Editors  
*Current Biology*

Dear Editors,

We are submitting our manuscript titled “Phosphatidylinositol 4,5-bisphosphate regulates cilium transition zone maturation in *Drosophila melanogaster*” to be considered for publication in *Current Biology*. In this paper, we demonstrate a novel role for the membrane lipid phosphatidylinositol 4,5-bisphosphate, or PIP2, in the development of the cilium transition zone using the male germline of *Drosophila melanogaster* as a model.

The transition zone forms a diffusion barrier at the base of the cilium, thereby controlling the transport of cargo entering and exiting this organelle. As a result, the proper formation and maturation of the transition zone is essential for the assembly of the cilium and its function as a sensory organelle.

In this paper, we present the following key findings:

1. We demonstrate that reducing PIP2 in the Drosophila male germline induces the formation of longer than normal transition zones.
2. We show that the type I phosphatidylinositol phosphate kinase Skittles regulates transition zone length.
3. We provide evidence that hyperelongated transition zones are functionally defective.
4. We show that the *onion rings* allele of Drosophila Exo84, a component of the exocyst complex, can decouple transition zone length from the loss of plasma membrane-cilium tethering observed in cells with reduced levels of PIP2.

This article is of broad interest for several reasons. First, we show that the poorly understood process of transition zone maturation, by which a nascent transition zone matures into a fully functional one, is regulated by the lipid PIP2, which is known to be enriched at the base of cilia from multiple studies. Second, we show that the Drosophila type I phosphatidylinositol phosphate kinase Skittles regulates transition zone maturation, and that it does so *in situ*, providing further evidence that these enzymes may be genetic modifiers of diseases of cilia. Third, we show that the exocyst, which has been shown to be important for cilium formation in multiple studies, regulates cilium maintenance by enabling plasma membrane-cilium attachment but not transition zone maturation.

Here are the names of six possible reviewers:

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We look forward to your favourable consideration of our manuscript.

Sincerely,

Julie Brill