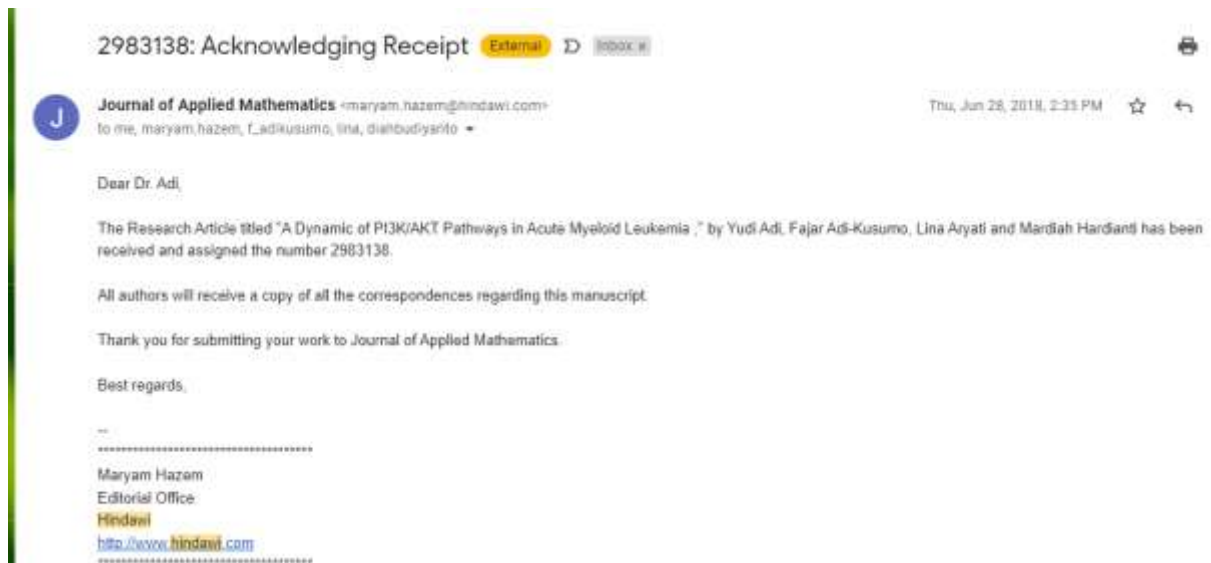
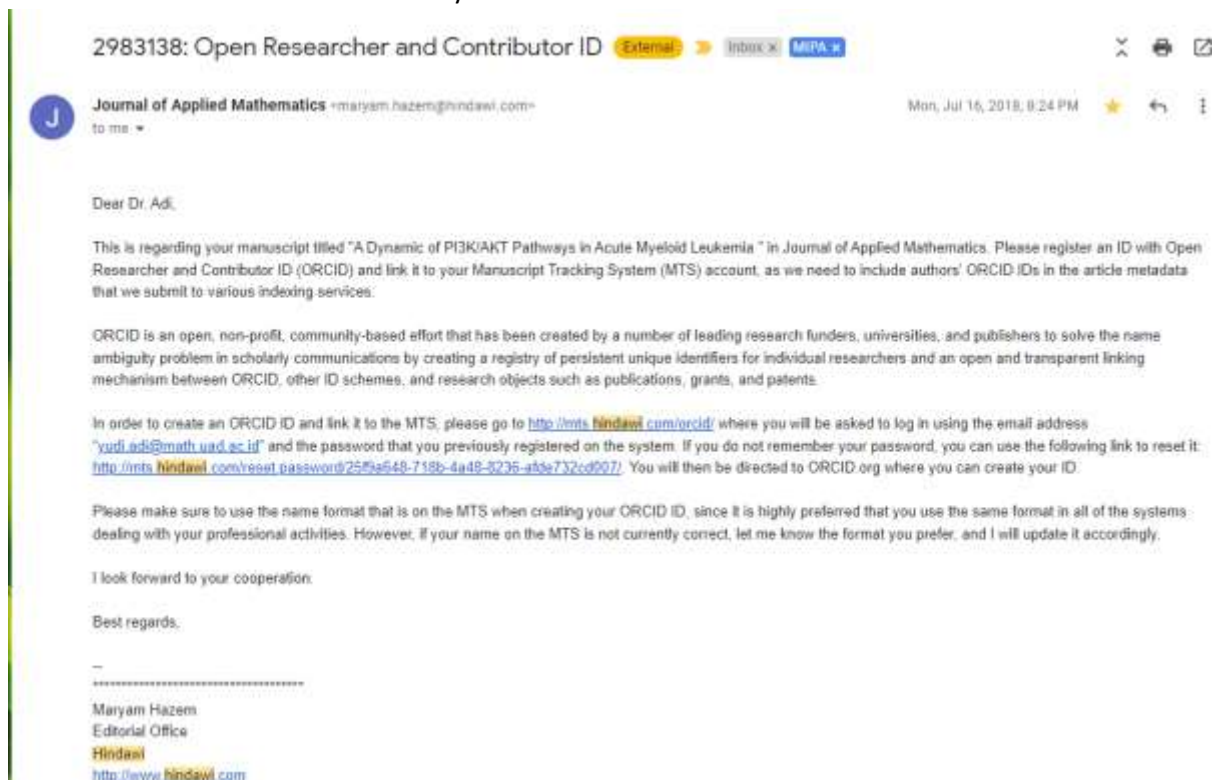


RIWAYAT KORESPONDENSI ARTIKEL DI JURNAL OF APPLIED MATHEMATICS (JAM)
(PENERBIT HINDAWI)

1. Artikel di submit melalui sistem OJS pada **28 Juni 2018**



2. Pada 16 Juli 2018 Editor meminta mnyertakan ID ORCID



3. Hasil review dengan kategori **revisi Mayor** diperoleh pada **1 Oktober 2018**

2983138: Major Revision Required    

 **Oluwale D. Makinde** <iamghindawi.com>
to me, makinde, f_adikusumo, lina, diabudiyanto

Mon, Oct 1, 2018, 7:34 AM

Dear Dr. Adi,

Following the review of Research Article titled "A Dynamic of PI3K/AKT Pathways in Acute Myeloid Leukemia" by Yudi Adi, Fajar Adi-Kusumo, Lina Aryati and Mardiah Hardianti, I recommend that it should be revised taking into account the changes request reviewer(s). Since the requested changes are major, the revised manuscript will undergo a second round of review by the same reviewer(s). Please login to the Manuscript Tracking System to read the submitted review report(s) and submit the revised version of your manuscript no later than Monday, October 29, 2018.

To submit the revised version of your manuscript, please access "Author Activities" in your account and upload the PDF file of your revised manuscript. Also, please submit your replies to the comments of the reviewer(s) as an additional PDF file.

Best regards,

Professor Oluwale D. Makinde
makindeo@gmail.com

 **Yudi Adi** <yudi.adig@math.ust.ac.id>
to Journal

Mon, Oct 1, 2018, 11:13 AM

Thank you, I will do that.

4. Revisi dikirim pada 10 Oktober 2018

2983138: Revised Version Received    

 **Journal of Applied Mathematics** <maryam.hazem@hindawi.com>
to me, maryam.hazem, f_adikusumo, lina, diabudiyanto

Wed, Oct 10, 2018, 10:03 PM

Dear Dr. Adi,

The revised version of Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia" by Yudi Adi, Fajar Adi-Kusumo, Lina Aryati and Mardiah Hardianti has been received. The editor assigned to handle the review process of your manuscript will inform you as soon as a decision is reached.

Thank you for submitting your work to Journal of Applied Mathematics.

Best regards,

.....
Maryam Hazem
Editorial Office
Hindawi
<http://www.hindawi.com>
.....

Komentar dan tanggapan seperti dalam Revision report seperti terlampir

Revision Report: “A Dynamics of PI3K/AKT Pathways in Acute Myeloid Leukemia”

Dear Editor:

Thank you for the opportunity to revise our manuscript, *A Dynamics of PI3K/AKT Pathways in Acute Myeloid Leukemia*. We thank the review panel for their critical but insightful comments. Addressing those comments resulted in an improved paper. We thank all reviewers for their kind words and positive comments on our paper.

In the table below, we document how we have addressed the comments from the three reviewers. We do hope that you will find the revisions meet the quality standard required by the journal.

Thank you for your consideration.

Sincerely,

Yudi Ari Adi.

REVIEW #1

No.	The reviewer's comments	Our responses
1	<i>The title looks incomplete and/or unclear. It should rather read like Dynamics of PI3K/AKT pathways in Acute Myeloid Leukemia or A Dynamic Model of PI3K/AKT pathways in Acute Myeloid Leukemia</i>	We have changed the title to A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia
2	<i>The grammar and typography in the article need to be improved.</i>	We have improved the Grammar and typography. In page 1, last line, we have changed “Untreated AML patient leading to fatal infection, bleeding or organ infiltration within 1-year diagnosis, ...” to “Untreated AML patient results in fatal infection, bleeding or organ infiltration within 1-year of diagnosis, ...” In page 2, second paragraph, line 11, we have changed “suppression” to “supressing” In page 2, third paragraph, line 5, we have changed “... there no...” to “...there are no known...” In page 3, first paragraph, line 2, we have changed “... extension...” to “...extended...” In page 3, first paragraph, line 14, we have changed “...reserved...” to “...reversed...” In page 4, we have not changed “...coefficient 3...” to “...a cubic of power...”, because for the Hill's Equation $\frac{X^n}{K^n + X^n}$, the exponent n, called the <i>Hill coefficient</i>, so we use the term coefficient instead of a power

3	There exists some dimensional inconsistencies in the model. For instance k_0 is said to have units μM which is inconsistent with the expected dimension ($\mu M/min$) of $\frac{dx_1}{dt}$. Considering the dimensions of k_4 and K_4, the term $\frac{k_3 x_3^2}{K_3^2 + x_3^2}$ will have dimension of $(\mu M)^2 min^{-1}$, which is inconsistent with that of $\frac{dx_4}{dt}$. If the dimensions of the parameters are correct, then the model needs to be reformulated. Authors should consider the definitions and/or units given to the parameters in Table 2.	According to the references, some dimensions of the parameters presented in table 2 are incorrect. Therefore, we make corrections as follows <table border="1"> <thead> <tr> <th>Parameter</th><th>Unit (Before)</th><th>Unit (After correction)</th></tr> </thead> <tbody> <tr><td>k_0</td><td>μM</td><td>$\mu M min^{-1}$</td></tr> <tr><td>b</td><td>min^{-1}</td><td>min^{-1}</td></tr> <tr><td>k_1</td><td>$\mu M min^{-1}$</td><td>$\mu M min^{-1}$</td></tr> <tr><td>d_1</td><td>min^{-1}</td><td>min^{-1}</td></tr> <tr><td>a_2</td><td>min^{-1}</td><td>$\mu M min^{-1}$</td></tr> <tr><td>k_2</td><td>$\mu M min^{-1}$</td><td>min^{-1}</td></tr> <tr><td>k_3</td><td>$\mu M min^{-1}$</td><td>$\mu M min^{-1}$</td></tr> <tr><td>d_2</td><td>min^{-1}</td><td>min^{-1}</td></tr> <tr><td>d_3</td><td>min^{-1}</td><td>min^{-1}</td></tr> <tr><td>p</td><td>$\mu M min^{-1}$</td><td>min^{-1}</td></tr> <tr><td>m</td><td>$\mu M min^{-1}$</td><td>$\mu M^{-1} min^{-1}$</td></tr> <tr><td>k_4</td><td>$\mu M min^{-1}$</td><td>min^{-1}</td></tr> <tr><td>k_5</td><td>$\mu M min^{-1}$</td><td>$\mu M min^{-1}$</td></tr> <tr><td>d_5</td><td>$\mu M min^{-1}$</td><td>min^{-1}</td></tr> <tr><td>K_1</td><td>μM</td><td>μM</td></tr> <tr><td>K_2</td><td>μM</td><td>μM</td></tr> <tr><td>K_3</td><td>μM</td><td>μM</td></tr> <tr><td>K_4</td><td>μM</td><td>μM</td></tr> <tr><td>K_5</td><td>μM</td><td>μM</td></tr> </tbody> </table> We also correct description d_5, “Constant rate of FOXO3a dephosphorylation” to “FOXO3ap degradation rate”. The complete of Tabel 2 is presented in the paper.	Parameter	Unit (Before)	Unit (After correction)	k_0	μM	$\mu M min^{-1}$	b	min^{-1}	min^{-1}	k_1	$\mu M min^{-1}$	$\mu M min^{-1}$	d_1	min^{-1}	min^{-1}	a_2	min^{-1}	$\mu M min^{-1}$	k_2	$\mu M min^{-1}$	min^{-1}	k_3	$\mu M min^{-1}$	$\mu M min^{-1}$	d_2	min^{-1}	min^{-1}	d_3	min^{-1}	min^{-1}	p	$\mu M min^{-1}$	min^{-1}	m	$\mu M min^{-1}$	$\mu M^{-1} min^{-1}$	k_4	$\mu M min^{-1}$	min^{-1}	k_5	$\mu M min^{-1}$	$\mu M min^{-1}$	d_5	$\mu M min^{-1}$	min^{-1}	K_1	μM	μM	K_2	μM	μM	K_3	μM	μM	K_4	μM	μM	K_5	μM	μM
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4	Authors should consider doing some basic mathematical analysis of the model, like biological and mathematical and/or possessedness of the model before the simulation. This is agreed on by authors in the conclusions section.	The model is not sufficiently accessible to allow us to conduct the mathematical analysis. It is due to the complexity of the model. The complexity comes from the use of the Hill's equation with coefficients according to the number of protein binding sites. For example, PIP3 has four binding sites so that the reaction will follow the Hill's equation with a coefficient four. We obtained a 26th degree polynomial equation when trying to analyze the model, so we couldn't find the solution. Furthermore, we can't analyze the positivity and stability of the model. Mathematical analysis can be obtained if we reduce or simplify some of the interaction terms, for example by reducing the Hill's coefficient or if the model does not follow the Hill's equation. In this paper, we want to show the dynamics of the protein with a model which the biochemical reaction follows the Hill's equation. Therefore, in this paper, we are only limited to providing numerical simulations and no theoretical analysis. We added a statement at the beginning of section Result and Discussions in page 5 as follows. “The model equations (1) – (5) is not sufficiently accessible to allow us to conduct the mathematical analysis. Therefore, in this paper, we only provide numerical simulations.”																																																												

REVIEW #2

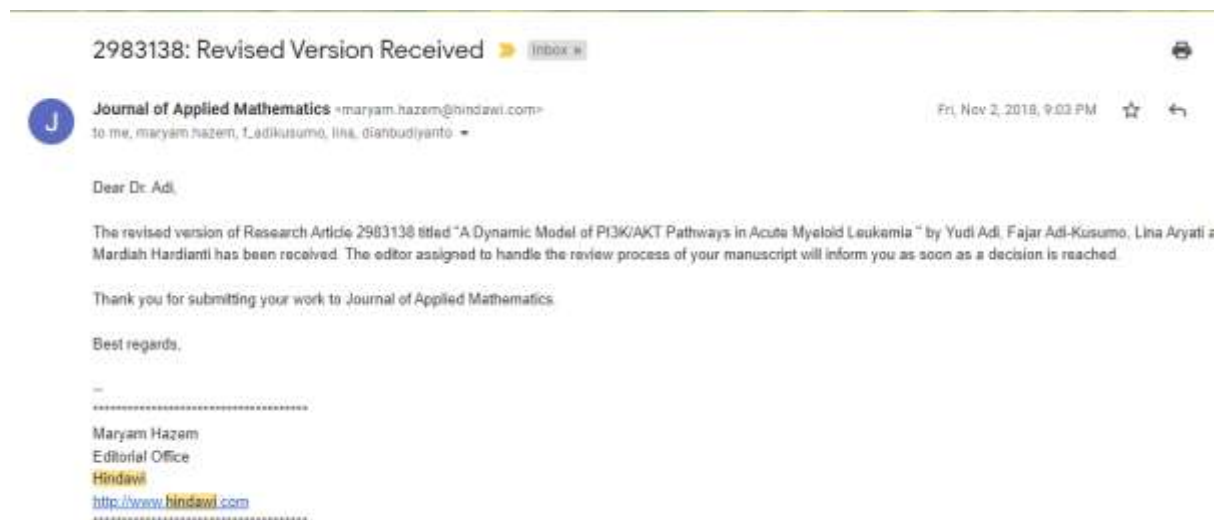
No.	The reviewer's comments	Our responses
1	<i>In page 2, third paragraph, line 10, change "Adi et al in [1] has been studied" to "Adi et al in [1] studied"</i> <i>In page 2, third paragraph, line 11, change "The model has not included .." to "The model did not include .."</i> <i>In page 3, line 5, change "Our model is focused to discuss" to "Our model is focused on discussing"</i>	<i>In page 2, third paragraph, line 10, We have changed "Adi et al in [1] has been studied" to "Adi et al in [1] studied"</i> <i>In page 2, third paragraph, line 11, We have changed "The model has not included .." to "The model did not include .."</i> <i>In page 3, line 5, We have changed "Our model is focused to discuss" to "Our model is focused on discussing"</i>

REVIEW #3

No.	The reviewer's comments	Our responses
1	<i>Introduction and model formulation parts are satisfactory</i>	Thank you
2	<i>Section of the analytical solution of the model is missing; the following should be included</i> <i>i) Boundedness of the model</i> <i>ii) Positivity</i> <i>iii) Stability analysis of the model</i> <i>Note: however in the conclusion part, the authors recommended these aspects will be captured in future work.</i>	The model is not sufficiently accessible to allow us to conduct the mathematical analysis. It is due to the complexity of the model. The complexity comes from the use of the Hill's equation with coefficients according to the number of protein binding sites. For example, PIP3 has four binding sites so that the reaction will follow the Hill's equation with a coefficient four. We obtained a 26th degree polynomial equation when trying to analyze the model, so we couldn't find the solution. Furthermore, we can't analyze the positivity and stability of the model. Mathematical analysis can be obtained if we reduce or simplify some of the interaction terms, for example by reducing the Hill's coefficient or if the model does not follow the Hill's equation. In this paper, we want to show the dynamics of the protein with a model which the biochemical reaction follows the Hill's equation. Therefore, in this paper, we are only limited to providing numerical simulations. We added statement in the begining of section Result and Discussions in page 5 as follows. "The model equations (1) – (5) is not sufficiently accessible to allow us to conduct the mathematical analysis. Therefore, in this paper, we only provide numerical simulations."
3	<i>In the numerical simulation part, some parameter values used which are different from the range of value</i>	We have revised the range of some parameter values The range of parameter value of K_1 should be 0.1 – 1.0 and the parameter value of K_3 should be written

	<i>as per Table 2. For example, K_1, K_3 and K_5, the author should explain why?</i>	between 0.08 – 0.4. The range of parameter value of k_5 should be written 0.000297 – 2.92. The value of the K_5 parameter is obtained from the assumption as given in the description at the bottom of the table and is appropriate. This range of parameter values is taken from Adi-Kusumo and Wiraya [2], Karabekmez [10] and from Wee and Aguda [21]. We have added Wee and Aguda in the references [21].
4	<i>The author refers to the wrong figure that Figure 3a instead of Figure 2a in page 6 “It can be seen that FOXO3ap reaches a peak in 100 minutes then decreases and oscillates to a certain level (see Figure 3a).”</i>	We have referred to the right figure.
5	<i>The caption of figure two is placed in the wrong place. The caption should be below the figure</i>	We have placed the caption in the right place.
6	<i>In page 7, the figure which justifies “We note that if the constant rate of FOXO3a phosphorylation set to be zero, the concentration of FOXO3ap will be zero (not shown in the figure).” Should be included</i>	We have added Figure 2c to justify the statement
7	<i>There are no explanations for the figure 3, the explanation should be given</i>	We have rewritten this part to provide explanation in first paragraph, page 8.

- Permintaan revisi minor pada 29 Oktober 2018 dan hasil revisi dikirim pada 2 November 2018



- Konfirmasi file diterima

2983138: Acknowledging Receipt of Electronic Files

Inbox x MIPA x



Journal of Applied Mathematics <maryam.hazem@hindawi.com>
to me, maryam.hazem, f_adikusumo, lina, diahbudiyanto

Tue, Nov 6, 2018, 11:16 AM ☆

Dear Dr. Adi,

This is to confirm the receipt of the electronic files of Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia" by Yudi Fajar Adi-Kusumo, Lina Aryati and Mardiah Hardianti. We will check all the uploaded files and contact you if anything else is needed.

Thank you for your cooperation.

Best regards,

—

Maryam Hazem
Editorial Office
Hindawi
<http://www.hindawi.com>

7. Artikel dinyatakan diterima pada **5 November 2018** dan permintaan biaya untuk open akses jurnal

2983138: Your manuscript has been accepted

Inbox x MIPA x



Oluwale D. Makinde <jamg@hindawi.com>
to me, makinded, f_adikusumo, lina, diahbudiyanto

Mon, Nov 5, 2018, 7:13 PM ☆ ↩ ⋮

Dear Dr. Adi,

The review process of Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia" by Yudi Adi, Fajar Adi-Kusumo, Lina Aryati and Mardiah Hardianti submitted to Journal of Applied Mathematics has been completed. I am pleased to inform you that your manuscript has now been accepted for publication in the journal.

The publication process of your manuscript will be initiated upon the receipt of electronic files. Please log in to the Manuscript Tracking System at the link below using your username and password, and upload the electronic files of your final accepted version within the next 2-3 days.

http://mts.hindawi.com/author/2983138/upload_files/

The electronic files should include the following:

- 1- Source file of the final accepted manuscript (Word or TeX/LaTeX)
- 2- PDF file of the final accepted manuscript
- 3- Editable figure files (each figure in a separate EPS/PostScript/Word file) if any, taking into consideration that TIFF, JPG, JPEG, BMP formats are not editable.

If you have deposited your manuscript on a preprint server (e.g. arXiv, bioRxiv, chemRxiv), now would be a good time to update it with the accepted version. If you have not deposited your manuscript on a preprint server, you are free to do so.

Thank you again for submitting your manuscript to Journal of Applied Mathematics.

Best regards,

Professor Oluwale D. Makinde
makinded@gmail.com

2983138: Article Processing Charges

Inbox X MIPA X



Journal of Applied Mathematics <nouthayla.magdy@hindawi.com>
to me, nouthayla.magdy, f.edikusumo, lina, diahbudyanto ▾

Mon, Nov 5, 2018, 7:13 PM



Dear Dr. Adi,

As an open access journal, Journal of Applied Mathematics levies Article Processing Charges that amount to USD 750. The total charges for your manuscript (2983138), before any taxes that may apply, are USD 750.

You can access the invoice for your article and make payments through the following URL:

<https://invoice.hindawi.com/502805f8-741f-43e1-a7f2-0650caea2f95/>

You will need to login to your account on the Manuscript Tracking System to access the link. After entering your billing address information, you will be able to pay by credit card or bank transfer.

If paying by bank transfer, please refer to invoice number 2983138 and return a scanned copy of the payment authorisation by email to facilitate our tracking of your payment.

The invoice is payable upon receipt and your prompt action would be appreciated.

If the payment will be made by an alternative source (e.g. your institution), you can provide contact details for the person who will be arranging payment via the invoice page.

If I can be of any assistance with the payment process, please let me know.

Kind regards,

Nouthayla Magdy
Accounts Receivable Specialist
Hindawi

8. Galleyproofs

2983138: Galley Proof Corrections

Inbox



Journal of Applied Mathematics <maryam.hazem@hindawi.com>
to me, diahtudiyanto, lina, f, adikusumo

Tue, Nov 13, 2018, 6:42 AM



Dear Dr. Adi,

This is to confirm the receipt of the first galley proof corrections of Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia."

Thank you for your cooperation.

Best regards,

—

Maryam Hazem
Editorial Office
Hindawi
<https://www.hindawi.com>

2983138: Galley Proofs

Inbox



Journal of Applied Mathematics <maryam.hazem@hindawi.com>
to me, diahtudiyanto, lina, f, adikusumo

Mon, Nov 12, 2018, 8:35 PM



Dear Dr. Adi,

I am pleased to let you know that the first set of galley proofs of your Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia" is ready. You can apply your corrections directly to the manuscript with the Online Proofing System (OPS).

Using the OPS, you can quickly and easily make corrections directly to your galley proofs and submit these corrections with a single click.

<https://ops.hindawi.com/author/2983138/>

If a new corresponding author is added, they must log into their manuscript tracking system account and add their ORCID ID. Any additional ORCID IDs added on during proofing will also need to be updated on that author's account. Delays can occur if this isn't done.

To expedite the publication of your manuscript, please send us your corrected galley proofs within three days.

Best regards,

—

Maryam Hazem
Editorial Office
Hindawi
<https://www.hindawi.com>

9. Pemberitahuan artikel dipublikasikan pada **14 November 2018**

