Organ Size Regulation in Rp mutants in Drosophila

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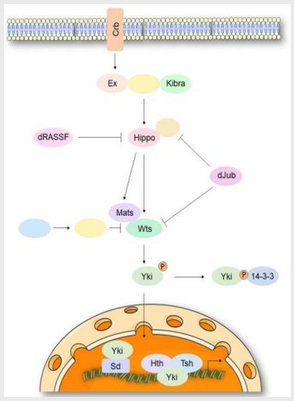
Abstract

Ribosomal proteins (Rp) function as components of ribosomes which are essential for the synthesis of proteins. Given how important ribosomes are for translation, organisms with homozygous mutations for Rp die, while heterozygous mutants present with abnormal disease in humans as can be seen in Diamond- Blackfan anemia and *Drosophila* with reduced size in bristles and an extended growth period (the minute phenotype). In the case of *Drosophila*, previous results in the lab suggests that Xrp1 are able to regulate this phenotype through a developmental delay that contributes to the extended growth period compensating for the missing copy of the Rp gene. The Hippo signaling pathway is a kinase cascade that plays a role in organ size control in animals by regulating the activity of a transcription co-activator yorkie (yki) that promotes organ growth. During the course of this research wing size was used as a measure for the genetic interactions of the manipulated genes. The question that we explored was whether Xrp1 regulates organ size in Rp mutants through the regulation of the hippo pathway. Our hypothesis is that there will be an increase of yki activity in Rp (ribosomal protein) mutants to maintain organ size. Crosses were set for the desired genotypes, wings from the obtained flies were dissected and measurements were taken. From the taken measurements we found evidence that RpS3 heterozygous flies display mild but significant increase in wing size and reduction in aspect ratio, a phenotype dependent on Xrp1. Moreover, additional genetic interaction data is presented with the members of the Hippo pathway. From results we were able to support our hypothesis in the case of yki but not in wts, suggesting that these measurements should be repeated with a greater number of flies.



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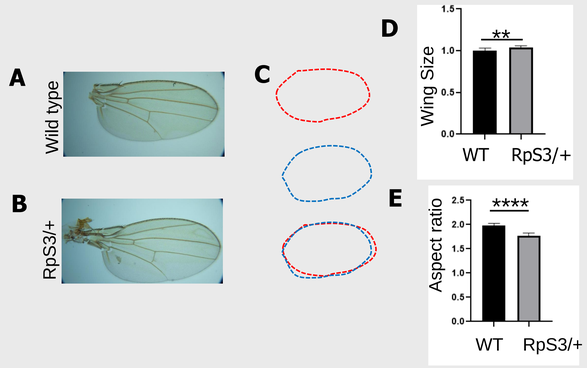
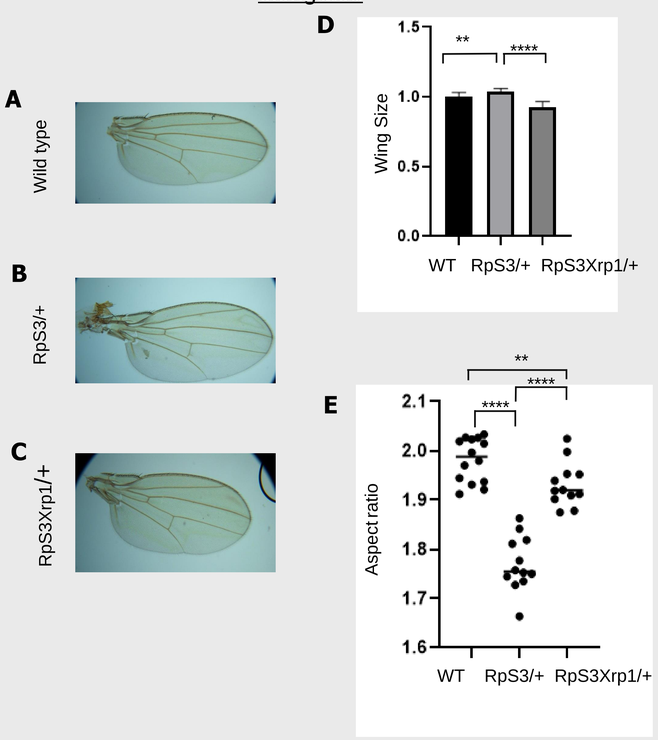
Results

RpS3 heterozygous flies display mild but significant increase in wing size and broader wing shape



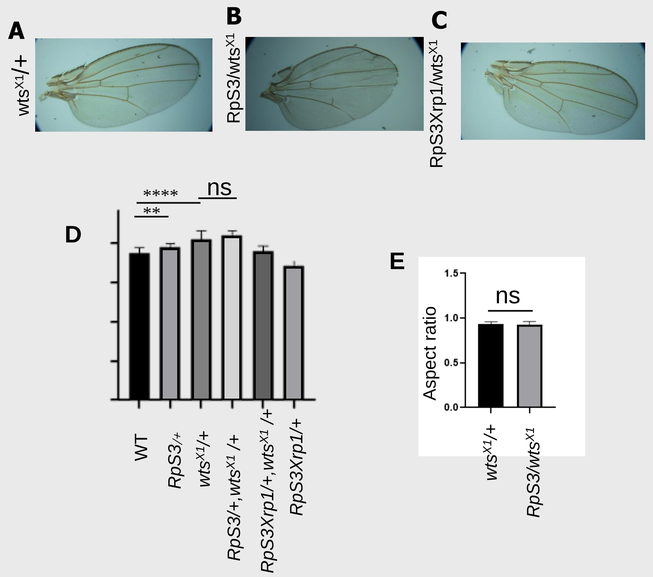
(A-B) Wing from wild type and RpS3/+ flies. (C) Schematic representation of wild type (red) and RpS3/+ (blue) wings. (D-E) Graphs compare the size (C) and shape of wild type and RpS3/+ wings. Wing size of wild type and RS3/+ were normalized with average wing size of wild type fly. RpS3/+ wing were found to be 3.7% bigger (C) and significantly broader than wild type wings (D). Similar change in wing shape was also observed in RpS18/+ flies, however, their wing size remain similar to wild type wings (data not shown).

Loss of one copy of Xrp1 make RpS3/+ wings smaller and elongated



(A-C) Wings from wild type, RpS3/+ and RpS3Xrp1/+ flies. Note change in wing size and shape in RpS3/+ wings upon loss of one copy of Xrp1. Quantification for same is shown in D & E.

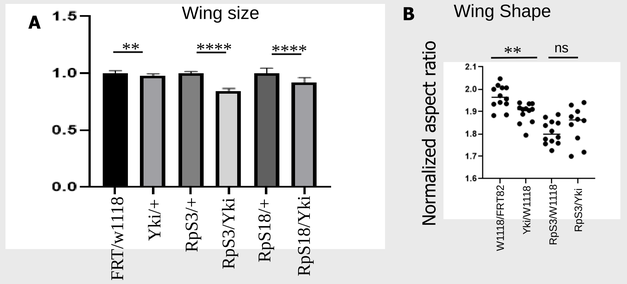
The loss of one copy of *wts* made the *Rp*/+ wings to grow similarly to *wts*/+ wings in regards to size



(A-C) Wings from wts^{X1}/+, $RpS3/wts^{X1}$ and $RpS3Xrp1/wts^{X1}$ flies.

Note, no significant change in size (D) and shape (E) of Rp/+ wings was observed upon the loss of one copy of *wts* compared to that in wild type background.

RpS3/+ displays genetic interaction with Yki with respect to wing size



(A) One copy loss of yki in wild type flies result in 2% reduction in wing size while that in RpS3/+ and RpS18/+ result in 15.5% and in 8.2% size reduction, respectively. (B) Aspect ratio of RpS3/+ and RpS3/Yki, Yki/+, W1118/FRT82.

Conclusion

- The increase in wing size in the RpS3 heterozygous flies showing a possible increase in yki activity due to the Rp mutation.
- In fig.2 where Xrp1, which regulates development delay in RpS3/+, was removed the decrease in wing size and elongation in RpS3 heterozygous flies phenocopy the loss of one copy of yki (Fig 4), suggesting that Xrp1 and Yki might work in a pathway.
- No genetic interaction was found between wts and RpS3 using wing shape and size as the measurable phenotype. The loss of one copy of *wts* made the wings bigger in wild type flies as well as in the RpS heterozygous flies to the same proportion showing the potential for research into whether this is caused by an increase in cellular growth or an impact on developmental delay in the wts/+.
- In comparison to the wild type reduction in yki activity have more drastic effect in RpS3 and RpS18 mutant showing that rp mutant recruit more yki in order to reach their final size.

Future Directions

Given the number of flies that were measured these results are still preliminary and these measurements should be repeated but with a larger number of flies. As only the wings were examined the question as to whether the effect of yki acts in a cell autonomous or a systemic manner could be posed. Lastly, since the Hippo pathway regulates Dilp8 and Xrp1 also regulates Dilp8 this study serves as a basis to check if Xrp1 regulates Dilp8 through yki.

References

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