Supplementary Figure 1. FH depletion did not cause fluid-phase C5 activation in either wild-type or P knockout mouse serum. Intact C5 levels did not change significantly in either WT (light gray bars) or $P^{-/-}$ (dark gray bars) mouse serum after passing through an anti-fH mAb column to deplete fH (fH dpl) or a control mAb column (control). fH depleted serum was incubated at 37 C for 60 minutes before C5 ELISA assay. Values normalized to intact C5 level in control mAb-treated serum at t=0. Data are representative of two independent experiments.

Supplementary Figure 2. C3 and IgG deposition in $fH^{m/m}/P^{-/-}$ mice with and without anti-C5 mAb treatment. (A). Representative immunofluorescence images of glomerular C3 and IgG staining in $fH^{m/m}/P^{-/-}$ mice that were untreated (pre-terminal disease) or treated with anti-C5 mAb for 4 months. Because kidneys collected from moribund control mAb-treated $fH^{m/m}/P^{-/-}$ mice had severe pathology which caused high non-specific immunofluorescence staining, we used non-treated $fH^{m/m}/P^{-/-}$ mice without terminal renal disease as controls for comparison in this analysis. **(B)** Quantification of glomerular C3 and IgG deposition in untreated $fH^{m/m}/P^{-/-}$ mice (n=5) and anti-C5 mAb treated $fH^{m/m}/P^{-/-}$ mice (n=3). C3 deposition appeared to be reduced in anti-C5 mAb treated mice but the difference did not reach statistical significance. In contrast, IgG deposition was significantly increased in anti-C5 mAb treated mice. Scale bars in A = 50μm. ** p = 0.002, student's t-test.

Supplemental Figure 3. C5 inhibition reduced glomerular inflammatory cell infiltration. (A) Quantification of CD11b+ cells in the glomeruli of untreated, control IgG-treated and anti-C5 mAb-treated $FH^{m/m}/P^{-/-}$ mice. Of the untreated mice, there were significantly more CD11b+ cells in the glomeruli of moribund mice (n=4) than in mice that did not yet develop terminal renal disease (n=5). $FH^{m/m}/P^{-/-}$ mice treated with control IgG (n=2) had significantly more glomerular CD11b+ cells than mice treated with anti-C5 mAb (n=3). ** $p<0.01$, *** $p<0.001$, one-way ANOVA with Tukey's test. **(B)** Representative immunofluorescence staining of CD11b+ cells in the glomeruli of the four groups of mice described in panel A. Counterstain = DAPI (blue). Scale bars = 25 μm.

Supplementary Figure 4. Histology of $C5aR^{-/-}$ and $fH^{m/m}/C5aR^{-/-}$ mice. (**A-B**) $C5aR^{-/-}$ mice showed normal renal histology by PAS staining (**A**) and EM (**B**), with only focal mesangial dense deposits noted on EM. (**C-D**) Untreated $fH^{m/m}/C5aR^{-/-}$ mouse kidney pathology was similar to young $fH^{m/m}$ mice, with mesangial proliferation observed by PAS staining (**C**) and early stages of GBM thickening and subendothelial dense deposits seen by EM (**D**). All samples from 2-3 month old mice. Scale bars A-B = 50μm; C-D = 2μm.

Supplementary Figure 5. Complement levels in $fH^{m/m}/C5aR^{-/-}$ and $C5aR^{-/-}$ mice. Intact C3 (**A**), activated C3 (**B**), and intact C5 levels (**C**) in $C5aR^{-/-}$ (n=5), $fH^{m/m}$ (n=5) and $fH^{m/m}/C5aR^{-/-}$ (n=4) mouse plasma demonstrated that C3 and C5 levels were unchanged by $C5aR^{-/-}$ deficiency. Plasma C3 and C5 in $C5aR^{-/-}$ mice were normal while circulating complement levels in $fH^{m/m}/C5aR^{-/-}$ mice were comparable to those found in $fH^{m/m}$ mice. ** $p<0.01$ and *** $p<0.001$, one-way ANOVA with Tukey's test. All samples from 2-3 month old mice.

Supplementary Figure 6. Quantification of glomerular C3 and C9 deposition in $fH^{m/m}$ and $fH^{m/m}/C5aR^{-/-}$ mice treated with anti-P mAb. Quantification of glomerular C3 (**A**) and C9 (**B**) staining demonstrated that C5aR deficiency did not lead to any significant differences in glomerular C3 or C9 deposition in $fH^{m/m}$ mice treated with anti-P mAb. Due to limitation of reagent availability, not all mice were assessed for C9 staining.

Supplemental Figure 7. Quantification of glomerular CD11b+ cell infiltration in $FH^{m/m}$ and $FH^{m/m}/C5aR^{-/-}$ mice treated with anti-P mAb. Glomerular and interstitial CD11b+ cell numbers were uniformly low in the $FH^{m/m}/C5aR^{-/-}$ mouse group (n=5), whereas the numbers were variable in $FH^{m/m}$ mice (n=4) with some showing significantly higher counts.