SUPPLEMENTAL DATA

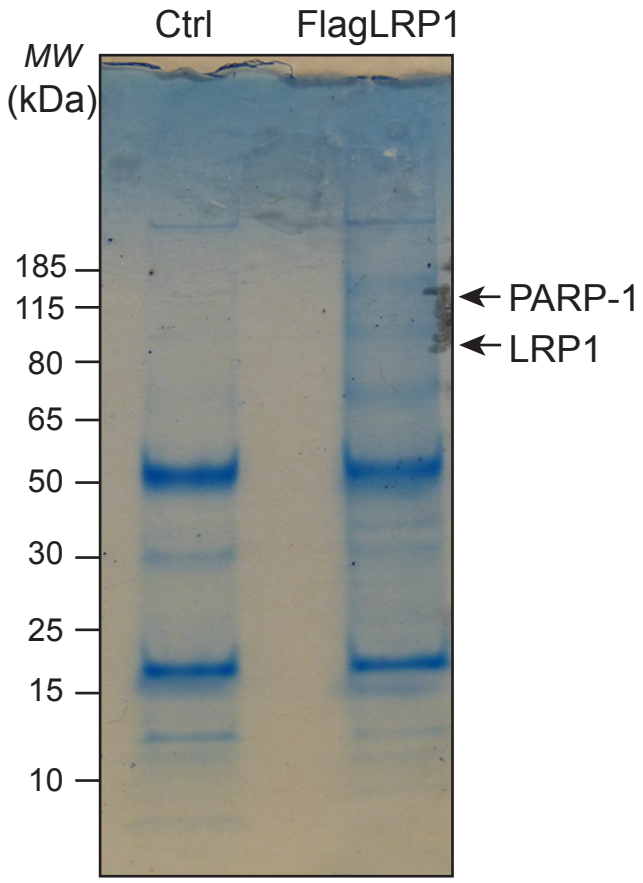

Figure Sl. PARP-1 is a candidate protein associating with LRP1. Lysates of HEK 293 cells with stably transfected Flag-tagged LRP1 β chain (Flag-LRP1) were immunoprecipitated with an anti-Flag antibody and stained with Coomassie blue. The positive bands were subjected to mass spectrometry analysis to identify interacting proteins. PARP-1 is one of these candidate proteins that are likely associated with LRP1.

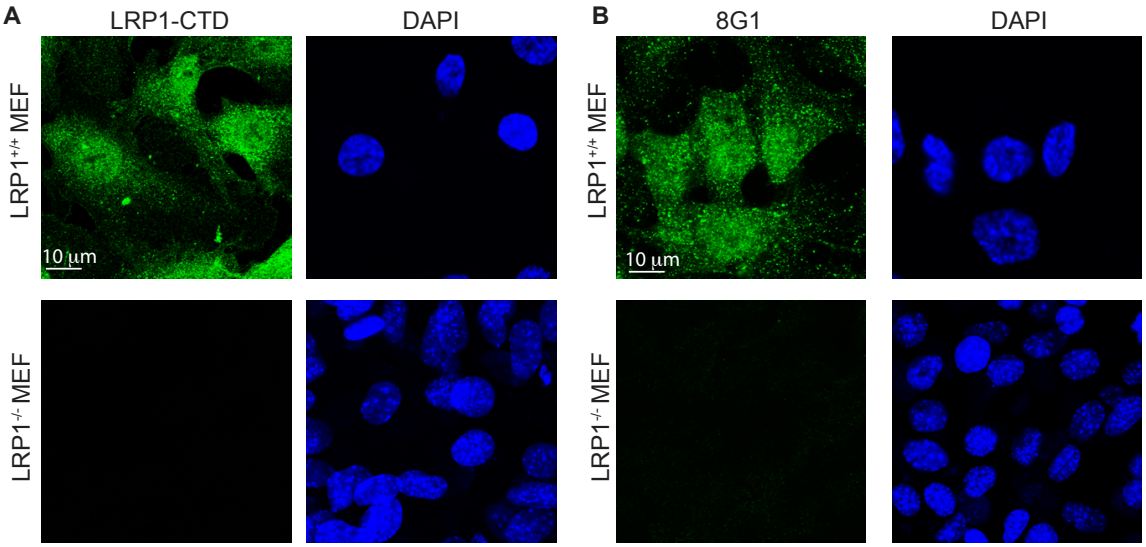

Figure SII. LRP1 antibodies are specific for LRP1 staining. $LRP1^{+/+}$ MEF and $LRP1^{-/-}$ MEF cells were stained with LRP1 (C-terminal) antibody (LRP1-CTD, Cat. No. L2170 from Sigma, in A) or 8G1 antibody (Cat. No. ab20384 from Abcam, in B), and DAPI for nucleus. In $LRP1^{+/+}$ MEFs, we observed LRP1 specific signals with some in vesicle-like structures. However, no detectable signals of LRP1 were observed with $LRP1^{-/-}$ MEF cells.

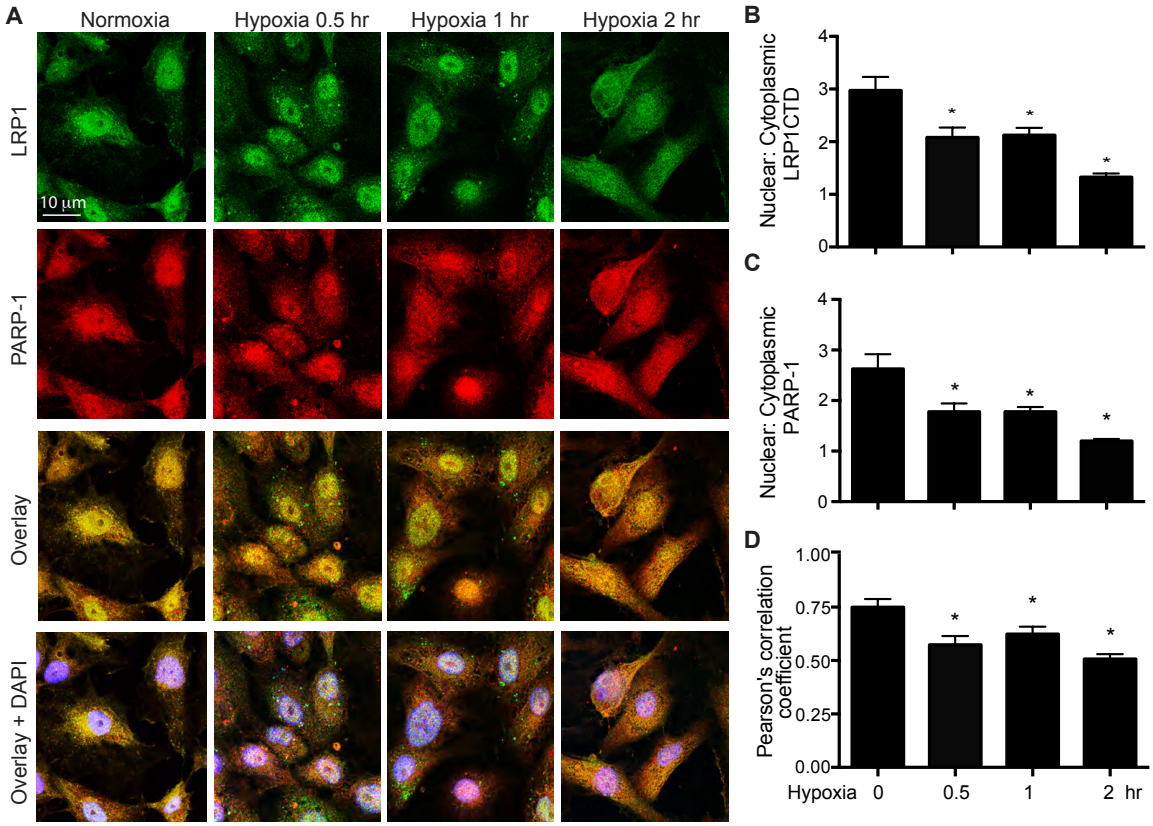

Figure SIII. Hypoxia affects the subcellular localization of LPR1 and PARP-1 and decreases their association. A, HREC cells were cultured with or without pretreatment of DAPT at 10 μM for 24 hours under normoxia condition, or exposed to hypoxia at 2% O_2 for the indicated time. After fixation, cells were stained with LRP1 (C-terminal) antibody (LRP1-CTD, Cat. No. L2170 from Sigma), PARP-1 antibody and DAPI for nucleus. **B-C,** The subcellular localization of LRP1 (B) and PARP-1 (C) is presented as a ratio of relative signals of LRP1 C-terminal or PARP-1 protein in the nucleus to that in the cytoplasm. **D,** The co-localization of LRP1 and PARP-1 was presented with Pearson's correlation coefficients. *, $P<0.05$, compared to cells cultured in normoxia, analyzed with one-way ANOVA followed by Bonferroni comparison test. n≥7.

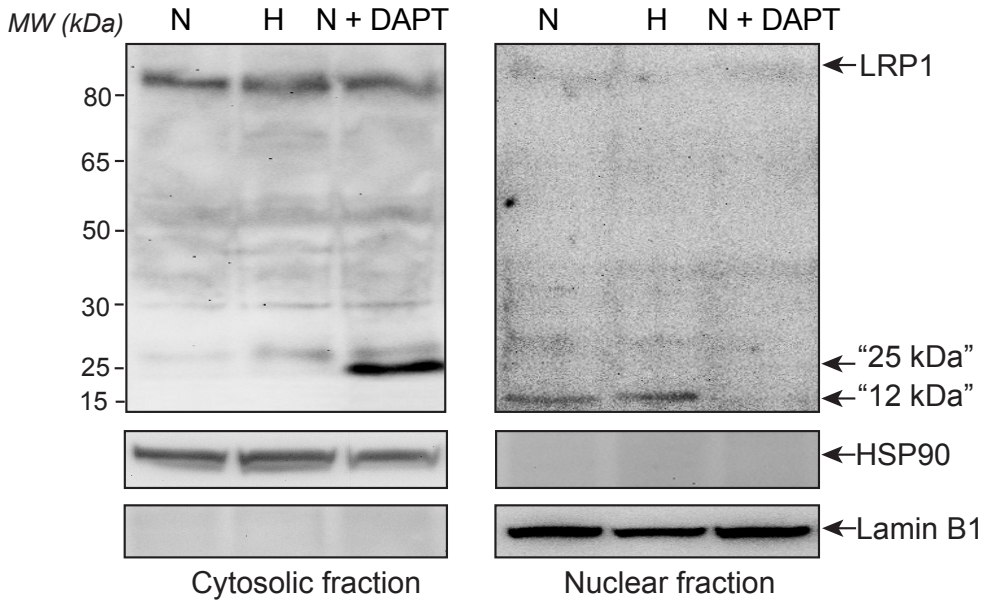

Figure SIV. The γ -secretase-dependent LRP1 processing is not affected by hypoxia. HREC cells were pretreated with DAPT (10 μM) for 24 hours and then cultured under normoxia (N) or hypoxia (H, 2% O_2) level for 2 hours. Cells were then harvested and separated into the indicated subcellular fractions. Western blotting with LRP1 (C-terminal) antibody (Cat. No. L2170 from Sigma) and markers for cytosolic fractions (Hsp90) and nuclear fractions (Lamin B1) was performed as indicated.

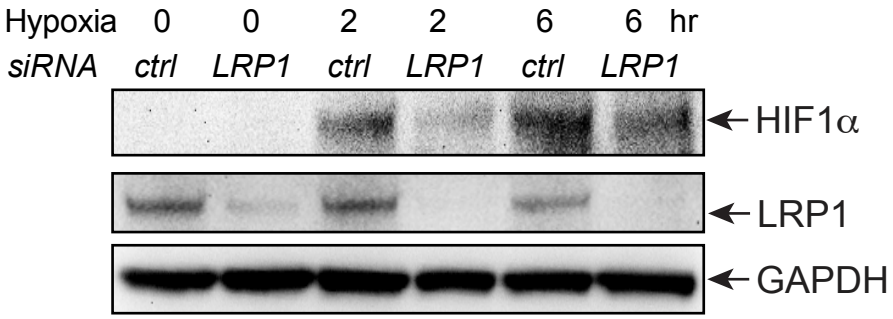

Figure SV. HIF1a induction is inhibited by LRP1 knockdown in HRECs. HRECs were exposed to 2% O2 for different time periods, followed by Western blotting analysis for the detection of HIF1α protein.

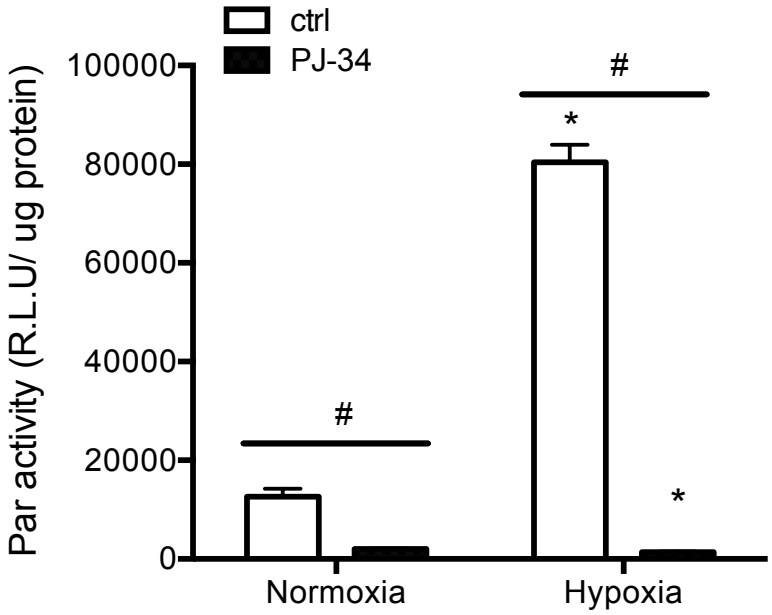

Figure SVI. PARP-1 activity is inhibited by its inhibitor PJ-34 in HRECs. Quantitative data were presented as a ratio of relative light unit (R.L.U.) to total protein amount in cell lysates. *, $P<0.05$, compared to same cells under normoxia. #, $P<0.05$, compared to control siRNA-transfected HRECs. n=3. Data was analyzed by two-way ANOVA followed by Fisher's LSD multiple comparison test.

Table SI. Proteins identified in LRP1-associated protein complexes by mass spectrometry.

Sample	Name	Accession	Species	Peptide Count[1]	%Coverage	Total score[2]
1	low density lipoprotein-related protein 1 variant	gi|62088576	Homo sapiens	10	3.518	12.7
2	poly(ADP-ribose) synthetase	gi|337424	Homo sapiens	30	26.23	38.92
3	heat shock protein HSP 90-alpha isoform 2	gi|154146191	Homo sapiens	20	35.52	29.01
4	topoisomerase I	gi|339806	Homo sapiens	14	22.88	20.13
5	DNA replication licensing factor MCM4	gi|33469917	Homo sapiens	9	22.94	16.68
6	LDL-receptor related precursor (AA -19 to 4525)	gi|34339	Homo sapiens	18	4.842	16.58
7	translational control protein 80	gi|5006602	Homo sapiens	14	20.16	13.45
8	HIST1H4F	gi|49457374	Homo sapiens	11	60.19	12.55
9	RNA binding protein	gi|5821153	Homo sapiens	41	12.28	51.25
10	DNA-dependent protein kinase catalytic subunit isoform 1	gi|13654237	Homo sapiens	12	3.852	23.27

Notes:

1= Number of peptides matched to the protein sequence (95% confidence)

2= Score of the quality of MS/MS peptide fragment ion matches