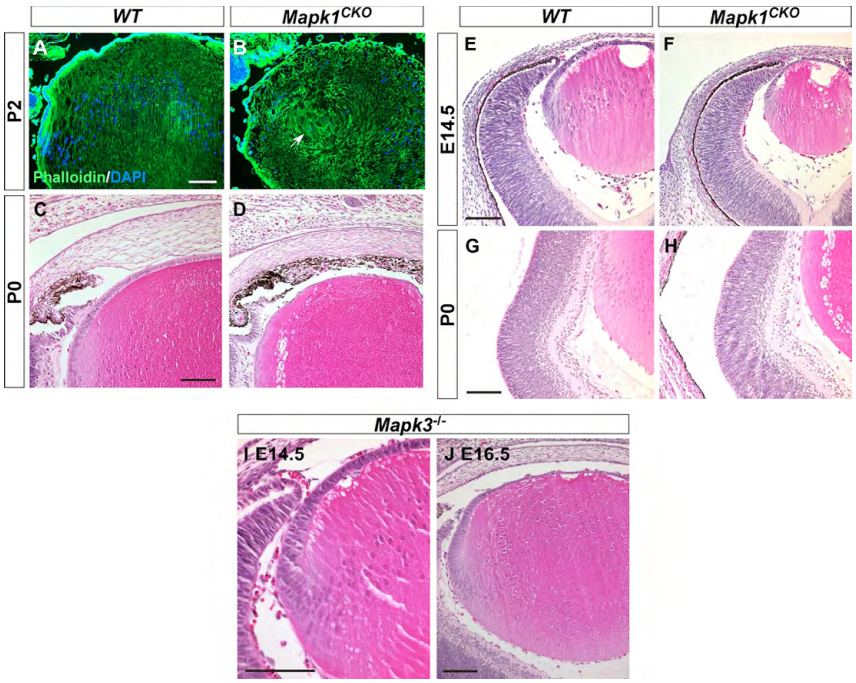

Fig. S1. Phalloidin staining and lens/eye histology. (**A**,**B**) Phalloidin labels F-actin in P2 mouse lenses. Compared with WT lens, *Mapk1*^{CKO} lens had disorganized fiber cells. Some areas showed a degenerative phenotype (arrow in B). (**C**,**D**) Anterior segment defects. The corneal endothelium and anterior chamber were absent in *Mapk1*^{CKO} eyes. The iris developed abnormally and was attached to the cornea in *Mapk1*^{CKO} eyes. (**E-H**) Despite the lens defects, retinal development did not seem to be affected at E14.5 (F) and P0 (H) in *Mapk1*^{CKO} eyes when compared with WT eyes (E,G, respectively). (**I**,**J**) No eye phenotype was observed in E14.5 or E16.5 *Mapk3*$^{-/-}$ mice. Scale bars: 100 μm.

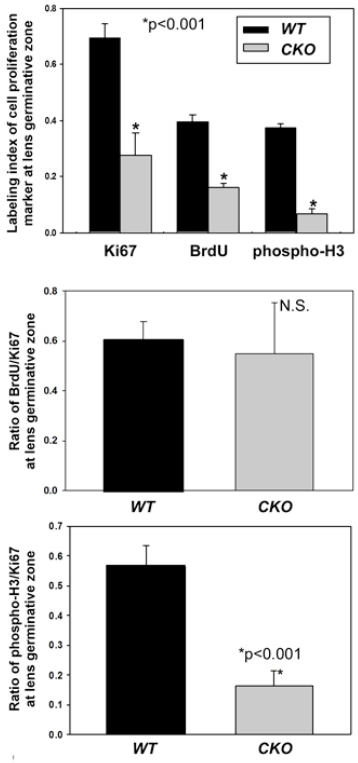

Fig. S2. Cell proliferation markers in the lens germinative zone (10-30º as shown in Fig. 3A,B). The labeling indices for all three markers were significantly reduced (top panel). When the ratios of BrdU/Ki67 and phospho-H3/Ki67 were calculated, we found no significant change in the BrdU/Ki67 ratio between WT and *Mapk1*^{CKO} lenses (middle panel), whereas the ratio of phospho-H3/Ki67 was significantly reduced in *Mapk1*^{CKO} lenses (bottom panel). These data suggest that the G2-M phase was most affected by MAPK1 deficiency. We also speculate that the decrease in Ki67 index in *Mapk1*^{CKO} lens could be a result of a shortened late G2/M phase, extended G0/G1 phase, or a combination of both.

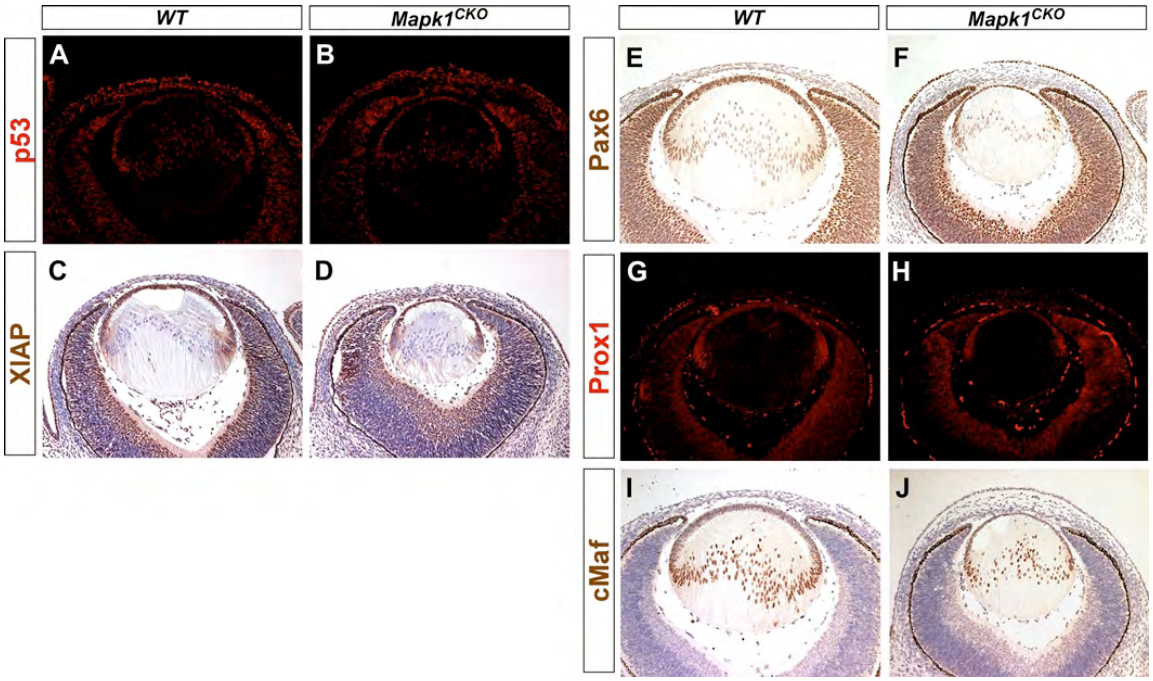

Fig. S3. Expression of apoptosis regulatory proteins (p53 and XIAP) and transcription factors (PAX6, PROX1 and cMAF) important for lens development in E14.5 mouse lens. (**A-J**) No change in expression patterns was observed for these proteins between WT and *Mapk1*^{CKO} lenses.

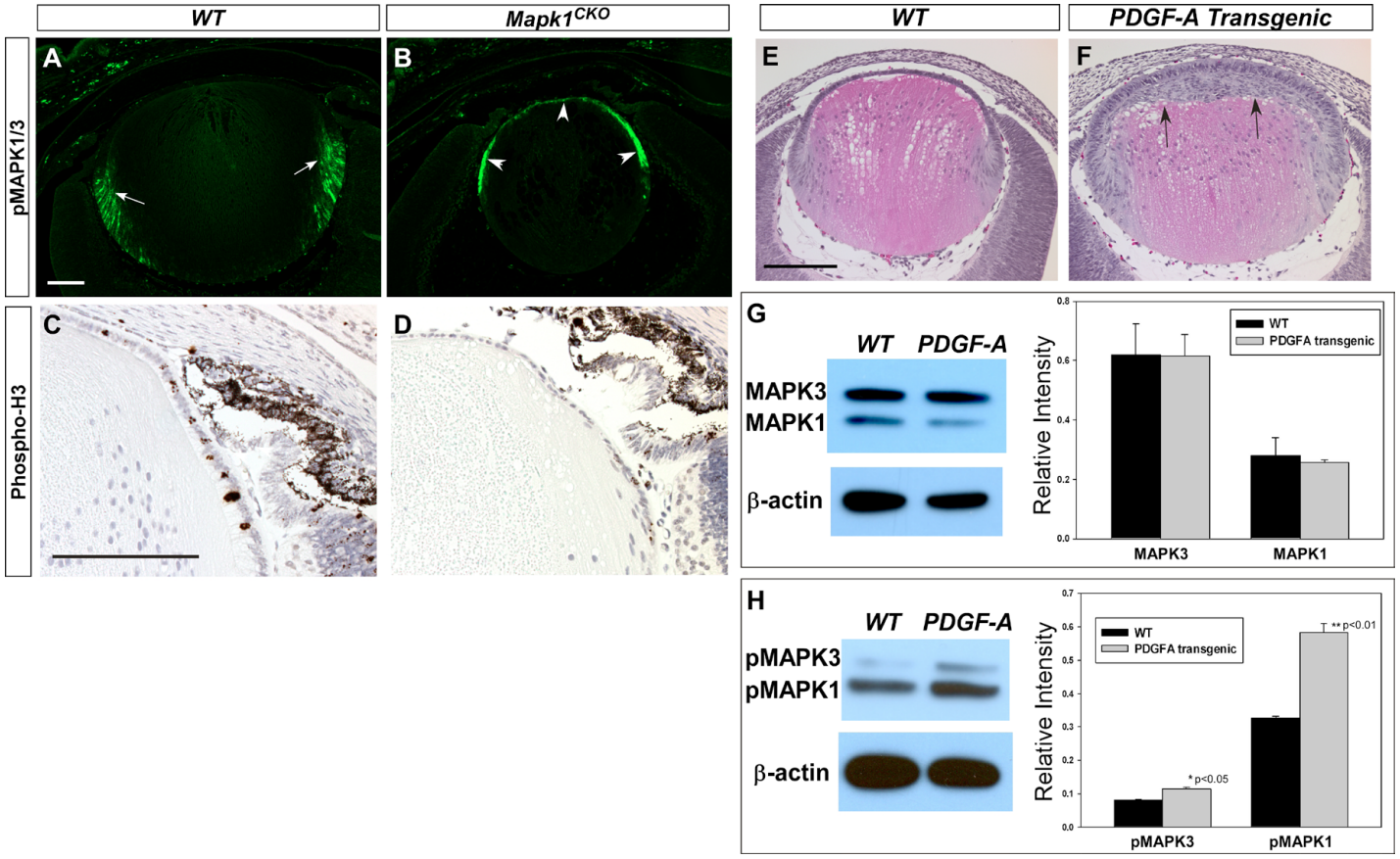

Fig. S4. MAPK activation and cell proliferation analysis. (**A**,**B**) pMAPK1/3 immunofluorescence was performed without TSA enhancement. In *Mapk1*^{CKO} lens, the level of pMAPK (equivalent to pMAPK3) was increased in the epithelium, likely as a result of an adaptive response to compensate for the loss of MAPK1 activity. Furthermore, the hyperactive region of pMAPK (arrows in A, WT) was shifted anteriorly in *Mapk1*^{CKO} lens (arrowheads in B). This change could be caused by the reduction in lens size and consequent anterior shift of the developing iris and ciliary body in the *Mapk1*^{CKO} eye. (**C**,**D**) Phospho-H3 immunohistochemistry. Increase of pMAPK3 did not rescue cell proliferation defects in *Mapk1*^{CKO} lens. (**E-H**) *PDGFA* transgenic mice. PDGF-A overexpression in the lens induced overproliferation of the lens epithelial cells (arrows in F). MAPK1/3 protein levels were unaltered, but pMAPK1/3 levels were higher in *PDGFA* transgenic lenses (G,H) than in WT lenses. A 40% increase in the pMAPK3 levels and an 80% increase in the pMAPK1 levels occurred in *PDGFA* transgenic lenses, compared with WT lenses, suggesting that MAPK1 is more responsive to PDGF-A stimulation. Scale bars: 100 μm. **P*<0.05, ***P*<0.01.