

## Reply to the reviewers' comments

Reviewer Number	Original comments of the reviewer	Reply by the author(s)	Changes done on the page number and line number
<b>REVISION</b>			
<b>Main Reviewer</b>	This case was not a candidate for combined PGT (PGT-A and PGT-M), why PGS was done for them?	<p>Dear reviewer</p> <p>We are grateful immensely to the main reviewer for providing us with suggestions. We apologize for very late response as we need to re-run the PCR process to complete the figure after enzymatic digestion as your suggestion.</p> <p>Here are our responses point-to-point according to your comments:</p> <p>As the incidence of obtaining embryos with abnormal chromosome(s) (aneuploidy) following an IVF program is relatively high, the patient has been suggested to check the ploidy status of the embryo before performing PGT-M. This strategy would be more effective to attain a high probability of pregnancy rather than performing PGT-M only.</p>	
	For what their abnormal embryo (17q11.2-17q24.2, 39.50Mbp) was frozen, this deletion is normal variant?	The procedures of IVF – PGT-A/PGT-M in our clinic begin with trophoctoderm biopsy. Well-trained embryologists will assess the quality and decide which blastocyst will be chosen for PGT-A/PGT-M. All biopsied embryos will be stored in liquid nitrogen until the clinicians and patients receive the	

		<p>report of genetic analysis.</p> <p>The deletion is not a normal variant. However, the termination of abnormal-frozen embryos is decided by the patient after having a round consultation with the expert geneticist in our clinics. The patient requested to keep the embryo up to now. Therefore, the abnormal embryo (17q11.2-17q24.2, 39.50Mbp) remains to be kept up to now.</p>	
	<p>Valuable work has been done for detecting SMN-1 and SMN-2 exon 7-8 deletion using the PCR- restriction fragment length polymorphism (RFLP) method, but you don't mentioned the size of expected bands resulting from enzymatic digestion?</p>	<p>Thank you very much for your reminder. We have added the data of expected band size before and after enzymatic digestion in the revised manuscript</p> <p>“The expected band for <i>SMN</i> Exon 7 and exon 8 after PCR was 187 bp and 186 bp. After enzyme digestion, the <i>SMN</i> exon 7 band in healthy embrio was expected to be cleaved into 2 bands, while exon 8 was into 3 bands, as shown in Figure 2. SMA positive and negative control samples were provided for comparison and quality control of the PCR and digestion process. Here, <i>SMN1</i> deletion was confirmed when the digestion only resulted in one band of <i>SMN</i> exon 7 and two bands of <i>SMN</i> exon 8.”</p>	<p>Page 3, Line 127-132</p>
	<p>In addition, the image of PCR product before and after enzymatic digestion was not presented.</p>	<p>The complete image of the PCR product has been provided, before and after the digestion, along with the expected size of the band and</p>	<p>Figure 2 Page 5, Line 147-160</p>

		marker.	
	<p>Finally and most importantly please explain how to control and verify the function of applied restriction</p>	<p>Thank you very much for your comment. In our deletion test analysis protocol, we always use, already established positive and negative control samples, as standards in each analysis. Thus, the function of applied restriction could be monitored and confirmed by observing the band separation of positive and negative control samples.</p> <p>On the other hand, our protocol used DraI and HcoB1 as restriction enzymes which digest the bands into two separated bands for exon 7 and three separated bands for exon 8. Thus, the malfunction of the restriction enzyme could be found easily when there was only single band present in the positive and negative control samples, after the digestion process.</p> <p>We provided the band image of enzymatic digestion in the manuscript and added additional sentences in the method section.</p>	<p>Figure 2 Page 5, Line 147-160</p>

Webmail interface showing an email from IJRM 99-329 (A-10-1821-1) with an attached file and a message body.

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**Left Sidebar:** polim.arie@irsi-bunda.org, 32, Search..., Inbox, Drafts, Sent, Junk (1), Trash, Archive

**Message List:**

- IJRM Yazd IVF Journal 2022-09-19 22:40
- Re: From IJRM A-10-1821-1 (99-329)
- IJRM Yazd IVF Journal 2022-08-24 18:17
- Re: Fw: From IJRM A-10-1821-1 (99-329)
- International Journal of Reprod... 2022-08-18 11:35
- Re: Some information about article A-10-182...
- aboedi17@gmail.com 2022-07-26 09:20
- **Fwd: From IJRM 99-329 (A-10-1821-1)**
- International Journal of Reprod... 2022-04-11 17:30
- Re: Some information about article A-10-182...
- APJR 2021-03-23 18:00
- final version of our manuscript (APJR\_189\_20)
- APJR 2021-03-23 17:54
- Re: Final Reading Proof (APJR\_189\_20)
- APJR 2021-03-23 16:38
- Final Reading Proof (APJR\_189\_20)
- APJR 2021-03-23 16:36
- Re: Urgency apjr\_189\_20 final proofreading (2...

**Message Content:**

**Fwd: From IJRM 99-329 (A-10-1821-1)**

To aboedi17@gmail.com on 2022-07-26 09:20

99-329 Acceptance.jpg (~1.1 MB)

----- Original Message -----  
Subject: From IJRM 99-329 (A-10-1821-1)  
Date: 2022-04-12 15:14  
From: IJRM Yazd IVF Journal <ijrmyazd@yahoo.com>  
To: "polim.arie@irsi-bunda.org" <polim.arie@irsi-bunda.org>

Dear Dr. Arie Adrainus Polim [1]

Thank you again for contribution to IJRM. I would like to inform you that your manuscript titled "\_Birth of spinal muscular atrophy unaffected baby from genetically at-risk parents following a pre-implantation genetic screening: A case report" \_written by Arie Adrainus Polim, Nining Handayani, Dian K Nurputra, Anggia Melanie Lubis, Batara Sirait, Dennis Jakobus, Arief Boediono, Ivan Sini with reference No: A-10-1821-1 (99-329) has been accepted by editorial board and it will be published in this journal. We will be look forward to receiving your future papers.

Please see the attached file.

Webmail interface showing an email thread. The browser address bar shows the URL: `sgx16.dewaweb.com:2096/cpsess5191737819/3rdparty/roundcube/index.php?_task=mail&_mbox=INBOX.Sent`. The email is from `polim.arie@irsi-bunda.org`.

**Re: Some information about article A-10-1821-1, from International Journal of Reproductive BioMedicine**

To International Journal of Reproductive BioMedicine on 2022-08-18 11:35

[Rev] article A-10-1821-1\_Reading Proof.docx (~409 KB)

On 2022-08-17 12:36, International Journal of Reproductive BioMedicine wrote:

Dear Dr. Arie Adrainus Polim

Regarding your paper accepted for publishing in the next issues of IJRM, it was reviewed by our journal English and scientific editors and final corrections should be done. Could you kindly indicate your corrections with underlying text? I would appreciate receiving your corrected manuscript within 2 days.

Best regards

Parisa Khani M.D.  
Managing Editor

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The interface also shows a list of other emails in the inbox, including messages from IJRM Yazd IVF Journal and APJR regarding article A-10-1821-1 and manuscript proofreading.