Supplemental Methods and experimental procedures:

Oxygen-induced retinopathy, retina dissection, vessel staining and flat mount:
To induce oxygen-induced retinopathy (OIR), neonatal mice were exposed to 75% oxygen from P7 to P12[1]. Mice at various ages in OIR or during development were anesthetized with Avertin (Sigma-Aldrich) and sacrificed by cervical dislocation. Eyes were enucleated and fixed in 4% paraformaldehyde for 1 h at room temperature, followed by isolation and subsequent dissection of the retina. To visualize vessels, retinas were stained overnight at room temperature with fluoresceinated *Griffonia Bandeiraea Simplicifolia* Isolectin B_4 (Alexa Fluor 594 conjugated; I21413; Invitrogen; 1:100 dilution) in PBS with 1 mM $CaCl_2$. Following 2 hr of washes in PBS, retinas were whole-mounted onto Superfrost/Plus microscope slides (12-550-15; Fisher Scientific) with the photoreceptor side down with SlowFade Antifade reagent (S2828; Invitrogen).

Quantification of vaso-obliteration, vaso-proliferation in OIR and vascular development:
Quantification of retinal vasculature during development, vaso-obliteration and vaso-proliferation in OIR was carried out as described previously in Adobe Photoshop or Image J [2-4]. Images of whole-mounted retina were taken at ×5 magnification on a Zeiss AxioObserver.Z1 microscope and merged using AxioVision 4.6.3.0 software to produce an image of the entire retina. Vascular growth during development, vaso-obliteration and vaso-proliferation in OIR were quantified in Adobe Photoshop or Image J. The number of pixels in vascular area during development is visualized with isolectin staining and outlined in Photoshop and compared to total number of pixels in the whole retina. Retinal areas with pathologic neovascular tufts structures were visually identified by their abnormal aggregated morphology that is distinctly different from the normal finely branched vascular network. The number of pixels in pathologic neovascular area is quantified and compared with the total number of pixels in the whole retina, by the SWIFT_NV method [4] which consists of a set of macros on NIH's free ImageJ platform to isolate the neovascular structures to stand out clearly against the background fluorescence of normal vessels. Evaluation was done blind to the identity of the sample. *n* is number of eyes quantified.

RNA isolation:
Total RNA was extracted from the retinas of 6 mice, each from a different litter; the RNA was pooled to reduce biologic variability (n=6). Retinas from each time point were lysed with a mortar and pestle and filtered through QiaShredder columns (Qiagen, Chatsworth, MD, USA). RNA was then extracted according to manufacturer's instructions using the RNeasy Kit (Qiagen). To generate cDNA, 1 μg total RNA was treated with DNase I (Ambion Inc.) to remove any contaminating genomic DNA, and was then reverse transcribed using random hexamers, and SuperScript III reverse transcriptase (Invitrogen Corp., Carlsbad, CA, USA). All cDNA samples were aliquoted and stored at –80°C.

Quantitative real-time PCR analysis of gene expression:
We used Primer Bank and NCBI Primer Blast Software.Express software (Applied BioSystems) to design the following primers: mouse *Sirt1* (F: 5'-GACGATGACAGAACGTCACAC,R: 5'-CGAGGATCGGTGCCAATCA), *Vegf* (F: 5'-GGAGATCCTTCGAGGAGCACTT, R: 5'-GGCGATTTAGCAGCAGATATAAGAA), *Epo* (F: 5'-AGAATGGAGGTGGAAGAACAG, R: 5'-GCGACATCAATTCCTTCTGAG), *PGC-1α* (F: 5'-GGAGCCGTGACCACTGACA, R: 5'-TGGTTTGCTGCATGGTTCTG), *TNFα* (F: 5'- CCAACATGCTGATTGATGACACC, R: 5'-GAGAATGCCAATTTTGATTGCCA), *IL-1β* (F: 5'- TTCAGGCAGGCAGTATCACTC, R: 5'-GAAGGTCCACGGGAAAGACAC), *IL-6* (F: 5'- TAGTCCTTCCTACCCCAATTTCC, R: 5'-TTGGTCCTTAGCCACTCCTTC), *SOCS3* (F: 5'- AGCTGGTGGTGAACGCCGTG, R: 5'-GCGTGCTTCGGGGGTCACTC), *TSP-1* (F: 5'- TTCTTACCCTTGACAACAACGTG, R: 5'-

CCACAGATAGCTTGGAGGTCC), *TSP-2* (F: 5'- GTGGGCTGCGATCTTATCGA, R: 5'-CAAGCCCCTGAAGTGACTCTCT), *TIMP-1* (F: 5'- GCAACTCGGACCTGGTCATAA, R: 5'-CGGCCCGTGATGAGAAACT), *PEDF* (F: 5'- AGGACATGAAGCTACAGTCGTTGTT, R: 5'-CTCGAAAGCAGCCCTGTGTT) and *cyclophilin A* (F: 5'-CAGACGCCACTGTCGCTTT, R: 5'-TGTCTTTGGAACTTTGTCTGCAA); rat *Vegf* (F: 5'-CAATGATGAAGCCCTGGAGT, R: 5'-AATGCTTTCTCCGCTCTGAA), *Epo* (F: 5'-CGAACGTCCCACCCTGCTGC, R: 5'-GTGGGGGAGCGCAGAGGACT), *TNFα* (F: 5'-CATCCGTTCTCTACCCAGCC, R: 5'-AATTCTGAGCCCGGAGTTGG); *IL-1β (*F: 5'-CCTTGTCGAGAATGGGCAGT, R: 5'-TTCTGTCGACAATGCTGCCT); *IL-6* (F: 5'-ACAGCGATGATGCACTGTCA, R: 5'-ACGGAACTCCAGAAGACCAG); *SOCS3* (F: 5'-TGTCGGAAGACTGTCAACGG, R: 5'-GCTAACTGGGAGCTACCGAC); *TSP-1* (F: 5'-TTCTTACCCTTGACAACAACGTG, R: 5'-CCACAGATAGCTTGGAGGTCC); *TSP-2* (F: 5'-CGTCTCTGCAACTCACCAGT, R: 5'-CTGTCACATCCCCGACACAA); *TIMP-1* (F: 5'-GCAACTCGGACCTGGTCATAA, R: 5'-CGGCCCGTGATGAGAAACT); *PEDF* (F: 5'-TGGCTTACTTCAAGGGGCAG, R: 5'-AGGGTCTGACATCATGGGGA); and *cyclophilin A* (F: 5'-CTTTGCAGACGCCGCTGTCTCTT, R: 5'- CTGCTGTCTTTGGAACTTTGTCTGC). Quantitative analysis of gene expression was determined using an ABI Prism 7700 Sequence Detection System (TaqMan) and the SYBR Green Master mix kit. Standard curves for each gene were plotted with quantified cDNA template during each real-time PCR reaction. Each target gene mRNA copy number was normalized to 10^6 copies of the house keeping gene, *cyclophilin A*.

Immunohistochemistry:
For retina cross-sections immunostaining, eyes were fixed in 4% paraformaldehyde for 1 h and incubated in 30% sucrose at 4°*C*, followed by embedding in OCT. 10-μm thick sections were blocked in PBS with 0.1% Triton X-100 and 5% goat serum. Sections were stained with isolectin to visualize vessels and/or primary antibodies followed by secondary antibodies. For whole-mount immunohistochemical staining, retinas fixed in 4% paraformaldehyde for 1 h were rinsed in 1x PBS, permeabilized overnight at 4°C with 0.5% Triton X-100 in PBS, stained with Isolectin B_4, followed by primary Sirt1 antibody (Millipore, 07-131) and secondary antibody staining (chicken anti-rabbit Alexa 488, A-21441, Invitrogen). Retinal whole-mounts were prepared and imaged as described previously

Immunoprecipitation, Western blot and ELISA assay:
For immunoprecipitation, RGC-5 cell lysate were incubated with acety-lysine antibody (Cell Signaling, #9814) overnight at 4°C, followed by incubated with protein A agarose beads for 1hour. After extensive washing, samples were eluted with 2XSDS sample buffer and analyzed by Western Blotting. For Western Blot, 25 μg protein of retinal lysate or RGC-5 cell lysate (or immunoprecipited samples) was loaded on an SDS-PAGE gel and transferred onto a PVDF membrane. After blocking, the membranes were incubated overnight with primary antibody followed by secondary antibody conjugated with horseradish peroxidase for one hour at room temperature. Chemiluminescence signals were generated with ECL plus substrate and captured with KODAK film. The following primary antibodies were used for Western Blot: anti-Sirt1 (Millipore, 07-131), anti-HIF1α (Abcam, ab1), anti- HIF2α (Abcam, ab199), anti-β–actin(Sigma-Aldrich, A1978), goat anti-rabbit conjugated with horse-radish peroxidase (NA934V, Amersham Pharmacia). For Epo and VEGF ELISA assay, RGC-5 medium were concentrated first using centrifugal filters (Millipore, UFC801024) followed by ELISA according to manufacturer's instruction (MyBioSource.com, MBS160249; R&D Systems, RRV00).

Reference:

[1] L. E. Smith*, et al.*, "Oxygen-induced retinopathy in the mouse," *Invest Ophthalmol Vis Sci,* vol. 35, pp. 101-11, Jan 1994.

[2] E. Banin*, et al.*, "T2-TrpRS inhibits preretinal neovascularization and enhances physiological vascular regrowth in OIR as assessed by a new method of quantification," *Invest Ophthalmol Vis Sci,* vol. 47, pp. 2125-34, May 2006.

[3] K. M. Connor*, et al.*, "Quantification of oxygen-induced retinopathy in the mouse: a model of vessel loss, vessel regrowth and pathological angiogenesis," *Nat Protoc,* vol. 4, pp. 1565-73, 2009.

[4] A. Stahl*, et al.*, "Computer-aided quantification of retinal neovascularization," *Angiogenesis,* vol. 12, pp. 297-301, 2009.