Supplementary Figure legends

Supplementary Fig.1. Color fundus photograph (upper left), fluorescein angiogram (FA, upper middle), indocyanine green angiogram (ICGA, upper right), spectral-domain optical coherence tomography (SD-OCT) image before treatment (lower left), and SD-OCT image after treatment with ranibizumab (lower right) in neovascular age-related macular degeneration (nAMD) patients. A, A 70-year-old woman with type 1 neovascularization (NV). Her best-corrected visual acuity (BCVA) was 20/60, and her WIF-1 level was 61.7 ng/mL. Three months after intravitreal injection of ranibizumab (IVR), the amounts of intra- and sub-retinal fluid decreased. BCVA improved to 20/30. Disruption in the level of the junction between the inner and outer segment of the photoreceptor (IS/OS) on SD-OCT persisted. B, A 66-year-old man with polypoidal choroidal vasculopathy (PCV). The BCVA was 20/25, and his WIF-1 level was 23.7 ng/mL. Three months after IVR, sub-retinal fluid resolved, with an intact external limiting membrane (ELM) and a small defect in the IS/OS on SD-OCT. Vision was maintained. C, A 63-year-old man with type 2 NV. The BCVA was 20/30, and his WIF-1 level was 29.9 ng/mL. Three months after IVR, intra- and sub-retinal fluid, as well as choroidal neovascularization, resolved. BCVA improved to 20/25. Intact ELM and IS/OS on SD-OCT were observed. D, An 81-year-old woman with type 3 NV. The BCVA was 20/60, and her WIF-1 level was 80.6 ng/mL. Although cystoid edema, PED, and intraretinal retinal angiomatous proliferation (RAP) lesions resolved three months after IVR, persistent large defects in ELM and IS/OS on SD-OCT were observed. Visual acuity was not improved.

Supplementary Fig.2. WIF-1 was increased in retinas of light-exposed C57BL/6 mice.

Mice were maintained in accordance with the policies of the Konkuk University Institutional Animal Care and Use Committee (IACUC). Mice were housed in a controlled barrier facility in the Laboratory Animal Research Center in Konkuk University. All animals were handled in compliance with the ARVO Statement of the Use of Animals in Ophthalmic and Visual Research. C57/BL6 mice (10 weeks) were exposed to a 20,000 lux bright light for
4 h. Eyes were enucleated 1 and 5 days after the exposure, and the retina was carefully pushed out to isolate the retinal pigment epithelial (RPE) cells. Retina and RPE cells were lysed in RIPA buffer (Thermo) containing phosphatase inhibitor (Thermo) and phenylmethylsulfonyl fluoride (PMSF, Sigma). Supernatants were obtained by centrifugation at 15,000 rpm for 10 min and used for western blot analysis of WIF-1.

For immunofluorescence, eyes were enucleated and fixed with 4% PFA/PBS for 1 h. Isolated eyes were punched with a 23G needle and further fixed with 4% PFA/PBS for 1 h prior to incubation in 20% sucrose/PBS for 16 h followed by freezing in OCT cryopreservation medium. Cryostat sections were taken at 10 μm. Frozen sections of OCT-embedded eyes were incubated in blocking solution (5% normal donkey serum in PBS with 0.1% Triton X-100) for 1 h prior to incubation with primary antibodies at 4°C for 16 h. Tissue sections were incubated with the secondary antibodies, Alexa488 (Molecular Probes) anti-mouse antibody for 1 h, and the nuclei were counterstained with To-pro3 iodide (Molecular Probes). Fluorescent images were obtained using a confocal microscope (Olympus).

A western blot analysis showed that was WIF-1 exclusively located in the retina and that the expression of WIF-1 increased upon bright light exposure. Immunofluorescence showed marked increased expression of WIF-1 in the inner segment of the photoreceptor layer, outer plexiform layer, inner nuclear layer, and ganglion cell layer 5 days after bright light exposure.