

Peer Review Information

Journal: Nature Ecology & Evolution

Manuscript Title: The earliest Denisovans and their cultural adaptation

Corresponding author name(s): Samantha Brown, Diyendo Massilani, Katerina Douka

Editorial Notes:

Reviewer Comments & Decisions:

Decision Letter, initial version:
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1st December 2020

*Please ensure you delete the link to your author homepage in this e-mail if you wish to forward it to your co-authors.

Dear Katerina,

Your manuscript entitled "The earliest Denisovans and their cultural adaptation" has now been seen by three reviewers, whose comments are attached. The reviewers have raised a number of concerns which will need to be addressed before we can offer publication in Nature Ecology & Evolution. We will therefore need to see your responses to the criticisms raised and to some editorial concerns, along with a revised manuscript, before we can reach a final decision regarding publication.

The reviewer comments seem mostly straightforward, though we ask you to pay particular attention to reviewer 1's remarks about Bayesian modelling, and reviewer 3's remarks regarding the lithic analyses--while it seems clear that some interpretation of cultural affiliation can be made based on the results presented here, demonstrating affiliation with the Acheulo-Yabrudian industry requires either detailed analysis or (possibly) full discussion of previously published work.

We therefore invite you to revise your manuscript taking into account all reviewer and editor comments. Please highlight all changes in the manuscript text file [OPTIONAL: in Microsoft Word format].

We are committed to providing a fair and constructive peer-review process. Do not hesitate to contact

us if there are specific requests from the reviewers that you believe are technically impossible or unlikely to yield a meaningful outcome.

When revising your manuscript:

- * Include a "Response to reviewers" document detailing, point-by-point, how you addressed each reviewer comment. If no action was taken to address a point, you must provide a compelling argument. This response will be sent back to the reviewers along with the revised manuscript.
- * If you have not done so already please begin to revise your manuscript so that it conforms to our Article format instructions at <http://www.nature.com/natecolevol/info/final-submission>. Refer also to any guidelines provided in this letter.
- * Include a revised version of any required reporting checklist. It will be available to referees (and, potentially, statisticians) to aid in their evaluation if the manuscript goes back for peer review. A revised checklist is essential for re-review of the paper.

Please use the link below to submit your revised manuscript and related files:

[REDACTED]

Note: This URL links to your confidential home page and associated information about manuscripts you may have submitted, or that you are reviewing for us. If you wish to forward this email to co-authors, please delete the link to your homepage.

We hope to receive your revised manuscript within four to eight weeks. If you cannot send it within this time, please let us know. We will be happy to consider your revision so long as nothing similar has been accepted for publication at Nature Ecology & Evolution or published elsewhere.

Nature Ecology & Evolution is committed to improving transparency in authorship. As part of our efforts in this direction, we are now requesting that all authors identified as 'corresponding author' on published papers create and link their Open Researcher and Contributor Identifier (ORCID) with their account on the Manuscript Tracking System (MTS), prior to acceptance. ORCID helps the scientific community achieve unambiguous attribution of all scholarly contributions. You can create and link your ORCID from the home page of the MTS by clicking on 'Modify my Springer Nature account'. For more information please visit <http://www.springernature.com/orcid>.

Please do not hesitate to contact me if you have any questions or would like to discuss these revisions further.

We look forward to seeing the revised manuscript and thank you for the opportunity to review your work.

[REDACTED]

Reviewer expertise:

Reviewer #1: ancient DNA

Reviewer #2: ancient proteomics and ZooMS

Reviewer #3: Acheulo-Yabrudian lithic industries

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

Brown et al are reporting the finding of 5 novel hominin bones from Denisova cave obtained using ZooMS-based identification. Four out of those were of sufficient preservation to yield complete mitochondrial DNA genomes via targeted enrichment of ancient DNA. Three samples (Denisova 19, 20, 21) are identified as Denisovan specimens, and one (Denisova 17) as a Neanderthal.

The authors use established protocols for ancient DNA data generation and authentication. The final coverage of the four individuals is no doubt sufficient for the phylogenetic placement on the Neanderthal and Denisovan lineages for Denisova 17 and Denisova 19, 20, 21 respectively. The authors also perform a simple molecular dating analysis based on the number of substitutions on their inferred maximum parsimony trees, which yield age estimates consistent with the archaeological date of the layer.

Overall, the conclusions of the manuscript are well supported by the presented analysis. However, the manuscript could benefit further from a more in-depth dating analysis using e.g. Bayesian phylogenetic methods such as those implemented in BEAST. The newly reported Denisovan sequences in particular in combination with their archaeological date estimates as calibration points could provide further insights into the timing of the divergences among the different Denisovan MT lineages and their common ancestor with Sima de los Huesos.

Minor comments

Supplement, line 163: Reference for the assumed substitution rate is missing

Fig 3: Denisova 17 should also be in bold font

Reviewer #2 (Remarks to the Author):

This is an important manuscript that furthers our knowledge on Denisovan distribution and genetics through both ZooMS (as a method of screening thousands of morphologically-unidentified bone fragments) and mtDNA (for ID verification and phylogenetics). The manuscript then discusses the biomolecular identifications of five new hominin bone samples from Denisova cave within the context of the other associated finds of the cave (lithics and zooarchaeological remains), culminating in the broader cultural significance of the results. Amongst these novel findings is the fact this manuscript reports the oldest Denisovan samples currently documented.

The study also shows evidence of excellent biomolecular preservation (both collagen and mtDNA) and

is a marvellous example of the use of ZooMS as a screening mechanism to uncover bones of great interest, that are eligible for more expensive and time consuming mtDNA analysis.

I do not consider this manuscript to have any major flaws which should prohibit its publication. I feel that the results presented are of immediate interest to researchers in the field of human palaeoproteomics, plus wider aspects of archaeology, palaeontology, human evolution and dispersal, and more generally to non-experts. I therefore recommend publication in Nature Ecology and Evolution.

I have suggested some minor points for the authors to consider.

Line 48-49

The use of the word 'reliable' here is misleading. Collagen fingerprinting is most likely to give genus or family-level identifications in most types of vertebrate due to the slowly evolving nature of the collagen molecule, but the reliability of the technique does not change in this sense. Please rephrase this to be clearer, otherwise it suggests that species-level IDs could be unreliably assigned.

Line 74

Table S2 doesn't indicate that the layers are sterile as such, other than by omitting them in the table. It might look better to include these layers in this supplementary table and then indicate that the layers were sterile by stating '0' in the second column. Is sterile the best word to use in this context? Sterile to me suggests no biological material, but there may be microscopic remains, and/or environmental DNA in the sediments.

Line 77

Should be a space between 20 and mg

Line 86-87

"Given that no great apes are known from the region these bones almost certainly belong to humans" – consider removing this sentence here as the topic is picked up again at line 96. Perhaps also consider including an additional sentence or two, at line 96, that explains why we cannot use collagen signatures to rule out great apes and must default to using geographical location and historic biodiversity. Although this tactic is fine, it would be of interest to clarify which (if not all) of the biomarkers in Table S1 hominins share with great apes and why can we not yet separate these. If there hasn't been any work done on this yet then this should be stated.

Line 111

Should be a space between 50 and km

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Space between 1 and 'm'

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Space between 20 and mg... and so on throughout (lines 256, 257, 259, 260... etc. etc). The manuscript shows inconsistencies whereby sometimes a space is present between the number and the unit, and sometimes it is not. E.g. line 284 contains both versions. Default to versions where a space is present unless the journal requires otherwise.

Line 256

1 uL of trypsin is not a good indication of the quantity/concentration of trypsin used, as it depends on

the dilution. Please update the material and methods with the quantity of trypsin used per sample (ug).

Hominid PMFs

When looking at the raw MALDI data, there appears to be some differences in the PMFs of Denisova 17 (of Neanderthal type) and Denisova 18, 19, 20 and 21 (of Denisova type), e.g. peak at 1446 versus 1455 (may not be homologous). This suggests potential differences in the amino acid sequences of each group. Can collagen separate these two groups? An addition of this information would be of great interest, if it is already known. Otherwise this would require a separate study.

General comments

- The references to the supplementary information are not as easy for the reader as they could be. For example, Table S2 is referenced before Table S1 which forces the reader to jump around a little. The same occurs with the figures within the manuscript, whereby there is no reference to Fig 1a before Fig 1b. There is also no reference to Table S4 in the manuscript. These are small points but if corrected would neaten up the manuscript and how it references the supplementary information.

Reviewer #3 (Remarks to the Author):

I have been asked to review the archaeological part of the paper, especially in the relation to the possible connection between the Levantine Acheulo-Yabrudian complex and the Early Middle Paleolithic at layer 15 in the Eastern Chamber of Denisova Cave. The authors suggest that the closest parallel to layer 15 industries can be found in the Acheulo-Yabrudian. This might be so, however, the evidence presented in the paper is not sufficiently detailed. The lithic assemblage at Denisova contains Levallois cores, discoidal cores, ventrally thinned flakes, scrapers retouched by Quina retouch, spur-like, denticulate, and notched forms. Among these characteristics, some are too general (i.e. notched forms), others are absent from the Acheulo-Yabrudian (i.e. Levallois). In other cases, the description is insufficient to claim for similarity, i.e. ventrally thinned flakes were never reported in the Acheulo-Yabrudian. However, cores-on-flake with ventral removals do occur in Acheulo-Yabrudian assemblages, as well as partial bifaces with ventral thinning. The description of the ventrally thinned pieces in the paper is not clear and not detailed enough to claim similarity. The main similarity is the presence of scrapers with Quina retouch in both Acheulo-Yabrudian and Denisova assemblages.

I find it very tricky to claim direct migration on the basis of lithic evidence. In several cases when compelling evidence for migrations was presented, it involved a direct comparison between industries and meticulous comparative study of technology, morphology, and style of the artifact (see for instance: Kolobova et al. 2020. Archaeological evidence for two separate dispersals of Neanderthals into southern Siberia. *Proceedings of the National Academy of Sciences of the United States of America*. 117, 2879–2885).

To claim for the similarity between Denisova and Acheulo-Yabrudian, more detailed technological and morphological analyses should be conducted. These should include a quantitative analysis in order to understand how frequent are the 'Acheulo-Yabrudian like' features at Denisova. These should also include a detailed study of the blank production methods, retouching techniques, and specific artifact types, such as ventrally thinned flakes. Ideally, it should also involve a direct comparison with the

Acheulo-Yabrudian.

On a more general note, it is not clear how the suggested interpretation of the lithic evidence contribute to the paper goals

*****END*****

Author Rebuttal to Initial comments

We thank the reviewers for their time and effort to assess our manuscript and offer their expertise. We reply to each review below and have incorporated most of their comments in our main text.

Reviewer #1: ancient DNA

Reviewer #2: ancient proteomics and ZooMS

Reviewer #3: Acheulo-Yabrudian lithic industries

Reviewers' comments:

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Overall, the conclusions of the manuscript are well supported by the presented analysis. However, the manuscript could benefit further from a more in-depth dating analysis using e.g. Bayesian phylogenetic methods such as those implemented in BEAST. The newly reported Denisovan sequences in particular in combination with their archaeological date estimates as calibration points could provide further insights into the timing of the divergences among the different Denisovan MT lineages and their common ancestor with Sima de los Huesos.

As suggested by the reviewer, we used BEAST to estimate molecular ages of the mtDNAs of the newly identified individuals and the divergence dates between the different hominin groups. We performed the analyses using both the whole mtDNA and the coding region only. For consistency with previous works, we report the estimates based on the coding region in the main text.

We have added a brief description of these analyses, as well as a table with the estimated ages of the archaic individuals (Table S7) and a table of the estimates of the divergence times between mtDNAs using as calibration points the archaeological age estimates of the individuals from Denisova Cave (Table S8).

We caution that since there are no directly dated Denisovan specimens that can be used as calibration points for analyses, the age estimates may be unreliable. We nevertheless report them as they may be used to gauge the differences in age between the different individuals (see Suppl. Info. Page 6).

We also note that the estimate of the divergence time between Denisovan and Sima de los Huesos mtDNAs has a very wide posterior distribution due to the uncertain age estimate of the Sima de los Huesos individual. We used as priors for the Sima de los Huesos mtDNA a range from 260ky (the divergence between Neandertal mtDNA lineages) to 780ky (the divergence between archaic and modern human mtDNA) as defined in Peyregne et al., Sci. Adv. 2019.

Minor comments

Supplement, line 163: Reference for the assumed substitution rate is missing

Thank you, this is now corrected.

Fig 3: Denisova 17 should also be in bold font

Thank you, this is now corrected.

Reviewer #2 (Remarks to the Author):

This is an important manuscript that furthers our knowledge on Denisovan distribution and genetics through both ZooMS (as a method of screening thousands of morphologically-unidentified bone fragments) and mtDNA (for ID verification and phylogenetics). The manuscript then discusses the biomolecular identifications of five new hominin bone samples from Denisova cave within the context of the other associated finds of the cave (lithics and zooarchaeological remains), culminating in the broader cultural significance of the results. Amongst these novel findings is the fact this manuscript reports the oldest Denisovan samples currently documented.

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I do not consider this manuscript to have any major flaws which should prohibit its publication. I feel that the results presented are of immediate interest to researchers in the field of human palaeoproteomics, plus wider aspects of archaeology, palaeontology, human evolution and dispersal, and more generally to non-experts. I therefore recommend publication in Nature Ecology and Evolution.

I have suggested some minor points for the authors to consider.

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This has been revised to say: “In vertebrates, it is commonly used to assign genus or family-level identifications and, in some instances, species-specific determinations are possible.”

Line 74

Table S2 doesn't indicate that the layers are sterile as such, other than by omitting them in the table. It might look better to include these layers in this supplementary table and then indicate that the layers were sterile by stating '0' in the second column. Is sterile the best word to use in this context? Sterile to me suggests no biological material, but there may be microscopic remains, and/or environmental DNA in the sediments.

We thank the reviewer for the thoughtful comment. In this instance sterile is used in the archaeological sense, as these are essentially layers of sediment deposit but with no cultural material to denote human presence. We have updated the draft to reflect this. We feel it would be misleading to add layers 10 and 16 to table S2 as no bones have been excavated from these layers and this may imply that we simply chose not to look at these layers.

Line 77

Should be a space between 20 and mg **Corrected**

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“Given that no great apes are known from the region these bones almost certainly belong to humans” – consider removing this sentence here as the topic is picked up again at line 96. Perhaps also consider including an additional sentence or two, at line 96, that explains why we cannot use collagen signatures to rule out great apes and must default to using geographical location and historic biodiversity. Although this tactic is fine, it would be of interest to clarify which (if not all) of the biomarkers in Table S1 hominins share with great apes and why can we not yet separate these. If there hasn't been any work done on this yet then this should be stated.

The sentence, “Given that no great apes are known from the region these bones almost certainly belong to humans” has been removed.

Line 111

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Space between 1 and 'm' **Corrected**

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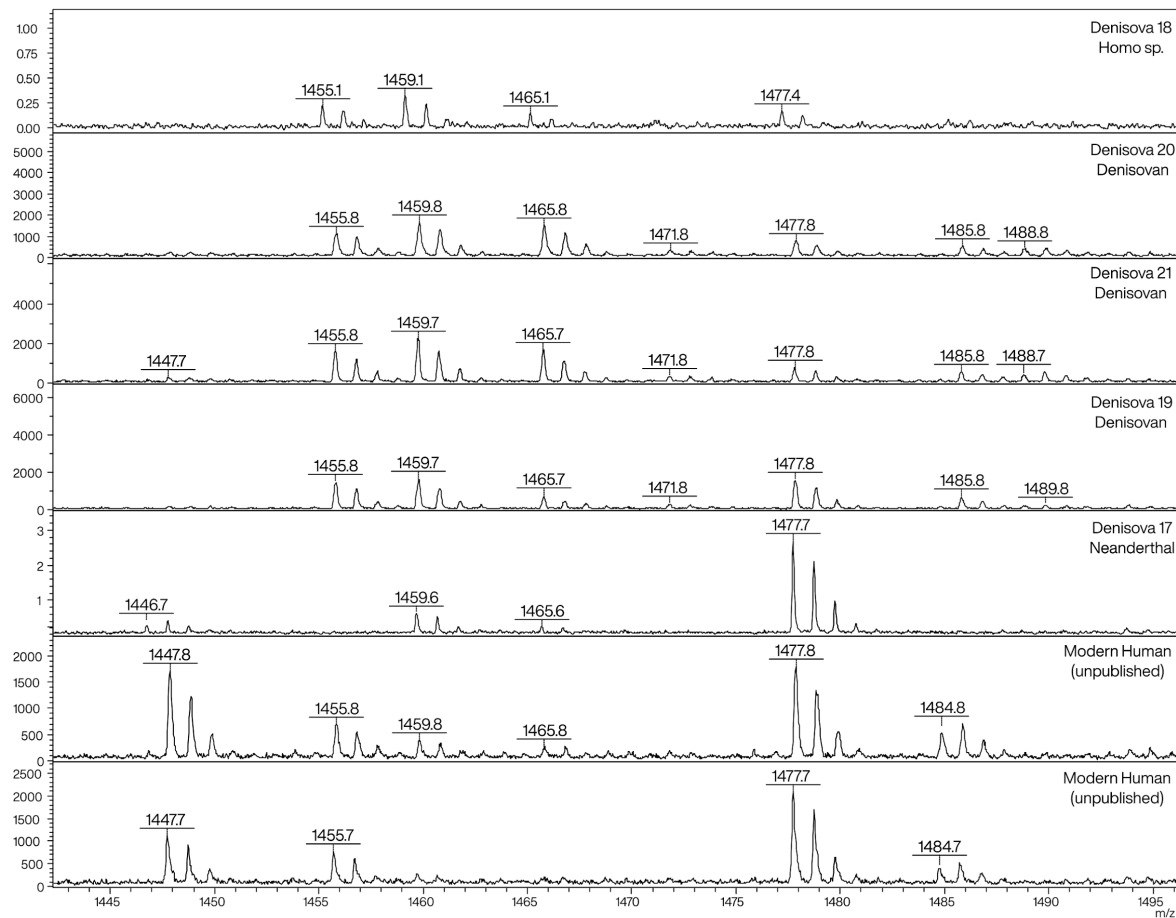
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It is not possible to use PMF results to differentiate Hominidae (see Buckley et al. 2009; Welker et al., 2016). Unfortunately, markers at 1446 and 1455 are not reliably present in either hominin population to allow for differentiation. To demonstrate this for the reviewers we have created a new figure (see below) which focuses on m/z 1400-1500 and includes two unpublished modern humans (from a Holocene-age site). 1446 appears in D17 (Neanderthal), D21 (Denisovan), and both modern humans (with a deamidation shift of 1 m/z). 1455 is only absent from D17, however this absence cannot be used to differentiate Neanderthals from other hominin populations. Recent proteomics research (see Welker et al., 2016 and Chen et al., 2019) have identified SAPs which might be useful in differentiating Neanderthals from Denisovans but at present this is beyond the scope of ZooMS analysis as they are not visible in PMF data.

We have added references to line 96 which reads, “Since peptide mass fingerprinting cannot be used for a more specific taxonomic assignment than Hominidae” to make this more clear.



General comments

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Thank you, this has been corrected.

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The main similarity is the presence of scrapers with Quina retouch in both Acheulo-Yabrudian and Denisova assemblages.

I find it very tricky to claim direct migration on the basis of lithic evidence. In several cases when compelling evidence for migrations was presented, it involved a direct comparison between industries and meticulous comparative study of technology, morphology, and style of the artifact (see for instance: Kolobova et al. 2020. Archaeological evidence for two separate dispersals of Neanderthals into southern Siberia. *Proceedings of the National Academy of Sciences of the United States of America*. 117, 2879–2885).

The reviewer is right, the typological descriptions are rough and could well be the result of different technological trajectories. We should point out that we do not favor either straight migrations or direct connections between the two places and groups. We merely observe similarities and acknowledge that there is indeed a small number of similarly aged lithic assemblages to compare against, yet none from Central Asia.

To claim for the similarity between Denisova and Acheulo-Yabrudian, more detailed technological and morphological analyses should be conducted. These should include a quantitative analysis in order to understand how frequent are the 'Acheulo-Yabrudian like' features at Denisova. These should also

include a detailed study of the blank production methods, retouching techniques, and specific artifact types, such as ventrally thinned flakes. Ideally, it should also involve a direct comparison with the Acheulo-Yabrudian.

On a more general note, it is not clear how the suggested interpretation of the lithic evidence contribute to the paper goals.

We agree with the reviewer's comment. At present, we cannot find any analogies to the industries from the lower layers of the Denisova Cave in adjacent regions, hence the need to turn to more distant ones. Our observations are preliminary and may well change in the near future. We are currently in the process of an in-depth analysis of the lithic industry and the development of an evidence-based approach.

In terms of the inclusion of the lithic information in our manuscript, even if we cannot identify direct parallels it is important to present it since layers 14 and 15 are uniquely associated with Denisovans at the site and this is the first time that can be shown that are linked to a specific material culture.

Decision Letter, first revision:

16th April 2021

*Please ensure you delete the link to your author homepage in this e-mail if you wish to forward it to your co-authors.

Dear Katerina,

Your Article, "The earliest Denisovans and their cultural adaptation" has now been seen by the same three reviewers. While the two referees with molecular expertise feel that those aspects are now suitable for publication, the archaeologist referee (with a specialism in Acheulo-Yabrudian industries) commented to editors that they did not feel that the revised manuscript had taken their recommendations into account. Unfortunately we have to agree with this--while we understand that the paper is reporting what are in some ways preliminary observations, we cannot publish technically unsubstantiated findings. In order to maintain the comparison with Acheulo-Yabrudian industries, it would be necessary to fully present the lithic data in order for our reviewer to technically assess it. I recognise that this might not be achievable for this manuscript (though it would be the ideal path to take), so we might be able to reach a compromise through editing. I think the text until about line 259 can probably stand, but the final paragraph will need to be removed and reworked: this appears to present a conclusion based solely on the lithic industry at Denisova rather than alluding to the other lines of evidence you present here, so would in any case require some overhaul prior to publication. But in the absence of reviewable lithic analysis, I don't think we can countenance publishing the possible interpretation (no matter how speculative/tentative) of either migration or convergence.

Please don't hesitate to get in touch to discuss this--I think we can achieve a publishable version of

this manuscript without too much further work, but I hope you understand the need to compromise on some aspects.

If revising your manuscript:

* Include a "Response to reviewers" document detailing, point-by-point, how you addressed each referee comment. If no action was taken to address a point, you must provide a compelling argument. This response will be sent back to the referees along with the revised manuscript.

* If you have not done so already we suggest that you begin to revise your manuscript so that it conforms to our Article format instructions at <http://www.nature.com/natecolevol/info/final-submission>. Refer also to any guidelines provided in this letter.

* Include a revised version of any required reporting checklist. It will be available to referees (and, potentially, statisticians) to aid in their evaluation if the manuscript goes back for peer review. A revised checklist is essential for re-review of the paper.

Please use the link below to submit a revised paper:

[REDACTED]

Note: This URL links to your confidential home page and associated information about manuscripts you may have submitted, or that you are reviewing for us. If you wish to forward this email to co-authors, please delete the link to your homepage.

If you wish to submit a suitably revised manuscript we would hope to receive it within 6 months. If you cannot send it within this time, please let us know. We will be happy to consider your revision so long as nothing similar has been accepted for publication at Nature Ecology & Evolution or published elsewhere.

Nature Ecology & Evolution is committed to improving transparency in authorship. As part of our efforts in this direction, we are now requesting that all authors identified as 'corresponding author' on published papers create and link their Open Researcher and Contributor Identifier (ORCID) with their account on the Manuscript Tracking System (MTS), prior to acceptance. This applies to primary research papers only. ORCID helps the scientific community achieve unambiguous attribution of all scholarly contributions. You can create and link your ORCID from the home page of the MTS by clicking on 'Modify my Springer Nature account'. For more information please visit www.springernature.com/orcid.

Please do not hesitate to contact me if you have any questions or would like to discuss the required revisions further.

Thank you for the opportunity to review your work.

[REDACTED]

Reviewer expertise:

as before

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

The newly included Bayesian phylogenetic analyses in the revised manuscript follows the established protocol from previous studies of ancient hominin mtDNA. It adds valuable insights to the manuscript, and as such I have no further comments and recommend it for publication.

Reviewer #2 (Remarks to the Author):

I have read all reviewer comments and author responses and I am very happy with all the responses and corrections. I feel this article is very well suited for publication in the journal Nature Ecology and Evolution.

Virginia L. Harvey

Decision Letter, second revision:

11th June 2021

Dear Katerina,

Thank you for submitting your revised manuscript "The earliest Denisovans and their cultural adaptation" (NATECOLEVOL-201011791B). Following your revision along the lines previously discussed, I'm pleased to tell you we can now accept the manuscript for publication in principle.

If the current version of your manuscript is in a PDF format, please email us a copy of the file in an editable format (Microsoft Word or LaTeX)-- we can not proceed with PDFs at this stage.

We are now performing detailed checks on your paper and will send you a checklist detailing our editorial and formatting requirements in about a week. Please do not upload the final materials and make any revisions until you receive this additional information from us.

Thank you again for your interest in Nature Ecology & Evolution. Please do not hesitate to contact me if you have any questions.

[REDACTED]

Our ref: NATECOLEVOL-201011791B

16th June 2021

Dear Dr. Douka,

Thank you for your patience as we've prepared the guidelines for final submission of your Nature Ecology & Evolution manuscript, "The earliest Denisovans and their cultural adaptation" (NATECOLEVOL-201011791B). Please carefully follow the step-by-step instructions provided in the attached file, and add a response in each row of the table to indicate the changes that you have made. Please also check and comment on any additional marked-up edits we have proposed within the text. Ensuring that each point is addressed will help to ensure that your revised manuscript can be swiftly handed over to our production team.

****We would like to start working on your revised paper, with all of the requested files and forms, as soon as possible (preferably within two weeks). Please get in contact with us immediately if you anticipate it taking more than two weeks to submit these revised files.****

When you upload your final materials, please include a point-by-point response to any remaining reviewer comments.

If you have not done so already, please alert us to any related manuscripts from your group that are under consideration or in press at other journals, or are being written up for submission to other journals (see: <https://www.nature.com/nature-research/editorial-policies/plagiarism#policy-on-duplicate-publication> for details).

In recognition of the time and expertise our reviewers provide to Nature Ecology & Evolution's editorial process, we would like to formally acknowledge their contribution to the external peer review of your manuscript entitled "The earliest Denisovans and their cultural adaptation". For those reviewers who give their assent, we will be publishing their names alongside the published article.

Nature Ecology & Evolution offers a Transparent Peer Review option for new original research manuscripts submitted after December 1st, 2019. As part of this initiative, we encourage our authors to support increased transparency into the peer review process by agreeing to have the reviewer comments, author rebuttal letters, and editorial decision letters published as a Supplementary item. When you submit your final files please clearly state in your cover letter whether or not you would like to participate in this initiative. Please note that failure to state your preference will result in delays in accepting your manuscript for publication.

Cover suggestions

As you prepare your final files we encourage you to consider whether you have any images or illustrations that may be appropriate for use on the cover of Nature Ecology & Evolution.

Covers should be both aesthetically appealing and scientifically relevant, and should be supplied at the best quality available. Due to the prominence of these images, we do not generally select images featuring faces, children, text, graphs, schematic drawings, or collages on our covers.

We accept TIFF, JPEG, PNG or PSD file formats (a layered PSD file would be ideal), and the image should be at least 300ppi resolution (preferably 600-1200 ppi), in CMYK colour mode.

If your image is selected, we may also use it on the journal website as a banner image, and may need to make artistic alterations to fit our journal style.

Please submit your suggestions, clearly labeled, along with your final files. We'll be in touch if more information is needed.

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Final Decision Letter:

23rd September 2021

Dear Katerina,

We are pleased to inform you that your Article entitled "The earliest Denisovans and their cultural adaptation", has now been accepted for publication in Nature Ecology & Evolution.

Before your manuscript is typeset, we will edit the text to ensure it conforms to house style.

Once your manuscript is typeset you will receive a link to your electronic proof via email, with a request to make any corrections as soon as possible. If you have queries at any point during the production process then please contact the production team at rjsproduction@springernature.com. Once your paper has been scheduled for online publication, the Nature press office will be in touch to confirm the details.

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