OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Zahedan Journal of Research in Medical Sciences
Article DOI: 10.5812/zjrms.9936
Published in: Zahedan Journal of Research in Medical Sciences: 21(4); e9936

Peer Review Report for "The Apoptotic Pathway Induced by Vincristine in Mouse Proliferating and Resting Normal Lymphocytes and Lymphoma Cell Line"

Author(s): Mohaddese Shahhosseini, Susan Kaboudanian Ardestani , Roya Yaraee

Review Timeline:

Submit Date:	5 Dec 2016
Revised Date:	28 Apr 2019
Accepted Date:	22 Jul 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) — 4 Jan 2017

Dear AE,
1. Please the authors correct the abstract according to the journal format
2. Please notify about different possible side effects of Vincristine
3. LDH assay is recommended for toxicity detection
4. The authors claim that "causes an increase in the activity of caspases 8 and 9 detectable 20 min after adding substrate to cell lysate" this is because of caspases auto-activation or increase in caspase transcription
5. What is your evidence for cell arrest after treatment by Vincristine
6. One of Vincristine side effect is on Cytochrome P450 3A5 that may affect your cell apoptosis how do you interprate that,
7. Please tell about Biological Half-Life of Vincristine in vitro.
Thanks.

REFEREE: Reviewer | **Revision** (0) — 21 Jan 2017

Dear AE

This manuscript might be of interest for ZJRMS readers, although there are several concerns:
1- The English writing needs vast editorial and language corrections to be fit for publishing.
2- It is needed to discuss the results better and more deeply in the discussion part. The discussion is very brief. On the other hand, the results are very long and they should be summarized and repetitions must be omitted.
3- References for protein and enzyme measurements should be written.
4- Statistical analysis and level of significance should be written. A number of samples or repetitions must be shown.
5- It seems to my opinion that the figures and absorbances are not necessary. Why the absorbances are not converted to enzyme activity and if they did way you repeat them? May explanations of the figure titles are repetition from text and are not necessary
6- Some results for enzyme assays in the tables are ZERO; while these may be under the detection limit of the method applied. On the other hand, may they be not delectable?
7- The manuscript must be reconsidered to fit the standard format of the journal. (For instance, abstract and references should be reconsidered)
8- Abbreviations should not be used in the manuscript without full name definition in the first time. (for instance in the abstract)
Thanks.

REFEREE: Reviewer | **Revision** (0) 10 Feb 2017

Dear AE,
In this article, the authors studied the effect of Vincristine on apoptosis induction in tumor cells in comparison to mouse splenocytes. The article is well written, however some modifications must be done before consideration for publication.
1- The most important issue is that statistical analysis should be used to present all the differences that have been observed between groups.
2- Instead of using general phrases such as “mild increase” (Discussion, Paragraph 6), authors must use p-value to show the differences.
3- The data are shown in Figure 4 without the error bar.
4- The data that are presented in table 1, 2 and 3, must be summarized, and should be presented in the figure 1, 2 and 3, respectively. Then the tables must be deleted.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 20 Feb 2017

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: EIC | **Revision** (0) 20 Feb 2017

Dear Author,
The manuscript needs MAJOR REVISION. Please sign in to your account and follow the

instruction to submit your revised paper. With respect to the time restriction, we are looking forward to hearing you soon and in the mentioned time frame. For further details refer to the end of this email and read the ATTACHMENT.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear editor,

Concerning manuscript # 9936

I have received the reviewer comments. Thank you and all of the reviewers for comments. Sorry for too long delay in response due to some personal and occupational issues. The answers are followed here one by one and the changes were shown with yellow marker in the revised text:

Reviewer #1:

1. please correct your abstract according to journal format
1- The abstract was revised according to journal format.

2.please notify about different possible side effects of Vincristine
2- Probable side effects of vincristine were mentioned.

3.LDH assay is recommended for toxicity detection
3- LDH assay is very useful test in this regard, unfortunately we had not included it in our research plan, yet no plan to perform it now.

4.you claim that "causes an increase in the activity of caspases 8 and 9 detectable 20 min after adding substrate to cell lysate" this is because of caspases auto-activation or increase in caspase transcription
4- According to our method in which enzymatic activity was assayed, we have observed the activity. In the case of caspases with strong regulatory mechanisms, an increase in transcription may not lead to activity.

5. what is your evidence for cell arrest after treatment by Vincristine
5- according to MTT assay in our project [Ref.13] and also various studies in literature.

6. one of Vincristine side effect is on Cytochrome P450 3A5 that may affect your cell apoptosis how do you interprate that,
6- It may have a role in toxicity induced by vincristine (as well as many other drugs, Ref) but we did not evaluate this mechanism in our study.

Quintanilha JCF, de Sousa VM, Visacri MB, Amaral LS, Santos RMM, Zambrano T, Salazar LA, Moriel P. Involvement of cytochrome P450 in cisplatin treatment: implications for toxicity. Cancer Chemother Pharmacol. 2017;80(2):223-233.

7. please tell about Biological Half-Life of Vincristine in vitro
7- Biological half-life of vincristine was added in text, although its half-life wide range as mentioned:

The strong antileukemic activity of vincristine has been limited by its variable and unpredictable pharmacological characteristics, narrow therapeutic index and neurotoxicity profile (Said R, Tsimberidou AM. Pharmacokinetic evaluation of vincristine for the treatment of lymphoid malignancies. Expert Opin Drug Metab Toxicol. 2014 Mar;10(3):483-94.) Pharmacokinetic studies in patients with cancer have shown a triphasic serum decay pattern following rapid intravenous injection. The initial, middle and terminal half–lives are 5 minutes, 2.3 hours, and 85 hours respectively; however, the range of the terminal half–life in humans is from 19 to 155 hours (https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=49596de6-ab18-49d1-9e5b-30968fc21c36&type=display).

Thanks for useful comments.

Reviewer #2:

This manuscript might be of interest for ZJRMS readers, although there are several concerns:
1- The English writing needs vast editorial and language corrections to be fit for publishing.
1- The English writing was revised as possible.

2- It is needed to discuss about the results better and more deeply in the discussion part. The discussion is very brief. On the other hand the results is very long and it should be summarized and repetitions must be omitted.
2- The results were summarized as possible (3 tables merged with figures) and some notes were added to discussion.

3- references for protein and enzyme measurements should be written.
3- References for protein and enzyme measurements were mentioned.

4-statistical analysis and level of significance should be written. Number of samples or repetitions must be shown.
4- Statistical analysis, level of significance and number of samples were written.

5-it seems to my opinion that the figures and absorbances are not necessary. Why the absorbances are not converted to enzyme activity and if done way you repeat them? May explanations of the figure titles are repetition from text and are not necessary
5- Figures and absorbances were merged.

6- Some results for enzyme assays in the tables are ZERO; while these may be under the detection limit of the method applied. On the other hand, does they may be not delectable?
6- Zero in tables were replaced by not delectable (ND).

7- The manuscript must be reconsidered to fit the standard format of the journal. (For instance abstract and references should be reconsidered)
7- The manuscript was revised according to journal format.

8- Abbreviations should not be used in the manuscript without full name definition in the first time. (for instance in the abstract)
8- Full name of abbreviations was mentioned first time in the main text (not the abstract).

Thanks for comments.

Reviewer #3:

In this article, the authors studied the effect of Vincristine on apoptosis induction in tumor cells in comparison to mouse splenocytes. The article is well written, however some modifications must be done before consideration for publication.
1- The most important issue is that statistical analysis should be used to present all the differences that have been observed between groups.
2- Instead of using general phrases such as "mild increase" (Discussion, Paragraph 6), authors must use p-value to show the differences.
1 and 2- Statistical analysis, level of significance and number of samples were written.

3- The data are shown in Figure 4 without the error bar.
3- The error bar in this test is too small and hardly observable.

4- The data that are presented in table 1, 2 and 3, must be summarized, and should be presented in the figure 1, 2 and 3, respectively. Then the tables must be deleted.
4- Figures and Tables were merged.

Thanks for comments.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 19 Jan 2019

Dear AE,
All the comments are revised in the manuscript.
best regards

REFEREE: Reviewer | **Revision** (1) 7 Apr 2019

Dear AE,
Previous comment and its response:
6- Some results for enzyme assays in the tables are ZERO; while these may be under the detection limit of the method applied. On the other hand, may they be not delectable?
6- Zero in tables were replaced by not detectable (ND)'
however, ND is not included in the table in the revised version.
Thanks.

REFEREE: Reviewer | **Revision** (1) 8 Apr 2019

Dear AE,
The manuscript is upgraded according to the comments of reviewers. However, the ANOVA test seems to be not an appropriate analysis method to compare the differences between groups. the analysis should be done by using a non-parametric method. The median and p-value of caspases activity and possible differences should be mentioned in the text.
Thanks.

REFEREE: Associate Editor | **Revision** (1) 9 Apr 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (1) 9 Apr 2019

Dear Author,

Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.

Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear editor,

Concerning manuscript # 9936

I have received the reviewer comments. The answers are followed here one by one and the changes were shown with yellow marker in the edited text:

Reviewer 1:

hello dear editor in chief
all the comments are revised in the manuscript.
best regards

Thanks for useful comments.

Reviewer 2:

The manuscript is upgraded according to the comments of reviewers. However, the ANOVA test seems to be not an appropriate analysis method to compare the differences between groups. the analysis should be done by using a non-parametric method. The median and p-value of caspases activity and possible differences should be mentioned in the text.

In old manuscript, the SDs had been shown only in graphs (although in some cases they were too low to be seen); now we included the SD of the mean caspase activity in the tables and the text.

The experiments were performed multiple times so there are enough data for parametric test. (attachment). We also reanalyzed the data Using G-instat. The results were not different in general; for example caspase 8 in BCL1:

The P value is 0.0002, considered extremely significant.
Variation among column means is significantly greater than expected by chance.

Tukey-Kramer Multiple Comparisons Test
If the value of q is greater than 5.910 then the P value is less than 0.05.

Comparison	Mean Difference	q	P value
5 ug/ml Vin vs 10 ug/ml Vin	-1.940	6.751	* P<0.05
5 ug/ml Vin vs 20 ug/ml Vin	-11.500	40.022	*** P<0.001
10 ug/ml Vin vs 20 ug/ml Vin	-9.560	33.270	*** P<0.001

But according to the point that in our experiments, the caspase activity in Negative Controls was not detectable, it was not possible to parametrically analyze the data and compare them with zero (C-) but other groups are statistically comparable.

As you mentioned precisely these data may be suitable for non-parametric analyses (it has caspase activity or not) which we not our interesting. The main point for us was that: in which type of cells which caspase (or which apoptotic pathway) is activated? So we have used "fold increase" according to resting + 5 µg/ml (and not C-)

Thanks for useful comments

Reviewer 3:

"previous comment and its response"
6- Some results for enzyme assays in the tables are ZERO; while these may be under the detection limit of the method applied. On the other hand, does they may be not delectable?
6- Zero in tables were replaced by not delectable (ND)'
however, ND is not included in the table in the revised version.

You are absolutely right and I just lost it. Sorry. It is now included.

Thank you and all of the reviewers for comments.

Attachments

BCL1

		caspase 3 activity		caspase 8 activity		caspase 9 activity	
	time	mean	SD	mean	SD	mean	SD
without sub	0	0.0695	0.002121	0.0635	0.006364	0.061	0.014142
	10	0.075	0.011314	0.074	0.009899	0.073	0.011314
	20	0.0625	0.007778	0.062	0.002828	0.069	0.009899
	30	0.059	0.008485	0.0685	0.012021	0.072	0
	40	0.063	0	0.0655	0.009192	0.0695	0.00495
	50	0.065	0.005657	0.063	0.002828	0.066	0.005657
	60	0.0555	0.00495	0.061	0.001414	0.065	0.004243
without cell lysis	0	0.0595	0.000707	0.0635	0.000707	0.0625	0.003536
	10	0.0615	0.00495	0.066	0.002828	0.0675	0.00495
	20	0.0615	0.002121	0.067	0.011314	0.059	0
	30	0.065	0.001414	0.0635	0.000707	0.0605	0.000707
	40	0.0635	0.002121	0.0665	0.000707	0.065	0.002828
	50	0.0645	0.00495	0.065	0.004243	0.0645	0.003536
	60	0.0545	0.006364	0.3725	0.434871	0.064	0.009899
- control	0	0.1105	0.055861	0.091	0	0.0575	0.000707
	10	0.1135	0.053033	0.096	0	0.0565	0.003536
	20	0.1035	0.04879	0.088	0	0.055	0.001414
	30	0.0985	0.041719	0.079	0	0.06	0
	40	0.1325	0.098288	0.095	0	0.0575	0.002121
	50	0.14	0.106066	0.099	0	0.0575	0.007778
	60	0.115	0.067882	0.5335	0.617304	0.058	0.001414
vin 5	0	0.1295	0.044548	0.0995	0.000707	0.113	0.007071
	10	0.2205	0.045962	0.1105	0.003536	0.116	0.005657
	20	0.2455	0.053033	0.1755	0.00495	0.2035	0.007778

	30	0.296	0.015556	0.293	0.002828	0.3065	0.006364
	40	0.2985	0.026163	0.358	0.014142	0.3575	0.00495
	50	0.324	0.056569	0.3795	0.006364	0.37	0.001414
	60	0.3235	0.060104	0.3765	0.012021	0.369	0
IC50	0	0.095	0.012728	0.1115	0.00495	0.0945	0.000707
	10	0.0825	0.016263	0.1095	0.007778	0.1245	0.014849
	20	0.0895	0.003536	0.121	0.025456	0.155	0.002828
	30	0.08	0.007071	0.1675	0.088388	0.195	0
	40	0.0825	0.007778	0.2075	0.133643	0.234	0.016971
	50	0.088	0.008485	0.2025	0.1393	0.241	0.004243
	60	0.1215	0.014849	0.2045	0.135057	0.241	0.019799

Resting lymphocytes

		caspase 3		caspase 8		caspase 9	
	time	mean	SD	mean	SD	mean	SD
without sub	0	0.0765	0.007778	0.057	0.002828	0.057	0.004243
	10	0.0765	0.007778	0.057	0.004243	0.059	0.009899
	20	0.0765	0.002121	0.0575	0.003536	0.0635	0.003536
	30	0.0775	0.003536	0.0565	0.000707	0.0595	0.000707
	40	0.08	0	0.0605	0.014849	0.069	0.014142
	50	0.0785	0.00495	0.067	0.008485	0.058	0.001414
	60	0.079	0.004243	0.0655	0.006364	0.061	
without cell lysis	0	0.072	0.004243	0.078	0.009899	0.083	0.016971
	10	0.07	0.002828	0.082	0.012728	0.0895	0.003536
	20	0.0625	0.003536	0.0745	0.006364	0.079	0.004243
	30	0.062	0.002828	0.0715	0.007778	0.0725	0.00495
	40	0.0715	0.000707	0.0775	0.009192	0.083	0.018385
	50	0.0675	0.002121	0.079	0.015556	0.0775	0.000707

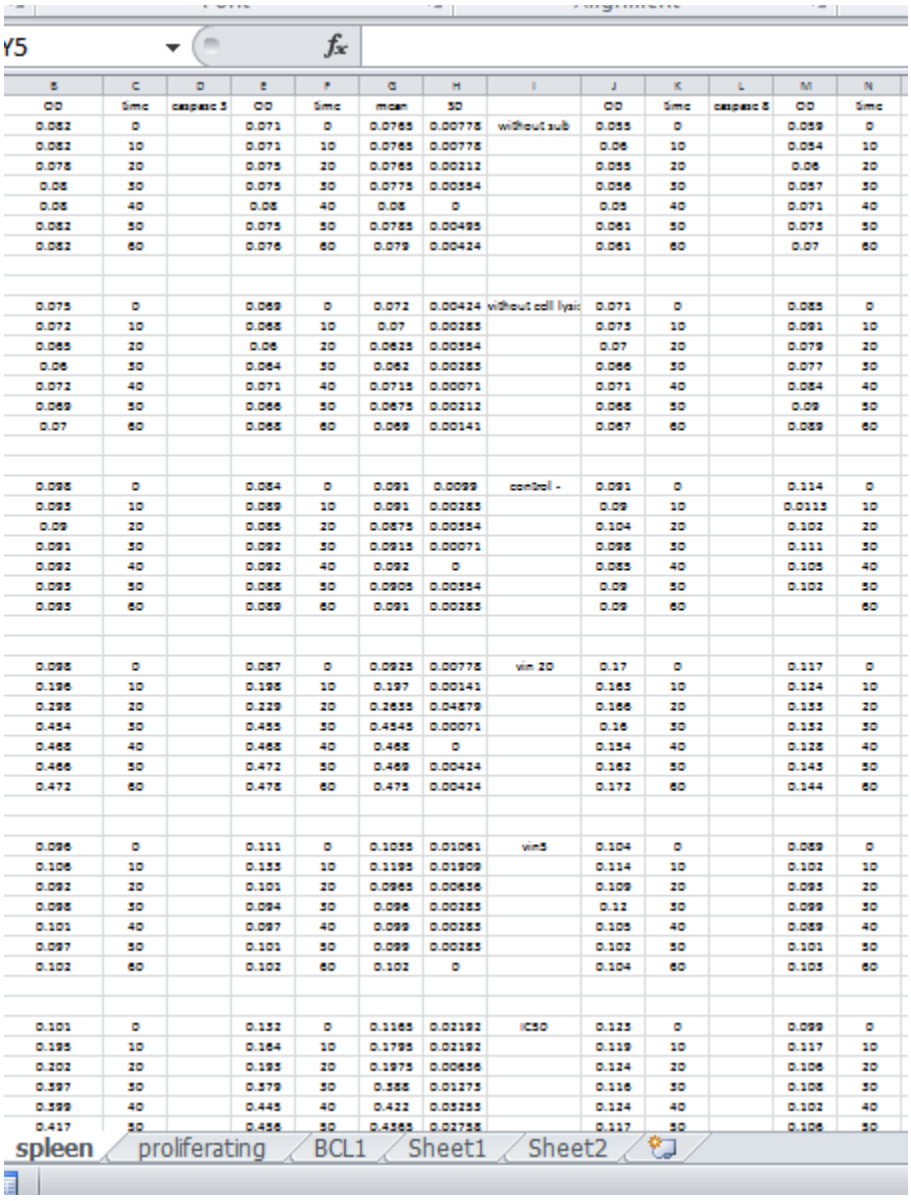
	60	0.069	0.001414	0.078	0.015556	0.095	
- control	0	0.091	0.009899	0.1025	0.016263	0.106	0.012728
	10	0.091	0.002828	0.05065	0.055649	0.1055	0.007778
	20	0.0875	0.003536	0.103	0.001414	0.1015	0.010607
	30	0.0915	0.000707	0.1045	0.009192	0.1035	0.000707
	40	0.092	0	0.095	0.014142	0.1055	0.013435
	50	0.0905	0.003536	0.096	0.008485	0.098	0.007071
	60	0.091	0.002828	0.09	!DIV/0#	0.1025	0.010607
vin 20	0	0.0925	0.007778	0.1435	0.037477	0.111	0.015556
	10	0.197	0.001414	0.1435	0.027577	0.2235	0.013435
	20	0.2635	0.04879	0.1495	0.023335	0.5105	0.020506
	30	0.4545	0.000707	0.146	0.019799	0.5215	0.02192
	40	0.468	0	0.141	0.018385	0.5325	0.017678
	50	0.469	0.004243	0.1525	0.013435	0.524	0.004243
	60	0.475	0.004243	0.158	0.019799	0.532	0.004243
vin5	0	0.1035	0.010607	0.0965	0.010607	0.105	0.022627
	10	0.1195	0.019092	0.108	0.008485	0.147	0.056569
	20	0.0965	0.006364	0.101	0.011314	0.2065	0.026163
	30	0.096	0.002828	0.1095	0.014849	0.199	0.024042
	40	0.099	0.002828	0.097	0.011314	0.285	0.024042
	50	0.099	0.002828	0.1015	0.000707	0.2915	0.012021
	60	0.102	0	0.1035	0.000707	0.2915	0.016263
IC50	0	0.1165	0.02192	0.111	0.016971	0.0995	0.003536
	10	0.1795	0.02192	0.118	0.001414	0.1175	0.009192
	20	0.1975	0.006364	0.115	0.012728	0.1995	0.007778
	30	0.388	0.012728	0.112	0.005657	0.393	0.007071
	40	0.422	0.032527	0.113	0.015556	0.4045	0.012021
	50	0.4365	0.02757	0.1115	0.00777	0.4035	0.00070

			7		8		7
	60	0.4325	0.036062	0.114	0.011314	0.406	0.008485

Proliferating Lymphocytes

		caspase 3		caspase 8		caspase 9	
	time	mean	SD	mean	SD	mean	SD
without sub	0	0.059	0.004243	0.0675	0.007778	0.0625	0.003536
	10	0.0615	0.007778	0.0695	0.00495	0.0665	0.000707
	20	0.0575	0.006364	0.0625	0.000707	0.054	0.001414
	30	0.06	0.004243	0.062	0.007071	0.058	0.001414
	40	0.0575	0.010607	0.0605	0.002121	0.0565	0.002121
	50	0.069	0.007071	0.073	0.001414	0.0685	0.000707
	60	0.061	0.007071	0.0605	0.003536	0.0625	0.000707
without cell lysis	0	0.0585	0.00495	0.076	0.001414	0.0665	0.00495
	10	0.06	0.005657	0.0775	0.000707	0.0675	0.003536
	20	0.0555	0.003536	0.066	0.011314	0.0675	0.00495
	30	0.0635	0.002121	0.0725	0.014849	0.0725	0.00495
	40	0.0655	0.003536	0.0685	0.000707	0.0685	0.002121
	50	0.0665	0.000707	0.0745	0.010607	0.068	0.001414
	60	0.062	0	0.0705	0.012021	0.0705	0.006364
- control	0	0.0895	0.000707	0.141	0.019799	0.083	0.001414
	10	0.093	0.001414	0.17	0.01	0.093	0.007071
	20	0.0865	0.00495	0.162	0.04	0.0865	0.002121
	30	0.0915	0.003536	0.157	0.02	0.087	0.001414
	40	0.0935	0.00495	0.152	0.009899	0.0935	0.002121
	50	0.094	0.002828	0.1715	0.010607	0.091	0.007071
	60	0.0915	0.002121	0.191	0.011314	0.0855	0.00495
vin 20	0	0.106	0.005657	0.1085	0.000707	0.144	0
	10	0.1935	0.003536	0.109	0.005657	0.285	0
	20	0.371	0.01272	0.109	0.00565	0.466	0

			8		7		
	30	0.556	0.029698	0.1225	0.02192	0.8275	0.000707
	40	0.595	0.012728	0.179	0.024042	0.883	0
	50	0.5835	0.023335	0.201	0.02687	0.927	0
	60	0.5975	0.020506	0.193	0.049497	0.926	0
Vin 5	0	0.125	0	0.1095	0.003536	0.114	0.015556
	10	0.1335	0.010607	0.1265	0.03	0.17	0.004243
	20	0.2845	0.010607	0.1205	0.00495	0.238	0.011314
	30	0.298	0	0.122	0.004243	0.301	0.002828
	40	0.299	0.002828	0.1215	0.04	0.3185	0.010607
	50	0.3055	0.000707	0.147	0.028284	0.327	0
	60	0.311	0.012728	0.12	0.008485	0.3875	0.009192
IC50	0	0.095	0	0.094	0.002828	0.181	
	10	0.191	0	0.1	0.001414	0.188	
	20	0.297	0.070711	0.102	0.001414	0.298	
	30	0.4	0.070711	0.106	0.004243	0.385	
	40	0.4715	0.006364	0.105	0.009899	0.408	
	50	0.53	0.070711	0.0915	0.000707	0.461	
	60	0.538	0.070711	0.0965	0.007778	0.455	



B	C	D	E	F	G	H	I	J	K	L	M	N
OD	time	caspase 3	OD	time	mean	SD		OD	time	caspase 8	OD	time
0.062	0		0.071	0	0.0765	0.00778	without sub	0.055	0		0.059	0
0.062	10		0.071	10	0.0765	0.00778		0.06	10		0.054	10
0.078	20		0.075	20	0.0765	0.00212		0.055	20		0.06	20
0.08	30		0.075	30	0.0775	0.00354		0.056	30		0.057	30
0.08	40		0.08	40	0.08	0		0.05	40		0.071	40
0.062	50		0.075	50	0.0755	0.00495		0.061	50		0.073	50
0.062	60		0.076	60	0.079	0.00424		0.061	60		0.07	60
0.075	0		0.069	0	0.072	0.00424	without cell lysi	0.071	0		0.085	0
0.072	10		0.068	10	0.07	0.00283		0.073	10		0.091	10
0.065	20		0.06	20	0.0625	0.00354		0.07	20		0.079	20
0.06	30		0.064	30	0.062	0.00283		0.066	30		0.077	30
0.072	40		0.071	40	0.0715	0.00071		0.071	40		0.064	40
0.069	50		0.066	50	0.0675	0.00212		0.068	50		0.09	50
0.07	60		0.068	60	0.069	0.00141		0.067	60		0.089	60
0.098	0		0.084	0	0.091	0.0099	control -	0.091	0		0.114	0
0.093	10		0.089	10	0.091	0.00283		0.09	10		0.0113	10
0.09	20		0.085	20	0.0875	0.00354		0.104	20		0.102	20
0.091	30		0.092	30	0.0915	0.00071		0.098	30		0.111	30
0.092	40		0.092	40	0.092	0		0.085	40		0.105	40
0.093	50		0.088	50	0.0905	0.00354		0.09	50		0.102	50
0.093	60		0.089	60	0.091	0.00283		0.09	60			60
0.098	0		0.087	0	0.0925	0.00778	vin 20	0.17	0		0.117	0
0.196	10		0.198	10	0.197	0.00141		0.165	10		0.124	10
0.298	20		0.229	20	0.2635	0.04879		0.166	20		0.133	20
0.454	30		0.455	30	0.4545	0.00071		0.16	30		0.132	30
0.468	40		0.468	40	0.468	0		0.154	40		0.128	40
0.466	50		0.472	50	0.469	0.00424		0.162	50		0.143	50
0.472	60		0.478	60	0.475	0.00424		0.172	60		0.144	60
0.096	0		0.111	0	0.1035	0.01061	vin5	0.104	0		0.089	0
0.106	10		0.133	10	0.1195	0.01909		0.114	10		0.102	10
0.092	20		0.101	20	0.0965	0.00636		0.109	20		0.093	20
0.098	30		0.094	30	0.096	0.00283		0.12	30		0.099	30
0.101	40		0.097	40	0.099	0.00283		0.105	40		0.089	40
0.097	50		0.101	50	0.099	0.00283		0.102	50		0.101	50
0.102	60		0.102	60	0.102	0		0.104	60		0.105	60
0.101	0		0.132	0	0.1165	0.02192	IC50	0.123	0		0.099	0
0.195	10		0.164	10	0.1795	0.02192		0.119	10		0.117	10
0.202	20		0.193	20	0.1975	0.00636		0.124	20		0.106	20
0.397	30		0.379	30	0.388	0.01273		0.116	30		0.106	30
0.399	40		0.445	40	0.422	0.05253		0.124	40		0.102	40
0.417	50		0.456	50	0.4365	0.02758		0.117	50		0.106	50

spleen | proliferating | BCL1 | Sheet1 | Sheet2

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (2) — 1 May 2019

Dear AE,
This revision could be acceptable.
Thanks.

REFEREE: Reviewer | **Revision** (2) — 21 Jul 2019

Dear AE,
The manuscript fulfills the minimum criteria for acceptance.
Thanks.

REFEREE: Associate Editor | **Revision** (2) — 22 Jul 2019

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) — 22 Jul 2019

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.