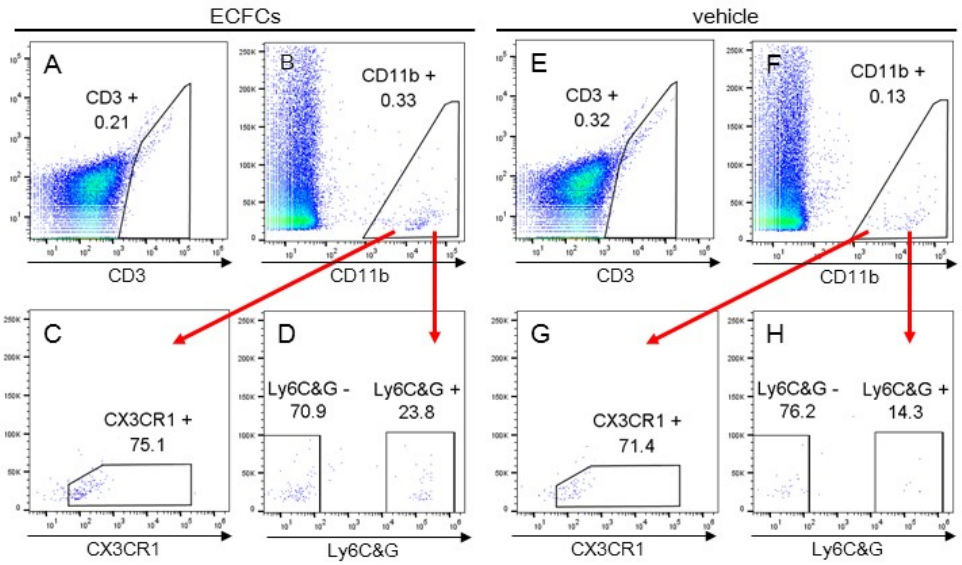
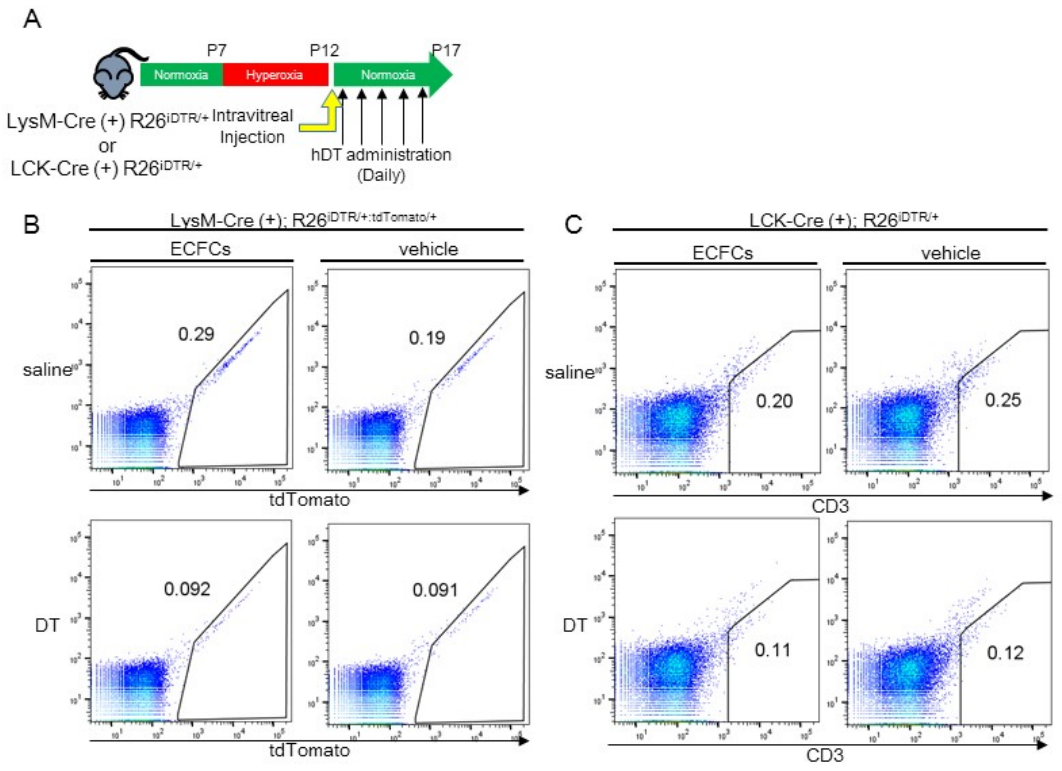
Supporting information



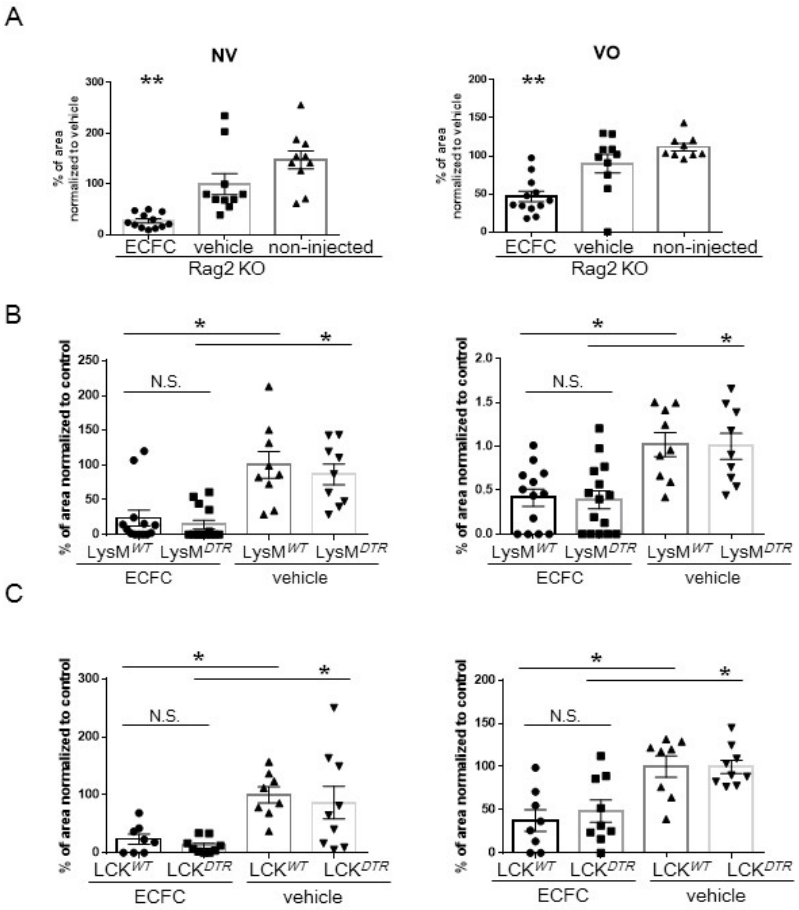
Supplementary Figure S1.

Immune cell profile in the retina after injection of human ECFCs for OIR mice. Representative flow cytometry analysis for single cell suspensions from wildtype OIR eyes at P17 injected ECFCs **(A-D)** or vehicle **(E-H)** at P12. **(A and E)** CD3+ T cells and **(B and F)** CD11b+ myeloid cells. CD11b+ cells are also labeled with CX3CR1 (microglia marker) antibody or Ly6C&G (monocyte and neutrophils marker) antibody.



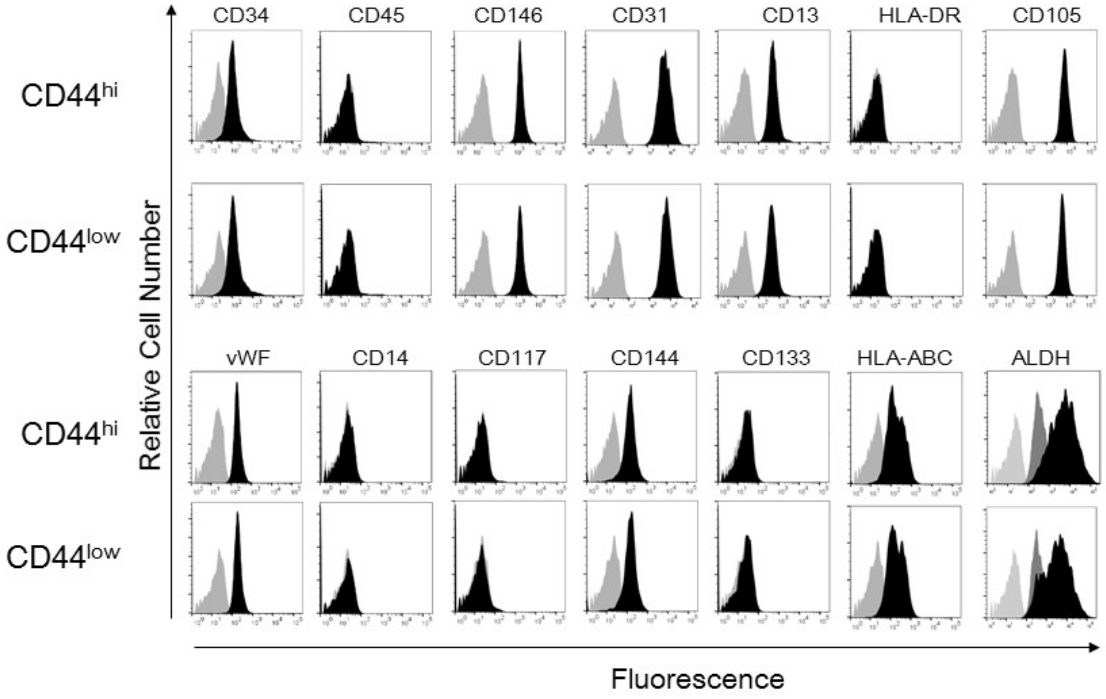
Supplementary Figure S2.

DT-mediated ablation of myeloid cells or T cells in iDTR transgenic mice. (A) Experimental scheme for DTR tg mice. **(B and C)** Representative flow cytometry analysis for single cell suspensions from **(B)** LysM-Cre(+); R26$^{iDTR/+:tdTomato/+}$ (myeloid cells) mice or **(C)** LCK-Cre(+); R26$^{iDTR/+}$ mice at P17 after injection of ECFCs or vehicle at P12. Mice subsequently received daily intraperitoneal injection of saline or DT. Number of cells was assessed with tdTomato fluorescence for LysM-Cre(+); R26$^{iDTR/+}$ mice (B) and CD3 immuno-labeling for LCK-Cre(+); R26$^{iDTR/+}$ mice (C).



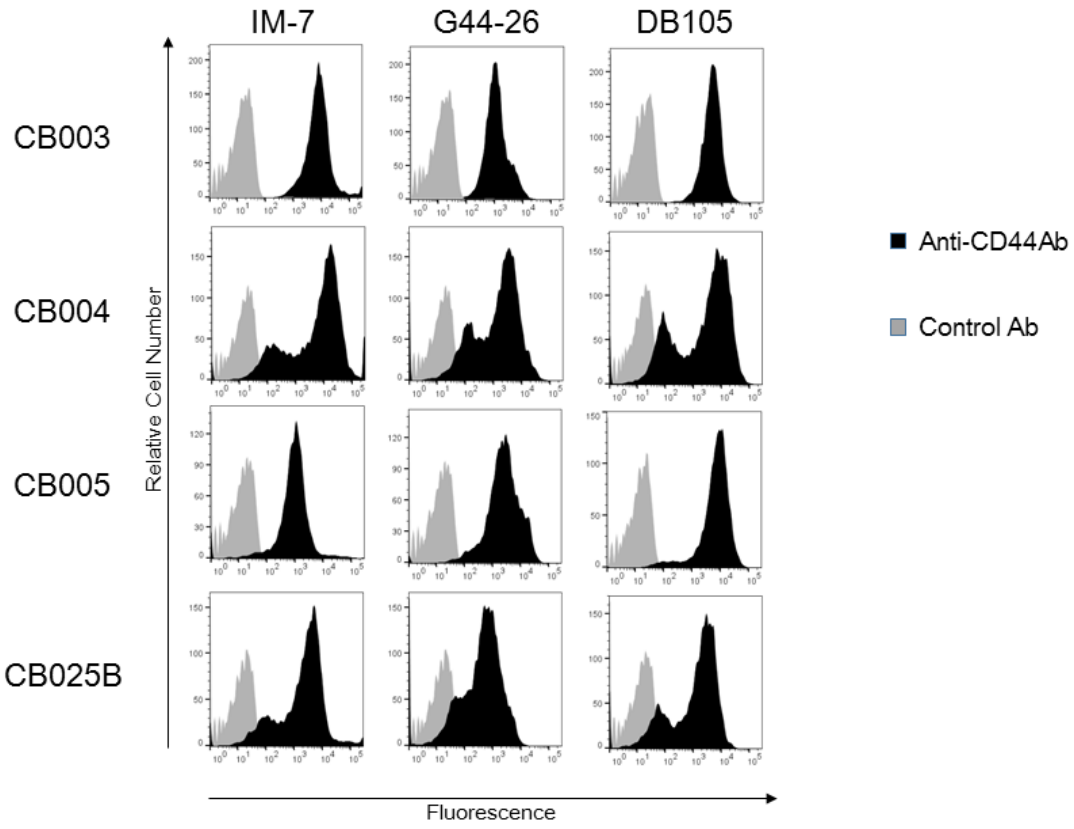
Supplementary Figure S3.

Human ECFCs rescues OIR in various immune competent cell-depleted mice. The rescue effect of ECFCs in OIR is not a simple consequence of immunologic reaction induced by ECFCs. **(A)** Quantification of OIR in Rag-2 knock-out mice injected with ECFCs or vehicle. **(B)** Comparison of NV and VO in OIR for $LysM^{WT}$ (LysM cre-) or $LysM^{DTR}$ (LysM cre+) mice after ECFCs injection or vehicle. No significant difference in ECFCs rescue effect was observed between myeloid cell knockout (cre+) and control (cre-) mice. **(C)** Comparison of NV and VO in OIR for LCK^{WT} (LCK cre-) or LCK^{DTR} (LCK cre+) mice after ECFCs injection or vehicle. No significant difference in ECFCs rescue effect was observed between T cell knockout (cre+) and control (cre-) mice. n>8 per group. Error bars represent SEM. *P < 0.05, **P < 0.01, Kruskal-Wallis test with Dunn's multiple comparison test.



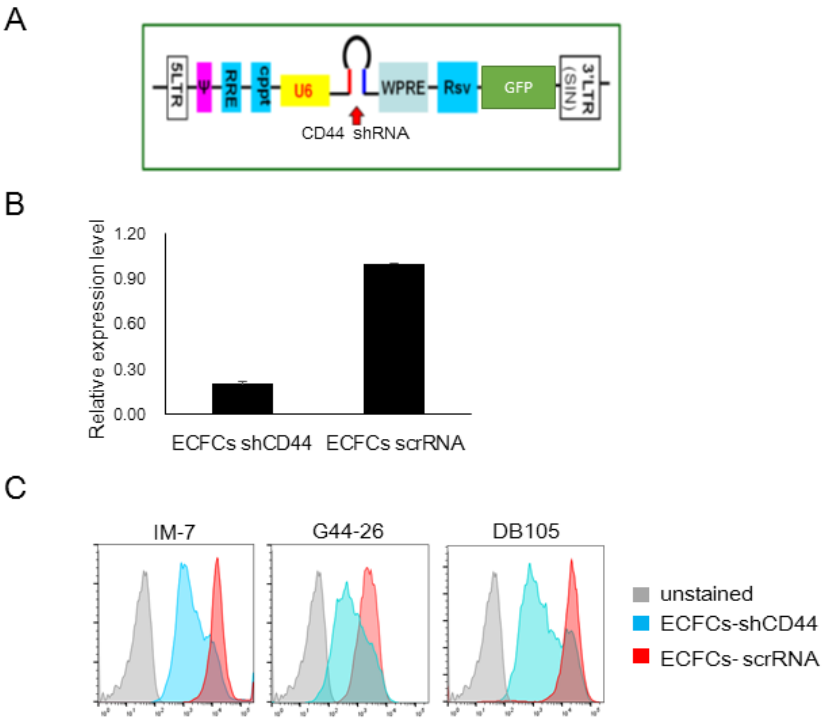
Supplementary Figure S4.

Phenotypic analysis for CD44 high or low cells with anti CD44 antibody (clone: IM-7) by FACS analysis for arrays of indicated antigens. Representative flow cytometry histograms of CD44 high/low ECFCs show reactivity with various marker molecules (right-shifted, black-filled curves compared with gray-filled curves of the appropriate isotype controls) in similar expression pattern. In ALDH panels, black-filled curves and dense gray curves represent $ALDH^{hi}$ populations and $ALDH^{low}$ populations, respectively.



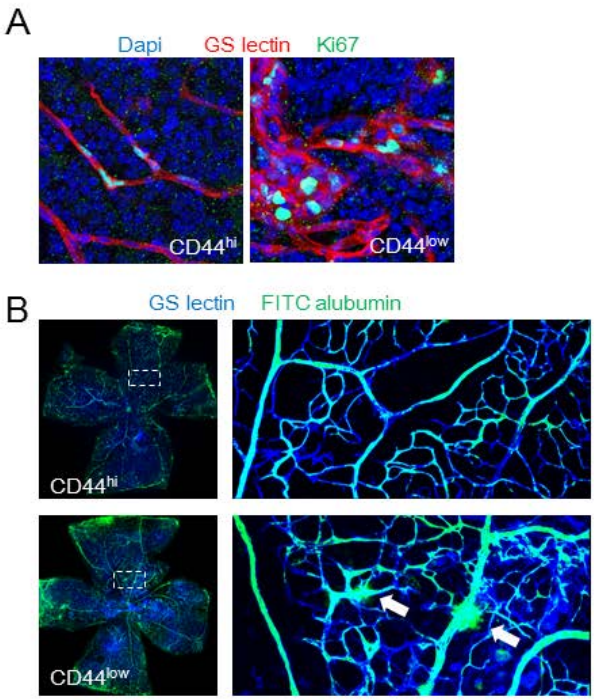
Supplementary Figure S5.

FACS analysis using different clone of CD44 antibody for ECFCs derived from 4 different donors of cord blood at passage 5. The percentage of $CD44^{hi}$ ECFCs was 47.5 ± 23.6 % and $CD44^{low}$ ECFCs was 23.1 ± 4.95 %. Titles on top: Name of antibody clone. Titles on left: Name of cord blood donor samples.



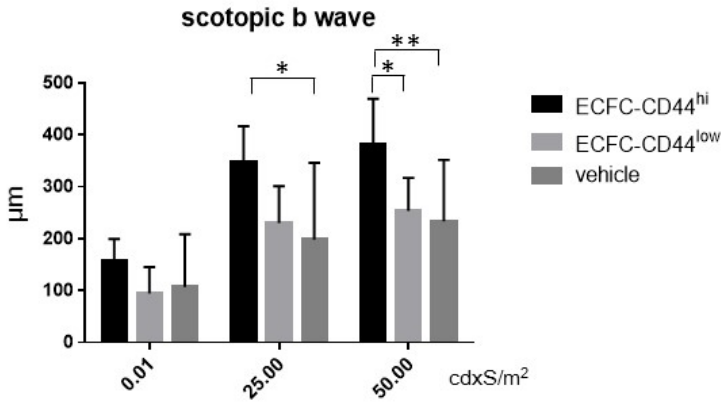
Supplementary Figure S6.

Knock-down (KD) efficiency for CD44 in ECFCs. **(A)** Scheme for KD for CD44. **(B)** qPCR result after lenti-virus mediated KD. **(C)** Flow cytometric analysis for KD-ECFCs. Each flow analysis is showing the name of clone of CD44 antibody.



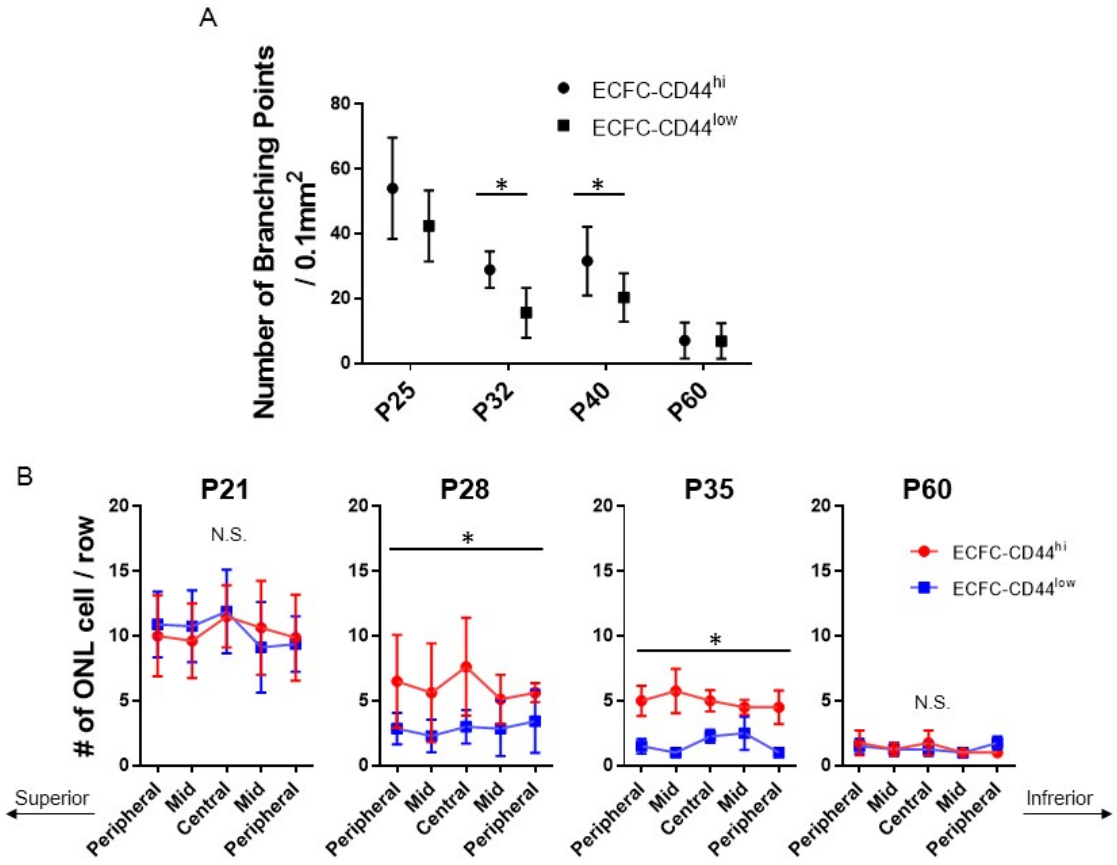
Supplementary Figure S7.

(**A and B**) Intravitreal injection of CD44^{hi} ECFCs promotes maturation of retinal vessels in oxygen induced retinopathy model. **(A)** Flat-mount staining of retinas injected with CD44^{hi} or CD44^{low} ECFCs with anti-Ki67 antibody. **(B)** FITC albumin perfusion with GS lectin staining (*n* = 4 mice per group).

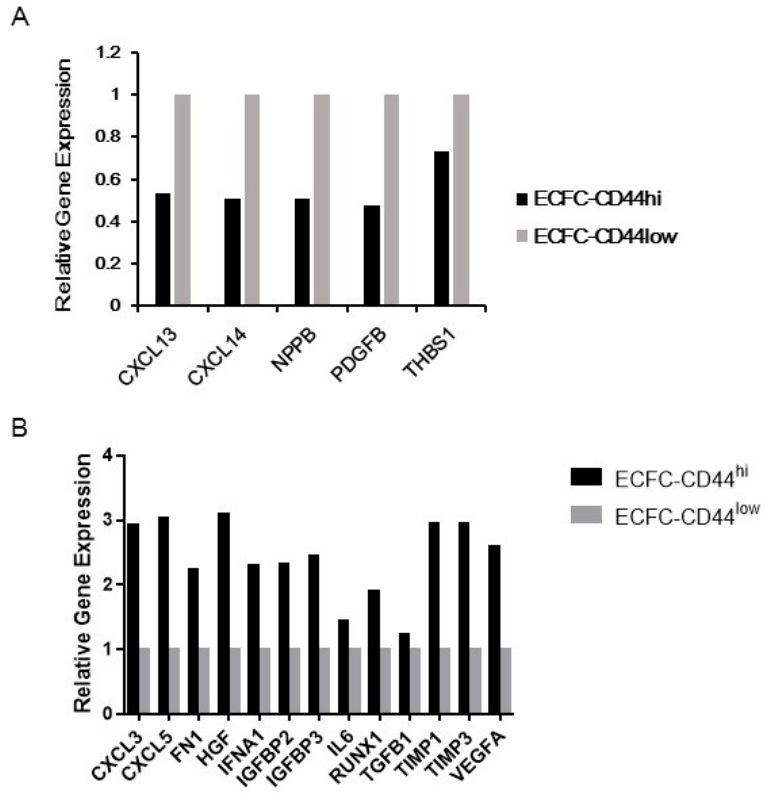


Supplementary Figure S8. Injection of ECFCs functionally rescue in OIR eyes.

Scotopic ERG at P30 for eyes injected ECFCs at P12. Error bars represent SD. n=9 per group, $^{**}P < 0.01$, $^{*}P < 0.05$, one-way ANOVA with Tukey analysis.



Supplementary Figure S9. The time course of retinal degeneration in RD10 mice after ECFCs injection. (A) Quantification of branch point in deep plexus of retinal vasculature on P25, P32, P40 and P60 and **(B)** quantification of number of ONL nuclear staining at P21, P28, P35 and P60 in RD10 mice after injection of ECFCs at P14. Error bars represent SD. *P<0.05, student's t test. n>4.



Supplementary Figure S10.

Results of qPCR based gene profile analysis for CD44$^{hi/low}$ ECFCs. **(A)** RNA from cells cultured in two-dimensional dish did not show higher angiogenic growth factor gene expression in CD44^{hi} ECFCs. **(B)** qPCR based gene profile analysis for human angiogenic growth factors expressed on ECFC-CD44^{hi} or ECFC-CD44^{low} cultured in 3D gel for 48h. Genes dysregulated by >1.5 fold with P values of less than 0.05 were plotted (n=4).

Supplementary Table S1. Flow and immunohistochemical staining antibodies

Name of reagent	Company	Host species	Catalog No.	Dilution factor
Flow Cytometry				
CD13 conjugated to APC	BioLegend	Mouse	301705	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD14 conjugated to FITC	BD PharMingen	Mouse	557153	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD31 conjugated to FITC	BD PharMingen	Mouse	555445	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD34 conjugated to FITC	BD PharMingen	Mouse	555821	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD45 conjugated to FITC	BD PharMingen	Mouse	555482	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD90 conjugated to PE	BD PharMingen	Mouse	555596	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD105 conjugated to APC	BD PharMingen	Mouse	562408	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD117 conjugated to PE	BD PharMingen	Mouse	555714	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD133 conjugated to PE	Miltenyi Biotec	Mouse	130-098-826	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD144 conjugated to PE	BioLegend	Mouse	348506	5 µL / test (1 x 10^6cells in 100 µL buffer)
HLA-DR conjugated to APC	BioLegend	Mouse	307609	5 µL / test (1 x 10^6cells in 100 µL buffer)
HLA-ABC conjugated to PE	BioLegend	Mouse	311405	5 µL / test (1 x 10^6cells in 100 µL buffer)
VEGF-R2 conjugated to PE	R and D Systems	Mouse	FAB357P	5 µL / test (1 x 10^6cells in 100 µL buffer)
vWF	BD PharMingen	Mouse	555849	6 µL / test (1 x 10^6cells in 100 µL buffer), cells were permialized with 0.2% Triton X-100 (Sigma).
CD44 conjugated to APC, clone IM-7	BD PharMingen	Mouse	559250	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD44 conjugated to APC, clone G44-26	BD PharMingen	Mouse	559942	5 µL / test (1 x 10^6cells in 100 µL buffer)
CD44 conjugated to PE, clone DB105	Miltenyi Biotec	Mouse	130-098-108	5 µL / test (1 x 10^6cells in 100 µL buffer)
Immunohistochemistry				
PECAM-1	BD PharMingen	Rat	553370	1:200
ki67	Abcam	Rabbit	ab15580	1:100
MAP2	Sigma	Mouse	M4403	1:1000
GFP	ThermoFisher	Rabbit	A-21311	1:200
anti human VE-cadherin	BioLegend	Mouse	348502	1:100
Arrestin	EMD Millipore	Rabbit	AB15282	1:200
rhodopsin	EMD Millipore	Mouse	MABN15	1:1000
opsin (Red/Green)	EMD Millipore	Rabbit	AB5405	1:200
isolectin GS IB-4	ThermoFisher	NA	I21413	1:200