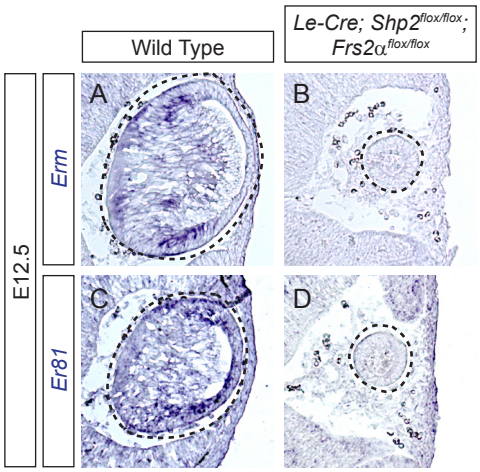
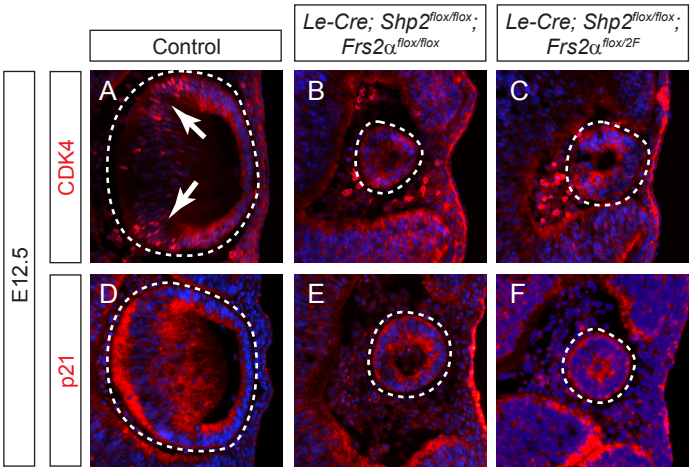
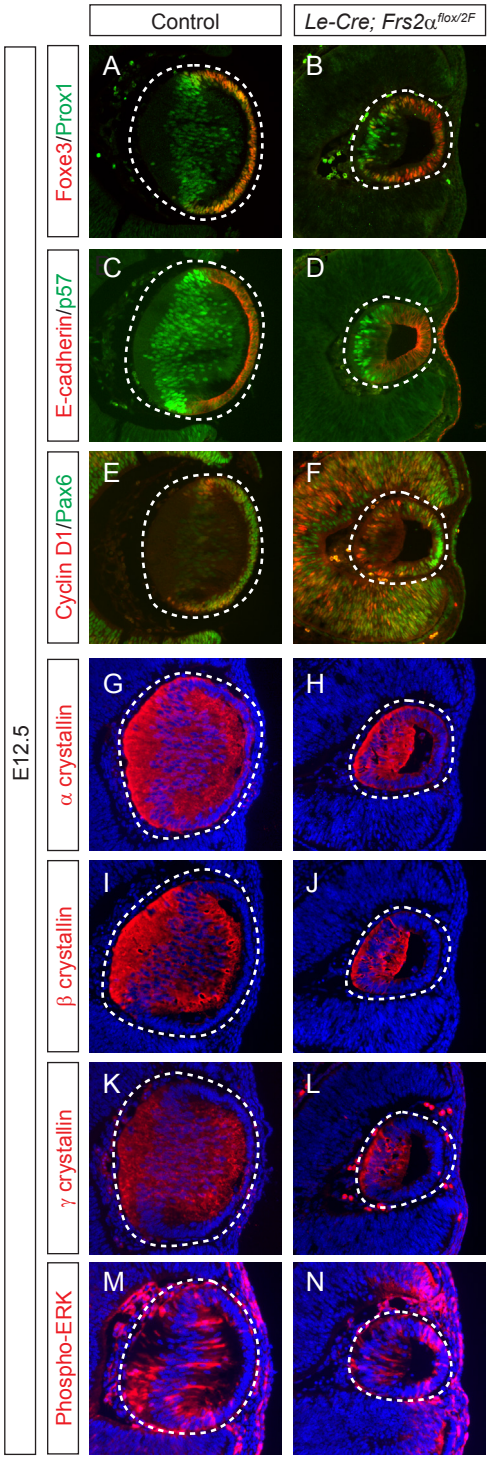


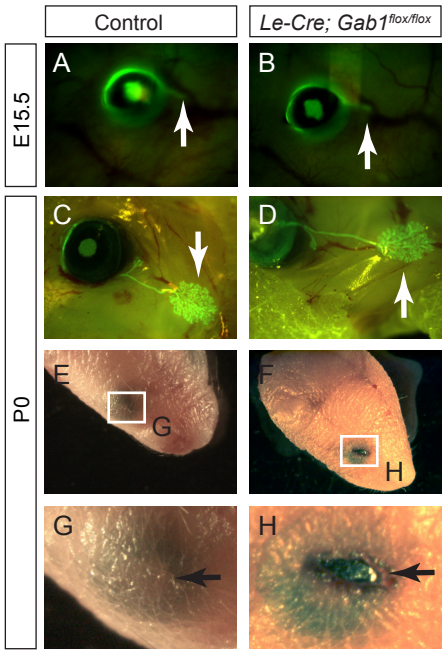
Supplementary Figure 1. (A-D) RNA in situ hybridization shows that FGF signaling-response genes *Erm* and *Er81* were down regulated in E12.5 *Le-Cre*; *Shp2*$^{flox/flox}$; *Frs2α*$^{flox/flox}$ lens. Three embryos of each genotype were analyzed. Dashed lines encircled lenses.



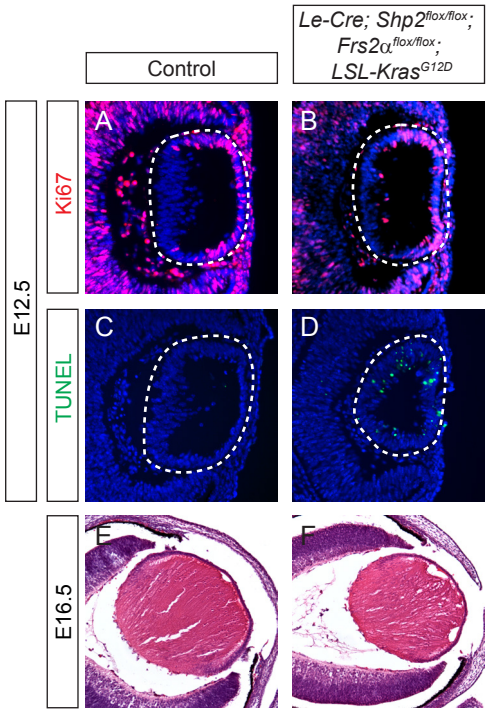
Supplementary Figure 2. (**A-C**) Nuclear staining of cyclin-dependent kinase 4 (CDK4) was detected in wild type lens cells that migrated to the transitional zone to proliferate (arrows in A), but not in either *Le-Cre*; *Shp2*$^{flox/flox}$; *Frs2α*$^{flox/flox}$ or *Le-Cre*; *Shp2*$^{flox/flox}$; *Frs2α*$^{flox/2F}$ mutant cells. (**D-F**) Staining of cell cycle arrest marker p21 was indistinguishable between control and mutant lenses.



Supplementary Figure 3. (**A-F**) Similar to *Le-Cre*; *Frs2α*$^{flox/flox}$ mutant, *Le-Cre*; *Frs2α*$^{flox/2F}$ lens was reduced in size at E12.5, but displayed normal expression of Foxe3, Prox1, E-cadherin, p57, cyclin D1 and Pax6. (**G-L**) α-, β- and γ-crystallins were also present in *Le-Cre*; *Frs2α*$^{flox/2F}$ lens. (**M-N**) Similar Phospho-ERK staining was observed in wild type control and *Le-Cre*; *Frs2α*$^{flox/2F}$ lenses. Three embryos of each genotype were analyzed.



Supplementary Figure 4. (**A-D**) As visualized by GFP expression from *Le-Cre* transgene (Pan et al., 2008), both budding and branching morphogenesis of lacrimal gland were unaffected in E16.5 and P0 *Le-Cre*; *Gab1*$^{flox/flox}$ mutants (n=10), respectively. (**E-H**) Open eyelids (arrows in G and H) were observed in P0 *Le-Cre*; *Gab1*$^{flox/flox}$ mutants (n=10).



Supplementary Figure 5. (**A-D**) Expression of cell proliferation marker Ki67 was recovered in E12.5 *Le-Cre*; *Shp2*$^{flox/flox}$; *Frs2α*$^{flox/flox}$; *LSL-Kras*^{G12D} mutant lenses. However, TUNEL staining remained significantly elevated as compared to controls. (**E-F**) At E16.5, *Le-Cre*; *Shp2*$^{flox/flox}$; *Frs2α*$^{flox/flox}$; *LSL-Kras*^{G12D} mutant (*n*=3) lenses was smaller in size, but morphologically similar to wild type controls.