Supplementary Figure 1. HCC are hypervascular tumors in which vessels were irregularly covered by pericytes. (A) Representative confocal images of pericyte coverage showing pericyte-covered vessels in three HCC tumors compared to three tumor adjacent normal tissues. Samples were probed by anti-CD31 antibody (red) and anti-NG2 antibody (green). Scale bar 50 μm.

Supplementary Figure 2. $CD34^+$ PLCs formed more aggressive microtumors compared to $CD34^-$ PLCs. (A) Representative confocal images and (B) protein expression of CA9 in $CD34^+$ microtumors compared to $CD34^-$ microtumors, quantified by MFI per microtumor. Samples were probed by anti-CA9 (red) antibody and counterstained by DAPI (blue). Scale bar 50 μm. ****$p < 0.0001$.

Supplementary Figure 3. Microcarriers as supporting matrices enhanced tumor cell-ECM interactions and promoted malignancy of tumor cells. (A) Bright-field microscopy images of spheroids and microtumors embedded in Matrigel on Day 3. Scale bar 50 μm. (B) Quantification of the migration area of spheroids and microtumors. ****$p < 0.0001$.

Supplementary Figure 4. ZA counteracted Sora-elicited vascular immature through enhancing the expression and activation of ErbB1/ErbB2 and PDGFR-β receptors of pericytes. (A) Representative confocal images of vascular pericyte coverage and (B) the quantification of NG2 and CD31 co-staining in microtumors. Microtumors were pretreated with 50 nM ZA, 10 nM SU 16f, 10nM canertinib, 10 nM SU 16f plus 10nM canertinib for 8 hours prior to exposure to ZA for 48 hours. Samples were probed by anti-CD31 (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. ****$p < 0.0001$.

Supplementary Figure 5. ZA enhanced pericyte coverage of vessels in HCC mouse model via upregulating the expression and activation of ErbB1/ErbB2 and PDGFR-β receptors in pericytes. (A) Representative confocal images of ErbB2 expression in pericytes (B) the quantification of ErbB2 expression in pericytes of tumors treated with Sora, ZA, Sora plus ZA. Samples were probed by anti-ErbB2 (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. (C) Representative confocal images of PDGFR-β expression in pericytes (D) the quantification of PDGFR-β

expression in pericytes of tumors treated with Sora, ZA, Sora plus ZA. Samples were probed by anti-PDGFR-β (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. ****$p < 0.0001$.

Supplementary Figure 6. ZA enhanced pericyte coverage of vessels in HCC mouse model via upregulating the expression and activation of ErbB1/ErbB2 and PDGFR-β receptors in pericytes. (A) Representative confocal images of phospho-ErbB1 expression in pericytes (B) the quantification of phospho-ErbB1 expression in pericytes of tumors treated with Sora, ZA, Sora plus ZA. Samples were probed by anti- phospho-ErbB1 (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. (C) Representative confocal images of phospho-ErbB2 expression in pericytes (D) the quantification of phospho-ErbB2 expression in pericytes of tumors treated with Sora, ZA, Sora plus ZA. Samples were probed by anti-phospho-ErbB2 (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. ****$p < 0.0001$.

Supplementary Figure 7. ZA enhanced pericyte coverage of vessels in HCC mouse model via upregulating the expression and activation of ErbB1/ErbB2 and PDGFR-β receptors in pericytes. (A) Representative confocal images of phospho-PDGFR-β expression in pericytes (B) the quantification of phospho-PDGFR-β expression in pericytes of tumors treated with Sora, ZA, Sora plus ZA. Samples were probed by anti- phospho-PDGFR-β (red) and anti-NG2 (green) antibodies. Scale bar 50 μm. ****$p < 0.0001$.

Supplementary Figure 8. (A) Establishment of 3D model of tumor-driven angiogenesis. (a) The mixture of HUVECs and pericytes was co-cultured with microcarriers. (b) HUVECs and pericytes formed pericyte-covered endothelial tubes on microcarriers. (c) Addition of $CD34^+$ PLCs and MSCs to microcarriers carrying pericyte-covered vessels to form multicellular aggregates. (d) The formation of vascularized tumor microtissue. (B) Schematic diagram of ZA enhanced pericyte recruitment to vessels. (C) Schematic diagram of the proposed mechanisms by which ZA promoted pericyte recruitment to vessels.

Figure S1

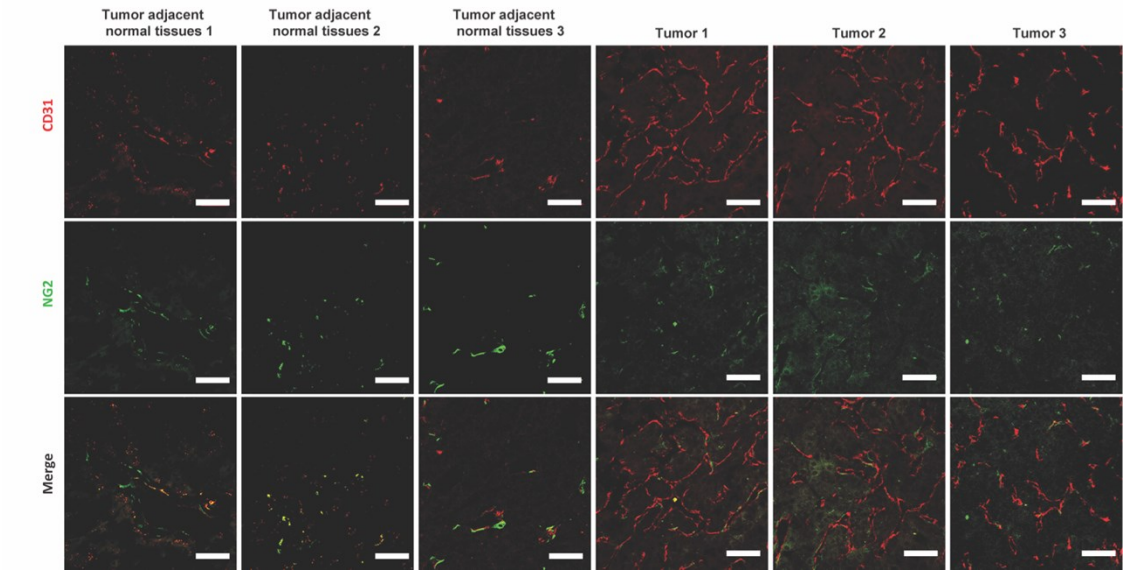


Figure S2

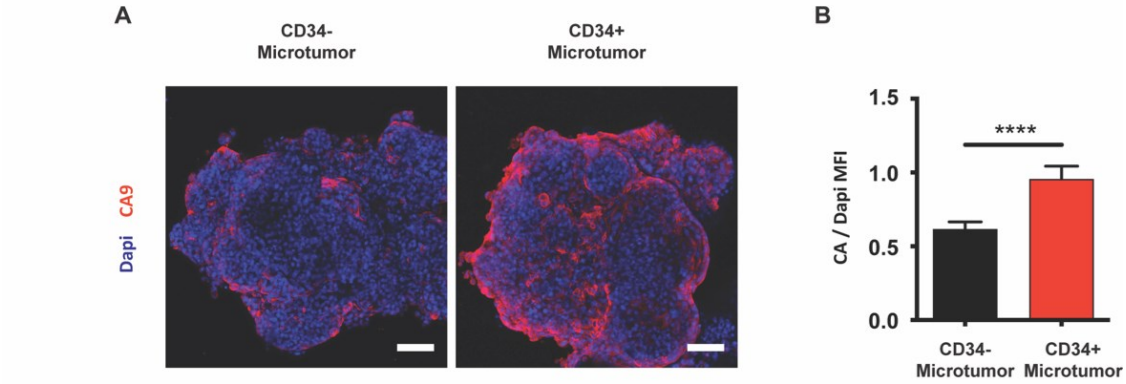


Figure S3

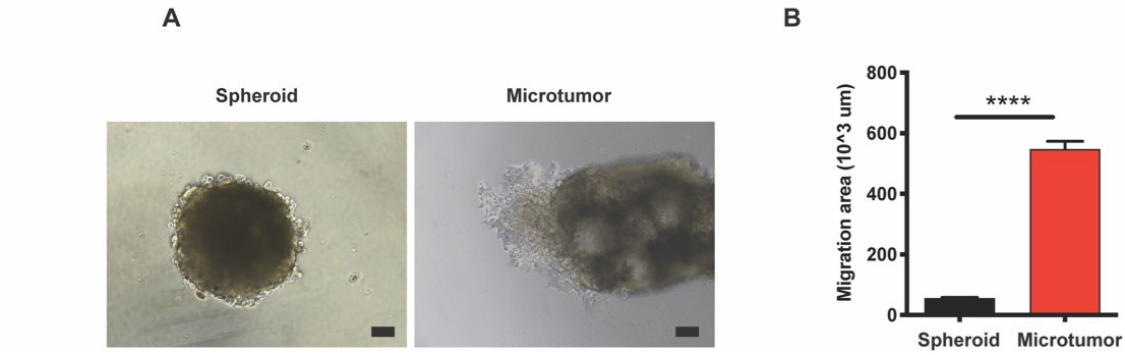


Figure S4

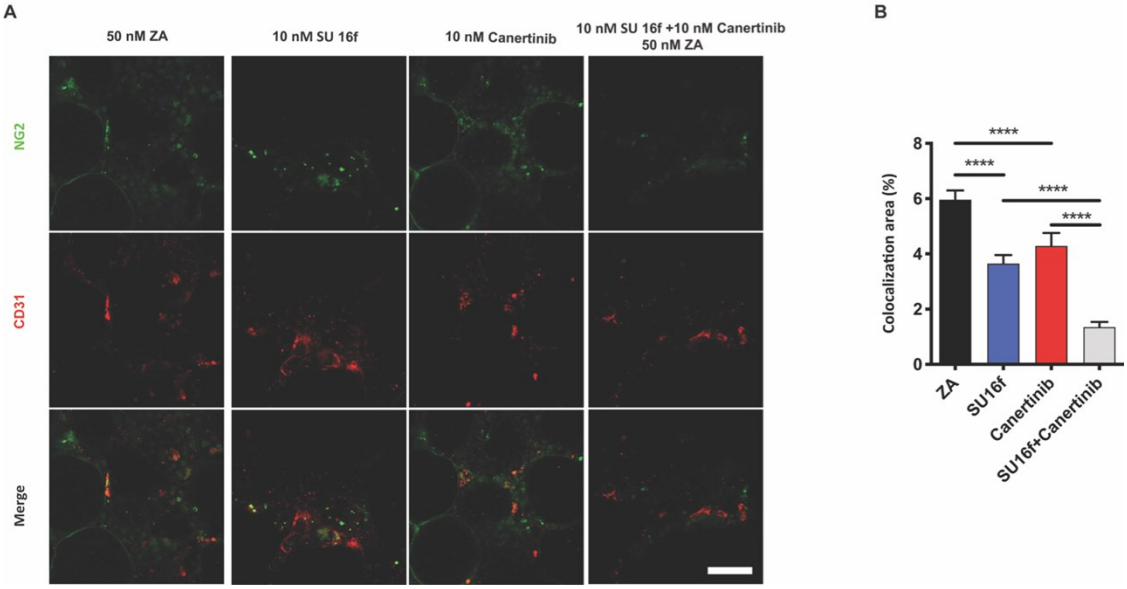

A
50 nM ZA
10 nM SU 16f
10 nM Canertinib
10 nM SU 16f +10 nM Canertinib
50 nM ZA
NG2
CD31
Merge
B
Colocalization area (%)
8
6
4
2
0
****
****
****
****
ZA
SU16f
Canertinib
SU16f+Canertinib

Figure S5

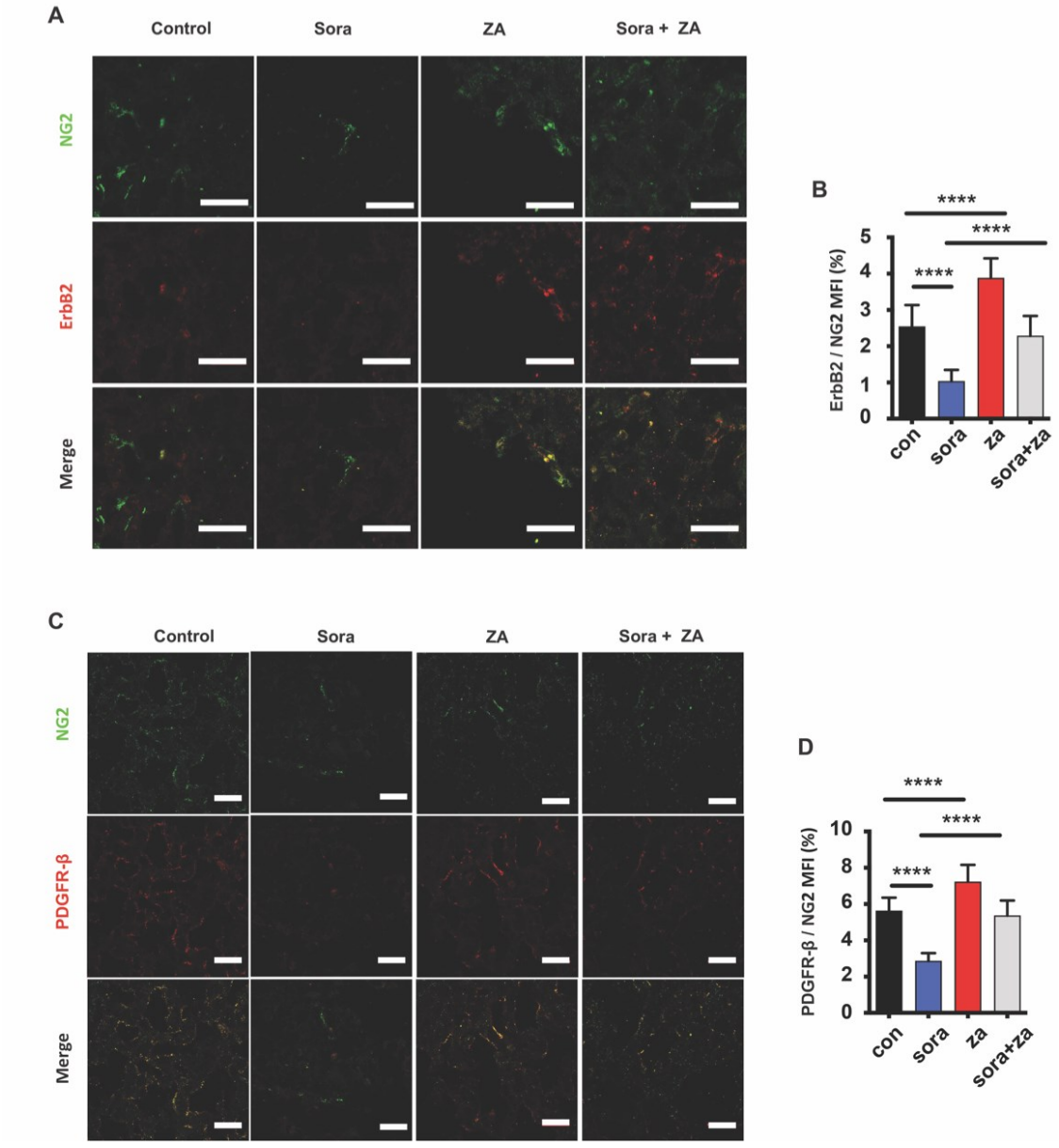

A
Control
Sora
ZA
Sora + ZA
NG2
ErbB2
Merge
B
ErbB2 / NG2 MFI (%)
0
1
2
3
4
5
****
****
****
con
sora
za
sora+za
C
Control
Sora
ZA
Sora + ZA
NG2
PDGFR-β
Merge
D
PDGFR-β / NG2 MFI (%)
0
2
4
6
8
10
****
****
****
con
sora
za
sora+za

Figure S6

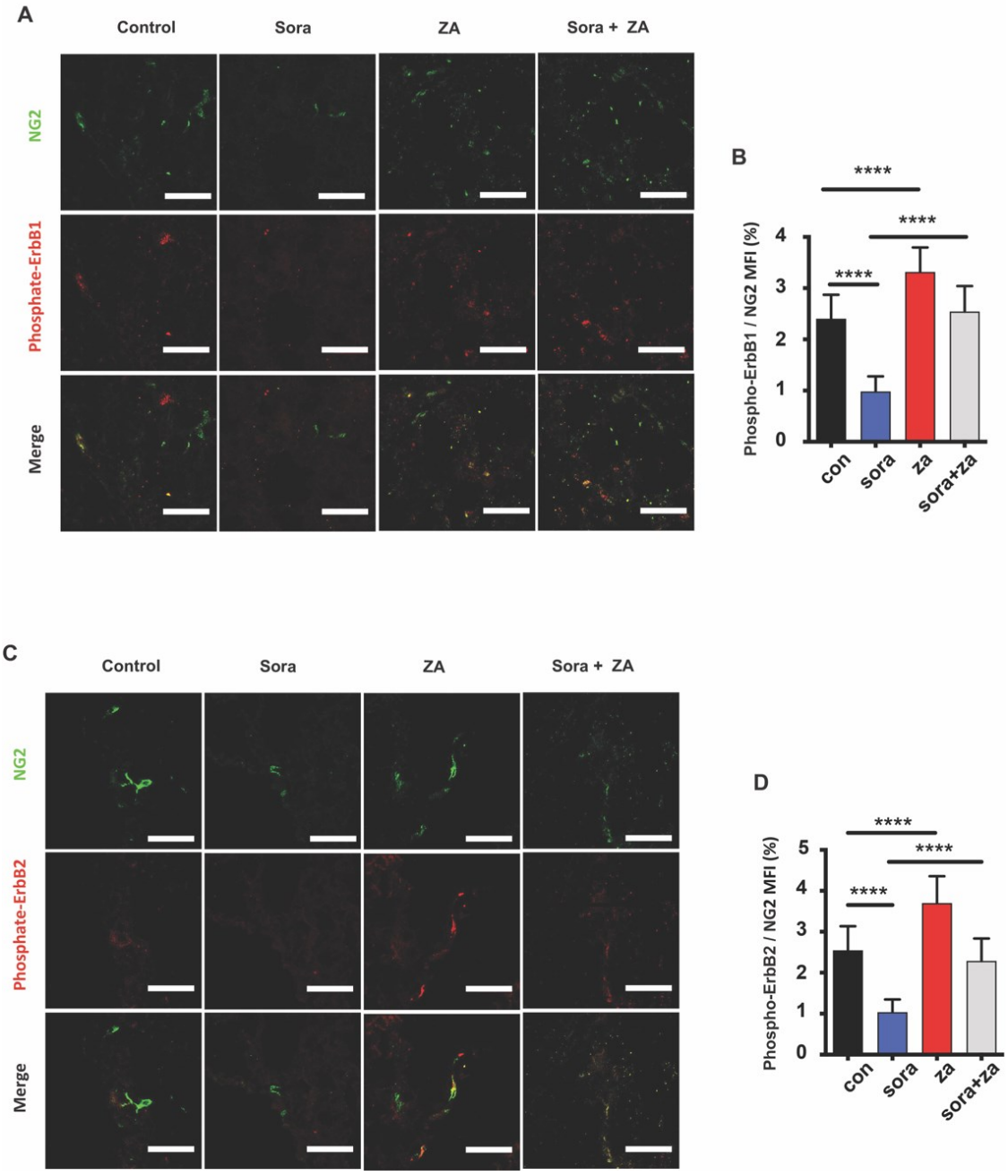

A
Control
Sora
ZA
Sora + ZA
NG2
Phosphate-ErbB1
Merge
B
Phospho-ErbB1 / NG2 MFI (%)
****
****
****
0
1
2
3
4
con
sora
za
sora+za
C
Control
Sora
ZA
Sora + ZA
NG2
Phosphate-ErbB2
Merge
D
Phospho-ErbB2 / NG2 MFI (%)
****
****
****
0
1
2
3
4
5
con
sora
za
sora+za

Figure S7

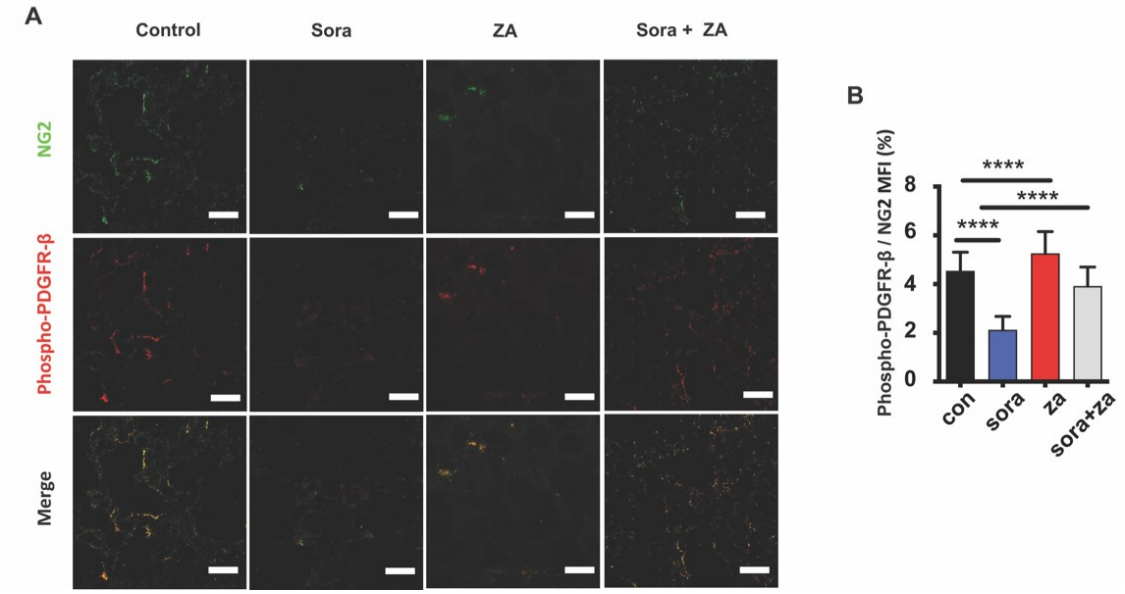
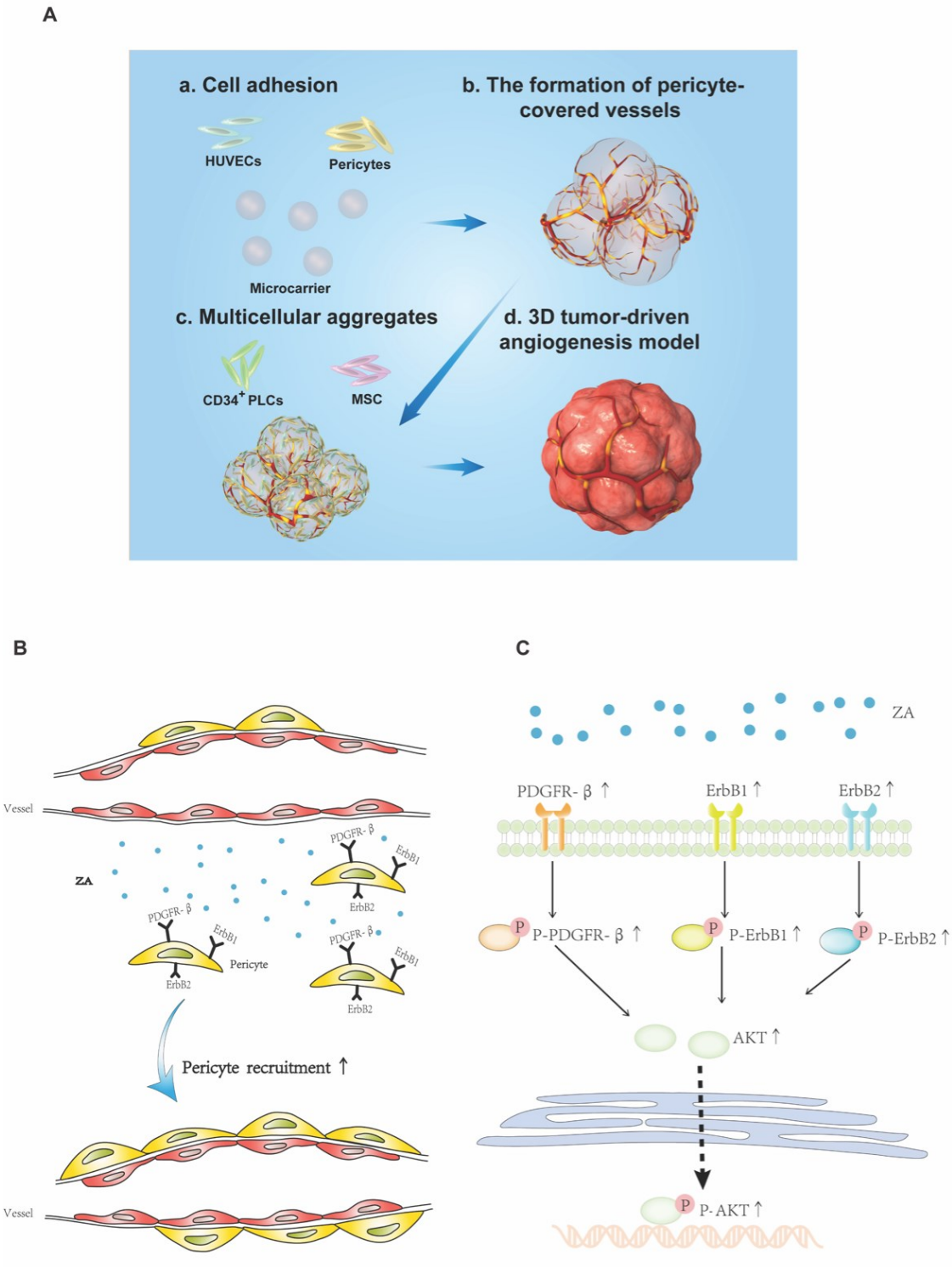

A
Control
Sora
ZA
Sora + ZA
NG2
Phospho-PDGFR-β
Merge
B
Phospho-PDGFR-β / NG2 MFI (%)
0
2
4
6
8
****
****
****
con
sora
za
sora+za

Figure S8


A
a. Cell adhesion
b. The formation of pericyte-covered vessels
HUVECs
Pericytes
Microcarrier
c. Multicellular aggregates
d. 3D tumor-driven angiogenesis model
CD34+ PLCs
MSC
B
Vessel
ZA
PDGFR- β
ErbB1
ErbB2
Pericyte
Pericyte recruitment ↑
Vessel
C
ZA
PDGFR- β ↑
ErbB1 ↑
ErbB2 ↑
P-PDGFR- β ↑
P-ErbB1 ↑
P-ErbB2 ↑
AKT ↑
P-AKT ↑