

Title: **Mechanisms of Lysosomal Positioning and Movement**
Authors: Birol Cabukusta and Jacques Neefjes
Article Type: Review

Monitoring Editor Rosa Puertollano
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Decision and Reviews

Dear Dr. Neefjes,

Thank you for taking the time recently to write your review “Mechanisms of Lysosomal Positioning and Movement” for *Traffic*. I asked two colleagues who are experts in the field to review this review and their verbatim comments are appended below. I share the enthusiasm of the referees about this review, and agree that this will be of interest to the readers of *Traffic*. The referees have made several suggestions for correcting and clarifying the presentation that you will find very easy to address. With these minor revisions I would be pleased to accept this review for publication.

Sincerely,

Rosa Puertollano, PhD
Guest Editor

Referee's Comments to the Authors

Referee: 1

Comments to the Author

In this review, Cabukusta and Neefjes bring together recent work on how lysosomes are positioned and move within the cytoplasm. Overall it is well written and informative. It discusses recent work from Neefjes lab and many others and so gives a nice overview of the field. Although I do not think it should preclude publication, my main concern is that it is not clear to me what differentiates it from Bonifacino and Neefjes recent review in *Current Opinion in Cell Biology* (2017) or Pu and Bonifacino *JCS* (2016). The authors might consider better defining what the USP of this review is in the revised manuscript.

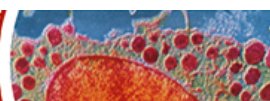
Minor comments:

Pg. 3.

“40 kinesin heavy chain genes” – kinesin heavy chain is typically only used to refer to the kinesin-1 heavy chains KIF5A,B,C. Would be better phrased as “the human genome encodes over 40 kinesin proteins that are grouped into 14 families” See 10.1083/jcb.200408113 for standardized nomenclature.

“there is only one dynein heavy chain identified” – this is a little misleading in this context as there is a separate DHC in IFT motor dynein 2 as well as the axonemal dyneins. Better phrased as “only one dynein family member – cytoplasmic dynein 1, has been implicated in transport within the cytoplasm”

Pg. 8



ALG2 is referred to as a “dynein adaptor”. This overstates the available data which, from reading the NCB paper on which this is based, appears to be little more (biochemically) than an overexpression co-IP with dynamitin.

Figure 4:

In panel B, Kif5B is shown as having a PH domain. This is an error. The paper describing its lipid binding mapped this site to a basic sequence within the tail.

Referee: 2

Comments to the Author

This is a very nice review for the lysosomal biology for its position and movement. The manuscript is well written and the reference are carefully cited. This review should benefit many cell biologists who are interested in lysosome, so it will fit for publication in Traffic. I only have two minor comments:

(1) When "dynein" was first shown in the article, it should be specific as "cytoplasmic dynein-1 ("dynein" hereafter)" in order to avoid any confusion.

(2) In addition to dynactin, RILP also interacts with dynein light intermediate chain, which has been reported by Richard Vallee and Ron Vale's groups, respectively. Please include this information in the review.

Author Rebuttal

Dear Lisa,

Many thanks for your handling of the manuscript and the favourable and helpful comments of the reviewers. The reviewers had only small comments and we have modified the text accordingly (Our point by point response to each reviewer comment can be found below). In addition, we prepared another illustration to be considered as the abstract figure. I hope you like this.

We include the modified text and please let us know whether you need further information.

All the best from the Low Countries,

Jacques

___ANSWER TO REFEREE COMMENTS___

REFEREE 1

Comments to the Author

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BC & JN: We thank the reviewer for his corrections and implement the changes accordingly.

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BC & JN: We made the corrections mentioned by the reviewer.

Figure 4:

In panel B, Kif5B is shown as having a PH domain. This is an error. The paper describing its lipid binding mapped this site to a basic sequence within the tail.

BC & JN: We made the corrections indicated by the reviewer. We thank the reviewer for noticing this mistake.

REFEREE 2

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This is a very nice review for the lysosomal biology for its position and movement. The manuscript is well written and the reference are carefully cited. This review should benefit many cell biologists who are interested in lysosome, so it will fit for publication in Traffic. I only have two minor comments:

(1) When "dynein" was first shown in the article, it should be specific as "cytoplasmic dynein-1 ("dynein" hereafter)" in order to avoid any confusion.

BC & JN: We thank the reviewer for pointing out this issue and implement the according change.

(2) In addition to dynactin, RILP also interacts with dynein light intermediate chain, which has been reported by Richard Vallee and Ron Vale's groups, respectively. Please include this information in the review.

BC & JN: We thank the reviewer for referring to this finding and include the missing information.

