Date:December 11,2021 Your Name:Beibei Wang Manuscript Title:Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis by upregulating endoglin signaling Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed) Time frame: Since the initial	Specifications/Comments (e.g., if payments were made to you or to your institution)
1	All support for the present manuscript (e.g., funding, provision of study materials,	the Health science and Technology Project of Zhejiang Province	2022RC047 to Beibei Wang
	medical writing, article processing charges, etc.) <b>No time limit for this item.</b>		
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None    Image: Constraint of the second seco
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None

The author reports funding support from the Health science and Technology Project of Zhejiang Province (2022RC047).

Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:\_<u>Nian Dong</u>\_\_\_ Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> <u>by upregulating endoglin signaling</u> Manuscript number (if known):\_\_\_\_\_

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) <b>No time limit for this item.</b>	Time frame: Since the initial	planning of the work
		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	None	
3	Royalties or licenses	None	
4	Consulting fees	None	

5	Payment or honoraria for lectures, presentations, speakers bureaus,	None	
	manuscript writing or		
	educational events		
6	Payment for expert	None	
	testimony		
_			
7	Support for attending meetings and/or travel	None	
8	Patents planned, issued or	None	
	pending		
9	Participation on a Data Safety Monitoring Board or	None	
	Advisory Board		
10	,	None	
	in other board, society,		
	committee or advocacy		
	group, paid or unpaid		
11	Stock or stock options	None	
- 10			
12	Receipt of equipment,	None	
	materials, drugs, medical writing, gifts or other		
	services		
13	Other financial or non-	None	
10	financial interests		

None

# Please place an "X" next to the following statement to indicate your agreement:

Date: <u>December 11,2021</u>
Your Name:_ <u>Dengmin Wu</u>
Manuscript Title: Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis
by upregulating endoglin signaling
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present	None	
	manuscript (e.g., funding,		
	provision of study materials,		
	medical writing, article		
	processing charges, etc.)		
	No time limit for this item.		
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None    Image: Constraint of the second seco
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None      Image: Constraint of the second se

None

### Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:<u>Ya Fang</u> Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> <u>by upregulating endoglin signaling</u> Manuscript number (if known):\_\_\_\_\_

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
1		Time frame: Since the initial	planning of the work
1	All support for the present	None	
	manuscript (e.g., funding, provision of study materials,		
	medical writing, article		
	processing charges, etc.)		
	No time limit for this item.		
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None

None

### Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:\_<u>Junjie Chen</u>\_ Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> <u>by upregulating endoglin signaling</u> Manuscript number (if known):\_\_\_\_\_

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) No time limit for this item.	the Natural Science Foundation of Zhejiang Province	LQ20H010002 to Junjie Chen
		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	None	
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None

*The author reports funding support from the Natural Science Foundation of Zhejiang Province (LQ20H010002).* 

Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:<u>Yuting Lin</u> Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> <u>by upregulating endoglin signaling</u> Manuscript number (if known):\_\_\_\_\_

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present	None	
	manuscript (e.g., funding,		
	provision of study materials,		
	medical writing, article		
	processing charges, etc.)		
	No time limit for this item.		
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None    Image: Constraint of the second seco
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None      Image: Constraint of the second se

None

### Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:<u>Saverio Bellusci</u> Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> by upregulating endoglin signaling Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) <b>No time limit for this item.</b>	the Deutsche Forschungsgemeinschaft the First Affiliated Hospital of Wenzhou Medical University	EXC 2026, Project ID: 390649896 and SFB1213-projects A02 and A04 to Saverio Bellusci a startup grant to Saverio Bellusci
		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	None	
3	Royalties or licenses	None	
4	Consulting fees	None	

5	Devenant or honoraris for	News
З	Payment or honoraria for	None
	lectures, presentations,	
	speakers bureaus,	
	manuscript writing or	
	educational events	
6	Payment for expert	None
	testimony	
7	Support for attending	None
	meetings and/or travel	
8	Patents planned, issued or	None
•	pending	
	pending	
9	Participation on a Data	None
9	Safety Monitoring Board or	None
	Advisory Board	
10	-	Alexa de la constante de la consta
10	Leadership or fiduciary role in other board, society, committee or advocacy	None
	group, paid or unpaid	
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical	None
	writing, gifts or other	
	services	
13	Other financial or non-	None
	financial interests	

The author reports funding support from the Deutsche Forschungsgemeinschaft (EXC 2026, Project ID: 390649896 and SFB1213-projects A02 and A04) and the First Affiliated Hospital of Wenzhou Medical University.

#### Please place an "X" next to the following statement to indicate your agreement:

Date: <u>December 11,2021</u>
Your Name:Jin-San Zhang
Manuscript Title: Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis
by upregulating endoglin signaling
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed) Time frame: Since the initial	Specifications/Comments (e.g., if payments were made to you or to your institution)
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) <b>No time limit for this item.</b>	Wenzhou Medical University	a startup package to Jin-San Zhang
		Time frame: past	36 months
2	Grants or contracts from any entity (if not indicated in item #1 above).	None	
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None

The author reports funding support from Wenzhou Medical University.

Please place an "X" next to the following statement to indicate your agreement:

Date:<u>December 11,2021</u> Your Name:<u>Kezhi Dai</u> Manuscript Title:<u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u> <u>by upregulating endoglin signaling</u> Manuscript number (if known):\_\_\_\_\_

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed) Time frame: Since the initial	Specifications/Comments (e.g., if payments were made to you or to your institution)
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article	the Natural Science Foundation of Zhejiang Province	LY20C070002 to Kezhi Dai
	processing charges, etc.) No time limit for this item.		
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	
4	Consulting fees	None	
5	Payment or honoraria for	None	

6	lectures, presentations, speakers bureaus, manuscript writing or educational events Payment for expert testimony	None
7	Support for attending meetings and/or travel	None
8	Patents planned, issued or pending	None
9	Participation on a Data Safety Monitoring Board or Advisory Board	None
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	None
11	Stock or stock options	None
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	None
13	Other financial or non- financial interests	None

*The author reports funding support from the Natural Science Foundation of Zhejiang Province (LY20C070002).* 

Please place an "X" next to the following statement to indicate your agreement:

Date: <u>December 11,2021</u>
Your Name: <u>Chengshui Chen</u>
Manuscript Title: <u>Sphingosine 1-phosphate receptor 1 governs endothelial barrier function and angiogenesis</u>
by upregulating endoglin signaling
Manuscript number (if known):

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The following questions apply to the author's relationships/activities/interests as they relate to the <u>current</u> <u>manuscript only</u>.

The author's relationships/activities/interests should be <u>defined broadly</u>. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
		Time frame: Since the initial	planning of the work
1	All support for the present manuscript (e.g., funding, provision of study materials,	the National Natural Science Foundation of China	81770074 to Chengshui Chen
	medical writing, article	the Science and	2020C03067 to Chengshui Chen
	processing charges, etc.)	Technology project of	
	No time limit for this item.	Zhejiang Province	
		the Key Technologies	2016YFC1304000 to Chengshui Chen
		Research and	
		Development Program of	
		China	
		Time frame: past	36 months
2	Grants or contracts from	None	
	any entity (if not indicated		
	in item #1 above).		
3	Royalties or licenses	None	

4	Consulting fees	None
5	Doumont or honoraria for	None
Э	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or	None
	educational events	
6	Payment for expert testimony	None
	testimony	
7	Support for attending meetings and/or travel	None
	meetings and/or traver	
8	Patents planned, issued or pending	None
9	Participation on a Data	None
	Safety Monitoring Board or Advisory Board	
10	Leadership or fiduciary role	None
	in other board, society, committee or advocacy	
	group, paid or unpaid	
11	Stock or stock options	None
12	Receipt of equipment	None
12	Receipt of equipment, materials, drugs, medical	
	writing, gifts or other services	
13	Other financial or non-	None
	financial interests	

the author reports funding support from the National Natural Science Foundation of China (81770074), the Science and Technology project of Zhejiang Province (2020C03067), and the Key Technologies Research and Development Program of China (2016YFC1304000). Please place an "X" next to the following statement to indicate your agreement: