A Screen for Genetic Modifiers of Protein Phosphatase 1 Function in Drosophila Collective Cell Cohesion and Migration

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INTRODUCTION

Collective cell migration is important in normal physiological processes, such as embryonic development, as well as abnormal processes such as cancer.

Drosophila melanogaster border cells demonstrate developmentally regulated collective cell migration during oogenesis making it an excellent genetically accessible model for identifying how cell collectives move in tissues.

During ovarian development, 6-8 cells form the border cell cluster, which migrate together as a cohesive cluster to reach the large oocyte at the posterior end of the egg chamber.

Previous experiments from our lab have found that inhibition of protein phosphatase (PP1) activity, through overexpression of the endogenous (and specific) PP1 inhibitor, nuclear inhibitor of PP1 (NiPP1), caused the border cell cluster to separate into single cells and limited migration ability.

Further experiments demonstrated that PP1 regulates actomyosin contractility and adhesion between border cells to promote collective migration.

METHODS

To gain additional insights into how PP1 activity controls collective cell migration, we performed a genetic modifier screen of the NiPP1-induced border cell phenotypes.

We screened the majority of deficiency lines from the 2nd and 3rd chromosome Bloomington Deficiency Kits, specifically looking for chromosomal regions whose altered gene dosage either enhanced or suppressed the effects of NiPP1 on border cell cohesion or migration.

The GAL4/UAS system is used to express NiPP1.

slbo-Gal4 (green, Figures 3 and 4) drives specific expression of UAS-NiPP1 in border cells, plus follicle cells.

RESULTS

We have now identified five distinct deficiencies that significantly enhance the NiPP1 migration defect and one deficiency that strongly enhances the NiPP1 cluster separation phenotypes.

We are currently mapping the relevant genetic enhancers through a combination of testing smaller overlapping deficiencies and testing for interaction with specific RNAi lines.

It is expected that the relevant smaller deficiencies will enhance the phenotype as well.

CONCLUSION AND FUTURE RESEARCH

By blocking PP1 activity in Drosophila border cells we were able to analyze deficiencies specifically to find which chromosomal segment enhanced or suppressed the NiPP1 phenotype such as migration defects, more "rounded" border cells, and weakened adhesion.

So far in our genome-wide screen of the 2nd and 3rd chromosomes, we have found five positive modifiers of the NiPP1 migration defects.

Small deficiencies from the positive modifiers are being analyzed and are expected to enhance the NiPP1 phenotype.

After completing this analysis, RNA interference will be used to knockout specific genes and proteins to identify the PP1 molecular targets and pathway members.

Identifying these targets and pathways members can be used to future study normal or abnormal processes in humans such as embryonic development and cancer.

REFERENCES AND ACKNOWLEDGEMENTS


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