



## Osteoblasts pattern endothelium and somatosensory axons during zebrafish caudal fin organogenesis

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Editor: Steve Wilson

### Review timeline

Original submission: 28 September 2021

Editorial decision: 12 November 2021

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### Original submission

#### First decision letter

MS ID#: DEVELOP/2021/200172

MS TITLE: Osteoblasts pattern endothelium and somatosensory axons during zebrafish caudal fin organogenesis

AUTHORS: Rosalind G Bump, Camille EA Goo, Emma C Horton, and Jeff Rasmussen

I have now received two referee reports on the above manuscript, and have reached a decision. The referees' comments are appended below, or you can access them online: please go to BenchPress and click on the 'Manuscripts with Decisions' queue in the Author Area.

The overall evaluation is positive and we would like to publish a revised manuscript in Development after you have addressed the referees' minor comments.

#### Reviewer 1

##### *Advance summary and potential significance to field*

The paper addresses an interaction between osteoblasts, blood vessels and axons during organogenesis of the zebrafish caudal fin. The authors applied the following functional approaches: a chemical inhibition to prevent angiogenesis, mutant fish to perturb dorsal root ganglion neurogenesis, and genetic depletion of osteoblasts to impair ray formation. Using confocal imaging of fluorescent reporters and immunostaining, the formation of fin structures was monitored in these functional studies. Indeed, it is surprising that in absence of blood vessels and somatosensory nerves, the larval fin skeleton morphogenesis was rather normal until a certain size of animals. By contrast, ablation of osteoblasts led to phenotypes in endothelial remodeling innervation in the developing fin.

Overall, the quality of figures with illustrations and movies is excellent and the result are well explained. The introduction provides a good background to the topic, and the discussion is interesting. I really enjoyed reading this clear and elegant manuscript.

*Comments for the author*

Minor suggestion:

Line 95: I would recommend to say “approximately 18 main bony rays”, as this number can vary plus/minus 1.

Reviewer 2*Advance summary and potential significance to field*

The article “Osteoblasts pattern endothelium and somatosensory axons during zebrafish caudal fin organogenesis,” by Bump et al. is a careful study that both characterizes the patterning and identity of the axons that innervate the caudal fin, and that identifies a hierarchy of tissue requirements for patterning. The results are significant because the authors are the first to characterize the types of axons that populate the fin, and because the results are the first to demonstrate through functional studies that osteoblasts are needed to pattern vessels and axons in the developing fin. This is important both for understanding the widely used zebrafish fin model, and also more generally for an understanding of how multiple tissues are patterned in an organ.

*Comments for the author*

I have two suggestions that I feel would further strengthen the significance of the findings.

1. For those interested in the zebrafish caudal fin, the authors should note if the *erbb3b* null allele has noticeable fin phenotypes.
2. There is another recent publication (Senk and Djonov, 2021, Scientific Reports) showing that collagen fibers are needed for angiogenesis during fin regeneration. The authors should comment on the findings from this paper, and discuss if they think that collagen fibers may be responsible for the dependence of vessel and axon outgrowth on osteoblasts (i.e. or if they believe another feature of osteoblasts is required).

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**First revision**Author response to reviewers' comments

Reviewer 1 Advance Summary and Potential Significance to Field:

The paper addresses an interaction between osteoblasts, blood vessels and axons during organogenesis of the zebrafish caudal fin. The authors applied the following functional approaches: a chemical inhibition to prevent angiogenesis, mutant fish to perturb dorsal root ganglion neurogenesis, and genetic depletion of osteoblasts to impair ray formation. Using confocal imaging of fluorescent reporters and immunostaining, the formation of fin structures was monitored in these functional studies. Indeed, it is surprising that in absence of blood vessels and somatosensory nerves, the larval fin skeleton morphogenesis was rather normal until a certain size of animals. By contrast, ablation of osteoblasts led to phenotypes in endothelial remodeling innervation in the developing fin. Overall, the quality of figures with illustrations and movies is excellent and the result are well explained. The introduction provides a good background to the topic, and the discussion is interesting. I really enjoyed reading this clear and elegant manuscript.

**We thank the reviewer for their positive comments.**

Reviewer 1 Comments for the Author:

Minor suggestion:

Line 95: I would recommend to say “approximately 18 main bony rays”, as this number can vary plus/minus 1.

**Thank you for the suggestion. Line 95 has been revised as suggested.**

## Reviewer 2 Advance Summary and Potential Significance to Field:

The article “Osteoblasts pattern endothelium and somatosensory axons during zebrafish caudal fin organogenesis,” by Bump et al. is a careful study that both characterizes the patterning and identity of the axons that innervate the caudal fin, and that identifies a hierarchy of tissue requirements for patterning. The results are significant because the authors are the first to characterize the types of axons that populate the fin, and because the results are the first to demonstrate through functional studies that osteoblasts are needed to pattern vessels and axons in the developing fin. This is important both for understanding the widely used zebrafish fin model, and also more generally for an understanding of how multiple tissues are patterned in an organ.

We thank the reviewer for their positive comments.

## Reviewer 2 Comments for the Author:

I have two suggestions that I feel would further strengthen the significance of the findings.

1. For those interested in the zebrafish caudal fin, the authors should note if the *erbb3b* null allele has noticeable fin phenotypes.

Thank you for the suggestion. The manuscript (lines 129-130) has been revised to include the following sentence: “*erbb3b* mutant caudal fins did not exhibit gross morphological alterations in ray patterning.”

2. There is another recent publication (Senk and Djonov, 2021, Scientific Reports) showing that collagen fibers are needed for angiogenesis during fin regeneration. The authors should comment on the findings from this paper, and discuss if they think that collagen fibers may be responsible for the dependence of vessel and axon outgrowth on osteoblasts (i.e. or if they believe another feature of osteoblasts is required).

Thank you for pointing out this interesting and relevant publication. The revised discussion (lines 412-415) now references this paper as follows: “*Collagen fibers promote endothelial growth during larval trunk vascular development and following adult fin amputation (Senk and Djonov, 2021). Whether the effect we observed of *sp7+* ablation on vessel remodeling in the fin is mediated by collagens or other factor(s) remains to be determined.*”

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## Second decision letter

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ARTICLE TYPE: Research Article

I am happy to tell you that your manuscript has been accepted for publication in Development, pending our standard ethics checks.