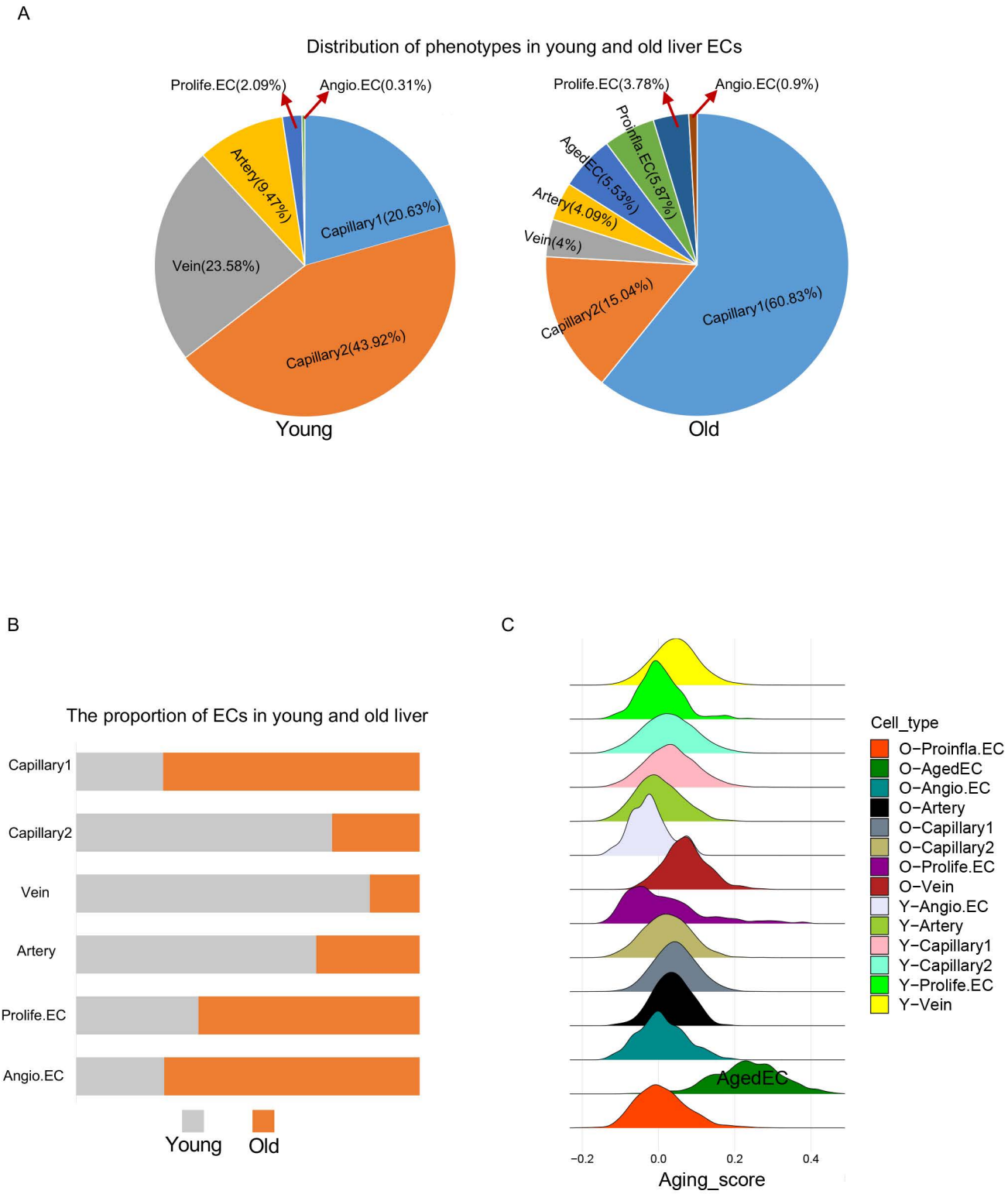
A
Distribution of phenotypes in young and old liver ECs
Prolife.EC(2.09%)
Angio.EC(0.31%)
Artery(9.47%)
Capillary1(20.63%)
Vein(23.58%)
Capillary2(43.92%)
Young
Prolife.EC(3.78%)
Angio.EC(0.9%)
Proinfla.EC(5.87%)
AgedEC(5.53%)
Artery(4.09%)
Vein(4%)
Capillary2(15.04%)
Capillary1(60.83%)
Old
B
The proportion of ECs in young and old liver
Capillary1
Capillary2
Vein
Artery
Prolife.EC
Angio.EC
Young
Old
C
Cell_type
O−Proinfla.EC
O−AgedEC
O−Angio.EC
O−Artery
O−Capillary1
O−Capillary2
O−Prolife.EC
O−Vein
Y−Angio.EC
Y−Artery
Y−Capillary1
Y−Capillary2
Y−Prolife.EC
Y−Vein
AgedEC
−0.2
0.0
0.2
0.4
Aging_score

Figure S1

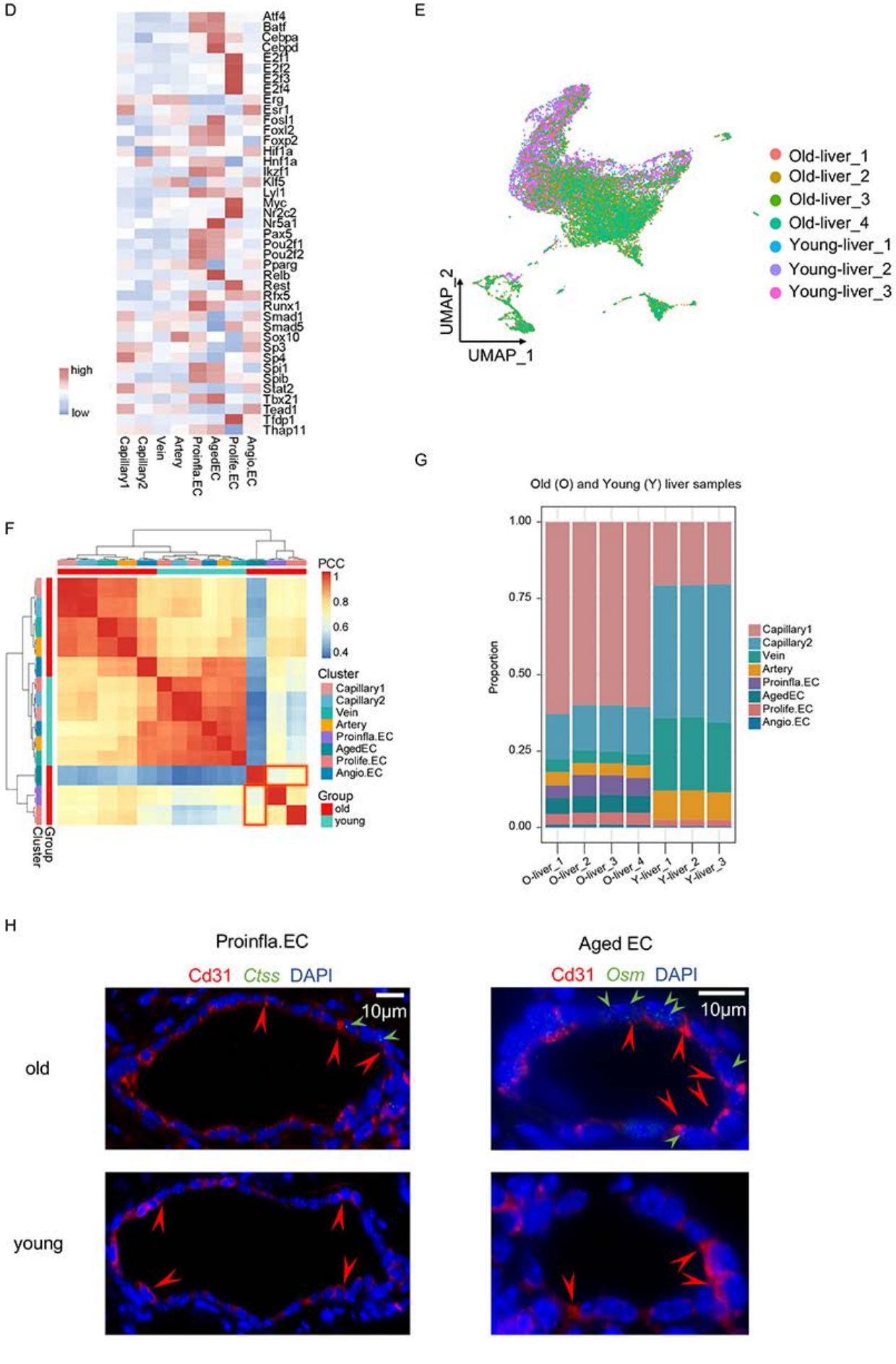
D
Atf4
Batf
Cebpa
Cebpd
E2f1
E2f2
E2f3
E2f4
Erg
Esr1
Fosl1
Foxl2
Foxp2
Hif1a
Hnf1a
Ikzf1
Klf5
Lyl1
Myc
Nr2c2
Nr5a1
Pax5
Pou2f1
Pou2f2
Pparg
Relb
Rest
Rfx5
Runx1
Smad1
Smad5
Sox10
Sp3
Sp4
Spi1
Spib
Stat2
Tbx21
Tead1
Tfdp1
Thap11
high
low
Capillary1
Capillary2
Vein
Artery
Proinfla.EC
AgedEC
Prolife.EC
Angio.EC
E
Old-liver_1
Old-liver_2
Old-liver_3
Old-liver_4
Young-liver_1
Young-liver_2
Young-liver_3
UMAP_2
UMAP_1
F
PCC
1
0.8
0.6
0.4
Cluster
Capillary1
Capillary2
Vein
Artery
Proinfla.EC
AgedEC
Prolife.EC
Angio.EC
Group
old
young
Group
Cluster
G
Old (O) and Young (Y) liver samples
Proportion
1.00
0.75
0.50
0.25
0.00
O-liver_1
O-liver_2
O-liver_3
O-liver_4
Y-liver_1
Y-liver_2
Y-liver_3
Capillary1
Capillary2
Vein
Artery
Proinfla.EC
AgedEC
Prolife.EC
Angio.EC
H
Proinfla.EC
Cd31 Ctss DAPI
Aged EC
Cd31 Osm DAPI
10μm
10μm
old
young

Figure S1

I

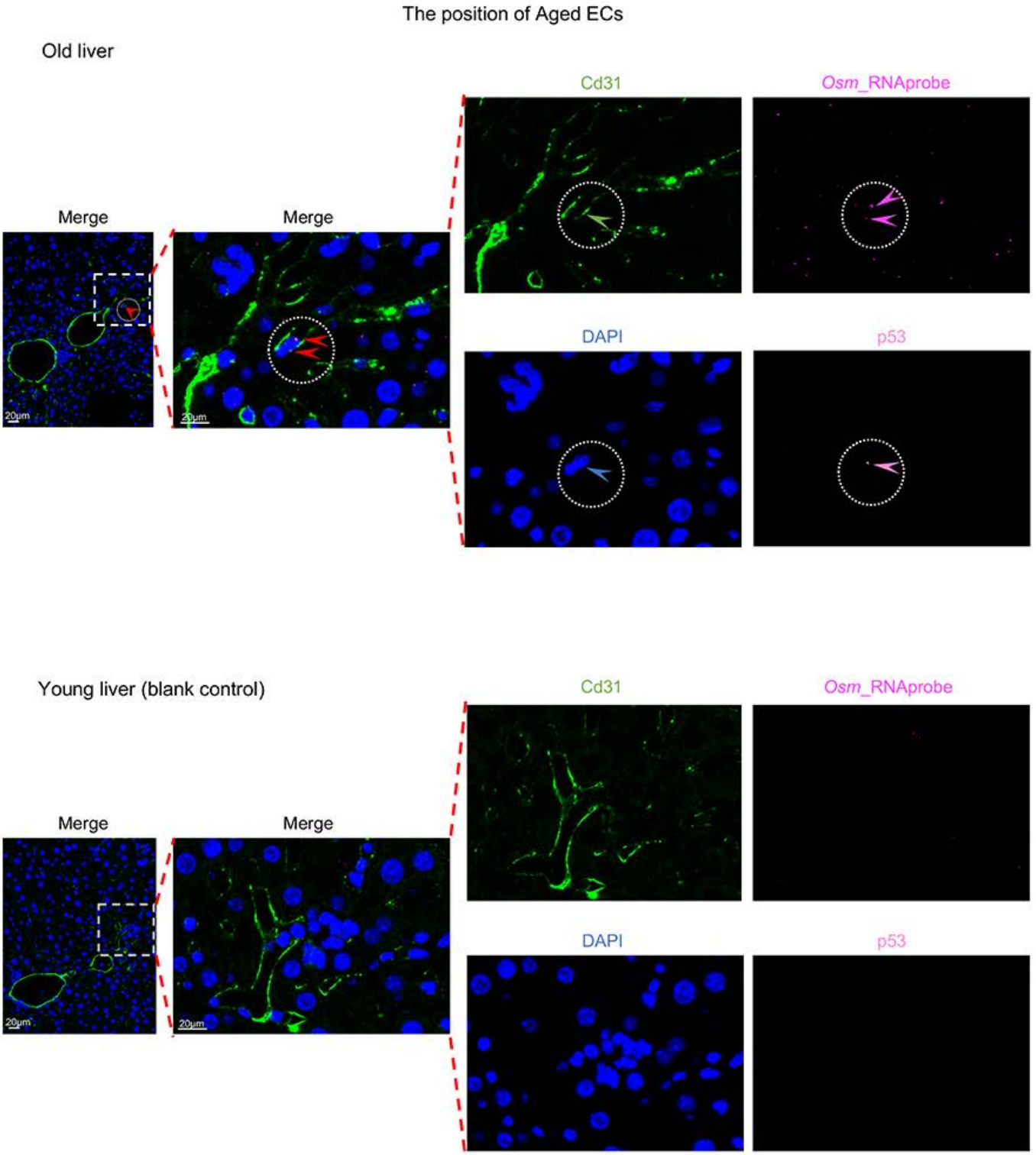
The position of Aged ECs
Old liver
Cd31
Osm_RNAprobe
Merge
Merge
DAPI
p53
20μm
20μm
Young liver (blank control)
Cd31
Osm_RNAprobe
Merge
Merge
DAPI
p53
20μm
20μm

Figure S1

Figure S1. Relative composition of EC phenotypes and gene set scores of senescence-associated secretory phenotype (SASP) in young and old mouse liver.

(A) Pie charts showing the relative composition of EC phenotypes in young and old mouse liver ECs.

(B) Phenotypic distribution of young and old common EC clusters in the liver.

(C) Density plot showing gene set scores of SASP genes in ECs of the mouse liver in the young (denoted by "Y") and old (denoted by "O") group.

(D) Heatmap showing the cell-type specific TF activity of mouse liver ECs.

(E) UMAP plot showing the integration of the seven liver ECs datasets with harmony.

(F) Hierarchical heatmap showing the PCC (Pearson correlation coefficient) of a normalized transcriptome between groups in cell type resolution. The color intensity of the heatmap suggests the PCC values. Hierarchical clustering analysis was performed on the basis of the PCC of the relative change in mean expression of highly variable genes. The color bars above the heatmap indicate the cell type and group comprised by all young and old samples. The red boxs, in the heatmap, indicated that Aged EC, Prolife.EC and Proinfla.EC had high correlations.

(G) Composition of the ratios of samples in the young liver (denoted by "Y-liver") and old liver (denoted by "O-liver") group.

(H) RNAscope experiments confirmed the expression of marker genes (*Ctss*, *Osm*) in Proinfla.EC and Aged EC. Micrographs of *Osm* (indicated by green arrowheads) and *Ctss* (indicated by green arrowheads) mRNA transcripts in old liver sections. Immunostaining for Cd31 was used to visualize ECs (indicated by red arrowheads). Nuclei were counterstained with DAPI. Images show the red-, green- and blue-channel images. Green arrowheads indicate *Osm* or *Ctss* RNAscope signals, respectively. Scale bars, 10 μm.

(I) RNAscope experiments and immunofluorescence staining confirmed *Osm* transcripts/p53 (the marker of senescent cells) /Cd31 coimmunostaining for Aged EC in liver sinusoidal region from old and young mice. Scale bar, 20 μm.