

## Supplemental Figure S1: Anti-C5a therapy enhances the efficacy of anti-VEGF therapy for "wet" AMD-like features seen in laser-induced choroidal neovascularization.

"Wet" AMD-like features were assessed using the laser-induced CNV model. CNV lesion size was assessed following administration of either IgG isotype control or anti-C5a alone or in combination with anti-VEGF. (A) Scanning laser ophthalmoscopy angiography images of anti-C5a therapy versus IgG isotype controls show a decrease in neovascular exudative lesions following anti-C5a therapy. (B) Comparing anti-VEGF therapy to combinatorial therapy (anti-VEGF with anti-C5a) decreased neovascular exudative lesions were seen with combinatorial therapy at 2 and 5 mg/kg of anti-VEGF.



Supplemental Figure S2: Overall trends of gene expression changes in inflammatory and ECM remodeling genes detected on pathway-focused PCR arrays of eye cups of aged Cfh+/-fed an HFC diet.

Graphic representation illustrating the change in expression of the 84 genes on the Inflammatory Processes and Autoimmunity and on the Extracellular Matrix and Adhesion Molecules pathwayfocused PCR arrays (Qiagen). For these analyses, a gene was considered to be upregulated or downregulated if the fold change was greater than  $\pm 1.25$  as previously described<sup>2</sup>. (**A**) An upregulation of 29 genes involved in inflammation was detected in the eye cups of aged *Cfh*+/mice fed an HFC diet compared to age-matched *Cfh*+/- mice fed a normal diet. (**B**) 47 genes involved in extracellular matrix remodeling were upregulated in the eye cups of aged *Cfh*+/mice fed an HFC diet. Together these gene expression changes indicate support that there is inflammation and extracellular matrix remodeling in the eyes of aged *Cfh*+/- mice fed the HFC diet. All genes and their fold changes are shown in **Supplemental tables 1** and **2**.

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Supplemental Figure S3: C5AR1 expression in human RPE and Choroid and immortalized human RPE.

RNA was isolated from RPE and choroid of a human donor eye as well as cultured ARPE19 RPE cells. (A) Expression of two RPE markers (*RLBP1* and *RPE65*) and (B) one choroid marker (*TIE2*) was examined in these RNA samples. (C) *C5AR1* expression was examined using these samples. *C5AR1* was abundantly detected in choroid-enriched RNA. No *C5AR1* expression was detected in isolated RPE or cultured ARPE19 cells. This supports the *C5ar1* expression pattern seen in primary mouse posterior tissues. nd: none detected