

1. Publication

Vidal RL, Figueroa A, Court FA, Thielen P, Molina C, Wirth C, Caballero B, Kiffin R, Segura-Aguilar J, Cuervo AM, Glimcher LH, Hetz C. **Targeting the UPR transcription factor XBP1 protects against Huntington's disease through the regulation of FoxO1 and autophagy.** *Hum Mol Genet.* 2012 May 15;21(10):2245-62. doi: 10.1093/hmg/ddc040. Epub 2012 Feb 14. PMID: 22337954; PMCID: PMC3335312.

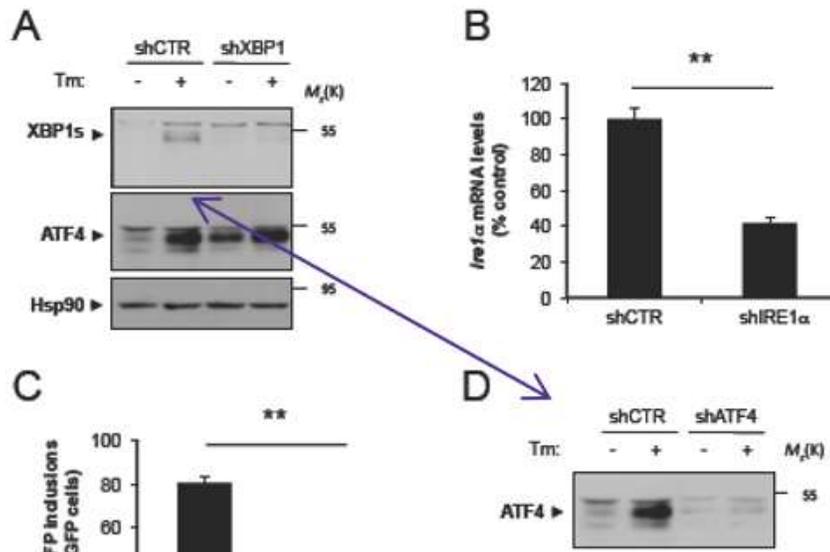
2. Pubpeer Comments

This article reports XBP1 and FoxO1 have roles in HD via an ER stress mechanism.

Supplementary Figure 4A and D are more related than not.

In both figures ATF4/shCTR lanes are identical but the two attached lanes to the right are different. In 4D, the splice is clearly visible.

In the Hsp90 lanes, three of the four bands are the same. They are bands 2-4 in part A, and the bands 1-3 in part D.



3. Answer

These experiments were performed by Dr. Rene Vidal (Postdoctoral fellow). We apologize for the initial mistake, but this error was corrected in the year 2012 (<https://academic.oup.com/hmg/article/21/10/2245/2900667>). The problem arises because there are two versions of the supplementary figure 4A are still available online in different platforms.

In the old version of this figure, in panels A and D we tested the efficiency of shRNA knockdown in stable cell lines for the genes XBP1, ATF4, and control and then monitored ATF4 and XBP1 expression by Western blot. These 3 cell lines were generated at the same time and thus used the same control shRNA in most experiments. This is why in

both panels A and D the control image (shCTR) were the same (from the same blot), repeated twice in both panels figure (Figure 1A). We apologize for this mistake since it was not mentioned in the figure legend. As soon as we noticed this error we contacted to the editor and send the original data to take actions, and performed an online replacement of the supplementary figure 4 including a new experiment (Figure 1B). They decided to replace the supplementary material for a new one without any correction since there was no error in the figure, just that it was not properly mentioned the splice (see interchange of emails during 2012 in Figure 2). This case was considered close in 2012 by HMG and no further actions needed.

Unfortunately, **we noticed an additional error when selecting the Hsp90 bands for loading control of the supplementary figure 4A**, because the selection of the bands moved one well including another lane that should not be considered (Figure 3A). For full clarity, here we provide the full scans of the online and corrected supplementary figure 4 (Figure 3). Importantly, the biological conclusion of the experiment is not altered by this mistake.

We have contacted the editorial office of Human Molecular Genetics to replace supplementary figure 4 with the corrected version of the figure if needed (see attached email). **The editors considered that our responses are satisfactory and no further actions are required (see email).** Raw data and explanation have been posted in Pubpeer.

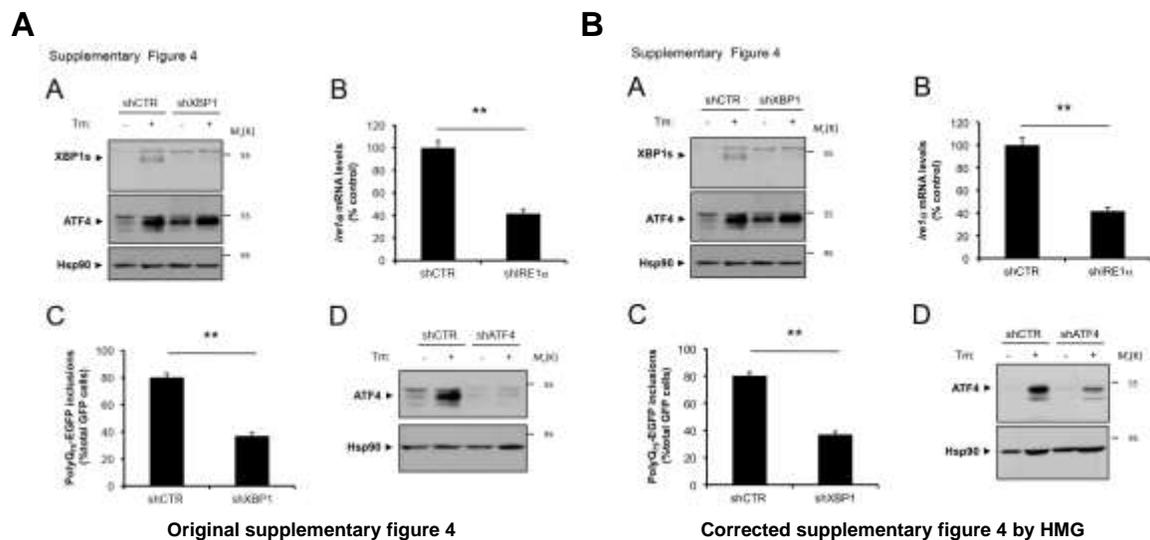


Figure 1. Side-by-side comparison of both online versions. (A) Original version of the supplementary figure 4 containing the image duplication as explained in the text. **(B)** Corrected supplementary figure 4 available online in the HMG site.



Claudio Hetz <claudio.hetz@gmail.com>

replacement supplementary figure HGM Manuscript

OUP Team (Pam) <oupteam@techset.co>
To: HMGeditorial <hmg_editorialoffice@oup.com>, claudio.hetz@gmail.com
Cc: oupteam <oupteam@techset.co>, HMG <hmg@oup.com>

Fri, Nov 2, 2012 at 7:35 AM

Dear Stephanie/Claudio

The supplementary data has been replaced as requested. Please let me know if there are any further queries or problems?

Regards

HMG team



Claudio Hetz <claudio.hetz@gmail.com>

Clarification/Erratum on figure legend HGM Manuscript?

Claudio Hetz <claudio.hetz@gmail.com>
To: hmg_editorialoffice@oup.com
Cc: Rene Vidal <renevidalg@gmail.com>
Bcc: chetz@hsph.harvard.edu

Mon, Oct 29, 2012 at 2:47 PM

Dear Editor
since I didn't receive an answer from this important email, I am sending it again.

Many thanks in advance.

Sincerely yours,

Claudio Hetz

Dear all
I am contacting you because we just realized we omitted some minor, but relevant, information in the legend of supplementary Figure 4 of our manuscript "Hum Mol Genet. 2012 May 15;21(10):2245-62"

In panels A and D we tested the efficiency of shRNA knockdown for the genes XBP1 and ATF4, and then monitored ATF4 expression by Western blot. Both cell lines were generated in parallel and used the same control shRNA line in most experiments.

This is why in both panels A and D the control image (shCTR) is the same (from the same blot), repeated twice in both panels figure. This was not mention in the figure legend.

To avoid misinterpretations, I wanted to discuss with you if it will be necessary to add an errata or clarification to the figure legend.

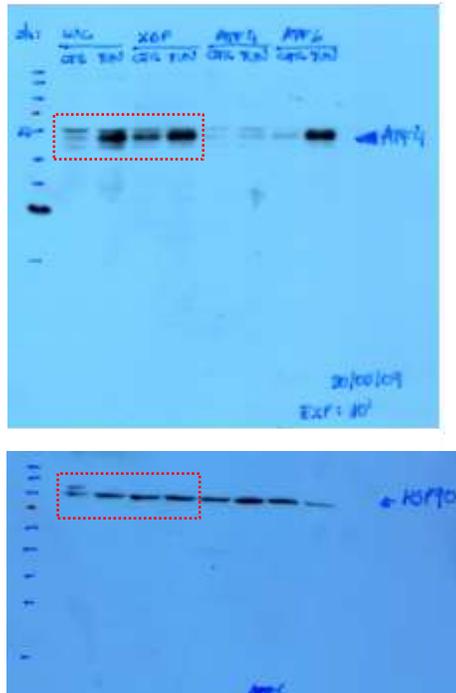
As you could see here in the attached file (full scan of the films), all the runs are from the same blot where we tested actually 3 shRNAs for different genes and one control. Since these are general reagents of the lab, these type of controls are done all the time, and we have dozens of independent repeats. There was an unintentional mistake when the loading of the image was added but as you could see from this full scan all correspond to the same experiment.

Normally when we repeat a control on a paper we state it in the legend and here we missed it. If you consider we need to add a clarification for the legend, the following text could be used:

"In the original legend of Supplementary Figure 4A and D authors have omitted the fact that the control shCTR in both panels correspond to the same Western blot image because all runs were done in the same gel. The loading control was cut in the wrong position to assemble the image. Full scans were provided to the editorial office of these experiments".

Figure 2. Exchange of email by the editorial office of HMG indicating that the correction was done online for the supplementary figure 4.

A



B

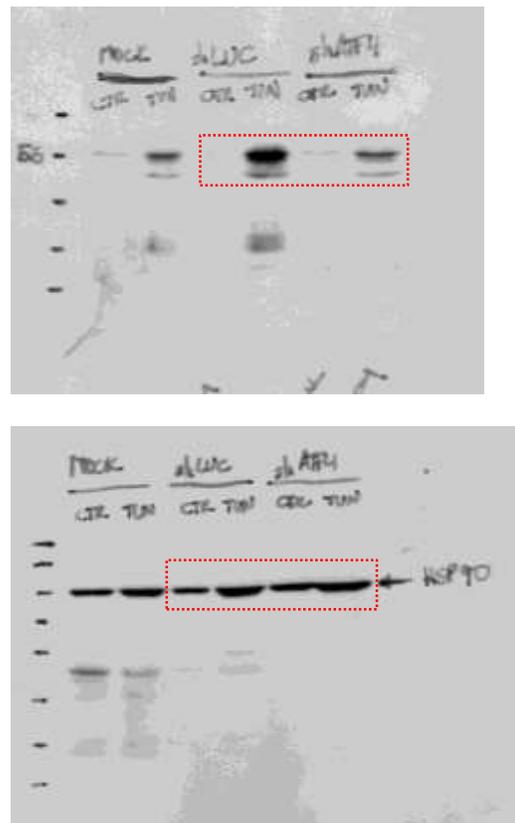
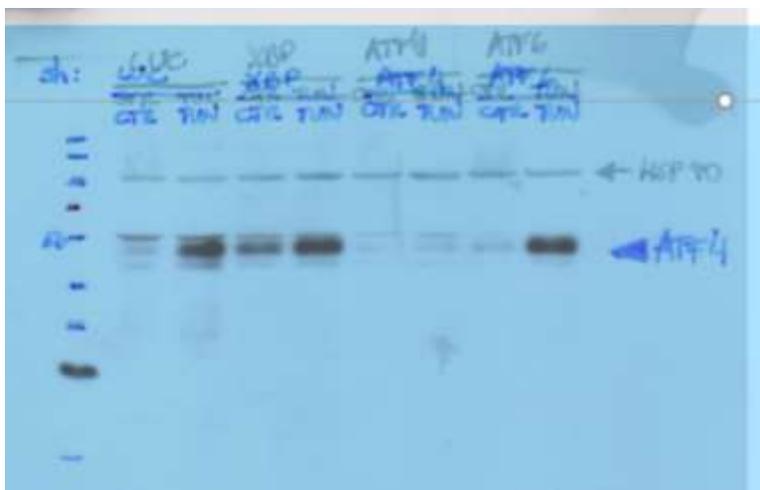


Figure 3. Raw data presentation (A) Raw data of the corrected supplementary figure 4A. **(B)** Raw data of the corrected supplementary figure 4D. Both figures are available online at the HMG site.

Overlap two images:



New email to editor:

Correo de Universidad de Chile - about our article Vidal et al HMG 2012

22-02-21 15:56



Claudio Hetz <chetz@uchile.cl>

about our article Vidal et al HMG 2012

Claudio Hetz <chetz@uchile.cl>

22 de febrero de 2021, 15:56

Para: hmgjournal@dpag.ox.ac.uk, Rene Vidal <renevidalg@gmail.com>

Cc: Claudio Hetz <chetz@uchile.cl>

Cco: Danilo Medinas <danilo.medinas@gmail.com>, Vicente Valenzuela <vicentevalenzuela@gmail.com>, Hery Urra <hery.urre@gmail.com>

Dear Professor Kay Davies

I am contacting you because there was a Pubpeer query on our article regarding the replacement of a supplementary figure that we performed internally with the editorial office years ago.

For your records, I am attaching here the response that we will upload to our lab webpage. We also posted a simpler version to Pubpeer for transparency. In the process of generating this file we realized the loading control was not properly cropped and moved one line, which did not alter the conclusions of the study. If you need further information please don't hesitate in contacting us.

Sincerely yours,

Claudio Hetz and Rene Vidal

Claudio Hetz

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 file to editor - Vidal et al Hum Mol Genet 2012.docx
3313K

Response editor:

Correo de Universidad de Chile - about our article Vidal et al HMG 2012

01-03-21 18:44



Claudio Hetz <chetz@uchile.cl>

about our article Vidal et al HMG 2012

HMG journal <hmgjournal@dpag.ox.ac.uk>
Para: Claudio Hetz <chetz@uchile.cl>, Rene Vidal <renevidalg@gmail.com>

1 de marzo de 2021, 7:22

Thank you for your response which satisfies the concerns raised.

Best wishes

Professor Dame Kay E Davies

Executive Editor

Human Molecular Genetics

<http://mc.manuscriptcentral.com/hmg>

[El texto citado está oculto]